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This symposium brought together engineers, physical scientists, physiologists, and psychologists, to discuss how nonionizing electromagnetic radiations deposits thermalizing energy in biological tissues and the means by which this energy may be detected and effectively managed by the conscious organism.

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ELEANOR R. ADAIR

John B. Pierce Foundation Laboratory
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This book is dedicated to
JAMES DANIEL HARDY
for his contributions to thermal physiology and his interest in the thermal consequences of microwave exposure.

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Preface

This volume is the proceedings of a symposium hosted by the John B. Pierce Foundation and held at Yale University, New Haven, Connecticut, on October 26–27, 1981. The goal of the symposium was to bring together engineers, physical scientists, physiologists, and psychologists to discuss how nonionizing electromagnetic radiation deposits thermalizing energy in biological tissues and the means by which this energy may be detected and effectively managed by the conscious organism.

Much is known about the mechanisms by which warm-blooded organisms achieve and maintain a characteristic, stable internal body temperature in the face of environmental thermal stresses. Exposure to nonionizing radiation of the microwave frequency range can provide a unique thermal challenge to deep, as well as peripheral, body tissues that must be dealt with by these same mechanisms.

Recent developments on two broad scientific fronts indicated that an interdisciplinary meeting would be both timely and productive. First, research into the biological effects of exposure to radiofrequency radiation has advanced considerably during the past 6–7 years, roughly since a symposium held at the New York Academy of Sciences. Many of the suggestions for future needs and directions, offered by Prof. Arthur W. Guy on that occasion, have already occurred and more are in various stages of accomplishment. Research emphasis in this field has shifted from high-intensity to low-intensity exposure as scientists probe more and more subtle biological effects. With this shift in emphasis has come the realization that an increase in body temperature of an experimental animal exposed to microwaves implies a breakdown of thermoregulatory mechanisms. On the other hand, low-intensity exposures, previously dubbed "nonthermal," usually initiate immediate and efficient thermoregulatory processes that ensure the constancy of the internal body temperature. Knowledge of basic thermoregulatory processes is clearly necessary for the full understanding of the responses of conscious animals in the presence of radiofrequency fields.

The second development is the recent surge of interest in the use of microwave diathermy and other means to produce highly localized hyperthermia as an adjunct to effective cancer treatment. Localized tissue heating is known to increase local tissue blood flow and to alter metabolic processes in the affected tissues. However, such treatments are employed only in the clinic, not in the laboratory, with the result that much potential data that could add significantly to our understanding of thermoregula-

tory processes are not recorded. Students of thermal physiology, as well as cancer therapists, would benefit from an increased awareness of microwave techniques for producing localized hyperthermia as well as the particular problems of energy absorption attendant upon microwave exposure.

It was most appropriate that the symposium on microwaves and thermoregulation be hosted by the John B. Pierce Foundation. This institution was founded in 1924 to " . . . promote research, educational, technical, or scientific work in the general fields of heating, ventilation, and sanitation, for the increase of knowledge to the end that the general hygiene and comfort of human beings and their habitations may be advanced."

In 1934, the Foundation sponsored the organization of The John B. Pierce Foundation of Connecticut, Incorporated which owns and operates the Laboratory in New Haven. Since its founding, the Laboratory has been affiliated with Yale University. Many of its staff contributed to this symposium; their cooperation and enthusiasm helped to make the symposium a reality.

The symposium and this volume would not have been possible without the generous support of the Tri-Service Electromagnetic Radiation Panel, TERP, representing the Army, Navy, and Air Force. These funds were administered through AFOSR Grant 81-0211. Additional support has been provided by the John B. Pierce Foundation.

To the participants, who enthusiastically exchanged ideas and thereby expanded our knowledge of this interdisciplinary research area, I extend my thanks. Many others made substantial contribution to the success of the symposium and the preparation of this proceedings volume. I thank Dr. James D. Hardy, former Director of the John B. Pierce Foundation Laboratory, who first urged me to convene this meeting, Dr. Lawrence E. Marks for his presentation at the symposium, not recorded herein, and Dr. A. Pharo Gagge and Dr. Hardy for serving as session chairmen. Ms. Janice Gore of the Yale University Medical School Office of Continuing Education worked tirelessly on the symposium arrangements. Special thanks are offered to Mrs. Barbara Adams for her assistance in all phases of this enterprise. I greatly appreciate the effort of Ms. Joan Batza who prepared the final copy used to reproduce these proceedings and the expertise of Mrs. Gillian Akel who prepared the subject index to this volume.

Eleanor R. Adair

MICROWAVES AND THERMOREGULATION: HISTORICAL INTRODUCTION

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I. INTRODUCTION

Building models of the thermoregulatory system and gaining insight about how RF energy is absorbed by the human body have been two distinct disciplines with very little cross-fertilization for several decades. Their historical developments have much in common. In both cases, models of the human body were introduced which were initially very simple. These models were eventually replaced by increasingly complex models providing ever-increasing predictive capability. Now these two discipline have begun to merge for several reasons:

1. Determination of thermal tolerances to radiofrequency (RF) energy absorption requires the use of advanced thermoregulatory models. Past and presently anticipated RF-safety standards for man are based on the concept that average total energy absorption should not exceed either the basal metabolic rate or about 40% of this value. More attention is directed now to strongly-localized energy absorptions. The concept of permissible total thermal load should be complemented by stating the permissible local SAR-values and temperature increases. Application of appropriate thermoregulatory models may be required to translate specific absorption rates (SAR) into temperatures.
2. The controlled application of RF energies may well become a valuable research technique to further our

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understanding of thermoregulatory processes, a point first made years ago by Hardy to this writer.

3. Local temperature elevations caused by absorption of RF and microwave (MW) energies may well become a valuable therapeutic technique to reduce abnormal tissue. Appropriate consideration of man's thermoregulatory system is required in order to translate local SAR distributions into temperature elevations in clinical hyperthermia.

I will first outline the history of thermal RF-tolerance and of thermoregulation and then conclude with a survey of recent attempts to merge these two areas. The models to be considered are indicated in Table I.

TABLE I. Models of Electromagnetic Heat Deposition and Thermoregulation

(1.) RF and MW Energy Deposition	
(2.) Human Thermoregulation	
(3.) Thermoregulation and Microwaves.	Perception Simple models for temperature increase Compartmental models and microwaves (Combinations of 1 and 2)

II. RADIO FREQUENCY AND MICROWAVE ENERGY DEPOSITION

A. Earlier Models of Microwave Energy Absorption

The first model considered a semi-infinite plane of soft tissue with high water content, such as muscle, with the radiation hitting the air-tissue interface at a right angle. Values for depth of penetration and percentage of absorbed energy could be calculated readily from available dielectric data. They were later confirmed experimentally.

As a next step, subcutaneous fat-muscle and then skin-fat-muscle configurations exposed to radiation were considered. Again the results could be readily predicted from electromagnetic propagation theory and available dielectric

data. In this case spatial patterns of local energy absorption (specific absorption rate, SAR) are more complex and depend on frequency, as well as amounts of skin and fat. In spite of the emerging complexity, it was possible to state some rather general conclusions for most of the microwave frequency range of dominant interest at that time:

1. Below 1 GHz, about 40% of the incident energy is absorbed in the deeper situated muscle and core tissue, and most of the other 60% is reflected.
2. Well above 3 GHz, the percentage of absorbed energy increases slowly at first and then more rapidly from about 40% to about 70%. This energy is almost entirely absorbed in the skin.
3. Between these two extremes, the SAR distribution depends critically on the thickness of the various tissue layers and the frequency. The percentage of total absorbed energy varies between 20% and 100%.

The conclusions from these studies have sometimes been criticized since they were based on such simple models. However, they can be expected to be applicable to partial body irradiations, such as applied with diathermy techniques and localized hyperthermia treatments. More recent work has also demonstrated that these results are applicable to the case of man's absorption of RF energy if appropriately superimposed on man's resonance with the impinging field. These earlier studies have been reviewed several times (Schwan and Piersol, 1954; Schwan, 1965).

B. Cross-Section Studies

During the Fifties interest shifted from microwave diathermy to hazard problems. It therefore became necessary to consider the absorption characteristics of the total man. In the early Sixties we approximated man first by a homogeneous tissue sphere and then by a tissue sphere surrounded by a subcutaneous fat layer. Work was conducted both theoretically and experimentally using a large anechoic chamber. Techniques were developed to scale experimental data obtained at one frequency to another frequency. This was accomplished by using appropriately-sized manikins and adjusting the conductivity of their interior saline solutions. The concept of the relative absorption cross-section was introduced to express the ratio of total absorbed energy to incident energy. It can readily be related to the concept of the body-averaged SAR (av.) and the total energy absorbed E_t:

$$E_t = A \times F \times RAC = W \times SAR\ (av.)$$

where W is body weight, RAC is relative absorption cross-section, F is incident flux level and A is illuminated body area (shadow cross-section).

The results of these studies demonstrated that RAC-values can be greater than one. This resonance effect typically occurs when man's size compares with about one-half wavelength. As frequency increases well above the resonance range, the relative absorption cross-section approaches values calculated for the cases of the plane tissue slab discussed above. Below resonance, RAC and SAR(av.) decrease rather rapidly with decreasing frequency. The mechanisms responsible for this pattern are well understood.

Almost one decade passed before this sort of work was again undertaken. These studies profited from advancements in computer capability and analytical techniques. More advanced models of man were introduced including spheroids, ellipsoids and cell block models. This very extensive effort over the past ten years that is still ongoing today has refined considerably our insight into the patterns of energy deposition in man. Some of the important conclusions include: The resonance phenomena can be much more pronounced than anticipated from the studies of the spherical model of the early Sixties; RAC values of 4 and more can be achieved for frequently-occurring exposure conditions. Extensive experimental work supported this theoretical conclusion, taking advantage of the development of advanced phantom models of man and their rapid thermographic evaluation. For more details see the review of Johnson and Guy (1972) and the collection of data presented by Durney, *et al.* (1976, 1978, 1980).

C. Local Hot Spot Phenomena

The work during the past decade has not only advanced considerably our detailed knowledge of RAC and average SAR values, but it has also provided insight into the spatial distribution of specific absorption rates. These spatial distributions are quite complex and depend critically on all parameters, such as field characteristics, body dimensions, body orientation to field, and proximity of other physical objects, including the ground. Nevertheless, some rather general conclusions can be drawn:

1. At frequencies well above 3 GHz, surface heating is pronounced.

2. Strong exchange currents between different body compartments, such as legs to ground, arms to trunk, or head to trunk, can exist.
3. Hot-spot-like patterns of energy deposition can be generated in the frequency range from about 500 to 2000 GHz. In these hot spots local SAR values can easily be tenfold larger than average SAR values.

Work in this area included both theoretical and experimental studies. During the early part of the past decade the focussing and resonance phenomena of curved tissues such as the human head were investigated in great detail and the mechanism responsible for hot spots identified. The theoretical studies from several groups of investigators and experimental observations using the thermographic scanning procedure developed by Guy fit well together. However, the cell block models of man are not yet detailed enough to indicate the dominant surface heating which should also prevail at frequencies near and below the resonance range, particularly in the trunk.

Table II attempts to summarize the modeling developments summarized in the preceeding sections on RF- and MW- energy deposition.

TABLE II. Energy Deposition by RF and MW

Semi-infinite plane of muscle
Skin-Fat-Muscle
Tissue sphere, homogenous, absorption cross-section RAC
Tissue sphere with fat shell, absorption cross-section RAC
SAR distribution (average and local)
Sphere and ellipsoid
Cell block models of man
Phantom techniques
Some Results:
Resonances (man, body segments, skin-fat-muscle)
Hot spots in 0.5 - 2 GHz range
Surface heating at high microwave frequencies
4 frequency ranges (below resonance, resonance, hot spot, surface heating.)
Exchange currents (segmental such as head and arms to trunk, to ground)

III. THERMOREGULATION

I am less competent to summarize the developments in the field of thermoregulation. However, a similarity to the history for the RF-field is apparent. In both cases the development of increasingly complex models occurred as shown in Table III. Gagge, one of the pioneers of the field, introduced a model which approximated man by a sphere generating metabolic heat and interacting thermally with the environment (Gagge, *et al.* (1969, 1971). Multiple-layer schemes were used with skin on top of subcutaneous fat on top of muscle and core tissues. Further refinements were introduced by Hardy, Wissler, Stolwijk and others and include:

1. Compartmentalization of the human body into regions or segments, including legs, feet, arms, hands, trunk and head. Each compartment was subdivided to account for skin, fat or bone, muscles, and organs.
2. Appropriate consideration of the role of heat conduction and blood flow between the various compartments and their subcomponents.

TABLE III. Models of Human Thermoregulation

Cylinder
Cylinder, stratified
Compartmental models:
Passive
With control features including
Body segments
Components of each segment (skin, subcutaneous fat, muscle, core)
Thermostat and feedback

3. Appropriate consideration of the mechanism of heat exchange of man with the environment, including radiation losses, sweating, and heat conduction.
4. Introduction of feedback loops into the model which incorporate temperature sensors and a thermostatic controller in the hypothalamus. This controller integrates the temperature signals received from

various body segments, compares the information with a reference signal, and initiates corrective measures.

Initially, models were "passive", i.e., with no feedback components useful for controlling and corrective action. Wissler introduced a system with some hundred components which describes in detail conductive, convective and counter-current heat exchange processes. Models incorporating thermoregulatory feedback control first emerged in the middle Sixties. For some detailed reviews of these developments, see Fan, *et al.* (1971), Wissler (1970), Stolwijk and Hardy (1977). For a recent, more detailed summary in the context of RF and microwave energies applied to man, see Michaelson and Schwan (1981).

Stolwijk's present model is probably the most sophisticated one. Its predictions have been experimentally checked by an appropriate evaluation of exercising man. This model with its many components and subcomponents requires advanced computer capabilities. In this regard it compares with the sophisticated block models of man exposed to RF- fields where the modeling of the human body has advanced to a state requiring large computational power and further refinement of the models becomes difficult.

Aside from temperature sensors in the skin and in the hypothalamus, there appear to exist additional temperature sensors with a controlling ability. The medulla and the spinal cord possess such an ability and the gut may as well. Further refinements of the Stolwijk model will increase computational demands correspondingly.

The question arises: Is the Stolwijk model a sufficiently refined one to predict the thermal responses of man to RF-energy deposition? A considerable amount of work has been done so far with thermodes which inject a known amount of energy at a chosen site in the body of test animals and much has been learned from this. But it will be difficult, if not impossible, to subject man to RF-energy inputs which are high enough to evoke a response and compare this response with the model. Furthermore, our ability to locate precisely, inside the human body, known amounts of RF-energy is not advanced, even though we have learned much about the principles which govern energy absorption in man.

Let us next look at what has been accomplished by applying physiological and regulatory considerations to RF-energy absorption studies.

IV. THERMOREGULATION AND MICROWAVES

A. Perception of Microwaves

Early interest in physiological responses to microwaves concerned the problem of whether microwaves can be perceived soon enough to prevent tissue damage. Extensive work had been done on the threshold of perception of infrared by Hardy and his colleagues. From their data it appears that perception occurs at intensity levels below those needed to cause injury. Microwaves of sufficiently low frequency do penetrate much deeper than infrared and the possibility remains that below the skin, higher temperature elevations could occur than at the surface. Adequate detection relies primarily on skin temperature receptors. It could be argued therefore that microwave perception cannot be necessarily relied upon to prevent damage. The question of whether undue heat input from RF radiation may lead to sufficient discomfort to motivate escape from such exposure was recently discussed again at a workshop on thermal physiology (1980). Dr. Adair stated: "Thermal comfort and discomfort are very strong motivating conditions for humans particularly, and for animals. When any form of thermal discomfort is produced either by the environment or deep in the body core, the organism immediately initiates behavioral action to remedy the situation."

She went on to state: "Although a source of thermal energy may not trigger the receptors in the skin so that it is directly sensed, there is a good deal of experimental evidence that shows that behavioral and physiological action can be initiated through thermal stimulation at specific sites inside the body in the absence of a specific sensory cue. It is unknown how many of these specific sites would be involved, for example, in a whole-body exposure to microwave radiation. However, the sites are there and a great many of them are sensitive and have implications for thermoregulatory behavior as well as physiological responses." The question of whether thermal discomfort resulting from microwave exposure can be relied upon to prevent harm should be pursued further.

Even in the simpler case of microwave perception, only a limited amount of data exists. Hendler, *et al.* (1963), in Hardy's laboratory, investigated threshold values of cutaneous warmth for 3 cm microwave radiation and infrared. Somewhat later, threshold determinations were carried out in our laboratory at about 10 cm (2880 MHz) (Schwan, *et al.*, 1966). Comparisons of infrared and 10 cm microwave

threshold values were also carried out by Vendrik and Vos (1958). Experimental procedures were different in these cases, making it somewhat difficult to state clearly absolute threshold values for all conditions of practical interest. It appears that warmth thresholds for microwaves are well above those for infrared. (See Chapters 9 and 10 for further discussion of these studies). For example, for 3 GHz radiation, the sensitivity is quoted by Vendrik and Vos to be about tenfold higher than for infrared, reflecting the great difference in absorption coefficients. Since absorption coefficients change strongly with frequency between 1 GHz and 10 GHz, differences between infrared and microwave sensitivities should also change significantly through this frequency range and somewhat less outside this range. This argument is based on the assumption that exposure times needed to achieve perception are much shorter than thermal time constants. Since the former are usually measured in seconds and the latter in minutes, this appears to be justified. The reported microwave flux at threshold is above flux levels listed in the current ANSI standard and therefore perception cannot be relied upon to prevent undue exposure.

B. Temperature Increase (Simpler Models)

Earlier attempts to treat mathematically the problems of temperature elevation assumed of necessity simple semi-infinite tissue slabs exposed to radiation. Cook treated this problem by relying on a solution of the pertinent differential equation given by Vendrik. Vendrik never published the derivation of his formula and his equation has no finite steady state solution. Recently Foster, *et al.* (1978) recognized that blood flow must also be considered to achieve a steady state solution.

The Foster, *et al.* solution provides a convenient appraisal of optimal temperature elevations with or without surface cooling. The results may be summarized as follows: Surface cooling can lower the temperature only to a depth equal to the thermal penetration depth from the surface. The spatial temperature distribution is independent of frequency if the radiation depth of penetration is shorter than the thermal penetration depth. Here the thermal penetration length is defined as the distance from the surface required to reduce the temperature by a factor of two if only surface heating is applied. For typical blood flow, it has a value of nearly 1 cm. Microwaves have a comparable penetration at about 2 GHz. Above this frequency, heat conduction rather

than microwave penetration is predicted to be largely responsible for observed temperature elevations. The solution of Foster, *et al.* also provided further justification for the 6-minute time constant incorporated in the ANSI standard.

The next model investigated in our laboratory was that of an idealized hot spot of 1 cm radius having the shape of a pedestal function (Kritikos and Schwan, 1978). The hot spot dimension was assumed to be small compared with that of the surrounding medium. Therefore, the temperature elevation in such a hot spot formed inside the human head is rather independent of the surface conditions. Heat conduction as well as blood flow were incorporated in the model and time-dependent as well as steady state solutions for the spatially-dependent temperature increase were calculated.

This model was later elaborated on by replacing the pedestal-type hot spot by the actual hot spots generated by 1000 MHz irradiation in a small head (Kritikos, *et al.* 1979, 1982; Burr, *et al.* 1980). The results predicted by the models of these two groups are virtually identical with regard to all important aspects. Both groups conclude that the simple pedestal hot spot function provides a good approximation for optimal temperature values. For example, Burr, *et al.* give for the exact hot spot a temperature elevation of 0.26 °C, while the pedestal-type hot spot yields 0.33 °C. Spatial SAR variations over distances smaller than

TABLE IV. Temperature Increase (Simple Models)

Semi-infinite plane (Cook; Foster, *et al.*)
"Pedestal" hot spot in tissue medium (Kritikos, *et al.*)
Actual SAR distribution in tissue sphere (Kritikos, *et al.*; Burr, *et al.*)
Some results:
Thermal penetration length D_t *vs* Radiant penetration length D_r (Importance of $D_r \gtrless D_t$ on temperature distribution.)
Comparison of "pedestal" *vs* actual SAR distribution
10 mW/cm^2 → 0.5 °C in head and slab models (dependent on blood flow)

the thermal penetration length are fairly well smoothed over by heat exchange. Furthermore, actual hot spot dimensions as reflected by their temperature profiles cannot have a radius smaller than the thermal penetration length, i.e., about 1 cm.

Table IV lists results from the model studies discussed above.

It is also of interest to compare the temperature elevation in the center of the hot spot with the average temperature elevation if no hot spot exists when the irradiated head is maintained at its steady state temperature by blood exchange with the rest of the body. In this case, the temperature increase is calculated to be almost a hundredfold lower than in the hot spot (Kritikos and Schwan, 1978).

C. Compartmental Models and Microwaves

During the past half decade several attempts were made to combine the thermoregulatory models with RF absorption data. Table V indicates these first attempts. Emery, *et al.* (1975, 1976) used Stolwijk's thermoregulatory model for two cases. In one case, heat deposition was assumed to be in the head alone and in the other case, the total body was exposed. Skin responses were stated to be more pronounced than core responses. The results were strongly dependent on the assumed model of sweat production. Later, Guy, *et al.*

TABLE V. Temperature Increase (Compartmental Models)

Whole body heat load Head heat load	Guy, Emery
Whole body, cell model	Spiegel
Hot spot (Hypothalamus)	Way, *et al.*
Some results:	
Significant heat load in legs and thighs for 10 mW/cm^2 in resonance range	
Significant physiological responses for hot spot in hypothalamus for 10 mW/cm^2, hot spot range.	

(1978) used the Stolwijk model again to investigate the exposure of man in the resonance range. For an incident flux of only 10 mW/cm^2, significant temperature elevations in man's legs were predicted. More recently, Spiegel, *et al.* (1980) carried out a detailed analysis for the same exposure conditions, using a cell model of man to account for the spatial variations in SAR. Unacceptable temperature elevations in the thigh were predicted.

In these attempts, the number of compartmental elements was of necessity small. For example, Spiegel used a modified Stolwijk model with 15 segments. The core of the trunk, head, etc., were each represented as one unit, even though their total input from radiant heat may have been accomplished by the use of a more detailed cell block model of man. Thus, it is not possible to predict the existence of large local temperature elevations in small parts of the total segmental volume. For example, the case of hot spots in the brain cannot be considered adequately. The case of a local hot spot in the position of the hypothalamus was investigated by Way, *et al.* (1982), utilizing Stolwijk's model but adding an extra segment for the hot spot. Considering SAR values for the hot spot in the 10 to 20 mW/g range, significant but tolerable physiological responses were predicted. The quoted SAR values correspond to a head exposure at about 10 mW/cm^2 in the frequency range which can be used to generate such hot spots, i.e., 0.5 to 2 GHz.

In the frequency range over which hot spots may occur model-builders may be faced with the task of combining the detailed cell block models developed for the study of RF- and microwave absorption with equally finely sub-divided thermoregulatory models of man. This may be beyond our present capabilities. Above the frequency range of hot spots, the situation simplifies since surface heating is dominant. The application of thermoregulatory models in the case of RF- or microwave energy input is possible in the case of surface heating, and perhaps outside the frequency range over which hot spots occur (i.e., from 0.3 to 3 GHz). In the hot spot range, the models must be refined to account for local strong effects. Clearly, we have a long way to go before we can fully predict man's thermal response to radio-frequency radiant energy.

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REFERENCES

Burr, J.G., Cohoon, D.K., Bell, E.L. and Penn, J.W. (1980). Thermal response model of a simulated cranial structure exposed to radiofrequency radiation. *IEEE Trans. BME*-27:452.

Cook, H.F. (1952). A physical investigation of heat production in human tissues when exposed to microwaves. *Brit. J. Appl. Physics* 3:1.

Durney, C.H., Johnson, C.C., Barber, P.W., Massoudi, H., Iskander, M. F., Lords, J. L., Ryser, K. K., Allen. S.J., and Mitchell, J.C. (1980). *Radiofrequency Radiation Dosimetry Handbook*, 3rd ed., Rep.SAM-TR-76-35/78-22 and 80-32(AFSC). Brooks Air Force Base, Texas.

Emery, A.F., Short, R.E., Guy, A.W., Kraning, K.K., and Lin, J.C. (1976a) (1976b). The numerical thermal simulation of the human body when absorbing nonionizing microwave irradiation - with emphasis on the effect of different sweat models. In: *Biological Effects of Electromagnetic Waves*. Vol. 2. Selected papers of the USNC/URSI Annual Mtg., Boulder, Colorado, Oct. 20-23, 1975. U.S. Dept. of HEW, Public Health Service, Food and Drug Administration. See also, *J. Heat Transfer, Trans. ASME* 98:284.

Fan, L.T., Hsu, F.T., and Hwang, C.L. (1971). A review of mathematical models of the human thermal system. *IEEE Trans. Biomed. Eng.* 18:218.

Foster, K.R., Kritikos, H.N., and Schwan, H.P. (1978). Effect of surface cooling and blood flow on the microwave heating of tissue. *IEEE Trans. Biomed. Eng.* 25:313.

Gagge, A.P., Stolwijk, J.A.J., and Nishi, Y. (1969). The prediction of thermal comfort when thermal equilibrium is maintained by sweating. *ASHRAE Trans.* 75:108.

Gagge, A.P., Stolwijk, J.A.J., and Nishi, Y. (1971). An effective temperature scale based on a simple physiological regulatory response. *ASHRAE Trans.* 77:247.

Guy, A.W., Webb, M.D., Emery, A.F., and Chou, C.K. (1978). Measurement of power distribution at resonant and nonresonant frequencies in experimental animals and models. Report, Contract F41609-76-C-0032, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Hendler, E., Hardy, J.D., and Murgatroyd, D. (1963). Skin heating and temperature sensation produced by infrared and microwave irradiation. In: *Temperature, Its Measurement and Control in Science and Industry - Part 3, Biology and Medicine* (J.D. Hardy, ed.). p. 211. Reinhold Publ. Corp. New York. Vol. 3.

Johnson, C.C. and Guy, A.W. (1972). Nonionizing electromagnetic wave effects in biological materials and systems. *Proc. IEEE* 60:692.

Kritikos, H.N., Foster, K.R., and Schwan, H.P. (1979.) Temperature profiles in spheres due to electromagnetic heating. *Proceedings of 1978 Symposium on Electromagnetic Fields in Biological Systems,* Ottawa, Canada, IMPI Ltd.

Kritikos, H.N., Foster, K.R., and Schwan, H.R. (1981). Temperature profiles in spheres due to electromagnetic heating. *J. of Microwave Power,* 16:327.

Kritikos, H.N., and Schwan, H.P. (1978). Potential temperature rise induced by electromagnetic field in brain tissues. *IEEE Trans. BME* 26:29.

Michaelson, S.M. and Schwan, H.P. (1981). Factors governing the use of microwave/radiofrequency energies in cancer therapy. In: *Advances in Radiation Biology.* Vol. 9 (J.T. Lett & H. Adler, eds.). p. 323. Academic Press, New York.

Schwan, H.P. (1965). Biophysics of Diathermy. In: *Therapeutic Heat.* 2nd ed. p. 63. Eliz. Licht Publ., New Haven, Conn.

Schwan, H.P., Anne, A., and Sher, L. (1966). Heating of living tissues. U.S. Naval Air Eng. Center, Phila., Penna. Report NAEC - ACEL 534.

Schwan, H.P. and Piersol, G.M. (1954). Absorption of electromagnetic energy in body tissues - review and critical analysis (Part 1, Biophysical aspects) *Am. J. of Physical Medicine* 33:371.

Spiegel, R.J., Deffenbaugh, D.M., and Mann, J.E. (1980). A thermal model of the human body exposed to an electromagnetic field. *Bioelectromagnetics* 1:253.

Stolwijk, J.A.J. and Hardy, J.D. (1977). Control of body temperature. In: *Handbook of Physiology.* Vol. 9 (D.H.K. Lee, ed.). p. 45. Williams & Wilkins, Balt., Md.

Vendrik, A.J.H. and Vos, J.J. (1958). Comparison of the stimulation of the warmth sense organ by microwave and infrared. *J. Applied Physiology* 13:435.

Way, W.I., Kritikos, H.N., and Schwan, H.P. (1981). Thermoregulatory physiologic responses in the human body exposed to microwave radiation. *Bioelectromagnetics* 2:341.

Wissler, E.H. (1970). The use of finite difference techniques in simulating the human thermal system. In: *Physiological and Behavioral Temperature Regulation* (J.S. Hardy, A.P. Gagge & J.A.J. Stolwijk, eds.). p. 367. Thomas, Springfield, Ill.

Workshop on Thermal Physiology, Proceedings (1980). (T. Whit Athey, ed.) HEW Publication (FDA) 80-8109.

CHARACTERIZING THE THERMAL ENVIRONMENT

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INTRODUCTION

The energy exchange between a man and the environment is an important determiner of his comfort, well-being, and physical health. These energy flows depend on a number of parameters of the thermal environment and the individual. Fortunately, due primarily to the work of Gagge and his associates (1940, 1941, 1967, 1970) at the Pierce Laboratory, many of these parameters can be combined for the purpose of characterizing the thermal environment's potential for heat transfer. Microwaves represent a new path in the energy exchange spectrum and it will be shown that this new type of sensible or dry heat exchange can be characterized using the traditional methods.

The heat transfer pathways are illustrated in Figure 1. Heat is produced in the body by metabolism (M); in addition, heat may enter the body from the absorption of microwave radiation (AMicro). For thermal stability, this energy must be continually transferred to the environment. The balance between energy production and loss is so regulated by behavioral and physiological adjustments that the temperatures of the body's core and skin are maintained within narrow limits.

Energy may be lost by doing work (force x distance) on the surroundings, through respiration and by heat transfer from the skin. Respiratory losses (Q_{res}) are generally small. In typical comfort situations, most of the heat is lost from the skin by convection (Q_c) to the surrounding air and radiation (Q_r) to the surrounding walls and surfaces. In nonsweating situations, there is an additional small loss

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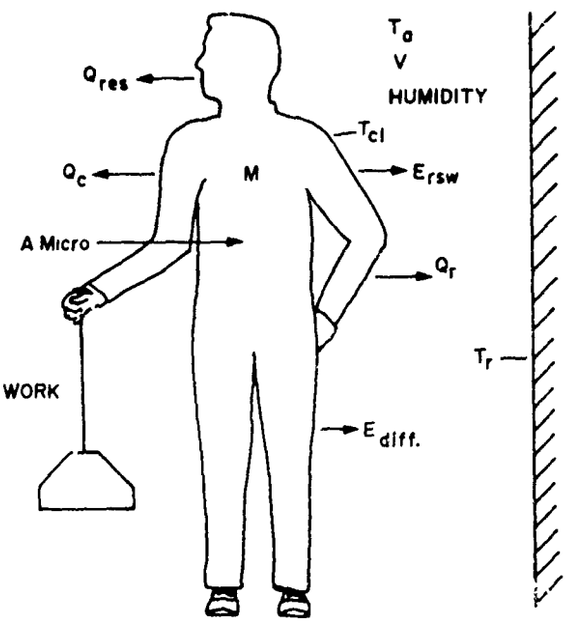

$$M + A\,Micro = WORK + Q_{res} + E_{diff} + E_{rsw} + Q_c + Q_r$$

Figure 1. The energy flows between man and the environment.

by the diffusion of water vapor through the skin (E_{diff}). In warm or hot conditions, the evaporation of regulatory sweat (E_{rsw}) can become a powerful mechanism for heat dissipation.

Convective heat loss increases with increasing air motion (V) and decreasing air temperature (T_a). At very low room air speeds, convection continues from the warm bouyant air rising next to the body. Radiation losses increase in proportion to the difference between the mean radiant temperature of the surrounding surfaces and the surface temperature of the individual. The mean radiant temperature (T_r) is defined as the temperature of an imaginary isothermal black enclosure in which an occupant would exchange the same amount of heat by radiation as in the actual nonuniform environment. In interior rooms of buildings away from

perimeter walls and in the absence of other heated or cooled surfaces, the air and mean radiant temperatures are usually approximately equal. Respiratory heat losses depend on air temperature, humidity, and the rate of ventilation, which in turn are proportional to metabolism. The mass or evaporative heat transfer terms, E_{diff} and E_{rsw}, are both affected by humidity and air motion.

Two other parameters that affect the energy flow are metabolism and clothing insulation. Metabolism is characterized by a unit called the met. The energy produced by a resting person per unit body surface area (58 W/m^2) is arbitrarily defined as 1 met. Clothing is also important since it adds thermal resistance to the heat path between the skin and surrounding environment. The resistance is characterized with the clo unit (1 clo or 0.155 $Wm^{-2}C^{-1}$). One clo of clothing insulation can keep a resting human "comfortable" at 21 °C (70 °F).

In cool environments, the resulting losses may be burdensome even with autonomic and behavioral adjustments. Under such conditions, the overall energy balance equation of Figure 1 indicates that absorbing microwave energy within the body is a novel way to supplement insufficient metabolic heat, balance the energy equation, and reduce the stress and discomfort of a cold environment.

OPERATIVE TEMPERATURE

The dry heat transfer per unit area for convection and radiation can be written as

$$q_c + q_r = h_c (T_s - T_a) + h_r (T_s - T_r) \qquad (1)$$

where h_c is the convective heat transfer coefficient, h_r is the linearized radiant heat transfer coefficient and T_s is the mean surface temperature of the individual, whether skin or clothing. For humans, h_c has a minimum value of about 2.9 $Wm^{-2}C^{-1}$ at low air speeds and can be predicted from $h_c = 8.6\ V^{0.53}$ for air speeds (V) above 0.15 m/s. The radiation coefficient (H_r) for energy transfer from a human to his equivalent black body surrounding can be shown to be

$$h_r = 4\ \varepsilon\ f_{eff}\ \sigma\ [(T_a + T_r)/2 + 273]^3 \qquad (2)$$

where σ is the Stefan-Boltzmann constant ($5.67 * 10^{-8}\ Wm^{-2}K^{-4}$). Assuming a skin or clothing emissivity (ε) of 0.95, the ratio of area effective for radiation to the total

surface area (f_{eff}) of 0.70 (some of the surface between legs, arms and fingers is ineffective) and a typical comfortable temperature of 25 °C, $h_r \approx 4.0$ $WM^{-2}C^{-1}$.

The dry heat transfer of equation 1 and the description of the environment can be simplified by some algebraic rearrangement as follows:

$$q_c + q_r = (h_c + h_r)\ T_s - (h_c\ T_a + h_r\ T_r) \quad (3)$$

and by factoring out $h_c + h_r$

$$q_c + q_r = (h_c + h_r)\ [T_s - (h_c\ T_a + h_r\ T_r)/(h_c + h_r)] \quad (4)$$

where now equation 4 quantifies the heat transfer by radiation and convection between the surface of the individual at temperature T_s and the environment, whose temperature is the average of the air and mean radiant temperatures, weighted by the respective heat transfer coefficients. This average environmental temperature is called the operative temperature (T_o) and characterizes the environment for dry heat transfer (Gagge, 1940). Thus equation 4 becomes

$$q_c + q_r = (h_c - h_r)\ (T_s - T_o) \quad (5)$$

where $T_o = (h_c\ T_a + h_r\ T_r)/(h_c + h_r)$. Operative temperature is the temperature of an imaginary uniform environment ($T_a = T_r$) that will transfer dry heat at the same rate as in the actual nonuniform environment ($T_a = T_r$).

Over a limited range, a person's thermal sensations on a scale from warm to cool are linearly related to the operative temperature (Gagge, 1973).

CLOTHING

Clothing acts as a buffer between the skin and the environment and adds resistance to the flow of dry heat from the skin. The resistance as previously mentioned is described by a unit called the clo. A business suit is about 1 clo and a pair of shorts about .05 clo. The clo unit is the effective resistance for the whole body even though the particular garment may cover only a small part. Numerically one clo has a thermal resistance of 0.155 m^2C/W (Gagge, 1941). The insulation of clothing is primarily due to air trapped in the fabric. This air is also the major source of vapor resistance. Thus, the clo value of an ensemble also provides a good method of estimating its water vapor

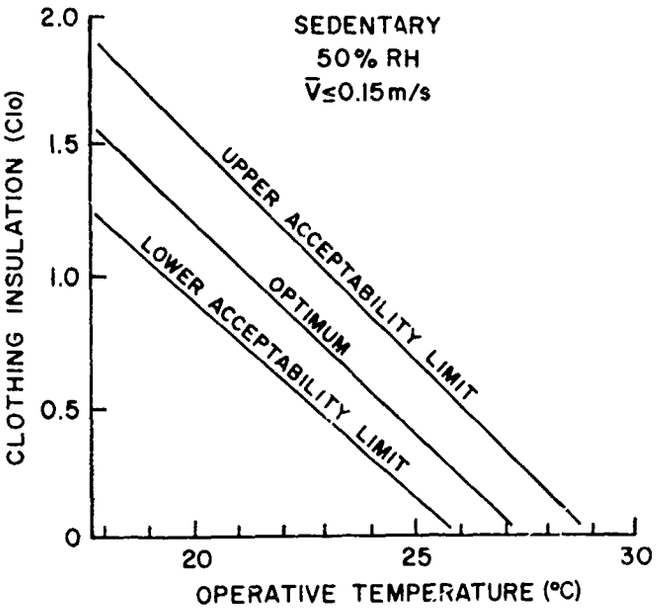

Figure 2. Clothing insulation necessary for various levels of comfort at a given temperature during light, mainly sedentary, activities ($\leq$ 1.2 met).

resistance. The vapor resistance in torr·m^2/W is approximately 0.065 times the clo value (Nishi, 1970).

The relationship between clothing insulation and operative temperature for the comfort of a sedentary person is shown in Figure 2. The figure shows that for a given operative temperature there is a range of clothing levels in which 80% or more of the population would find the environment thermally acceptable (ASHRAE, 1981). For example, at 22 °C (72 °F), the clothing range is 0.6 to 1.2 clo. The insulation value of a long sleeved shirt and trousers is about 0.6 clo; a winter business suit with a vest is about 1.2 clo. At 22 °C a person wearing 1.2 clo would feel "slightly warm" while the person wearing 0.6 clo would feel "slightly cool". Similarly, Figure 2 indicates that with a business suit, an environment between 18 °C (65 °F) and 22 °C (72 °F) would be thermally acceptable to sedentary persons while the 0.6 clo shirt and trousers ensemble would be acceptable in the 22-25.5 °C (72-78 °F) range.

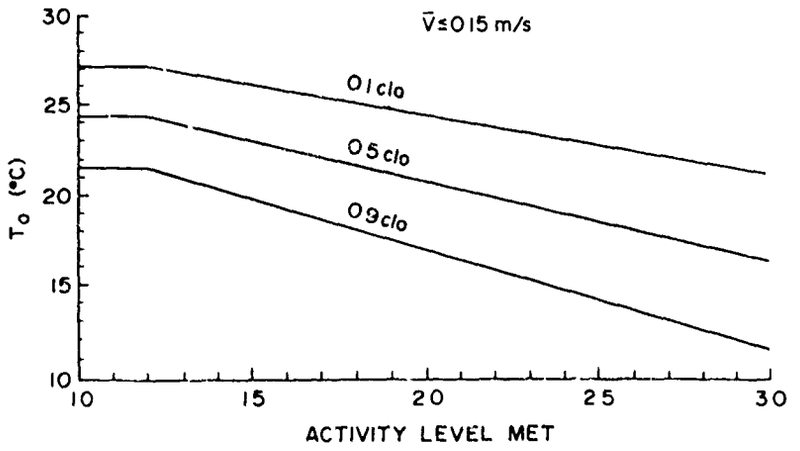

Figure 3. Optimum operative temperature for active people in environments of low air movement.

ACTIVITY

Since heat production increases with activity, to transfer the increased heat and maintain comfort, the ambient operative temperature must decrease (Figure 3). Fortunately, the increased activity results in increased relative air motion and convective heat transfer so that the operative temperature need not be decreased as much as it would if there were no increased air motion.

EFFECTIVE RADIANT FLUX

Another way to characterize the radiant component of the thermal environment is with effective radiant flux (ERF). This concept, proposed by Gagge, *et al.* (1967), is applicable to microwave comfort heating and its introduction here may increase the understanding of microwave heating of humans. The energy balance for heat exchange at the surface of an individual is

$$M_{sk} = h_c (T_s - T_a) + h_r (T_s - T_r) + E_v \qquad (6)$$

where M_{sk} is the net metabolic energy to be dissipated from

the skin and E_v is for the evaporative heat losses. By adding $+T_a - T_a$ to the radiation term of equation 6 it can be rearranged to

$$M_{sk} = (h_c + h_r)\ (T_s - T_a) - h_r(T_r - T_a) + E_v \qquad (7)$$

where the first term on the right represents the convective and radiant heat transfer between the individual and a uniform environment at air temperature (T_a). The second term on the right is the effective radiant flux (ERF) and represents the radiant energy absorbed by the body that occurs when the mean radiant temperature (T_r) is greater than the air temperature. Thus, the energy balance becomes

$$M_{sk} + ERF = h(T_s - T_a) + E_v \qquad (8)$$

where $h = h_c + h_r$. The equation states that at equilibrium the net metabolic energy plus the absorbed radiant energy equals the energy transferred to a uniform environment at temperature T_a. In terms of operative temperature, the dry heat transfer terms of equation 7 or 8 can be expressed as

$$h(T_s - T_o) = h(T_s - T_a) - ERF \qquad (9)$$

or

$$T_o = T_a + ERF/h. \qquad (10)$$

The ERF concept was demonstrated experimentally at the Pierce Laboratory through the use of two IR quartz lamps directed 45° downward at a seated subject (Figure 4). As the air temperature was increased and decreased in 1 °C steps, the subject was asked to adjust the power to the IR heaters to maintain thermal comfort. Simultaneous observations of ERF and T_a, chosen for comfort by four normal male subjects, both unclothed and clothed, are shown in Figures 4 and 6. The negative slopes of the ERF vs T_a lines for either clothed or unclothed conditions are essentially identical, as expected from equation 10. The values of ERF and T_a describe a locus of constant operative temperature, T_o, whose value is indicated by the temperature intercept with ERF = 0. The T_o for comfort decreases approximately 6.7 °C/clo (12 °F/clo) as clothing insulation is added. In Figure 7, the loci of ERF and T_a have been drawn for three clothing insulations - unclothed, 0.6 clo and 1.2 clo (Berglund and Gagge, 1979). The lines have been calculated with a dynamic digital model of temperature regulation (Gagge, *et al.*, 1976). Each locus represents a condition where

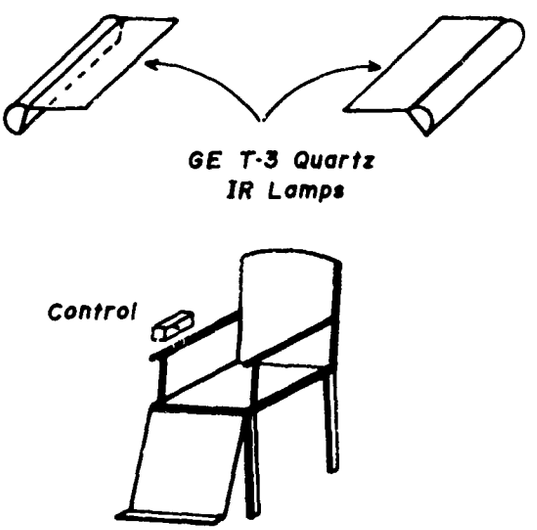

Figure 4. Diagram showing relation of subject's chair to the two sources of infrared radiation.

regulatory sweating is negligible and a state of thermal comforts exists. The negative slope of each locus is approximately h. Increasing air movement (V) causes the loci to become more vertical and thus reduces the effectiveness of ERF for producing comfort. Increased clothing insulation as noted experimentally in Figures 5 and 6 does not change these negative slopes but only displaces the comfort loci to lower temperatures.

MICROWAVES AND OPERATIVE TEMPERATURE

The overall energy balance equation including absorbed microwaves (AMicro) can be written as

$$M + AMicro = Work + Q_{res} - Evap = Q_c + Q_r. \quad (11)$$

If this equation is rewritten with all the sensible or dry forms of energy exchange grouped on the right, the result is

$$M - Work - Q_{res} - Evap = Q_c + Q_r - AMicro. \quad (12)$$

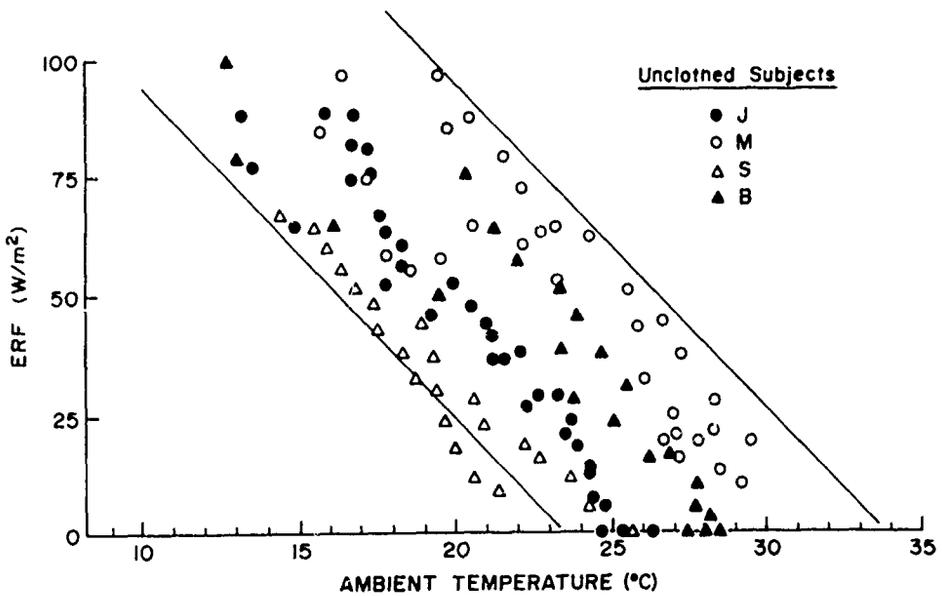

Figure 5. Radiant heat required for comfort of unclothed sedentary subjects.

The Q_c and Q_r terms represent heat flow away from the body; AMicro is a flow into the body. The dry energy flow can be normalized by dividing by the body surface area (A_D)

$$(Q_c + Q_r - AMicro)/A_D = h_c(T_s - T_a + h_r (T_s - T_r) - AMicro/A_D. \quad (13)$$

Previously, the environment's potential for dry heat transfer has been characterized with the operative temperature. In this case:

$$(h_c + h_r) (T_s - T_o) = h_c (T_s - T_a) + h_r (T_s - T_r) - AMicro/A_D. \quad (14)$$

Solving for operative temperature T_o

$$T_o = (h_c T_a + h_r T_r)/h + AMicro/(h A_D). \quad (15)$$

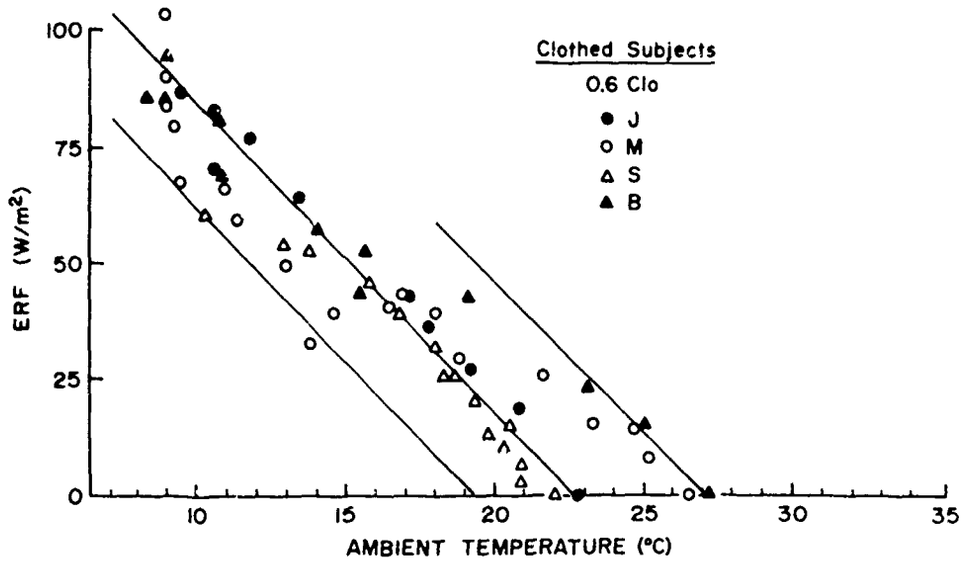

Figure 6. Radiant heat required for comfort of sedentary subjects in normal clothing.

Equation 13 can also be written in terms of ERF as

$$T_o = T_a + ERF/h + AMicro/(h\ A_D). \qquad (16)$$

With the exception of the AMicro term, the equations are familiar from the prior discussion about ERF. In equations 15 & 16 one sees the effect of microwave radiation is similar to that of infrared; it increases the effective operative temperature and thus the space feels warmer than the air temperature. If the air and wall temperatures are approximately equal ($T_a = T_r$, ERF = 0) as is often the case

$$T_o = T_a + AMicro/(h\ A_D). \qquad (17)$$

The operative temperature of an environment is a good indicator of the comfort and thermal sensations experienced. For a given level of thermal sensation, activity, and clothing, the operative temperature is constant. Thus equation 17 can be rearranged to equation 18 which predicts the air temperature for comfort defined by the operative temperature

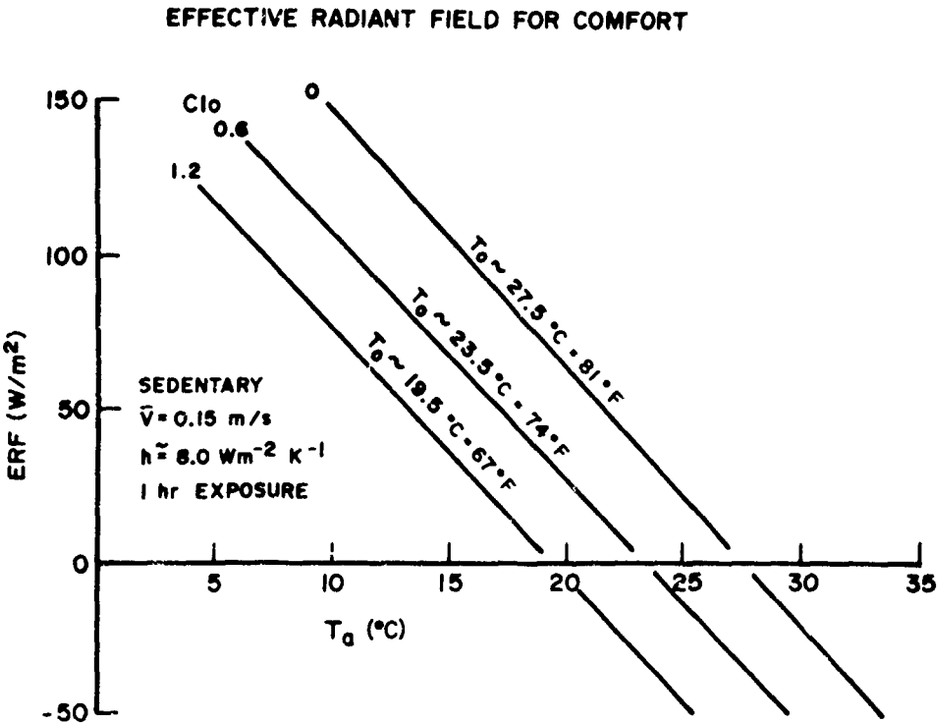

Figure 7. Effective Radiant Field (ERF) for comfort with various levels of clothing insulation.

at a given microwave energy level

$$T_a = T_o - AMicro/(h\ A_D). \qquad (18)$$

The absorbed microwaves can be expressed more quantitatively in terms of the incident power density (IPD), the projected area of the person that intercepts the radiation (A_p) and the fraction of the incident radiation that is absorbed (α). The absorbed microwaves can also be expressed in terms of the specific absorptance rate (SAR, Watts absorbed per kilogram of body weight) and body weight (wt).

$$AMicro = \alpha\ A_p\ IPD \qquad W \qquad (19)$$

or

$$AMicro = SAR\ wt. \qquad W \qquad (20)$$

Using these quantities, equation 17 becomes

$$T_o = T_a + \alpha\ f_p\ IPD/h \qquad (21)$$

and

$$T_o = T_a + SAR\ wt/(h\ A_D) \qquad (22)$$

where f_p = ratio of projected to total area or A_p/A_D.

Human data to demonstrate the operative temperature concept with microwaves is unknown or unavailable but Adair and Adams (1980, 1982) have carried out some applicable microwave experiments with squirrel monkeys. The monkeys were trained to sit in a chair and to regulate the temperature of the air flowing through a microwave anechoic chamber. The monkeys were instrumented for the measurement of skin and rectal temperatures. Results are shown in Figure 8 for microwave exposures lasting 10 and 150 minutes to one side of the monkey. As the power density increased, the monkeys chose to regulate the temperature of the flowing air to lower and lower levels. The air speed during the 10 minute exposures was slower (0.11 m/s) than during the 2 1/2 hr exposures (0.35 m/s) and may account for the slope differences in Figure 8. The animals may be assumed to have regulated the environmental temperature behaviorally to maintain a constant level of comfort. Their skin and rectal temperatures remained constant throughout each experiment. With zero radiation the monkeys regulated the air temperature to about 35.5 and 35.8°C for the 150 and 10 minute exposure experiments. Thus, the lines can be considered constant operative temperature lines of 35.5 and 35.8°C and to correspond to equation 18. The response of the monkeys to microwaves in Figure 8 is analogous to the human responses to infrared in Figures 5 and 6.

The behavioral data together with the theory of operative temperature can be used to evaluate some of the elusive microwave parameters such as absorptance (α) and SAR. For example, if equation 21 is rearranged and solved for absorptance

$$\alpha = (T_o - T_a)\ h/(f_p\ IPD). \qquad (23)$$

This equation was used to determine α from the 2 1/2 hr behavioral data of Adair and Adams in Figure 8 where at a

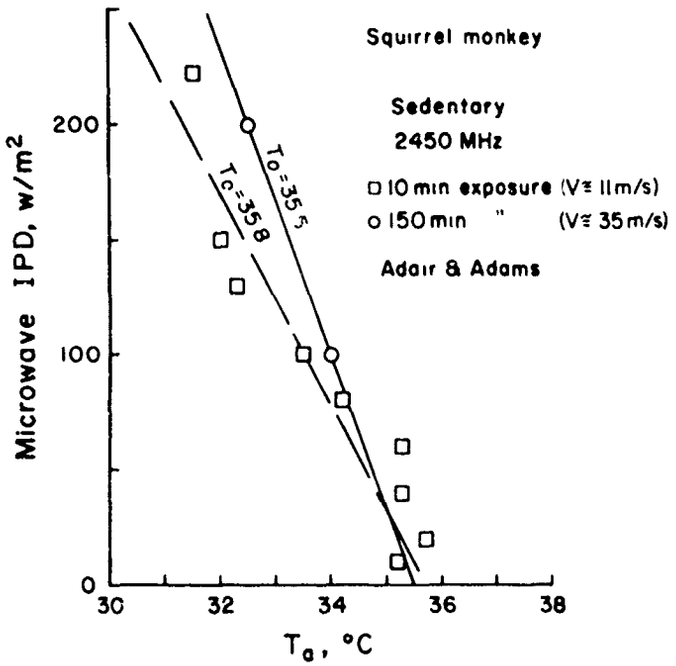

Figure 8. Air temperature chosen by sedentary squirrel monkeys exposed unilaterally to a homogeneous microwave field in an anechoic chamber.

IPD of 20 mW/cm^2 (200 W/m^2) the animals chose to decrease air temperature 3°C. The convective heat transfer coefficient (h_c) was calculated as that of an equivalent sphere with a surface area equal to that of the monkey. This is a procedure advocated by Rapp (1968) for seated humans. The surface area of the monkey was estimated using the equation developed for squirrel monkeys ($Am = 0.11\ wt^{2/3}m^2$) by Stitt, *et al.* (1971). These assumptions allowed the combined heat transfer coefficient ($h_c + h_r$) to be estimated at 12.3 W $m^{-2}C^{-1}$. The projected area (A_p) was determined from photographing the silhouette of some seated monkeys of average body mass. The resulting projected area factor ($f_p = A_p/A_D$) was thus determined to be 0.295. Substituting these values into equation 23

$$\alpha = 3 * 12.3/(0.295*200) = 0.63$$

which is a reasonable value for the absorptance of a

squirrel monkey.

The specific absorption rate (SAR) can also be estimated from the behavioral data of Figure 8. Rewriting equation 20

$$SAR = AMicro/wt \tag{24}$$

and substituting equation 19 for AMicro into 24, it follows

$$SAR = \alpha f_p \text{ Am IPD/wt.} \quad W/kg \tag{25}$$

Substituting the squirrel monkey surface area equation into the above, SAR becomes

$$SAR = 0.2 \text{ IPD}/wt^{1/3} \quad W/kg \tag{26}$$

where IPD is in mW/cm^2. Since a squirrel monkey weighs about 1 kg,

$$SAR \tilde{=} 0.2 \text{ IPD} \tag{27}$$

MICROWAVE COMFORT HEATING OF HUMANS

Comfort heating of humans by microwaves as a means to conserve energy has been proposed by Pound (1980). If the operative temperature characterization that includes microwave energy is valid, then the traditional analytical methods may be used to make predictions and estimates about comfort heating with microwaves. Some predictions of what the air temperature should be for various levels made with equation 21 for sedentary humans in still air are demonstrated in Figure 9. Two families of curves are shown. One family is for nude persons (0 clo) and the other is for persons wearing a warm vested suit or similar clothing (1.2 clo). The curves are loci of constant operative temperature (19.5 and 27.5 °C) and thereby constant comfort is assumed. For each clothing level there are operative temperature lines for beam and diffuse microwave radiation. The beam radiation is incident on just one side of the individual (f_p = .17), while the diffuse microwave radiation impinges uniformly from all directions (f_p = .70) Shadowing between arms, legs, fingers, etc., prevents f_p from reaching unity. The operative temperature lines are further divided into two absorptance classes (α = 0.5 and 0.9). Absorptance varies with microwave frequency. It is seen that the differences between beam and diffuse radiation are great; much larger reductions in air temperature for a given level of incident

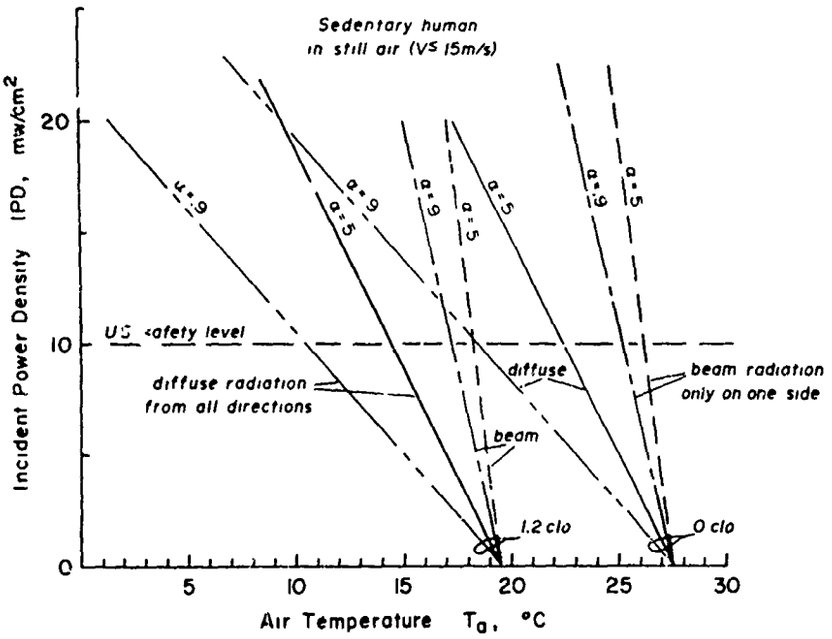

Figure 9. Predicted incident power density required for comfort of sedentary persons in various air temperatures at two levels of clothing insulation. The effect of radiation received from one side and simultaneously from all directions is shown as is the effect of 0.5 and 0.9 radiation absorptance.

flux density are possible with diffuse than with beam radiation The absorptance effect is smaller. Figure 9 shows that comfort for sedentary persons wearing typical winter clothing should be possible in a 10.5 °C (51 °F) environment with diffuse microwave radiation at the currently permitted 10 mW/cm^2 level (ANSI, 1966) i.e., in a 10 mW/cm^2 diffuse radiation field at 10 °C with α = 0.9 the person will feel as if he were in a non-microwave, thermally-uniform room at 19.5 °C (67 °F). With beam radiation at the 10 mW/cm^2 level the temperature of the environment would have to be raised to about 17 °C (63 °F) for comfort.

CONCLUSION

Operative temperature (T_o) is a convenient and traditional way to characterize the environment for dry heat transfer. The relationships between operative temperature, comfort and thermoregulation are well understood. Microwave energy may be included in the evaluation of operative temperature, making possible the prediction of microwave energy effects on comfort over a wide range of conditions. The concept of microwave heating for comfort appears to have the potential for improving the thermal environment in many situations and possibly for saving energy as well.

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REFERENCES

Adair, E.R. and Adams, B.W. (1980). Microwaves modify thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics* 1:1.

Adair, E.R. and Adams, B.W. (1982). Behavioral thermoregulation in the squirrel monkey: adaption processes during prolonged microwave exposure. *Journal of Comparative and Physiological Psychology*. (In Press).

ASHRAE Standard 55-81 (1981) "Thermal Environmental Conditions for Human Occupancy," American Society of heating, Refrigerating and Air-Conditioning Engineers, Atlanta, Georgia.

Berglund, L.G. and Gagge, A.P (1979). Thermal Comfort and Radiant Heat. In *Third National Passive Solar Conference Proceedings*, Office of the American Section of the International Solar Energy Society, Inc. p. 250. University of Delaware: Newark, Delaware.

Gagge, A.P. (1940). Standard operative temperature, a generalized temperature scale, applicable to direct and partitional calorimetry, *American Journal of Physiology* 131:93.

Gagge, A.P., Burton, A.C., and Bazett, H.C. (1941). A practical system of units for the description of the heat exchange of man with his environment. *Science* 94:428.

Gagge, A.P., Rapp, G.M., and Hardy, J.D. (1967). The effective radiant field and operative temperature necessary for comfort. *ASHRAE Transactions*, 73 (I): 1.2.1.

Gagge, A.P., Stolwijk, J.A.J., and Nishi, Y. (1971). An effective temperature scale based on a simple model of human physiological regulator response. In *ASHRAE Transactions* 77:247.

Gagge, A.P., Nishi, Y., and Gonzalez, R.R. (1973). Standard effective temperature-a single temperature index of temperature sensation and thermal discomfort. In *Bldg. Res. Symposium: Thermal Comfort and Moderate Heat Stress*. p. 229. Building Research Station, London.

Gagge, A.P., Nishi, Y., and Nevins, R.G. (1976). The role of clothing in meeting Federal Energy Agency conservation guidelines. *ASHRAE Transactions* 82:234.

Nishi, Y. and Gagge, A.P. (1970). Moisture permeation of clothing-a factor governing thermal equilibrium and comfort. *ASHRAE Transactions* 76:111.1.1.

Pound, R.V. (1980). Radiant heat for energy conservation. *Science* 208:494.

Rapp, G.M. (1968). Convective mass transfer and the coefficient of evaporative heat loss from human skin. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, Eds.) p. 55. C.C. Thomas, Springfield.

"Safety Level of Electromagnetic Radiation with Respect to Personnel" (1966). American National Standards Institute, New York.

Stitt, J.T., Hardy, J.D., and Nadel, E.R. (1971). Surface area of the squirrel monkey in relation to body weight. *J. Appl. Physiol.* 31:140.

THE MICROWAVE STIMULUS

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I. INTRODUCTION

In the past, significant exposure of people to microwave energy has been limited mostly to diathermy at the frequencies of 27 MHz and 2450 MHz. As the technological uses of the microwave spectrum multiply, however, there will be growing exposure of people to significant microwave levels, not only as incidental and possibly undesired but also as desired exposures in beneficial applications such as that of hyperthermia (Short and Turner, 1980) as well as radiant heating for comfort (Pound, 1979). It is anticipated that the frequencies of exposure will cover a wide range from low frequencies such as 27 MHz to the upper limits of the microwave spectrum around 300 GHz - a range of more than 10,000 to 1.

There is much knowledge of the properties of sensation derived from infrared stimuli consisting of spectral components above 300 GHz. Although some isolated data exist on sensation derived from microwave stimuli (see Michaelson, 1972) there is no knowledge for sensation of microwave stimuli comparable to that existing for infrared. (See Chapter 9.)

The task of developing information on microwave sensations will involve scientific researchers from a wide variety of disciplines. In particular, physiologists, psychophysicists and other life scientists, previously involved in the study of responses to infrared (IR) stimuli will be asked to turn their attention to the study of microwave stimuli.

It is the aim of this chapter to convey to such life

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scientists an understanding of the microwave stimulus in simple terms, how it differs from the infrared stimulus, and some idea of how microwave energy is generated, transmitted, and measured. Many experimental microwave exposures (of animals to date) are done in "closed" systems (e.g., waveguides and cavities) as well as "open" systems (e.g., free space or anechoic chamber). I will try to point out some of the technical pitfalls of microwave exposure systems, particularly the closed systems.

Although this chapter will not review in detail the nature of electromagnetic energy at frequencies below the microwave range, it will show how the microwave stimulus exhibits to some degree properties of energy at both higher and lower frequency ranges of the electromagnetic spectrum. At times microwave stimuli behave like infrared stimuli and induce "radiant" (warmth) sensations while at other times the microwave stimulus can excite body currents and responses more akin to that produced by lower frequency electrical signals, e.g., ordinary household electricity at 60 Hz.

Finally, I will review some of the practical aspects of experience with microwave stimuli involving sensation and exposure artifacts peculiar to the microwave part of the spectrum.

II. BASIC MICROWAVE CONCEPTS

Researchers experienced with basic aspects of radiant energy in the optical part of the spectrum may appreciate a reminder on general aspects of electromagnetic waves applicable to the whole non-ionizing radiation part of the spectrum and in particular the microwave part of the spectrum. For a supplementary tutorial see Osepchuk, 1979.

A. Properties of Electromagnetic Waves

The basic concept of an electromagnetic wave applies to the whole spectrum of interest which ranges from household electricity at the low end to the visible spectrum at the high end. Energy in any part of this spectrum which radiates or exists in space is pictured as one or more component waves. Each wave is a disturbance moving with unchanged form much as one sees waves move on the surface of water (radiate or propagate). The disturbance that is the essence of electromagnetic waves is analogous to the mechanical

forces that make the water move up and down and is described by quantities called fields. There is an electric field E oriented in a direction transverse to that of propagation. One can picture this as the quantity that exists between two electrodes with a battery across them. Thus, the electric field E is a quantity expressed in volts per meter. This field has the ability to move charges which exist in all matter in one form or another. This field alternates in direction as we progress along the wave - just as the mechanical force alternates in causing the crests and valleys of a water surface wave. This alternating electric field or force causes currents, or charges in motion, within a material. Such currents are measured in amperes and their density is expressed in amperes per square centimeter (A/cm^2) or milliamperes per square centimeter (mA/cm^2). Because the wave is moving or propagating, the charge motions (currents) and the fields causing the former are not steady but alternate in direction at a rate, for an observer at rest, called frequency.

All electromagnetic waves move with the same velocity in free space, namely, 3×10^8 meters/sec or 186,000 miles/sec. This is difficult to conceive, but frequency and a spatial distance called wavelength are more easily appreciated. The wavelength is simply the distance or period between neighboring points of similar or the same field value - magnitude and direction - analogous to the distance between peaks of water waves. The wavelength is expressed in terms of meters or centimeters.

Because the disturbance or wave is moving at a speed of $c = 3 \times 10^8$ m/sec the sense of the field experienced at a fixed point varies or oscillates, repeating itself periodically at a rate equal to the distance the wave moves in one second ($c = 3 \times 10^8$ meters) divided by the distance between field peaks (i.e., the wavelength λ), i.e., the number of positive or negative peaks that sweep by in one second. This is the frequency f and the calculation simply is

$$f = c/\lambda \qquad (1)$$

The electromagnetic wave consists not only of an alternating electric field disturbance but also a magnetic field, which is in a direction at right angles (perpendicular) to that of the electric field. This field H or force is that associated with moving charges and is expressed in terms of amperes per meter (A/m). A related form of a magnetic field is denoted B and is expressed in units of Tesla. These magnetic fields and the forces they produce are more important if the material is "magnetic," e.g., a ferrite. In general,

the magnetic field is of little significance with regard to the biological effects of microwave exposure. It is primarily the electric field that is of interest because it is the internal electric field E that causes internal currents within bodies as well as the associated heating.

Note that the internal field will be different from the external field or incident field because of the effect of the body in reflecting or shunting the outside field as well as attenuating the waves as they penetrate the body.

It should be stressed that generally in the interaction of microwaves with biological systems, it is only the *internal electric* field E that is of direct significance. Note, however, that *external magnetic* fields in general may create internal electric fields by a process called induction. This distinction is of importance at the lower microwave frequencies.

All electromagnetic waves consist of moving patterns of alternating fields, the latter being familiar concepts of low-frequency electricity. Electromagnetic waves, however, also exhibit general radiant characteristics more familiar in the description of optical or infrared radiation. The term radiation, when applied to any non-ionizing radiation, applies only in the far field of some source where there is a radiating plane wave. The far field for small radiating apertures or antennae exists at distances R given by $2\pi R/\lambda >> 1$. In addition, for large apertures, like a "dish" reflector, there is the far-field condition $R > D^2/2\lambda$ where D is the diameter or large dimension of the radiating aperture.

In the far field where there is a meaningful plane wave, it makes sense to use the terms radiation and radiation flux or power density p. The latter is simply the power flow, or rate of energy transfer, and is related to the E field by

$$p(W/m^2) = \frac{E^2(V/m)}{120\ \pi} \tag{2}$$

or

$$P(mW/cm^2) \simeq \frac{E^2(V/m)}{4000} \tag{3}$$

The H field is given by

$$H(A/m) = \frac{E(V/m)}{120\ \pi} \tag{4}$$

and the B field is given by

$$B(gauss) = \frac{E(V)/m)}{30,000} \tag{5}$$

At high frequencies where radiation fields are more significant, there are unique relationships between the fields and power density and both concepts have value. At low frequencies, however, it is quite possible to have either an E or H field in some region of space without the other and without significant radiation. In this case the fields are called quasistatic and no definite relation exists between E and H at a given point.

In this chapter we will not discuss extensively how materials interact with electromagnetic fields or waves. We will describe the most fundamental concepts of dielectric constant ε (actually the so-called relative dielectric constant) and the loss tangent $\tan \delta$. The dielectric constant tells a lot about reflection properties and reduction in wavelength. The latter is reduced from the free-space value by the ratio ε. Wave reflection at a surface of a material will increase as ε increases. For example, for a substance like water where $\varepsilon \sim 60$, the power reflection is about 60%.

The loss tangent is a measure of how absorptive the material is, or how quickly it causes a wave to attenuate as it propagates in the material. A simple formula for penetration depth D, the depth at which the power density is reduced by $1/e^2$ or the fields by 1/e, is

$$D = \frac{0.318\ \lambda_o}{\varepsilon \tan \delta} = \frac{0.318\ \lambda}{\tan \delta} \qquad (6)$$

where λ_o is free space wavelength.

The energy or power absorbed by the body as the wave attenuates produces local heating at a rate called the specific absorption rate, and is given by

$$SAR = \frac{1}{2\rho}\ \omega\varepsilon_o\ \varepsilon\ \tan \delta\ E_{in}^2 \text{ watts/kg.} \qquad (7)$$

where

- SAR is the power transferred to the absorber by the electric field in the body
- ρ is the mass density of the body, in kg/m^3
- ε_o is the permittivity of free space, in farads/m
- ε is the relative dielectric constant
- $\tan \delta$ is the loss tangent
- ω is the radian frequency given by $\omega = 2\Pi f$
- E_{in} is the electric field in volts/m at the point in the body, with the subscript "in" to emphasize that the field inside the body is not the same as the field in the incident radiation.

The dielectric parameters ε and the tan δ are essential in determining the properties of electromagnetic waves as they are incident on and are transmitted through material bodies. These parameters will vary with frequency and greatly so across many decades in frequency. Since we are interested primarily in the microwave frequency range we have tabulated in Table I a few values of dielectric parameters for common materials at the microwave frequency of 2.45 GHz - the frequency of the microwave oven.

TABLE I. A Partial List of Dielectric Properties of Foods and Other Materials at 2,450 MHz (at Room Temperature, 20 °C)

Material	ε	tan δ
Distilled water	78	.16
Muscle	50	.422
Fat	9	.268
Raw beef	49	.33
Mashed potato	65	.34
Cooked ham	45	.56
Peas	63	.25
Ceramic (alumina)	8-11	.0001-.001
Most plastics	2-4.5	.001-.02
Some glasses (pyrex)	∿ 4.0	∿ .001-.005
Papers	2-3	.05-.1
Woods	1.2-5	.01-.2
Sand	2-5	.01-0.1
Formica	4.0	.04

Table I shows that materials like glasses, paper and plastic are generally transparent whereas foods and biological tissue are heavy absorbers, primarily because of high water content. Furthermore, the variability of tan δ in materials such as paper and wood is due to variable moisture content. In general, the ranges of tan δ shown apply for moisture content less than 10%. Higher values of tan δ will result for moisture content greater than 10%.

B. The Electromagnetic Spectrum

In this chapter we are interested primarily in the microwave/radiofrequency portion of the electromagnetic spectrum. Figure 1 shows a spectrum chart designating in order different ranges of frequency (cycles per second or Hertz) and wavelengths (centimeters). (Note that frequency and wavelength are inversely related through Eq. (1) and either quantity by itself specifies the waves under discussion.) The frequency scale is divided into decades by vertical dashed lines. The solid vertical lines denote various frequencies designated for "industrial, scientific and medical" (ISM) use by governmental authorities on frequency allocations. (The FCC in the U.S.)

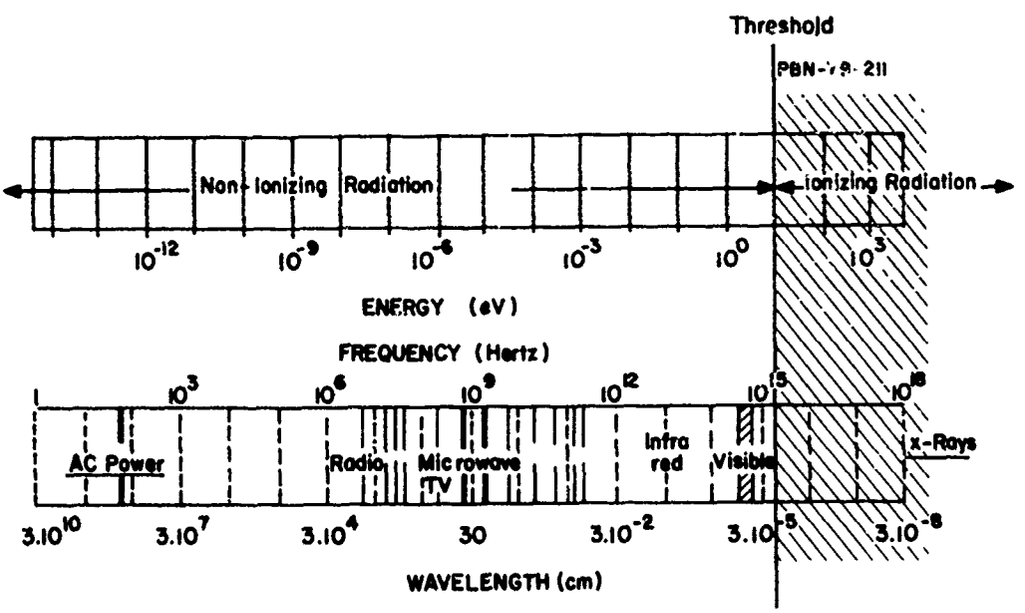

Figure 1. The Electromagnetic Spectrum. A threshold line is drawn between the regions of non-ionizing and ionizing radiation to emphasize the distinction. In the lower chart the vertical undashed lines in the microwave region denote officially-designated ISM bands centered at the following frequencies: 6.78, 13.56, 27.12, and 40.68 MHz; 0.43342, 0.915, 2.45, 5.80, 24.125, 61.25, 122.5 and 245 GHz.

At the low end of the spectrum is the frequency of household electricity (60 Hz). For low frequencies, engineers normally talk of currents in conductors, voltages across

circuit elements, and the fields around circuit elements but usually the concept of radiated flux is not applicable. At the high end of the non-ionizing part of the spectrum is the visible range along with its bordering regions of infrared and ultraviolent. In these optical regimes one talks of radiant flux or power density but there is less practical need to invoke the concepts of fields. In between optical and power frequencies lie microwaves which have some relation to both ends of the spectrum, i.e., both the E and H fields and such radiation terms as power flux (mW/cm^2) are important in describing microwave effects.

The definition of the microwave portion of the electromagnetic spectrum is usually somewhat arbitrary but it can be based alternatively on the property of maximum coupling of electromagnetic energy to macroscopic objects of common use and interest to man, a "microwave" resonance effect. We shall discuss both viewpoints.

Many groups or authorities choose to define "microwaves" as applying to a *specific* region of the spectrum. For example, the Scientific Committee 53 of the National Council on Radiation Protection and Measurement (NCRP, 1981) states, "For the purposes of this report, radio-frequency radiation refers primarily to electromagnetic radiation in the frequency range of 300 kHz to 300 GHz. Such a range includes microwave radiation, i.e., the frequency range from approximately 300 MHz to 300 GHz." On the other hand, the International Telecommunications Union (RCA, 1969) in 1959 designated the "radio" spectrum as extending from 3 kHz to 3000 GHz with no use made of the term "microwaves".

Many authors of scientific and technical texts (e.g., Muchmore, 1964) define microwaves more uniquely as that portion of the spectrum where "the wavelength to size ratio is of the order of unity" for the objects or apparatus under study. This then means that there are only a few "modes" possible for the system. (A mode is a state or distribution of electromagnetic energy that can exist by itself in a given system as distinguished from a "component" or "spatial harmonic". For example, a waveguide usually functions in its "dominant" mode region of frequency, a band of about 40% width where only one propagating mode can exist. In this region of frequency the width of the guide is approximately 3/4 λ).

Scientifically, or from the viewpoint of logical exposition, it makes sense to define "microwaves" in this fashion. If so, we can present Table II as a logical way to divide the electromagnetic spectrum (non-ionizing) with respect to any object considered under interaction with electromagnetic energy. This scheme of definition is always related to the

TABLE II. Breakdown of EM Spectrum

Name:	Static	Quasistatic	Microwave	Quasioptical	Optical
Frequency Range:	$\lambda \to \infty$ or $\lambda >>> L$	$\lambda >> L$	$\lambda \sim L$	$\lambda << L$	$\lambda <<< L$

size L of the object under study.

Alternative names are sometimes suggested, e.g., "RF" for "quasistatic" or "nanowave" for "quasioptical" (Zimmerer, 1966). In any case, the organization in Table II is useful in interpreting microwave literature in general and specifically the literature on microwave-biological interactions. If these interactions are uniquely related to the requirement that $\lambda \sim L$, then clearly one must scale in frequency from animal to man. On this basis, one can justify the choice by ANSI C 95 of the range of 10 MHz to 100 GHz as the microwave range for human exposure standards (Guy, 1980).

It is expected that the heating, cooking, and biological effects of non-ionizing or RF radiation depend on the penetrating power of the radiation, and the latter is expected to peak in the microwave region. This is confirmed in many studies of absorption of electromagnetic energy by man (Gandhi, 1979). A peak absorption of energy occurs in a resonance range of roughly 30-300 MHz for humans, decreasing as f^2 at low frequencies and decreasing slowly to about 1/10 of its resonance value at high frequencies.

At low frequencies the radiation is shunted out (or reflected) by the conducting nature of the body. (The dielectric constant also becomes very large at low frequencies.) At high frequencies the energy is absorbed in a small skin depth as given by Eq. (6). Thus the internal field is large only in a finite range which we call microwave. This property is depicted in Figure 2 from a rough calculation of the field in the center of a man when exposed to radiation at a given frequency. It is important to note that the resonance range is around 100 MHz for man but is about 3 GHz for a mouse or hamburger. If the microwave range is taken to extend to 300 GHz, then the portion above roughly 10 GHz is characterized by essentially surface (skin) absorption in man. Here viewpoints comparable to those for infrared exposure seem probable.

This discussion has centered primarily on electric fields since they are believed to be the significant physical

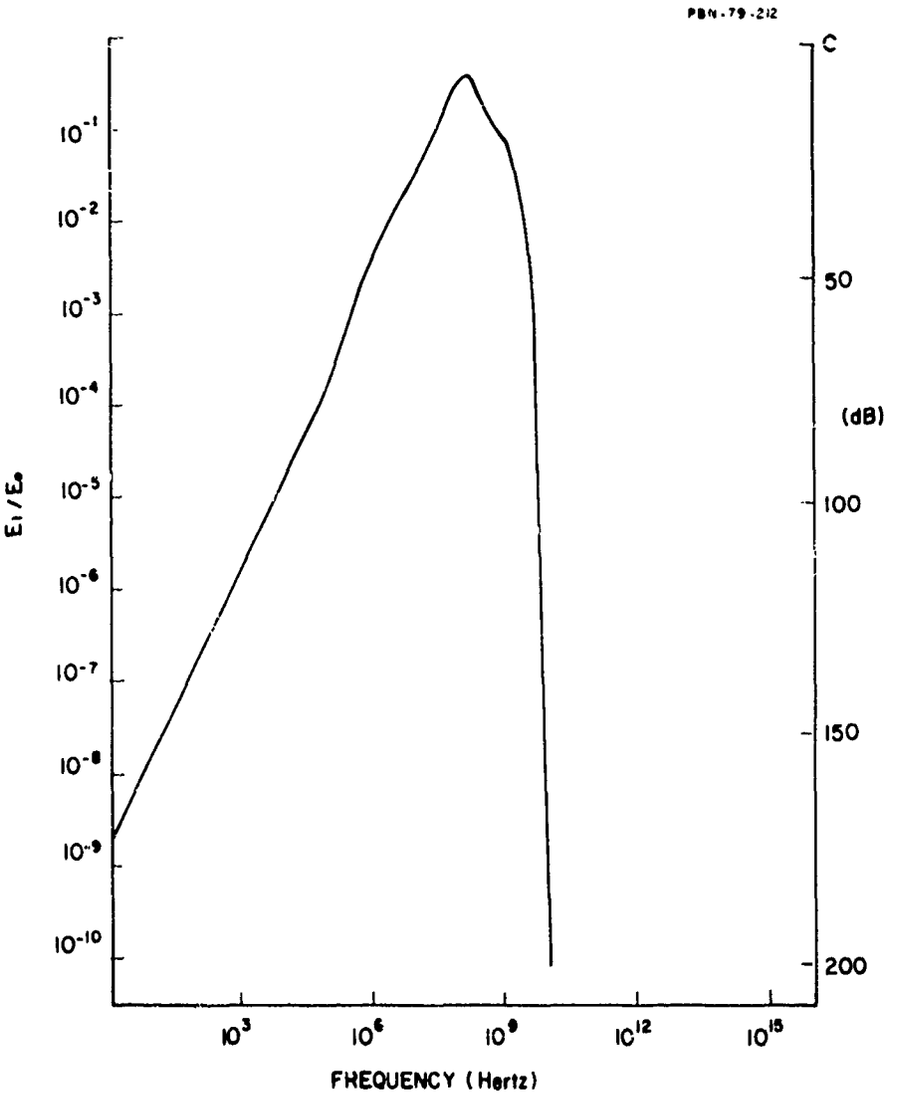

Figure 2. Estimated dependence on frequency of penetration capability of non-ionizing radiation in model of human body with minimum dimension of 15 cm. Ordinate is ratio of electric field in *center* of body (E_i) to incident (external) electric field (E_o). Every reduction of E by 20 dB represents a factor of 10^2 in E or 100 in power density.

parameter in biological interactions either through heating, Eq. (7), or in hypothesized non-thermal effects (NCRP, 1981). Although magnetic fields are believed to be less significant, one should recognize that at low frequencies the human body and most objects are transparent to magnetic fields except as countered by the H fields of induced currents in the body. This induced current phenomenon also produces internal electric fields, the more so near the surface, but the induced E fields also decrease as frequency is lowered.

The microwave range as variously defined is also characterized by low ambient levels of natural radiation (Osepchuk, 1979). This is why the microwave range is of particular interest for communication to objects in space. On the other hand, we have significant fields at low frequency (e.g., several kV/m before a storm) and significant radiation flux at optical frequencies (e.g., $\sim$ 60 mW/cm^2 from the sun at noon). The naturally-occurring microwave fluxes are not entirely trivial compared to commonly-occurring man-made fluxes in the environment. The latter typically are in the range of a nanowatt/cm^2 (10^{-9} W/cm^2) to a microwatt/cm^2 (10^{-6} W/cm^2) (Janes, 1979). It has been suggested (NCRP, 1981, p. 93) that "man-made sources in the microwave and RF region have power outputs many orders of magnitude above background." This statement is misleading, especially if one adopts the NCRP definition of "microwaves" as 0.3 to 300 GHz. The thermal or black-body fluxes from the earth at temperature T_e (assuming an emissivity of unity) is give by

$$S = 0.3 \left(\frac{f}{300}\right)^3 \left(\frac{T_e}{300}\right) \mu W/cm^2 \qquad (8)$$

for the spectrum up to f in GHz; T_e in °K. This yields 0.3 μW/cm^2 for the "microwave" background. This clearly is very significant compared to long-term man-made environmental exposure levels. Even the value up to 30 GHz (0.0003 μW/cm^2) is significant compared to long term man-made exposure.

This is not to say that the comparison is not dramatic at some frequencies, particularly in the resonance range of man. This is surely related to the perceived need for most stringent exposure standards for man in the microwave resonance range of frequencies, 30-300 MHz (Guy, 1980). On the other hand, it is clear that the upper part of the range denoted "microwave" may turn out to have more in common with the infrared spectrum, at least with regard to sensation phenomena and biological effects in man, a fact reflected in the revised standard.

One can note that the meager data (Michaelson, 1972) on

sensation of microwave radiation indicate rising thresholds for sensation as frequency is lowered (*cf* Chapters 9 and 10). Presumably this is correlated with increasing penetration depth at lower frequencies.

Sensation phenomena, as well as exposure safety limits, should in an approximate way exhibit an adiabatic region for short-exposure duration below an applicable time constant where the phenomenon depends on *energy* (dose) absorbed. (This corresponds to the region of "temporal summation" as described in Chapter 9, and occurs only for sensations near threshold in the infrared range.) Beyond this time the phenomenon depends on *rate* of energy transfer or simply the radiant flux or power density, i.e., under conditions of equilibrium in the process, thermal or otherwise. The applicable time constants are expected to depend on penetration depth. One might expect shorter time constants at the higher microwave frequency range where penetration is superficial as it is in the infrared range.

In addition, the study of human sensation of microwave energy may already be complicated by psychological factors. The perceived risk of exposure to microwave radiation appears to be heightened under modern societal viewpoints which are often somewhat irrational (Osepchuk, 1981).

III. PROPERTIES OF MICROWAVE GENERATORS

Microwave energy is generated by either a variety of microwave tubes or solid-state devices, either as power oscillators or a low-power oscillator followed by a chain of amplifiers. With conventional microwave tubes, very large output power is feasible up to at least 1 megawatt at frequencies up to 10 GHz (Osepchuk, 1979). Efficiencies of low-power oscillators or amplifiers may be less than 10% but higher power tubes typically can be designed with at least 40% and even up to 90% efficiency at the lower microwave frequencies. Microwave tubes include linear-beam tubes (klystrons and traveling-wave tubes and crossed-field tubes), magnetrons, and crossed-field amplifiers. In addition, there exist voltage-tunable oscillators called "carcinotrons" or backward-wave oscillators (BWO).

Above 10 GHz, conventional microwave tubes drop in power capability rapidly as f^{-5} but there now exist in development a new class of "fast-wave" tubes like the gyrotron which is likely to extend the frequency boundary at a given power level upwards by a factor of ten.

Solid-state (semiconductor) devices include transistor

amplifiers and oscillators at the lower microwave frequencies and a variety of diode oscillators and amplifiers at the higher frequencies. Below 1 GHz the efficiency of transistors can be quite high, > 60%, but this value drops rapidly for frequencies above 1 GHz. Diode devices can exhibit efficiencies up to 30 or 40% but 10 to 20% is more typical. To achieve substantial power, many discrete solid-state devices are combined in various ways.

Whereas solid-state devices involve low d.c. voltages and high currents, microwave tubes at the higher power levels > 50 kW may involve high voltage > 30 kV. Thus a potential by-product of high-power microwave tubes includes x-radiation and spurious products of infrequent voltage breakdown such as corona, air ions, and ozone. In well designed modern power sources these phenomena are minimized.

Ideally, microwave power sources produce a coherent signal, i.e., a single frequency carrier or at least a narrowband signal. Energy at frequencies other than the carrier, though much smaller than the carrier, can exist and can be quite significant, especially for crossed-field tubes which tend to be noisy.

For example, consider the magnetrons used in microwave ovens. These produce about 700 watts at 2450 MHz at ∿ 70% efficiency and cost less than $25 to the oven manufacturer. They are provided with filter elements to reduce noise and

Figure 3. Spectrum between 0 and 1 GHz of power from unfiltered cathode of cooker magnetron. Vertical scale: 10 dB/division, Horizontal scale: 100 MHz/div. Magnitude of peak at ∿ 200 MHz is 36 dBm/MHz.

spurious signals. Without these elements this non-carrier power can be intolerably significant. Figure 3 shows the spectrum of unfiltered power emitted at the cathode of the magnetron amounting to a few watts. This power is divided by a spurious signal at ∿ 200 MHz and its harmonics and broad-band noise. Such spurious energy is potentially more troublesome as a source of radio-frequency interference than microwave leakage at 2450 MHz from an oven which typically is less than 1 watt even at the limits imposed by Federal standards.

Other tubes may produce less spurious signals but may produce excessive harmonic signal levels. For example, traveling-wave tubes (TWT's) of the broadband (helix) variety typically can produce a second-harmonic signal up to 10% of the fundamental output signal when operated at the low end of its band.

Any tube or solid-state device can in principle become unstable, at least momentarily, and shift into abnormal modes of operation - producing undesired signals at generally low efficiency. Careful monitoring of power sources is necessary to insure absence of such moding during microwave experiments.

Most power sources can not only be operated in a continuous (CW) fashion but usually can be pulsed-modulated in amplitude, or amplitude modulated. Some sources (e.g., BWO's) can be frequency-modulated. High power pulsed tubes (e.g., megawatts peak) are generally designed for radar application and in most cases are limited in pulse widths to the range of 1 to 50 microseconds.

IV. ARTIFACTS IN CLOSED EXPOSURE SYSTEMS

In some respects, the irradiation of a biological subject in a closed system (e.g., waveguide or cavity) is more attractive than in an open system. Total power absorbed can be monitored and there is no radiation leakage or RFI (radio-frequency interference) problem. There are numerous potential artifacts in closed systems, however.

Waveguide systems propagate a single mode over only a 40% range in frequency. TEM (transverse electromagnetic) systems can be used over a broad range extending to zero frequency but there are finite upper limits. Recently, there has been a dispute (Weil, *et al.*, 1981) over the potential problem of higher modes in a TEM cell. If such a cell of finite length is only lightly loaded by an absorbing object, the cell is likely to exhibit fields in these higher modes

only at frequencies of axial resonance (where the length of cell is n x $\lambda/2$) because the higher modes do not propagate in the usual feed lines. If a cell is heavily loaded, these higher modes will be significant in establishing the distribution of external field around the object. It was suggested (Weil, 1981) that a better exposure system for freedom from higher modes would be an open parallel-plate guide. Even for this system, however, there will be higher modes even if they are damped somewhat by radiation loss, hence the term "leaky waves".

Figure 4 illustrates an example of waveguide-systems artifact. A section of WR430 waveguide is excited by a TWT power source driven by a BWO swept from 2 to 4 GHz. The signal from an arbitrary off-axis probe is shown in Figure 4(a). There appear to be some resonant responses in the range below 2.75 GHz where only the TE_{10} mode is supposed to propagate. If a low-pass filter is introduced, however, to cut off signals above 4.0 GHz, then these resonant responses disappear (Fig. 4(b)). In fact, the responses are due to spurious waveguide resonances excited by the *2nd* harmonic output of the TWT. This is filtered in the output circuit of the TWT, preferably after a circulator or protective ferrite device. The 2nd harmonic is not removed by a filter in the input circuit of the TWT.

Similarly, in multi-mode cavities, like that of the microwave oven (Heynick, *et al.*, 1977) the intent is to provide uniform irradiation of a biological subject without resonant responses. For this purpose, some means of making the fields vary randomly in time is provided, e.g., a "mode-stirrer". There is no complete assurance of the absence of resonances, however. Figure 5 shows the input impedance of a microwave oven cavity containing a 1000 ml water load on a *Smith Chart** as the frequency varies from 2415 to 2485 MHz, for a fixed position of a mode stirrer. The two loops indicate resonances that suggest weak coupling to the water and a possible source of other artifacts, e.g., microarcing if high fields are generated someplace in the cavity where a close spacing between conducting objects exists.

Figure 6 shows acoustic pulses detected with a microphone

*The radial coordinate of the Smith Chart corresponds to the magnitude of the reflection coefficient of a given load impedance which terminates a transmission line. The azimuthal coordinate corresponds to the phase of the reflection. The reflection coefficient varies from 0 to 1. Equivalent impedance or admittance contours are usually provided on the Smith Chart, also.

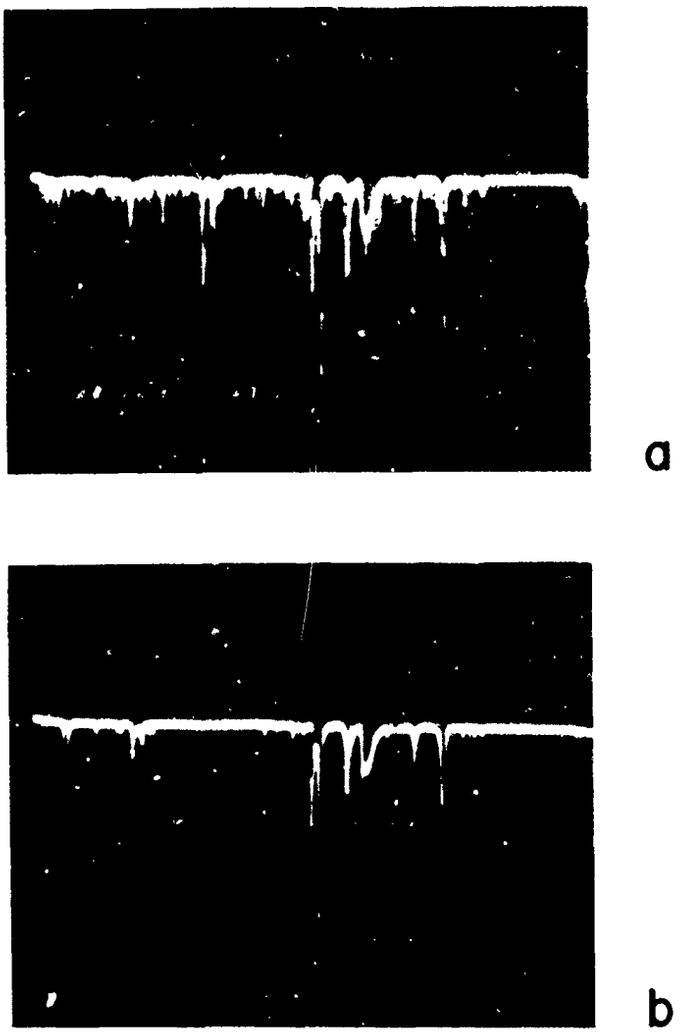

Figure 4. Signal detected at side wall of WR430 waveguide with an E-field probe as power source frequency is swept from 2 to 4 GHz. Vertical scale: linear with power; Horizontal scale: ∿ 0.2 GHz per division. (a) Without 2nd harmonic filter in detection circuit or output circuit. (b) With 2nd harmonic filter.

at two distances from a source of microarcing in a coaxial line. Higher frequencies in the range above 10 kHz tend to be generated as determined by local geometries. These sounds, though weak, may be perceptible to some animals.

All possible artifacts cannot be reviewed here but a few

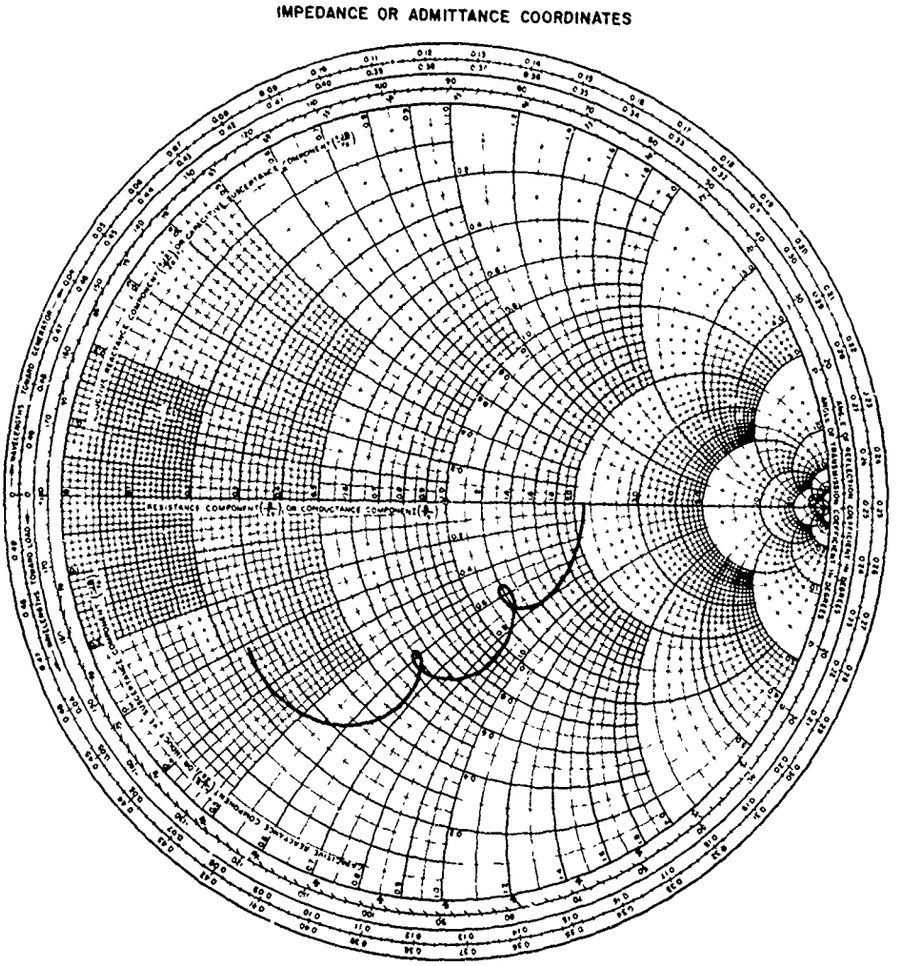

Figure 5. Impedance of a microwave oven on Smith Chart as frequency is swept from 2415 to 2485 MHz; fixed position of mode stirrer; 1000 ml water load.

more can be mentioned: the difference in infrared environment in space surrounded by low emissivity metal walls and difficulties in controlling both the temperature and the humidity of the air.

Some artifacts are potential problems in both open and closed systems. A prime example concerns the use of metal probes or leads which, besides perturbing and concentrating fields, can introduce low-frequency currents through rectification effects in the metallic assemblies or from the instrumentation attached to the probes.

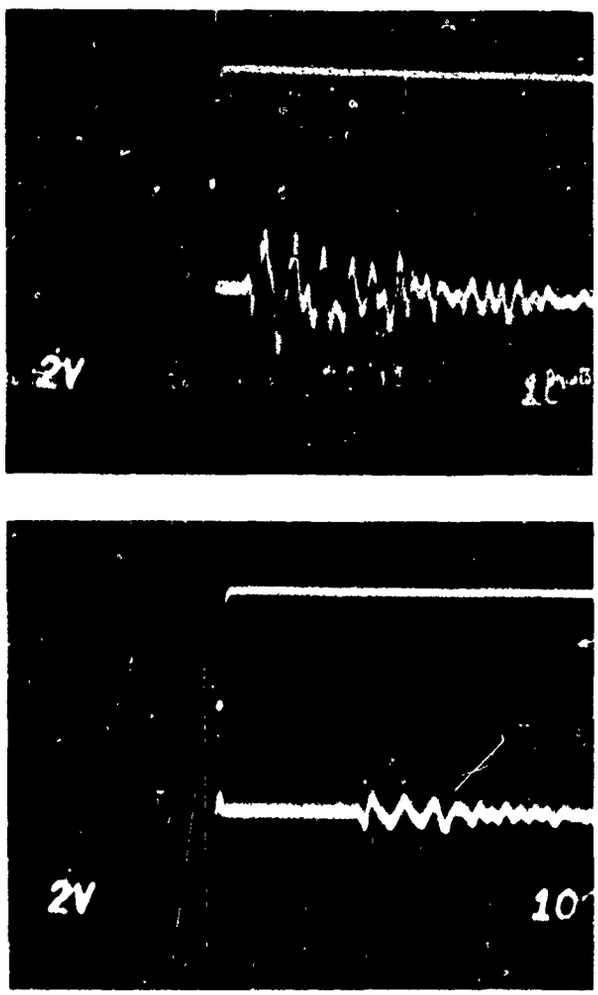

Figure 6. Acoustic signals detected near a site of microarcing in a coaxial line. Vertical scale: 2 volts/div.; Horizontal scale: 100 μsec/div. Gen. Rad. Microphone Model 1962, Gen. Rad. Preamplifier Model 1560-P42. (a) Distance: 1.5 cm; (b) Distance: 6 cm.

V. TEMPORAL ASPECTS OF MICROWAVE FIELDS

It is almost always the case that the microwave/RF fields in practice or in experiments exhibit considerable variation in space and in time. Even if the fields at a fixed point did not vary with time an observer in motion would almost

certainly experience a temporal variation. In practice the spatial variations arise from scattering of waves from objects around the subject. In addition, various sources have variation with time for reasons peculiar to the source. Broadcast sources are usually steady in strength except for fluctuations caused by moving scattering objects. Other sources like CB or mobile radio are intermittent and transient at a fixed point. Radar sources illuminate a fixed point with a burst of about 0.1 second duration as a rotating antenna moves with a rotation period of the order of 5-15 seconds.

Figure 7 shows leakage from a microwave oven as measured close to its point of maximum leakage. A variety of temporal variations can be caused by heating of the food or water load, thermal drift of the properties of the tube or

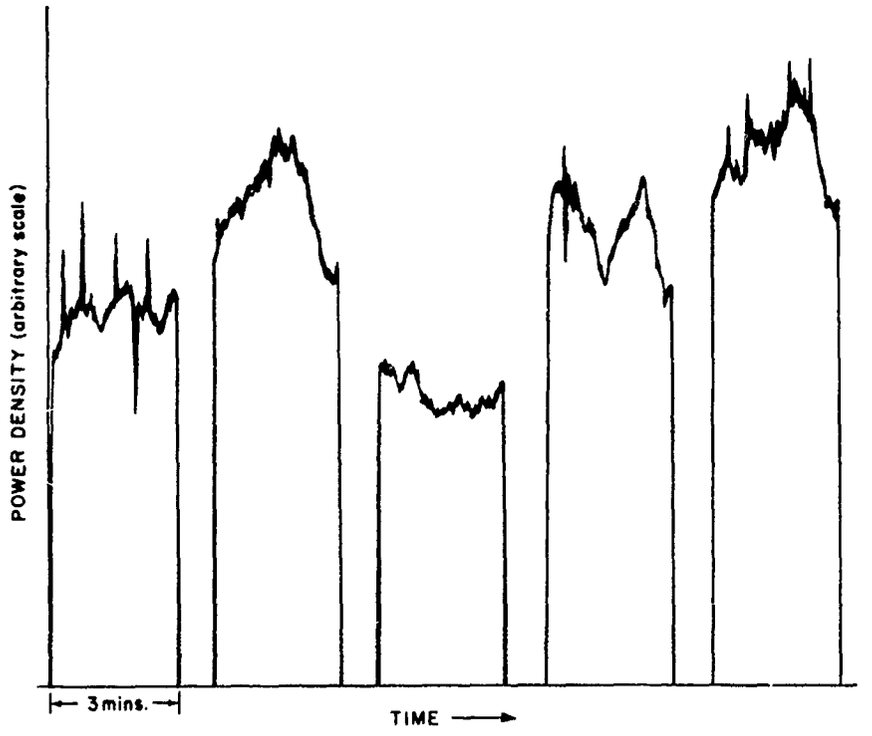

Figure 7. Maximum leakage of a microwave oven under standard test conditions as a function of time. A fresh water load (275 ml) is introduced for each run with initial water temperature conforming to BRH regulations (20 ± 5 °C).

the cavity as well as infrequent instabilities of one sort or another.

Figure 8 shows the fields from an RF heat sealer as monitored at a distance of about 150 feet from the source (linear power scale). In this case the level of this signal was the dominant signal in the environment - a peak level of about 0.5 $\mu W/cm^2$. Note the quasi-repetitive intermittent operation which, however, is subject to great changes from time to time. It is interesting to note that while fields at 27 MHz were not monitored in EPA surveys (Janes, 1979), they appear to be major sources of environmental fields in localized and transient situations, the dominant sources being those of CB radio, RF heat sealers, and RF diathermy.

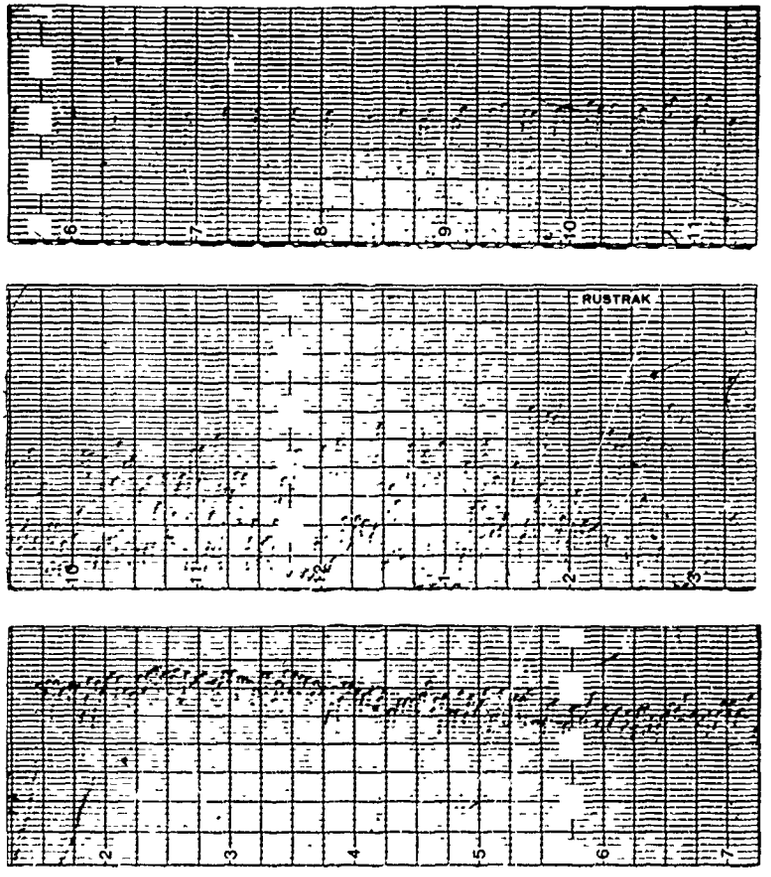

Figure 8. Radiation from a heat-sealer at a distance of ∿ 150 feet. Vertical scale: arbitrary linear power scale; Horizontal scale: 30 seconds/division.

VI. ENGINEERING ASPECTS OF MICROWAVE SENSATION

At high frequencies, e.g., the infrared, sensation is produced by superficial absorption of radiant beams on the skin. At low frequencies, 60 Hz or below 10 kHz, sensation or pain from electrical energy is induced usually by *contact* situations. Thus we have distinct nervous sensations of electrical current with threshold values for sensation, pain, immobilization, and injury usually without burns (Dalziel, 1972). We have the phenomenon of microarcing and shock when one touches a doorknob and discharges static charge or touches a grounded object when immersed in a high value of electric field (Delaplace and Reilly, 1978). In addition, we have the more extreme situation where people or animals perceive very high electric fields through the erection of hair on the skin, either near high-voltage lines or in exposed mountain areas before a thunderstorm (Bridges and Preache, 1981).

Across the microwave/RF spectrum one can expect some aspects of both low and high frequency sensations to be relevant. At the higher microwave frequencies radiant perception at the skin, as with infrared, appears straightforward. At the lower microwave frequencies (< 1 GHz) where penetration is considerable, the rules governing perception of radiation remain largely unknown (cf Chapters 9 and 11).

In practice, the perception of microwave energy by engineers and technicians is mostly by localized contact rather than radiant perception. For example, perception of microwave energy at the end of a coaxial connector is usually at the pain threshold with or without a very localized burn. Table III lists the threshold power for pain sensation as experienced by two subjects holding a finger against a type N male coaxial connector. It is seen that over almost two decades in the microwave frequency range the pain threshold occurs at roughly 0.15 watts absorbed. This is compatible with the hypothesis of localized heating to the pain threshold temperature of 44.5 °C in a few seconds. Rough calculations using the formulae and data of Pittaway (1964) and Hardy (1958) confirm the reasonableness of this interpretation.

Table III also notes the existence of a detection of arcing or corona between a finger and connector. This sensation is not painful if the duty cycle is kept low enough.

TABLE III. Thresholds for Sensation (5 Seconds) by Finger Contact with Small Coaxial Connectors (Type N, Male)

Frequency (GHz)	Pain (Watts, Ave.)		Corona-Arc (Watts, Peak)
	Incident	Absorbed	Incident
.25	.6	.2	
.50	.6	.15	
1.0	.6	.15	
2.0	.5	.15	100
4.0	.3	.10	100
8.0	.2	.15	100
11.0	.2	.15	100

VII. CONCLUSIONS

A review of the physical aspects of microwave systems for study of the effects of microwave exposure or sensation is presented. It is pointed out that aspects of low-frequency electricity and optical radiant heating both play a role within the microwave range in sensation phenomena. Resonant absorption and penetration in the microwave range will possibly produce unique sensations.

A review of sources and the engineering aspects of closed exposure systems reveals a host of potential artifacts that need to be isolated and controlled in experiments involving exposure of biological targets. Temporal variations and local concentrations of microwave energy will play a prominent role in sensation phenomena, both in the laboratory and in real life.

REFERENCES

ANSI C95.1 (1982). *Safety Levels with Respect to Human Exposure to Electromagnetic Fields (300 kHz to 100 GHz).* American National Standards Institute, 1430 Broadway, New York.

Bridges, J.E. and Preache, M. (1981). Biological influences of power-frequency electric fields - A tutorial review from a physical and experimental viewpoint. *Proc. IEEE* 69: 1092.

Dalziel, C.F. (1972). Electric-shock hazard. *IEEE Spectrum*, 9: 41.

Delaplace, L.R. and Reilly, J.P. (1978). Electric and magnetic-field coupling from high-voltage AC power transmission lines - classification of short-term effects on people. *IEEE Trans. on Power Apparatus and Systems*, 97: 2243.

Gandhi, O.P. (1979). Dosimetry-the absorption properties of man and experimental animals. *Bull. N.Y. Acad. Med.* 55: 999.

Guy, A.W. (1980). Non-ionizing radiation: Dosimetry and interaction. *Non-Ionizing Radiation*, Proc. of a Topical Symposium, American Conf. of Governmental Industrial Hygienists, Cincinnati, Ohio, p. 75.

Hardy, J.D. (1958). Thermal radiation, pain and injury. In: Licht, *Therapeutic Heat*, New Haven, p. 170.

Heynick, L.N., Polson, P. and Karp, A. (1977). A microwave exposure system for primates. *Radio Science* 12, No. 6(5): 103.

Janes, D.E., Jr. (1979). Radiation surveys - Measurement of leakage emissions and potential exposure fields. *Bull. N.Y. Acad. Sci.* 55: 1021.

Michaelson, S.M. (1972). Cutaneous Perception of Microwaves. *J. Mic. Power* 7(2): 67.

Muchmore, R.B. (1964). Microwave Techniques. In: Bleuler, E. and Hazby, R., *Methods of Experimental Physics*, Vol. 2, Electronic Methods. Academic Press, N.Y., p. 705.

NCRP (1981). *Radiofrequency Electromagnetic Fields*. NCRP Report No. 67, National Council on Radiation Protection and Measurement, Washington, D.C.

Osepchuk, J.M. (1979). Sources and basic characteristics of microwave/RF radiation. *Bull. N.Y. Acad. Med.* 55: 976.

Osepchuk, J.M. (1981). On the costs of perceived versus real risks of microwave radiation. *Proc. Conf. on Cost/Benefit Analysis and Microwave/RF Radiation*, Univ. of Michigan (in press).

Pittaway, L.G. (1964). The temperature distributions in thin foil and semi-infinite targets bombarded by an electron beam. *Brit. J. Appl. Phys.* 15: 967.

Pound, R.V. (1979). Radiant heat for energy conservation, *Science* 208: 494.

RCA (1969). *Frequency Allocations*, published by RCA Frequency Bureau, RCA Corporation.

Short, J.G. and Turner, P.F. (1980). Physical hyperthermia and cancer therapy. *Proc. IEEE* 68(1): 133.

Weil, C.M., Joines, W.T. and Kinn, J.B. (1981). Frequency range of large-scale TEM mode rectangular strip lines. *Microwave J.* 24: 93.

Zimmerer, R.W. (1966). Suggested name "Nanowave Region" for the E-M spectrum between 10 micrometers to 10 millimeters wavelength. *IEEE Trans. MTT* 14: 157.

ELECTROMAGNETIC HEATING FOR THERAPY

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INTRODUCTION

Electromagnetic heating is used in clinics for physical therapy and for the treatment of cancer. Originally, natural sources of heat, such as sunshine or hot water, were used for therapeutic purposes (Licht, 1965). However, the heating was achieved only at a superficial level, since changes in vasomotor tonus of the blood vessels in the skin aid in the maintenance of a constant temperature in deep tissues during exposure to the sun, immersion in hot water, or contact with other conductive heat sources. Thus, the usefulness of heat in therapy was limited until relatively recently. It was only in the early twentieth century that diathermy ("through heat" in Greek) became available, making the heating of deep tissues possible. Three methods are now used in clinics for producing heat in deep tissues -- ultrasound, shortwave, and microwave diathermy -- which are based on the principles of propagation and absorption of acoustic or electromagnetic waves in the tissue.

Used in physical therapy for almost a century, diathermy

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has also been used in combination with ionizing radiation for the treatment of cancer. Recently there has been a vast increase of interest in this latter application. The problem of producing controllable heating patterns in the body has become a popular topic of research. In this paper we will review the biophysics of tissue heating with electromagnetic waves and discuss methods of quantifying the energy absorption and associated temperature increases.

BIOPHYSICS OF ELECTROMAGNETIC HEATING

The fundamental difference between wave propagation in free space and in tissue is due to the dielectric properties of tissue, the dielectric constant and conductivity. In general, biological tissues can be classified into two major categories according to their dielectric properties. Those with high water content, such as muscle, skin, kidney, and liver tissues, have higher dielectric constants and conductivity than those with low water content, such as fat or bone. Brain, lung, and bone marrow tissues contain intermediate amounts of water and have dielectric constants and conductivities that fall between the values for the two groups. Dielectric properties are a function of the frequency. The dielectric constant decreases while the conductivity increases with increasing frequency. Numerical data have been published by Schwan (1957), Johnson and Guy (1972), Stuchly, *et al.* (1981), and Foster and Schepps (1981).

The action of electromagnetic fields on tissues produces two types of effects that determine their dielectric properties: (1) the oscillation of free charges on ions, and (2) the rotation of polar molecules at the frequency of the applied field (Johnson and Guy, 1972). Free charge motion gives rise to conduction currents with an associated energy loss due to the electrical resistance of the medium. The rotation of polar molecules generates displacement current in the medium with an associated dielectric loss due to viscosity. These two losses are the basis of electromagnetic energy absorption which produces heating in the medium.

The rate of temperature rise in tissue heated with electromagnetic energy is related to the rate of energy absorption W_a, metabolic heating rate W_m, power dissipation by thermal conduction W_c and blood flow W_b, as expressed in the following equation:

$$\frac{d(\Delta T)}{dt} = \frac{1}{4186c}(W_a + W_m - W_c - W_b)$$

where c is the specific heat of the tissue (Guy, *et al.*, 1974). In a typical clinical treatment using about 50 watts output power, the temperature, T, will increase as shown in Figure 1. Initially there is a linear rate of increase

$$\frac{d(\Delta T)}{dt} = W_a/4186c$$

lasting approximately three minutes.

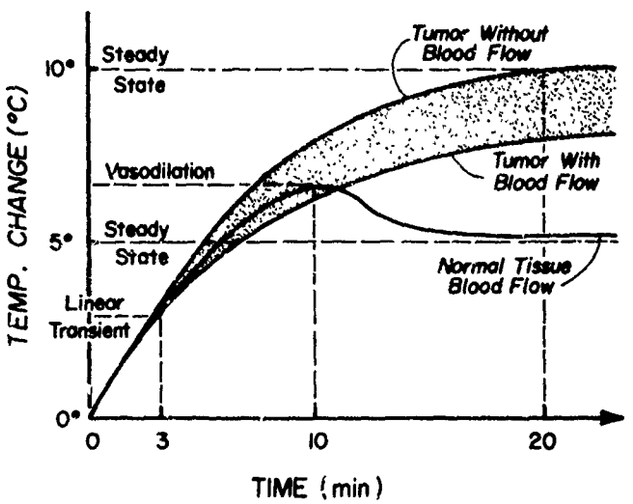


Figure 1. The temperature change in tumor and normal tissues under hyperthermia showing the differences in heating of tumor tissue without blood flow, tumor tissue with blood flow, and normal tissue. (Reprinted with permission from Guy and Chou, 1982).

In normal tissue, after this linear increase in temperature, there is a period of nonlinear temperature rise usually lasting another 7 to 10 minutes, where ΔT becomes sufficiently large ($\sim$6 °C) that blood flow becomes important in dissipating the absorbed energy. In tissues with a low

or negligible blood flow rate, the temperature will monotonically approach a steady state value dictated by the magnitude of W_a, as shown on the upper curve in Figure 1, with equilibrium reached when $W_a = W_c$. For vascular tissues, a marked increase in blood flow will occur due to vasodilation when the temperature reaches the range of 42 - 44 °C, as shown in Figure 1, when $W_a = W_c + W_b$.

In many tumors the blood flow is vigorous at the periphery and sluggish in the center (Song, *et al.*, 1980). Since the blood vessels in tumors are often fully open during ordinary conditions, there is, in many cases, no vasodilation during the heat treatment. After steady state conditions are reached, the final temperature of the tumor is higher than that of the surrounding normal tissue. The shaded area in Figure 1 indicates the range of temperature rise in tumors. The lower boundary is for the periphery of the tumor and the upper curve is for the center, where no blood flow exists.

The rate of energy absorption W_a must be sufficiently high so that the therapeutic level of temperature can be maintained over the major portion of the treatment period. If too little power is applied, the period or the level of temperature elevation will not be long enough or high enough for any benefits, while with too high a level, the temperature of the normal tissue may not be maintained at a safe level by vasodilation. The pain sensors are a reliable and sensitive means for alerting the patient to an unsafe temperature. If the applied power level is set so that only mild pain or discomfort is experienced by the patient, the vasodilation in normally vascular tissues will be sufficient to limit or even lower the temperature to a level that is both tolerable and therapeutically effective.

METHODS OF ELECTROMAGNETIC HEATING

Electromagnetic heating of tissues may be accomplished by three methods: (1) Direct application of current by contacting electrodes or non-contacting capacitive plates; (2) Induction of eddy currents in the tissue by alternating magnetic fields from solenoidal or "pancake" magnetic coils; or (3) Radiation at ultra-high (UHF) and microwave frequencies.

Shortwave Applicators

1. Capacitor Electrodes. The earliest diathermy equipment consisted of a high-frequency generator from which currents were applied directly to the tissues by contacting electrodes (Licht, 1965). Because of uneven or poor contact, one of the greatest hazards was the production of burns at the electrode-tissue interface. As the operating frequency of diathermy equipment increased, the electrodes were redesigned so that they did not have to make direct contact with the tissues, since displacement currents between the electrode plates and the anatomical surfaces are sufficient to couple energy to the tissue. Although direct contact and capacitor electrode arrangements are still used at the surface of the body to treat patients with present day 13.65 and 27.12 MHz diathermy equipment, there are some fundamental problems. Figure 2 illustrates how induced conduction currents in the tissue produce much greater power absorption in the subcutaneous fat than in the skin and

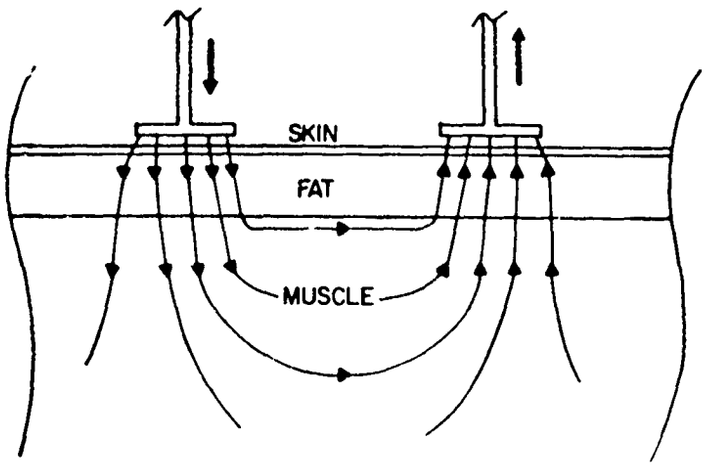


Figure 2. Field distribution in layered tissues exposed to capacitor-type electrode diathermy. Heating is greater by an order-of-magnitude in subcutaneous fat than in skin or muscle, which have higher water content. (Guy, *et al.*, © 1974 IEEE).

deeper tissue of high water content. It also shows that the divergence of the current tends to concentrate the power absorption in the superficial tissue adjacent to the electrodes. This, along with the lower specific heat in fat, results in a rate of heating more than 17 times greater in fat than in the deeper tissue of high water content. In addition, the rate of cooling by blood circulation is significantly less in fat, so the final steady-state temperature of fat is considerably higher than in tissue of high water content.

2. Induction Coils.

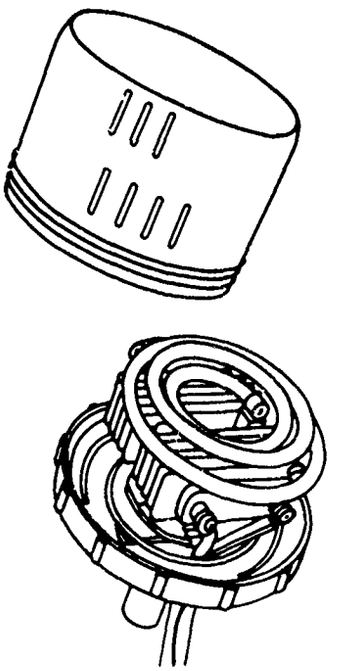


Figure 3. A compact induction coil applicator for the magnetic induction of circular eddy currents in tissue (courtesy of Siemens-Reiniger Werke Ag). (Guy, *et al.*, © 1974 IEEE).

Coils have been used for the magnetic induction of circular eddy currents in the tissues. The applicator shown in Figure 3, a "monode," is a compact coil-and-capacitor combination that may be placed at various distances from the patient by an adjustable supporting arm (not shown). A cross-sectional view of the induced currents (Figure 4) illustrates the superiority of the inductive coil over the

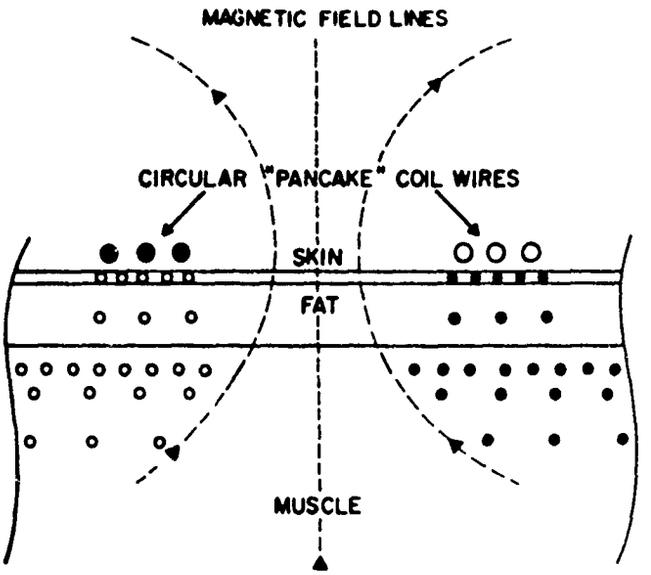


Figure 4. A cross-sectional representation of induced current distribution in layered tissues exposed to induction coil diathermy which shows the superiority of the heating over that from the capacitor type electrode. (Guy, *et al.*, © 1974 IEEE).

capacitor type of electrode. In this case, the induced electric fields are parallel to the tissue interfaces, and therefore are not greatly modified by the tissue boundaries. Ideally, the current density and heating will be higher in the tissue of high water content where the conductivity is greater.

Microwave Applicators

When microwave diathermy was first introduced in 1946, there was great hope that it would provide significantly improved heating patterns over those produced by shortwave diathermy. The shorter wavelength made it possible to direct and focus the power so as to couple it to the patient by direct radiation from a small, compact applicator. This was originally believed to be a distinct improvement over the quasi-static and inductive coupling of the field to the tissues provided by the cumbersome capacitor and coil-type applicators. The cross-sectional area of the directed power could be made smaller and used to provide much more flexibility in controlling the size of the treatment area.

1. Radiating Type. The 2450 MHz diathermy equipment that is currently available commercially consists of a 100 W magnetron generator with a variable-power control calibrated in percentage of total power output. Various types of standard dipole and monopole applicators used with this generator are illustrated in Figure 5.

2. Direct Contact Type. The superiority of frequencies lower than 2450 MHz for therapeutic heating was predicted by Schwan and Piersol (1954) and experimentally verified by Lehmann, *et al.* (1962a, 1962b, 1965) and Guy and Lehmann (1966). Plane wave or radiating-type sources become impractical to use at these lower frequencies, since it is impossible to focus the energy into a beam using applicators of reasonable size; thus, the near-zone fields of the applicators extend to greater distances. Under these conditions, a pure radiation or far-zone field can be maintained only by placing the applicator at distances at which large areas of the body would be exposed and excessive power levels would be required. Thus, in order to obtain selective heating with reasonable input power levels (50 to 100 W), one must necessarily expose the tissues to the near-zone fields of the source. The fields induced in the tissue are then highly dependent on the field distribution and frequency of the source and may be considerably different from those produced by plane-wave or radiation fields. The aperture source provides a reasonable model for studying the effect of shape, size, and frequency of a source on the fields induced in the tissues. Under such conditions, the size and distribution of the induced fields may be controlled, resulting in improved diathermy applicators.

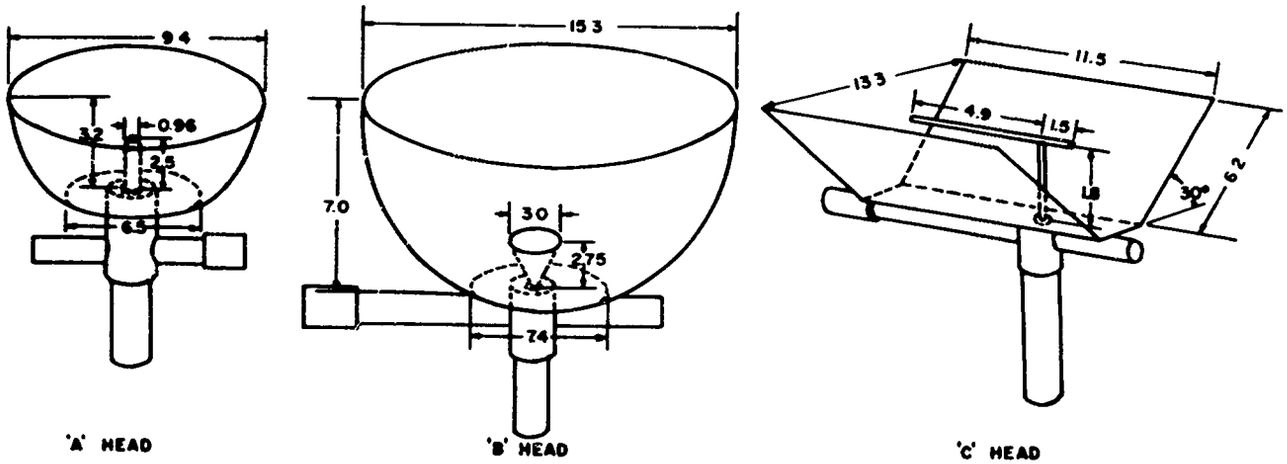


Figure 5. Standard dipole and monopole applicators used with the 100 W magnetron generator for 2450 MHz diathermy. (Guy, *et al.*, © 1974 IEEE).

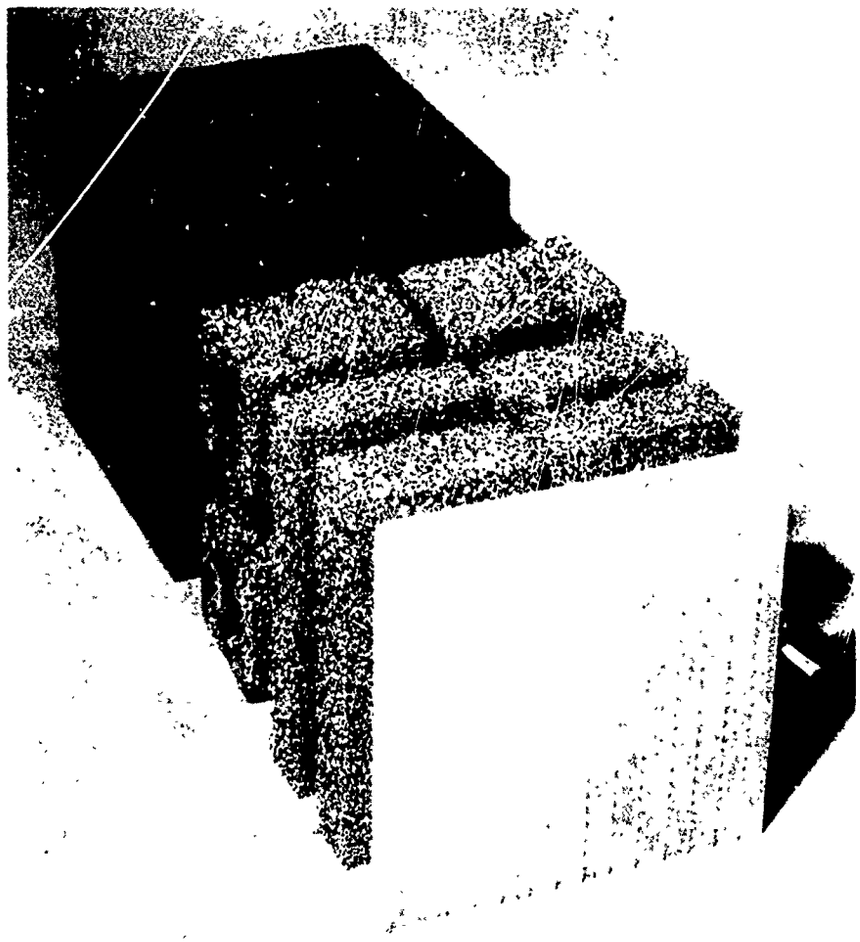


Figure 6. A 915 MHz direct-contact applicator (13 x 13 cm) composed of two separate TE_{10} mode waveguides. (Guy, *et al.*, © 1978[a] IEEE).

Figure 6 illustrates a 915 MHz direct-contact applicator developed by Guy, *et al.* (1978a). This 13 x 13 cm cavity applicator is composed of two separate TE_{10} mode waveguides. A light weight dielectric foam (Emerson & Cumming, Inc.) with a dielectric constant of 4 is used to load the applicator to allow 915 MHz wave propagation in the small size waveguide feed system. The foam is also porous which allows cooling air to be blown through the applicator and onto the surface of the tissue being treated. This makes greater heating of the deeper tissue possible without an excessive

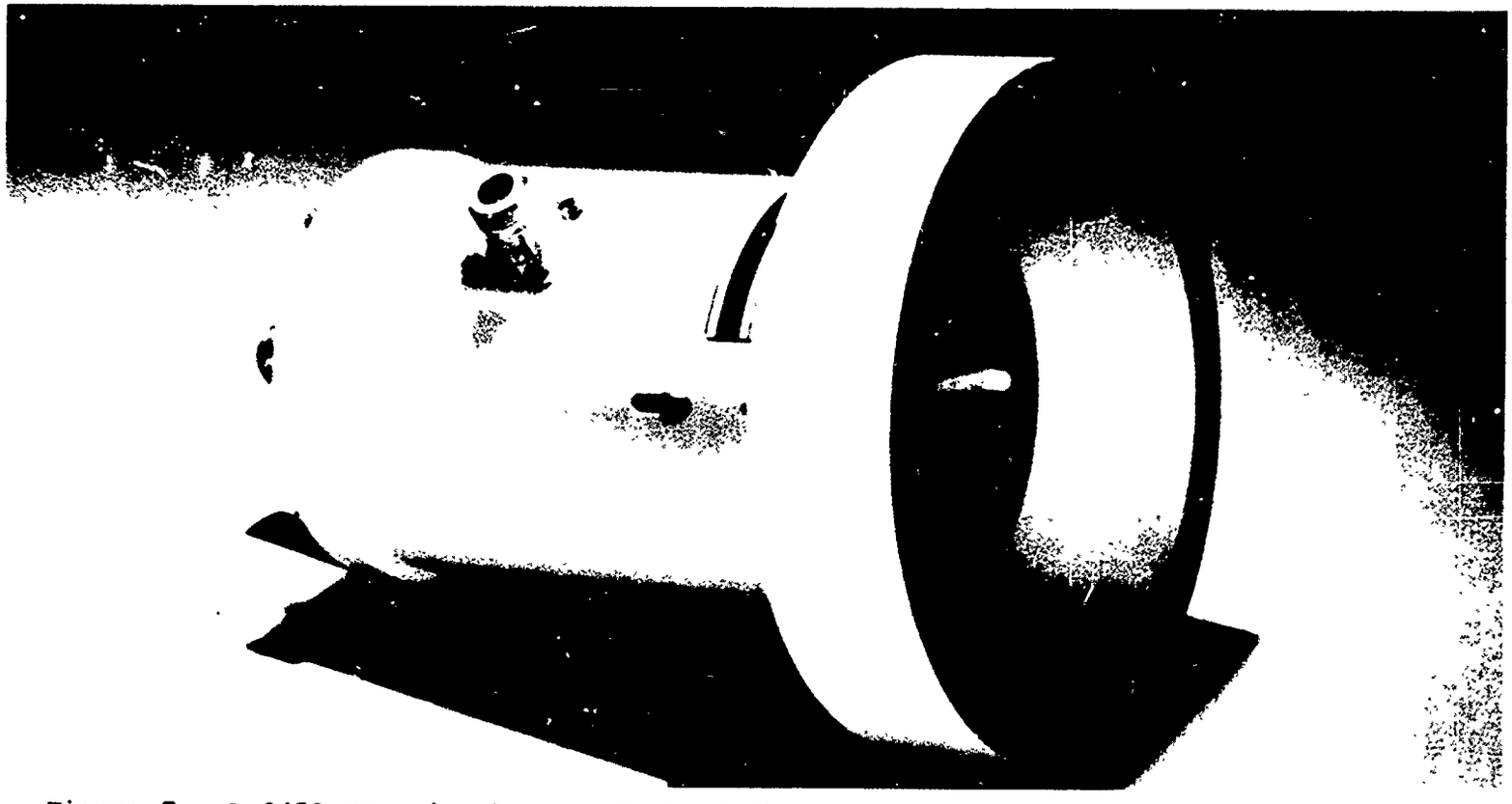


Figure 7. A 2450 MHz circularly polarized direct-contact applicator with a single feed and a pair of phase shifters for producing a circularly polarized TE_{11} mode. (Kantor, *et al.*, © 1978 IEEE).

rise in the temperature of the surface tissue. An acrylic radome is placed at the aperture to separate the metal edges of the applicator from the tissue to prevent hotspots.

Kantor, *et al.* (1978) described a 2450 MHz circularly polarized applicator, shown in Figure 7, which has a single feed and a pair of phase shifters for producing a circularly polarized TE_{11} mode. The circularly polarized fields provide more uniform heating than linearly polarized fields. There is also an annular choke to control the leakage level within the required 5 mW/cm^2.

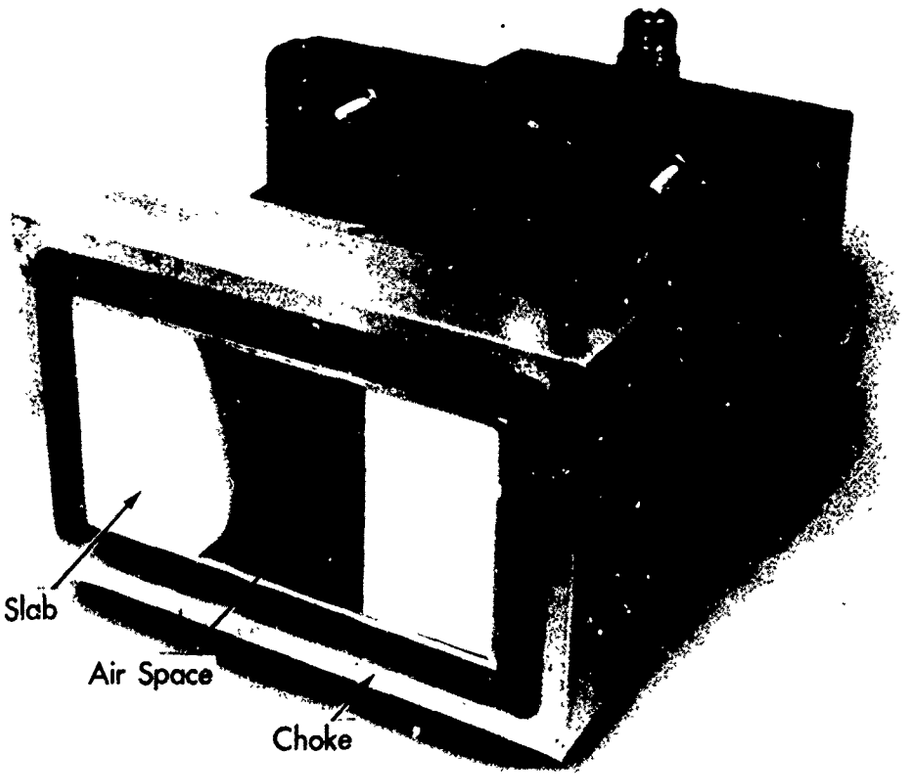


Figure 8. A 2450 MHz slab-loaded direct-contact applicator consisting of a standard WR-430 waveguide loaded with Teflon slabs of dielectric constant=2. (Kantor and Witters, © 1980 IEEE).

A slab-loaded rectanglar waveguide applicator was also described by Kantor and Witters (1980). This applicator, shown in Figure 8, is a standard WR-430 waveguide loaded with Teflon slabs of dielectric constant 2. These slabs provide more uniform heating patterns by forcing the fields to be uniform in the air space between the slabs. The aperture is also surrounded by a choke to minimize leakage.

3. Phased Array Contact Applicator. Heating in deep tissues may be significantly increased by the use of a phased array of applicators rather than a single applicator (Guy and Chou, 1982). For example, if two identical applicators are placed on opposite sides of a body member, such as the leg or arm, and the applicators are fed by the same source so that the aperture field distributions are in electrical phase, the electric fields at the center of the cylinder will be doubled due to the two applicators. Since the heating is proportional to the square of the electric field, the heating will be increased by a factor of four. If two additional applicators are placed in the same way, with the center line of each perpendicular to the center line of the first two applicators, and they are also fed in phase, the total heating from the four applicators will greater by a factor of 8 than that achieved with a single applicator. The fields of the two pairs of applicators do not add directly since they are orthogonal. If we consider a spherical object being exposed in the same way with four applicators and another two applicators are added to the remaining two open sides of the sphere, the heating could be increased by a factor of 12 over that of a single applicator. The results of an experimental study of the use of a phased array consisting of 915 MHz rectangular aperture applicators exposing a cylindrical phantom model of the human arm is shown in Figure 9. In these experiments, the applicators were fed in phase using a system of hybrid couplers.

MEASUREMENT OF ELECTROMAGNETIC HEATING

The rate of energy absorption in tissue W_a depends on many factors. One of these factors relates to the dielectric properties of the tissue. The fat thickness and the amount of bone in the treated area can affect the amount of energy absorption because of the disparity in dielectric properties of tissues with high and low water contents. The

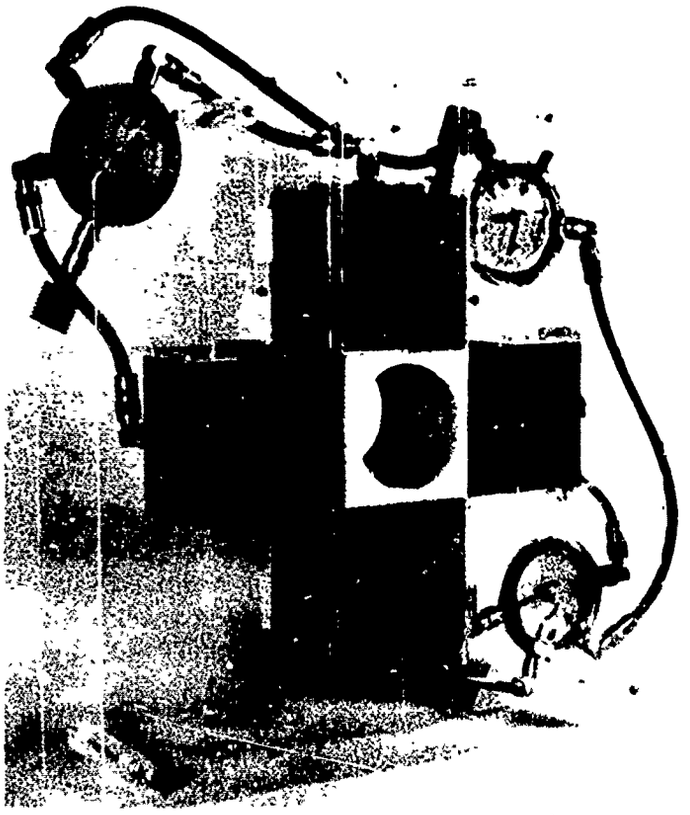


Figure 9. A phased array of four 915 MHz direct-contact applicators for heating a human arm. The four applicators fed in phase provide heating greater by a factor of 8 than that provided by a single applicator. (Reprinted with permission from Guy and Chou, 1982.)

shape, size, and depth of the tissue to be treated also greatly influence the energy absorbed. For example, the absorption in the head will be very different from that in the arm or back. The factors affecting the coupling of energy between the applicator and the tissue are: frequency of operation, the type of applicator, the size and geometry of the applicator, the orientation of the fields, the spacing between the applicator and tissue, and, of course,

the input power to the applicator. This rate of energy absorption W_a is defined by the National Council of Radiation Protection and Measurements (1981) as the Specific Absorption Rate (SAR).

The final temperature pattern in the tissue, as discussed above (BIOPHYSICS OF ELECTROMAGNETIC HEATING), is determined by the SAR (i.e., W_a), the duration of exposure, the metabolic heat generation, and the heat loss due to thermal conduction and blood flow. Since the heat transfer and the blood flow differ at various locations in the treated areas and are usually unknown during treatment, it is not possible to measure the final temperature for every treatment before a suitable heating method is applied. However, the SAR can be quantified for many general cases. This SAR is very useful for the comparison of different applicators. It provides a criterion for the evaluation of the efficiency of specific applicators for raising tissue temperature to a therapeutic level.

The SAR in a particular volume of tissue may be determined from the initial linear increase in temperature following exposure to electromagnetic fields. This must be done before the temperature of the tissue is significantly altered by heat diffusion and blood flow: thus such measurements are usually made with an application of high power of short duration. Since the power need only be applied long enough to measure a change of a few degrees, the measurement can be made without thermal damage to the tissue.

Temperature probes used for accurately determining the true rate at which temperature changes must have a rapid response and must also perturb electromagnetic fields minimally. Several temperature probes that meet these criteria have been described and are available commercially (Bowman, 1976; Rozzell, *et al.*, 1975; Wickersheim and Alves, 1979). Since the heating pattern may vary considerably over a three-dimensional volume of tissue, a single point measurement will not define the pattern or quantify the maximum SAR or temperature increase. Multiple probes, such as used on BSD-1000 hyperthermia equipment, can provide better information about the pattern of heating, but only to a limited extent.

Guy (1971a) has described a thermographic method for rapid measurement of the SAR in tissue through the use of models. This method uses a thermographic camera for recording temperature changes induced by radiofrequency fields over an internal surface of the exposed object. The models are composed of materials with dielectric and geometric properties similar to those of the tissue structures which they represent. Special materials have been developed that

simulate human fat, muscle, brain, and bone. Models are designed to separate along planes perpendicular to the tissue interfaces so that, after exposure to radio frequency fields, a cross-sectional temperature distribution can be measured with a thermographic camera. A silk screen is placed over the pre-cut surface on each half of the model to hold the tissue material in place and to provide electric contact between the two halves of the model. A plane of separation is first scanned with the thermographic camera in order to record the pre-exposure distribution of temperatures. The assembled model is then exposed to the same electromagnetic source that will be used to expose actual human tissue. After a short exposure to a power level much higher than normally used for therapy, the model is quickly disassembled and the new temperature pattern over the surface of separation is measured and recorded by means of the thermographic camera. Since the thermal conductivity of the tissue model is low, the rate of the change in the distribution of temperatures measured during the short exposure will closely approximate the SAR pattern over the flat surface, except in regions of high temperature gradients where errors may occur due to appreciable heat diffusion. The thermographic techniques described for use with models can also be used to quantify the SAR patterns in sacrificed animals exposed to radiofrequency fields (Chou and Guy, 1977; Johnson and Guy, 1972) and the skin surface of live animals (Guy, *et al.*, 1978b; Chou and Guy, 1982).

HEATING PATTERNS

In this section, we will discuss the SAR patterns obtained theoretically and experimentally from models and human subjects.

Shortwave Applicators

Guy, *et al.* (1974) analyzed the SAR patterns in plane layers of tissues exposed to 27.12 MHz shortwaves with an induction coil as shown in Figure 10. The SAR patterns were calculated for different thicknesses of fat and different applicator spacings using the variables defined in Figure 10. An example of the relative SAR patterns is shown in Figure 11. The predicted SAR patterns agree very well with measurements obtained using pig tissues (Lehmann, *et al.*, 1968). Figure 12 illustrates temperature measurements made

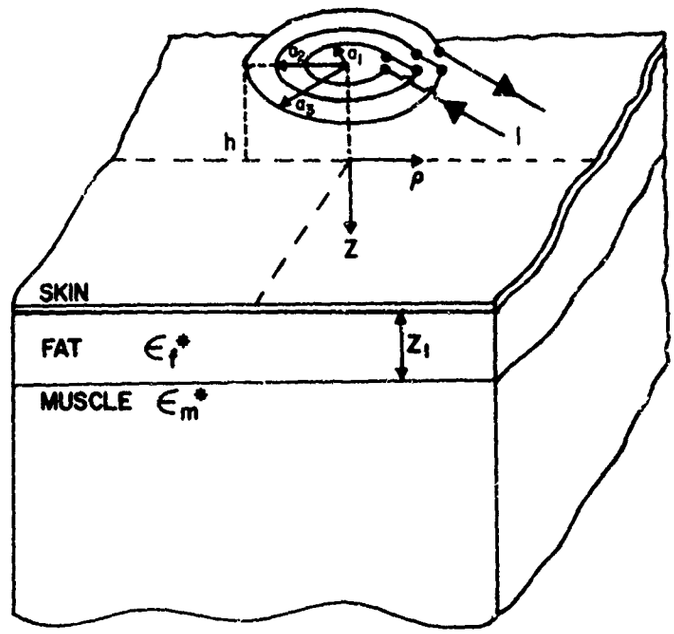


Figure 10. Geometry and coordinates for plane layers of skin, fat, and muscle tissue exposed to 27.12 MHz shortwaves with a flat "pancake" diathermy induction coil. (Guy, *et al.*, © 1974 IEEE).

in the thighs of human subjects exposed to shortwave diathermy. The inductive shortwave diathermy is more effective than capacitive heating in elevating the temperature of deep tissue while maintaining a cool temperature at the surface. The major disadvantage of the inductive applicator is the toroidal SAR pattern which is not efficient for heating small tumors.

Microwave Applicators

If other than a plane wave source is used to expose biological tissues, the SAR patterns will be highly dependent on the size of the source and the distribution of the field. Many applications of microwave power in medicine require a quantitative understanding of the possible SAR patterns in tissues that can result from the use of aperture and waveguide sources. Guy (1971b) has analyzed a case where a two-layered fat (thickness z_1) and muscle tissue model was

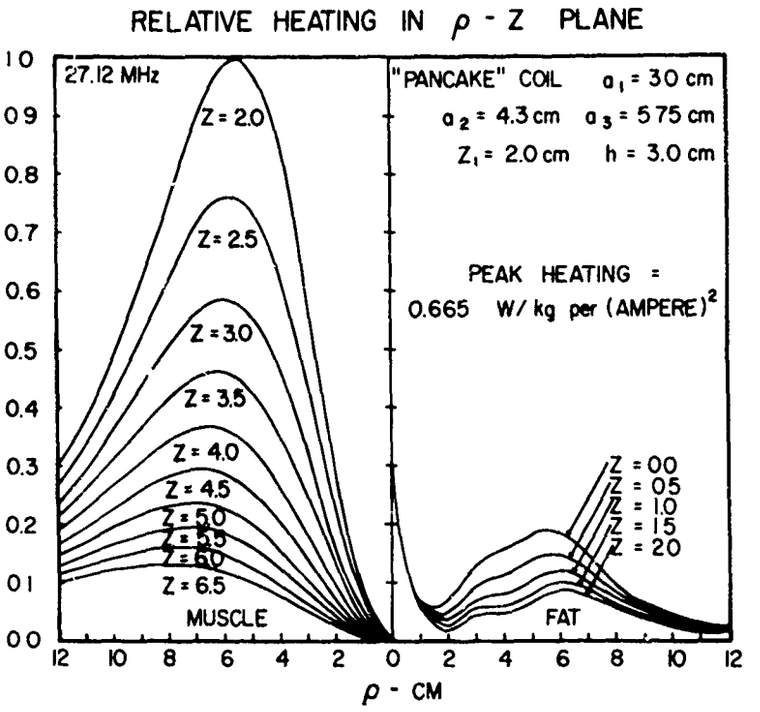


Figure 11. Calculated SAR patterns in fat (2 cm thick) at different depths exposed to a 27.12 MHz "pancake" diathermy induction coil. (Guy, *et al.*, © 1974 IEEE).

exposed to a direct-contact aperture source of width a and height b as shown in Figure 13. Figure 14 illustrates the results of this work where the relative SAR levels in the x-z plane are plotted for width a=12 cm and height b=2, 4, 12, and 26 cm (Figure 14, A, B, C, D). For comparison, the SAR at the surface of the fat due to a plane wave exposure is denoted by a dashed line in each figure. With small aperture heights, the applicator produces considerable superficial heating, in excess of that produced by plane wave exposure, and minimal heating in the underlying musculature. As the aperture height is increased, the relative heating in the deeper musculature increases greatly, compared to the superficial heating in the fat layer.

The SAR patterns in multi-layered cylindrical tissues exposed to an aperture source can also be determined by representing the fields in the region as a summation of three-dimensional cylindrical waves, expressing the aperture field as a two-dimensional Fourier series, and matching the

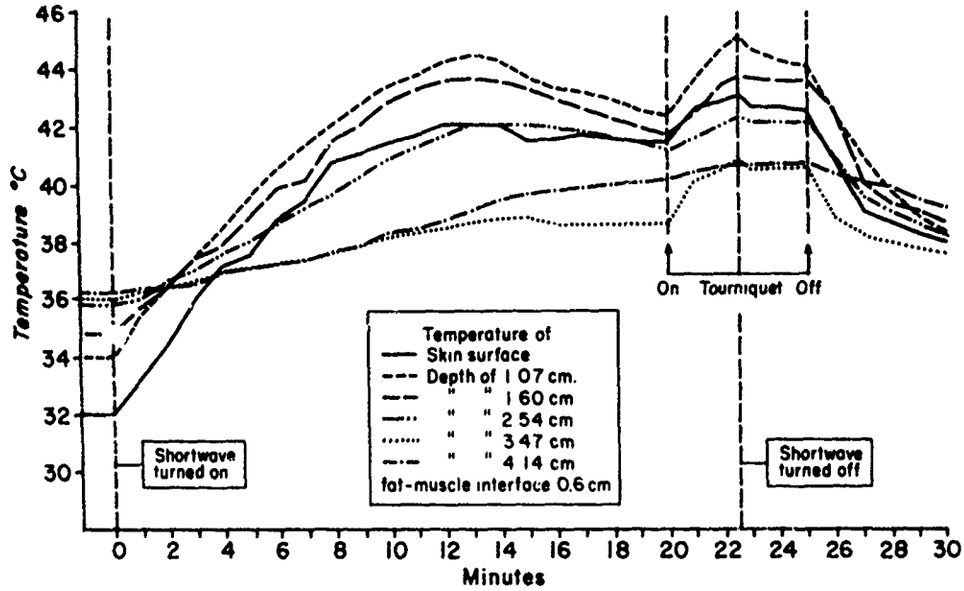


Figure 12. Temperature measurements in the thighs of human subjects (Z_1 = 0.6 cm and h = 3.5 cm as defined in Figure 10) exposed to a "pancake" diathermy induction coil. (Reprinted with permission from Lehmann, *et al.*, 1968).

boundary conditions. Ho, *et al.* (1971) have calculated the SAR patterns for a number of different sizes of apertures and cylinders. Typical results are shown in Figure 15 for a human-arm-sized cylinder exposed to a surface aperture source 12 cm long with the electric field polarized in the direction of the cylinder axis. The patterns are plotted as a function of the radial distance from the center of the cylinder for various circumferential angles, $\emptyset$, measured with respect to the reference at the center of the aperture. The patterns are normalized to the values calculated at the reference ($\emptyset$-0) on the fat-muscle interface. The difference between the SAR patterns calculated for cylindrical tissues and plane-layered tissues demonstrates the significant role of tissue curvature in assessing the effectiveness and safety of devices designed for the medical applications of microwave energy.

All of the theoretical results discussed in this section strongly indicate the ineffectiveness of 2450 MHz for diathermy, as pointed out in earlier reports by Schwan and

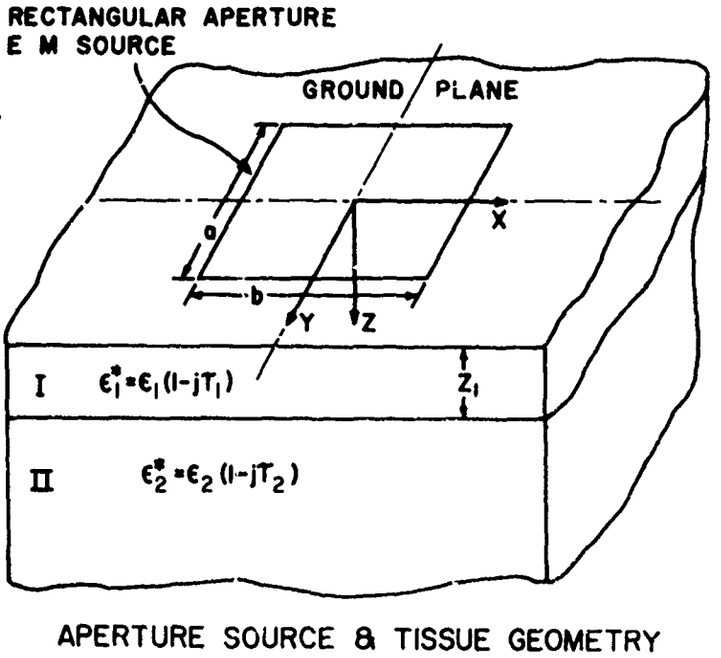


Figure 13. Exposure of a two-layered fat and muscle tissue model to microwave power from a direct-contact aperture source. (Guy, © 1971[b] IEEE).

Piersol (1954, 1955), Lehmann, *et al.* (1962a, 1962b, 1965), Lehman (1971), Guy and Lehmann (1966), and Guy (1971a, 1971b). Although the lower frequencies of 915 MHz authorized in the United States or 433 MHz authorized in Europe appeared to be better choices, the theoretical data show that 750 MHz would be the best choice for an applicator of convenient size for heating 100-200 cm^2 regions in the clinic.

1. Radiation Type Applicators. Figure 16 illustrates the absorption patterns in fat-muscle layers of tissue exposed to the diathermy C director as measured by the thermographic method for different thicknesses of fat. The spacing between the applicator (plastic cover) and the surface of the tissue was set to the clinically-recommended value of 5 cm. The models used for these studies were assembled by first constructing a 30 cm x 30 cm x 14 cm box

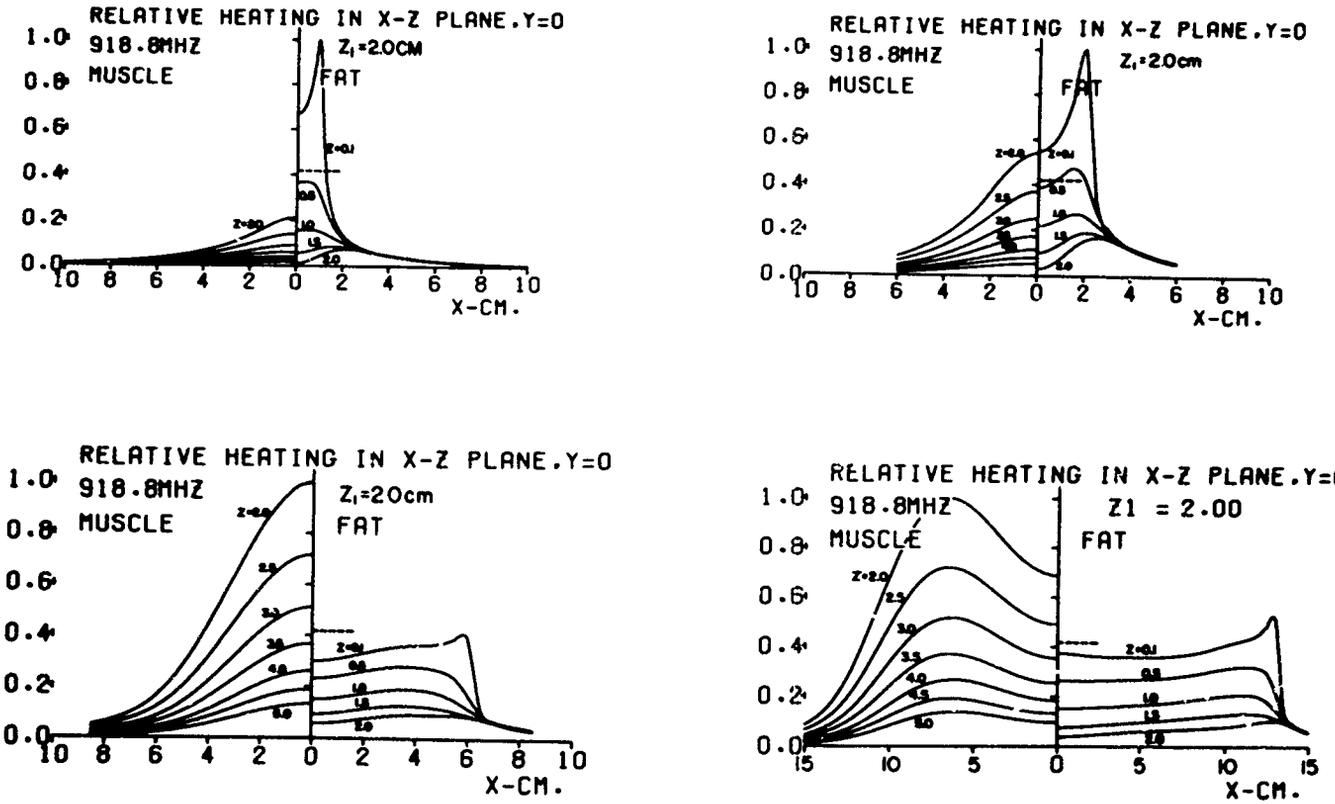


Figure 14. Results of the exposure of a two-layered fat and muscle tissue model to microwave power from a direct-contact TE_{10} mode waveguide aperture source showing the relative SAR levels in the x-z plane plotted for width a = 12 cm and height b = 2, 4, 12, and 26 cm. The dashed line is the SAR at surface of the fat due to a plane wave exposure. (Guy, © 1971[b] IEEE.)

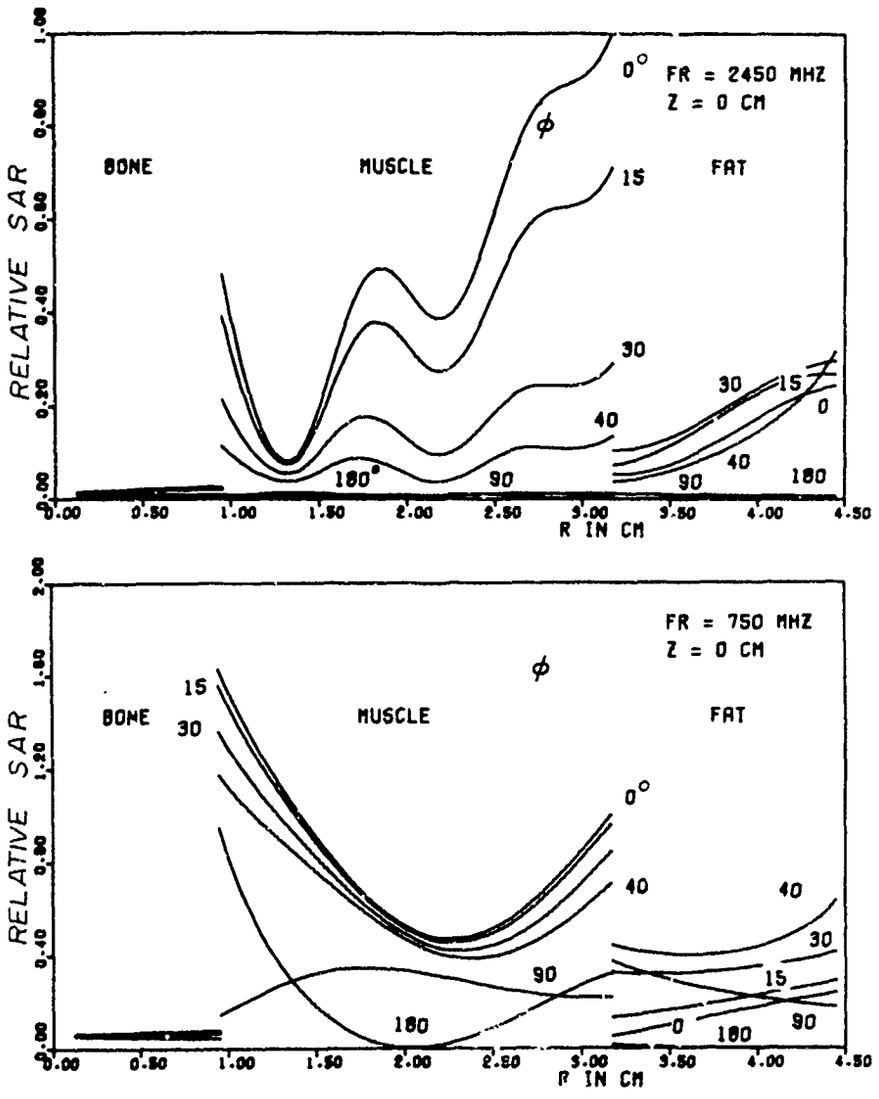
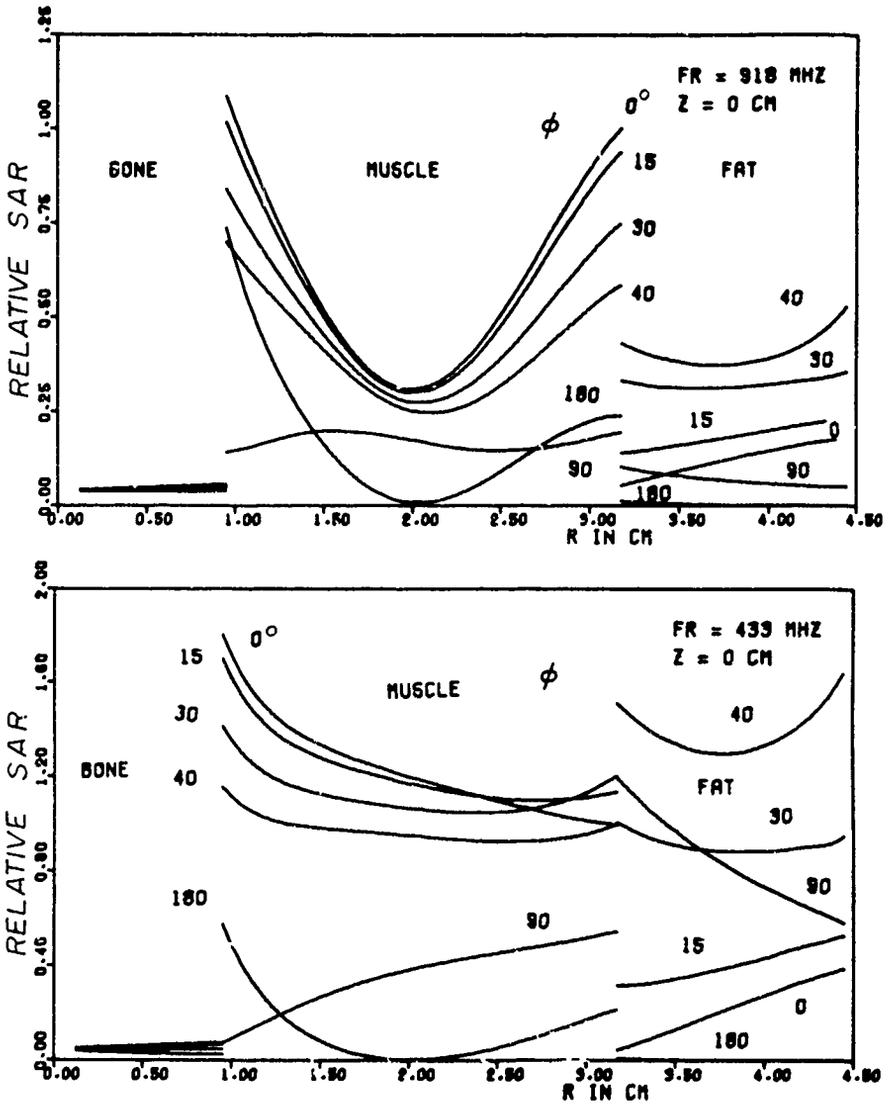


Figure 15. SAR patterns for a multi-layered human-arm-sized cylinder (20 cm long) exposed to a direct-contact aperture source (90° angle and 12 cm long) at four different frequencies with the electric field polarized in the direction of the cylinder axis. (Ho, *et al.*, © 1971 IEEE.)



ARM SIZE TE_{10} E_θ APERTURE SOURCE

TR = 90°, ZR = 12 CM, L = 20 CM

Figure 15 (cont.)

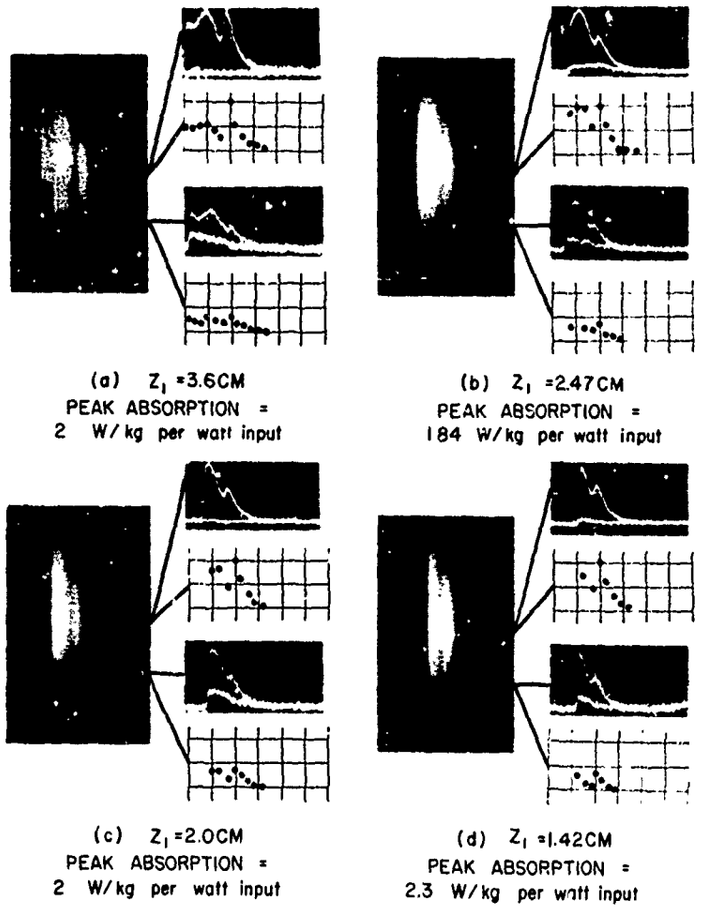


Figure 16. Thermograms and relative SAR patterns for different thicknesses of fat in plane fat-muscle tissue models exposed to 2450 MHz from a diathermy C director at 5 cm spacing. B scans taken at midline of the model and 4 cm below the midline. The dotted lines represent calculated SARS. (Guy, *et al.*, © 1974 IEEE.)

with Plexiglas sides of 1/4" thickness, and top and bottom surfaces of solid synthetic muscle. The thermographic camera was set to obtain a C scan (intensity proportional to temperature) over a two-dimensional area, as shown by the large photographs in Figure 16. The B scans consisted of

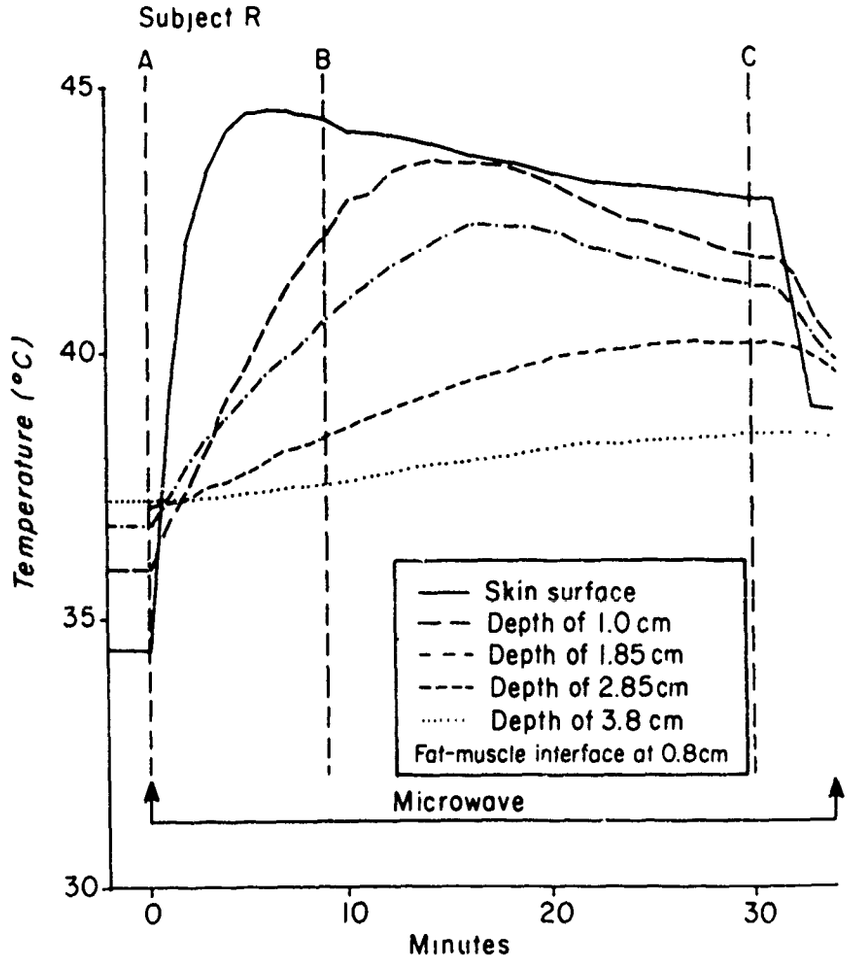


Figure 17. Measurements of temperature in the thigh of a human volunteer exposed to microwaves at 2456 MHz using a C director. (Reprinted with permission from Lehmann, *et al.*, 1965).

two one-dimensional scans, one before and one after exposure, with the same horizontal scale as the C scans and a vertical deflection proportional to temperature (scale is given under each figure). The B scans were taken along the horizontal midline and also along a parallel line 4 cm below the midline of the model.

Lehmann, *et al.* (1965) have reported measurements of temperature made in the thighs of human volunteers (with a fat layer 0.8 cm thick and the applicator spaced at 2 cm intervals) exposed to the C director as shown in Figure 17. For these cases, the applied power was adjusted to the level where discomfort or mild pain was felt temporarily at the surface of the skin. The heating pattern of the B director

was shown to be toroidal like that of a shortwave inductive applicator (Kantor, 1977).

The depth of the heating patterns obtainable with

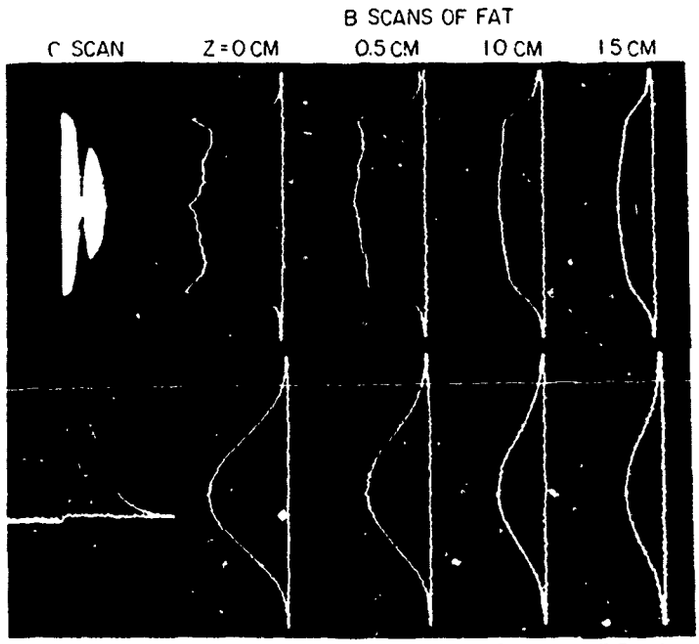


Figure 18. Thermograms of the exposure of a plane fat-muscle tissue model to a 918 MHz direct-contact applicator. The maximum SAR in the muscle is 3.27 W/kg per watt input. (Guy, *et al.*, © 1974 IEEE).

radiation microwave applicators is somewhat less than that obtainable with shortwave inductive applicators. When all aspects are considered, the heating characteristics of the shortwave inductive diathermy applicator discussed in the previous section appear to be superior to those obtained with 2450 MHz modalities in terms of therapeutic value.

2. Direct-Contact Type Applicators. The thermograms illustrated in Figure 18 show SAR patterns in a model of

human muscle tissue exposed to the 915 MHz direct-contact applicator. The results show that the maximum absorption in the muscle is 3.27 W/kg per W input to the applicator. Thus, an input power of approximately 50 W will produce an SAR of approximately 164 W/kg in the tissue, more than adequate for typical clinical applications. Taking density and specific heat into account, the maximum SAR in the fat using the 915 MHz applicator was approximately 40 percent of that in the muscle. The maximum SAR per unit of incident power density was greater than that for plane wave exposure. This

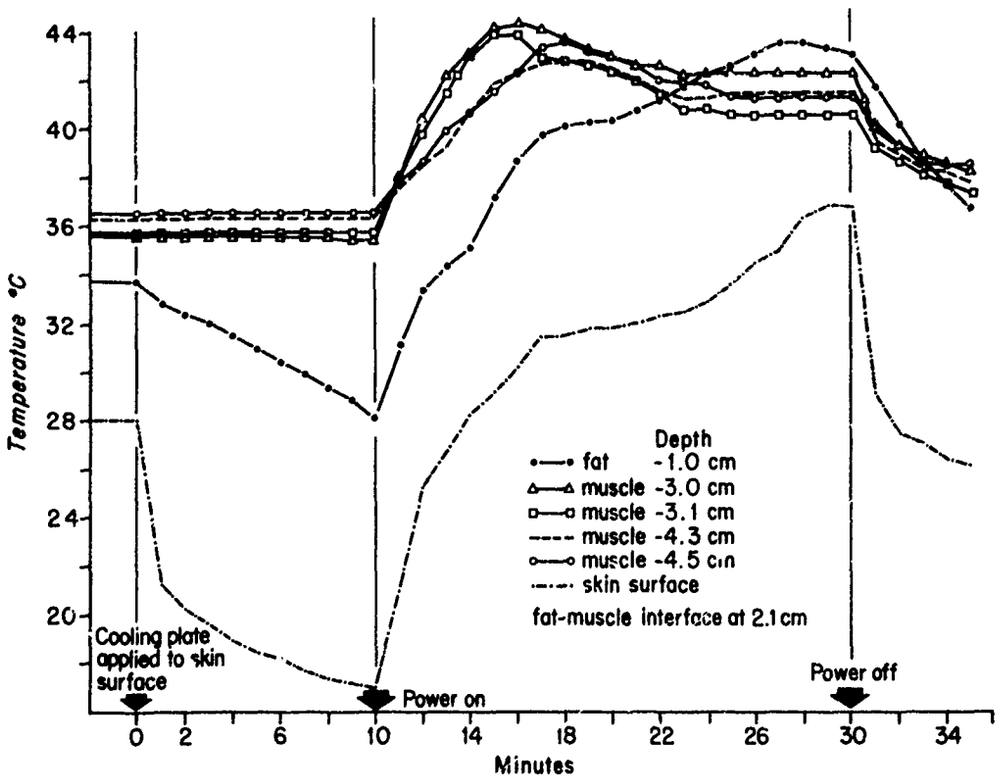


Figure 19. A record of the temperatures in the thigh of a human volunteer with 2.1 cm of subcutaneous fat exposed to microwaves with a 918 MHz direct-contact applicator with surface cooling. (Reprinted with permission from deLateur, *et al.*, 1970.)

was expected since this applicator was designed to couple all of the applied energy to the tissue, whereas, with a plane wave source, a considerable amount of energy is

reflected from the surface. The characteristics of deep penetration and minimal heating of fat demonstrated in models compare favorably with those using shortwave diathermy. An additional advantage is that the heating pattern is reasonably uniform, in contrast with the undesirable toroidal pattern produd by shortwave diathermy.

The 915 MHz UHF applicator was tested under clinical conditions by Lehmann, *et al*. (1978) and de Lateur, *et al*. (1970) by exposing the thighs of human volunteers. The experiments were conducted both with and without cooling of the skin surface. Figure 19 shows the results of a typical experiment for a subject with 2.1 cm of subcutaneous fat. The initial 5 minutes of cooling lowered the skin temperature below 17 °C and the fat temperature to 28 °C. The temperature of the muscle tissue was unaffected. when power was applied, the usual linear transient was observed, from which SARs of 87 W/kg and 54 W/kg, calculated in the muscle at depths of 1.4 cm and 2.1 cm respectively, were obtained. An SAR of 56 W/kg at the center of the fat layer was also calculated. During the 20 minute heating period, the muscle temperature as a function of time followed the characteristic trend illustrated in Figure 1. The temperature reached a maximum oi 45 °C at a location 0.5 to 0.6 cm below the fat-muscle interface after a typical 6 min. exposure period. Sekins, *et al* (1980) and Sekins (1981) have used the Xe^{133}

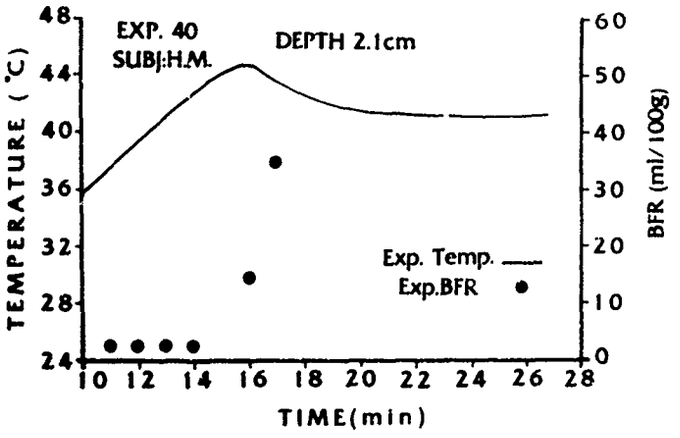


Figure 20. Temperature and blood flow rate (BFR) measured at the site of a xenon injection in the thigh muscle of a human subject during 915 MHz direct-contact microwave diathermy treatment. (Reprinted with permission from Sekins, 1981.)

clearance technique to measure the rate of blood flow in the thigh muscle during microwave diathermy treatment. Figure 20 shows an example of the temperature and blood flow data in one subject. The blood flow increased from 4 to 36 ml/min per 100 g tissue during the diathermy treatment. It is interesting to see that the blood flow stayed at the resting value even when the temperature was 42 °C. The blood flow increased only when the temperature reached 43 °C. The blood flow stayed high to keep the temperature near 41 °C (not shown in Figure 20).

Lehmann, *et al.* (1968) conducted experiments on human volunteers that demonstrated that the 13 cm^2 radome cooled direct-contact microwave applicator heated muscle tissue selectively, to a maximum level between 43 and 45 °C at a depth of 1 to 2 cm in the muscle. By increasing power levels sufficiently to compensate for blood cooling, it would be possible to return the muscle temperature to 43-45 °C and keep it there for long periods of treatment.

Kantor and Cetas (1977) measured thermographically the widths and depths of heating patterns of four 2450 MHz direct-contact applicators, including a circular applicator and a slab-loaded waveguide applicator. The depth of heating was the same (2.2 cm) for all four applicators. The widths of the heating patterns were related to the size of the aperture and distribution of the field. When the choke was added to the slab-loaded waveguide, the width of the heating pattern was reduced slightly as compared with that of the original flange applicator (Kantor and Witters, 1980). No data were reported on the clinical use of these applicators.

The direct contact applicators not only provide better coupling of energy into the tissue, but also reduce the stray radiation considerably (Guy, *et al*, 1974; Kantor and Cetas, 1977; Lehmann, *et al.*, 1979). This reduction in stray radiation is an important safety consideration for both the patient and the therapist.

3. Phased-Array Applicators. The thermographically-determined SAR distribution for a single applicator was similar to the theoretical value shown in Figure 15. When the same model was exposed with the four phased-array applicators, the results shown in Figures 21 and 22 were obtained. The results show a marked change of the SAR pattern, with the maximum SAR occurring at the bone-muscle interface and a uniform SAR occurring around the periphery of the bone. This configuration would appear to be ideal for treating bone tumors since the maximum heating would

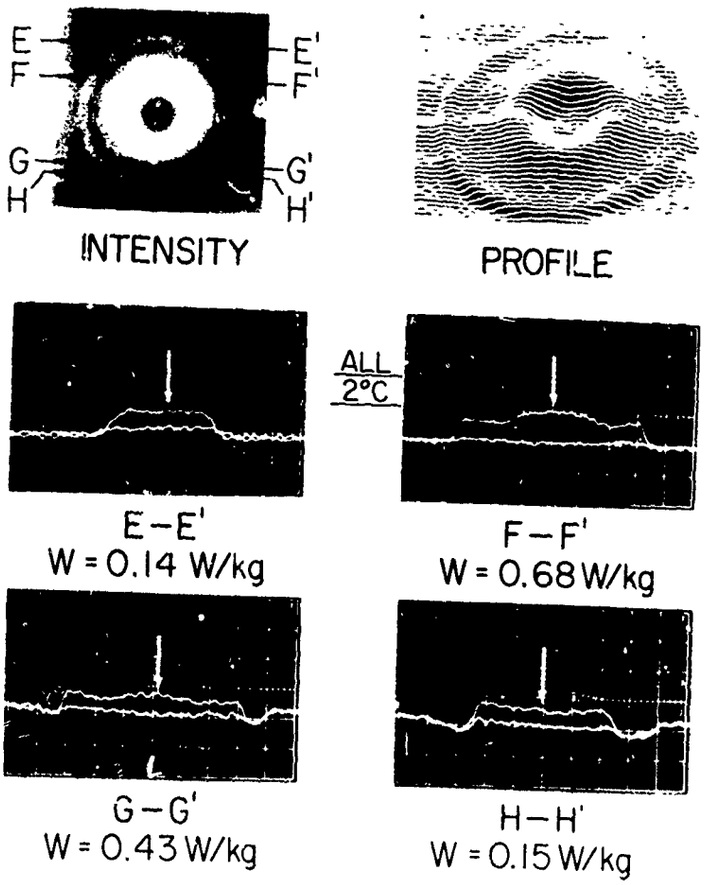


Figure 21. Thermographic results of the exposure of a human arm model (cross-sectional surface) to 915 MHz microwaves from four phased array direct-contact applicators normalized to 1.0 W input. (Reprinted with permission from Guy and Chou, 1982.) The applicators are shown in Figure 9.

always occur at the interface between healthy bone and the tumor tissue of higher water content.

DISCUSSION

Controlled electromagnetic heating of tissues in humans requires considerable study of a theoretical and

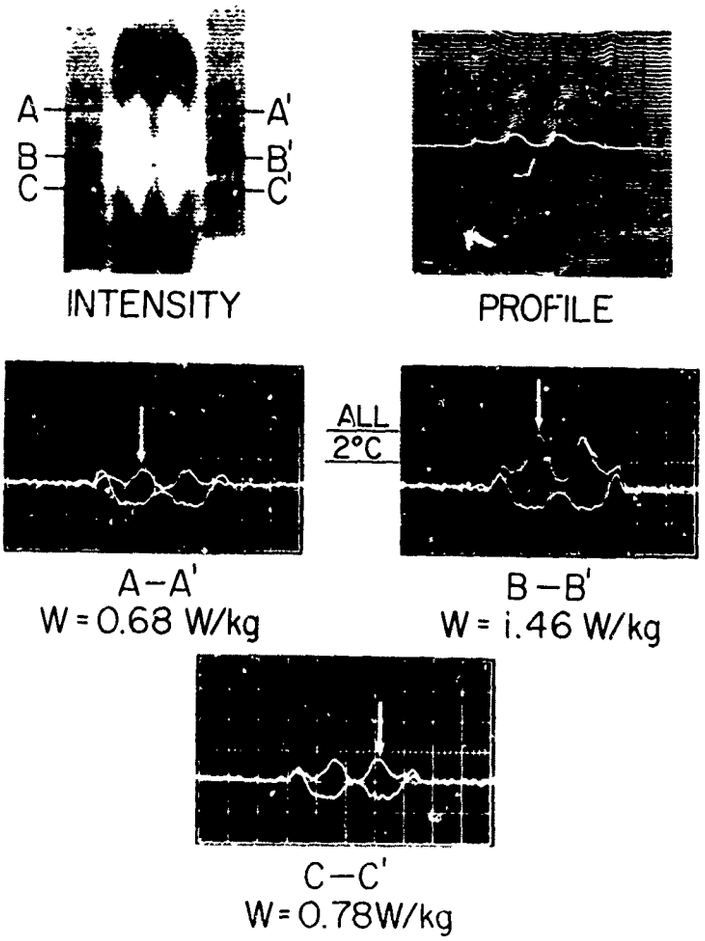


Figure 22. Thermographic results of the exposure of a human arm model (longitudinal surface) to 915 MHz microwaves from four phased array direct-contact applicators normalized to 1.0 W input. (Reprinted with permission from Guy and Chou, 1982.)

experimental nature before an optimal heating modality may be utilized in the treatment of patients in the clinic. Patterns of energy deposition in tissues exposed to electromagnetic fields are highly dependent on the size, shape, and electrical characteristics of the tissue, the frequency of the applied fields, and the size and geometry of the electromagnetic applicator. The location, size, and

shape of the tumor are important considerations in the selection of a proper source of electromagnetic radiation. The pattern of transient or steady state temperatures within a volume of exposed tissue is not only dependent on the SAR pattern but also on the blood flow, thermal properties, and boundary conditions in the tissue medium. The selection of a proper modality for a particular clinical situation must involve the solution of the following three problems.

Problem I

Clinical hyperthermia has been severely restricted by unsatisfactory equipment with limited power output for heating tissue. Most of the clinical experience to date has been gathered from patients treated with "homemade" components. Elementary designs of applicators for clinical hyperthermia have, for the most part, allowed heating of superficial tumors only. In any case, the distribution of heat tends to be uneven. When radiobiological data indicate a threshold of effective heat for killing tumor cells that lies within a narrow range of temperatures, the problem of inhomogeneity of tissue temperature becomes a major obstacle to successful treatment.

The successful treatment of a tumor without damage to surrounding healthy tissues requires that temperatures in the tumor be sufficiently high to be effective, but at the same time temperatures in the surrounding tissues must remain at the safe levels to avoid damage to healthy tissues. This pattern must be prescribed by a clinician or a specialist in the life sciences who is knowledgeable about the physical characteristics and the thermal sensitivity of both the neoplastic and the surrounding healthy tissue. In addition, the time-temperature relationship for providing the most effective treatment must be defined.

Problem II

Once the required spatial and temporal pattern of temperatures is defined, the next step would ideally involve the determination of the required SAR as a function of time and position to produce the desired pattern of temperatures. This requires a careful theoretical analysis based on information concerning the thermodynamic properties of the tissues, including blood flow rates, thermoconductivity, specific heat, and boundary conditions of the tissues within the treatment region.

Since the desired result of a protocol of tissue heating is the development of high local temperatures, it is necessary that the clinician or the thermal analyst be able to specify both the level of heating and its spatial and temporal characteristics. To do so is a twofold problem since it is usually not clear what effect a given distribution of heating will have on tissue temperatures and, even if this is known, whether such deposition patterns can be achieved. In fact, it is most probable that a range of different energy depositions may yield essentially the same temperature profiles. Which of these several deposition patterns can be achieved most expeditiously is open to question, particularly when it is recognized that by varying the temporal characteristics or the thermal boundary conditions quite disparate results may be obtained.

Problem III

The final problem is the selection or design of an electromagnetic source for producing the required SAR patterns. This is probably the most difficult of the three problems, requiring the selection of the optimum frequency, source configuration, and method of application. Electromagnetic modalities now being used for physical therapy and cancer treatment include low frequency currents, high frequency magnetic or electric sources, very high frequency, and microwave sources.

In the use of electromagnetic heating modalities, one is faced with many formidable limitations, the major one being the decreasing depth of penetration as frequency increases. This limitation makes it difficult to focus or transmit microwave energy to deep-seated tumors. However, by using phased arrays of sources or scanning antennas which illuminate a relatively large surface area of the body with moderate power densities but produce beams that intersect deep within the body, one can produce higher levels of SAR at the site of a tumor than that possible from a single or nonscanning source. Thus some of the most formidable obstacles and the greatest number of difficulties are encountered in the solution of Problem III due to the physical limitations in the design of suitable electromagnetic sources. From a practical standpoint most research and experimentation with electromagnetic heating modalities have started with Problem III, rather than Problem I, since the limitations of electromagnetic heating are the controlling factors in determining the final distributions of temperatures in treated tissues. It has proved more efficient to determine the SAR

or heating patterns that are possible with electromagnetic sources and define the limitations of this type of heating rather than to rigorously attempt to solve a problem that may not have a solution. Thus, there must be trade offs and compromises between the clinical requirements and the limitations of the electromagnetic heating modalities.

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REFERENCES

Bowman, R.R. (1976) A probe for measuring temperature in radio frequency heated material. *IEEE Trans. Microwave Theory Tech.* MTT-24: 43.

Chou, C.K. and Guy, A.W. (1977) Microwave and RF dosimetry. In *Workshop on the physical basis of electromagnetic interactions with biological systems.* (L.S. Taylor and A.Y. Cheung, eds.) Workshop held at Univ. of Maryland, College Park, MD, June 15-17.

Chou, C.K. and Guy, A.W. (1982) Systems for exposing mice to 2450 MHz electromagnetic fields. *Bioelectromagnetics* (in press).

deLateur, B.J., Lehmann, J.F., Stonebridge, J.B., Warren, C.G., and Guy, A. W. (1970) Muscle heating in human subjects with 915 MHz microwave contact applicator. *Arch. Phys. Med.* 51: 147.

Foster, K.R. and Schepps, J.L. (1981) Dielectric properties of tumor and normal tissues at radio through microwave frequencies. *J. Microwave Power* 16: 107.

Guy, A.W. (1971a) Analyses of electromagnetic fields induced in biological tissues by thermographic studies on equivalent phantom models. *IEEE Trans. Microwave Theory Tech.* MTT-19: 205.

Guy, A.W. (1971b) Electromagnetic fields and relative heating patterns due to a rectangular aperture source in direct contact with bilayered biological tissue. *IEEE Trans. Microwave Theory Tech.* MTT-19: 214.

Guy, A.W. and Chou, C.K. (1982) Physical aspects of localized heating by radiofrequency waves. In *Hyperthermia in Cancer Therapy*, (K. Storm, ed.) Boston, Mass: G.K. Hall (in press).

Guy, A.W. and Lehmann, J.F. (1966) On the determination of an optimum microwave diathermy frequency for a direct contact applicator. *IEEE Trans. Biomed. Eng.* BEM-13: 76.

Guy, A.W., Lehmann, J.F., and Stonebridge, J.B. (1974) Therapeutic applications of electromagnetic power. *Proc. IEEE* 62: 55.

Guy, A.W., Lehmann, J.F., Stonebridge, J.B., and Sorensen, C.C. (1978a) Development of a 915 MHz director contact applicator for therapeutic heating of tissues. *IEEE Trans. Microwave Theory Tech.* MTT-26: 550.

Guy, A.W., Webb, M.D., Emery, A.F., and Chou, C.K. (1978b) Measurement of power distribution at resonant and nonresonant frequencies in experimental animals and models. Scientific Report No. 11, Bioelectromagnetics Research Laboratory, Univ. of Washington, Seattle, WA: Final report for USAF/SAM Contract #41609-76-C-0032.

Ho, H.S., Guy, A.W., Sigelmann, R.A., and Lehmann, J.F. (1971) Microwave heating of simulated human limbs by aperture sources. *IEEE Trans. Microwave Theory Tech.* MTT-19: 224.

Johnson, C.C. and Guy, A.W. (1972) Nonionizing electromagnetic wave effects in biological materials and systems. *Proc. IEEE* 60: 692.

Kantor, G. (1977) New types of microwave diathermy applicators - comparison of performance with conventional types. In *Proceedings of Symposium on Biological Effects and Measurement of Radiofrequency Microwaves* (D.G. Hazzard, ed.) HEW publication (FDA) 77-8026, pp. 230-249.

Kantor, G. and Cetas, T.C. (1977) A comparative heating pattern study of direct contact applicators in microwave diathermy. *Radio Science* 12: 111.

Kantor, G. and Witters, D.M., Jr., (1980) A 2450 MHz slab-loaded direct contact applicator with choke. *IEEE Trans. Microwave Theory Tech.* MTT-28: 1418.

Kantor, G., Witters, D.M., Jr., and Greiser, J.W. (1978) The performance of a new direct applicator for microwave diathermy. *IEEE Trans. Microwave Theory Tech.* MTT-26: 563.

Lehmann, J.F. (1971) Diathermy. In *Handbook of Physical Medicine and Rehabilitation*. (F.H. Krusen, F.J. Kottke, P. Ellwood, eds.) p. 273 Philadelphia: Saunders.

Lehmann, J.F., Guy, A.W., deLateur, B.J., Stonebridge, J.B., and Warren, C.G. (1968) Heating patterns produced by shortwave diathermy using helical induction coil applicators. *Arch. Phys. Med.* 49: 193.

Lehmann, J.F., Guy, A.W., Johnston, V.C., Brunner, G.D., and Bell, J.W. (1962a) Comparison of relative heating patterns produced in tissues by exposure to microwave energy at frequencies of 2450 and 900 megacycles. *Arch. Phys. Med.* 43: 69.

Lehmann, J.F., Guy, A.W., Stonebridge, J.B., and deLateur, B.J. (1978) Evaluation of a therapeutic direct-contact 915-MHz microwave applicator for effective deep-tissue heating in humans. *IEEE Trans. Microwave Theory Tech.* MTT-26: 556.

Lehmann, J.F., Johnston, V.C., McMillan, J.A., Silverman, D.R., Brunner, G.D., and Rathbun, L.A. (1965) Comparison of deep heating by microwaves at frequencies 2456 and 900 megacycles. *Arch. Phys. Med.* 46: 307.

Lehmann, J.F., McMillan, J.A., Brunner, G.D., and Guy, A.W. (1962b) A comparative evaluation of temperature distributions produced by microwaves at 2456 and 900 megacycles in geometrically complex specimens. *Arch. Phys. Med.* 43: 502.

Lehmann, J.F., Stonebridge, J.B., and Guy, A.W. (1979) A comparison of patterns of stray radiation from therapeutic microwave applicators measured near tissue-substitute models and human subjects. *Radio Science* 14: 271.

Licht, S. (1965) *Therapeutic Heat and Cold*, 2nd Edition, New Haven, Connecticut: Elizabeth Licht.

National Council of Radiation Protection and Measurement (1981) *Radiofrequency Electromagnetic Fields: Properties, Quantities and Units, Biophysical Interaction and Measurement*. NCRP Report No. 67.

Rozzell, T.C., Johnson, C.C., Durney, C.H., Lords, J.L., and Olson, R.G. (1975) A nonperturbing temperature sensor for measurements in electromagnetic fields. *J. Microwave Power* 9: 241.

Schwan, H.P. (1957) Electrical properties of tissues and cells. *Advan. Biol. Med. Phys.* 5: 147.

Schwan, H.P., and Piersol, G.M. (1954) The absorption of electromagnetic energy in body tissues, Part I. *Amer. J. Phys. Med.* 3: 371.

Schwan, H.P., and Piersol, G.M. (1955) The absorption of electromagnetic energy in body tissues, Part II. *Amer. J. Phys. Med.* 34: 425.

Sekins, K.M., (1981) Microwave hyperthermia in human muscle: An experimental and numerical investigation of the temperature and blood flow fields occurring during 915 MHz diathermy. Ph.D. Dissertation, University of Washington, Seattle, WA.

Sekins, K.M., Dundor, D., Emery, A.F., Lehmann, J.F., McGrath, P.W., and Nelp, W.B. (1980) Muscle blood flow changes in response to 915 MHz diathermy with surface cooling as measured by Xe^{133} clearance. *Arch. Phys. Med. and Rehab.* 61: 105.

Song, C.W., Kang, M.S., Rhee, J.G., and Levitt, S.H. (1980) Effect of hyperthermia on vascular function in normal and neoplastic tissues. *Ann. N.Y. Acad. Sci.* 335: 35.

Stuchly, M.A., Athey, T.W., Stuchly, S.S., Samaras, G.M., and Taylor, G. (1981) Dielectric properties of animal tissues in vivo at frequencies 10 MHz - 1 GHz. *Bioelectromagnetics* 2: 93.

Wickersheim, K.A., and Alves, R.B. (1979) Recent advances in optical temperature measurement. *Industrial Research Development.* 21: 82.

IN VIVO TEMPERATURE MEASUREMENTS DURING WHOLE-BODY EXPOSURE OF *MACACA MULATTA* TO RESONANT AND NONRESONANT FREQUENCIES

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INTRODUCTION

As early as 1953, Brady recognized the potential for thermal hazards from whole-body exposure to radiofrequency radiation (RFR) in operational situations. A critical analysis of the absorption of such energy by humans and the thermal consequences of such absorption was undertaken by Schwan and Piersol (1954, 1955) adding greatly to the current understanding of the problem. Crucial to the development of dosimetric techniques was the documentation that whole-body energy absorption is a function of the frequency of the incident wave (Schwan and Li, 1956). On this basis, simple plane-layer models were developed that dominated the science of RFR dosimetry for several years.

In the late 1960s, burgeoning reports of biological effects produced by RFR exposure kindled renewed interest in dosimetry. Most of the research at that time involved small rodents exposed to RF fields that were characterized, at best, by frequency and incident power density. Clearly, improved dosimetric techniques were called for. Early work by Guy (1971a) extended the plane-layer analysis to more complex objects utilizing infrared thermography of man-equivalent models and more realistic multi-layer slabs (Guy, 1971b). Guy and his co-workers noted the unequal distribution of the absorbed energy in the man-like figurines and this thermographic evidence was used to support the concept of "hot spots." About this time, Ho and his colleagues

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(1971) constructed mathematical models of human body parts, incorporating frequency and geometric interactions, that also predicted inhomogeneous energy absorption. Dosimetric theories and models mushroomed in the 1970s. In his summary of known interactions of RFR with biological systems, Schwan (1971) expressed doubts regarding resonance phenomena, neurological effects, and the like, emphasizing the importance of gross thermal effects. On the other hand, Johnson and Guy's excellent summary (1972) reiterated the concept of hot spots, proposed specific absorption rate (SAR) as the most useful quantity to correlate with biological effects, and suggested internal temperature measurement in the intact system as the only realistic way to evaluate potential hazards.

Livesay and Chen (1974) developed a theoretical method to determine internal field distributions inside heterogeneous biological bodies of irregular shapes. Kritikos and Schwan (1975) contributed to our understanding of unequal distribution of heating potential inside lossy spheres and specified the radius-to-frequency ratios under which a hot spot appears. Additional insight was provided by characterizing the absorption effects in terms of frequency and orientation in the RF field (Gandhi, 1975a; Guy, *et al.*, 1976), as well as by demonstration of resonance phenomena (Gandhi, *et al.*, 1975; Barber, 1977). Foci of unequal SAR as a function of orientation, frequency, or presence or absence of ground plane in mathematical models (Chen and Guru, 1977) as well as in dead or anesthetized animals (Gandhi, 1975b) were reported. The unavailability of a truly nonperturbed temperature sensor for use in RF fields hampered the latter work. Gandhi and Hagmann (1977) also predicted partial body resonance that was later measured in a monkey model by Olson and Griner (1980). Attempts to modify mathematical models of SAR in man by including thermoregulatory terms for sweating (Emery, *et al.*, 1976) and by irradiation of simulated biological materials (Foster, *et al.*, 1978) did not generate accurate estimates of energy absorption and accompanying temperature distribution in tissues. Further refinements of earlier mathematical simulations subsequently produced more agreement with geometric model and figurine data (Hagmann, 1979). Spiegel, *et al.* (1980) presented a more ambitious attempt to include thermoregulatory responses and blood flow effects in such a simulation. They predicted enhanced local SARs and an attendant sharp local temperature increase in the upper arm and lower thigh at whole-body resonant frequencies and in the wrist and ankle region when exposure occurred at frequencies resonant for the extremities.

Burr and Krupp (1980) first used *in vivo* temperature measurement techniques to map the distribution of energy absorption in the head of a live rhesus monkey and compared the findings with measurements made in models, detached monkey heads and the head of an intact carcass. In these experiments, blood flow effects significantly modified temperature distribution in the mid-brain, when compared to the sharp peak observed in the 3.3 cm sphere. The results clearly showed the difference between the heating potential referred to by Kritikos and Schwan (1979) and the real-time temperature rise in the presence of blood flow. Way, *et al.* (1981) modified Stolwijk's thermoregulatory model to consider hot spots in the region of the hypothalamus. They concluded that thermoregulatory action serves to prevent any drastic temperature rise until an SAR threshold of about 5 W/kg is reached.

One result of the accumulation of data based on measurements in models, figurines, and mathematical simulations was to blur the distinction between electrical hot spots resulting from the unequal distribution of absorbed energy and thermal hot spots representing true localized temperature increases in biological tissue under realistic physiological conditions. The concept of average SAR was called into question as a reliable gauge for comparing experiments performed at differing exposure frequencies and incident power levels for objects or subjects of varying size and shape.

Although no empirical evidence exists for the occurrence of elevations in tissue temperature significantly above core temperature at the foci where enhanced energy absorption occurs, the informed literature on this subject is replete with references to tissue hot spots, target organs and extensions of the concept to justify drastic reductions in permissible exposure levels for humans. Temperature hot spots have become an accepted fact, and regulatory agencies are now seriously considering their impact on standards for exposure to RFR.

The invention of RFR-transparent thermometers, particularly the Vitek Electrothermia Monitor developed by Bowman (1976), allowed for temperature determinations *in vivo* during RFR exposure. Beginning in 1980, several studies addressed the impact of exposure to head resonant frequencies (Adair and Adams, 1980) partial body resonances (Krupp, 1981) and core temperature response during whole-body exposure to a near-resonance frequency (Lotz, *et al.*, 1981). The research reported below was designed to measure the change in local tissue temperature to unilateral plane wave (whole-body) exposure at a frequency near resonance, in an

intact animal, at anatomical sites where hot spots could be expected, based on predictions from the literature cited above.

EXPERIMENTAL METHODS

Radiofrequency Radiation Exposures

All near-resonance RFR exposures were performed in the far field of an anechoic chamber, 3 x 3 x 5 m (Emerson and Cummings, Inc.) using 219 MHz, continuous wave RFR, produced by an amplifier (MCL Inc. Model 10670) with an open-ended waveguide antenna. Incident power densities were measured prior to each exposure using a 10-cm dipole built and calibrated by the National Bureau of Standards. Values read at either edge of a 100-cm-wide field were 10-15% lower than those measured at the center of the field. Differences in the vertical dimension were not measured but the height of the vertical field utilized was less than one-third the horizontal distance. For purposes of this report, the three readings were averaged (Table I). SAR values for wrist, ankle, biceps, and thigh were calculated from temperature rises following 30-second exposures to 27 mW/cm^2 in monkey models made of muscle equivalent material using the method

Table I. Representative Values of Measured Field Intensity

Amplifier Output (watts)	Incident Power Density (mW/cm)[a]			
	Left[b]	Center	Right[b]	Average
100	4.74	5.76	5.02	5.17
200	8.27	10.19	8.49	8.98
450	15.85	19.06	16.12	17.01
900	24.80	29.44	25.42	26.55

[a]Readings taken 1 meter from horn along horizontal midline of beam.

[b]Distance from center--50 cm.

TABLE II. SAR Measurements in a Monkey Model[a]

Probe Site	Depth of Probe (cm)[b]	SAR (mW/g/mW/cm^2)
Ankle	1.0	2.6 ± 0.12[c]
Thigh	2.7	2.9 ± 0.22
Wrist	1.25	1.5 ± 0.06
Biceps	1.9	0.4 ± 0.14
Umbilicus	3.8	0.9 ± 0.2

[a]Measurement sites correspond to probe location in living animal. Model of muscle-equivalent material, and equal in anatomical shape and posture to its live counterpart. All dimensions and mass two-thirds life size.

[b]Distance from front of animal with probe equidistant from all surfaces.

[c]Average of four readings ± SD.

of Guy (1971a) (Table II). The model is three-fourths life size (65 cm), and, therefore, represents a more severe exposure than in the live monkey exposure, as the model size is very close to the true resonance length of 54 cm for 219 MHz (wave length 136 cm x 0.4 = 56 cm). The whole-body average SAR was 0.49 (W/kg)/mW/cm^2), calculated from average animal dimensions and body mass, using the methods of Durney, *et al.* (1980).

Animals

The animals exposed were male *Macaca mulatta* weighing between 4.5 and 6.5 kg and measuring 83-75 cm, crown to heel. Initial anesthesia was induced by intramuscular injection of 0.1 ml/kg of a mixture made by combining 1 ml of a 100 mg/ml solution of ketamine HCl (Vetalar, Parke Davis, Inc.) and 3 ml of a 20 mg/ml solution of zylazine (Rompun, Haver-Lockhart, Inc.). Subsequent intramuscular injections of 10 mg/kg of ketamine alone were made hourly to

prolong anesthesia. The pharmacological effect was to provide a uniform plane of anesthesia which permitted surgical procedures without pain and without extreme depression of respiration or the cardiovascular system.

Following induction of anesthesia, the sites to be implanted were clipped and washed with an iodine-base soap (Betadine). The animal was then positioned on a Styrofoam board. For each site, a 1-2 cm skin incision was made, and deeper tissues were separated by blunt dissection to allow a Vitek probe to be positioned at a depth where the greatest temperature rise would be expected to occur, based on theoretical predictions and our measurements of temperature increments in tissue-equivalent models. A suture around the probe was used to maintain this locus and was fixed to any convenient tissue structure, e.g., a tendon or muscle sheath. The skin was closed tightly around each exiting lead with a horizontal mattress suture, and the lead was then taped to the exposure board to prevent movement.

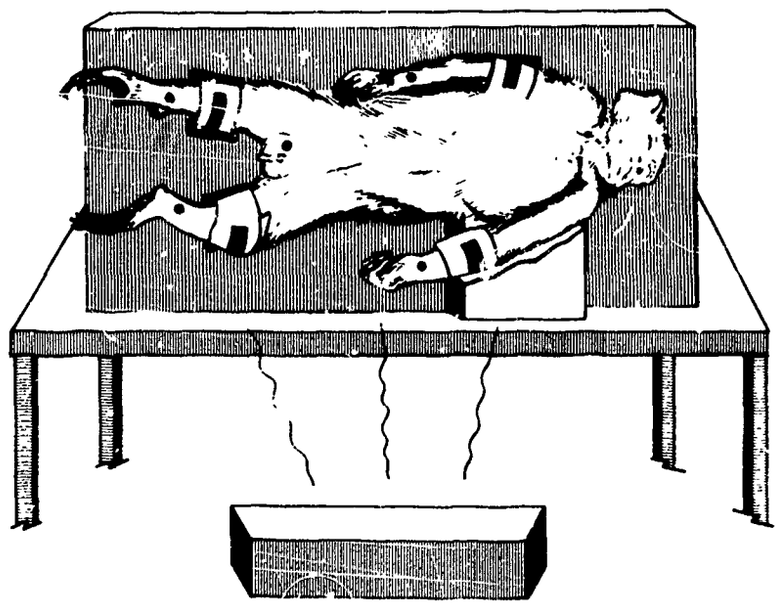

Figure 1. Drawing of a rhesus monkey positioned for RF exposure. A block to support the head has been omitted for clarity. Dots mark the positions mentioned in the text where Vitek temperature probes were surgically implanted.

Figure 1 depicts an animal prepared for exposure, with sites of implantation marked by dots; the long axis of the animal's body was oriented parallel to the E-field during the exposure.

Two animals with Vitek probes implanted in the ankle and wrist were exposed to each of four power densities, 5.0, 7.5, 10.0 or 27.0 mW/cm^2 for a total of eight experiments. Two additional animals had Vitek probes implanted in a lower bicep and in the distal one-third of the thigh and were exposed to an incident power of 10 mW/cm^2. Exposure duration was four hours or until rectal temperature reached 41.5 °C. Data from replicate exposure conditions in comparable-sized animals were nearly identical. For clarity, the data shown in Figures 2 and 4 are from a single animal. Data in Figure 3 represent the mean rectal

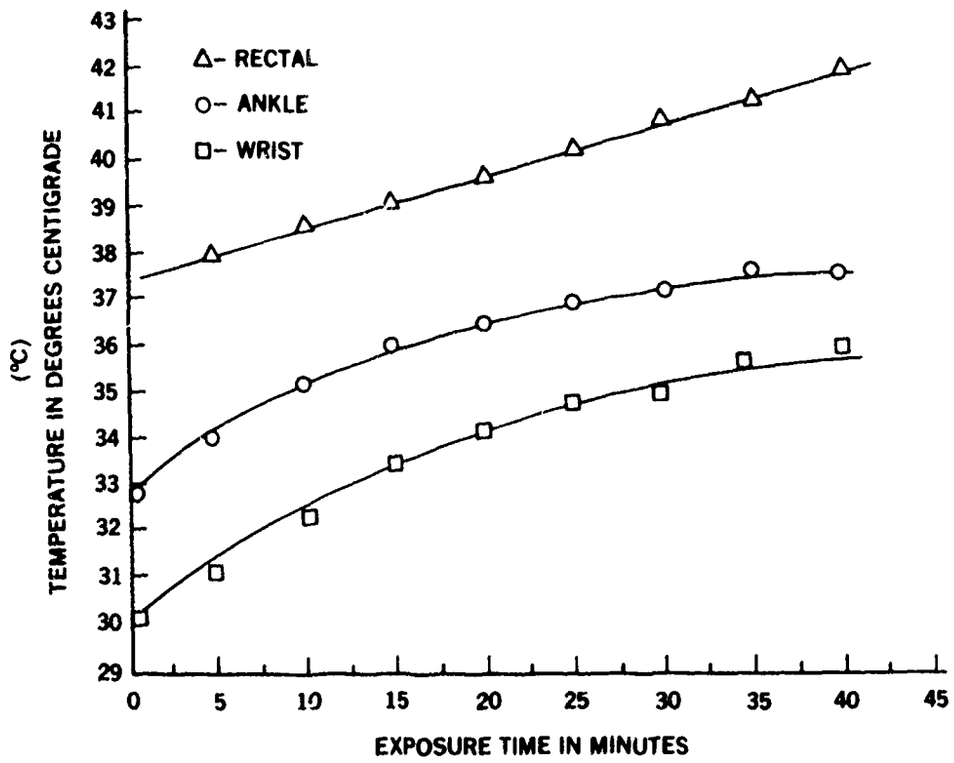

Figure 2. Typical temperature response of one monkey to 40 minutes of 219 MHz, 27 mW/cm^2 whole-body exposure. Body temperature measured in the rectum, ankle, and wrist. Chamber temperature = 23 ± 0.5 °C.

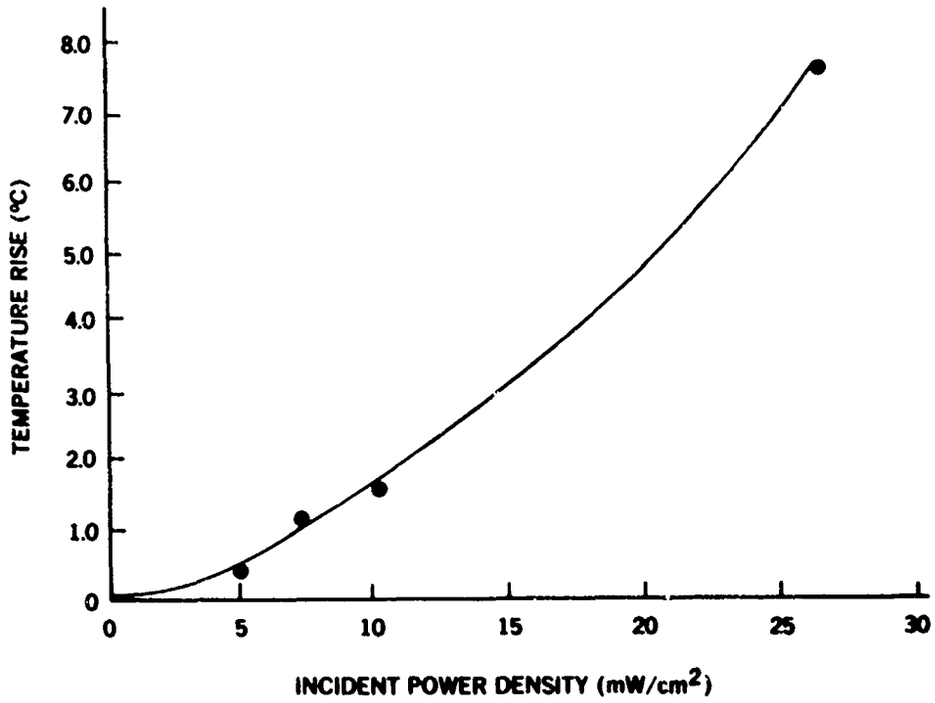

Figure 3. Mean rise in rectal temperature of 2 monkeys after 1 hour of exposure to 219 MHz continuous wave RF radiation at the power densities indicated. Data at 27 mW/cm^2 represents the predicted total rise in rectal temperature had the rate of rise occurring at the termination of exposure continued for a full hour of exposure. Chamber temperature = 23 ± 0.5 °C.

temperature rise measured in two animals following one hour of exposure to four different levels of incident power.

RESULTS AND DISCUSSION

Initial exposures were made at the highest incident power level available, 27 mW/cm^2, at an ambient temperature of 23 °C. Probes were located in one wrist and one ankle, and a deep rectal probe was used to determine core temperature. The exposure was continued until deep body temperature reached 41.5 °C (40 minutes), at which time the exposure was terminated. The effects of exposure to a near-resonant

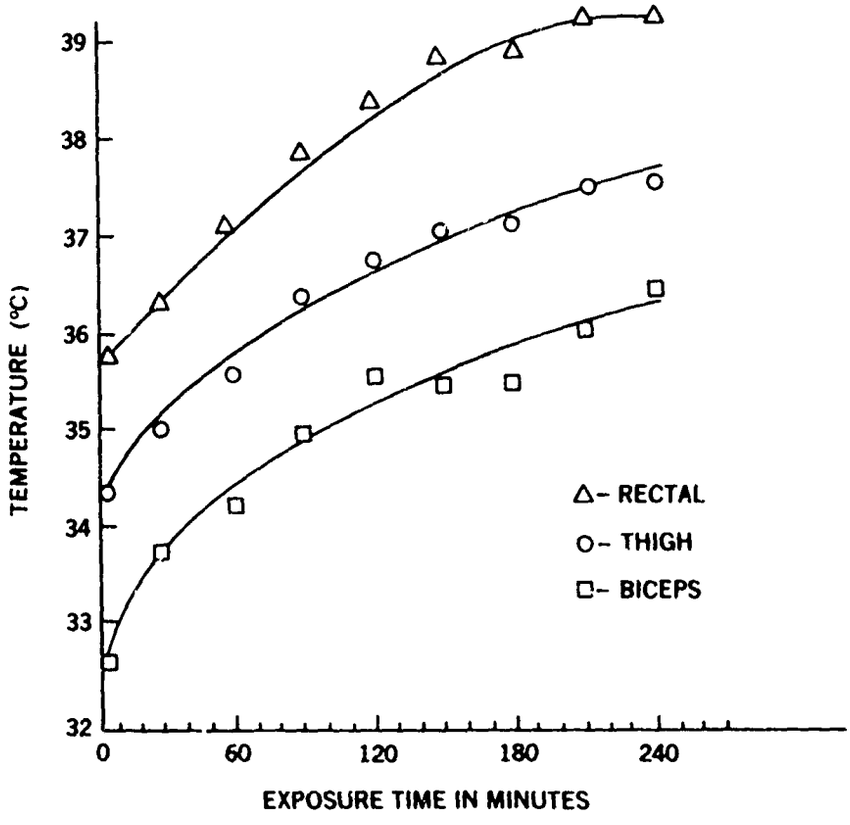

Figure 4. Typical temperature response of 1 monkey to a 219-MHz RF exposure at an incident power density of 10 mW/cm^2, for 4 hours. Body temperature measured in the rectum, thigh, and biceps. Chamber temperature = 23 ± 0.5 °C.

frequency were readily apparent: wrist, ankle, and rectal temperature rose precipitously (Figure 2). Additional exposures at 10, 7.5, and 5 mW/cm^2 produced increases in rectal temperature roughly proportional to the incident energy (Figure 3), with a threshold for marked temperature rise near 7.5 mW/cm^2. At no time did any wrist or ankle temperature surpass the measured rectal temperature.

Subsequent exposures at 10 mW/cm^2 involved implanted probes in the distal one-third of the biceps and quadriceps muscles of the arm and leg respectively. Once again, the tissue temperature rise at these sites paralleled that of the body as a whole, and no evidence for any hot spot could

be detected (Figure 4).

The results obtained are similar to those in a preliminary report by Lotz, *et al.* (1981) in spite of several important differences between the two test situations. Lotz used awake monkeys restrained in a seated position; hourly withdrawals of blood were made. Control of chamber temperature was not mentioned by Lotz. Details of SAR measurements were not available, but earlier data reported by Olson (1981) were obtained in a model with a mass almost three times that of the monkey used by Lotz. The monkeys in the present study were larger and were anesthetized; they were exposed in the far-field in a position designed for maximum RFR absorption. The average whole-body SAR of 0.49 $(W/kg)/(mW/cm^2)$ is a level where significant body heating could occur. Given these differences, the agreement is remarkable. Both studies confirm the fact that whole-body exposure at or near the resonant frequency for that body results in a rapid rise in body temperature, at much lower power levels than in the nonresonant case. In the case of this study, however, the average SAR at 7.5 mW/cm^2 was near the 4 W/kg level (7.5 x 0.49 = 3.76 W/kg), generally considered the threshold for significant physiological response. If the value measured in the model at the level of the umbilicus is used as an estimate of whole-body average SAR, the 5 mW/cm^2 exposure gives an SAR just above the threshold (5 x 0.95 = 4.5 W/kg).

Experiments at 2.066 GHz (Krupp, 1981), using the same techniques for implantation and exposure, produced a somewhat different pattern. An incident power density of 15 mW/cm^2 produced no increase in rectal temperature following one hour of exposure. Vitek probes implanted in the neck and groin (see Figure 1) also did not detect any increase in tissue temperature. Wrist and ankle temperatures, where the initial local set point was 3 to 4 °C below rectal temperature, rose slowly over the one-hour exposure, but in six trials never reached the rectal value. Squirrel monkeys exposed unilaterally to a head-resonant frequency (2450 MHz) tolerated incident field strengths up to 22 mW/cm^2 and exhibited no rectal temperature rise; however, thermoregulatory behavior was ongoing during the experiments (Adair and Adams, 1980).

The inability of the present study and others to detect the predicted isolated high temperature rise in wrist, arm, ankle, or leg reflects the failure of current mathematical models to include an adequate blood flow term, specifically to account for the contribution to heat redistribution made by the large blood vessels of the extremities. Measurements of blood flow changes in the brachial and femoral arteries

during RFR exposure would be helpful in refining the predictive capabilities of geometric models and mathematical simulations.

CONCLUSIONS

Anesthetized rhesus monkeys, implanted with Vitek temperature probes (in the wrist, ankle, thigh and biceps) and fitted with a rectal probe, were exposed ventrally to plane-wave 219 MHz RFR (E polarization) at controlled environmental temperature. Temperature responses were recorded during 1- to 4-hour exposures to several power densities that ranged from 5 to 27 mW/cm^2. Several conclusions may be drawn from the results of this study:

(1) The variety of exposure parameters and anatomical sites, explored in many combinations, failed to reveal the existence of tissue hot spots, localized regions of greatly-elevated temperature.

(2) Exposure to a frequency near whole-body resonance (219 MHz) produced a significant rise in body temperature at relatively low incident power levels when compared to comparable exposures to a frequency well above resonance (2.06 GHz) explored in an earlier study. Whole-body SAR, however, was at a level where temperature increase would be anticipated.

(3) Lower set-point temperatures in the limbs, as well as increases in peripheral blood flow that are unaccounted for by models, probably act to negate the predicted effects of unequal energy absorption on local tissue temperature.

REFERENCES

Adair, E.R. and Adams, B.W. (1980). Microwaves modify thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics* 1:1.

Barber, P.U. (1977). Electromagnetic power deposition in prolate spheroid models of man and animals at resonance. *IEEE Trans. Biomed. Eng.* 24:513.

Bowman, R.R. (1976). A probe for measuring temperature in radiofrequency-heated material. *IEEE Trans. MTT* 24:43.

Brady, S.I. (1953). Operational hazards of microwave radiation. *J. Aviation Med.* 24:328.

Burr, J.G. and Krupp, J.H. (1980). Real-time measurement of RFR energy distribution in the *Macaca mulatta* head. *Bioelectromagnetics* 1:21.

Chen, K.M. and Guru, B.S. (1977). Internal EM field and absorbed power density in human torsos induced by 1-500-MHz EM waves. *IEEE Trans. MTT* 25:746.

Durney, C.H., Iskander, M.F., Massoudi, M., Allen, S.J., and Mitchell, J.C. (1980). 3rd Ed. Radiofrequency Radiation Dosimetry Handbook. USAFSAM Tech Rept. 80-22. USAFSAM/RZP, Brooks AFB, TX 78235.

Emery, A.F., Short, R.E., Guy, A.W., Kraning, K.K., and Lin, J.C. (1976). The numerical thermal simulation of the human body when undergoing exercise or nonionizing electromagnetic irradiation. *J. Heat Transfer* 98:284.

Foster, K.R., Kritikos, H.N. and Schwan, H.P. (1978). Effect of surface cooling and blood flow on the microwave heating of tissue. *IEEE Trans. Bicmed. Eng.* 25:313.

Gandhi, O.P. (1975a). Frequency and orientation effects of whole animal absorption of electromagnetic waves. *IEEE Trans. Biomed. Eng.* 22:536.

Gandhi, O.P. (1975b). Conditions of strongest electromagnetic power deposition in man and animals. *IEEE Trans. MTT* 23:1021.

Gandhi,O.P. and Hagmann, M.J. (1977). Some recent results in the deposition of electromagnetic energy in animals and models of man. In *The Physical Basis of Electromagnetic Interactions with Biological Systems* (L.S. Taylor and A.Y. Cheung, eds.), p. 243. HEW (FDA) 78-8055, USGPO, Washington, D.C. 20402.

Gandhi, O.P., Sedigh, K., and Beck, G.S. (1975). Distribution of electromagnetic energy deposition in models of man with frequencies near resonance. In *Biological Effects of Electromagnetic Waves* (C.C. Johnson and M.L. Shore, eds.), Vol. 2:44. HEW(FDA)77-8011, USGPO, Washington, D.C. 20402.

Guy, A.W. (1971a). Analysis of electromagnetic fields induced in biological tissues by thermographic studies on equivalent phantom models. *IEEE Trans. MTT* 19:205.

Guy, A.W. (1971b). Electromagnetic fields and relative heating patterns due to a rectangular aperture source in direct contact with bilayered biological tissue. *IEEE Trans. MTT* 19:214.

Guy, A.W., Webb, M.D. and Sorensen, C.C. (1976). Determination of power absorption in man exposed to high frequency EM fields by thermographic measurements on scale models. *IEEE Trans. Biomed. Eng.* 23:361.

Hagmann, M.J. (1979). Numerical calculation of electromagnetic energy deposition for a realistic model of man. *IEEE Trans. MTT* 27:804.

Ho, H.S., Guy, A.W., Sigelmann, R.A., and Lehmann, J.F. (1971). Microwave heating of simulated human limbs. *IEEE Trans. MTT* 19:224.

Johnson, C.C. and Guy, A.W. (1972). Nonionizing electromagnetic wave effects on biological materials and systems. *Proc. IEEE*, 60:692.

Kritikos, H.N. and Schwan, H.P. (1975). The distribution of heating potential inside lossy spheres. *IEEE Trans. Biomed. Eng.* 22:457.

Kritikos, H.N. and Schwan, H.P. (1979). Potential temperature rise induced by electromagnetic field in brain tissues. *IEEE Trans. Biomed. Eng.*-26:29.

Krupp, J.H. (1981). In vivo measurement of radiofrequency radiation absorption. In *Proceedings of a Workshop on the Protection of Personnel Against Radiofrequency Electromagnetic Radiation* (J.C. Mitchell, ed.) USAFSAM Aeromedical Review 3-81. USAFSAM/RZP, Brooks AFB, TX 78235.

Livesay, D.E. and Chen, K.M. (1974). Electromagnetic fields induced inside arbitrary shaped biological bodies. *IEEE Trans. MTT* 22:1273.

Lotz, G.W., Podgorski, R.P., and Bley, J.A. (1981). Exposure of rhesus monkeys to a frequency (225 MHz) near whole-body resonance. Abs., 3rd Annual Conference, BEMS, Washington, D.C., p. 76.

Olson, R.G. and Griner, T.A. (1980). Partial body resonances in a sitting rhesus model at 1.29 GHz. *Bioelectromagnetics* 1:242.

Schwan, H.P. (1971). Interaction of microwave and radiofrequency radiation with biological systems. *IEEE Trans. MTT* 19:146.

Schwan, H.P. and Li, K. (1956). Hazards due to total body irradiation by radar. *Proc. IREE* 44:1572.

Schwan, H.P. and Piersol, G.M. (1954). The absorption of electromagnetic energy in body tissues: a review and critical analysis. Part 1. *Am. J. Phys. Med.* 33:371.

Schwan, H.P. and Piersol, G.M. (1955). The absorption of electromagnetic energy in body tissues: a review and critical analysis. Part 2. *Am. J. Phys. Med* 34:425.

Spiegel, R.J., Deffenbaugh, D.M., and Mann, J.E. (1980). A thermal model of the human body exposed to an electromagnetic field. *Bioelectromagnetics* 1:253.

Way, W.I., Kritikos, H.N., and Schwan, H.P. (1981). Thermoregulatory physiologic responses in the human body exposed to microwave radiation. *Bioelectromagnetics* 2:341.

INFRARED RADIATION AND HUMAN THERMAL COMFORT

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INTRODUCTION

This chapter describes the essential characteristics of thermal (infrared) radiation as related primarily to its effect on exchange in humans and accompanied physiological and sensory responses, most importantly certain aspects of human comfort. The first section reviews those basic properties and nomenclature associated with thermal radiation. The last section embodies a sequence of relevant research which has led to present concepts of thermal comfort: early pain studies, thermal sensation, as differentiated from comfort, and hedonics. Special attention is directed to those studies which have used thermal radiation as a tool in physiological studies.

BIOPHYSICS OF INFRARED (THERMAL) RADIATION

Infrared radiation (beyond the red end of the visible spectrum) includes wavelengths from 0.4 μm to about 150 μm (far infrared) (Sparrow and Cess, 1966). Radiant heat is thought to have been first quantified by W. Herschel in 1800 using a thermometer at various points in a prismatic spectrum (Phillips, 1974). He found that visible light transmits some heat but the effect is more pronounced beyond the red end of the spectrum. Although infrared radiation is more penetrating than visible light, it is nevertheless effective in warming substances.

Microwaves and Thermoregulation

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Table I. Schematic Diagram of the Electromagnetic Spectrum (from Sparrow & Cess, 1966; Birkebak, 1966; Phillips, 1974).

Energy changes	Nuclear		Inner shell electrons	Ionization of atoms and molecules		Valence electrons	Molecular vibrations: stretching		bending	Spin orientation (in magnetic field)	
Region in thermal radiation							(0.4 μm to 150 μm)				
Region in electromagnetic spectrum	Gamma rays	X rays	"Soft" X rays	Vacuum UV	Near UV	Visible	Near IR (overtone)	(fundamental)	Far IR	Micro-waves	Radio waves
Wavelength	1 Å	10 Å	100 Å	2,000 Å	4,000 Å	8,000 Å 0.8 μm	2.5 μm	25 μm	0.04 cm 400 μm	25 cm	

All materials are absorbers and emitters of thermal radiation. The second law of thermodynamics requires that, for a given wavelength, each substance's emissivity and absorptance be the same. Emissivity is here defined as the ratio, for a given wavelength interval, of the energy emitted per unit area divided by the energy emitted by a black-body of the same area. For real materials, the actual absorptance is a fraction of the wavelength. A so-called black-body is defined as one that absorbs all wavelengths. Such a cavity, held at a given temperature, will generate radiant energy according to a function of wavelength (λ) (Hardy, 1939).

The total energy of radiation in a cavity is proportional to the fourth power of the absolute temperature (T^4), a property first found experimentally in 1879 by J. Stefan but derived theoretically by L. Boltzmann in 1884 (Phillips, 1974). Their independent efforts are incorporated in the Stefan-Boltzmann law describing the rate of emission of energy per unit time and area (W_b) of a black-body surface. Wien later (1893) showed that the distribution of radiant energy (dW) according to a specific wavelength change ($d\lambda$) has the form:

$$dW = W(\lambda)\,d\lambda \qquad (1)$$

$$= C_2 T^5 f(\lambda T)/(\lambda T)^5\, d\lambda$$

where $f(\lambda T)$ is a function of the product of wavelength and absolute temperature solely, and C_2 is a constant (See Table II). The function ($W\lambda$) has a maximum: the wavelength at which the energy distribution is a maximum (λm) times the absolute temperature is (Sparrow & Cess, 1966)

$$\lambda_m T = 0.2898 \text{ cm} \cdot °K \qquad (2)$$

$$= 2898\ \mu\text{m} \cdot °K$$

Roughly 25% of spectral energy is radiated at shorter than λ_m and the rest radiates at wavelengths > λ_m (Hardy, 1939).

Radiant energy is transported by electromagnetic waves (or photons, the quantization of the waves). Radiation properties of certain materials can be described adequately by electromagnetic theory and classical concepts, but quantum theory is necessary for precise descriptions of absorbing and emitting media. From classical electromagnetic theory the waves describing infrared radiation travel at the speed of light in vacuum. In a quantum description, energy is transported by photons: minute energy packets of

Table II. Some Black-Body Radiation Constants

Constant	Symbol	Unit
Boltzmann	k	1.38×10^{-16} erg/° K
Planck	h	6.6×10^{-27} erg/ s
Speed of light	c_o	3×10^{10} cm/ s^1
Stefan-Boltzmann	σ	5.67×10^{-8} W/($m^2 \cdot K^4$)
Aggregate	C_1	1.19×10^{-16} W/m^2
Aggregate	C_2	1.44 cm/° K

From Sparrow & Cess (1966), Birkebak (1966)

electromagnetic radiation at the same velocity. In 1900, Planck first explained that blackbody radiation is emitted and absorbed in such distinct units; in 1905 Einstein postulated that energy must be absorbed only in the same units. The energy of a photon is hν (h is Planck's constant and ν is frequency). However, it is wise to keep in mind that there are photons of all energies: from the high energy photons of gamma rays to low-energy photons of infrared radiation and the very low energy photons of radio-waves (Table I).

The frequency, ν, and wavelength in a vacuum, λ, are related by the relation $c = \lambda \cdot \nu$. The problem is whether to choose ν or λ to characterize the radiation. *Frequency* is often used because it does not change when travelling from one medium to the other. However, radiation is more frequently classified according to *wavelength* (λ).

Thermal radiation is considered in this paper as "radiant energy emitted by a medium that is due solely to the temperature of the medium." (Sparrow & Cess, 1966). It is therefore the temperature of the medium which governs the actual *emission* of thermal radiation. Of concern to thermal biologists are the two distinct bands: solar (shortwave) radiation occurring in the range 0.3 μm and longer waves occurring at about 0.7 to 150 μm.

The total black-body emissive power (W_b) over all frequencies (or wavelengths) can be described by Planck and

Stefan-Boltzmann laws (Phillips, 1974; Sparrow & Cess, 1966; Hardy, 1939).* But, radiation properties concerned with human skin surfaces and the microenvironment cannot be wholly predicted from the physics of solids because of the heterogenous nature of the skin surface. The following publications summarize some of the results garnered from extensive studies of the properties of transmission of thermal radiation through human skin (Birkebak, 1966; Hardy, 1962; Fanger, 1972; Mitchell, 1970).

Human skin has variable thickness over different parts of the body and is therefore heterogenous to incident radiation. In the spectral region from 0.3 μm to 3 μm there is a maximum reflectivity (Figure 1) for white and black skin at about 0.8 to 1.2 μm, roughly the λ_m of maximum radiation for most infrared heaters. From 3 μm to 20 μm, reflectance becomes independent of skin pigmentation and is quite low.

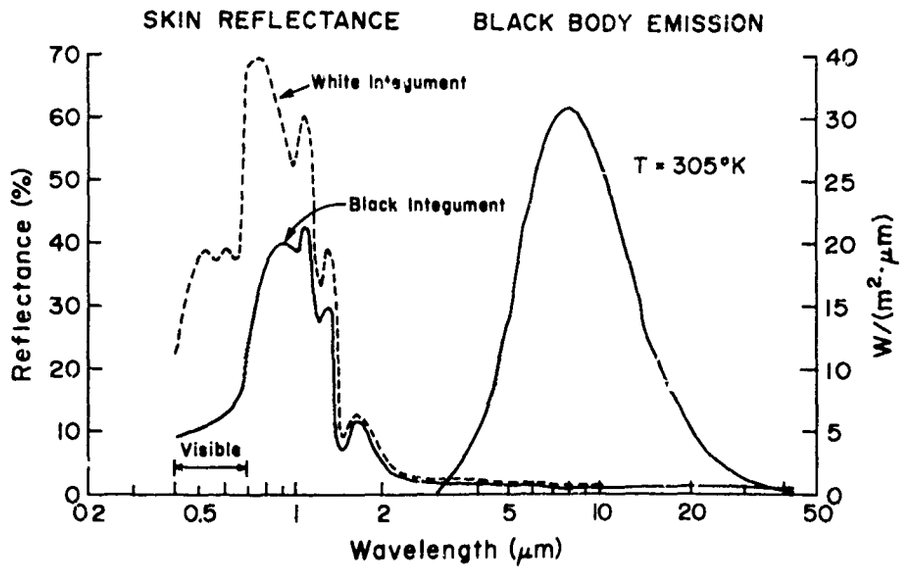

Figure 1. Human skin reflectance (%) for black and white skin and emissive power of a black body ($W/(m^2 \cdot \mu m)$) as a function of wavelength (μm). (Redrawn from Hardy, 1962).

*The actual Stefan-Boltzmann equation $W_b(T) = n^2 \sigma T^4$ is derived formally (if n, the index of refraction, is independent of frequency or λ and c_o = speed of light) by

The actual skin pigmentation is an important variable at short wavelengths near 0.4 to 0.7 μm; a darkly pigmented person will become markedly more heated by direct radiation $\geq$ 2500 K than would one of lighter skin (*cf.* Figure 2).

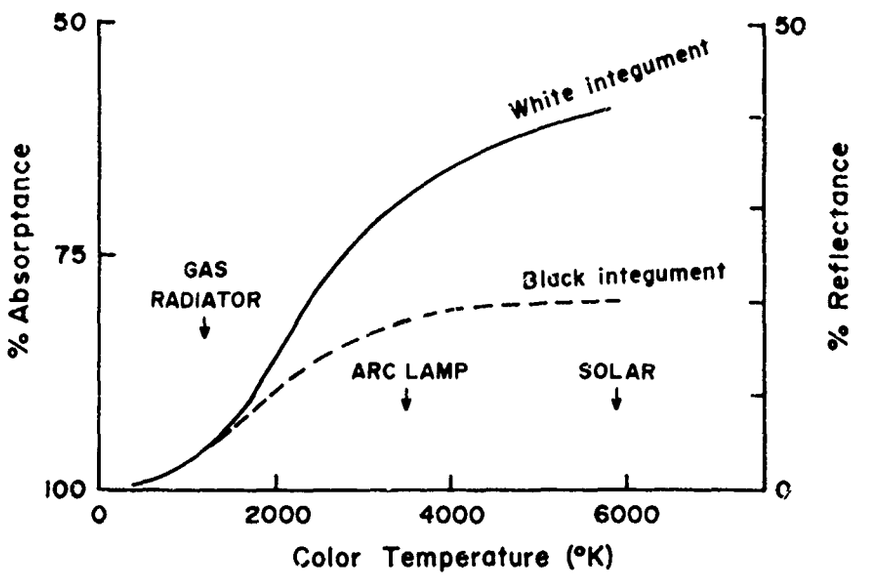

Figure 2. Absorptance (%) and reflectance (%) for black and white skin in relation to color temperature (°K). (Redrawn from Hardy and Gagge, 1967).

Clothing, however, minimizes the above differences. By decreasing emissivity of clothing, a reduction in radiative heat loss adds an additional protection against heat stress. Emissivity (e_s) of human skin varies with spectral region, but skin emits in the infrared spectrum (5 μm to 20 μm). It

---

$W_b(T) = n^2 T^4 (2 \pi k^4/C_o^2 h^3) \int e_{b\lambda} d\lambda$

where the definite integral for Planck's eq. = $\pi^4/15$. Additionally, $\sigma = 2\pi^5 k^4/15 C_o^2 h^3$ and becomes incorporated in the constant value 5.67×10^{-8} W/(m^2 · K^4); $W_b T = \sigma T^4$ where the index of refraction (n) = 1. The units of the other Blackbody constants (in SI) are in Table II for the reader's convenience.

is the emissivity value in this range that is important in human heat exchange.

The two ways of measuring emissivity of skin, analysis of reflecting power or analysis of absorbing power in the above λ ranges, are technically difficult. Hardy (1939) compared the emitting power of the skin by analyzing skin temperature accurately with an infrared radiometer and compared this with the temperature of a "perfect black-body" using the Stefan-Boltzmann law. Hardy found $e_s = 0.98 \pm 1\%$, a value constant for $\lambda > 4$ μm; e_s is therefore $\sim$1.0 (Mitchell, 1970).

Actual transmission of thermal radiation into the skin is variable and dependent on skin and blood pigments and scattering properties of the skin. Most of the absorption properties of the skin are related to its water moiety. The greatest penetration of a skin site (breast) to infrared radiation has been measured at λ of 1.2 to 1.4 μm (Hardy, 1962), where some 40 to 50% of the total flux entered to a depth of 1 cm. Conceivably, at this depth the free nerve endings, small blood vessels and individual sweat glands could be affected directly. As shown in Figure 3, the actual changes in skin temperature caused by thermal radiation depend on thermal conductivity (k_s), density (p), and specific heat (c) of the skin site (Hardy, 1962; Piergallini & Stoll, 1974).

When radiant energy falls on a surface (skin or clothing), it can be absorbed, reflected or transmitted and

$$\alpha + \tau + \rho = 1 \qquad (4)$$

where α = fraction of incident radiation absorbed;
τ = fraction of incident radiation transmitted;
ρ = fraction of incident radiation reflected.

Since most integument or clothing is opaque, as most solids are in the infrared, τ or transmission is negligible and $\alpha + \rho = 1$.

A good deal of information has been provided on radiative heat exchange between the human body and its surroundings. For the most part this exchange can be expressed by the Stefan-Boltzmann law (Gagge & Hardy, 1967) and is included in the heat balance equation (insensible loss and storage are not considered) in which the sensible heat loss $(R + C)$ from the body and clothing surface at T_{cl} is

$$(R + C) = h_r (T_{cl} - T_r) + h_c (T_{cl} - T_a) \quad W/m^2 \quad (5)$$

or $$= h (T_{cl} - T_o)$$

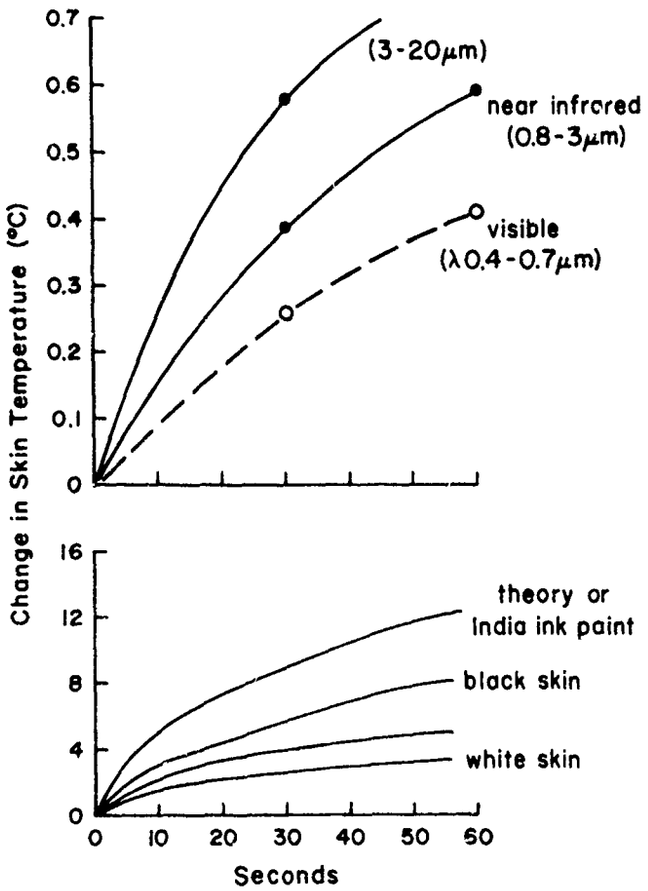

Figure 3. Changes in forehead skin temperature (°C) during solar radiant heating. Upper panel: irradiation by same intensity of visible, near- and far- infrared. Lower panel: comparisons of different skin pigmentations; painted skin, black pigmented and white. (Redrawn from Hardy, 1962).

where the left side of eq. 5. includes radiative (R) and convective (C) heat losses, and

h_r = a linear radiation exchange coefficient $(W/(m^2 °C)$

h_c = the convective heat transfer coefficient $W/(m^2 °C)$

h = the combined heat transfer coefficient and equal to $(h_r + h_c)$ $W/(m^2 °C)$

T_{cl} = the clothing or outer body surface temperature °C

T_a = the ambient air temperature °C

T_r = the mean radiant temperature °C

T_o = operative temperature which is an average of T_r and T_a, weighted by the transfer coefficients involved and given by $(h_r T_r + h_c T_a)/h$ (Winslow, *et al.*, 1937) °C

Mean radiant temperature (T_r) is defined as the temperature of an imaginary uniform "black" enclosure in which man would exchange the same heat by radiation as in the actual non-uniform environment (Gagge, *et al.*, 1971).

A linear radiative coefficient (Hardy and Gagge, 1967) is

$h_r = 4\ \sigma\ \varepsilon\ (A_r/A_d)\ f_{acl}\{\ [(T_{cl} + T_o)/2] + 273\}^3$ and eq. 5

becomes

$$R = 4\ \sigma\ \varepsilon\ (A_r/A_d)\ f_{acl}\{[(T_{cl} + T_o)/2] + 273\}^3 \cdot (T_{cl}-T_r) + C \qquad (5')$$

In eq. (5'), σ is the Stefan-Boltzmann constant (Table II) and ε includes the emissivities of human skin ($\sim$0.98) and clothing ($\sim$0.95) (Hardy, 1939; Fanger, 1972).

The term (A_r/A_D) is the ratio of a 4 π radiating area of the body surface "open" to thermal radiation over its Dubois total surface area (A_D, m^2). A_r is always less than A_D because extremities or other surfaces radiate to each other, rather than to exterior surfaces. Other variables in the assumption of A_r depend on posture (sitting, standing, or crouching) and clothing folds. Several researchers have provided useful methods to establish A_r in respect to A_d and these are compiled in Table III.

The factor (f_{cl}) expresses the increase in A_D due to clothing and can range from 1.0 for 0 clo to as high as 1.5 for 3 clo (Fanger, 1972).

The development of the *effective radiant field* (ERF) describing the net radiant exchange with all sources that radiate at temperatures different from the isotropic ambient T_a was a major step in thermobiology (Gagge & Hardy, 1967). It has allowed another dimension to our understanding of the energy exchange between the total radiant environment and the human being (Gagge, 1970).

Effective radiant field (ERF) is here defined as the *net*

Table III. Relationship of DuBois surface area (A_D) and posture.

Body Posture	$A_r(m^2)$	Method
Standing	$0.725 \cdot A_D$	optical
"	$0.71 \cdot A_D$	heat balance
"	$0.78 \cdot A_D$	envelope
"	$0.78 \cdot A_D$	photographic
Sitting	$0.696 \cdot A_D$	optical
"	$0.65 \cdot A_D$	heat balance
"	$0.72 \cdot A_D$	heat balance
Cycling ergometer	$0.81 \cdot A_D$	optical
Spread eagle	$0.85 \cdot A_D$	heat balance

Compiled from Fanger (1972); Gagge and Hardy (1967).

radiant heat exchange between all enclosing surfaces and directional heat sources and sinks by an occupant whose surface is hypothetically at the ambient temperature T_a. In other words, ERF is the net radiant energy exchanged by the occupant with only those surfaces and sources whose temperatures differ from the ambient air (T_a).

In general, any $(ERF)_n$ is a function of the radiating temperature of the source n in absolute temperature, the absorptance α of the exposed body or clothing surface for the emission of σK^4 by the source, and an appropriate view factor (F_{hn}) that describes the fraction of man's total body surface irradiated by the source. (Oleson, 1981; Fanger, *et al.*, 1980; McIntyre, 1976).

Any radiant source n contributing to the total ERF may take the generalized form (Gagge & Hardy, 1967):

$$(ERF)_n = f_{acl}(A_r/A_D)F_{h-n}\alpha_n[(T_n+273)^4-(T_a+273)^4]. \ W/m^2 \quad (6)$$

The view factor F_{h-n}, refers to the body area A_D itself,

rather than the radiating area of the body surface ($A_r f_{acl}$) corrected for clothing. Only for the simplest geometrical arrangements can values of F_{m-n} be easily evaluated (Olesen, 1981).

In every case during thermal equilibrium, $(ERF)_n$ is the energy absorbed by the body system via the outer surface of the body and is solely a function of T_r and T_a and is not a function of T_{sf}. The relationships between ERF (W/m^2) and T_r, T_a, and T_o (°C) are:

$$ERF = h_r(T_r - T_a) \quad (7)$$

$$ERF = h(T_o - T_a) \quad (8)$$

$$T_r = T_a + ERF/h_r \quad (9)$$

$$T_o = T_a + ERF/h \quad (10)$$

$$T_r = T_a + (h/h_r)\ (T_o - T_a) \quad (9')$$

$$T_o = T_a + (h_r/h)\ (T_r - T_a) \quad (10')$$

Solar radiation contributes appreciably to the ERF. We recently studied (Arens, *et al.*, 1980) how ERF can be used to measure net radiant heat flux to or from the human body due to radiation at outside (anisotropic) air temperatures. For solar radiation, total (direct plus diffuse) radiation falling on a horizontal surface (I_{TH}) varies with solar elevation. In addition, A_D exposed to solar radiation, and therefore the solar energy received by a body, also varies with solar elevation. Total radiation I_{TH} is plotted in Figure 4 for a specific solar elevation using an elevation of 45 degrees as an average value for the contiguous United States and is about 665 W/m^2. The equivalence between ERF, T_r, and I_{TH} involves the following assumptions:

a. *R* and *C* are assumed equal in plotting T_r.

b. The surface area of the standard person (A_D = 1.8 m^2).

c. The projected area of standard man exposed to direct beam sunlight (A_p), where solar elevation $\beta = 45°$:

$$A_p/A_D = 0.23 \quad \text{(Fanger, 1972)}$$

$$A_p = (0.23)\ (1.8) = 0.41\ m^2$$

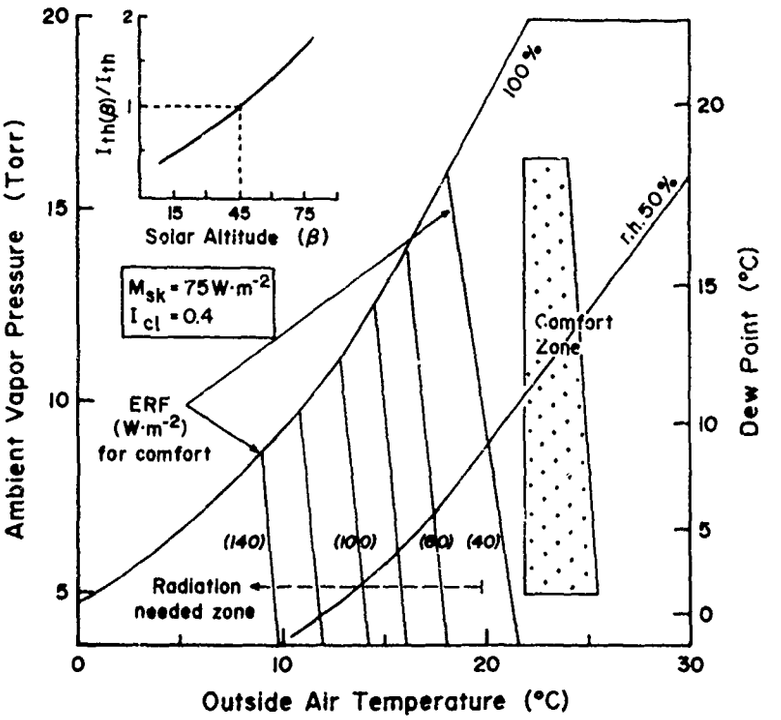

Figure 4. Effective Radiant Field (ERF) needed for comfort plotted on a psychrometric chart. Ordinates are ambient vapor pressure (Torr) and dewpoint temperature (°C). The activity is normal walking (1.3 met or M_{sk} 75 W/m^2). Top insert is factor to adjust I_{th} for solar altitude (From data in Arens, *et al.*, 1981).

d. Area of the standard man exposed to diffuse, reflected, and long-wave radiation (from Table III):

$$A = 0.72 \cdot 1.8 = 1.28 \text{ m}^2$$

where

$$f_{eff} = 0.72 \quad \text{(Fanger, 1972)}$$

e. Diffuse-sky solar radiation is assumed to radiate to the upper half of the human body and the ground-reflected solar radiation is assumed to be uniformly distributed over the lower half of the body.

The absorbed energy on the human body from long-wave and short-wave radiation sources is therefore measured by:

$$ERF \cdot \alpha_{LW} = [0.72 \cdot 0.9/1.8 \cdot (I_d + I_r) + 0.41/1.8 \cdot I_N] \cdot \alpha_{SW} \quad (11)$$

where

α_{LW} is long-wave absorptivity, $\approx$ 0.95

α_{SW} is short-wave absorptivity, $\approx$ 0.67 for (white) skin and average clothing

I_N is direct beam solar radiation measured perpendicular to the beam, W/m^2

I_d is diffuse irradiance, on an upward-facing horizontal surface (165 W/m^2)

I_r is reflected irradiance, on a downward-facing horizontal surface, 1 meter above the ground (W/m^2).

Because $I_N = (I_{TH} - I_d)/\sin \beta$, where I_{TH} is total solar irradiance of a horizontal surface, (Birkeback, 1966) equation (11) can be rewritten:

$$ERF \cdot 0.95 = [0.72/2 (I_d + I_r) + 0.41/(1.8 \cdot \sin \beta) (I_{TH} - I_d)] \cdot 0.67 \quad (12)$$

where I_r is assumed to be 0.20 I_{TH}.

Substituting in (12), ERF = 190 W/m^2. ERF is thermally equivalent to 0.29 $\cdot$ I_{TH}, or $I_{TH} = 3.5 \cdot ERF$.

ERF therefore allows one to assess the "radiation-needed" zone when outdoor air temperature drops below 20 °C. The radiation is based on a direct, easily-quantified concept taking into account the possible solar radiation load necessary to maintain an optimum comfort zone. This is an important development which is not handled by other indices ("plane", mean, or vector radiant temperatures, [McIntyre, 1976]) which work solely in isotropic environments.

THERMAL COMFORT

Up to now, we have concentrated on how thermal radiation affects the biophysical properties of the skin. How thermal radiation affects the thermal state of the body will now be discussed. A detailed description of how the thermal information is channeled to the central nervous system is beyond the scope of this chapter. Briefly, signals are generated in skin receptors sensitive to touch, pain, warmth and cooling (Hardy, 1971; Hensel, 1981). Their sensitivity is quite exact. Temperature receptors respond to local energy increments in the skin of as little as 0.63 $mW/cm^2 \cdot s$). Another receptor is sensitive to temperature decreases as small as 0.004 °C s (Bullock and Diecke, 1956; Hardy and Oppel, 1937).

Extensive research has led to a description of a zone of environmental temperatures in which the body is in a state of physiological thermal neutrality. The resting person maintains thermal steady-state (i.e., heat balance) such that internal body and skin temperatures are constant without excessive physiological regulatory activity such as sweating, vasoconstriction or vasodilation of skin blood vessels (see Chapter 13). This is also the zone of "neutral" temperature sensation. Studies by Fanger (1972) equate thermoneutrality with preferred comfort state or preferred temperature and show that for individuals at 0.6 clo, air velocity near still conditions (v at 0.10 to 0.15 m/s), 50% rh and sedentary activity, the thermoneutral (comfort) temperature is invariable regardless of age, sex, or season. Fanger demonstrated that other preferred comfort temperatures during thermal balance may be ascertained for any metabolic heat production ($\leq$ 3 met), for various clothing insulations (I_{cl}), dry bulb and mean radiant temperatures, and ambient vapor pressures as well as various coefficients of heat and mass transfer. During thermal neutrality there occurs: a) a linear relationship between skin temperature (T_{sk}) and metabolic rate (M) and b) a linear function between evaporation of sweat and (M). Fanger suggested a predicted mean sensation (PMV) for an individual from the thermal load on the body; a thermal load is presumed to occur whenever there is a difference between heat production and the heat loss to the actual environment for a person supposedly kept near heat balance (i.e. comfort) at the mean skin temperature and sweat secretion determined for a specified activity level. Thus, a change in heat loss is the prominent effect which occurs if a person (having a given metabolic rate, clothing insulation value, etc.) is

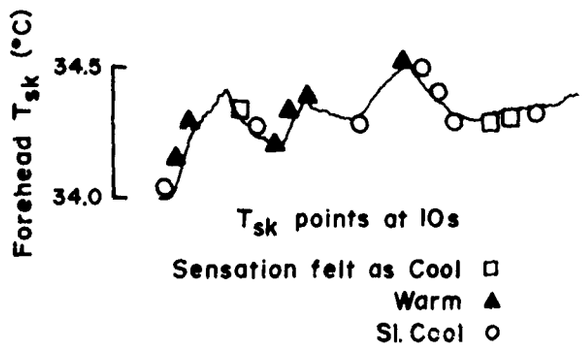

Figure 5. Effect of weak thermal radiation on the temperature of forehead skin (T_{sk}) and accompanied votes of thermal sensation. (Redrawn from Hardy, 1962).

displaced from a comfortable environment to a warmer or colder environment.

The implication that thermal comfort is equivalent to a sensation of neutral temperature is not wholly accurate or adequate. Other variables such as fatigue, endocrine (humoral) factors, and sensitivity to pain play a significant role.

As an example, Figure 5 shows measurements made by Hendler and Hardy (1960) on a subject asked to assess particular thermal sensations at given intervals while skin temperature was fluctuating normally in a "comfortable" environment. Although the subject was in thermal balance, the ratings given are closely linked with the temperature of the skin which was rising (slightly warm) or falling (slightly cool) even though these fluctuations amounted to no more than 0.2 °C. Hardy (1962) pointed out that ". . . a thermally neutral sensation is thus not the absence of temperature sensation."

Pain is a fundamental input to human comfort. Hardy, *et al.* (1951) showed that pain caused by over-heating a skin site by infrared radiation exhibits quite different thresholds from those discrete sensations stemming from rising ambients (increasing skin temperature) and lowering ambients (decreasing skin temperature) as shown in Figure 6. This figure indicates that between a T_{sk} of 27 to 36 °C there is no change in the threshold of warmth. An increase in the threshold for cold is evident for accompanied increases in T_{sk} of 32 to 34 °C. The threshold for thermally-irradiated

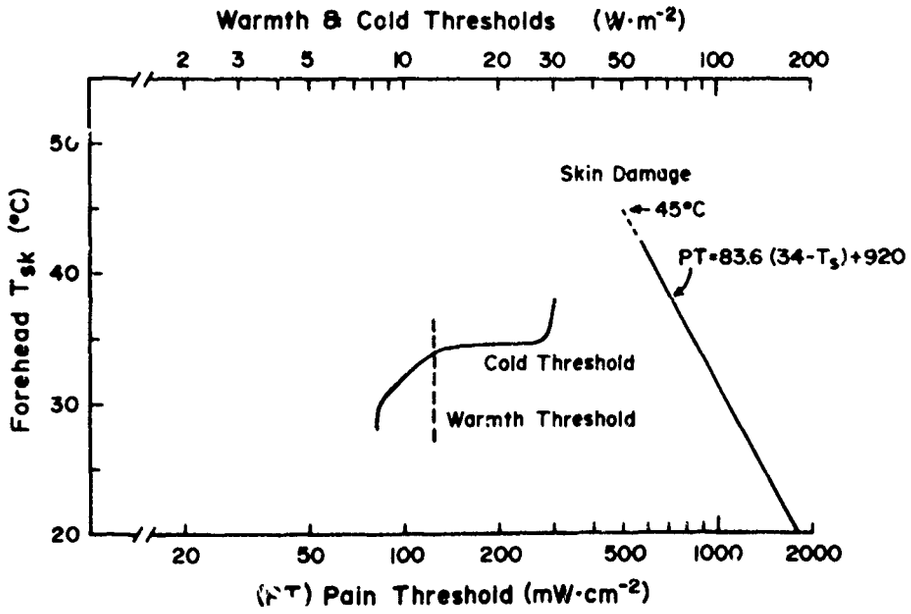

Figure 6. Relation of forehead skin temperature (°C) to thresholds of warmth, and cold (top abscissa-W/m^2) and rate of heat flux required for pain threshold (bottom abscissa-mW/cm^2). (From data in Hardy, *et al.*, 1951).

pricking pain is described as the rate of heat flux to the skin that just exceeds the rate of heat loss by an amount which drives T_{sk} to 45 °C within a given time period (3s) (Hardy, *et al.*, 1951). A skin temperature of 45 °C is a standard requirement for eliciting pricking pain by infrared radiation. This threshold is independent of age, sex, fatigue, or mood and occurs at an estimated intensity of thermal radiation of 861 $mW/cm^2 \pm$ 88 SD (present author's calculation) at the end of a 3-s exposure. Interestingly, magnitude estimates of warmth converge for 3-s duration, at about 800 mW/cm^2 (see Chapter 9) regardless of area of skin stimulated. Other types of pain (burning, aching) have cutaneous or subdermal origins which have different thresholds and thereby change the state of thermal comfort.

In humans, the origin of dissatisfaction with the thermal environment may thus be psychological, physiological, or physical. Winslow, *et al.* (1937) related unpleasant cold conditions in sedentary subjects to skin temperatures below 33.5-34 °C and unpleasant warm conditions to accumulation of

sweat on the skin surface (skin wettedness). Chatonnet and Cabanac (1965) showed that the judgment of thermal displeasure was relative to the state of hyper- or hypothermia of the body. Gagge, *et al.* (1967) showed that any sudden thermal transient towards a comfortable environment caused an immediate sensation of comfort although at the moment of the initial change the actual skin temperature and rate of sweating could be at levels not associated optimally with a feeling of comfort.

Benzinger (1963) contends that internal body temperature is the important variable affecting thermal comfort. His subjects, resting in a water bath at 38.5 °C, felt comfortable until tympanic temperature began to rise, at which time thermal discomfort increased. The inference was that the sensation of overheating was a function of deep body temperature with minimal effect from elevated skin temperature. However, in a study by Berglund and Gonzalez (1977) in which $T_{sk} = T_a = 35$ °C and skin wettedness was close to 100%, a spray of water caused immediate shivering and cold discomfort with no drop in esophageal temperature. Allnutt and Allen (1973) elevated internal body temperature to 38 °C but cooled the skin to 30 °C. Under these conditions subjects judged themselves as comfortable. In an elegant study, Gagge (1966) showed, by using infrared radiation, that onset of thermal sweating at T_a from 20 to 31 °C was immediate and accompanied a sensation of warmth induced by radiant heat prior to any increase in internal (tympanic) body temperature. These studies indicate that T_{sk} and internal body temperature (as an integrated drive) are both important parameters in judgments of the state of thermal comfort.

Another powerful effector output is behavioral thermoregulation which is highly developed in humans. It has been investigated in sub-human primates (Adair, 1977 and Chapter 17) and in other species. In one study, Stitt, *et al.* (1970) showed that small changes in average skin temperature or hypothalamic temperature from a constant reference point evoke appropriate autonomic responses which maintain the animal in a thermoneutral state. In humans, thermoregulatory behavior is also guided strongly by thermal sensations, but these sensations also have other components. One of these is the affective (hedonic) component: pleasantness and unpleasantness. Whether a particular property of the environment (air movement, infrared heating, ambient temperature) is perceived as pleasant or unpleasant depends on a combination of signals.

Marks and Gonzalez (1974) explored the way pleasantness and unpleasantness of a thermal stimulation of the blackened forehead depend on both the intensity and areal extent of a

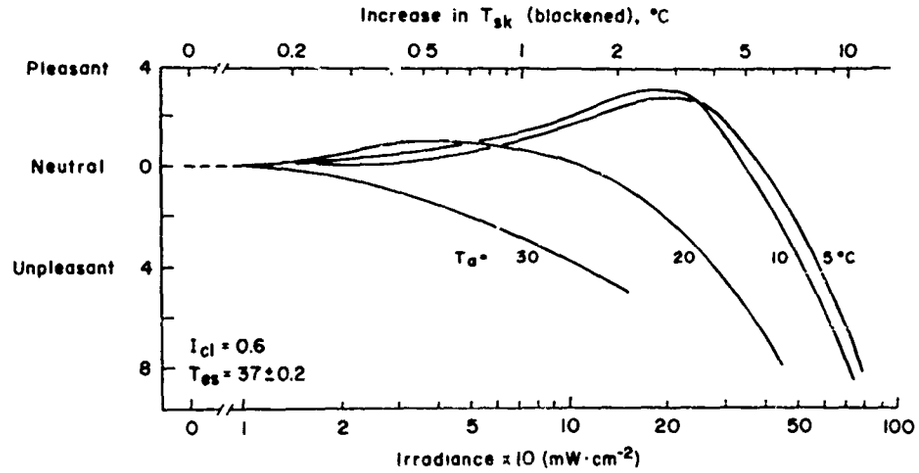

Figure 7. Relationship between hedonic estimates (pleasantness-unpleasantness) of radiant stimuli to the forehead and thermal irradiance (mW/cm^2) at 4 different air temperatures (T_a). Associated changes in forehead skin temperature (°C) are also shown. (Redrawn from Marks and Gonzalez, 1974).

radiant stimulus. While air temperatures were held constant at 5, 10, 15, 20, and 30 °C, irradiance was varied randomly from no stimulus to as high as 800 mW/cm^2. Figure 7 shows averaged results from two subjects. When radiant intensity increases, the estimation of that stimulus first becomes gradually pleasant then markedly unpleasant; the shape of the curve is dependent upon the air temperature. A 2 °C increase in forehead skin temperature, produced by the radiation, feels pleasant in the cold but unpleasant in warm air. The hedonic value and the intensity of sensation, which could not be totally characterized in the early Hendler and Hardy study (1959), therefore both depend on size and duration of stimulation. These are indications of spatial and temporal summation.

In these experiments, internal body temperature (T_{es}) remained close to normal levels (37-37.2 °C). Therefore, in the absence of any strong internal drive resulting from hyper- or hypothermia, the hedonic value is strongly governed by superficial skin temperatures. But as Cabanac (1969) has emphasized, deviations in internal temperature can promote, and often dominate, overall sensations of

thermal affect, a phenomenon for which he coined the term "alliesthesia" (Cabanac, 1969).

The sense of warm discomfort, especially while sedentary and during thermal radiation, is affected by two other principal physical properties of the skin. These properties are its temperature (T_{sk}) and wettedness (w) (Gonzalez and Gagge, 1973; Gagge, 1937), both intimately involved in heat exchange with the environment. The following processes are involved: (1) the heat transported by blood (SkBF or K_s) flowing from the body core to the periphery, (2) the sensible heat exchange between the skin surface and the environment by radiation and convection, (3) the combined effect of skin and internal body temperature on the sweating drive necessary for regulation of body temperature, and (4) the ability of the sweat to evaporate and thus provide cooling of the body.

The characterization of these major physiological factors, so important to thermal comfort, was first done by Hardy (1971). His account, garnered from his own extensive

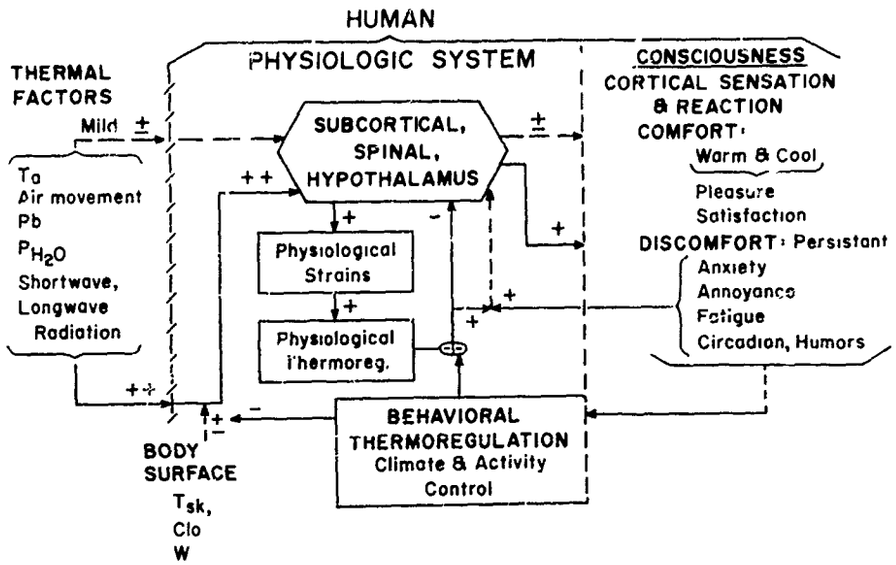

Figure 8. Summary of effects of common physical factors on human physiological thermoregulatory systems and comfort. Note additive effects from sources of discomfort such as skin wettedness (w), clothing insulation (clo), fatigue, etc. (Redrawn from Hardy, 1971).

studies and those of his colleagues, on pain, thermal radiation, and physiological measurements, makes a clear argument that perception of thermal comfort and discomfort is both detected by and a product of an integrated state of thermoregulation. The basic elements are shown in Figure 8.

Hensel (1981) has recently summarized certain aspects suggested by Figure 8 that are related to neurophysiological inputs having a common pathway. He has shown that peripheral thermal sensors feed directly to higher C.N.S. structures and play an important role in autonomic and behavioral responses of organisms to the thermal environment. Therefore from Hardy's (1972) and Hensel's (1981) conclusions, sensations of warmth follow directly from skin warming; but, warm discomfort depends upon an interaction between many physiological and physical factors, including sweating, fraction of skin areas wet with sweat, peripheral blood flow, and central and peripheral temperatures.

Warmth discomfort occurs whenever physiological mechanisms such as sweating and increased skin blood flow are activated to bring heat loss into balance with metabolic heat production. Cold discomfort arises predominantly from vasoconstriction and a subsequent decrease in skin temperature necessary for heat conservation. In humans, cold discomfort imposes a greater challenge to behavior than body heating because autonomic mechanisms of heat loss (vasodilation and sweating) allow facile means for maintaining thermal balance. However, in animals, the reverse may often be the case. Although an adequate description of sensory responses to cold environments can be made in terms of either cold discomfort or cold sensation, quantification of warm discomfort or warmth sensation is possible only by assessing multiple physiological responses.

It must be pointed out that neither T_{sk} nor w is a simple index of any one regulative process such as the secretion of sweat or the vasodilation of peripheral blood vessels during heat exposure. However, when thermal equilibrium is maintained by both of these efferent responses, it can be shown that they both may be linearly related to each other and to T_{sk}.

All of the above variables have been incorporated by Gagge, *et al.* (1972) in a single temperature index by which a prediction of thermal comfort and thermal sensation can be made. A simple model of human temperature regulation was used to simulate thermal responses in any environment; the model includes the applicable transfer coefficients for both sensible and insensible heat exchange and a humid operative temperature (T_{oh}) for any given environmental condition derived in terms of operative temperature (T_o), ambient

vapor pressure, and skin wettedness.

In later studies, Gagge, *et al.* (1972) proposed that a 50% rh base be included in a new index, which was defined as the temperature of an imaginary *standard* environment with a pre-fixed transfer coefficient in which the total heat exchange (sensible plus insensible) from the skin surface would be the same as in the actual environment. This standard index was called Standard Effective Temperature (SET*). How this rational index can be used to predict phasic sensations and thermal discomfort by cycling infrared radiation during increases in humidity was studied by Gonzalez and Gagge (1973). The experimental arrangement for exposing seated subjects to radiant heat was similar to earlier studies (Gagge and Hardy, 1967). Two infrared quartz heaters, fitted with shutters, were mounted at a 45° angle from the vertical and 2 meters from each side of the subject. The heaters were set at 7000 kW; this level caused the subject to receive an Effective Radiant Field (ERF) of 70 W/m^2 when the shutters were open, equivalent to raising the mean radiant temperature (T_r) by approximately 14 °C or the operative temperature (T_o) by approximately 9 °C above the T_a. The T_{db} was held constant near 32 °C. At τ=0 (experimental time), the subject had been in the chamber at least 15 min and had begun sweating lightly, while the instrumentation was adjusted. At this time, the radiant heat cycling pattern was initiated: 3 min on and 2 min off. During this cycling process, test observations were made just prior to radiant heat "on", after 2 min of exposure to radiant heat, and after one minute of no radiant heat. During the cyclic radiant heat the ambient vapor pressure was raised continuously from 8 Torr to 35 Torr.

Figure 9 shows the relationships between the discomfort index and physiological and physical measurements. The square-wave pattern for T_o and T_a represents the periods when the shutters were opened and closed. $\bar{T}_{sk}$ is also plotted on the same ordinate scale. The lower curves of Figure 9 show the relative changes in vapor pressure and ET* during the cyclic experiment. Discomfort, skin wettedness, skin, and rectal temperatures all show a progressive increase as the humidity rose.

Figure 10 shows the relationship between warm discomfort and skin wettedness as well as mean skin temperature $\bar{T}_{sk}$. Discomfort rose linearly with increasing skin wettedness for observations both with and without heating. The discomfort observations during radiant heat rose at approximately twice the rate of those without radiant heat in terms of changes in mean skin temperature, $\bar{T}_{sk}$.

Figures 10a and 10c relate discomfort to the ET* Index.

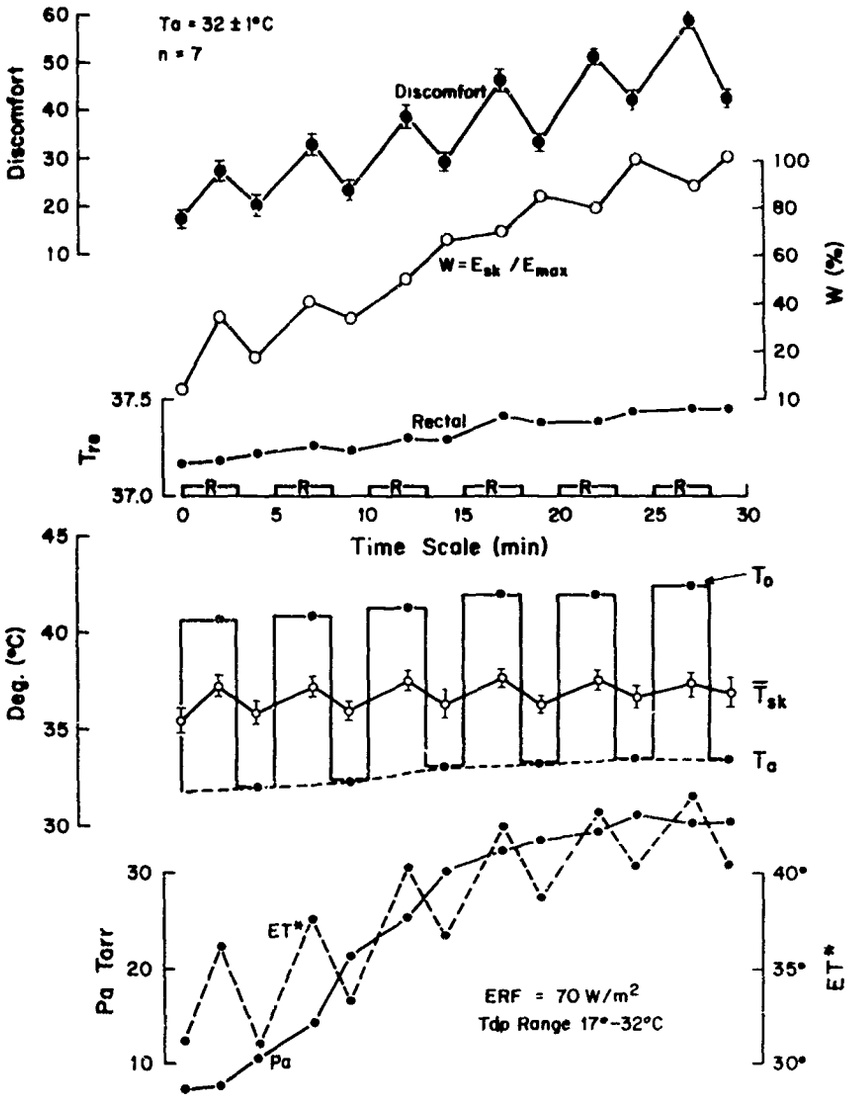

Figure 9. Variation with time of magnitude estimates of discomfort, skin wettedness (w), average skin temperature ($\bar{T}_{sk}$), and rectal temperature during changes in operative temperature (T_o) caused by infrared radiation (ERF) and rising ambient vapor pressure (P_a). Changes in effective temperature (ET*) are also shown. (From data in Gonzalez and Gagge, 1973.)

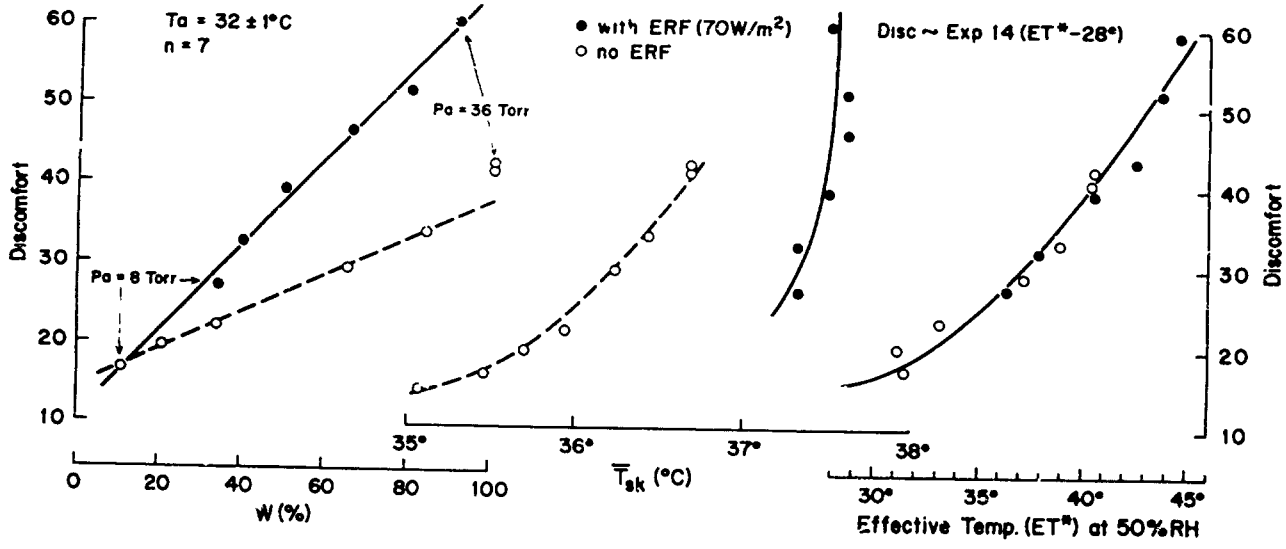

Figure 10. Warm discomfort as a function of % skin wettedness (w), mean skin temperature ($\bar{T}_{sk}$), and effective temperature (ET*). Data taken from Fig. 9.

Both of these curves show that thermal discomfort may be predicted by use of the ET* Index and the curves are described by the general power relation (cf. Chapter 9)

$$\text{Discomfort} \sim \exp \beta\ (ET^* - ET^*_n),$$

where β is the exponent of the power function and ET^*_n is the effective temperature at physiological thermoneutrality. The value of β for the radiation data is 1.4 when an ET^*_n value of 28 °C is used as the threshold.

Gonzalez, *et al.* (1974) reported data taken on clothed and unclothed sedentary subjects in both warm and cold environments in which thermal discomfort was assessed by magnitude estimation and compared with $\overline{T}_{sk}$ and w. In warm environments (ERF = 40 to 70 W/m^2), T_a and P_a were independently varied; in cold environments, only T_{db} was varied. Discomfort estimates, observed for various clothing insulations, humidity, and operative temperature, were compared to the Standard Effective Temperature (SET*) as shown in Figure 11. In the cold, $\overline{T}_{sk}$ is the principal input. Cold discomfort is a linear function of (25-SET*) in °C. In terms of SET*, warm discomfort displays a function of (SET*-25) to a power in the range of 1.5 to 2.0.

SET* is therefore a suitable temperature scale to describe the effects of the thermal environment on resting man. It is important to recognize that the extremities of the body during sedentary activity do not produce enough heat to maintain normal temperature in these sites; their local skin temperature is a major input in discomfort. The heat comes from the core of the body. During exercise, however, active muscle masses may increase their heat production by some 10 times the resting level increasing internal conduction thereby. The result is that changes in skin blood flow (K_s) (see Chapter 13) during exercise will provide an important addition to changes in the comfort thresholds shown in Figures 10 and 11.

CONCLUSIONS

This chapter highlights some biophysical and physiological variables important to our understanding of human responses to infrared radiation. Yet, there are many other aspects of the field which are fundamentally important but could not be adequately covered here. These include the following research areas which need fuller study.

Our understanding of pain and temperature sensation at

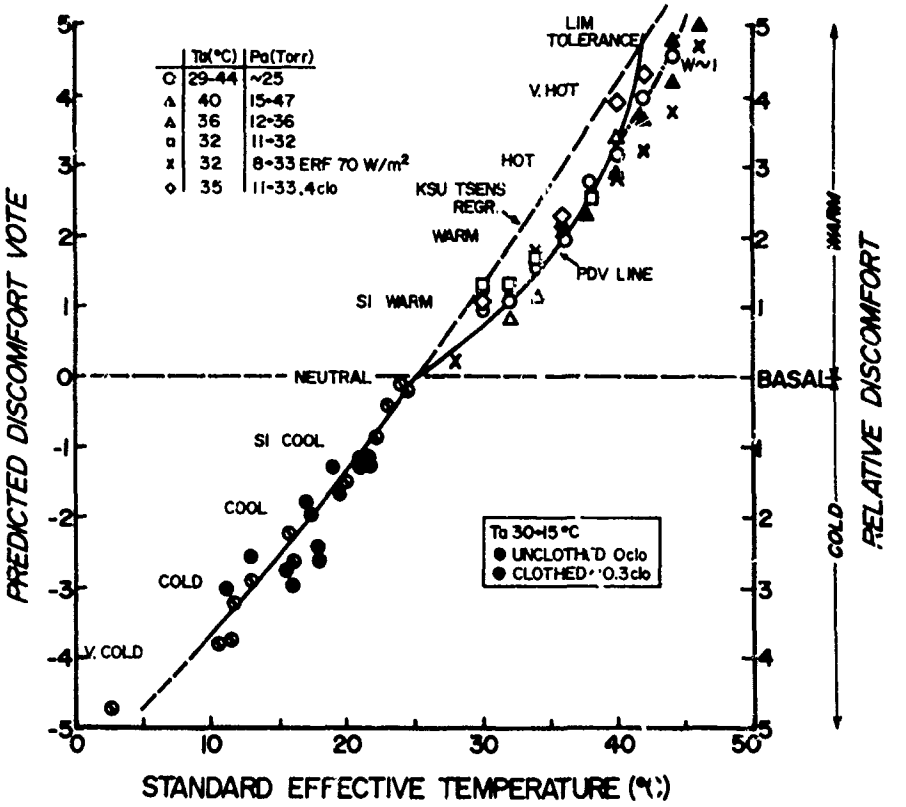

Figure 11. Relation of predicted discomfort and actual discomfort votes to various complex environments, normalized by standard effective temperature (°C). (From data in Gonzalez, *et al.*, 1974.)

the neurophysiological level is still limited. For example, Boulant and Gonzalez (1977) showed in rabbits that warm peripheral temperatures decreased markedly the thermosensitivity of heat loss (panting) responses to changes in preoptic temperature. These latter responses parallel similar neuronal responses occurring in hyperthermic conditions (Hensel, 1981) which suggest a common competitive link between peripheral excitatory afferents and local excitatory (preoptic) influences in the control of thermoregulatory heat loss. If true, this result could explain the close association of estimates of discomfort with efferent drive for thermal sweating shown in Figure 8 and in earlier studies by Gagge, *et al.* (1969).

Hendler and Hardy (1960) first pointed out for infrared heating that the rate of change of skin temperature (dT_s/dt) has a minimal effect in eliciting thermal sensation. Also interesting is the remarkable after-sensation felt with heating at the pricking pain threshold (800 mW/cm^2). These effects could possibly be attributed to slow kinetics of excitatory transmitters (a neuropeptide?) from nociceptive afferents, suggesting a biochemical mediator of pain and thermal discomfort. Some modulators of the perception of pain have been linked to pituitary endorphins (Holaday, *et al.*, 1978).

Studies on the effects of non-thermal stimulation (pressure), which has been shown to affect sweating (Ogawa, *et al.*, 1980), need to be pursued during phasic exposures to ERF and during heat acclimation.

Marks and Gonzalez (1974) showed that thermal radiation affects hedonic estimates as warm intensity increases (Figure 7). More intense radiation at a given ambient temperature above the comfort zone makes a person warmer and creates diverse behavioral responses (irritability, aggressiveness). It is important to assess what occurs during whole-body assymetric thermal radiation since assymetric radiant fields have a strong hedonic influence (e.g., basking in the sun, warm fireplaces, etc.). Some recent studies (McIntyre, 1976; Fanger, *et al.*, 1981; Olesen and Nielsen, 1981) have added to this understanding. Limits as high as 17 °C by clothed individuals but 11 °C by unclothed subjects have been tolerated. However, measurements of skin blood flow or skin heat flow have yet to be made during assymetric radiation.

Finally, the single and consistently reliable physical-physiological index of warm discomfort is still skin wettedness. Yet, how this signal is transduced and conveyed to the consciousness (whether by mechanical deformation or hydration of skin receptors) ~~(Figure 8)~~ still eludes thermobiologists.

ACKNOWLEDGMENTS

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REFERENCES

Adair, E.R. (1977). Skin, preoptic, and core temperatures influence behavioral thermoregulation. *J. Appl. Physiol.* 42: 559.

Allnutt, M.F., and Allan, J.R. (1973). The effects of core temperature elevation and thermal sensation on performance. *Ergonomics* 16: 189.

Arens, E., Gonzalez, R., Berglund, L.G., McNall, P.E., and Zeren, L. (1980). A new bioclimatic chart for passive solar design. *Proc. Amer. Soc. Intl. Solar Energy.* 5: 1202.

Benzinger, T.H. (1963). Peripheral cold-and central warm reception, main origins of human thermal discomfort. *Proc. Nat. Acad. Sci.* 49: 832.

Berglund, L.G., and Gonzalez, R.R. (1977). Evaporation of sweat from sedentary man in humid environments. *J. Appl. Physiol: Respirat. Environ. Exercise Physiol.* 42: 767.

Birkebak, R.C. (1966). Heat transfer in biological systems. *Int. Rev. Gen. Exp. Zool.* 2: 269.

Boulant, J.A. and Gonzalez, R.R. (1977). The effect of skin temperature on the hypothalamic control of heat loss and heat production. *Brain Research* 120: 367.

Bullock, T.H. and Diecke, F.P.J. (1956). Properties of an infra-red receptor. *J. Physiol. (London)* 134: 47.

Cabanac, M. (1969). Plaisir ou deplaisir de la sensation thermique et homeothermie. *Physiol. Behav.* 4: 359.

Chatonnet, J. and Cabanac, M. (1965). The perception of thermal comfort. *Int. J. Biometeorol.* 9: 183.

Fanger, P.O. (1972). *Thermal Comfort.* McGraw-Hill, New York.

Fanger, P.O., Banhidi, L., Oleson, B.W., Lankilde, I.G. (1980). Comfort limits for heated ceilings. *ASHRAE Trans.* 86: 259.

Gagge, A.P. (1937). A new physiological variable associated with sensible and insensible perspiration. *Am. J. Physiol.* 120: 277.

Gagge, A.P. (1966). Response of evaporative loss to high temperature radiant heat. *Fed. Proc.* 25: 400.

Gagge, A.P. (1970). Effective radiant flux, an independent variable that describes thermal radiation in man. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, J.A.J. Stolwijk, and A.P. Gagge, eds.), p. 34. C. Thomas, Springfield, Ill.

Gagge, A.P., and Hardy, J.D. (1967). Thermal radiation exchange of the human by partitional calorimetry. *J. Appl. Physiol.* 23: 248.

Gagge, A.P., Stolwijk, J.A.J., and Hardy, J.D. (1967). Comfort and thermal sensations and associated physiological responses at various ambient temperatures. *Env. Res.* 1: 1.

Gagge, A.P., Nishi, Y., and Gonzalez, R.R. (1972). Standard effective temperature - a single temperature index of temperature sensation and thermal discomfort. *Bld. Res. Bulletin.* 45: 1.

Gonzalez, R.R., and Gagge, A.P. (1973). Magnitude estimates of thermal discomfort during transients of humidity and operative temperature and their relation to the new ASHRAE effective temperature (ET*). *ASHRAE Trans.* 79: 88.

Gonzalez, R.R., Nishi, Y., and Gagge, A.P. (1974). Experimental evaluation of standard effective temperature: a new biometeorological index of man's thermal discomfort. *Int. J. Biometeor.* 18: 1.

Hardy, J.D. (1939). The radiating power of human skin in the infra-red. *Am. J. Physiol.* 127: 454.

Hardy, J.D. (1962). Physiological effects of high intensity infrared heating. *ASHRAE Journal* Nov: 19.

Hardy, J.D. (1971). Thermal comfort and health. *ASHRAE Journal* 13: 43.

Hardy, J.D., Goodell, H., and Wolff, H.G. (1951). The influence of skin temperature upon the pain threshold as evoked by thermal radiation. *Science* 114: 149.

Hardy, J.D. and Oppel, T.W. (1937). Studies in temperature sensation. III. The sensitivity of the body to heat and spatial summation of the end organ responses. *J. Clin. Invest.* 16: 533.

Hendler, E. and Hardy, J.D. (1959). Temperature Sensation. *ASME paper No. 58*, Aug: 69.

Hendler, E. and Hardy, J.D. (1960). Infrared and microwave effects on skin heating and temperature sensation. *IRE Trans. Med. Elect.* ME-7: 143.

Hensel, H. (1981). Neural Processes in long-term thermal adaptation. *Fed. Proc.* 40: 2830.

Holaday, J.W., Wei, E., Loh, H.H., and Li, C.H. (1978). Endorphins may function in heat adaptation. *Proc. Natl. Acad. Sci.* 75: 2923.

Marks, L.E., and Gonzalez, R.R. (1974). Skin temperature modifies the pleasantness of thermal stimuli. *Nature* 247: 473.

McIntyre, D.A. (1976). Radiant heat from lights, and its effect on thermal comfort. *Lighting Research and Technology.* 8: 121.

Mitchell, D. (1970). Measurement of the thermal emissivity of human skin *in vivo*. In *Physiological and Behavioral Temperature Regulation*. (J.D. Hardy, J.A.J. Stolwijk, and A.P. Gagge, eds.) p. 25. C. Thomas, Springfield, Ill.

Ogawa, T., Asayama, M. Ito, M. and Miyagawa, T. (1980). Dermatomal inhibition of sweating by skin pressure. In *Contributions to Thermal Physiology*. (Z. Szelenyi and M. Szekely, eds.) p. 413. Pergamon, N.Y.

Olesen, B.W. and Nielsen, R. (1981). Radiant spot cooling of hot working places. *ASHRAE Trans*. 87: 81.

Phillips, M. (1974). Electromagnetic Radiation. In *Encyclopedia Britannica* p. 644. W. Benton Publ., Chicago, Ill.

Piergallini, J.R. and Stoll, A.M. (1974). Optical Effects of pigmentation on temperature rise in a two-layer skin stimulant system during irradiation. *Aerospace Med*. 45: 485.

Planck, M. (1959). *The Theory of Heat Radiation*. Dover Publications, New York.

Sparrow, E.M. and Cess, R.D. (1966). *Radiation Heat Transfer*. Wadsworth Publ. Co., Belmont, California.

Stitt, J.T., Adair, E.R., Nadel, E.R., and Stolwijk, J.A.J. (1970). The relation between behavior and physiology in the thermoregulatory response of the squirrel monkey. *J. Physiol. (Paris)* 63: 423.

Winslow, C-E.A., Herrington, L.P. and Gagge, A.P. (1937). Physiological reactions of the human body to varying environmental temperatures. *Am. J. Physicl*. 120: 1.

BODY TEMPERATURE REGULATION DURING EUTHERMIA AND HYPERTHERMIA

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I. EUTHERMIA

A. Heat Balance Equation

Conservation of energy is the most important law for the study of thermoregulation. It is usually expressed in the following equation form and referred to as the heat balance equation (although work rate can enter into the equation):

$$M - W = R + C + E \pm S$$

On the left side of this equation, M is metabolic energy production and W is power or the rate at which useful work is performed by the body, if any. The strictest definition of work is used in the heat balance equation: that is, a force operating through a certain distance in the direction of the force. A man walking along level ground is not performing any work because of the absence of any force in the direction of motion. However, a person climbing stairs is performing work which is equal to his mass times the acceleration of gravity (the force) times the vertical height of the stairs. The difference between M and W in the heat balance equation is equal to heat production. Animals perform work with a low efficiency near 20-25% at best; i.e., if a subject performs a certain amount of work, then the metabolic production of the subject during the work

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performance would be at least four to five times larger than the amount of work performed.

The first three items on the right side of the heat balance equation are heat transfer terms which, under most conditions, represent heat losses from the body. R represents heat transfer due to radiation, C is that due to convection, and E is heat loss due to the evaporation of water. A detailed account of these heat transfer modes for humans is given by Gagge and Nishi (1977). All objects with a temperature above absolute zero emit electromagnetic radiation. This emission causes a net flow of heat from a warm object to a cool one. Heat transfer through conduction is usually insignificant under normal conditions. However, conduction combined with mass transfer forms the mode of heat transfer known as convection which is a significant form of heat transfer. Convection occurs when a cool fluid, usually air or water, surrounds a warmer object. The amount of heat removed by the fluid depends upon the temperature difference between the object and the bathing medium, and also the velocity of the fluid bathing the object. The third term, E, represents heat loss due to the evaporation of water. When water changes phase from a liquid to a gas at normal body temperature, nearly 600 cal/gm are required, the latent heat of vaporization. The body loses this amount of heat when water is evaporated from its surface. Water which diffuses through skin is constantly being evaporated along with water in the breath lost from respiratory surfaces. Evaporation depends on the difference between vapor pressures at the evaporative surface and of the ambient air. This is most important in hot environments when the temperature gradient between the body and the environment is small or even reversed. Such environments render radiation and convection useless as avenues of heat loss. Fortunately, evaporation can remove large amounts of heat, and sweating, wallowing and other methods of keeping the skin wet are effective in preventing dangerous increases in body temperature from occurring in hot environments.

Finally, the term S in the heat balance equation is the rate of heat storage. It is merely the difference between heat production on the left side of the equation and heat losses on the right side. Positive or negative heat storage can be directly related to an increase or decrease in body temperature by knowing the mass and the specific heat of the body. The aim of temperature regulation is to minimize S, to balance heat loss with heat gain, thereby maintaining body temperature at its normal value. This normal value for body temperature in man is cited by most people as 98.6 °F, but, in fact, there is a distribution of normal values. Ivy

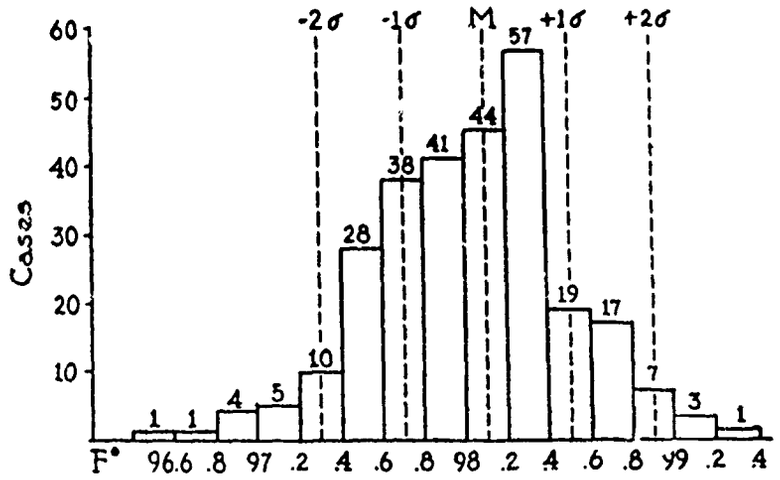

Figure 1. This frequency histogram shows the wide range of body temperature (oral temperature) found in normal, healthy individuals. M=mean temperature and σ=standard deviation. From Ivy (1944).

(1944) measured the temperature in a number of normal, healthy medical students. Figure 1 shows a histogram from his survey of these subjects. One can see that the average is 98.1 °F and the mode is 98.3 °F but there is also a wide variation from 96.5 to 99.3 °F. Although body temperature is, on average, a constant value, it is usually changing, a factor which accounts for some of the variation in normal body temperature. Long term observations of body temperature have revealed a number of periodicities. In an early study, Kleitman (1923) recorded the body temperature from subjects deprived of sleep. Figure 2 shows data from one such subject who endured 115 hours without sleeping. Clearly illustrated is a circadian rhythm in body temperature, with a maximal value occurring in the afternoon and a minimum, in the early morning. These data also showed that the daily rhythm was not due to periods of sleep because they persisted despite the elimination of sleep during the observational period, although insomnia seemed to attenuate the magnitude of this periodicity. There have been other body temperature oscillations reported such as those correlated with the rest-activity cycle which has a period of

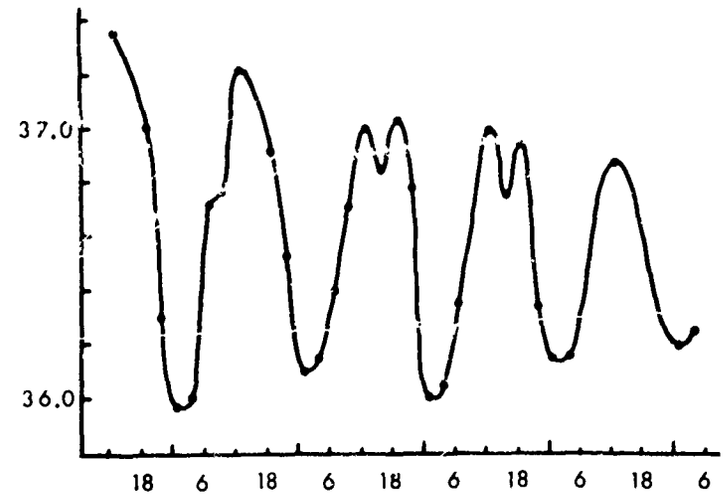

Figure 2. The prominent circadian rhythm in body temperature is illustrated by this 5 day record of oral temperature from a study by Kleitman (1923). The subject did not sleep during this experiment. Clock times of 0600 hr. and 1800 hr. are indicated along the abscissa. Body temperature (°C) is on the ordinate.

60-90 minutes in man, a periodicity in women which is coincident with the menstrual cycle, and seasonal variations.

B. The Thermoregulatory System

The thermoregulatory system seems to operate in a manner similar to an automatic negative feedback control system. A simplified diagram is shown in Figure 3. It contains a body whose temperature is regulated at a reference or set value. There are sensors to detect various temperatures of the body and a controller to integrate this sensory information and to control the effectors for heat production and heat loss. If a disturbance offsets body temperature from the set temperature, then the controller detects this change through the thermal sensors, and appropriate effector activity is elicited to bring body temperature back towards the desired level.

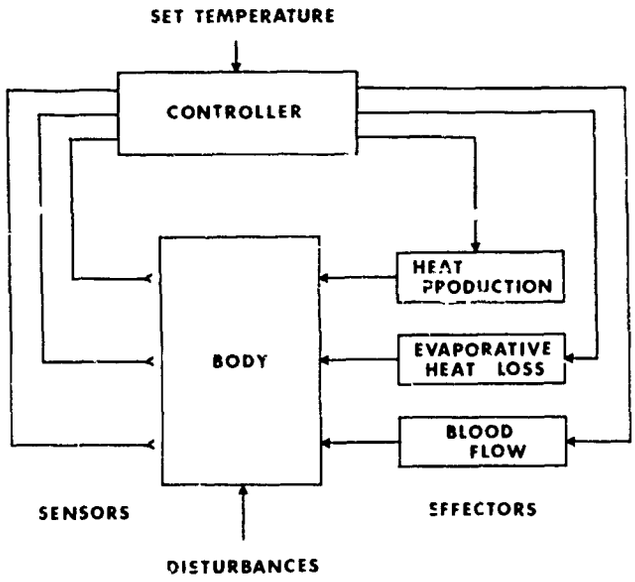

Figure 3. The thermoregulatory system is depicted here as a simple automatic control system. Thermodetectors sense various body temperatures and relay this information to a central controller. The controller processes the information and determines the appropriate effector activity to alleviate any disturbances and maintain body temperature within normal limits.

Effector activity depends upon the level of skin temperature and, thus, it has been reasoned that thermal sensors must exist which detect skin temperature. In fact, free nerve endings in the skin can be found which increase their activity to warming the skin, warm receptors, or to cooling the skin, cold receptors. Examples of such neurons are illustrated in Figure 4 which is taken from the work of Hensel and his coworkers (Hensel and Kenshalo, 1969; Hensel and Wurster, 1969). In this particular study, skin on portions of the nose of cats was either locally heated or cooled while recordings were taken from fibers in the infraorbital nerve which supplies this region. The average firing rates of these neurons are shown as a function of skin temperature. When the skin temperature was increased from a thermoneutral value (32-34 °C), warm fibers increased their impulse frequencies while cold fibers decreased theirs. Conversely, cold fibers increased their activity when the skin was cooled while the activity of the warm

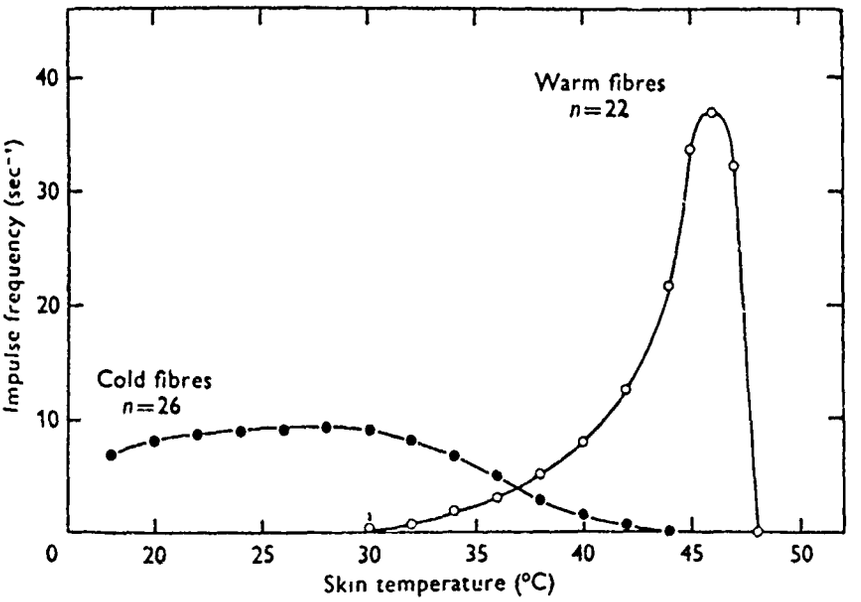

Figure 4. Neurons exist which alter their activities in response to changes in skin temperature. The curves above show the average impulse frequencies as a function of skin temperature for two populations - warm fibers and cold fibers. These data are from neurons innervating the nose of a cat (Hensel and Kenshalo, 1969).

fibers was suppressed. Mechanical stimulation of the same area did not elicit any neuronal activity indicating a specificity of these fibers to the thermal stimuli. Similarly, localized heating or cooling of the preoptic anterior hypothalamus evokes appropriate effector activity for heat loss or heat storage and, therefore, thermal sensors are thought to exist in this region. Again, neurons can be found which react to local heating or cooling. In an early study, Nakayama, *et al.* (1961) warmed the preoptic area of cats using radio frequency heating while recording from single neurons in the same area. As shown in Figure 5, single units were discovered whose activities increased simultaneously with rising hypothalamic temperature accompanied a few minutes later by polypnea, a heat loss response. Many other reports (for example, Nakayama, *et al.* 1963 ; Hellon, 1967; Cabanac, *et al.*, 1968) have since confirmed and established the presence of both warm-sensitive and cold-sensitive neurons in this region. The behavior of these neurons has led many to believe that these neurons are

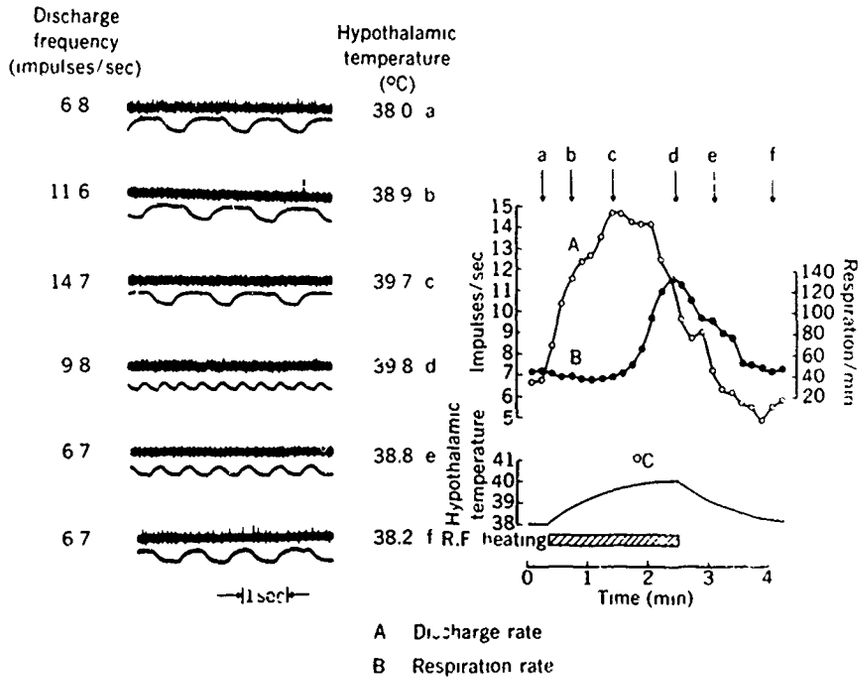

Figure 5. Localized radio-frequency heating of the preoptic/anterior hypothalamus causes polypnea, a heat loss mechanism, and an increase in the discharge rate of certain neurons residing in the same area of the brain. From Nakayama, T., Eisenman, J.S., and Hardy, J.D. (1961). Single unit activity of anterior hypothalamus during local heating. *Science* 134:560-561. Copyright 1961 by the American Association for the Advancement of Science. Reprinted by permission.

indeed the thermodetectors present in the preoptic area of the hypothalamus. Thermal sensors are also thought to exist elsewhere in the body such as the spinal cord (Simon, 1974), midbrain (Hensel, 1974), and viscera (Rawson and Quick, 1970). Unfortunately, there is still no direct proof that these thermally responsive neurons are actually the thermal sensors involved with thermoregulation.

The signals from the various thermal sensors are integrated by the controller for temperature regulation which in turn organizes the appropriate effector outputs. Early studies concerned with the central nervous system revealed that temperature regulation is compromised when hypothalamic tissue is destroyed and, thus, the controller for thermo-

regulation is thought to exist in this region. The most powerful inputs to the controller are apparently provided by the thermal information from the skin and the hypothalamus. The skin sensors are important because they can detect changes in the environment. For instance, if ambient temperature decreases, then heat loss from the skin is increased, leading to a reduction in its temperature. This occurrence evokes cutaneous vasoconstriction to reduce heat transfer from the body core to the skin through the circulation. In addition, shivering is induced if necessary, leading to increased heat production. On the other hand, hypothalamic sensors detect internal changes, the most common being the rise in body temperature during exercise due to the increased heat production from skeletal muscle. This rise elicits cutaneous vasodilation to carry heat from the core to skin, and it stimulates sweating to increase the transfer of heat from the skin to the environment. Together, peripheral and internal thermodetectors allow the controller to quickly and accurately regulate body temperature under most conditions.

How these two sets of thermoreceptors are integrated is of current interest. Recent experiments from our laboratory indicate a multiplicative interaction between the two. Figure 6 shows metabolic rates measured in rabbits at various skin and hypothalamic temperatures (Stitt, 1978). By varying ambient temperature, one can control skin temperature, and by employing chronically implanted, water perfused thermodes, one can set hypothalamic temperature as desired. The three lines represent constant values of mean skin temperature as indicated. Each line has a different slope, increasing with decreasing skin temperature, and all lines appear to converge at the same point. Such an arrangement can be modelled by the multiplicative interaction shown by the equation in Figure 6. Another study (Stitt, 1976) revealed that a heat loss effector mechanism, respiratory evaporative heat loss in rabbits, also displayed a multiplicative interaction. Other researchers have also argued for a multiplicative interaction (e.g., Jacobson and Squires, 1970). However, there are some who have argued for an additive integration of skin and hypothalamic information by the regulator of body temperature (Hammel, *et al.*, 1963; Hellstrøm and Hammel, 1967); the debate continues.

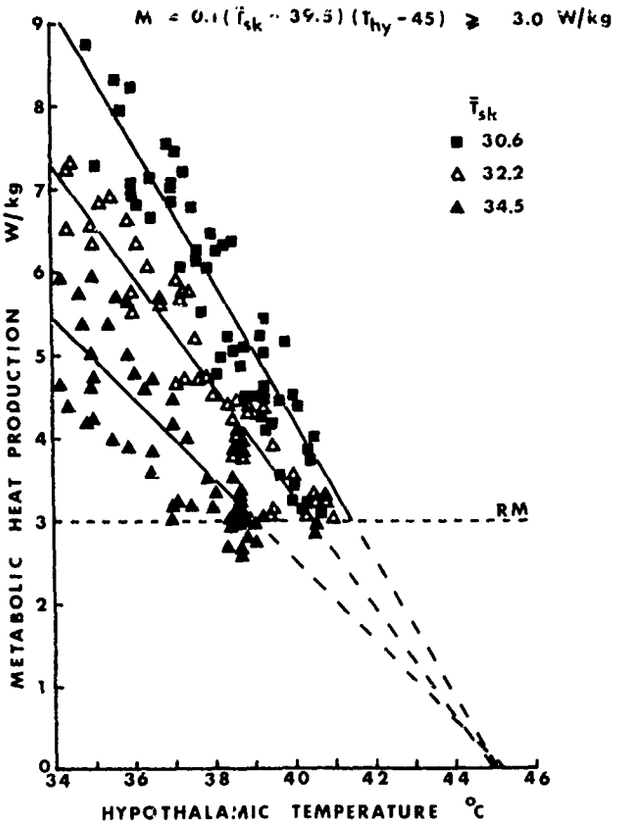

Figure 6. Metabolic heat production (in watts/kg) in rabbits is shown for different hypothalamic temperatures (Thy) at three levels of mean skin temperature ($\bar{T}$sk) indicated by the symbols. Least squares regression analysis of the data produces three converging lines which can be modelled by the multiplicative equation shown in this figure. This model sets resting metabolic rate (RM) as 3.0 W/kg. From Stitt (1978).

II. HYPERTHERMIA

Hyperthermia is the condition where body temperature is elevated above normal values. Referring back to the heat balance equation, hyperthermia ensues when heat production

exceeds heat loss leading to the storage of heat and a rise in body temperature. If this imbalance is not corrected, body temperature will continue to rise resulting in heat stroke, then death. There are many ways for such an imbalance to occur. For instance, a hot, humid environment can overwhelm the cooling power of radiation, convection, and evaporation, leading to hyperthermia. In some cases the function of heat loss effector mechanisms might be impaired due to autonomic nervous system dysfunction or certain types of drug therapy. Thus, if sweating or cutaneous vasodilation were unable to increase as they would normally in response to a warm environment, then body temperature would rise. Two common forms of hyperthermia are the hyperthermia of exercise and fever. During exercise, increased heat production creates a temporary imbalance between heat gain and heat loss. This causes a higher-than-normal body temperature throughout the exercise period. Fever is a specialized case of hyperthermia which is usually associated with illness and infection.

A. Exercise

Exercise produces a condition where the thermoregulatory system must operate in the presence of an internal disturbance. When a proportional negative feedback control system encounters such a disturbance, the system generally operates with an offset in its regulated variable. Apparently this happens during exercise. Figure 7 shows how this increment in body temperature is generated. Heat production rises immediately and produces a temporarily large rate of heat storage. Rising body temperature generates a negative error signal, -e. This increasing signal drives heat loss mechanisms at an ever-increasing rate until heat loss equals heat production. When a balance is attained, body temperature will equilibrate in a state of hyperthermia. This elevated body temperature is maintained as long as exercise generates an increased level of heat production.

The analysis in Figure 7 assumes that exercise affects body temperature only by creating internal heat. Exercise does not change the "set point" or the normal operation of the thermoregulatory system. Nielsen and Nielsen (1965) provided experimental evidence that these assumptions are valid, at least for moderate levels of exercise. These researchers used short wave diathermy to deposit heat in the deep tissues of the torso in human subjects. The same subjects also exercised on a cycle ergometer at a work rate which was adjusted so that the heat production during

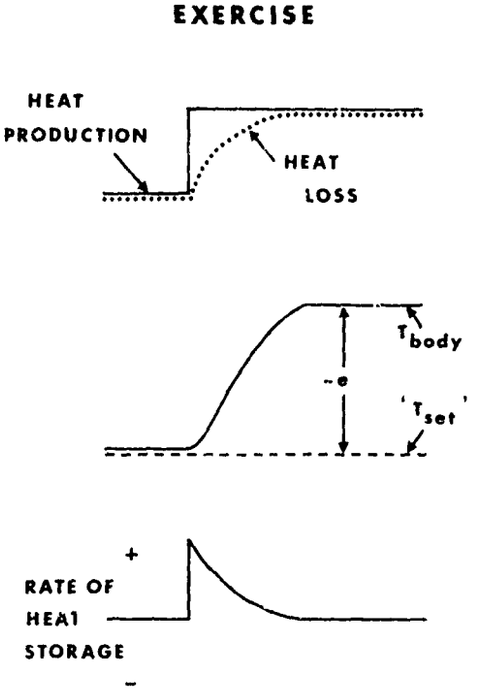

Figure 7. The events leading to a rise in rectal temperature during exercise. Hyperthermia is caused by the sustained increase in heat production during exercise. The set temperature appears to remain unchanged during exercise. From Stitt (1979).

diathermic heating and cycling was equal (almost 400 kcal/hr which is approximately 5 times basal levels). During steady state conditions, Nielsen and Nielsen found that rectal temperature increased by the same amount in both procedures. Similar thermal conductances indicated that skin blood flow increased equally during diathermy and exercise. Finally, the two procedures resulted in only a small difference in sweat rates. Since they altered body temperature and thermoregulatory effector mechanisms in a similar manner, exercise and diathermic heating appeared to be equivalent disturbances.

It is difficult to imagine that diathermy or exercise can affect body temperature regulation in a nonthermal manner. More likely, diathermy and exercise produce similar responses because they both effect changes in thermoregulation only by generating internal heat. Low frequency microwaves

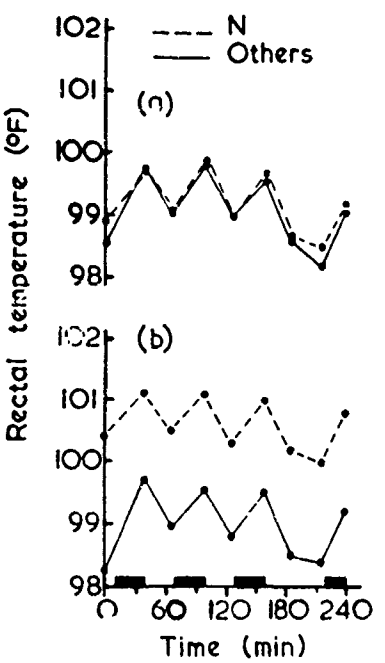

Figure 8. An early observation by Macpherson (1959) of body temperature regulation during fever. Subjects exercised (climbed steps) during the bars above the time axis and rested in between. Rectal temperature for subject N is shown (a) before and (b) during a febrile respiratory illness. The other subjects were healthy in both cases. Although rectal temperature for N was elevated during fever, it responded to the exercise regimen in a manner similar to the others. During fever, temperature regulation appears to occur normally, except at an elevated level.

which deposit heat in deep tissues of the body are probably not unlike the shortwaves used for diathermic heating by Nielsen and Nielsen. Thus, one might expect that the steady state thermoregulatory response to irradiation by microwaves of this type would be the same as that produced by diathermic heating and moderate exercise, all represented by the analogy in Figure 7.

B. Fever

By contrast, fever increases the level at which body temperature is regulated. During fever, the behavior of the thermoregulatory system is consistent with an elevation of its set temperature. The febrile temperature is defended against disturbances as it is during regulation in the afebrile condition. Figure 8 shows one of the earliest demonstrations of this point in man. Macpherson (1959) had been conducting long term experiments involving soldiers who were on a daily regimen of alternating exercise and rest periods. By chance, one subject, N, contracted a febrile illness during the course of the study, but insisted upon performing the experimental procedures. Figure 8(a) compares the response of rectal temperature for subject N while healthy with the mean values of rectal temperature for the other subjects in the study. Rectal temperature for N rose during exercise periods and fell during rest periods in a manner almost identical to the others. Figure 8(b) makes the same comparison when N was in the febrile state. Rectal temperature was 2 °F above that for the other subjects. However, when the exercise bouts were performed, N's rectal temperature again rose and fell in a manner similar to the others, except at a higher level. Thus, temperature regulation during exercise was not impaired by fever.

How is the elevated body temperature of fever attained? This depends upon the thermal environment and the potency of the fever. Heat losses are first reduced to a minimum. If this action does not provide an adequate rate of heat storage, then heat production rises. Figure 9 depicts an experiment which demonstrates different ways a fever can be achieved. Intravenous injections of leukocyte pyrogen (LP) produced fever in a rabbit, first in a warm environment, and then in a cold one. In addition to rectal temperature, Figure 9 also displays metabolic heat production (M), ear blood flow (EBF), and respiratory evaporative heat loss (E_{res}). At the high ambient temperature, the animal was obliged to vasodilate (high EBF) and pant (high E_{res}) to remain in thermal balance. LP produced fever by suppressing the elevated activity of these heat loss mechanisms. However, in the cold environment, heat loss mechanisms were minimized to maintain body temperature. When LP was injected in the cold, heat losses could not be further reduced. Instead, increased heat production was the only way to raise body temperature, and, thus, the rabbit shivered vigorously. These experiments show that once a pyrogen displaces the set temperature, the controller for thermoregulation utilizes any appropriate effector

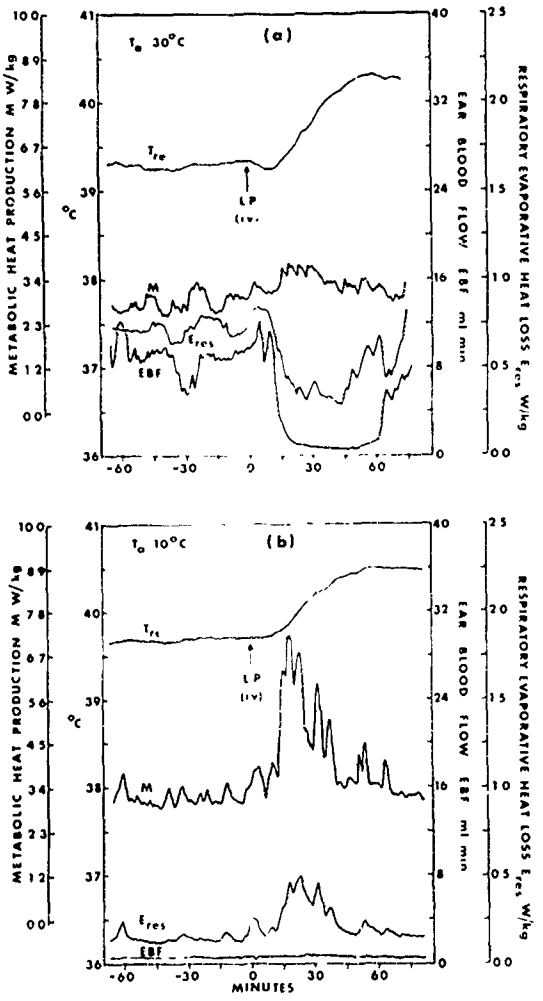

Figure 9. Identical doses of leukocyte pyrogen (LP) were injected into a rabbit to produce fevers in an ambient temperature (Ta) which was hot (a) and one which was cold (b). Although the change in rectal temperature (Tre) was about the same in both cases, the thermoregulatory effector mechanisms utilized to raise rectal temperature were different. In the hot environment, heat loss mechanisms - ear blood flow (EBF) and respiratory evaporative heat loss (Eres) - were suppressed, leading to heat storage. However, in the cold environment, heat production (M) was increased, again leading to heat storage. From Stitt (1979).

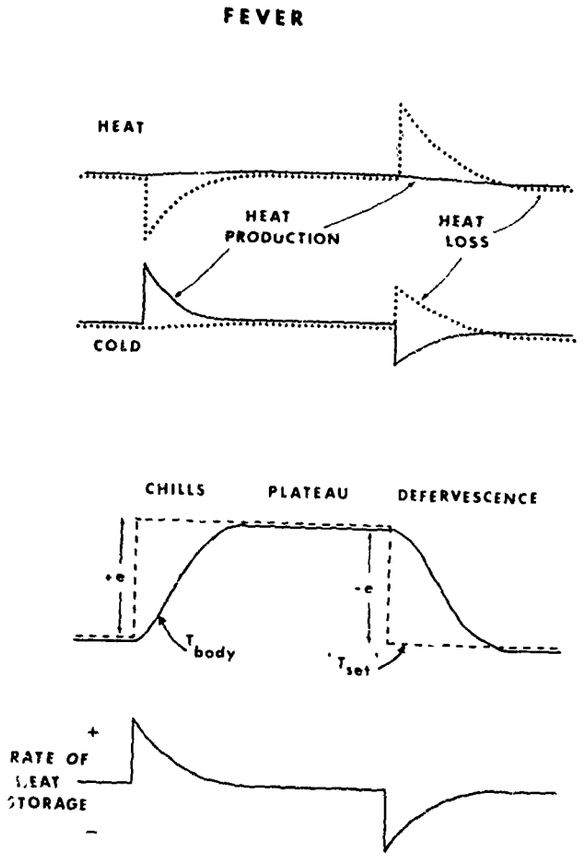

Figure 10. The events occurring during a fever. The primary cause of fever is an increase in the set temperature which leads to a temporary increase in heat storage. During defervescence, set temperature returns to normal. This leads to negative heat storage and return of body temperature back to normal. As seen in Figure 9, the mechanisms used to generate a fever depend upon the ambient temperature. Decreased heat loss produces fever in the heat; increased heat production produces fever in the cold.

mechanisms available to raise body temperature.

The events which produce fever and those which terminate it are illustrated in Figure 10. When a circulating pyrogen affects the central nervous system, the set temperature (shown in the third panel as a dashed line) is elevated. Because body temperature is below this new set point, a large error signal, e, is generated which activates effectors to increase body temperature. This is the "chill" phase of a fever. It is characterized by pallor, indicative of cutaneous vasoconstriction, and intense shivering. This effector activity leads to heat storage and a rapid elevation of body temperature to the febrile level whereupon the "plateau" phase begins. At this stage, the error signal has been eliminated, effector activity is close to the level existent before fever, and normal regulation now occurs at this new and higher level. The plateau phase is maintained until either the illness runs its course or an antipyretic drug is administered after which the fever breaks and the "crisis" phase begins. The set temperature reverts back to its normal value, but actual body temperature is still at febrile levels. Thus, a large negative error signal, -e, is now produced which drives heat loss mechanisms. Profuse sweating occurs along with cutaneous vasodilation, bringing about a large heat loss (negative heat storage) which rapidly returns body temperature to the normal level.

C. Differences Between Exercise and Fever

Even though the final temperature attained during fever and during the hyperthermia of exercise might well be the same, there are obvious differences between the two states. The febrile person will appear normal with no heat dissipating mechanisms active (assuming a thermoneutral environment). Conversely, the exercising person will exhibit sweating and cutaneous vasodilation: these are active heat loss mechanisms which are counteracting the increased heat production of exercise. A febrile person initially feels cold, then thermally comfortable during the plateau phase, while an exercising person will report a sensation of warmth or overheating. In addition, there is a difference in the temperature which is judged as comfortable or pleasant. This can be illustrated by the following experiments. Figure 11 presents an experiment where a squirrel monkey was allowed to select ambient air at a temperature of either 10 or 50 °C before and after an injection of prostaglandin E_1 (PGE_1), a pyrogenic substance when administered directly into the brain. The PGE_1 injection not only caused an

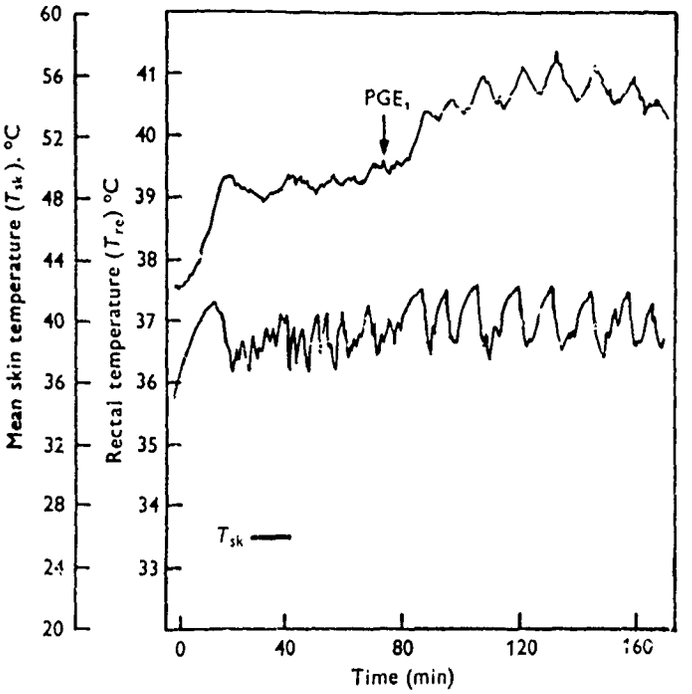

Figure 11. This experiment demonstrates that fever increases the preferred temperature chosen by a monkey. The monkey was trained to select as it wished either 10 °C ambient air or 50 °C ambient air. The monkey's selections produced a mean skin temperature averaging about 38 °C before fever. Injection of prostaglandin (PGE_1) into the hypothalamus produced a fever and increased the amount of hot air chosen by the animal. This action led to an increase in mean skin temperature, averaging about 40 °C during the fever. Mean skin temperature which was controlled by the monkey itself rose during fever. From Crawshaw and Stitt (1975).

increase in rectal temperature, but it also produced a rise in mean skin temperature because the monkey had selected more warm air than it had before the fever. Thus, fever causes a hyperthermia accompanied by an *increase* in the preferred temperature. On the other hand, Figure 12 shows an experiment where a human subject had his hand inserted into a water perfused glove. The subject was instructed to adjust the water temperature to that temperature which felt pleasant, before and during an exercise period. This figure shows that exercise induced both a rise in esophogeal temperature and a fall in the temperature of the glove

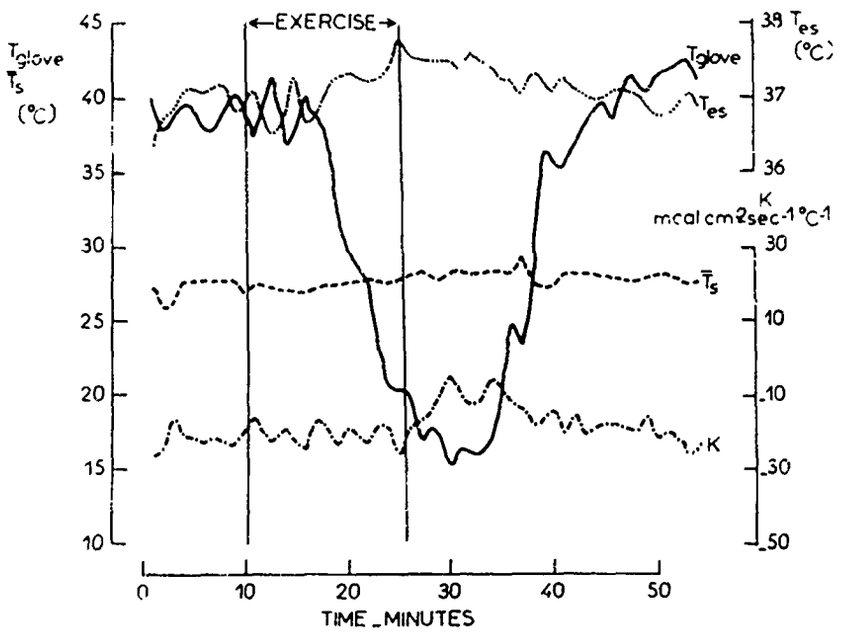

Figure 12. During this experiment a subject wore a water perfused glove and was instructed to maintain a comfortable glove temperature by controlling water temperature. Glove temperature (Tglove), esophogeal temperature (Tes), mean skin temperature ($\bar{T}s$), and the thermal conductance of the palm (k) were measured before, during, and after exercise (bicycle ergometer). During the second half of the exercise period, the temperature (Tglove) selected by the subject fell as body temperature rose. Conversely, Tglove gradually rose during the recovery period as body temperature returned to normal. The hyperthermia of exercise produces a decrease in the preferred temperature. From Cabanac, M., Cunningham, D.J., and Stolwijk, J.A.J., (1971). Thermoregulatory set point during exercise: a behavioral approach. *J. comp. physiol. Psychol.* 76:94-102. Copyright 1971 by the American Psychological Association. Reprinted by permission of the publisher and author.

perfusion water. The subject selected progressively cooler water as his body temperature rose due to the exercise. Contrary to fever, exercise produced hyperthermia which was accompanied by a *decrease* of the preferred temperature.

III. SUMMARY

In this paper we have presented a few fundamental principles which are essential for an understanding of how microwaves might affect body temperature regulation. Application of the heat balance equation requires an accounting of all heat losses and heat gains. Thus, experimental measurements of these two processes are usually required to explain any thermoregulatory response. Knowledge of the individual elements of the thermoregulatory system and their integrative operation is imperative. Without such information one cannot hope to analyze or predict the consequences of microwave irradiation, or to separate simple heating effects from possible nonthermal effects. Finally, we have tried to emphasize that hyperthermia can be produced in different ways. Thus, there may be several forms of microwave hyperthermia, differing in their causality. Deposition of microwave energy in deep tissues might produce a response similar to exercise hyperthermia. On the other hand, microwaves with a higher frequency which are absorbed by skin might produce another type of response, perhaps similar to that produced by exposure to extremely high ambient temperatures. And it is not impossible that certain microwaves could disturb neural elements in the central nervous system, leading to thermoregulatory dysfunction and hyperthermia.

ACKNOWLEDGMENTS

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REFERENCES

Cabanac, M., Cunningham, D.J. and Stolwijk, J.A.J. (1971). Thermoregulatory set point during exercise: a behavioral approach. *J. Comp. Physiol. Psychol.* 76:94.

Cabanac, M., Stolwijk, J.A.J., and Hardy, J.D. (1968). Effect of temperature and pyrogens on single-unit activity in the rabbit's brain stem. *J. Appl. Physiol.* 24:645.

Crawshaw, L.I., and Stitt, J.T. (1975). Behavioural and autonomic induction of prostaglandin E_1 fever in squirrel monkeys. *J. Physiol. London.* 244:197.

Gagge, A.P. and Nishi, Y. (1977). Heat exchange between human skin surface and thermal environment. In *Handbook of Physiology. Reactions to Environmental Agents* (D.H.K. Lee, H.L. Falk, and S.D. Murphy, eds.). sect. 9, p. 69, *Am. Physiol. Soc.*, Bethesda, MD.

Hammel, H.T., Jackson, D.C., Stolwijk, J.A.J., Hardy, J.D., and Strømme, S.B. (1963). Temperature regulation by hypothalamic proportional control with an adjustable set point. *J. Appl. Physiol.* 18:1146.

Hellon, R.F. (1967). Hypothalamic neurons responding to temperature in conscious rabbits. *J. Physiol. London.* 193:381

Hellstrøm, B. and Hammel, H.T. (1967). Some characteristics of temperature regulation in the unanesthetized dog. *Am. J. Physiol.* 213: 547.

Hensel, H. (1974). Thermoreceptors. *Ann. Rev. Physiol.* 35:233.

Hensel, H. and Kenshalo, D.R. (1969). Warm receptors in the nasal region of cats. *J. Physiol. London.* 204:99.

Hensel, H. and Wurster, R.D. (1969). Static behavior of cold receptors in the trigemimal area. *Pflügers Arch. ges. Physiol.* 313:153.

Ivy, A.C. (1944). What is normal or normality? *Quart. Bull. Northwestern Univ. M. School* 18:22.

Jacobson, F.H. and Squires, R.D. (1970). Thermoregulatory responses of the cat to preoptic and environmental temperatures. *Am. J. Physiol.* 218:1575.

Kleitman, N. (1923). Studies on the physiology of sleep. I. The effects of prolonged sleeplessness on man. *Am. J. Physiol* 66:67.

Macpherson, R.K. (1959). The effect of fever on temperature regulation in man. *Clin. Sci.* 18:281.

Nakayama, T., Eisenman, J.S., and Hardy, J.D. (1961). Single unit activity of anterior hypothalamus during local heating. *Science* 134:560.

Nakayama, T., Hammel, H.T., Hardy, J.D., and Eisenman, J.S. (1963). Thermal stimulation of electrical activity of single units in the preoptic region. *Am. J. Physiol.* 204:1122.

Nielsen, B. and Nielsen, M. (1965). Influence of passive and active heating on the temperature regulation of man. *Acta Physiol. Scand.* 64:323.

Rawson, R.O. and Quick, K.P. (1970). Evidence of deep-body thermoreceptor response to intra-abdominal heating of the ewe. *J. Appl. Physiol.* 28:813.

Simon, E. (1974). Temperature regulation: the spinal cord as a site of extrahypothalamic thermoregulatory functions. *Rev. Physiol. Biochem. Pharmacol.* 71:1.

Stitt, J.T. (1976). The regulation of respiratory evaporative heat loss in the rabbit. *J. Physiol. London.* 258:157.

Stitt, J.T. (1978). Hypothalamus and Thermoregulation. Control of metabolic heat production and the determinants of a normal regulated body temperature in rabbits in the cold. In *Current Studies of Hypothalamic Function. Metabolism and Behavior* (W.L. Veale and K. Lederis, eds.) Vol. 2, p. 44, S. Karger, New York.

Stitt, J.T. (1979). Fever versus hyperthermia. *Fed. Proc.* 38:39.

CENTRAL NERVOUS MECHANISMS REGULATING BODY TEMPERATURE

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INTRODUCTION

Microwave radiation generates heat in tissues, and therefore body temperatures and thermoregulatory responses are variables of primary interest to those conducting research on the effects of microwave irradiation on animals. However, the vertebrate thermoregulatory system is extremely effective in maintaining thermal homeostasis of the body in the face of extreme and varied thermal stresses. Therefore, the effects of microwave irradiation cannot be evaluated on the simple basis of a change in some body temperature; the integrated response of the thermoregulatory system must be considered. The microwave biologist should have an appreciation for the relationships between changes in various body temperatures and the compensatory responses of thermoregulatory effectors. Such an appreciation can only be enhanced by an understanding of the central nervous system (CNS) integrative mechanisms underlying these relationships between stimuli and responses. In this chapter I shall discuss current concepts of the organization of the central nervous thermoregulatory system. I shall pay particular attention to features of the system which may present special problems or opportunities for biologists studying the effects of microwave radiation on organisms.

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REPRESENTATION OF BODY TEMPERATURE TO THE CNS

The influence of microwave irradiation on inputs to the thermoregulatory system will depend on the distribution of energy deposition in the body and the distribution of thermal sensitivity in the body. Let's assume that the microwave engineer can model the deposition of energy. What quantitative information do we have on the organization of thermal sensitivity?

The thermal status of tissues is transduced into neural signals at many locations in the body. Let's begin with the skin. The skin is well supplied with undifferentiated, unmyelinated endings of small myelinated fibers which are sensitive to either warm or cold (cf. Figure 4, Chapter 7). Both classes of cutaneous thermoreceptors are characterized by phasic responses to changes in temperature as well as rates of static firing which are directly proportional to temperature in the case of warm receptors and inversely proportional to temperature in the case of cold receptors. These receptors do not respond to mechanical stimuli. There have been several recent reviews of cutaneous thermoreceptors (Iggo, 1969; Hensel, 1976, 1981; Necker, 1982). For our purposes it is sufficient to note that the CNS receives abundant information about the actual temperature of skin surfaces and also about any changes which occur in skin temperatures. But the important issues in the context of microwave exposure are the relative representations of different skin areas to the central regulatory system and the weighting of these inputs relative to inputs from thermosensors deep in the body. As we might expect, the representation of peripheral temperatures in the control of thermoregulatory responses is not simply proportional to the area of the skin surface stimulated nor are the inputs from cold and warm receptors strictly symmetrical.

The most dramatic localized thermosensitivity has been demonstrated in the scrotum of rams (Waites, 1962; Hales, *et al.*, 1971) and pigs (Ingram, *et al.*, 1972). In most mammals and birds it is difficult to stimulate thermal polypnea or panting by a generalized heating of the skin if deep body temperature remains normal. However, heating of the scrotum of rams and pigs to slightly above 40 °C stimulated polypnea in spite of a gradual fall in deep body temperature. These studies also showed that an increased thermogenesis stimulated by low overall skin temperatures could be suppressed by heating of the scrotum. The high thermosensitivity of the scrotum may be a very special adaptation related to the

influence of high temperatures on spermatogenesis. Normally the immediate response to overheating of the scrotum is a relaxation of the scrotal musculature so that the scrotum and the testes are cooled convectively. In the artificial situation of thermal stimulation of the scrotum, or perhaps whole body exposure to microwave radiation, the relaxation of the scrotal musculature is not an effective local thermoregulatory response, and a large input to the central thermoregulatory system results. Therefore, the effect of whole body microwave radiation on the temperature of the testes may result in a thermal stimulation out of proportion to the induced rise in overall skin and body temperature.

Other less specialized skin areas are also weighted differentially relative to the influence of their temperatures on thermoregulatory responses. An excellent example comes from the work of Necker on pigeons (1977). The beak of the pigeon has numerous cold receptors (Necker, 1972); nevertheless, heating and cooling the beak and the nonfeathered skin of the legs are very ineffective in modulating ongoing shivering induced by a lowered body temperature. In contrast, heating and cooling feathered skin areas have strong influences on shivering. Per unit area, back skin is the most sensitive, followed by wing skin, and then skin of the breast.

Man is the only other species for which the thermosensitivity of different skin areas has been quantified in terms of influence on thermoregulatory responses. The measured response variable was sweating rate as influenced by radiant warming (Nadel, *et al.*, 1973) or cooling (Crawshaw, *et al.*, 1975) of specific skin areas. The results of these studies are shown in Table I. The facial skin is about 3 times more sensitive to warm or cool stimuli than the skin covering either trunk or extremities, and it appears to be approximately equally sensitive to warming or cooling. For the trunk and extremities an asymmetry in sensitivity to warming or cooling is apparent. The extremities are more sensitive to cooling and the trunk is more sensitive to warming. These results have been confirmed in psychophysical studies of warmth sensation in different body regions (cf. Chapter 9).

Deep body temperatures also play a role in stimulating thermoregulatory responses. Classically, the hypothalamus, particularly the preoptic and anterior hypothalamic nuclei, and the spinal cord have been considered important inputs to the thermoregulatory system (Bligh, 1973; Hammel, 1968; Simon, 1974; and Necker, 1982). In mammals hypothalamic thermosensitivity is high -- extremely high in some species of small mammals (Heller, 1978). Birds have minimal or even

Table I. Relative Thermosensitivity of Different Skin Areas as Measured by Sweating

	A	B	C
Face	0.07	0.21	0.19
Chest	0.09	0.10	0.08
Upper back	0.09	0.11	0.09
Abdomen	0.18	0.17	0.12
Trunk	0.36	0.38	0.29
Upper legs	0.16	0.15	0.12
Lower legs	0.16	0.08	0.15
Upper arms	0.13	0.12	0.13
Lower arms	0.12	0.06	0.12
Extremities	0.57	0.41	0.52

Column A lists the relative surface areas of different parts of the human body. Column B lists weighting factors for skin temperatures of these areas in the stimulation of sweating as measured on the thigh. Column C lists weighting factors for the effectiveness of cooling of these areas on reducing sweating (measured on the thigh) which has been stimulated by whole body heating (data from Crawshaw, *et al.*, 1975).

nonhomeostatic hypothalamic thermosensitivity; spinal temperature has been considered the dominant deep body feedback loop in the avian thermoregulatory system (Simon, 1974). Figures 1 and 2 present examples of thermoregulatory responses induced by perturbations of hypothalamic or spinal

temperatures. In both cases the responses of the animals in terms of actual heat exchange are much greater than the quantities of heat put into or taken out of the animal by the experimental manipulation. The result is that the stimulation causes a strong shift in overall body temperature in the opposite direction to that of the stimulus. It is commonly taken for granted that such highly thermosensitive

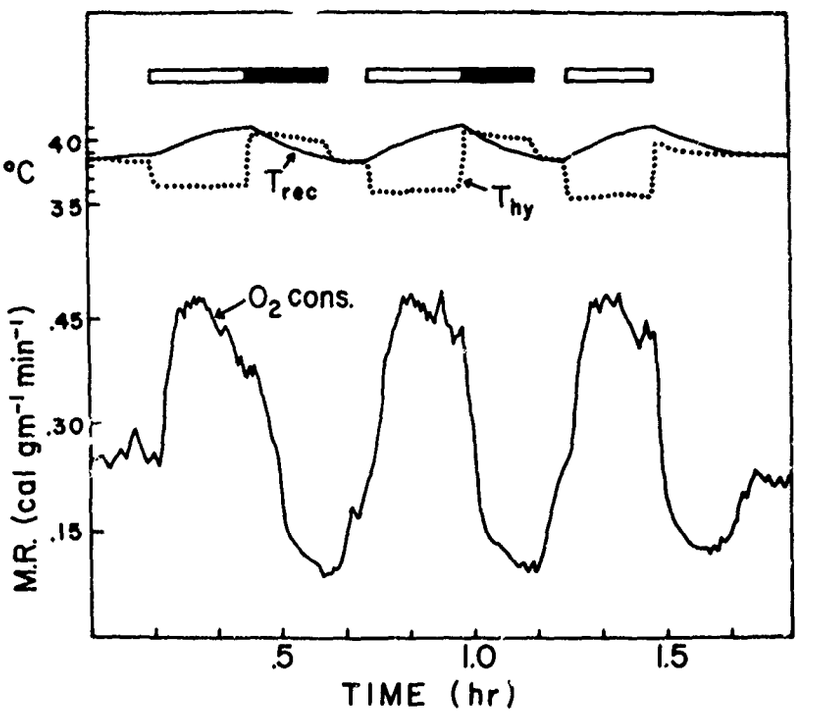

Figure 1. This recording was made during an experiment in which the hypothalamic temperature of an unanesthetized ground squirrel was cooled (open bar) and heated (black bar) while O_2 consumption and rectal temperature were measured. The experiment was conducted at 10 °C which is below thermoneutrality for this animal, and therefore the O_2 consumption was above the basal rate at the beginning of the record. Lowering of hypothalamic temperature (dotted line) caused marked elevations in O_2 consumption which resulted in steep increases in overall body temperature. Raising hypothalamic temperature suppressed O_2 consumption to basal levels which in this cold environment resulted in falls in overall body temperature (from Heller, *et al.*, 1974).

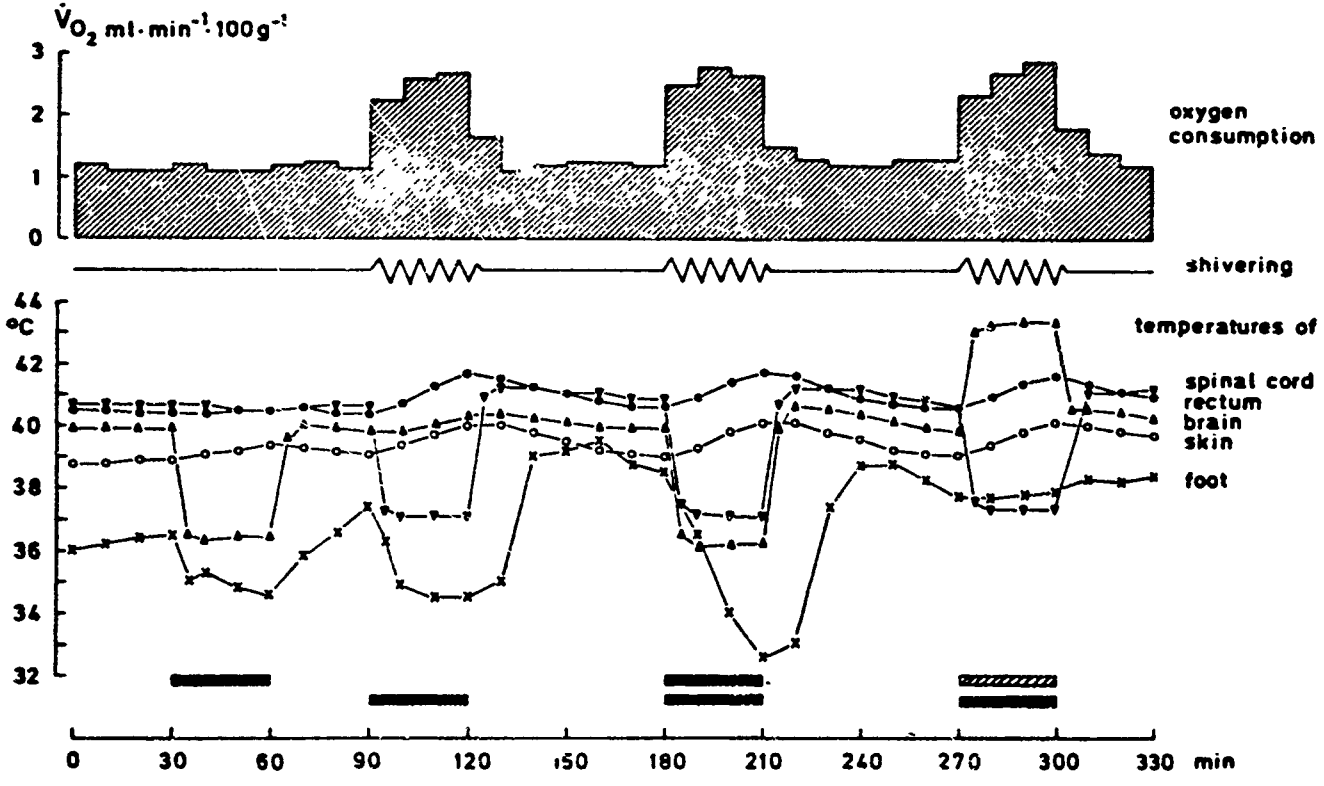

Figure 2. In this experiment the hypothalamus and the spinal cord of a pigeon were thermally manipulated while O_2 consumption and various body temperatures were measured. Cooling the hypothalamus had no effect other than causing a slight vasoconstriction in the feet. Spinal cooling induced a large increase in O_2 consumption as well as vasoconstriction in the feet, and other body temperatures rose due to the excess heat production. The metabolic response to spinal cooling was not augmented by simultaneous hypothalamic cooling or diminished by simultaneous hypothalamic warming. The vasomotor responses in the feet were influenced by both hypothalamic and spinal temperatures (from Rautenberg, *et al.*, 1972).

sites must be playing important roles in normal thermoregulation.

Deep body sites outside of the CNS also have been shown to be highly thermosensitive and influence thermoregulatory responses. Intraabdominal thermosensitivity, for example, has been demonstrated in sheep (Rawson, *et al.*, 1970), goats (Mercer, *et al.*, 1978), monkeys (Adair, 1971), and rabbits (Riedel, *et al.*, 1973). However, the quantitative distribution of extra-CNS thermosensitivity has been little studied.

In a series of extremely interesting and ingenious experiments in several species, Jessen and colleagues have been able to give us some idea of the relative weighting of the temperatures of different body areas in the stimulation of thermoregulatory responses. They have used a variety of techniques in concert to stimulate or change skin temperature, spinal temperature, hypothalamic temperature, and deep body temperature. An intravascular heat exchanger placed in the aorta of the goat was used to control deep body temperature (Jessen, *et al.*, 1977) while spinal and hypothalamic thermodes were used to independently manipulate the temperatures of these two CNS sites (Jessen, 1977). Skin temperature was influenced by the temperature of the surrounding air (Jessen, 1977) or else the animal was placed in a water bath (Jessen, 1981). In controlling the shivering response, the temperature of the body core had 3 times the influence of the skin temperature. The thermosensitivity of the body core was about equally divided between CNS and extra-CNS components, and within the CNS, hypothalamic temperature had about twice the power of the spinal temperature to drive heat production.

The weighting of thermal stimuli that drive respiratory evaporative heat loss in the goat has not been as extensively documented by Jessen and colleagues as have the stimuli driving metabolic heat production. But, enough work has been done to reveal that the integration of stimuli driving heat loss responses is not symmetrical with those driving heat production. If increased respiratory evaporative heat loss is induced by hypothalamic warming, it can be enhanced by spinal warming, but it cannot be inhibited by spinal cooling (Jessen, 1977).

Quantitation of stimuli that drive thermoregulatory responses has also been undertaken for the dog (Jessen, *et al.*, 1971) but is less complete than the work on goats. An accurate comparison of peripheral versus central thermosensitivity does not yet exist for the dog. However, for central thermosensitivity, the weighting of hypothalamic to all other deep body thermosensitivity is about 1:2.3 (Mercer,

et al., 1980), and the thermosensitivity of the hypothalamus is about equal to that of the spinal cord in driving responses of both heat loss and heat production. Therefore, the weighting of deep body thermosensitivities in the dog seems to be about equally divided between hypothalamus, spinal cord, and extra-CNS structures.

The Jessen group has also partitioned whole-body thermosensitivity of the goose into its spinal, supraspinal, and extra-CNS components (Helfmann, *et al.*, 1981), and the results are quite different from those obtained on the mammals discussed above. As expected from previous work on birds, the supraspinal thermosensitivity was very low -- 1/12 of total whole body thermosensitivity. An unexpected finding was that spinal thermosensitivity was also extremely low -- only 1/40 of total whole body thermosensitivity. Therefore, most of the input driving heat production in the goose is derived from thermosensitivity of structures outside of the CNS.

Quantitative partitioning of thermosensitivity does not exist for any other species. This is unfortunate for microwave research, because it is just this sort of information which is required to predict and assess the effects on the thermoregulatory system of the deposition of microwave energy in tissues. Also, we should expect considerable differences between species. Major differences in sites of CNS thermosensitivity exist between birds and mammals (Necker, 1982). Within mammals there appears to be an inverse relationship between hypothalamic thermosensitivity and body size (Figure 3). Comparable data on peripheral thermosensitivity of mammals does not exist, but we might expect the relationship to be reversed -- namely an increase in peripheral thermosensitivity with an increase in body size (Heller, 1978). Clearly, interpretation of the effects of microwave irradiation on the thermoregulatory system of a particular species will not be a simple task.

INTEGRATION OF INFORMATION AND CONTROL OF THERMOREGULATORY RESPONSES

The identification of sites deep within the body which are highly thermosensitive provides us with the basic components of a thermostat. When body temperature falls, the cold-sensitive structures are activated and can stimulate heat conservation/production responses. When core temperature rises, the warm-sensitive structures can stimulate heat loss responses. In this way deep body temperature

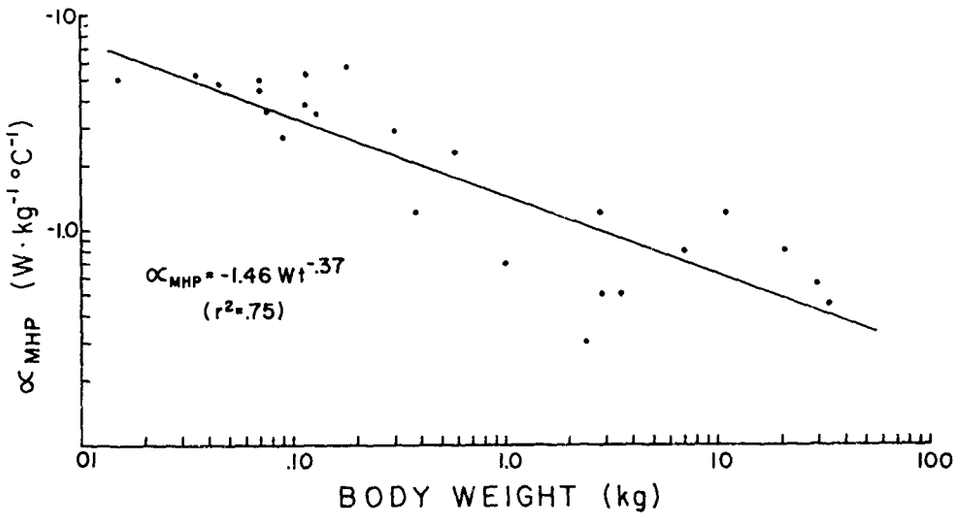

Figure 3. The proportionality constants relating metabolic rate to hypothalamic temperature plotted as a function of body weight for 21 species of mammals (from Heller, 1978).

should oscillate around a "set point" temperature at which the activities of both cold and warm receptors are minimal. Unfortunately, the thermoregulatory systems of mammals and birds do not function in this simple fashion. Major changes in thermoregulatory responses are not naturally associated with changes in body temperature. In studies on rats (Abrams, *et al.*, 1964), dogs (Rawson, *et al.*, 1965) and pigeons (Graf, *et al.*, 1979), long term recordings of deep body temperature and rate of metabolic heat production were made leading to the conclusion that the two responses were not correlated. What then is the function of the ubiquitous high thermosensitivity in deep body CNS structures of birds and mammals? Is it only a fail-safe adaptation of importance under extreme conditions, or is it integrally involved in moment-to-moment regulation of body temperature?

An answer to this seeming dilemma was first proposed by Hammel, *et al.* (1963) in the form of a hypothesis about the organization of the CNS thermoregulatory system. They termed their model a proportional regulator with an adjustable set point. Rather than assuming that the process of integration in the central nervous thermoregulatory system consisted of a simple weighted summing of inputs from all thermosensitive sites, they proposed that the process of

integration involves the generation of a reference signal which is compared to some feedback signal. Differences between the reference signal and the feedback signal are translated into commands to the appropriate effector mechanisms. In this scheme the authors considered hypothalamic temperature to be the major feedback element in this control system, and they proposed that other variables such as skin temperature, extrahypothalamic deep body temperatures, and sleep have their influence on the system by changing the reference signal. This model was later cast in the form of a control systems engineering model (Hammel, 1965; Hardy, 1965) reproduced in Figure 4. Data supporting this model were obtained in experiments on dogs in which hypothalamic thermosensitivity was characterized in terms of heat loss and heat production responses, and then the influences of skin temperature and extrahypothalamic body temperature on the hypothalamic thermosensitivity curves were determined (Hellstrøm and Hammel, 1967). An example of these important experiments is presented in Figure 5. In response to manipulations of hypothalamic temperature (T_{hy}) at a normal laboratory air temperature of 25 °C, the dog began to shiver when T_{hy} was cooled below about 37.5 °C and the intensity of shivering, as revealed by oxygen consumption, was proportional to the difference between this threshold of 37.5 °C and lower T_{hy}'s. When the dog was placed in a colder environment ($T_a \cong 15$ °C), it was already shivering vigorously at a T_{hy} of 37.5 °C and continued to shiver until T_{hy} was warmed to 40 °C. The slope of the response curve was very similar at T_a's of 15 °C and 25 °C, but the threshold T_{hy} for initiation of shivering was 2.5 °C higher at the lower T_a. When the dog was placed in warm environments, the threshold T_{hy} for the shivering response declined so that the warmer the T_a, the more hypothalamic cooling was required to initiate shivering. Depending on the prevailing T_a, it was possible to observe shivering or panting in the same dog at the same T_{hy}. Hellstrøm and Hammel suggested that these results could be interpreted to mean that inputs from peripheral thermosensitive elements serve to alter the reference signal against which the actual T_{hy} was being compared. In other publications, Hammel put forward a simple neuronal model which had the properties of the block, engineering model and accounted for the observed results (Hammel, 1965; Hammel, *et al.*, 1973).

The importance of these papers by Hammel and his colleagues was not that they offered models which uniquely explained the data on characteristics of hypothalamic and extrahypothalamic thermosensitivities and how those inputs were integrated to control thermoregulatory responses; other

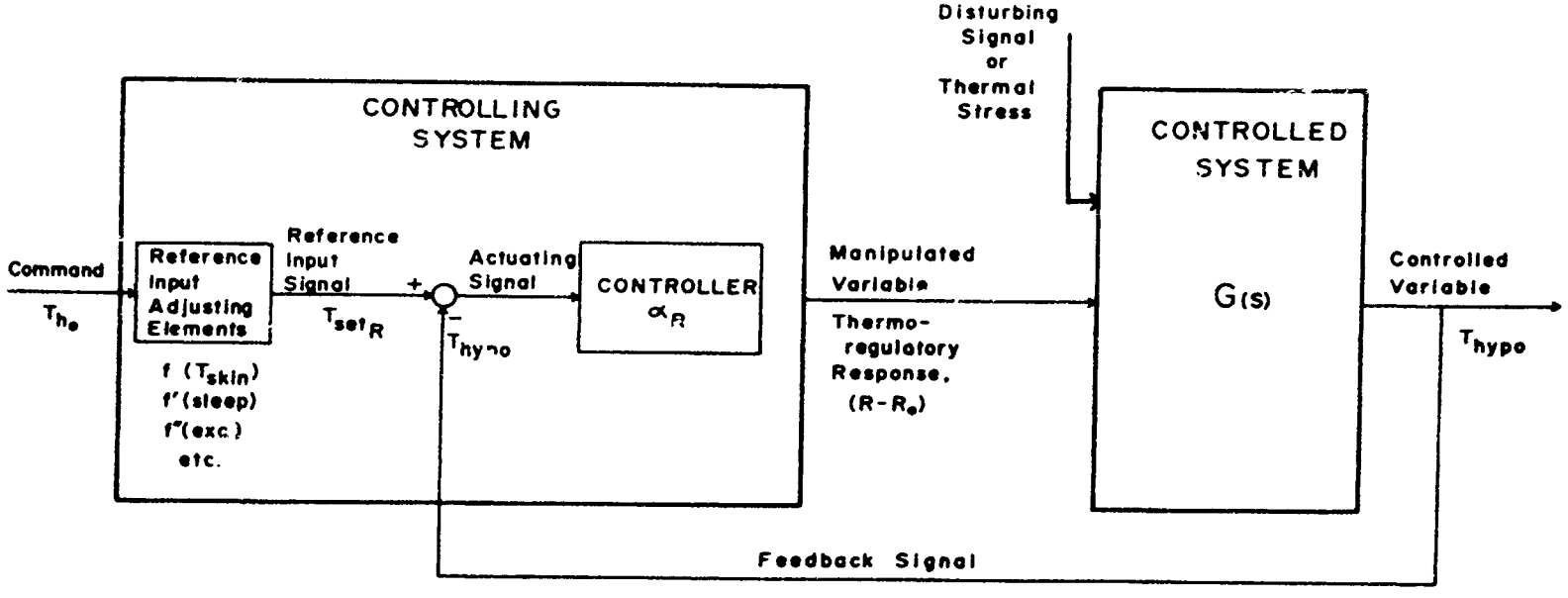

Figure 4. Block diagram of the mammalian thermoregulatory system. The controlled system represents all of the responses the animal can activate to alter its heat content. The controlling system resides in the CNS (from Hammel, 1965).

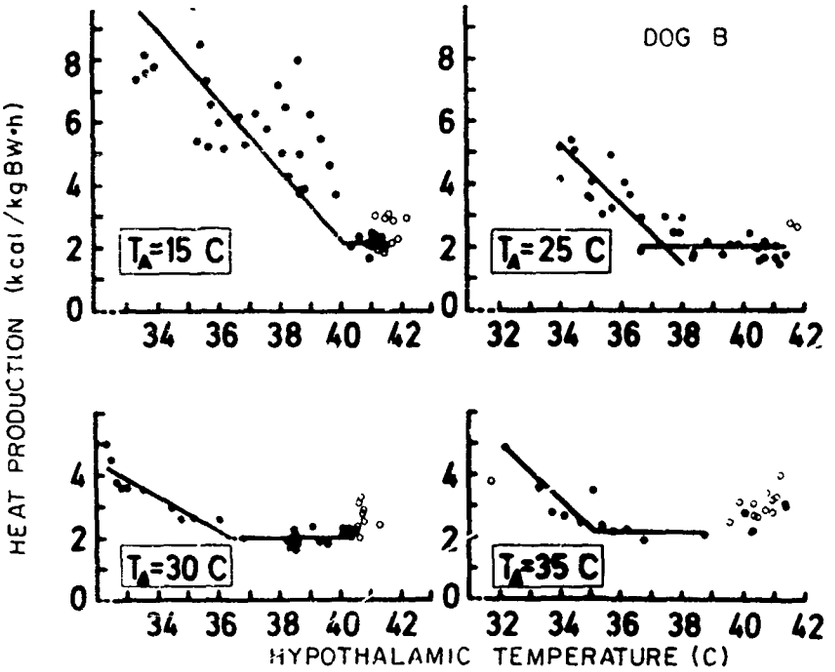

Figure 5. Metabolic responses of a dog to manipulations of hypothalamic temperature at four different ambient temperatures. Data represented by open circles were not included in calculations of basal levels or regression lines (from Hellstrøm and Hammel, 1967).

models which are equally tenable have been proposed (e.g., Wyndham, *et al.*, 1968; Brück, *et al.*, 1970; Bligh, 1972; Boulant, 1977). The real value of these early papers was in the concept of a highly adjustable central reference point against which a constant homeostatic variable could be compared. In other words, the sensitivity to the feedback variable changed rather than the feedback variable itself. Such a design feature imparts to the regulatory system a feed-forward nature or a predictive capability which greatly enhances the homeostatic ability of the system. Consider in this case that hypothalamic temperature is both the major feedback element in the regulatory system and the homeostatic variable which the system has evolved to regulate. Changes in skin temperatures or temperatures of exercising muscles threaten to perturb the homeostasis of T_{hy}. In a simple feedback regulator, T_{hy} would have to be displaced before an error signal would be generated to drive the

appropriate responses to return T_{hy} to its optimum level. With the feed-forward feature of the system, however, the peripheral perturbation causes a change in hypothalamic *thermosensitivity* before it can cause a change in hypothalamic *temperature*. Therefore, an error signal is generated and a response is initiated in *anticipation* of a change in the homeostatic variable, T_{hy}. Such a scheme offers a very satisfying explanation of why the hypothalamus is highly temperature sensitive even though its temperature rarely changes. In actuality, it is the sensitivity of the hypothalamus to temperature which changes in order to keep hypothalamic temperature constant.

Over the last 15 years or so, the concept of a relatively constant feedback signal and an adjustable reference or sensitivity to that feedback signal has remained of central importance as we have learned more about the details of the CNS thermoregulatory system. As mentioned above, a variety of other tenable models of the CNS thermoregulatory system have been proposed and supported by experimental results. Our appreciation for the diversity which probably exists in the design of the vertebrate thermoregulatory system has increased as a consequence. We know now, for example, that changes in hypothalamic thermosensitivity due to inputs from extrahypothalamic thermosensitive structures can be reflected by changes in slope of the curves (eg., harbor seal in Figure 6), thresholds as we saw for the dog (Figure 5), or both (Figure 7). We have learned a great deal more about the neuroanatomy, neuropharmacology, and electrophysiology of the thermoregulatory system -- topics beyond the scope of this chapter. And, we are also reaching a greater appreciation of the fact that the overall organization of the thermoregulatory system is much more complex than is expressed in simplistic models of a unitary hypothalamic regulatory center upon which all inputs converge and from which arises an integrated output which activates all effector mechanisms.

In recent years, Satinoff (1978) has proposed a view of the thermoregulatory system more complex than the classical models of a unitary hypothalamic regulator. The basic concept underlying Satinoff's model is that the thermoregulatory system consists of an evolutionary amalgamation of subsystems which have certain possibilities for independent action but are normally organized in a hierarchial fashion and held in check by the highest level in that hierarchy -- the hypothalamic regulatory circuit. The support for this concept comes largely from work with lesioned animals which has produced a plethora of fascinating and puzzling phenomena. For example, dogs (Thauer, 1935; Keller, *et al.*,

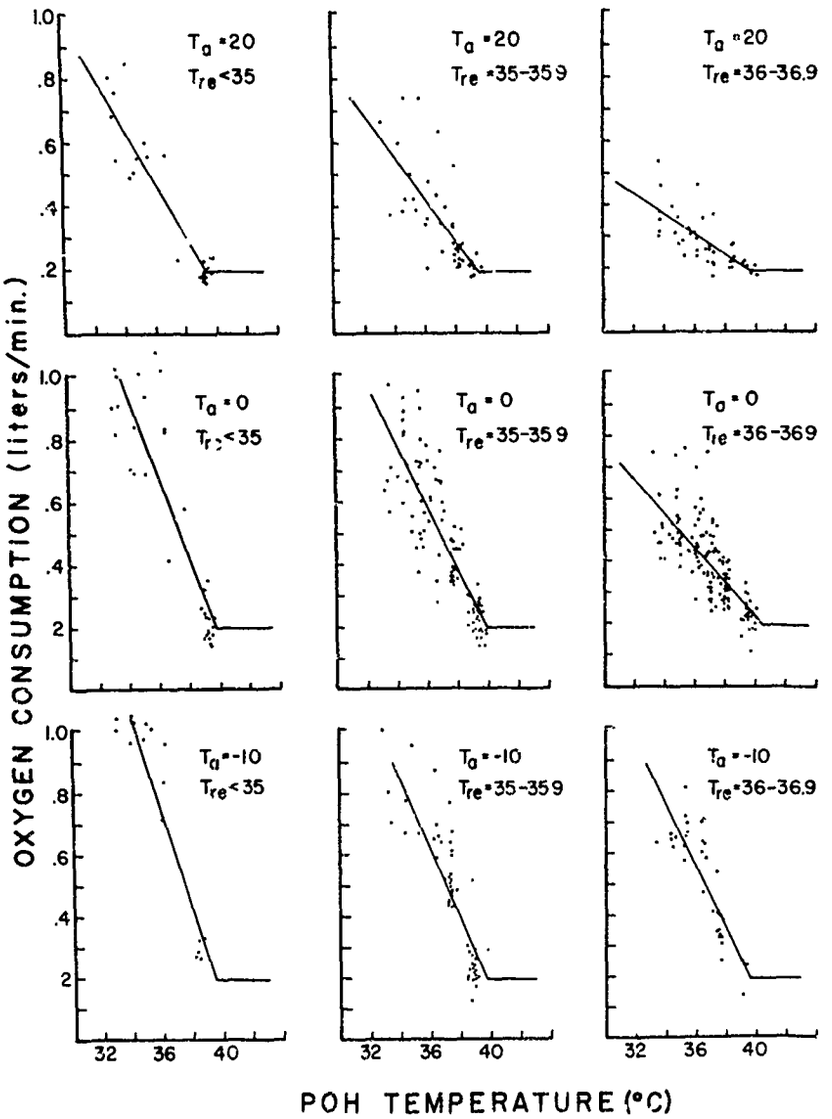

Figure 6. The rate of oxygen consumption of a harbor seal as a function of preoptic/hypothalamic temperature for nine combinations of ambient temperature (T_a) and rectal temperature (T_{re}) (from Hammel, *et al.*, 1977).

1964), cats (Chambers, *et al.*, 1974), and monkeys (Liu, 1979) with the brain transections in the midbrain and rabbits with high cervical transections (Thauer, *et al.*, 1957) retain or regain surprising abilities to make appropriate thermoregulatory responses and crudely regulate their body temperatures. Apparently some thermoregulatory reflexes

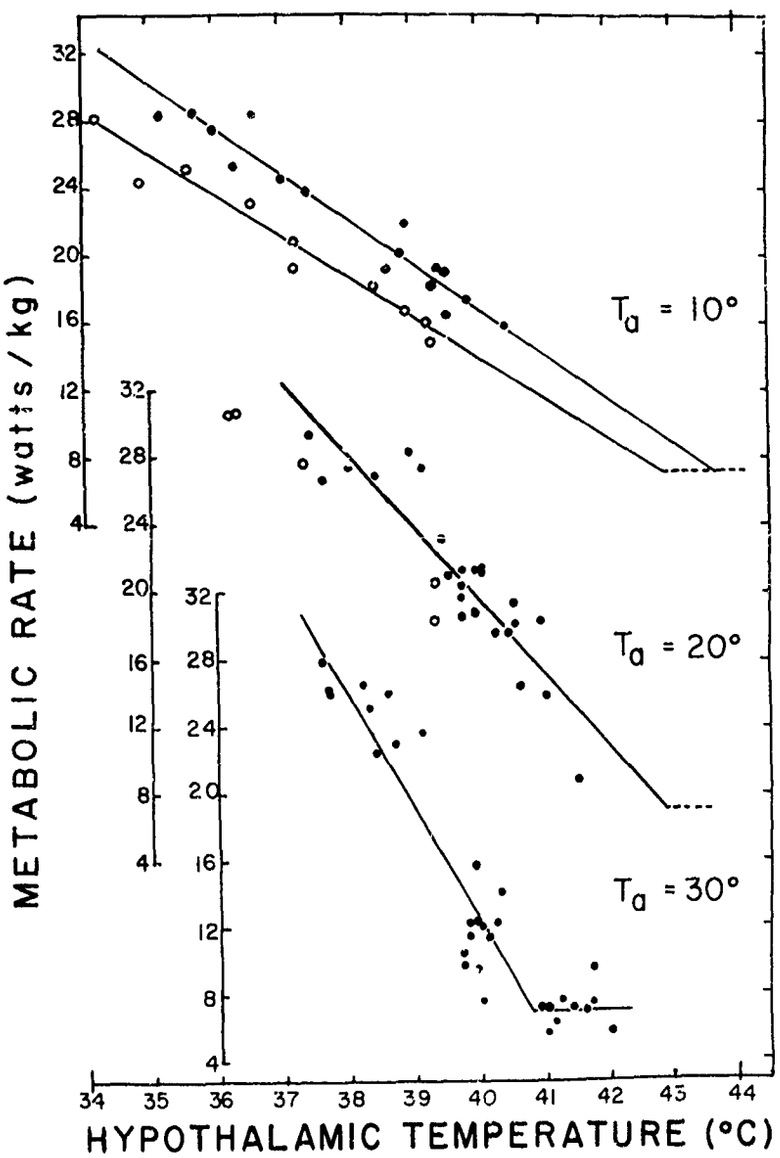

Figure 7. The rate of oxygen consumption of a desert ground squirrel (*Ammospermophilus nelsoni*) as a function of hypothalamic temperature at three ambient temperatures. Data points indicated by open circles were responses to hypothalamic coolings immediately following strong hypothalamic heatings. In this species both T_{hy} threshold for the metabolic response and the proportionality constant for the response are influenced by ambient temperature. The unique feature, however, is that the proportionality constant (slope of response curve) becomes more negative (steeper) at T_a increases (from Heller and Henderson, 1976).

remain in the absence of the hypothalamic regulator.

The nature of the control of the hypothalamus over lower level thermoregulatory reflexes was revealed in some fascinating experiments on cats (Chambers, *et al.*, 1974) and monkeys (Liu, 1979). Animals with brain transections just below the hypothalamus lost all autonomic thermoregulatory responses to skin chilling. If, however, an additional transection was made in the caudal midbrain or hindbrain, crude autonomic responses to skin chilling returned. Apparently a midbrain area exists which exerts tonic inhibition over lower level thermoregulatory reflexes, but this midbrain area itself is normally held in check by the hypothalamic thermoregulatory structures.

Discrete lesion experiments in rats have also produced results not readily explained by a unitary regulatory model. Lesions in the preoptic and anterior hypothalamic nuclei may eliminate autonomic thermoregulatory responses while leaving behavioral responses intact (Lipton, 1968; Carlisle, 1969; Satinoff, *et al.*, 1970). The conclusion drawn by Satinoff is that if a unitary regulator were integrating information and generating an error signal activating all thermoregulatory responses, then a lesion eliminating autonomic responses should also eliminate behavioral ones. An alternative interpretation which is not ruled out is that the preoptic/anterior hypothalamic area normally does integrate all relevant information and activates both autonomic and behavioral responses, but in the absence of this regulator the behavioral responses can be consciously controlled on the basis of conscious thermal sensation. Behavior to minimize perceived thermal discomfort could result in an apparent regulation of body temperature.

Other experiments have also succeeded in separating behavioral and autonomic thermoregulatory responses. Lateral hypothalamic lesions in rats (Satinoff, *et al.*, 1971) left the metabolic heat production response to cold exposure intact, but severely impaired behavioral responses. In a thermal stimulation study not involving lesions, Adair (1974) also demonstrated a separation of autonomic and behavioral thermoregulatory responses in squirrel monkeys. Thermal stimulation of either the preoptic area or the posterior hypothalamus elicited behavioral responses, but thermal stimulation of the posterior hypothalamus did not result in autonomic responses. Results such as these are not easily explained by a model such as that shown in Figure 4.

Satinoff's challenge to the classical concepts may be extremely relevant to research on the thermoregulatory effects of microwaves. Unusual patterns of energy deposition in tissues may disrupt normal organization of

hierarchical control and stimulate expression of lower-level thermoregulatory reflexes. Just such an anomalous situation was recently demonstrated by Graf (1980) as a result of long-term spinal warming in pigeons. The spinal warming stimulated panting which in turn caused extraspinal temperatures to fall, resulting in shivering coincident with the panting! The caveat is that the influences of microwave deposition of energy on normal thermoregulation may not be very easy to interpret. On the other hand, microwave techniques may offer the thermoregulatory physiologist a valuable tool for selective thermal stimulation of specific thermosensitive structures.

REGULATED CHANGES IN BODY TEMPERATURE

So far in this Chapter I have emphasized the constancy with which the CNS regulates body temperature, and I have pointed out that thermal energy deposited by microwaves in tissues would generate inputs to the regulatory system which would result in compensatory thermoregulatory responses. Thus the effects of microwave irradiation should be seen in activities of thermoregulatory effector organs which may be more significant than actual measured changes in body temperatures. Now I should like to turn to the question of regulated changes in body temperature which are normal adaptations of the thermoregulatory system and must be taken into consideration when interpreting any data on changes in body temperatures or thermoregulatory responses. The adaptations I shall discuss will include fever, circadian rhythms, arousal state, natural torpidity, and broad band regulation.

Fever

Fever (cf. also Chapter 7) is a classical symptom of infection or disease and was commonly assumed to be a pathological hyperthermia, a disruption of normal regulatory mechanisms. However, the sequence of events associated with fever seem to represent a coordinated integration of thermoregulatory responses. The onset of fever is characterized by both autonomic and behavioral responses to increase heat production and decrease heat loss. The plateau of the fever is accompanied by declines and modulations of heat production/conservation responses to maintain body temperature at the elevated, febrile level. When the fever

breaks, autonomic and behavioral heat loss responses result in a decline in body temperature to the normal level. This orderly sequence of events suggests that fever is not due to a disruption of thermoregulation, but instead may be a change in the level of regulation.

This supposition that fever is a regulated change in body temperature has now been amply demonstrated. Sharp and Hammel (1972) characterized rates of thermoregulatory saliva production in dogs as a function of hypothalamic temperature, ambient temperature, and level of exercise. The hypothalamic temperature threshold for increased saliva production decreased in response to increased ambient temperature and/or increased level of exercise. The production of fever by I.V. injection of endogenous pyrogen caused an increase in hypothalamic temperature threshold which was added to the threshold shifts due to the other variables. In other words, the thermoregulatory system appeared to integrate, directly or indirectly, the presence of the pyrogen along with other inputs in the setting of the hypothalamic temperature threshold for this heat loss response.

Other studies have also demonstrated shifts in hypothalamic temperature thresholds associated with fever. A particularly elegant quantitative study on prostaglandin-induced fevers and the hypothalamic temperature threshold for heat production responses was reported by Stitt, *et al.* (1974). Figure 8 taken from this study illustrates the precise graded changes in the characteristics of the thermoregulatory system during fever. The fact that fever is a precise regulated rise in body temperature leads to the speculation that it is an adaptive, protective response. This topic has been explored extensively by Kluger (1979), and is beyond the scope of our concerns here. However, it should be kept in mind that microwave damage of tissues could result in cell degeneration with associated release of pyrogenic substances and subsequent thermoregulatory disturbances.

Circadian Rhythms

Probably since Galileo invented the thermometer, a daily cycle of body temperature has been recognized in man and then in many other mammals and birds. The simple hypotheses that the daily cycle of body temperature is a consequence of daily patterns of food intake, muscular activity, or sleep/wakefulness have all been disproven (for reviews see Aschoff, 1970; Heller, *et al.*, 1977). More and more evidence is accumulating that there exists a circadian input to the thermoregulatory system which results in a circadian

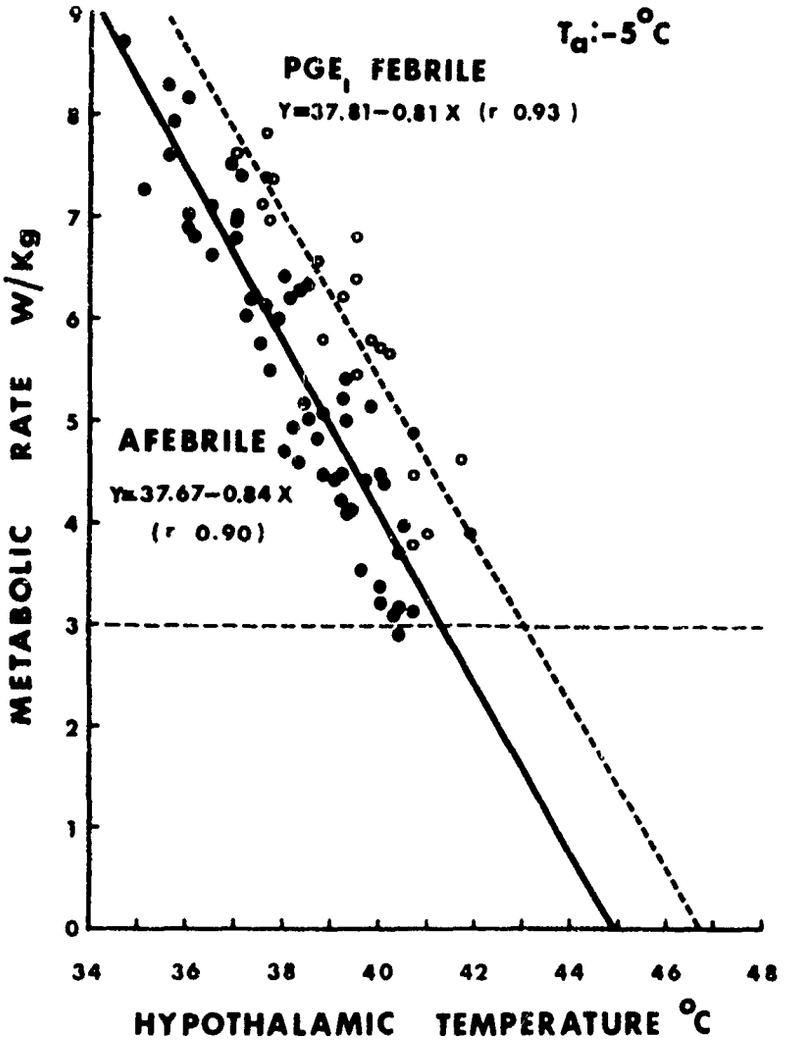

Figure 8. The metabolic rate of a rabbit as a function of hypothalamic temperature when afebrile and during the plateau of a fever induced by an intrahypothalamic injection of prostaglandin E_1 (from Stitt, *et al.*, 1974).

rhythm of regulated changes in body temperature. For example, in a study of forearm blood flow as a function of deep body temperature in exercising humans, Wenger, *et al.* (1976) showed a clear shift in the relationship with time of day (Figure 9). At night, forearm blood flow began to rise

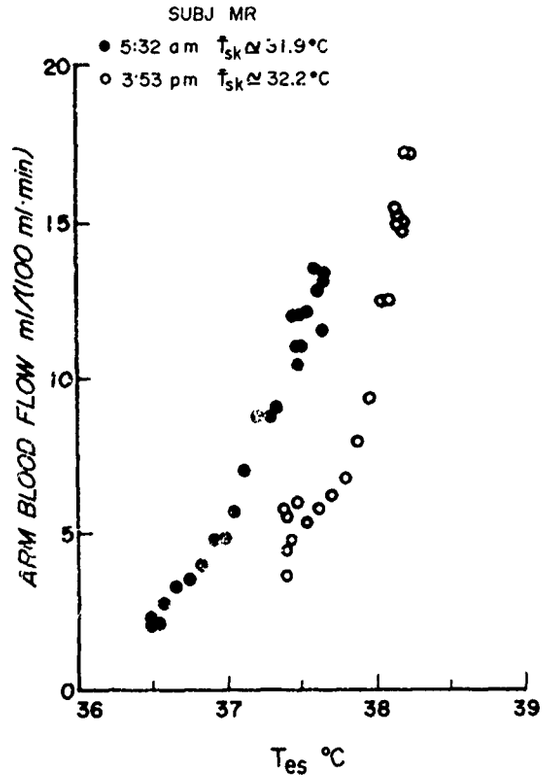

Figure 9. The forearm blood flow of a human subject as a function of esophageal temperature measured simultaneously during two experiments, one conducted during the daytime, the other at night. (From Wenger, *et al.*, 1976).

steeply at a lower deep body temperature than during the day. In a study of spinal thermosensitivity in pigeons, I have shown in collaboration with Graf and Rautenberg that the spinal temperature thresholds for shivering and panting in *awake* birds are both lower at night than during the day (Figure 10). Clearly, in any quantitative thermoregulatory studies it is important to have entrained subjects and to do measurements over the same time periods for comparisons within or between subjects. An example of the influence of the circadian rhythm of body temperature on the response to microwave exposure is discussed by Lotz in Chapter 22.

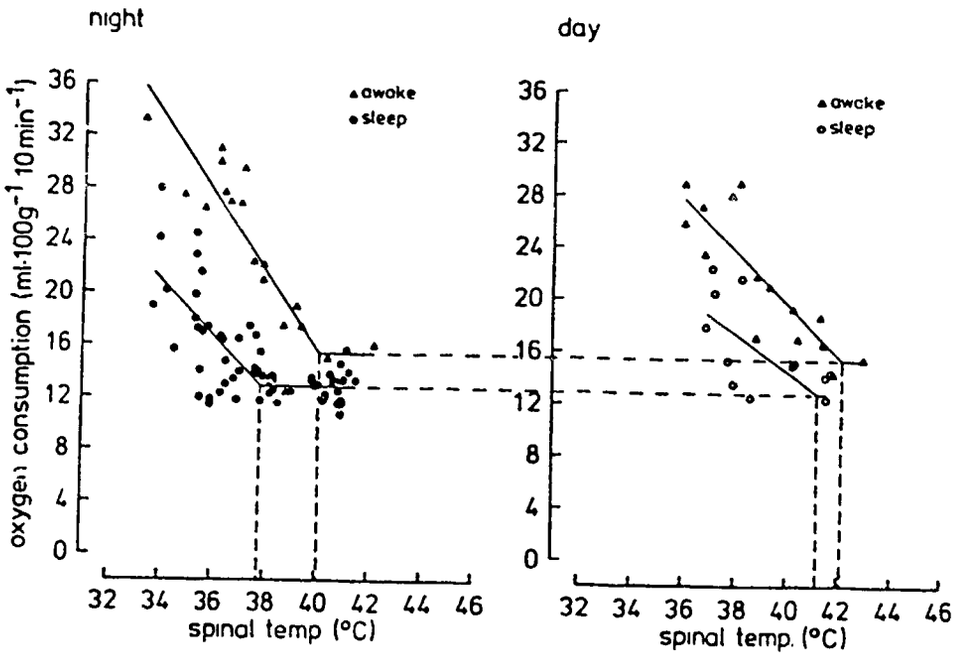

Figure 10. The metabolic responses of a pigeon to manipulations of the temperature of its spinal cord during sleep and wakefulness at night and in the day.

State of Arousal

To prove that a daily cycle of body temperature is not dependent upon the sleep/waking cycle is not to prove that the regulation of body temperature is independent of arousal state. In fact, changes in thermoregulatory responses coincident with transitions between wakefulness and sleep have been recognized in many studies of both man and animals (for reviews see Heller and Glotzbach, 1977 and Heller, *et al.*, 1978). More to the point of this discussion however, the characteristics of the thermoregulatory system in terms of hypothalamic thermosensitivity are strongly dependent upon arousal state. In non-human mammals sleep states are generally designated as REM (for rapid eye movement) sleep or non-REM sleep. These states can be easily distinguished by their EEG characteristics. In experiments in which hypothalamic temperature was manipulated while EEG and oxygen consumption were continuously monitored, hypothalamic thermosensitivity was distinctly lower in non-REM sleep than in wakefulness and appeared to be totally suppressed during REM sleep as shown in Figure 11 (Glotzbach, *et al.*, 1976).

The influence of sleep or arousal state on the thermo-

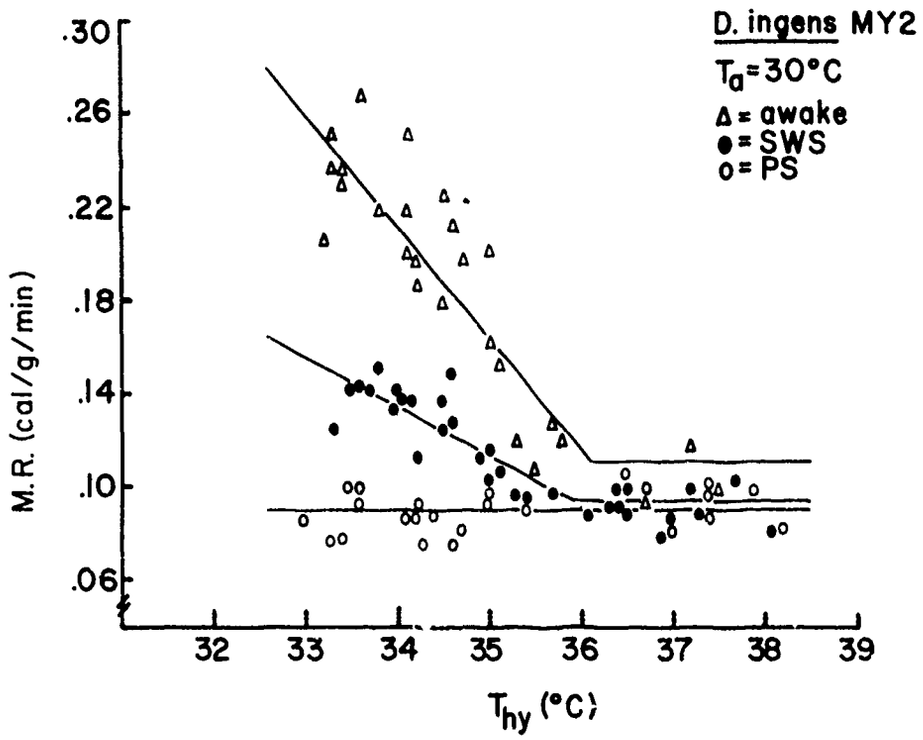

Figure 11. The metabolic responses of a kangaroo rat to manipulations of its hypothalamic temperature during wakefulness, REM sleep, and non-REM (slow wave) sleep.

regulatory system must be kept in mind in thermoregulatory experiments in which EEG is not being recorded. Frequently the conditions of experimentation may have a decided influence on arousal state. Clearly thermal stimulation of the skin and hypothalamus influence distribution of arousal states. Ambient temperatures in the upper thermoneutral range and/or mild hypothalamic warming are very conducive to non-REM sleep. REM sleep is maximized when both skin and hypothalamus are mildly warmed (Sakaguchi, *et al.*, 1978; Szymusiak, *et al.*, 1981). The potential complication, therefore, in experiments probing thermoregulatory responses to microwave irradiation is that the microwaves may influence skin and core temperatures which in turn influence arousal states, thereby effecting the characteristics of the thermoregulatory system.

Torpor

Natural torpidity in many species is an extension of normal euthermic arousal states. Specifically, mammalian torpor seems to consist mostly of non-REM sleep (for a review see Walker *et al.*, 1980). A bit of a problem derives from the fact that the EEG criteria on which definitions of arousal state are based become non-operational as brain temperature (T_{br}) falls below 25 °C. Therefore, until we have a more direct measure of the control of arousal state, we can only make conclusions about distribution of arousal states in situations in which T_{br} is above 25 °C, namely the early part of entrance into torpor, shallow torpor, and hibernation at a high T_a. In all such cases the predominant arousal state is non-REM sleep.

The fact that body temperature is regulated at a lower level during non-REM sleep than during wakefulness, coupled with the fact that natural torpor appears to be an extension of non-REM sleep, leads to the expectation that torpidity is a lowering of the regulated body temperature and not simply a turning off of thermoregulation. This is certainly the case. The hypothalamic temperature threshold for thermoregulatory heat production declines during entrance into hibernation and exists throughout bouts of hibernation (for a review see Heller, *et al.*, 1978). An open question concerns what happens to the hypothalamic temperature thresholds for heat dissipation responses during hibernation. Although the hibernating animal may be peripherally vasodilated, active heat loss responses do not seem to be stimulated by hypothalamic or peripheral heating. One report has described apparent heat loss behavior resulting from hypothalamic heating during hibernation (Mills, *et al.*, 1972) but it is possible that this behavior was more of an arousal response than a thermoregulatory response. More work must be done. Meanwhile the possibility exists that the animal in deep hibernation is regulating with a greatly expanded dead band between heat production and heat loss thresholds. If that is true, it would be of great utility for microwave research as a model system for studying heat deposition in tissues. The animal in deep hibernation is exceedingly still, and if it is regulating, with a wide dead band width, then there is much scope for studying the distribution of heat deposition due to microwave radiation without activating arousal or thermoregulatory responses.

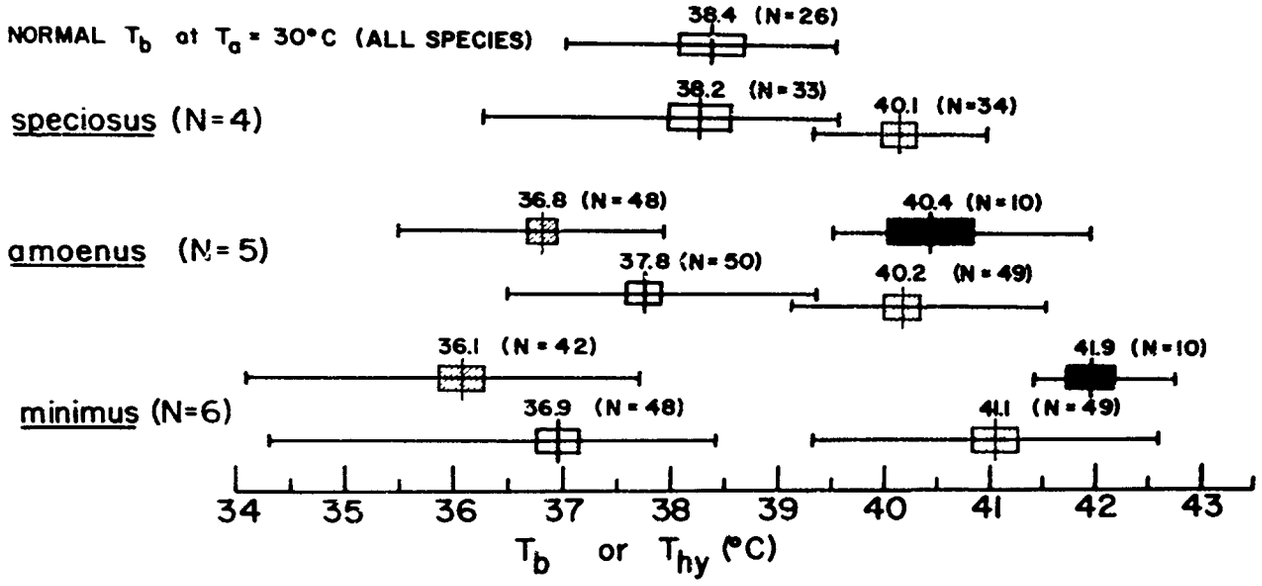

Figure 12. Maximum and minimum body temperatures tolerated by three species of chipmunks. Lines indicate ranges of data, bars indicate two standard deviations each side of the mean, open bars are data from awake animals, striped bars are data from sleeping animals, stippled bars are data obtained during whole-body heating, and solid bars are data obtained during hypothalamic heating. *Speciosus* is from pine forests, shows little tolerance of hyperthermia and no tendency to become hypothermic during recovery from heat exposure. *Amoenus* and *minimus* are from progressively hotter, more arid habitats. They tolerate hyperthermia before initiating active heat loss or escape responses, and during recovery they become hypothermic wnich is most pronounced during sleep which commonly occurs after heat exposure (from Chappell, *et al.*, 1978).

Broad band regulation

The last thermoregulatory adaptation I shall discuss as relevant to microwave research is another case of broad dead band regulation, but not associated with torpor. Active heat dissipation by evaporation of water is not a viable thermoregulatory response for many animals which face extreme heat stress. They simply don't have the body water to squander. In some species of highly adapted desert mammals, a thermoregulatory behavior pattern has evolved to obviate the need for excessive water loss for heat dissipation, and therefore, its corollary is a cycle of body temperature which does not stimulate active thermoregulatory responses, or broad dead band regulation. The best known case is the camel which allows its body temperature to rise during the day and fall during the night over a total range of about 10 °C (Schmidt-Nielsen, *et al.*, 1957). Small mammals, however, heat much more rapidly than larger ones because of their higher surface-to-volume ratio. They cannot wait until night to dissipate an acquired heat load, but they do have access to cooler microclimates such as burrows and small patches of shade. By moving between open areas and microclimates where they can passively dissipate heat, they use heat storage behavior over a much shorter time scale than does the camel. But, this behavior, along with their broad dead band width between thresholds for active thermoregulatory responses, enables them to exploit very hot, arid environments. Figure 12 (from Chappell, *et al.*, 1978) summarizes a study of three species of chipmunks living in contiguous habitats varying greatly in temperature and aridity. The study revealed that the potential for broad band width thermoregulation may be significantly different even in closely related species. The relevant message in the context of this discussion is that enormous species differences may be expected in responses to deposition of heat in tissues by microwave radiation. These differences may be due to adaptive characteristics of the thermoregulatory systems of the species involved rather than to the physics of microwave penetration and absorption.

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I would like to acknowledge the fruitful and exciting intellectual interactions I have had over the years with the associates and colleagues whose work I have discussed in

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REFERENCES

Abrams, R. and Hammel, H.T. (1964). Hypothalamic temperature in unanesthetized albino rats during feeding and sleeping. *Am. J. Physiol.* 206:641.

Adair, E. (1974). Hypothalamic control of thermoregulatory behavior: preoptic-posterior hypothalamic interaction. In *Recent Studies of Hypothalamic Function* (K. Lederis and K.E. Cooper, eds.), p. 341. Karger, Basel.

Aschoff, J. (1970). Circadian rhythm of activity and of body temperature. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 905. C.C. Thomas, Springfield, Illinois.

Bligh, J. (1972). Neuronal models of mammalian temperature regulation. In *Essays on Temperature Regulation* (J. Bligh and R. Moore, eds.), p. 105. American Elsevier Publishing Co., New York.

Bligh, J. (1973). *Temperature Regulation in Mammals and Other Vertebrates*. North Holland Publishing Co., Amsterdam.

Boulant, J.A. (1977). A hypothalamic neuronal model for thermoregulation. In *Selected Topics in Environmental Biology* (B. Bhatia, G.S. Chhina, and B. Singh, eds.), p. 41. Pergamon Press, Oxford.

Brück, K. and Wünnenberg, W. (1970). "Meshed" control of two effector systems: nonshivering and shivering thermogenesis. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 562. C.C. Thomas, Springfield, Illinois.

Carlisle, H.J. (1972). Effect of preoptic and anterior hypothalamic lesions on behavioral thermoregulation in the cold. *J. comp. physiol. Psychol.* 64:391.

Chai, C.Y. and Lin, M.T. (1973). Effects of thermal stimulation of medulla oblongata and spinal cord on decerebrate rabbits. *J. Physiol. (London)* 234:409.

Chambers, W.W., Seigel, M.S., Lin, J.D., and Lin, C.N. (1974). Thermoregulatory responses of decerebrate and spinal cats. *Exp. Neurol.* 42:282.

Chappell, M.A., Calvo, V.A., and Heller, H.C. (1978). Hypothalamic thermosensitivity and adaptations for heat-storage behavior in three species of chipmunks (*Eutamias*) *J. Comp. Physiol.* 125:175.

Crawshaw, L.I., Nadel, E.R., Stolwijk, J.A.J., and Stamford, B.A. (1975). Effect of local cooling on sweating rate and cold sensation. *Pflügers Arch.* 354:19.

Graf, R. (1980). Simultaneously activated heat gain and heat loss mechanisms in pigeons. *Proc. I.U.P.S.* 14:442.

Graf, R. and Necker, R. (1979). Cyclic and non-cyclic variations of spinal cord temperature related with temperature regulation in pigeons. *Pflügers Arch.* 380:215.

Glotzbach, S.F. and Heller, H.C. (1976). Central nervous regulation of body temperature during sleep. *Science* 194:537.

Hales, J.R.S. and Hutchison, J.C.D. (1971). Metabolic respiratory and vasomotor responses to heating the scrotum of the ram. *J. Physiol. (London)* 212:353.

Hammel, H.T. (1965). Neurons and temperature regulation. In *Physiological Controls and Regulations* (W.S. Yamamoto and J.R. Brobeck, eds.), p. 71. W.B. Saunders Co., Philadelphia.

Hammel, H.T. (1968). Regulation of internal body temperature. *Ann. Rev. Physiol.* 30:641.

Hammel, H.T., Jackson, D.C., Stolwijk, J.A.J., Hardy, J.D., and Strømme, S.B. (1963). Temperature regulation by hypothalamic proportional control with an adjustable set point. *J. Appl. Physiol.* 18:1146.

Hammel, H.T., Elsner, R., Heller, H.C., Maggert, J.A., and Bainton, C.R. (1977). Thermoregulatory responses to altering hypothalamic temperature in the harbor seal. *Am. J. Physiol.* 282:R18.

Hardy, J.D. (1965). The "set-point" concept in physiological temperature regulation. In *Physiological Controls and Regulations* (W.S. Yamamoto and J.R. Brobeck, eds.), p. 98. W.B. Saunders Co., Philadelphia.

Helfmann, W., Jannes, P., and Jessen, C. (1981). Total body thermosensitivity and its spinal and supraspinal fractions in the conscious goose. *Pflügers Arch.* 391:60.

Heller, H.C (1978). Hypothalamic thermosensitivity in mammals. *Experientia*, Suppl. 32:267.

Heller, H.C., Colliver, G.W., and Anand, P. (1974). CNS regulation of body temperature in enthermic hibernators. *Am. J. Physiol.* 277:576.

Heller,, H.C. and Glotzbach, S.F. (1977). Thermoregulation during sleep and hibernation. *Int. Rev. Physiol.* 15:147.

Heller, H.C. and Henderson, J.A. (1976) Hypothalamic thermosensitivity and regulation of heat storage behavior in a day-active desert rodent *Ammospermophilus nelsoni*. *J. Comp. Physiol.* 108:255.

Heller, H.C., Walker, J.M., Florant, G.L., Glotzbach, S.F., and Berger, R.J. (1978). Sleep and hibernation: electrophysiological and thermoregulatory homologies. In *Strategies in Cold: Natural Torpidity and Thermogenesis* (L. Wang and J. Hudson, eds.), p. 225. Academic Press, New York.

Hellstrøm, B. and Hammel, H.T. (1967). Some characteristics of temperature regulation in the unanesthetized dog. *Am. J. Physiol.* 213:547.

Hensel, H. (1976). Functional and structural basis of thermoreception. *Prog. in Brain Res.* 43:105.

Hensel, H. (1981). *Thermoreception and Temperature Regulation*. Academic Press, New York.

Iggo, A. (1969). Cutaneous thermoreceptors in primates and subprimates. *J. Physiol. (London)* 200:403.

Ingram, D.L. and Legge, K.F. (1972). The influence of deep body and skin temperatures on thermoregulatory responses to heating of the scrotum in pigs. *J. Physiol. (London)* 224:477.

Jessen, C. (1977). Interaction of air temperature and core temperatures in thermoregulation of the goat. *J. Physiol. (London)* 264:585.

Jessen, C. (1981). Independent clamps of peripheral and central temperatures and their effects on heat production in the goat. *J. Physiol. (London)* 311:11.

Jessen, C. and Mayer, E.T. (1971). Spinal cord and hypothalamus as core sensors of temperature in the conscious dog. I. Equivalence of responses. *Pflügers Arch.* 324:189.

Keller, A.D. and McClaskey, E.B. (1964). Localization, by the brain slicing method, of the level or levels of the cephalic brainstem upon which effective heat dissipation is dependent. *Am. J. Phys. Med.* 43:181.

Kluger, M.J. (1979). *Fever: Its Biology, Evolution, and Function*. Princeton University Press, Princeton.

Lipton, J.M. (1968). Effects of preoptic lesions on heat escape responding and colonic temperature in the rat. *Physiol. Behav.* 3:165.

Liu, J.C. (1979). Tonic inhibition of thermoregulation in the decerebrate monkey (*Saimiri sciureus*). *Exp. Neurol.* 64:632.

Mercer, J.B. and Jessen, C. (1978). Central thermosensitivity in conscious goats: hypothalamus and spinal cord versus residual inner body. *Pflügers Arch.* 374:179.

Mercer, J.B. and Jessen, C. (1980). Thermal control of respiratory evaporative heat loss in exercising dogs. *J. Appl. Physiol.* 49:979.

Mills, S.H. and South, F.E. (1972). Central regulation of temperature in hibernation and normothermia. *Cryobiology* 9:393.

Nadel, E.R., Mitchell, J.W., and Stolwijk, J.A.J. (1973). Differential thermal sensitivity in the human skin. *Pflügers Arch.* 340:71.

Necker, R. (1972). Temperature-sensitivity of thermoreceptors and mechanoreceptors on the beak of pigeons. *J. Comp. Physiol* 87:279.

Necker, R. (1977). Thermal sensitivity of different skin areas in pigeons. *J. Comp. Physiol.* 116:239.

Necker, R. (1982). Thermoreception and temperature regulation in homeothermic vertebrates. *Prog. in Sens. Physiol.* 2:1.

Rautenberg, W., Necker, R., and May, B. (1972). Thermoregulatory responses of the pigeon to changes of the brain and spinal cord temperatures. *Pflügers Arch.* 338:1122.

Rawson, R.O., Stolwijk, J.A.J., Graichen, H., and Abrams, R. (1965). Continuous radiotelemetry of hypothalamic temperatures from unrestrained animals. *J. Appl. Physiol.* 20:321.

Rawson, R.O. and Quick, K.P. (1970). Evidence of deep-body thermoreceptor response to intra-abdominal heating of the ewe. *J. Appl. Physiol.* 28:813.

Riedel, W., Siaplauras, S., and Simon, E. (1973). Intra-abdominal thermosensitivity in the rabbit as compared with spinal thermosensitivity. *Pflügers Arch.* 340:59.

Sakaguchi, S., Glotzbach, S.F., and Heller, H.C. (1979). Influences of hypothalamic and ambient temperatures on sleep in kangaroo rats. *Am. J. Physiol.* 237:1280.

Satinoff, E. (1978). Neural organization and evolution of thermal regulation in mammals. *Science* 201:16.

Satinoff, E. and Rutstein, J. (1970). Behavioral thermoregulation in rats with anterior hypothalamic lesions. *J. comp. physiol. Psychol.* 71:77.

Satinoff, E. and Shan, S.Y.Y. (1971). Loss of behavioral thermoregulation after lateral hypothalamic lesions in rats. *J. comp. physiol. Psychol.* 77:302.

Schmidt-Nielsen, K., Schmidt-Nielsen, B., Jarnum, S.A., and Houpt, T.R. (1957). Body temperature of the camel and its relation to water economy. *Am. J. Physiol.* 188:103.

Sharp, F.R. and Hammel, H.T. (1972). The effects of fever on the salivation response in the resting and exercising dog. *Am. J. Physiol.* 223:77.

Simon, E. (1974). Temperature regulation: the spinal cord as a site of extrahypothalamic thermoregulatory functions. *Rev. Physiol. Biochem. Pharmacol.* 71:2.

Stitt, J.T., Hardy, J.D., and Stolwijk, J.A.J. (1974). PGE_1 fever: its effect on thermoregulation at different low ambient temperatures. *Am. J. Physiol.* 227:622.

Szymusiak, R. and Satinoff, E. (1981). Maximal REM sleep time defines a narrower thermoneutral zone than does minimal metabolic rate. *Physiol. Behav.* 26:687.

Thauer, R. (1935). Wärmeregulation und Fieberfähigkeit nach operativen Eingriffen am Nervensystem homoiothermer Saugetiere. *Pflügers Arch.* 236:102.

Thauer, R. and Peters, G. (1938). Wärmeregulation nach operativer Ausschattung des "Wärmezentrums." *Pflügers Arch.* 239:483.

Waites, G.M.H. (1962). The effect of heating the scrotum of the ram on respiration and body temperature. *Quart. J. Exp. Physiol. and Cogn. Med. Sci.* 47:314.

Walker, J.M. and Berger, R.J. (1980). Sleep as an adaptation for energy conservation functionally related to hibernation and shallow torpor. *Prog. Brain Res.* 53:255.

Wenger, C.B., Roberts, M.F., Stolwijk, J.A.J., and Nadel, E.R. (1976). Nocturnal lowering of thresholds for sweating and vasodilation. *J. Appl. Physiol.* 41:15.

Wyndham, C.H. and Atkins, A.R. (1968). A physiological scheme and mathematical model of temperature regulation in man. *Arch. Ges. Physiol.* 303:14.

THERMAL SENSATION: INFRARED AND MICROWAVES

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The number of studies of how microwaves arouse warmth sensations can be counted on the fingers of one hand. They leave many, many unanswered questions, but the nature of the questions to be asked will in general take shape in the light of the much larger amount of information that we have about the perception of infrared radiation. So the main substance of this paper is to use present knowledge to help formulate a hypothetical program of psychophysical experiments with microwaves that will take account of the main variables that determine the subjective response.

One important question concerns what levels of power density are needed to trigger a just-detectable sensation, i.e., what is the absolute threshold of warmth sensation for microwaves versus infrared radiation. We shall see below that this phrasing of the question is deceptively oversimplified. Nevertheless, we address first the question of how infrared and microwave thresholds compare when measured in the same subjects under comparable test procedures. Two studies give first-order answers to the question. Hendler, Hardy, and Murgatroyd (1963) compared thresholds of infrared and 3-cm microwaves for a 37 cm^2, circular area of the forehead. Four subjects were tested by a variety of standard psychophysical procedures, including the classical methods of constant stimuli and limits. The threshold depended on the duration of the stimulation (the shorter the stimulation, the higher was the threshold). At all durations, however, the microwave thresholds were about twice as high as the infrared thresholds.

The second study (Justesen, Adair, Stevens, and Bruce-Wolfe, 1982) employed microwaves of 12.4 cm wavelength,

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used a different psychophysical method, the double-staircase method (Cornsweet, 1962), and stimulated about 100 cm^2 of the forearm for 10 sec at a time. (Six subjects were tested with microwaves, but because of constraints of time only four of these same subjects were tested with infrared.) On the average the 12.4-cm microwave stimulation yielded thresholds that were about 15 times higher than the infrared thresholds. Hence there seems little doubt that the warmth threshold is inversely related to the penetration depth of the radiation.

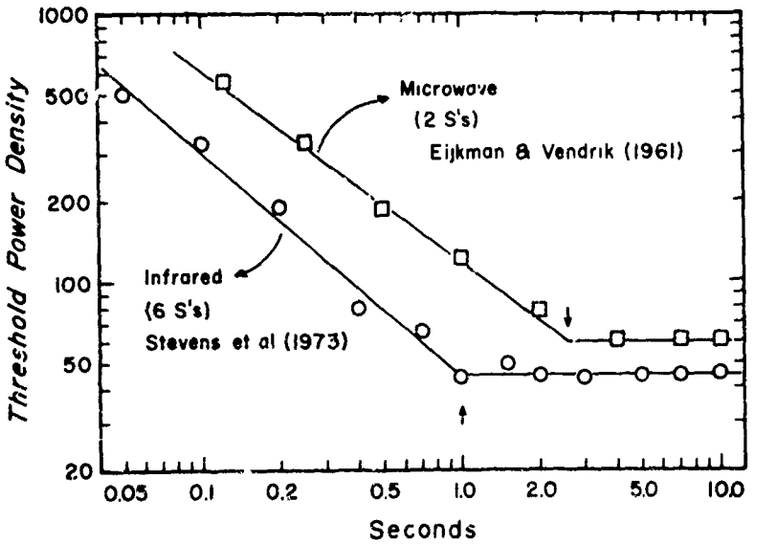

Figure 1. Relative threshold power density as a function of stimulus duration, comparing microwave and infrared stimulation. The relative up-down positions of the two functions is arbitrary because of the author's uncertainty of the absolute power density levels employed in Eijkman and Vendrik's study. However, the points illustrated here have to do with the relative shapes of the two functions, and it is known from other studies (see text) that microwaves yield higher thresholds than infrared.

One cannot stress too much that the understanding of the perception of radiation of any kind is not simply a matter of what level of stimulation a person can feel. The picture

is far more complicated, and my main interest in the paper is to try to convey something of this complexity. Consider, for example, Figure 1 which compared threshold measurements of infrared by Stevens, Oculicz, and Marks (1973) with threshold measurements of 10-cm microwaves by Eijkman and Vendrik (1961). The abscissa is the duration of the stimulus, and the ordinate is the relative power density needed to arouse a just-detectable sensation. The absolute up-down position of the microwave function I was unable to determine with certainty, but the studies just detailed above suggest that infrared produces lower thresholds than microwaves.

There are two noteworthy features illustrated by the figure. First, the threshold of power density depends on the duration of stimulation, almost (but not quite) by a reciprocity (power density counts slightly more, proportionally, than does duration). This phenomenon is called *temporal summation*, a psychophysical property exhibited by most of the human senses. However, this near complete reciprocity comes rather abruptly to a halt at a critical duration beyond which duration no longer matters. This is in itself remarkable because the skin temperature continues to rise beyond the critical duration. A second noteworthy feature is the difference in critical duration -- about 1 sec for infrared and 2.5 sec for microwaves. It will be interesting to see whether this difference holds with more extensive testing and whether critical duration varies systematically with wavelength. But to return to the main point: whether or not one detects radiation depends nearly as much on duration as on power density. We shall see later that the same statement could be made of stimulus area, body region stimulated, conditions of adaptation, and in all likelihood the wavelength of the radiation.

Absolute thresholds are only one way to examine the sensory effects of radiation. One might, for example, want to measure *difference thresholds* or what percentage increment to any given level of microwaves can be detected by the human observer. Analogous measurements made with infrared radiation by Herget, Granath, and Hardy (1941) showed that just-noticeably to increase a warmth sensation requires roughly a 20% stimulus increment on the forehead.

Another question of interest is the relation between the *magnitude* of the sensation and the level of radiation and other variables. One way to assess this is to have subjects make numerical estimates of arrays of stimuli that vary in level, area, duration, etc. Below is given an explicit illustration of this method. Still other measures of sensory function concern the *latency*, both of onset and offset of sensation. Observations by Hendler, Hardy, and

Murgatroyd (1963), by Schwan, Anne, and Sher (1966) and by Justesen, *et al.* (1982) suggest that microwave sensations yield very long onset and offset times compared with infrared.

Variables That Affect Temperature Sensation. I wish now to review some of the parameters of stimulation that seem likely to play key roles in the study of microwave-induced sensation. One obvious variable is the *wavelength* of the radiation. Here we have only a little information. Vendrik and Vos (1958) reported that 10-cm waves required for sensation about 10 times the power density of non-penetrating infrared waves. The work on 12.4-cm waves (Justesen, *et al.*, 1982) yielded a corresponding ratio of roughly 15. The less penetrating 3-cm waves used by Hendler, Hardy, and Murgatroyd (1963) required only about twice the levels of infrared.

I have already touched on another variable, namely *duration*, which we know counts heavily for both microwaves and infrared. However, the data in Figure 1 are restricted

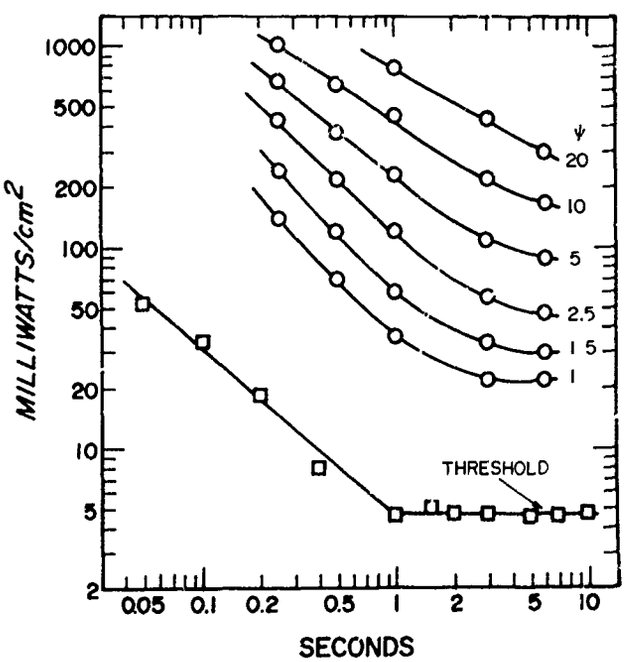

Figure 2. Showing the combinations of duration and power density (infrared) that produce a constant threshold and various constant warmth levels from weak to moderate.

solely to absolute thresholds, and it turns out that for infrared the rules of temporal summation change with increasing levels of warmth sensation. Figure 2 shows data of Marks and Stevens (1973). Each contour specifies the combinations of power density and duration that cause a constant warmth level. Although it is not so obvious to the naked eye, these contours tend to lose slope with increasing warmth level; that is, duration counts proportionally less and less than power density. On the other hand, the duration over which some summation can take place is extended to at least six seconds. Marks and Stevens argued that the heat transfer properties of the skin can basically explain the nature of this family of contours. Similar studies of microwaves could provide a rich source of information to test this theory further.

An even more important variable is the *areal extent* of stimulation. When a spot of radiation is enlarged one generally feels a greater degree of warmth level, not an increase in apparent area. This property is called *spatial summation*, and it is one of the most salient features of thermal sensation. In contrast, the sense of vision shows only trifling summation compared with warmth and cold. Changing the size of a spot of light typically leaves the brightness unchanged, and one sees instead simply an increase in the perceived area.

The rich summation of the thermal senses precludes good spatial acuity and localization of pure thermal sensations. Multiple spots of radiation usually fuse into a unitary sensation vaguely localized. Such fusion probably takes place in the central nervous system because two spots to the extreme sides of the forehead, for example, fuse to a single sensation vaguely localized near the midline. Localization of single spots is characteristically poor. Cain (1973) found that people often even confuse stimulation of the front and back of the torso, the typical error rate running about 20%. One suspects that microwaves will prove at least as difficult to localize and discriminate spatially.

There are alternative ways to study spatial summation. The first real quantitative data were the threshold studies of Hardy and Oppel (1937), and these have been confirmed and extended by more recent investigations (Kenshalo, Decker, and Hamilton, 1967; Stevens, Marks and Simonson, 1974). These studies show that in all regions of the body, power density and area trade by a near reciprocity to produce a just-detectable sensation. The area of threshold summation may be as large as 60 cm^2 or more.

As was true for temporal summation, the rules of spatial summation change as the criterion warmth level changes from

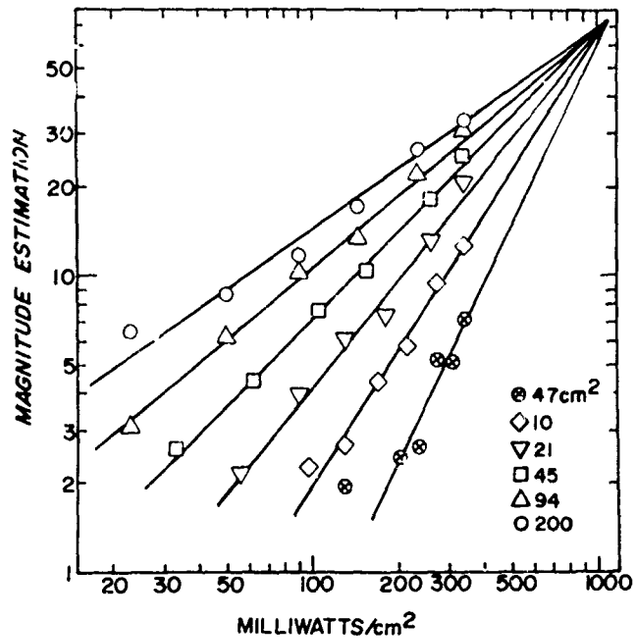

Figure 3. Magnitude estimation of warmth aroused by stimulating various areal extents of the back with various levels of infrared power density. This family of functions is fairly well described by straight lines in log-log coordinates, and they are therefore power functions of varying slopes.

a threshold sensation to a near painful level. Stevens, Marks, and Simonson (1974) studied these rules in several regions of the body. The procedure was to present various levels of radiation to various areal extents of the skin. In the course of testing, the subjects were generally unaware that area varied, and their instruction was simply to assign numbers to the apparent warmth level experienced in 3-sec exposures. This simple procedure generates data like those shown in Figure 3. Here one sees how apparent warmth level grows as a function of radiation level. There are four features to point out. (1) The thresholds for the small areas are high, but above threshold warmth grows fast with radiation level, i.e., the functions have steep slopes in log-log coordinates; (2) All of the functions converge at the threshold of thermal pain where there is no spatial summation; (3) For any given radiation level, the greater the area the greater the warmth experienced; (4) By making a

horizontal cross-section through these functions one can specify the various combinations of level and area that produce the same apparent warmth levels; in other words, one can use this figure to generate trade-off functions for area and level.

Figure 4 shows some typical trade-off contours for the back. We see here that at low warmth levels the trade-off is a near-reciprocity. With increasing level, power-density comes to count more and more than area, although the area over which some summation can occur expands to include

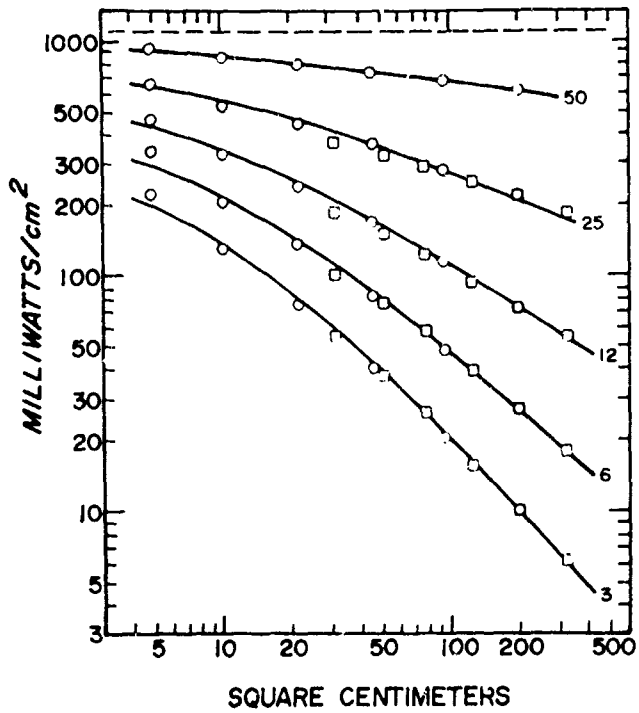

Figure 4. Showing the combinations of areal extent and infrared power density that produce various levels of constant warmth from weak (contour marked 3) to strong (contour marked 50). The dashed line represents the approximate thermal pain threshold for 3-sec exposures. The squares were generated from the data in Figure 4, the circles from an earlier similar study by Stevens and Marks (1971) done at a different time of year.

virtually the whole back of the torso. At the pain threshold, spatial summation ceases and localization improves. There is little question that spatial summation will also characterize microwave sensations, so one must be on guard against talking about a power density threshold, for example.

Body *region* also counts. Figure 5 shows the level of infrared necessary to produce various levels of warmth sensation from weak to strong (Stevens, Marks, and Simonson, 1974). At low levels the face is the most sensitive region, the trunk intermediate, and the limbs least sensitive. However, the regions become more uniformly sensitive at higher warmth levels. Very likely microwaves would also reflect these regional differences.

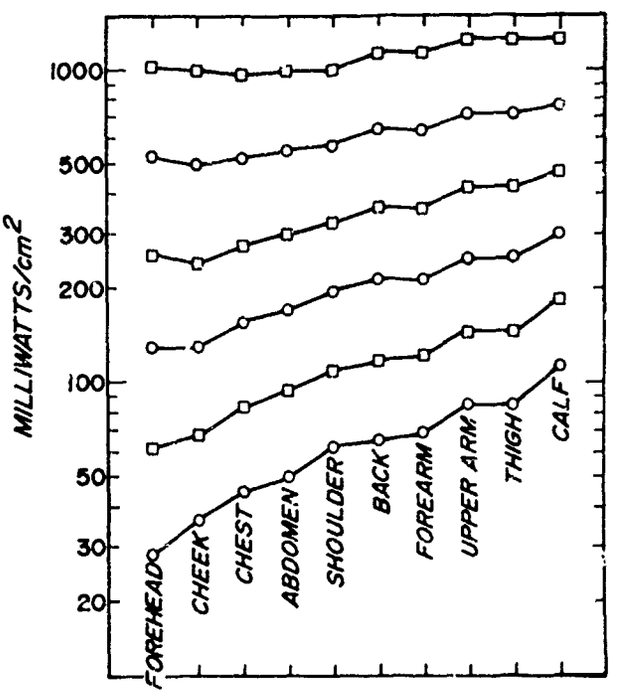

Figure 5. Showing the infrared power density needed to arouse the same warmth levels in ten regions of the skin. The contours become flatter as criterion warmth varies from weak to painful.

This listing of relevant parameters is not meant to be exhaustive. I have, for example, confined myself to studies using relatively transient stimulation and thereby avoided the complexities of thermal adaptation. It is commonplace in thermal psychophysics, however, that sensations aroused by infrared stimulation or by contact stimulation tend to fade over time. There is every reason to think that microwave-induced sensations will do the same. In fact, Justesen, *et al.* (1982) made some casual observations that resembled adaptation. The problem of adaptation may turn out to have a central role in understanding the behavior of organisms exposed to microwave radiation over long periods of time. I have also left out of discussion potential personal variables such as age, sex, and body dimensions. Finally, I have said nothing about the arousal of pain by microwave stimulation. Cook (1952) measured pain thresholds, and again the picture appears complex in that

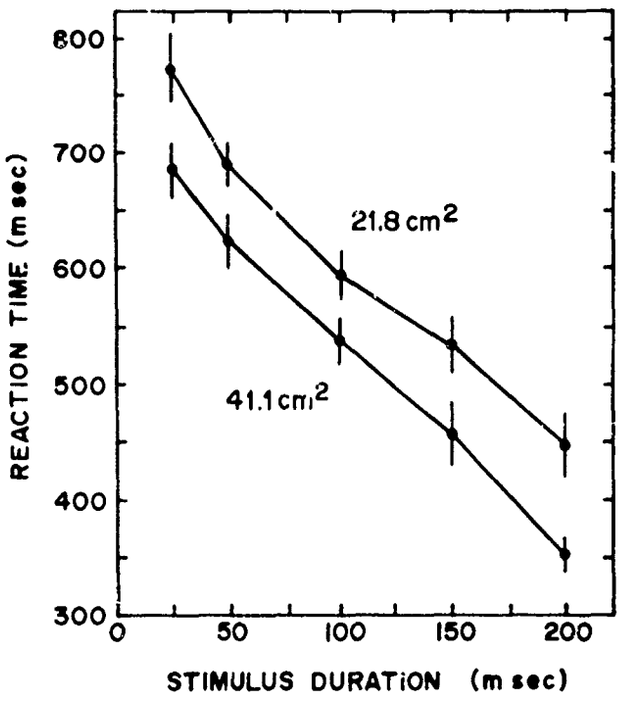

Figure 6. Showing how the reaction time for a constant power density (infrared) varies as a function of five different durations and two areal extents of the forehead. Redrawn from Banks, 1976.

the threshold depends not only on power density, but also on duration and area of exposure.

In conclusion, one must emphasize that the three most potent variables governing warmth sensation appear to be power density, area, and duration. These three can be traded one for another to produce a given sensory effect. As a final example, in Figure 6 we see data of W. P. Banks (1976) showing that the speed of reaction (i.e., onset latency) for infrared improves with both the duration and area, just as it does with power density. In other words, onset latency is related to spatial and temporal summation. It will be especially interesting to learn how microwaves behave in this respect, both as regards onset and offset latencies. Casual measurements of onset latency by Justesen, *et al.* (1982) came to about 3.5-6.0 sec, about an order of magnitude longer than onset latencies shown in Figure 6. In Chapter 10 in this volume D. R. Justesen explores the unfavorable implications of these long latencies in the learning of escape behavior by murine organisms exposed to microwave radiation. The long offset latencies observed by Hendler, Hardy, and Murgatroyd (1963) and by Justesen, *et al.* (1982) are also of interest (a kind of "afterglow" that can last up to at least 15 sec). In contrast, infrared sensations extinguish quite abruptly when stimulation ceases.

Although it is at present impossible to say much about thermal sensations aroused by microwaves, it is doubtless expedient that any future psychophysical programs of studies be guided by past experience with more conventional means of thermal stimulation. Only then will we be able to come to grips with the complexity of the problem and to avoid simplistic generalizations from limited kinds of testing.

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REFERENCES

Banks, W.P. (1976) Areal and temporal summation in the thermal reaction time. *Sens. Proc.* 1:2.

Cain, W.S. (1973) Spatial discrimination of cutaneous warmth. *Amer. J. Psychol.* 86:169.

Cook, H.F. (1952) The pain threshold for microwave and infra-red radiations. *J. Physiol.* 118:1.

Cornsweet, T.N. (1962) The staircase method in psychophysics. *Amer. J. Psychol.* 75:485.

Eijkman, E.G. and Vendrik, A.J.H. (1961) Dynamic behavior of the warmth sense organ. *J. Exp. Psychol.* 62:403.

Hardy, J.D. and Oppel, T.W. (1937) Studies in temperature sensation. III. The sensitivity of the body to heat and the spatial summation of the end organ responses. *J. Clin. Invest.* 16:533.

Hendler, E., Hardy, J.D., and Murgatroyd, D. (1963) Skin heating and temperature sensation produced by infrared and microwave irradiation. In *Temperature: Its measurement and Control in Science and Industry* (C.M. Herzfeld, ed), p.211. Reinhold, New York.

Herget, C.N., Granath, L.P., and Hardy, J.D. (1941) Warmth sense in relation to the area of skin stimulated. *Amer. J. Physiol.* 135:20.

Justesen, D.R., Adair, E.R., Stevens, J.C., and Bruce-Wolfe, V. (1982) Human sensory thresholds of microwave and infrared irradiation. *Bioelectromagnetics* 3:117.

Kenshalo, D.R., Decker, T., and Hamilton, A. (1967) Spatial summation on the forehead, forearm, and back produced by radiant and conducted heat. *J. comp. physiol. Psychol.* 63:510.

Marks, L.E. and Stevens, J.C. (1973) Temporal summation related to the nature of the proximal stimulus for the warmth sense. *Percept. & Psychophys.* 14:570.

Schwan, H.P., Anne, A., and Sher, L. (1966) Heating of living tissues. U.S. Naval Air Engineering Center, Philadelphia, Report NAEC-ACEL-534.

Stevens, J.C. and Marks, L.E. (1971) Spatial summation and the dynamics of warmth sensation. *Percept. & Psychophys.* 9:391.

Stevens, J.C., Marks, L.E., and Simonson, D.C. (1974) Regional sensitivity and spatial summation in the warmth sense. *Physiol & Behav.* 13:825.

Stevens, J.C., Okulicz, W.C., and Marks, L.E. (1973) Temporal summation at the warmth threshold. *Percept. & Psychophys.* 14:307

Vendrik, A.J.H. and Vos, J.J. (1958) Comparison of the stimulation of the warmth sense organ by microwave and infrared. *J. Appl. Physiol.* 13:435.

SENSORY DYNAMICS OF INTENSE MICROWAVE IRRADIATION: A COMPARATIVE STUDY OF AVERSIVE BEHAVIORS BY MICE AND RATS

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INTRODUCTION

My intent in this paper is to present and discuss original data that bear on a seeming paradox in mammalian perception of non-pulsatile microwave fields. The paradox is related to the *sensory dynamics* of perception, by which I mean the temporal and spatial characteristics of the sensations of warmth that attend irradiation at levels below the threshold of pain. First, however, a reprise of pertinent data is needed to characterize and define the paradox.

Absolute thresholds in the detection of microwave irradiation have been determined for human observers in several formal studies, all of which have involved short exposures (<10 s) of the body, typically of a circumscribed area of the forehead or forearm (Vendrik and Vos, 1958; Hendler, *et al.*, 1963; Schwan, *et al.*, 1966; and Hendler, 1968; see also the review by Michaelson, 1972, and the discussion by Stevens in Chapter 9). In most studies, thresholds have been couched solely in terms of exposure duration and of composite strength of the incident field (irradiance in W/cm^2), although indirect measures of energy absorption in conjunction with direct measures of irradiance have

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recently been reported (Justesen, *et al.*, 1982). Collectively, the findings from the cited studies indicate that field strengths, latencies to detection, and quantities of energy absorbed at the threshold of just-detectible warming decrease at shorter wavelengths. For example, Hendler, *et al.* (1963) found that a 4-s exposure of a 37-cm^2 area of the forehead to a 3-GHz field required a mean irradiance of 33.5 mW/cm^2 at the warmth threshold, which fell to 12.6 mW/cm^2 at 10 GHz and to 4.2 mW/cm^2 under far-infrared irradiation (>1000 GHz). Even allowing for differential scatter--about half of the energy in a 3-GHz or 10-GHz plane-wave field that is incident on the human body is not absorbed (see, e.g., Schwan, 1970), while far infrared waves are virtually perfectly absorbed (Hendler, *et al.*, 1963; Justesen, *et al.*, 1982)--it is apparent that greater quantities of the more deeply penetrating microwave energy are required to elicit a sensation of warmth. The greater depth of penetration by fields of longer wavelength is tantamount to a lower energy density per absorbed photon in the superficial layers of the skin that contain the thermal receptors. If some finite ΔT (or if some finite rate of increasing temperature) is required to excite a superficial thermal receptor, a greater quantity of the more deeply penetrating and more diffusely absorbed energy will be required to hyperthermalize the tissue that shelters the receptor.

The data of Justesen, *et al.* (1982), which are based on 10-s exposures of the human forearm (average area 107 cm^2), indicate that energy dosages near 10 joules ($\sim$90 mJ/cm^2) of 2450-MHz energy and near 2 joules ($\sim$20 mJ/cm^2) of far-infrared energy were required to elicit a sensation of warmth. Strictly comparable data on absorbed-energy thresholds of detection by infrahuman subjects do not exist because of marked differences in relative surface areas of exposed tissue. For example, King, *et al* (1971) found that *whole-body* exposures of the adult male rat to a 2450-MHz multi-path field required an energy dosage approximating 14 joules to promote a threshold level of detection. As another example, Adair and Adams (1980), during unrestricted, plane-wave exposures of squirrel monkeys to a CW 2450-MHz field, obtained evidence of a power-density threshold of detection near 7 mW/cm^2 (for a 10-min. duration of exposure), which extrapolates to a whole-body energy dosage approximating 10 joules (see Chapter 18 for a detailed discussion of data from infrahuman studies).

The paradox associated with perception of non-pulsatile microwaves inheres, on the one hand, in the ease with which human observers and infrahuman subjects detect the presence of a relatively weak field and, on the other hand, in the

difficulty that murine animals encounter in attempting to escape from a potentially lethal field (Carroll, *et al.*, 1980; Levinson, *et al.*, 1981, 1982). Rats exposed *ad libitum* in a 918-MHz multi-mode cavity to fields that resulted in a whole-body-averaged dose rate ($\dot{D}$ of 60 mW/g could attenuate or extinguish the field simply by moving into and remaining in a well-demarcated *safe* area, which bordered the rear wall of the cavity and comprised 25% of the area of its false floor of Plexiglas. Although the rats frequently entered and left the safe area, thereby frequently extinguishing and reactivating the field, they exhibited virtually no evidence of escape learning--as defined by an increasing habitation of the safe area--unless provided auxillary cueing by a photic stimulus, i.e., by a house light synchronized to illuminate during periods of the behaviorally contingent irradiation (Levinson, *et al.*, 1982). In contrast, rats motivated solely by faradic shock to the feet rapidly learned the same simple escape response. The failure of irradiated-but-uncued rats to learn an escape response would have had a lethal outcome had not a 2-min. interval of surcease intervened between each of five, 2-min. periods of available irradiation (Carroll, *et al.*, 1980).

These observations of rat behavior give rise to the question: If the animal can detect warming by a field that imparts energy at a whole-body averaged rate near 600 μW/g (King, *et al.*, 1971), why doesn't it take refuge from a field that is depositing energy in its body at a rate that is a hundredfold higher and that exceeds the resting metabolic rate by more than tenfold? *That* is the paradox. One likely possibility relates to the factor of *thermal inertia*. Hendler, *et al.* (1963) and Schwan, *et al.* (1966) reported that detection latencies of part-body warming under moderate-to-intense microwave fields (to $\sim$75 mW/cm^2) by human observers sometimes extended to tens of seconds; moreover, the sensation of warmth often persisted for tens of seconds to minutes after extinction of the field. Since rapid escape learning requires a close temporal contiguity between the act of escaping and the cessation of annoying or painful stimulation, it is quite possible that the rats of Carroll, *et al.* (1980) and of Levinson, *et al.* (1982) readily perceived and were discomfited by excessive warming but, given its persistence, were unable to associate an adaptive locomotor response with extinction of the field. The assay of detection used by King, *et al.* (1971), conditional suppression (Estes and Skinner, 1941), did not require a rapidly discerned onset of sensation. The field was presented aperiodically for relatively lengthy (60-s) periods, served as a conditional stimulus that warned of impending

shock to the feet, and eventually resulted in learned suppression of operant behavior, which was the criterion of detection. Also, the foot shock was brief (<1 s) and provided a highly salient signal that a period of warning stimulation was concluded.

Another, non-exclusive possibility in the rats' failure to escape attaches to the factor of *state dependence*. An abundance of data confirms defects of memory--specifically, of memory *retrieval*--in animals after they have learned to perform a response under one physiological state and then are tested for retention under another state (Overton, 1964; Nielson, 1968; Nielson, *et al.*, 1968). For example, rats well trained to make an avoidance response failed selectively to manifest it when lightly dosed with chlordiazepoxide (Sachs, *et al.*, 1966). It follows that if incorporation of a drug can selectively inhibit retrieval of a learned response, a rapid, systemically pervasive increase of temperature might create a succession of differing internal states that could defeat or obtund learning or retention (Jacobs and Sorensen, 1969; Misanin, *et al.*, 1979).

Yet another and still non-exclusive possibility attaches to the factor of *thermal preference*. The experimental psychologist has embraced the rat for its docility, availability, and ease of upkeep but, cavaliarly in return, has usually maintained it in an environment preferred by psychologists, not by the rat. *Homo sapiens'* preferred ambient temperature lies near 24 °C, that of domesticated *Rattus norvegicus*, near 28 °C (Hardy, 1970; Murgatroyd and Hardy, 1970; Altman and Dittmer, 1968). Is it not possible that the rat in an environment a few degrees too cool for comfort will initially enjoy the warming afforded by an intense microwave field? If so, an eventual shift from comfortable to uncomfortable levels of warming could make for a confusing wrinkle in the sensory dynamics attendant to continued irradiation. Stated differently, the cognitive apparatus of the rat or of any mammal may be taxed in discerning the connection between a little of something that feels good and more of the same thing that eventually feels bad (Cabanac, *et al.*, 1968; Cabanac, 1971).

Along with other concerns, the factors of thermal inertia, state-dependent memory, and shifting hedonic tone led me and my colleague, Daniel Levinson, to embark three years ago on a long-term multifactorial study of murine escape behaviors. Gender, species (rat vs. mouse), regimen (adventitious acquisition vs. successive approximation), field condition (plane-wave vs. multi-path, carrier frequency, modulation, and dose rate), environment (low, moderate, and high ambient temperatures and air velocities), training

schedule (massed vs. spaced trials), auxilliary cueing (photic vs. acoustic stimulation), and task difficulty are among the variables of interest. In this paper, I shall recount some findings from a still largely unfinished effort; collectively, the findings shed some light on the variables of species, field intensity, schedule, training regimen, and difficulty of task.

EXPERIMENT I

Materials and Methods

Fourteen adult female rats of the Long-Evans strain (Blue Spruce Farms, Altamont, New York) and 24 adult male mice of the CF1 strain (Harlen Sprague-Dawley Company, Madison, Wisconsin) served as subjects. They were maintained in separate vivaria of the Kansas City VA Medical Center under the following conditions: ambient temperature, 22 ±2 °C; housing, mice group caged, rats individually caged; and food, all animals had *ad lib.* access to Purina Lab Chow and water in the home cage. The daily light-dark cycle was 12/12 h (lights on at 0600 h).

Two false floors of opaque, white Plexiglas (Figure 1) and identical dimensions (45.6-cm wide x 35.7-cm deep x 0.6-cm thick) were used interchangeably in the 2450-MHz, Tappan-R3L multi-mode cavity described by Justesen, *et al.* (1971a). Each floor was inscribed with a circular safe area formed by a 1-cm-wide border of black-plastic tape. The circle's diameter was 22.75 cm and was centered on and comprised 25% ($\sim$407 cm^2) of the floor's total surface. One of the floors contained a grid of conductive silver paint, virtually white in hue, by which nonavoidable faradic shock could be applied to the feet and tail (Justesen, *et al.*, 1971b; Carroll, *et al.*, 1980). The other floor was inscribed only with the black-bordered circle and was used exclusively with animals exposed to microwave irradiation. The layout of the two floors, because the safe area was in the center, constitutes the most difficult task used to date in my laboratory in studies of escape learning by mice and rats.

Calorimetric dosimetry was performed on Styrofoam-insulated, 40- and 300-g models of water according to the procedure of Justesen, *et al.* (1971a). When an animal of a given mass was irradiated, available energy in the cavity was adjusted to result in a D of 60 or 120 mW/g (±10%). Excitation and extinction of the field was controlled by manual depression and release of a microswitch by an investigator, operation of which simultaneously resulted in

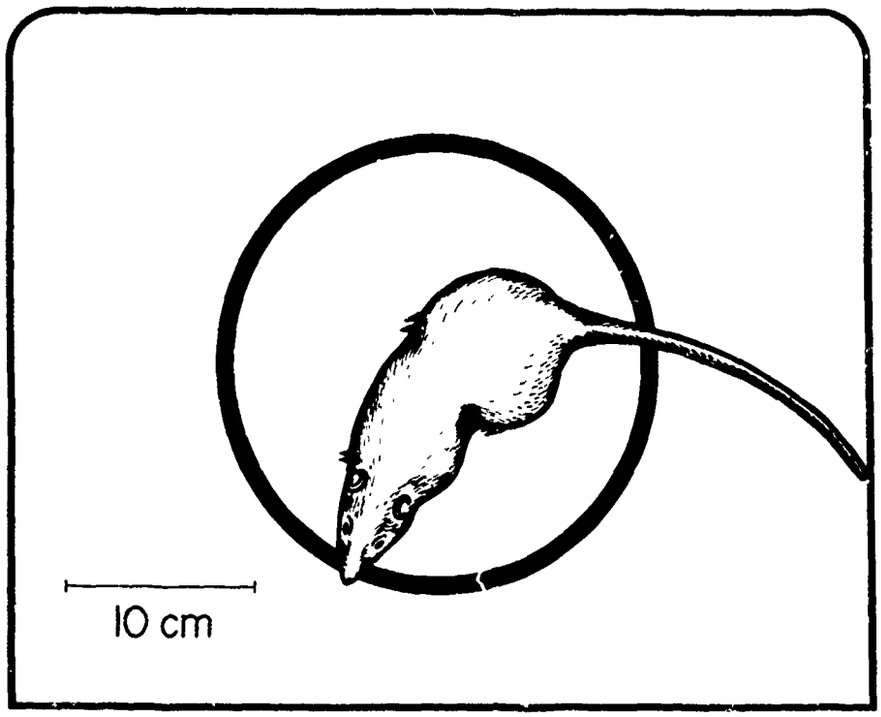

Figure 1. Overhead drawing of a rat on a false floor of white, opaque Plexiglas, which was installed in a 2450-MHz multi-mode cavity. The black-bordered circle enclosed the *safe* area, entry into which by a rat or mouse resulted in cessation of microwave irradiation or of faradic footshock. Exit from the safe area resulted in immediate reintroduction of irradiation or shock. Two interchangeable floors were used; one contained a grid of silver paint, which was used to apply faradic shock to active-control animals.

displacements of a pen of a 20-pen event recorder (Esterline-Angus Model-AW). The microswitch was also used to initiate and terminate faradic shock (at levels between 150 and 300 μA rms) during trials involving active-control animals. Periodically, a second microswitch was independently operated by a second investigator to provide a measure of inter-observer reliability. Movements of an animal within the cavity were easily viewed through a radiopaque grille, and independently recorded entries to, durations

within, and exits from the safe area all yielded reliabilities (Pearson product-moment *rs*) approaching unity.

Procedure

Mice and rats were measured daily for body mass on a Mettler Model-P1210 analytic balance and then were individually placed on the floor of the cavity (Fig. 1) for a 15-min. session per day either until completion of a 6-day sequence of sessions or until they expired from hyperthermia. The rats' body masses averaged 246 (±15.7 SD) g; the mice, 39.2 (±2.1 SD) g at initiation of experimentation. During the first day, baseline frequencies of entry to the safe area and times spent therein were recorded. During the sessions of days 2, 3, 4, and 5, irradiation or faradic shock was continuously presented unless an animal entered and remained in the safe area; irradiation or shock resumed immediately upon an animal's exit. Entry was defined as movement of the animal's head across the border of the safe area; conversely, an exit was defined as movement of the head across the border into the unsafe area. During day 6, irradiation or faradic shock was withheld; occupancy time in the safe area on that day provided a measure of resistance to extinction. Across the six days, temperatures in the cavity ranged between 22 and 25 °C (relative humidity, 50 ±10%), and the spatially averaged flow of air, as measured by a Kurz Model-441-M air-velocity meter, was 0.1 m/s. Ten rats and 20 mice were exposed to microwaves; four of each species, to faradic shock. The experiment was conducted in two segments. During the first segment, in which 10 mice and 10 rats were individually subjected to irradiation at 60 mW/g, outcomes dictated the need for an additional group of mice. Ten additional, experimentally naive mice were subjected to irradiation at 120 mW/g. Active controls--animals motivated by faradic shock--numbered four mice and four rats and were also observed at this time.

Results and Discussion

The data are summarized in Table 1 and Figure 2. Table 1 presents means of the frequencies with which mice and rats entered the safe area during baseline measures (day 1), during sessions in which microwave irradiation or faradic shock was terminated each time an animal entered the safe area (days 2 through 5), and during the final session of day 6 in which resistance to extinction was measured. The entry

Table I. Mean Frequency of Entries to Safe Area
(±Standard Error)

Species	Original n	Condition	Day 1 Baseline Entries	Day 2 Entries	Day 3 Entries	Day 4 Entries	Day 5 Entries	Day 6 Entries in Ext.	Mortality
Mouse	10	MW-60 mW/g	4.5(0.86)	4.9(1.72)	5.2(2.3)	4.8(1.73)	6.6(2.42)	5.1(2.68)	1, day 3; 1, day 5
Mouse	4	Shock	12.5(1.85)	4.3(0.85)	3.0(0.71)	2.3(1.25)	2.5(0.65)	8.8(5.12)	None
Rat	10	MW-60 mW/g	14.5(1.10)	4.6(0.58)	-	-	-	-	All 10, day 2
Rat	4	Shock	11.0(2.64)	8.3(1.65)	3.8(0.85)	2.3(1.32)	2.8(1.25)	0	None
Mouse	10	MW-120 mW/g	7.7(1.51)	4.4(1.54)	3.0(0.0)	-	-	-	9, day 2; 1, day 3
		Weighted Mean = (n = 38)	9.5	4.9*					

*Although this mean is based on all 38 animals, 22 expired from microwave irradiation before the end of the session.

Mean frequencies of entries to the safe area of a multi-mode cavity by the animals (24 mice and 14 rats) of Experiment I. During days 2, 3, 4, and 5, cessation of microwave (MW) irradiation at a whole-body-averaged dose rate of 60 or 120 mW/g was behaviorally contingent upon an animal's entry to the safe area. Irradiation resumed upon departure. Shocked animals received faradic current through the feet (∿150-300 μA rms) under the same contingency during the same four days. Baseline means of entries were recorded during day 1. The entries recorded during day 6 provide a measure of resistance to extinction. All daily sessions were of 15-min. duration.

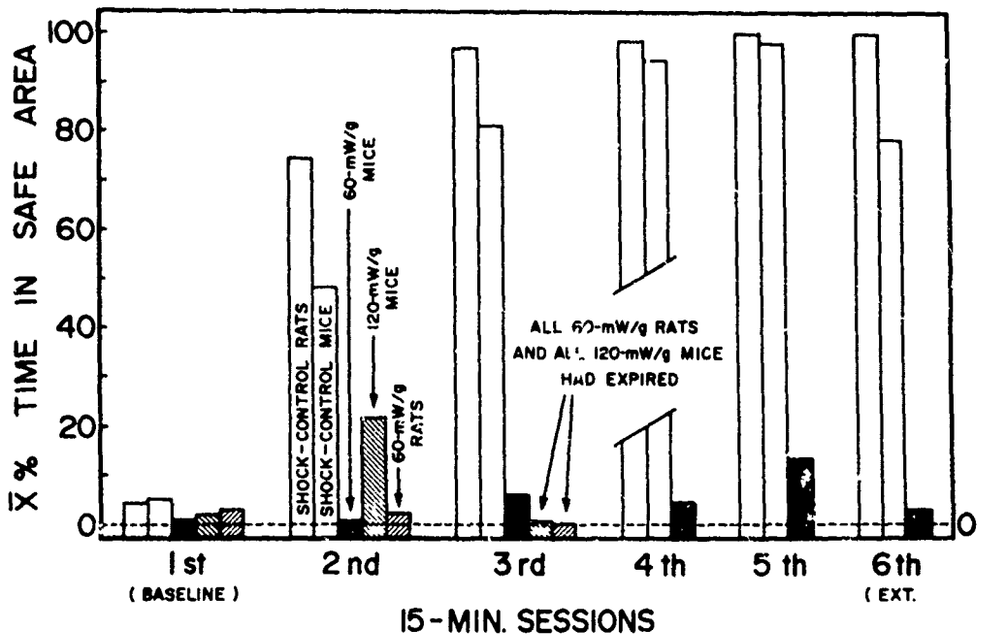

Figure 2. Experiment I: Mean-percent cumulative time spent by rats and mice in the safe area of a multi-mode cavity during a succession of six 15-min. sessions per animal under baseline (day-1), stimulation (day-2 through day-5), and extinction (day-6) conditions. Four rats and four mice (open bars) were reinforced upon entry to the safe area by cessation of faradic shock. Each of ten rats and ten mice was reinforced upon entry by cessation of microwave irradiation at 60 mW/g; ten mice of another group were reinforced by cessation of irradiation at 120 mW/g (hatched bars). All of the rats and two of the mice dosed at 60 mW/g expired, as did all mice dosed at 120 mW/g.

datum recorded in Table 1 is not a measure of escape learning but indexes pertinent locomotor activity; unless an animal entered the safe area there was no opportunity for negative reinforcement by surcease of annoying stimulation. The mean numbers of entries associated with initial exploration (day 1) were reliably different among the five groups of animals (F = 4.01; at 4 and 33 *df.*, P<.05) but were much more uniform during day 2 when irradiation or shock was first presented (F = 0.73; at 4 and 33 *df.*, P >.10). Animals of all groups exceeded a mean of four reinforced

entries during the first session of encounter with shock or radiation (day 2).

The measure of escape learning by groups of animals, which is the mean percentage of cumulative time spent per session in the safe area, is plotted in Fig. 2. Baseline means of occupancy time were low in animals of all five groups, ranging from 1 to 5%. Analysis of variance revealed a moderate but reliable difference among these means ($F = 4.83$; at 4 and 33 *df.*, $P<.05$). The shocked animals rapidly mastered the escape task and, although mice lagged somewhat behind rats during the first two sessions, near-complete avoidance of shock was demonstrated by animals of both species by the third and fourth sessions. In contrast, reliable evidence of escape, which was assessed by comparing baseline times of occupancy in the safe area with times during sessions of irradiation, was not demonstrated by any group of irradiated animals during any session (all Fs $\sim$1.0, all Ps > .10).

The failure of rats to escape from irradiation at 60 mW/g is associated with a high incidence of lethality; all ten animals expired during the first session of exposure. Median time to *cessation* of a *grand-mal* convulsion, which was observed in all ten rats, is 593 seconds. The whole-body-averaged dose of energy ($\dot{D}$) associated with this median, 35.6 J/g, doubtless overestimates the median lethal dose since termination of irradiation at *onset* of a *grand-mal*, microwave-induced convulsion is associated with a high incidence of lethality (Justesen, *et al.*, 1977; Justesen, 1979). The failure of mice to escape from irradiation at 60 mW/g is not associated with large-scale lethality; only two of ten animals expired, one during the second session of irradiation, one during the fourth. Scrutiny of individual occupancy times revealed two mice that respectively spent 25 and 52 percent of their time in the safe area during the fourth and final session of irradiation as compared with a mean of 4.8% for the remaining survivors. Whether the two higher percentages represent chance variation, indications of early acquisition, or, perhaps, evidence of behavioral thermoregulation, were uncertainties that dictated the decision to subject another 10 mice to irradiation at 120 mW/g.

Nine of the ten mice irradiated at 120 mW/g convulsed and died during the first session of irradiation. The medium time to cessation of convulsions, which were observed in all nine mice, is 346 seconds, which yields an average (supra-lethal) dose of 41.5 J/g. The tenth mouse expired during the second session of exposure, after 242 seconds. The energy dose was 29 J/g.

That intense and seldom-mitigated energy dosing at a rate of 60 mW/g was fatal for all ten Long-Evans' rats but for only two of ten CF1 mice presumably reflects the greater surface-area to body-mass ratio of the smaller species, i.e., the greater surface area affords more efficient dissipation of thermalized energy to a cooler surround. This interpretation comports with the findings of Monahan and Ho (1977a, 1977b) who found that female CF1 mice at ambient temperatures of 20 to 25 °C survived continuous, 15- to 20-min. exposures in a waveguide to 2450-MHz fields at a D that ranged as high as 65 mW/g. A mitigating factor that doubtless aided survival of these mice was the relatively high velocity (>1 m/s) of air that flowed through the authors' waveguide-exposure system.

The day-6 measure of resistance to extinction yielded some interesting findings. All four of the previously shocked rats spent 100% of their time in the safe area compared with an average of 78% by the previously shocked mice. These high percentages indicate that the escape-response habit was well established, albeit reliably more strongly in the rats ($P<<.01$, non-overlapping distributions). The eight surviving mice that had been subjected to irradiation at 60 mW/g spent an average of 2.7% of their time in the safe area during the extinction measure. When compared with the mean of the animals' control (baseline) percentages of day 1, 1.6%, the difference failed to depart from chance ($t = 0.7$; at 7 *df.*, $P > .10$). The mouse that had spent 52% of its time in the safe area during its final session of irradiation, spent 19% of its time in the safe area during the extinction session. This percentage does represent a relatively sizeable increase over the animal's control baseline of 1.4% and may represent an isolated case of escape learning.

Temperatures of the 38 animals were not measured (because of the potential confounding effects on memory when manual handling is conjoined with intense microwave irradiation [Bryan, 1966]), but the behavior of irradiated animals is fully compatible with the supposition of hyperthermalization. After a period of intense exploratory activity, an irradiated mouse or rat would spread saliva on its pelt, urinate, and become prostrate. *Grand-mal* convulsions were observed in all animals that expired. All of the irradiated animals that survived were palpably warmer upon removal from the cavity than they were just prior to irradiation.

Oddly enough, but fully in keeping with prior observations of the rat in my laboratory (see, e.g., Bermant, *et al.*, 1979; Carroll, *et al.*, 1980), not one mouse that survived a previous session of irradiation exhibited aggressive behavior upon being returned to the cavity; in contrast,

all mice and rats that had been subjected to faradic shock had to be handled carefully to prevent them from escaping from or biting the hands of the experimenter. Either or both of two possibilities could explain the absence of aversive and agonistic behaviors in the animal with a history of intense irradiation: analgesia and amnesia. Elevation of body temperature is reciprocally associated with elevation of circulating endorphins (Millan, *et al.*, 1981), the presence of which is associated with obtunding of pain (Terenius, 1978). Amnesia or analgesia borne of temperature-dependent changes of internal chemistry might therefore explain the failure of animals to learn the escape response during repeated sessions of irradiation. Indeed, it is tempting to speculate that a state-dependent retrograde amnesia akin to that induced by electroconvulsive shock or febrile convulsions was operating (Bryan, 1966; Murphy, *et al.*, 1967; Oke, *et al.*, 1974; Lovely, *et al.*, 1978; Guy, & Chou, 1982). If an intense but subconvulsive dose of microwave irradiation also results in retrograde amnesia, every visit to the cavity might be lost to the animal's memory. Alternately, given the difficult task--for the positively thygmotactic animal--of abandoning the periphery of the cavity to enter the open area of the circle might have conduced to immobilization borne of *learned helplessness* (Maier, *et al.*, 1969). Immobilization would be associated with reduced metabolic activity, which could, at least for the mouse, be the lower margin of total energy production that afforded survival.

None of the shocked animals exhibited immobilization. A recent report by Bermant, *et al.* (1979) revealed that rats developed high but stable colonic temperatures near 39 °C simply on being brought into a laboratory that housed the cavity in which they had been subjected to repeated faradic shock. This stable, locale-dependent rise of temperature in rats after exposure to electric shock has also been reported by Delini-Stula (1970) and could be a potent factor in facilitating retrieval of memory. One might be dealing with a literal as well as figurative "warm-up" phenomenon. That is, if memory is dependent on body temperature, retention will be most nearly intact when the temperature is the same under conditions of original learning and later measures of retention. Learning to escape from and to avoid shock would be accomplished much more rapidly therefore at the same elevated body temperature than would learning in which temperature is constantly rising--is constantly changing the body's physical and physiological state. It follows that faradic shock as a negative reinforcer might be less effective in promoting learning of an escape response if an animal were

subjected concurrently to intense microwave irradiation. It also follows that if the irradiated rat were able to utilize early, acceptable, even preferred levels of warming as a cue that predicts later, excessive warming, it might establish a regulated *steady-state* temperature, mediated behaviorally, by alternately escaping from and re-entering an otherwise eventually-lethal field.

My colleagues and I have yet to use the microwave field to alter the thermal state of shock-motivated animals, but there are preliminary findings that bear on the steady-state hypothesis (see Experiment II below).

The results of Experiment I demonstrated unequivocally that experimentally naive mice and rats under an *ad libitum* regimen do not quickly learn to escape from an intense, potentially lethal, multi-path field at 2450-MHz. These results confirm and extend earlier studies of rats subjected to intermittent bouts of irradiation at 60 mW/g in the multi-path field of a 918-MHz cavity (Carroll, *et al.*, 1980; Levinson, *et al.*, 1982). In addition to the difference in carrier frequencies, there are procedural differences between the present and earlier studies that are worthy of note. The earlier studies employed five 2-min. bouts of irradiation, each bout separated by a 2-min. interval, which would result in a maximal exposure time of 10 minutes per daily session. The intervals allowed dissipation of thermal energy by the intensely irradiated animal and were intended to preclude lethality. Since alternating periods of irradiation and respite might have interfered with learning of escape, it was necessary to turn to the sink-or-swim (actually, *learn-or-burn*) format of Experiment I, i.e., irradiation was continuously available during the 15-min. sessions of days 2 through 5. Although I doubt, given the behavioral evidence cited earlier, that the hyperthermalized animal suffers unduly or long, I hope no one perceives the need for parametric experiments that portend lethality on a large-scale.

As noted earlier, the task required of mice and rats in Experiment I is the most difficult yet employed in my laboratories. The task employed by Carroll, *et al.* (1980) and Levinson, *et al.* (1982) was of intermediate difficulty, although it, too, involved a safe area that comprised 25% of a cavity's false floor. However, the area used by them was located against the back wall of the cavity, which should and did result in relatively longer basal occupancy times by the positively thygmotactic animal. In other studies, (Levinson, *et al.*, 1981), data were obtained from experimentally naive animals subjected to a shuttle-box task, i.e., the false floors of 918- and 2450-MHz cavities were equally

partitioned into safe and unsafe areas. Sometimes the left half of the floor was safe, sometimes the right half, in accord with the need to counterbalance for a potential position preference. Lethality was nil when behaviorally contingent irradiation at a dose rate of 60 mW/g was scheduled. The absence of lethality is hardly surprising since, given equiprobable times of residence in both sides of the cavity, an animal's energy dose would approximate 18 J/g (300 s x 60 mW/g), which at moderate ambient temperatures is well below the rat's threshold of lethality (Justesen, 1975; Justesen, 1979).

The shuttle-box studies revealed that both mouse and rat will locomote repeatedly in and out of the safe area, perhaps to maintain a preferred body temperature, but the possibility of behavioral thermoregulation is clouded by the possibility of a *random walk*. That is, moderate thermalization during the initial period of irradiation may lead to behavioral arousal, to an increase of exploratory activity, and thus to an increased probability that the animal will locomote fortuitously to the safe area. The fall of temperature after entry to the safe area presumably would reduce the level of arousal and attendant motor activity to the end of increasing the relative amount of time spent therein. Either mechanism therefore--behavioral thermoregulation or a random walk under field-contingent excitation of arousal--could explain the finding that cumulative time spent in the safe side of the cavity increased across sessions until it was reliably above the basal level. However, at best, the asymptote of safe-area occupancy never reached the high, virtually 100% levels associated with foot-shock motivation.

One of my research assistants, Donald Riffle, took an interesting tack toward resolution of the random-walk question. He selected individual rats with a history of escape training akin to that of the microwave-irradiated rats of Levinson, *et al.* (1982), who exposed their animals during five 2-min. periods to behaviorally contingent radiation at 60 mW/g; 2-min. intervals were used between periods of available irradiation. Mr. Riffle began with a total of eight animals, four that had been assessed for escape from microwaves only and four for whom an acoustic cue had been paired with periods of behaviorally contingent irradiation. None of the animals had previously exhibited reliable indications of escape behavior, but all had been extensively handled and had been irradiated on several occasions. Four of the eight rats failed to survive a 10-min. session in which 2450-MHz energy was *continuously* available in the cavity; a relatively difficult escape task, entry to a centered circle, was used. The other four rats survived.

EXPERIMENT II

Materials, Methods, and Procedure

Four Long-Evans rats, with a history of exposure to a 2450-MHz multipath field that is summarized in the preceeding paragraph, were subjected to irradiation in the 2450-MHz cavity. Behaviorally contingent bouts of irradiation were scheduled as in Experiment I during a total of four sets of sessions. Each set comprised six sessions, each session of 10-min. duration per animal and separated by ∿24 h. The first session of each set was scheduled without irradiation, to permit recording of control baselines of cumulative time each animal spent in the safe area. The sixth session of each set was also scheduled without irradiation, to obtain measures of resistance to extinction. Whole-body-averaged dose rates of irradiation were at a given level during a given set of sessions, but differed across sets of sessions: Set 1, 60 mW/g; Set 2, 30 mW/g; Set 3, 120 mW/g; and Set 4, 60 mW/g. Two of the four rats received auditory cueing (2900 Hz at 80 dB) synchronized with periods of irradiation, as they had in a previous study. The other two rats, as before, were exposed only to microwave radiation. Colonic temperatures of each rat were measured before and after most sessions by a Bailey Model BAT-8 thermometer with a Bailey Model OT-1 thermocouple probe. The thermometer and probes were calibrated against a Taylor Model-21002 certified standard; readings were accurate within ±0.1 °C.

Results and Discussion

Figure 3 summarizes mean-percent times in the safe area and associated means of post-session measurements of colonic temperature. During the first session of irradiation at 60 mW/g, the two rats that received acoustic cueing spent much more time in the safe area than did the two uncued rats. In consequence of the longer durations spent in the unsafe area under irradiation, both of the uncued rats exhibited a high elevation of colonic temperature (to 44.1 °C) that probably would have been lethal to a non-acclimated animal--one without a recent history of several exposures to an intensely thermalizing field (Gelineo, 1940, 1964; Michaelson, *et al.*, 1965). During the 2nd, 3rd and 4th sessions at 60 mW/g, all four rats exhibited relatively moderate elevations of temperature and spent 40 to 60% of their time in the safe area.

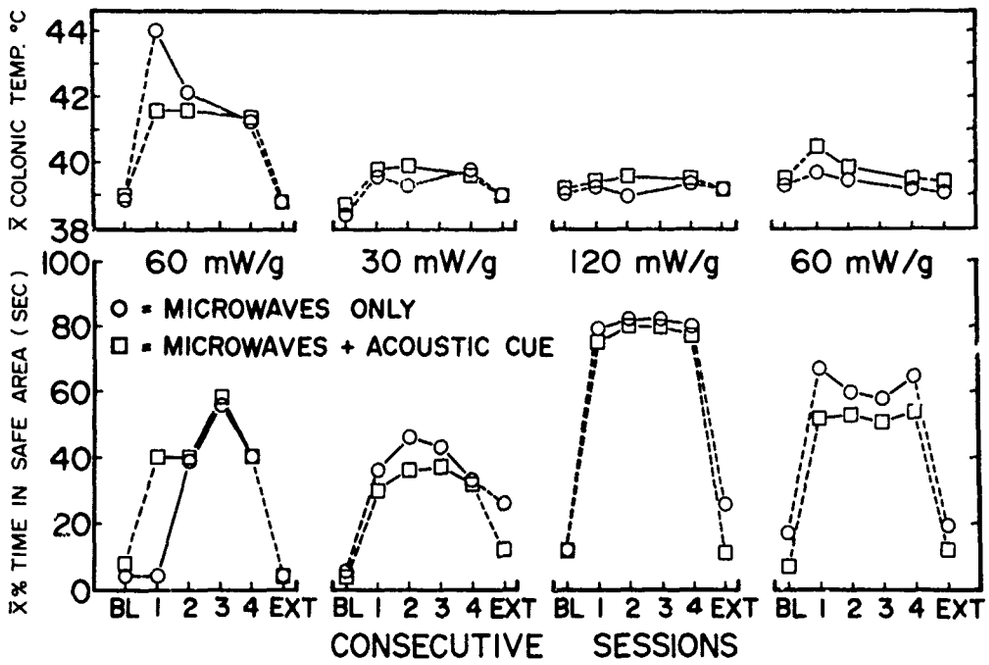

Figure 3. Experiment II: Mean-percent cumulative time per session and associated means of post-session colonic temperatures of four radiation-experienced rats that were individually observed for time in the safe area during four sets of sessions. Each set involved a series of six sessions, the first and last of which were conducted without irradiation to determine baseline times of occupancy (BL) and measures of resistance to extinction (Ext). Four daily sessions of irradiation intervened. Each set of sessions was separated by ∿48 hours. During the first and fourth set, irradiation resulted in microwave irradiation of an animal at 60 mW/g. The second and third set resulted in irradiation at, respectively, 30 and 120 mW/g. Squares represent means of two rats that were exposed to microwaves in synchrony with a 2900-Hz acoustic cue at 80 dB; circles represent means of two rats exposed to microwaves without acoustic cueing.

The initial set of sessions apparently was an effective tutorial in the acquisition of an efficient thermoregulatory response, since subsequent performances during session sets 2, 3, and 4 at, respectively, 30, 120, and 60 mW/g, were occasioned by mean times in the safe-area that covaried

markedly with dose rate. When the means of safe-area occupancy times were pooled for each set of exposure sessions and then were regressed against the three levels of energy dosing, the Pearson product-moment r was found to be .97 ($P < .025$ at 1 *df.*, single-tail distribution). Means of temperatures that were measured immediately after sessions of irradiation are relatively stable and combine to average 39.6, 39.3, and 39.7 °C with respect to dose rates of 30, 120, and 60 mW/g. Data on pre- and post-session temperatures are presented in Table 2.

The data of Mr. Riffle's experiment unequivocally indicate that *some* rats under an *ad-libitum* regimen can master a relatively difficult escape task and, indeed, can learn to thermoregulate by shuttling in and out of a highly intense field. The demonstration of adventitious acquisition of escape and thermoregulatory behavior by some rats does not force the conclusion that successful escape learning and thermoregulation would be general for all rats if they were given the careful shaping, discrete trials, and time-limited exposures that characterize the "permissive" method of successive approximation. However, I would be surprised if such a method were not productive of successful mastery by most mice and rats.

The critical question in the decision to study escape behavior of animals under a demanding or a permissive regimen turns on the question of what the investigator wishes to model. For several years, my colleagues and I have been concerned about the technically naive worker in the industrial milieu in which exist highly powered sources of HF, VHF, and UHF fields that could result in adventitious exposure of the unsuspecting individual (Guy and Justesen, 1979; Harris, *et al.*, 1977). Thus my initial selection of a procedural model was, by deliberate choice, the "worst-case." If there is a lesson that can be extrapolated from laboratory mouse and rat to industrial man and woman, it is that education of the latter--successive approximation or preventive hygiene by verbal communication--in the sensations and symptoms that may arise from adventitious exposure to intense fields should enable them to make timely retreat and thereby prevent discomfort, malaise, even serious injury. This concern, if mundane and practical, requires no apology from the laboratory scientist, who can gain a firm grasp of a phenomenon only by systematically evaluating all of the critical variables by which it is conditioned. The permissive case, which is much more fully represented in the traditional literature on escape and avoidance behaviors of animals under motivation by conventional noxious stimuli, will be the object of future endeavors.

Table II. Summary of Temperature Data

	1st Set of Sessions (60 mW/g)			2nd Set of Sessions (30 mW/g)			3rd Set of Sessions (120 mW/g)			4th Set of Sessions (60 mW/g)		
	BL	Irrad.	Ext.	BL	Irrad.	Ext.	BL	Irrad.	Ext.	BL	Irrad.	Ext.
Pre-Session Mean	38.2	37.8	37.8	37.2	37.5	37.3	38.1	37.7	37.6	38.0	37.5	37.7
Standard Deviation	0.48	0.55	0.52	0.29	0.35	0.13	0.69	0.40	0.29	0.57	0.65	0.46
No. of Measurements	4	12	4	4	12	4	4	12	4	4	12	4
Post-Session Mean	38.9	42.0	38.7	38.5	39.6	39.0	39.2	39.3	39.2	39.4	39.7	39.2
Standard Deviation	0.21	1.72	0.13	0.43	0.34	0.25	0.30	0.27	0.13	0.01	0.48	0.22
No. of Measurements	4	12	4	4	12	4	4	12	4	4	12	4
Mean ΔT	+0.7	+4.2	+0.9	+1.3	+2.1	+1.70	+1.1	+1.6	+1.5	+1.4	+1.7	+1.5

A summary of means and standard deviations of colonic temperatures is shown for four rats that were observed for evidence of escape or behavioral thermoregulation during four consecutive sets of sessions involving microwave irradiation at the indicated dose rates. Data based on two rats with and two rats without acoustic cueing (see text) were pooled. Irradiation was withheld during baseline (BL) and extinction (Ext) sessions. Each session within a set was conducted at 24-h intervals and colonic temperature of each animal was measured immediately before and immediately after a 10-min. period in a multi-mode cavity. In all four sets of sessions, temperatures were not measured before or after the third session of irradiation; this, to reduce the probability of colonic puncture by the thermal probe.

GENERAL DISCUSSION

The data of Experiment I reconfirm the general ineffectiveness of cessation of intense, multipath irradiation by microwaves as a negative reinforcer of adventitious escape by the murine animal. The data of the pilot study of Experiment II, even given the caveats of the animals' exposure history and a basis of selection that militates against generality, constitute a novel finding for a mammal: Behavioral thermoregulation in which sensory discriminative control is mediated *solely* by the microwave field. D'Andrea, *et al.* (1978) demonstrated such regulation in the whiptail lizard (*Cnemidophorus tigris*), an ectotherm whose existence in its natural habitat is dependent on behavioral control of--locomotion within--environments of widely ranging temperature. Stern, *et al.* (1979) demonstrated behavioral control of body temperature by rats in a very cold environment. Their rats were continuously irradiated for 15-min. periods by 2450-MHz microwaves at each of several power densities, none of which were presumably able to elevate the body temperature to preferred levels; control was vested in an infrared lamp, which could be switched on for a discrete period by a rat. As the background level of microwave irradiation was decreased (or increased) across sessions, the number of lever presses to incur the infrared field increased (or decreased). Adair and Adams (1980) employed a background of 2450-MHz radiation that was stepped in intensity across 10-min. periods while their experimental animal, the squirrel monkey (*Saimiri sciureus*) thermoregulated via operant control of warm and cool air. Each tug of a cord by a monkey shifted the temperature of continuously flowing air in the exposure milieu from 55 to 15 °C (or the reverse). Fifteen seconds after each tug, the temperature of the flowing air automatically returned to 55 (or 15) °C. As the intensity of microwave irradiation increased, the animals selected an increasingly cooler environment, which resulted in maintenance of a stable core temperature.

More recently, Bruce-Wolfe and Adair (1981) observed squirrel monkeys that had been trained to select alternate bouts of cold air (10 °C) and hot air (50 °C) by successive tugs of a cord. After stable levels of the operant cord-tug response (and thermal steady-state of core temperature) were achieved, microwave irradiation was paired with a flux of thermoneutral air (30 °C). Successive tugs of the cord then resulted in alternate bouts of microwave irradiation (with thermoneutral air) and the 10-°C air in the absence of irradiation. Given access to 2450-MHz irradiation that ranged

in intensity from 20 to 30 mW/cm^2, the monkeys exhibited highly efficient thermoregulatory behavior. However, the extent to which the successive, response-contingent shifts of air temperature from 10 to 30, and from 30 to 10 °C, etc., might have served as discriminative cues is unknown --only by maintaining a flux of air at a constant, less-than-preferred temperature would it be possible to control for convective cueing--but the demonstration of thermoregulation indicates convincingly that microwave heating *per se* is readily utilized by the primate to achieve a thermal steady-state.

The rats of Stern, *et al.* (1979), the monkeys of Adair and Adams (1980), and the monkeys of Bruce-Wolfe and Adair (1981) regulated their body temperatures by controlling, respectively, a source of visible radiant heating in a cold environment, a source of convective heating and cooling in a microwave environment, and microwave irradiation that alternated with a draft of cold air. Both visible light and a draft of cold air are highly salient as sensory stimuli. And a draft of cold air, and the warmth and visible light associated with activation of a conventional infrared lamp, should be *immediately* discernible to the attentive mammal.

The question of whether a stable body temperature will be maintained by a mammal in a cool surround solely through operant control of a microwave field was answered in the affirmative in Experiment II, albeit with strong qualifications regarding history and generality. Unknown is whether the experimentally naive rat or monkey will *acquire* such control without prior operant training and without the presence of salient sensory cues that covary with periods of microwave irradiation.

If an animal were required adventitiously to learn a conventional lever-pressing response to inactivate (escape from) a highly intense field in a surround of moderate temperature, I fear that the low probability of such a response in the absence of shaping by successive approximation would conspire for hyperthermal lethality. However, the high-probability and ecologically pertinent response of traversing within a shuttle box--locomotion between hotter and cooler loci of frequently inhabited areas--should afford a behavioral operant suitable to test the question of adventitious acquisition. In the light of the shuttle-box findings of Levinson, *et al.* (1981) cited above, much higher dose rates of irradiation than 60 mW/g would have to be employed to eliminate the possibility of non-discriminated survival borne of a random walk.

I shall go out on a speculative limb and predict that a significant proportion of mice and rats subjected to intense

irradiation under the adventitious, shuttle-box format would expire because of failure to discriminate the contingency between spatial locus and intense irradiation. My prediction is without direct empirical warrant but is based on factors that condition the sensory and perceptual dynamics of microwave irradiation: The relatively long latencies to detection of warming during irradiation and, even more so, the persistence of the warmth sensation after extinction of an intense field (Hendler, *et al.*, 1963; Schwan, *et al.*, 1966; and Carroll, *et al.*, 1980); the positive-to-negative shift of hedonic sign that presumably attends continuous, intense irradiation in a moderately cool environment (Cook, 1952; Cabanac, 1971); the possibility that incrementing temperature of the body constitutes a changing internal state that interferes with efficient mnemonic function (Overton, 1964; Nielson, 1968; Misanin, *et al.*, 1979); and the datum that thresholds of thermal pain in mammals are well above thresholds of irreversible cellular damage (Lowenstein and Dallenbach, 1930; Cook, 1952; Hardy, *et al.*, 1952; Hellon and Mitchell, 1975). I suspect in connection with the high threshold of thermal pain that whole-body exposure of an animal to an intense, multipath field results in loss of consciousness before painful stimulation occurs--and pain, of course, is the preeminent signal of retreat from injurious stimulation. It is possible that a thermal hotspot associated with an intense but uneven investment of absorbed energy in the tegument might exceed the threshold of pain but, were this to occur, the factor of thermal inertia might still prevent timely association between the act of escape and cessation of pain.

If the prediction of significant incidence of lethality is confirmed, I venture another with respect to *far*-infrared irradiation of the mammal: That it, too, will serve as an ineffective reinforcer of adventitious escape. The conventional wisdom is that exposure of the body to an infrared field, because of its shallow depth of penetration into the skin, will rapidly excite the superficial thermal receptors and quickly promote escape from a source, thereby precluding injury. The conventional wisdom may be sound, but is clouded by a potential artifact that is present in the natural scheme* and in the artifices of the laboratory, *visible light*.

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*The hot tip of a soldering iron and the live ash of a burning cigarette, etc., have inspired rapid retreat by legions of human beings who have made accidental contact,

The sun and the infrared lamp, which respectively are the primary sources of infrared waves in the natural and laboratory environments, also emit visible photons that can give sharp sensory definition of a temporal and spatial sort to the infrared field. Richard Lovely and colleagues at the University of Washington (Personal Communication, 1977) found that photic cueing of rats enabled rapid learning of escape from, then avoidance of, an intense microwave field, a feat not observed in the absence of photic cueing. Subsequently, Levinson, *et al.* (1982) confirmed this finding in the same species. Given Satinoff and Hendersen's observation (1977) that visible light, not excessive warming, might be the controlling discriminative stimulus of operant escape or avoidance behaviors in the field of an infrared lamp, and the observations by Cain (1973) that spatial discrimination of infrared warming by human observers is sometimes associated with gross errors of localization, there is reason to question whether far-infrared energy *per se* will function as an effective negative reinforcer of adventitious escape, at least when large areas of the body are irradiated. Since my hypothesis is so readily falsifiable, I hope someone beyond my laboratory will soon attempt to infirm it.

Future studies of the mouse and the rat in my laboratory will be directed to comparisons of near- (visible) and far- (non-visible) infrared energy as a motivator of escape to determine the role played by visible light in the acquisition function. There is need as well for human psychophysical studies that can provide precise comparative data on the spatial and temporal characteristics of microwave and infrared fields both weak and intense. Much work obviously remains to be done in resolving the vagaries of the sensory dynamics incumbent with exposure to long- and short-wave electromagnetic radiations.

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nor has photic cueing of retreat been necessary. My concern does not lie with these discrete, highly focal applications of thermal energy, which are painful (and do result in irreversible albeit limited injury to cells of the skin). Rather, I question whether application of far-infrared fields to large areas of the body will affect a mammal's aversion in a manner that differs qualitatively from that of the more deeply penetrating microwaves.

SUMMARY

The results of two experiments are reported, the first on 24 mice and 14 rats, all experimentally naive, that were observed for evidence of adventitious escape from faradic shock or from a potentially lethal, 2450-MHz microwave field in a multi-mode cavity. A relatively difficult task for the positively thygmotactic animal, entry into a circular area centered on a false floor of Plexiglas and thus remote to the walls of the cavity, was required to extinguish the shock or the field. Irradiation (or faradic footshock at 150-300 μA rms for eight, active-control animals, four of each species) was continuously available during each of four 15-min. sessions repeated at 24-h intervals. Control baselines of cumulative time spent in the safe area of the circle were recorded during an initial 15-min. session; resistance to extinction of escape responding in the absence of irradiation or footshock was measured during a sixth and final session. All of ten rats irradiated at a whole-body-averaged dose rate of 60 mW/g convulsed and expired, presumably from radiation-induced hyperpyrexia. Eight of ten mice irradiated at 60 mW/g survived the four sessions of irradiation, but reliable evidence of escape learning was not observed. All of ten mice irradiated at 120 mW/g convulsed and expired. In contrast, the mice and rats motivated by faradic footshock exhibited mastery of learning and, collectively, gave singular evidence of high resistance to extinction.

The data of the second experiment, which was a pilot study of four rats with an extensive history of exposure to intense but intermittently applied microwave fields, revealed that the animals learned to thermoregulate behaviorally by locomoting in and out of the safe-area circle. A strong relation between dose rate (30, 60, and 120 mW/g) and proportion of time spent in the safe area was observed (r = .97). Post-exposure means of colonic temperature during three sets of sessions under the different rates of energy dosing were highly stable and averaged 39.6 °C.

Several factors are discussed that might play roles in the failure-to-escape phenomenon and in the contrasting observation of fine-grained thermoregulation. The factors subsume under extrinsic (procedural) and intrinsic (biopsychological) categories. Among the extrinsic factors are task difficulty, regimen of training, environment, and field conditions. The intrinsic factors relate to the dynamics of sensation and perception and include hedonic tone, temporal and spatial attributes, and state-dependent mnemonics as

these may vary in association with the sizable elevations of body temperature that are induced by intense electromagnetic irradiation at radio and infrared frequencies.

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REFERENCES

Adair, E.R. and Adams, B.W. (1980) Microwaves modify thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics* 1: 1.

Altman, P.L. and Dittmer, D.S. (Eds.). (1968) *Metabolism*. Federation of American Societies for Experimental Biology: Bethesda, MD.

Bermant, R.I., Reeves, D.L., Justesen, D.R., and Levinson, D.M. (1979) Classical conditioning of microwave- and shock-induced hyperthermia in the rat. *Radio Science* 14/6S: 201.

Bruce-Wolfe, V. and Adair, E.R. (1981) Operant control of microwave radiation by squirrel monkeys. *Abstracts, 3rd Annual Meeting of the Bioelectromagnetics Society*, BEMS: Gaithersburg, MD., p. 42.

Bryan, R.N. (1966) Retrograde amnesia: Effects of handling and microwave radiation. *Science* 153: 897.

Cabanac, M. Physiological role of pleasure. (1971) *Science* 173: 1103.

Cabanac, M., Minaire, Y., and Adair, E.R. (1968) Influence of internal factors on the pleasantness of a gustative sweet sensation. *Comm. Behav. Biol.* 1: 77.

Cain, W.S. (1973) Spatial discrimination of cutaneous warmth. *Am. J. Psychol.* 86: 169.

Carroll, D.R., Levinson, D.M., and Justesen, D.R. (1980) Failure of rats to escape from a potentially lethal microwave field. *Bioelectromagnetics* 1: 101.

Cook, H.F. (1952) The pain threshold for microwave and infrared radiations. *J. Physiol. (London)* 118: 1.

D'Andrea, J.A., Cueller, C., Gandhi, O.P., Lords, J.L., and Nielson, H.C. (1978) Behavioral thermoregulation in the whiptail lizard (*Cnemidophorus tigris*) under 2450-MHz CW Microwaves. Abstracts, Open Symposium on the Biological Effects of Electromagnetic Waves, p. 88. International Union of Radio Science: Helsinki.

Delini-Stula, A. (1970) The development and extinction of hyperthermia induced by conditioned avoidance behavior in rats. *J. Exp. Anal. Behav.* 14: 213.

Estes, W.K. and Skinner, B.F. (1941). Some quantitative properties of anxiety. *J. Exp. Psychol.* 29: 390.

Gelineo, S. (1940) Sur la thermorégulation et la thermogenèse du rat durant un séjour prolongé aux températures provoquant hyperthermie. *Bull. Acad. Royale Serbe* 9: 149.

Gelineo, S. (1964) Organ systems in adaptation: The temperature regulating system. In: *Handbook of Physiology, Section 4: Adaptation to the Environment.* (D.B. Dill, E.F. Adolph, C.G. Wilber, eds.). p. 259. Amer. Physiological Soc.: Washington, D.C.

Guy, A.W. and Chou, C.-K. (1982) Effects of high-intensity microwave-pulse exposure of rat brain. *Radio Science* 17 (In Press).

Guy, A.W. and Justesen, D.R. (1979) *Panel--Research Opportunities and Problems*: Hearing before the Subcommittee on Natural Resources and Environment, U.S. House of Representatives, July 12, 1979. No. 70 [*Research on Health Effects of Nonionizing Radiation*]. pp. 63-78, 108-112. U.S. Government Printing Office: Washington, D.C.

Harris, E.H., Parr, W.H., Murray, W.E., and Glaser, Z.R. (1979) *Testimony before U.S. Senate Committee on Commerce, Science, and Transportation. Hearings on Irradiation, Health and Safety.* [Ser. No. 95-49], p. 586. U.S. Government Printing Office: Washington, D.C.

Hardy, J.D., Wolff, H.G., and Goodell, H. (1952) *Pain Sensations and Reactions.* pp. 78-79. Williams and Wilkins: Baltimore.

Hardy, J.D. (1970) Thermal comfort: Skin temperature and physiological thermoregulation. In: *Physiological and Behavioral Temperature regulation,* (J.D. Hardy, A.P. Gagge, J.A.J. Stolwijk, eds.) p. 856. Chas. C. Thomas: Springfield, Illinois.

Hellon, R.F., and Mitchell, D. (1975) Characteristics of neurones in the ventral-basal thalamus of the rat which respond to noxious stimulation of the tail. *J. Physiol. (London)* 50: 29.

Hendler, E., Hardy, J.D., and Murgatroyd, D. (1963) Skin heating and temperature sensation produced by infrared and microwave irradiation. In: *Temperature: Its Measurement and Control in Science and Industry*. (J.D. Hardy, ed.) p. 211. Reinhold: New York.

Hendler, E. (1968) Cutaneous receptor response to microwave irradiation. In: *Thermal Problems in Aerospace Medicine* (J.D. Hardy, ed.), p. 149. Unwin Ltd.: Surrey.

Jacobs, B.L. and Sorensen, C.A. (1969) Memory disruption in mice by brief post-trial immersion in hot or cold water. *J. comp. physiol. Psychol.* 68: 239.

Justesen, D.R. (1979) Behavioral and psychological effects of microwave radiation. *Bull. Acad. Med.* 55: 1058.

Justesen, D.R., Adair, E.R., Stevens, J.C., and Bruce-Wolfe, V. (1982) A comparative study of human sensory thresholds: 2450-MHz microwaves vs. far-infrared radiation. *Bioelectromagnetics* 3: 117.

Justesen, D.R., Levinson, D.M., Clarke, R.L., and King, N.W. (1971a) A microwave oven for behavioural and biological research: Electrical and structural modifications, calorimetric dosimetry, and functional evaluation. *J. Microwave Power* 6: 237.

Justesen, D.R., King, N.W., and Clarke, R.L. (1971b) Unavoidable gridshock without scrambling circuitry from a faradic source of low-radio-frequency current. *Behav. Res. Methods and Instrument.* 3: 131.

Justesen, D.R., Morantz, R.A., Clark, M., Reeves, D.L., and Mathews, M. (1977) Effects of handling and surgical treatment on convulsive latencies and mortality of tumor-bearing rats to 2450-MHz microwave radiation. *Abstracts, USNC/URSI 1977 Meeting*, p. 40. National Academy of Sciences: Washington, D.C.

King, N.W., Justesen, D.R., and Clarke, R.L. (1971) Behavioral sensitivity to microwave irradiation. *Science* 172: 398.

Levinson, D.M., Riffle, D.W., Justesen, D.R., Carroll, D.R., Bruce-Wolfe, V., and Clarke, R.L. (1981) Escape behavior by mice and rats in 2450- and 918-MHz fields: Evaluation of sonic stimulation as a cue. *Abstracts, 3rd Annual Meeting of the Bioelectromagnetics Society*, p. 40 BEMS: Gaithersburg, MD.

Levinson, D.M., Grove, A.M., Clarke, R.L., and Justesen, D.R. (1982) Photic cueing of escape by rats from an intense microwave field. *Bioelectromagnetics* 3: 105.

Lovely, R.H., Johnson, R.B., Chou, C.-K. and Guy, A.W. (1978) Induction of retrograde amnesia for classically conditioned fear by a single microwave pulse. *Abstracts, Open Symposium on the Biological Effects of Electromagnetic Waves*, p. 78. International Union of Radio Science: Helsinki.

Lowenstein, E. and Dallenbach, K.M. (1930) The critical temperatures for heat and for burning heat. *Am. J. Psychol.* 42: 423.

Maier, S.F., Seligman, M.E.P., and Solomon, R.L. (1969) Pavlovian fear conditioning and learned helplessness: Effects on escape and avoidance behavior of (a) the CS-US contingency and (b) the independence of the US and voluntary responding. In: *Punishment and Aversive Behavior* (B.A. Campbell and R.M. Church, eds.), p. 299. Appleton: New York.

Michaelson, S.M. (1972) Cutaneous perception of microwaves. *J. Microwave Power* 7: 67.

Michaelson, S.M., Thomson, R.A., and Howland, J.W. (1965) Comparative studies of 1285 and 2800 MC/Sec pulsed microwaves. *Aerospace Med.* 36: 1059.

Millan, M.J., Przewlocki, R., Jerlicz, M., Gramsch, C., Hoellt, V., and Herz, A. (1981) Stress-induced release of brain and pituitary beta-endorphin: Major role of endorphins in generation of hyperthermia, not analgesia. *Brain Res.* 208: 325.

Misanin, J.R., Vonheyn, R.E., Bartelt, S.W., and Boulden, W.E. (1979) The effect of hyperthermia on memory in rats. *Physiol. Psychol.* 7: 339.

Monahan, J.C. and Ho, H.S. (1977a) Microwave-induced avoidance behavior in the mouse. In: *Biological Effects of Electromagnetic Waves* (DHEW Publication No. 77-8010) (C.C. Johnson and M.L. Shore, eds.) p. 274. U.S. Government Printing Office: Washington, D.C.

Monahan, J.C. and Ho, H.S. (1977b) The effect of ambient temperature on the reduction of microwave energy absorption by mice. *Radio Science 14/6S,*73: 257.

Murgatroyd, D. and Hardy, J.D. (1970) Central and peripheral temperatures in behavioral thermoregulation of the rat. In: *Physiological and Behavioral Temperature Regulation*, (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.) p. 874. Chas. C. Thomas: Springfield, Illinois.

Murphy, R.M., Klausen, J., Justesen, D.R., and Pendleton, R.B. (1967) Enhanced relearning following electroshock- and febrile-[microwave] convulsions. *Sci. Proc.* American Psychiatric Association: Washington, D.C. 123: 166.

Nielson, H.C. (1968) Evidence that electroconvulsive shock alters memory retrieval rather than memory consolidation. *Exper. Neurol.* 20: 3.

Oke, A.F., Mendelson, J., and Justesen, D.R. (1974) Cortical hypothermia is a sequela of electroconvulsive shock. *Nature* 248: 437.

Overton, D.A. (1964) State-dependent or "dissociated" learning produced with pentobarbital. *J. comp. physiol. Psychol.* 57: 3.

Sachs, E., Weingarten, M., and Klein, N.W. (1966) Effects of chlordiazapoxide on the acquisition of avoidance learning and its transfer to the normal state and other drug conditions. *Psychopharmacologia* 9: 17.

Satinoff, E. and Hendersen, R. (1977) Thermoregulatory behavior. In: *Handbook of Operant Behavior.* (W.K. Honig and J.E.R. Staddon, eds.) p. 153. Prentice-Hall: Englewood Cliffs, N.J.

Schwan, H.P. (1970) Interaction of microwave and radiofrequency radiation with biological systems. In: *Biological Effects and Health Implications of Microwave Radiation.* (S.F. Cleary, ed.) p. 13. (USPHS No. BRH/DBE 70-2), U.S. Public Health Service: Rockville, Maryland.

Schwan, H.P., Anne, A., and Sher, L. (1966) *Heating of Living Tissues*, Report NAEC-ACEL-534, U.S. Naval Air Engineering Center: Philadelphia.

Stern, S., Margolin, L., Weiss, B., Lu, S.-T., and Michaelson, S.M. (1979) Microwaves: Effect on thermoregulatory behavior of rats. *Science* 206: 1198.

Terenius, L. Significance of endorphins in endogenous antinociception. In: *The Endorphins*, (E. Costa and M. Trabucchi, eds.) p. 321. Raven Press: New York.

Vendrik, A.J.H. and Vos, J.J. (1958) Comparison of the stimulation of the warmth sense organ by microwave and infrared. *J. Appl. Physiol.* 13: 435.

SENSATION, SUBTLETIES, AND STANDARDS: SYNOPSIS OF A PANEL DISCUSSION

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INTRODUCTION

A serious problem with regard to sensory awareness may present itself when an organism is exposed to a radiofrequency field. Under conditions when electromagnetic energy is deposited at some depth in the body tissues, as may occur when a human being is exposed to 3- or 10-cm microwaves, the thermosensitive neural endings in the skin may be bypassed, compromising normal sensation. Thus, as demonstrated in Figure 1 of Chapter 9 of this volume, a threshold warmth sensation derived from such microwave exposure may require a relatively longer duration and higher intensity of stimulation than would be necessary for a threshold warmth sensation derived from an infrared stimulus of comparable areal extent. On the other side of the coin, Justesen, in Chapter 10, has provided compelling evidence that rats and mice, under certain conditions, seem not to experience any thermal sensations when irradiated by high intensity microwave fields; at least these animals are not guided by changes in sensation alone to escape from potentially-lethal fields. These facts pose questions that are reminiscent of those investigated by psychophysiologists some years ago as they

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sought experimental evidence for the direct perception or appreciation of changes in the temperature of restricted brainstem areas as produced by implanted thermodes (Corbit, 1969, 1973; Corbit and Ernits, 1974; Adair, 1977). These facts also raise a fundamental question to be considered by those who would establish standards for the exposure of human beings to radiofrequency fields: shall sensation play a role in standard setting? During a panel discussion held at the Symposium on Microwaves and Thermoregulation (New Haven, Connecticut, October 26-27, 1981), these general questions were examined from many points of view, although no specific recommendations were made by the panelists. The major views aired during this discussion are summarized below.

THERMAL GRADIENTS IN TISSUE PRODUCED BY MICROWAVES AND INFRARED

A clear difference exists between the infrared stimulus and the microwave stimulus as these are represented to consciousness. This difference clearly derives from differences in absorption and heat flow in the skin produced by the two types of stimuli. In the case of infrared radiation, absorption occurs within the first millimeter or so of the skin surface; indeed, a large proportion occurs within the first 1/10th of a millimeter. As a result, the heat flowing into the skin proceeds along avenues that are very characteristic for the way the system was designed to operate; i.e., the way it has evolved. We do not yet know precisely what the relationships are between the physics of the heat transfer and the temperature changes in the skin, on the one hand, and the sensations that are evoked on the other hand. There are still many unanswered questions regarding these precise relationships, even for the case of infrared, despite a large body of psychophysical data describing the parameters of warmth sensation (cf. Chapter 9). For example, our knowledge of neurophysiological dynamics does not correlate very well with the sensory dynamics measured in the intact observer. A primary question among those yet to be resolved relates to the way in which the receptors are stimulated. Since the normal heat flow is decidedly inward from the skin, the receptors at their strategic location within the first millimeter, are certainly closely related to the normal path of the heat transfer. This particular location affords a much greater yield than deeper tissues in terms of temperature rise. Thus even very

short stimulations can produce substantial increases in the temperature of the skin surface and in receptor temperature as well.

However, stimulation of the skin by microwaves may give rise to a very different situation. Different microwave frequencies will have different penetration characteristics and hence different penetration profiles. Of the greatest importance is the fact that simultaneously a much larger mass of tissue must be raised in temperature than is the case for infrared. Clearly, there will be more absorption on the skin surface than there is at depth, but nevertheless the thermal gradient through the tissues will now be totally different. In addition, the heat losses that take place at the skin surface will result in an inverted thermal gradient, a most unusual situation for the thermal receptors to deal with and one for which they have certainly not evolved.

The difference of a factor of 10-15 in the power density required to arouse a just-perceptible sensation of warmth during stimulation by microwave *vs* infrared is not particularly surprising. This can be almost completely explained by considering the amount of tissue that has to be heated in a short period of time by penetrating and non-penetrating radiation. The surprising part is the diffuse nature of the sensation aroused by the microwave stimulus. This sensory diffusion makes the perception of warmth much less clear, even at threshold. According to the way the sensation derived from microwaves is described in the literature, the onset and offset of stimulation are much more difficult to recognize than when infrared stimuli are used. This result may have to do with a reversed or absent thermal gradient compared to the tissue gradient that is characteristically present when infrared irradiates the skin. One current theory of temperature perception holds that its basis lies in the recognition of a cutaneous thermal gradient. This is certainly a provocative point in this context.

IMPORTANCE OF FAMILIARITY AND ASSESSMENT OF RISK

When considering the relationship of sensation to the setting of standards for exposure to radiofrequency radiation, the general public's familiarity with radiation sources and perception of the risks involved with exposure to such sources must be considered. A lack of familiarity with devices from which radiation may emanate can color the public's view on whether regulatory control over a given

source is warranted or not. An informal survey conducted by Osepchuk was offered as a case in point. A group of 25 subjects (consisting of scientists, engineers, secretaries, administrators, etc.) rated a series of spectral sources on a scale that ranged from 1 to 5, each number indicating a different level of perceived risk. On this scale, "5" signified that the source (e.g., gamma rays) was unsafe at any level or exposure duration and that regulatory control was essential. At the other end of the scale, "1" indicated that the source was obviously safe and that regulation was unnecessary. An index of the familiarity of the sources was gained from the percentage of respondents who completed the risk assessment of each entity presented. This particular group of subjects (hardly representative of the public at large) felt quite familiar with and fearful of all sources of radioactivity or anything related to the generation of nuclear power and they rated these sources with high numbers. Radio and television broadcasting towers, as well as CB radios were familiar sources held to be of low risk. However, radar and microwave ovens ranked quite high in terms of both familiarity and perceived risk (comparable to X-rays). Interestingly enough, "nonionizing radiation," a somewhat less familiar term, carried a lower risk index.

What is the implication of a survey such as this for the assessment of sensations derived from radiofrequency electromagnetic radiation? Clearly, the sensory judgment made by an individual who is exposed to a microwave stimulus may be distorted by his knowledge that the source of stimulation is microwave radiation. It may be that the results of the few studies conducted 20-odd years ago (Eikman and Vendrik, 1961; Hendler, Hardy, and Murgatroyd, 1963; Hendler and Hardy, 1960; Schwan, *et al.*, 1966; Vendrik and Vos, 1958) would have been different had the assessments been made in the same climate of fear that is prevalent today. It is reassuring that some of these early data have been generally confirmed in a recent study that featured sophisticated human observers (Justesen, *et al.*, 1982).

DETECTABILITY AS A FUNCTION OF FREQUENCY

It is clear that within the broad range of microwave frequencies to which humans and animals may be exposed there is wide variation in the depth of penetration of the absorbed energy. The old ANSI standard (ANSI, 1974) did not take this fact into account when it specified the exposure limit

at 10 mW/cm^2 for all frequencies within the range from 10 MHz to 100 GHz. The new protection guide recently adopted by the American National Standards Institute is frequency dependent as shown in Table I. For exposure of human beings to electromagnetic energy at radiofrequencies from 300 kHz to 100 GHz, the protection guides are specified in the table in terms of the equivalent plane-wave free-space power density, and in terms of the mean squared electric (E^2) and magnetic (H^2) field strengths as a function of frequency. Over the frequency range that provides the greatest penetration depth in humans of all ages (30-300 MHz), the recommended maximum permissible exposure has been lowered by an order of magnitude relative to the old standard.

Table I. Radio Frequency Protection Guides (ANSI, 1982)

Frequency Range (MHz)	Power Density (mW/cm^2)	E^2 (V^2/m^2)	H^2 (A^2/m^2)
0.3-3	100	400,000	2.5
3-30	$900/f^2$	$4,000(900/f^2)$	$0.025(900/f^2)$
30-300	1.0	4,000	0.025
300-1500	f/300	4,000(f/300)	0.025(f/300)
1500-100,000	5.0	20,000	0.125

Note: f is the frequency in MHz.

Since the patterns of energy deposition vary with both the frequency and the size of the biological target, detectability will also vary greatly at different frequencies. It seems clear that at the higher frequencies (e.g., 30 GHz), where penetration below the skin surface is negligible, the stimulus intensity necessary to arouse a thermal sensation will be little different from infrared. Indeed, at these high frequencies, humans may be able to sense radiation intensities that fall within the exposure guidelines. Such

will not be the case, however, over the entire radiofrequency spectrum. We know that the lower the frequency, the more energy will be required to reach a threshold sensation and the longer will be the latency to detection. It should be possible to take advantage of electronic detectors in the intermediate frequency range (e.g., S-band) so as to supplement the human sensory system. Most such devices on the market today, such as small leak detectors for microwave ovens, are crude and unreliable and many are temperature dependent. It should be possible to manufacture reliable detectors, however, particularly if the general public remains fearful of radiofrequency radiation and demands such commercial adjuncts. At the lowest frequencies, where sensation deteriorates markedly, electronic equipment is enormously susceptible to the radiation. The resulting interference with complex electronics gear, such as home entertainment systems, can serve as a warning signal over this frequency range.

It is important to bear in mind, in the context of the present discussion, that the exposure standards are not related to what an individual can feel. The standards are related to what is an acceptable deposition of thermalizing energy in an individual relative to normal rates of heat production and heat dissipation. Over much of the radiofrequency spectrum, the standard is set at levels that are below what most would consider detectable by sensation. A question posed to the panel was . . ."If I can feel it, is it injurious to my health?" While a definitive answer to this question can not be given at the present time, an answer to a slightly different question can. If you can feel it, it almost certainly exceeds the new exposure standard unless the exposure is very brief.

SOME CHARACTERISTICS OF THE THERMAL SENSATION DERIVED FROM MICROWAVE RADIATION.

The experimental evidence is clear that when a human being is exposed to a microwave field (within the frequency range where there is at least 10% absorption efficiency), that field will be perceptible at a power density in excess of 50 mW/cm^2. Perceptibility has also been demonstrated in several infrahuman species by many investigators. Perceptibility per se is often not the problem, but the temporal dynamics of the sensation may be. There appears to be a

dissociation between physical and psychological time that characterizes microwave sensation. That is, there is a finite time during which the field is on before one perceives it and there is a finite period after the field goes off during which one continues to feel it. In other words, the temporal boundary of the sensation is fuzzy.

In this context, it is important to note that the skin, even with its exquisite sensitivity, is a very poor discriminator of absolute temperature or steady state temperature. We humans get very poor signals about the actual level of skin temperature at any one time. On the other hand, although we are uncertain about the underlying processes involved, we appear to be very sensitive to *changes* in temperature, presumably mostly to the rate of change of temperature. On-signals or off-signals at the thermoreceptor level are correlated in some way with positive or negative rates of change of temperature. Whatever these changes are will invariably be much slower during microwave heating because a block of tissue has to be heated, and as a result the thermal gradients that are created will be much softer. So also with the off-signal which will be created by the re-establishment of the normal thermal gradient in the tissues. Thus, purely on the basis of the physical situation, the expectation would be for sensations derived from microwave stimuli to have fuzzy beginnings and ends.

Fading or adaptation of the sensation derived from microwaves may also occur. One panelist described an informal pilot experiment in which he participated as an observer; its purpose was to measure latencies to detection both for onset and offset of microwave-induced sensation. Several stimuli, of suprathreshold intensity but of different durations, were presented to the skin of the subject's forearm. His task was to report when the field went on and off. Typically, the onset latency of the 2450 MHz field was about 5-sec but sometimes the sensation disappeared before the field was extinguished. The subject admitted he had a mental bias that all presentations would be of equal duration, a factor that may have contributed to the premature disappearance of his sensations. However, adaptation of warmth sensation during the long exposures should not be ruled out. On some occasions, the warmth sensation persisted for some time after the microwaves had been turned off, as has been reported by others. In order to begin to resolve the myriad of unanswered questions about sensations derived from microwave exposure, it is imperative that ways be found to conduct psychophysical studies using human subjects. A program of research such as that outlined by Stevens in Chapter 9, involving several microwave frequencies as well as infrared,

would provide a solid psychophysical basis for understanding how temperature reception in the skin actually occurs.

REFERENCES

Adair, E.R. (1977) Studies on the behavioral regulation of preoptic temperature. In *Drugs, Biogenic Amines and Body Temperature*. p. 84. Karger, Basel.

AN AMERICAN NATIONAL STANDARD (1974). Safety level of electromagnetic radiation with respect to personnel. ANSI C95.1-1974. Institute of Electrical and Electronic Engineers, New York.

AN AMERICAN NATIONAL STANDARD (1982). American national standard safety levels with respect to human exposure to radio frequency electromagnetic fields (300 kHz-100 GHz). ANSI C95.1-1982. American National Standards Institute, New York.

Corbit, J.D. (1969). Behavioral regulation of hypothalamic temperature. *Science* 166:256.

Corbit, J.D. (1973). Voluntary control of hypothalamic temperature. *J. comp. physiol. Psychol.* 83:394.

Corbit, J.D. and Ernits, T. (1974). Specific preference for hypothalamic cooling. *J. comp. physiol. Psychol.* 86:24.

Eijkman, E. and Vendrik, A.J.H. (1961). Dynamic behavior of the warmth sense organ. *J. Exp. Psychol.* 62:403.

Hendler, E. and Hardy, J.D. (1960). Infrared and microwave effects on skin heating and temperature sensation. *IRE Trans. Med. Electronics* ME7:143.

Hendler, E., Hardy, J.D. and Murgatroyd, D. (1963). Skin heating and temperature sensation produced by infrared and microwave irradiation. In *Temperature. Its Measurement and Control in Science and Industry. III Vol. 3* (J.D. Hardy, ed.). p. 211. Reinhold Publishing Corp., New York.

Justesen, D.R., Adair, E.R., Stevens, J.C., and Bruce-Wolfe, V. (1982). A comparative study of human sensory thresholds: 2450 MHz microwaves *vs* far-infrared radiation. *Bioelectromagnetics* 3:117.

Schwan, H.P., Anne, A., and Sher, L. (1966). *Heating of living tissues*. U.S. Naval Air Engineering Center, Philadelphia, Report NAEC-ACEL-534.

Vendrik, A.J.H. and Vos, J.J. (1958). Comparison of the stimulation of the warmth-sense organ by microwave and infrared. *J. Appl. Physiol.* 13:435.

BEYOND THERMOREGULATION

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It is my pleasant task to touch briefly on a topic that extends beyond the subject of this symposium--the deposition, detection, and effects of thermalizing microwave energy in organisms--to a consideration of what happens at energy levels below those at which one might reasonably expect heating. Numerous observations have been recorded that suggest physiological and psychological effects at such "nonthermal" levels. Rather fewer publications have attempted to suggest a mechanism by which interactions at such levels might be explained. Such attempts usually rely on a single explanation. No one has considered the relative merits of explanations offered by other observers--in fact, no one has even made a list of the various explanations that come to mind, which would be a necessary first step. Let me try to do at least that; but since I am interested in the history of technology and the history of medicine, let me first place the subject in an appropriate historical context.

I have done that before for audiences very much like the present one, most recently at the meeting at the New York Academy of Medicine that some of you attended (Süsskind, 1979). By the way, I was quite certain that interest in my remarks on that occasion would be limited to the symposium participants and did not even order reprints, but to my surprise there were many requests; some are still coming in now, nearly two years after the proceedings were published, the majority of them from behind the Iron Curtain. Abstracts of papers published by the New York Academy of Medicine must be read assiduously from the Elbe to the Volga.

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Interest in the history of one's subject is one thing, but it is somewhat unnerving to find oneself the object of historical research. That has already happened to some of us. As you know, an historian at the University of Michigan has published an account of U.S. microwave standard setting (Steneck, *et al.*, 1980) and subsequently organized a conference on the risks and benefits of microwaves (Steneck, 1982); and several of us have received his inquiries about the beginnings of this research field. One has the subjective feeling that this research was done so recently as to be practically contemporary; but on checking I find that the first publication in which I advocated the approach that also characterizes the present symposium, a paper on "Electromagnetic radiation as a tool in the life sciences" (Jaski and Süsskind, 1961), appeared in *Science* fully twenty years ago.

I have no wish to trespass on the historical introduction presented earlier (Chapter 1), but I want to say a few words about what we may call the prehistory of our subject. We know that interest in thermoregulation derives partly from interest in the hazards of microwaves, and partly from their positive use in biomedical research and therapy. At the turn of the century Tesla (1891) published his observation that passage of high-frequency currents through a human subject resulted in perceived heating; he said he was not sure whether it would be beneficial. In one sense, that question is still before us today, ninety years later. That is, we are interested in a phenomenon that may be of therapeutic value but may be dangerous in excessive doses; and one of our jobs is to determine the equivalent of what might also be called the risk/benefit ratio. By the way, it is a good thing that Tesla and his successors were not hampered by regulations on the protection of human subjects, else his original observations might have never been made. Of course, he *was* conscious of a potential problem--in his case we may even say, a high-potential problem (about a million volts). Tesla took one precaution: he did all those experiments on himself, and he noted the effects of the various wave shapes and other electrical quantities--not only heating but also perspiration, blood circulation, even getting sleepy. The risk/benefit ratio must have been all right, since he lived to be eighty-seven. It is true he was a bit ga-ga at the end, but wait till you are eighty-seven!

Those were conduction experiments. Meanwhile, D'Arsonval (1893) was doing induction experiments. It is a fact that there was interest in the biomedical effects of radio waves before they were employed for communications. Marconi's first experiments did not take place until 1895; his basic

patent dates from 1896. Yet in 1893 D'Arsonval was irradiating people for therapeutic purposes and carrying out controlled experiments on groups of patients--and also on bacteria and on several toxins. He was far ahead of his time, a true pioneer. That is why the recently formed Bioelectromagnetics Society first wanted to call itself the D'Arsonval Society, but unfortunately decided otherwise.

I need not rehearse for you the subsequent history--the advent of diathermy, the uses of high-frequency currents in surgery, the worries about the hazards of microwaves beginning with the war of 1939-1945, and the more recent techniques of enhancing the therapeutic effects of ionizing radiation by simultaneous irradiation with microwaves. Nor is interest in the thermal effects of microwaves limited to human beings. An entire industry has grown up concerned with materials processing and treatment, including cooking. The advent of microwave ovens, of which millions are now sold in the USA each year, also served to revive concern with the hazards of nonionizing radiation and played a major part in the passage of our Radiation Control for Health and Safety Act of 1968. So microwave heating is a daily concern to industrial specialists, to be sure in vitro. At least I hope none of you has tried in vivo experiments in your microwave oven, like the lady we have all read about who gave her toy poodle a shampoo and tried to dry him in a microwave oven. She created an explosive situation.

Why should we be interested in the "nonthermal" effects when nonionizing energy at thermalizing levels is of growing importance both in practical applications and in basic research? ("Nonthermal" is an imperfect descriptor, since there may be thermal effects on the microscopic and molecular scales that do not result in bulk heating; the term "subtle" introduced by Lovely in Chapter 20 of this volume is better.) To begin with, we are interested in these effects for the same reasons we concern ourselves with thermalizing effects: because of their practical importance (especially as possible hazards) and because of their potential as research tools. Many investigators have tried to demonstrate effects at progressively lower levels. For a time, it seemed almost like a competition: no sooner would someone show an effect below 10 mW/cm^2--say, at 1 mW/cm^2 --than someone else would show one at 0.1 mW/cm^2. The literature of these subtle effects is enormous, in several languages, especially Russian. Many of the underlying studies are summarized in a book translated from the Czech (Marha, *et al.*, 1971).

So the prime motivation for research in this field comes from possible hazards; and the second, which corresponds to

the concerns of the present symposium, from the hope that low-level nonionizing radiation might also prove to be a useful tool in elucidating the behavior of organisms. I would go even further in this direction and echo the hope expressed in the aforementioned paper of twenty years ago (Jaski and Süsskind, 1961) that we might learn something in that way not only about the behavior of organisms but also about their basic nature; that low-level nonionizing radiation might be used not only in the study of organs but also of cellular and subcellular phenomena, and help show us how they work.

But there is a third reason as well, which derives from the simple fact that low-level effects must be present during high-level irradiation, even though they may be masked by the more obvious thermal effects of such irradiation. In this regard, I find it highly suggestive that some of the low-level effects can be demonstrated only when the irradiation is above--and sometimes well above--10 mW/cm^2. For example, in a series of experiments we did on mice some years ago, autopsies showed that there were some anomalies among the irradiated animals--not many, just a few per cent, but there were some malignancies that did not show up among the controls (Prausnitz and Süsskind, 1962). On the other hand, the irradiated group showed greater longevity than the controls. This finding puzzled us--no one had previously proposed that microwaves might be a Good Thing--but it has been since confirmed by Don Justesen and his group (Preskorn, *et al.*, 1978).

As another example, consider the survey of the teratogenetic effects of nonionizing radiation made by Mary Ellen O'Connor (1980). Almost every effect reported showed up only when the irradiation was above 10 mW/cm^2. Now if we take this number, or something like it, as a measure of what is thermal and what is nonthermal, as a sort of boundary between these two concepts, we see at once that we cannot regard the matter in such simplistic terms. A teratogenetic effect might not be *a priori* considered to be a thermal effect; but if we only observe it at intensities we associate with thermal effects, what should we call it? The boundary is not sharp--it is quite fuzzy; and some of the thinking about it tends to be fuzzy, too.

As mentioned, there is not only no consensus about the mechanisms by which the low-level effects could be taking place, no one has even taken a systematic look at the various possibilities. So the first step would be to let our imaginations soar, put down anything we can think of, and subject each item on the list to theoretical analysis; and if it survives analysis, examine the remaining possibilities

experimentally. It is rational to demand that experiment should be guided by theory; if it is not, one is proceeding by trial and error and the probability of success is reduced to what is to be expected from fortuitous observation. Yet our funding agencies seem uninterested in such a rational approach. At least, when I proposed it to the National Institutes of Health, the proposal was dismissed out of hand; it did not even go to one of the Institutes for review by a study group. I was brusquely told that a theoretical study such as I proposed was an assessment, not research, and hence outside NIH's province. But let us look at it, anyway.

One can approach the problem either as a physicist would, or as a biologist--or both. A physicist might ask: are we dealing with resonant or nonresonant absorption? That is, are the phenomena highly frequency dependent? And are they truly absorption or are they perhaps inductive phenomena? How do they relate to material in the liquid state--which in turn may have varying degrees of order, extending perhaps to a variety of solid-state behaviors?

Or one could look at it like a biologist and classify the phenomena according to the various levels of biological organization at which such interactions may occur. That is, the site of the interaction could be at the molecular, macromolecular, or molecular-aggregate levels; it could be at the membrane, subcellular, cellular, or possibly higher biological levels, all the way up to systemic. Right away, such a correlation would facilitate the analysis of any mechanisms that are proposed. The goal would be eventually to relate the mechanisms to specific biological effects. In other words, one would focus first on the physical changes that may result from irradiation, and then evaluate the biological consequences.

What are some of these mechanisms, mechanisms that have been proposed, and others that may occur to us as we go along? One of the difficulties, as I have already suggested, is that a low-level effect may be masked by a high-level effect. The low-level effect does not become apparent until the field is strong enough to produce heating. People worry about long-term effects of even slight amounts of heating--and it is true we do not know yet what a chronic rise of, say, 1°C in the body temperature may portend--and this heating then tends to mask the low-level effect, not only in a physical sense but also in our thinking. So we have to be extra clever to know how to go about it, how to propose means of testing whether one or another mechanism is responsible for effects that might be buried under a mass of the effects of heating.

Of course heating itself is a mechanism; it is in fact *the* classical mechanism. Dielectric heating was observed even before there was much in the way of dielectric theory: the effect was known before the mechanism was understood. The same goes for dielectric forces and, for that matter, for magnetic effects that have been known for some time, such as the behavior of homing pigeons. Homing pigeons have been used for a long time--look up the history of the U.S. Army Signal Corps--but it is only recently that traces of permanently magnetized materials were discovered in pigeons, and bees, even bacteria. So dielectric heating, dielectric forces, and permanent magnetism are our "classical" mechanisms. And then we can look at a range of other mechanisms that we shall call "semiclassical". They would include for example the various models that have been offered to explain the calcium efflux experiments. These are mechanisms in which extraordinarily weak fields may trigger long-range cooperative processes. I am using the terms "classical" and "semiclassical" as a physicist would, in distinction from modern physics. There may well be mechanisms that could have a basis only in modern physics--in quantum mechanics. That is, there is a class of possible mechanisms in which it is postulated that very weak electric and magnetic fields could induce macroscopically significant effects by one of two possibilities: either a long-range, quantum-mechanically cooperative interaction; or by the elicitation of a quasi-resonance mode over a narrow range of special frequencies. Relatively little attention has been paid to date to such mechanisms as superconductivity at room temperature; to quantized magnetic flux; to tunneling through energy barriers; to semiconductivity and other solid-state behavior. The literature of this field is scant and highly speculative, but it is entirely possible that one of these mechanisms may prove to be the relevant one in the end.

It may be difficult to obtain support for the investigation of one of a long list of putative mechanisms if we do not know in advance which one, but there is one area of some practical interest: the mechanism of fields at very low frequencies, below 100 Hz. There is public concern with high-voltage transmission at 50-60 Hz, and with extremely low frequency (ELF) communication systems. I am not suggesting that a scientist should concentrate on a particular field simply because funding for it is available--although it *is* surprising how wonderfully it concentrates his mind. When the National Cancer Institute first announced it would support studies of symbiotic relationships between ionizing and nonionizing radiation, it is said to have received several thousand proposals. Yet there are perfectly valid

scientific reasons to look at low-frequency radiation very carefully. For one thing, many electrophysiological phenomena take place at low frequencies, including nerve conduction and EEG rhythms. Then there are various well-established experimental observations, including field-induced magneto-phosphenes, calcium efflux that I have already mentioned, and possibly some of the more respectable behavioral studies. There is the further observation that microwave or at least uhf radiation when *modulated* by low frequencies becomes a way of getting the low frequencies into the organism; the microwaves then act as a carrier of the low frequencies of interest. So here is a good example of low-level nonionizing radiation used as a tool for scientific investigation, especially at the membrane level. We certainly need to know more about membranes, and if our leaders propose to justify paying for it because some farmers in Wisconsin are worried about their cows grazing on top of buried antennas, who are we to argue?

What we are up against may ultimately come down to various ways of making measurements--the various ways in which an unknown quantity may be measured to provide some assurance of independent confirmation. That brings to mind the story told by Barney Oliver when he was in charge of research at the Hewlett-Packard Co. and also served as president of the Institute of Electrical and Electronics Engineers. It seems a student who had not done well in a physics examination importuned the professor into giving him one more chance--a make-up examination on which the grade would turn, and consisting of just one question. The professor agreed, and set the following problem: given a building and a barometer, how can one measure the height of the building? The student sat and sat, staring at the blank paper; and when only ten minutes remained of the examination period, the professor said, "Well, I see you can't work out the answer even to this one simple question, so hadn't we best forget about a better grade?" It wasn't that, said the student, he had thought of several answers, but could not decide which was the best. Put them all down, said the professor; and that is what the student did. One way, he wrote, would be to take the barometer to the top of the building, drop it to the ground, and with a stopwatch time the period of the fall, from which the height of the building could be readily computed.--A second way would be to go out on a sunny day, measure the height of the barometer and the length of its shadow, and the length of the building's shadow, and compute the height of the building from simple proportionality.--In a third way, one could suspend the barometer from a known length of string like a

pendulum and time the period of the pendulum, both on the ground and at the top of the building, which would lead to two different values of the gravitational constant, from which the height of the building could be computed.--Or, one could mark off the known height of the barometer on the wall of the stairwell and continue doing it as he went up the stairs; then, by counting the number of marks and multiplying the barometer height by it, one would arrive at the building's height.--Finally, how about finding the superintendent in the basement, and telling him, "Look, I have this fine barometer--if you will tell me the height of the building, you can have the instrument!"

We have imaginative students like that at Berkeley, and not long ago I said to one of them, Ross Flewelling, suppose *you* were asked to deal with the question, how may weak electric and magnetic fields interact significantly with biological systems? Say we shall stay below 10 mW/cm^2 and below 100 V/m--quite a bit below: in tissue, we could go as low as 1 $\mu V/m$; and between microwave frequencies and dc. Mr. Flewelling disappeared for a couple of weeks, and when he came back, he had a little list.

First of all, he said, there is macro heat deposition; that is, dielectric relaxation, dielectric resonant absorption, and various reflection and refraction effects such as hot spots in the human body (Cleary, 1973, 1977, 1978; Johnson and Guy, 1972; Schwan, 1957, 1978). *Second*, micro heat deposition: micro thermal gradients, effects on ordered systems, and effects of heat on osmosis, on elasticity, thermoelectric and thermo-acoustic effects (Frey, 1971; Seaman, 1977; Schwan, 1978; Straub, 1978). *Third*, there are the effects of induced currents--ionic effects and effects such as polarization (Barański and Czerski, 1976; Frey, 1971; Little, 1977; Wachtel, *et al.*, 1975). *Fourth*, we have biopolymer interactions: relaxation, resonance due to vibration and rotation, charge transfer, and tunneling effects (Barnothy, 1964; Cleary, 1973, 1977, 1978; Dubrov, 1978; Frey, 1971; Illinger, 1970, 1974; Löwdin, 1963; Presman, 1970; Prohofsky, 1978; Schwan, 1977; Straub, 1978; Takashima, 1966). *Fifth*, there are the field-induced forces, forces that play a part in orientation, deformation, movement, destruction; macro and micro dielectric forces; dielectrophoresis; coordinated induced-dipole interactions; and magnetomotive and electromotive forces (Barnothy, 1964; Cleary, 1973, 1977; Frey, 1971; Schwan and Foster, 1980; Straub, 1978; Stuchly, 1979). *Sixth*, we should look at special magnetic and electric characteristics, not only diamagnetism, paramagnetism, and ferromagnetism, but also antiferromagnetic states, electrets, magnetoelastic and

magnetostrictive effects; at pyroelectricity and piezoelectricity, at magnetoconductivity, Hall effect, cyclotron resonance, and a couple of others (Barnothy, 1964; Dubrov, 1978; Frey, 1971; Grodsky, 1975, 1976; Tanner and Romero-Sierra, 1970). *Seventh*, there are the membrane interactions: their role in action potentials, in synaptic activity, vesicle fusion, receptors, axonal transport and the various transmitters, channels, and pumps; and of course effects on membrane structure and order (Barański, *et al.*, 1974; Barnes and Hu, 1977; Bawin, *et al.*, 1978; Frey, 1971; Grodsky, 1975, 1976; Schwan, 1977, 1978; Schwan and Foster, 1980; Straub, 1978; Wachtel, *et al.*, 1975). And *eighth*, there are cooperative processes like those related to ferroelectric and ferromagnetic effects, nonlinear oscillations, and limit cycles (Bawin, *et al.*, 1978; Fröhlich, 1977, 1980; Grodsky, 1975, 1976; Kaczmarek, 1977; Kaiser, 1978; Schwan and Foster, 1980; Schwartz, 1970; Taylor, 1981).

Well, Mr. Flewelling, I said, is that all?

Not really, he said. I left out the Zeeman effect and the Stark effect, because they would almost certainly come in only at the very highest field strengths. And I suppose we should really look at the whole question of the role of water, and possibly synergistic effects with ionizing radiation and with other fields, such as biofields and gravity. And then there are some possible effects or mechanisms that are so far out we could call them Exotic Mechanisms; you want to hear about Exotic Mechanisms?

Such as?

Well, thin-film effects, and liquid-crystal effects, and coherent vibrations, solitons, surface plasmas, superconductivity, tachyons (Beischer, 1971; Cope, 1973, 1976, 1979; Dubrov, 1978; Frey, 1971; Grodsky, 1977; Little, 1977; Straub, 1978; Taylor, 1981). . . . I finally had to stop him--I did not dare to ask him how he would measure the height of a building with nothing but a barometer--but wouldn't it be nice if funding were available to follow up some of these ideas?

REFERENCES

Barański, S. and Czerski, P. (1976). *Biological Effects of Microwaves*. Dowden, Hutchinson, and Ross, Stroudsburg, Penna.

Barański, S., Szmigielski, S., and Moneta, J. (1974). Effects of microwave irradiation in vitro on cell membrane permeability. In Czerski (1974), p. 173.

Barnes, F.S. and Hu, C-L.J. (1977). Model for some nonthermal effects of radio and microwave fields on biological membranes. *Trans. IEEE MTT*-25: 742.

Barnothy, M.F., ed. (1964). *Biological Effects of Magnetic Fields*. Plenum Press, New York.

Bawin, S.M., Sheppard, A., and Adey, W.R. (1978). Possible mechanisms of weak electromagnetic field coupling in brain tissue. *Bioelectrochem. Bioeng.* 5: 67.

Beischer, E.D. (1971). The null magnetic field as reference to the study of paramagnetic differential effects in animals and man. Ann. N. Y. Acad. Sci. 188: 324.

Cleary, S.F., ed. (1970). *Biological Effects and Health Implications of Microwave Radiation*. U.S. Department of Health, Education, and Welfare, Washington, D.C.

Cleary, S.F. (1973). Uncertainties in the evaluation of the biological effects of microwave and radiofrequency radiation. *Health Physics* 25: 287.

Cleary, S.F. (1977). Biological effects of microwave and radiofrequency radiation. *CRC Critical Rev. Environ. Control* 7: 121.

Cleary, S.F. (1978). Survey of microwave and radiofrequency biological effects and mechanisms. In Taylor and Cheung (1978), p. 1.

Cope, F.W. (1976). Biological sensitivity to weak magnetic fields due to superconductive Josephson junctions. *Physiol. Chem. Phys.* 5: 173.

Cope, F.W. (1976). Superconductivity--A possible mechanism for non-thermal biological effects of microwaves. *J. Microwave Power* 11: 267.

Czerski, P., ed. (1974). *Biological Effects and Health Hazards of Microwave Radiation*. Polish Medical Publishers, Warsaw.

D'Arsonval, J.A. (1893). Influence de la frèquence sur les effets physiologiques des courants alternatifs. *C. r. Acad. Sci.* 116: 630; 117: 34.

Dubrov, A.P. (1978). *The Geomagnetic Field and Life: Geomagnetobiology*. Plenum Press, New York.

Frey, A.H. (1971). Biological function as influenced by low-power modulated rf energy. *Trans. IEEE MTT*-19: 153.

Fröhlich, H. (1977). Long-range coherence in biological systems. *Riv. nuovo cimento* 7: 399.

Fröhlich, H. (1980). The biological effects of microwaves and related questions. In *Advances in Electronics and Electron Physics* (L. and C. Marton, eds.), vol. 53, p. 85. Academic Press, New York.

Grodsky, I.T. (1975). Possible physical substrates for the interaction of electromagnetic fields with biological membranes. *Ann. N. Y. Acad. Sci.* 247: 117.

Grodsky, I.T. (1976). Neural membrane: A physical synthesis. *Math. Bio. Sci.* 28: 191.

Illinger, K.H. (1970). Molecular mechanisms for microwave absorption in biological systems. In Cleary (1970), p. 112.

Illinger, K.H. (1974). Interaction between microwave and millimeter-wave electromagnetic fields and biologic systems: Molecular mechanisms. In Czerski (1974), p. 160.

Illinger, K.H. (1977). Atomic and molecular mechanisms underlying biological interaction with EM radiation. *Neurosciences Res. Prog. Bull.* 15: 64.

Jaski, T. and Süsskind, C. (1961). Electromagnetic radiation as a tool in the life sciences. *Science* 133: 443.

Johnson, C.C. and Guy, A.W. (1972). Nonionizing electromagnetic wave effects in biological materials and systems. *Proc. IEEE* 60: 692.

Kaczmarek, L.K. (1977). Cation binding models for the interaction of membranes with EM fields. *Neurosciences Res. Prog. Bull.* 15: 54.

Kaiser, F. (1978). Coherent oscillations in biological systems: I. *Z. Naturforsch.* 33a: 294.

Little, W.A. (1977). The physical characteristics of EM field interaction with molecular systems. *Neurosciences Res. Prog. Bull.* 15: 62.

Löwdin, P. (1963). Proton tunneling in DNA and its biological implications. *Rev. Mod. Physics* 35: 724.

Marha, K., Musil, J., and Tuhá, H. (1971). *Electromagnetic Fields and the Life Environment.* San Francico Press, San Francisco.

O'Connor, M.E. (1980). Mammalian teratogenesis and radiofrequency fields. *Proc. IEEE* 68: 56.

Prausnitz, S. and Süsskind, C. (1962). Effects of chronic microwave irradiation in mice. *Trans. IRE BME*-9: 104.

Preskorn, S.H., Edwards, W.D., and Justesen, D.R. (1978). Retarded tumor growth and greater longevity in mice after fetal irradiation by 2450-MHz microwaves. *J. Surg. Oncol.* 10: 483.

Presman, A.S. (1970). *Electromagnetic Fields and Life.* Plenum Press, New York.

Prohofsky, E.W. (1978). Microwave frequencies and the structure of the double helix. In Taylor and Cheung (1978), p. 133.

Schwan, H.P. (1957). Electrical properties of tissue and cell suspensions. *Adv. Biol. Med. Phys.* 5: 147.

Schwan, H.P. (1977). Some tissue determinants of interactions with electric fields. *Neurosciences Res. Prog. Bull.* 15: 88.

Schwan, H.P. (1978). Classical theory of microwave interactions with biological systems. In Taylor and Cheung (1978), p. 90.

Schwan, H.P. and Foster, K.R. (1980). Rf-field interactions with biological systems: Electrical properties and biophysical mechanisms. *Proc. IEEE* 68: 104.

Schwartz, G. (1970). Cooperative binding to linear biopolymers. *Eur. J. Biochem.* 12: 442.

Seaman, R.L. (1977). Effects of microwave radiation on Aplysian ganglion cells. *Neurosciences Res. Prog. Bull.* 15: 45.

Steneck, N.H., Cook, H.J., Vander, A.J., and Kane, G.L. (1980). Origin of U.S. safety standards for microwave radiation. *Science* 208: 1230.

Steneck, N. ed. (1982). *Risk/Benefit Analysis: The Microwave Case*. San Francisco Press, San Francisco.

Straub, K.D. (1978). Molecular absorption of non-ionizing radiation in biological systems. In Taylor and Cheung (1978), p. 35.

Stuchly, M.A. (1979). Interaction of radiofrequency and microwave radiation with living systems. *Rad. Environm. Biophysics* 16: 1.

Süsskind, C. (1980). The "story" of nonionizing radiation research. Bull. N. Y. Acad. Med. 55: 1152.

Takashima, S. (1966). Studies on the effect of radiofrequency waves on biological macromolecules. *Trans. IEEE BME*-13: 28.

Tanner, J.A. and Romero-Sierra, C. (1970). Bird feathers as sensory detectors of microwave fields. In Cleary (1970), p. 185.

Taylor, L.S. (1981). The mechanism of athermal microwave biological effects. *Bioelectromagnetics* 2: 259.

Taylor, L.S. and Cheung, A.Y., eds. (1978). *The Physical Basis of Electromagnetic Interactions with Biological Systems*. Proceedings of a workshop held at the University of Maryland, 1977. U.S. Department of Health, Education, and Welfare, Washington, D.C.

Tesla, N. (1891). "Massage" with currents of high frequency. *Electrical Engineer*, December 23.

Wachtel, H., Seaman, R., and Joines, W. (1975). Effects of low-intensity microwaves on isolated neurons. *Ann. N.Y. Acad. Sci.* 247: 46.

CIRCULATORY AND SWEATING RESPONSES DURING EXERCISE AND HEAT STRESS

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Skin blood flow works in tandem with sweating to eliminate heat from the body core, since skin blood flow carries heat to the skin surface, where it is dissipated by evaporation of sweat. Moreover, the skin itself is a large organ whose blood vessels drain into a large and compliant venous bed. All these factors play a major role in the circulatory consequences of heat stress in sweating animals.

From the perspective of heat balance in an animal, the law of conservation of energy may be expressed as

$$M = E + R + C \qquad (1)$$

in which M = metabolic energy production, and E, R, and C are heat lost to the environment by evaporation, radiation, and convection respectively. If the organism gains heat from the environment by any of the foregoing routes, the corresponding term is negative. (For a more complete discussion see Chapters 2 and 7).

By Newton's law of cooling, R is proportional to the difference between skin temperature (T_{sk}) and mean radiant temperature of the environment (T_r), and C is proportional to the difference between T_{sk} and air temperature (T_a):

$$R = h_r \cdot A \cdot (T_{sk} - T_r) \qquad (2)$$

and

$$C = h_c \cdot A \cdot (T_{sk} - T_a) \qquad (3)$$

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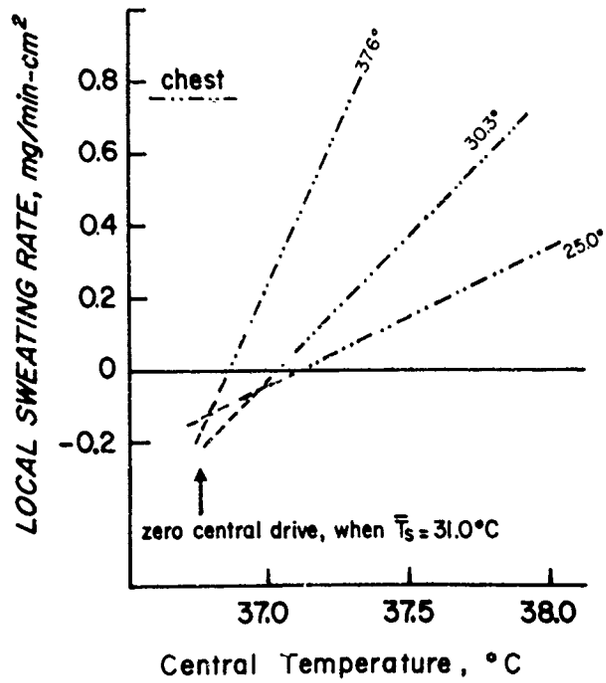

Figure 1. Effect of local skin temperature on sweat rate. The lines show the relation of chest sweating rate to esophageal temperature during leg exercise, when chest skin temperature at the site of sweat rate measurements was 25.0, 30.3, and 37.6 °C. Ambient temperature = 26 °C, and whole-body mean skin temperature ($\bar{T}_s$) = 31 °C. Modified from Nadel, *et al.* (1971b).

where h_r and h_c are the respective heat transfer coefficients, and A = surface area. Thus, the organism can control R and C by altering T_{sk} by adjustment of skin blood flow (SkBF): increasing SkBF brings T_{sk} nearer to blood temperature, and decreasing SkBF brings it nearer to ambient temperature. In a thermoneutral environment, a resting human can maintain heat balance solely by adjusting R and C through the control of SkBF. If the environment is so warm, or M so great (as during exercise), that these means are not sufficient to maintain heat balance, sweating begins.

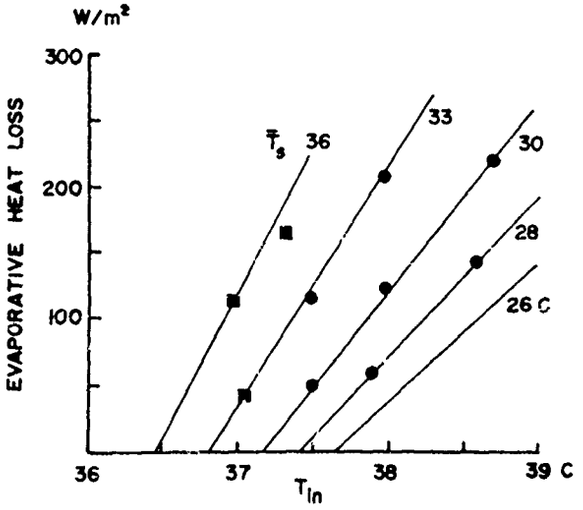

Figure 2. Relation of total evaporative heat loss (an index of whole-body sweat rate) to internal (T_{in}) and mean skin ($\bar{T}_s$) temperatures. Data were obtained at steady state during resting heat exposure (squares) and exercise (circles) in a wide range of ambient temperatures. Solid lines are calculated from $E = [197\ (T_{in} - 36.7\ °C) + 23\ (T_s - 34.0\ °C)] \cdot e^{(T_s - 34.0\ °C)/10}$. In this equation, the weighted sum of T_{in} and $\bar{T}_s$ represents the sympathetic nervous signal to the sweat glands, and the exponential factor represents the effect of local temperature on sweat gland response. From Nadel *et al.* (1971a), with permission of the American Physiological Society.

THERMOREGULATORY RESPONSES

Sweating

Evaporation of 1 liter of sweat removes 2,426 kJ as latent heat of evaporation (Wenger, 1972). Typical maximum rates of sweating are 2-3 liters/h and 10-15 liters/day. (For comparison, it is hard to attain a metabolic heat production greater than about 550 W, viz. 1,980 kJ/h.) Thermoregulatory sweat in human beings is secreted by about 3,000,000 eccrine sweat glands, which have a cholinergic sympathetic innervation, and are widely distributed over the skin surface (Montagna, *et al.*, 1962).

The sympathetic signal to the sweat glands is controlled

according to a) body core temperature, whose defense is the function of thermoregulation, and b) a weighted average of skin temperature over the body ($\bar{T}_{sk}$), which provides an index of the environmental thermal stress (cf. Chapter 7). Esophageal temperature (T_{es}) is a convenient index which responds rapidly to changes in core temperature, and was used in most of the experiments presented in this chapter. The reflex signal can be expressed as a linear combination of T_{es} and $\bar{T}_{sk}$, with T_{es} weighted about 9 times as heavily as $\bar{T}_{sk}$ (Nadel, *et al.*, 1971a). Furthermore, the warmer the sweat glands are, the greater is their response to sympathetic stimulation (Fig. 1). Thus the overall sweating response to T_{es} and $\bar{T}_{sk}$, including both local and reflex effects of $\bar{T}_{sk}$, is an summarized in Fig. 2, which presents measurements made both during leg exercise and during rest. As the figure indicates, the relation of sweating rate to T_{es} and $\bar{T}_{sk}$ is unaffected by leg exercise (Stolwijk and Nadel, 1973). By contrast, Tam, *et al.* (1978) reported that sweating rate during arm exercise is higher than during rest at the same internal and mean skin temperatures. Since arterial blood pressure is substantially higher during arm exercise than during leg exercise (Åstrand, *et al.*, 1965), it is likely that non-thermal activation of the sympathetic nervous system accounts for part of the sweating response during arm exercise.

Skin Blood Flow

In a cool or thermoneutral environment, the body controls R + C by varying SkBF and thus $\bar{T}_{sk}$, as noted above. When the heat stress is so great that this mechanism is not enough to maintain heat balance, sweating begins. SkBF continues to rise under these conditions, but now serves to deliver to the skin the heat which is being removed by evaporation of sweat, so that $\bar{T}_{sk}$ undergoes little furtner change.

Sympathetic control of SkBF is not uniform over the whole body: skin arterioles in the hands, feet, ears, and nose receive only constrictor nerves, whereas skin arterioles in most other places also receive dilator nerves (Fox and Edholm, 1963). Since forearm skin receives both constrictor and dilator nerves, and since forearm blood flow (FBF) can be measured readily by venous occlusion plethysmography, FBF is commonly used as an index of SkBF. Fig. 3 shows the relation of FBF to T_{es} during exercise, at two levels of $\bar{T}_{sk}$. The relationships seen in Fig. 3 are probably not greatly affected by the use of exercise to raise T_{es}.

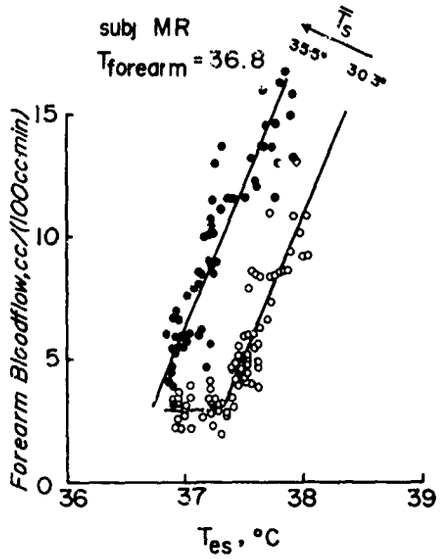

Figure. 3. Relation of forearm blood flow to esophageal temperature (T_{es}) during cycle exercise in ambient temperatures of 15 (open circles) and 35 °C (filled circles), with mean skin temperatures ($\bar{T}_s$) of 30.3 and 35.5 °C respectively. Forearm skin temperature was kept at 36.8 °C during these experiments. From Wenger, *et al.* (1975), with permission of the American Physiological Society.

Although the FBF:T_{es} relation is altered by exercise at $\bar{T}_{sk}$ of 38 °C (Johnson, *et al.*, 1974a), in cooler conditions the FBF:T_{es} relationship during submaximal exercise is the same as during recovery (Roberts and Wenger, 1979). Furthermore, Nielsen and Nielsen (1965) reported that at any given steady-state internal and mean skin temperatures, SkBF (estimated from whole-body thermal conductance) and sweating rates were the same during leg exercise as during passive heating by diathermy.

During the experiments shown in Fig. 3, forearm skin temperature was kept at 36.8 °C, whatever the level of $\bar{T}_{sk}$, so that unlike Fig. 2, Fig. 3 shows only the reflex effect of skin temperature. The reflex control of FBF, like that of sweating, can be approximated mathematically by a linear combination of T_{es} and $\bar{T}_{sk}$, with T_{es} weighted about 10 times as heavily as $\bar{T}_{sk}$ (Wenger, *et al.*, 1975). This close similarity is just what we should expect from the tandem

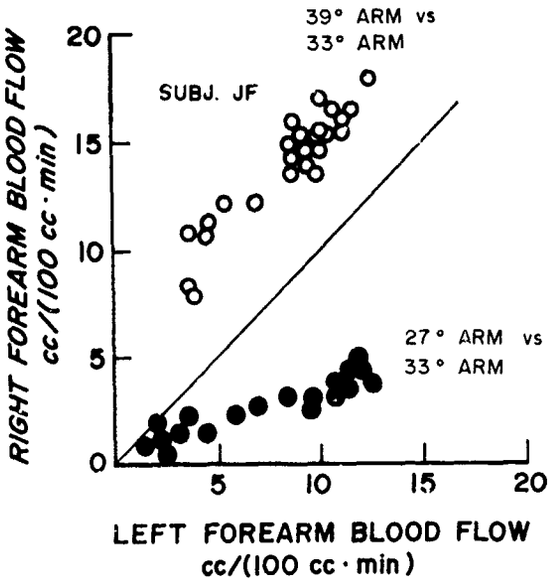

Figure 4. Effect of local temperature on forearm blood flow (FBF) during cycle exercise. The plotted points show the relation of FBF in the right arm to FBF measured simultaneously in the left arm. Skin of the left forearm was always kept at 33 °C, and skin of the right forearm was kept at either 27 °C (filled circles) or 39 °C (open circles). If there were no effect of local temperature, plotted points would lie on the line of identity, the 45° line passing through the origin.

operation of SkBF and sweating during heat stress. As with the sweat glands, the response of the skin arterioles to sympathetic stimulation depends on local skin temperature, as seen in Fig. 4. If the forearm is cooled to 27 °C, the sensitivity of the arterioles decreases, paralleling the effect of local temperature on sweating seen in Fig. 1; if the forearm is heated to 39 °C, however, the effect of local heating on forearm blood flow seems to be added to the effect of sympathetic stimulation, rather than modifying the sensitivity of the skin arterioles to sympathetic stimulation.

During heat stress, cardiac output and myocardial work must increase substantially to bring about the accompanying increases in SkBF. Patients with impaired myocardial

function may tolerate this load poorly (Berenson and Burch, 1952; Burch and Miller, 1969), but as a factor limiting heat tolerance in the young and healthy, this effect is less important than impairment of cardiac filling secondary to peripheral pooling of blood (Rowell, 1977), which is discussed below.

Capacity of Superficial Veins

The limbs have a dual venous drainage, consisting of a) superficial veins, which lie in the subcutaneous tissue and receive blood primarily from the skin, and b) deep veins, which receive blood primarily from muscle. However, the superficial and deep veins are connected with each other by many penetrating veins, so that potentially blood from anywhere in the limbs can return to the heart via either superficial or deep veins. Although the deep veins have a relatively poor sympathetic innervation (Webb-Peploe and Shepherd, 1968b), the superficial veins are well innervated, and constrict in response to cooling the body core (Webb-Peploe and Shepherd, 1968a). Dilation of the superficial veins will favor return of venous blood from the limbs to the heart via the superficial veins, and is thus equivalent to an increase in SkBF; constriction of the superficial veins will have the opposite effect. Since the superficial tissues are cooler than the tissues deeper in the limb, these veins can play a role in maintaining heat balance, favoring heat conservation when they are constricted, and heat loss when they are dilated (Goetz, 1950). The thermoregulatory role of the superficial veins is probably most important in and near the thermoneutral range, since they are well dilated in subjects who are not uncomfortably warm (Thauer, 1965).

Forearm venous volume (FVV), which can be measured easily by venous occlusion plethysmography (Wenger and Roberts, 1980), is a useful index of the compliance of the superficial veins and is inversely related to their tone (i.e., the activity of their smooth muscle). FVV is measured in a forearm which is elevated above shoulder level, so that its veins can drain freely by gravity. Forearm volume is measured with a Whitney mercury-in-silicone-rubber strain gauge, and the forearm veins are periodically congested to a certain pressure (e.g., about 19 Torr) by inflation of a pneumatic cuff surrounding the arm proximal to the gauge. FVV is taken as the difference in forearm volume between the congested and uncongested states.

Figures 5 and 6 show how FVV may be influenced by

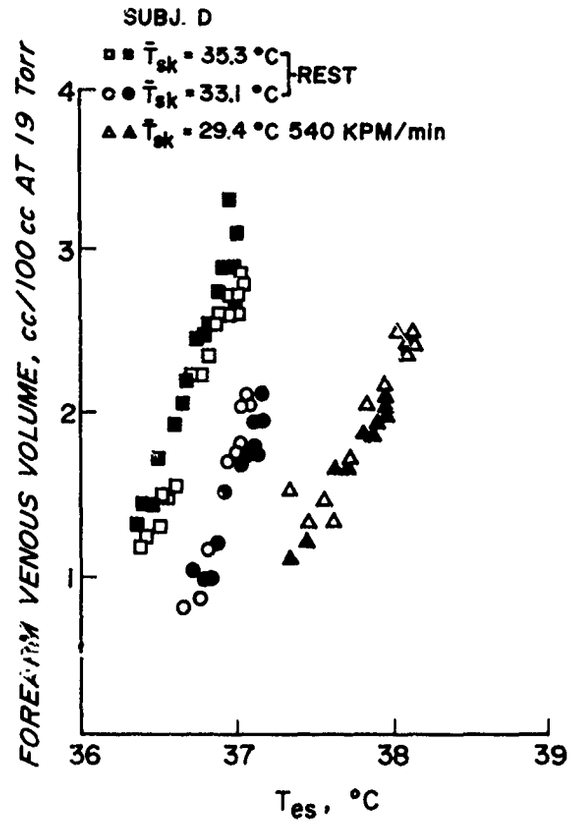

Figure 5. Effect of esophageal (T_{es}) and mean skin ($\bar{T}_{sk}$) temperatures on forearm venous volume (FVV). Triangles: ambient temperature (T_a) = 15 °C. Circles: T_a = 25 °C. Squares: T_a = 35 °C. Each symbol shape includes data from two duplicate experiments, one of which is indicated by open symbols and the other by filled symbols. Each experiment began with a state of near-maximal venoconstriction attained by eating ice. From Wenger and Roberts (1980), with permission of the American Physiological Society.

environmental temperature and by exercise. Immediately before these experiments, subjects ate chopped ice to lower their core temperatures enough to constrict their superficial veins maximally. During each experiment, as metabolic heat was retained and T_{es} rose, FVV increased. During these experiments, forearm temperature was maintained at about 35 °C, so that the effect of skin temperature in Figs. 5 and

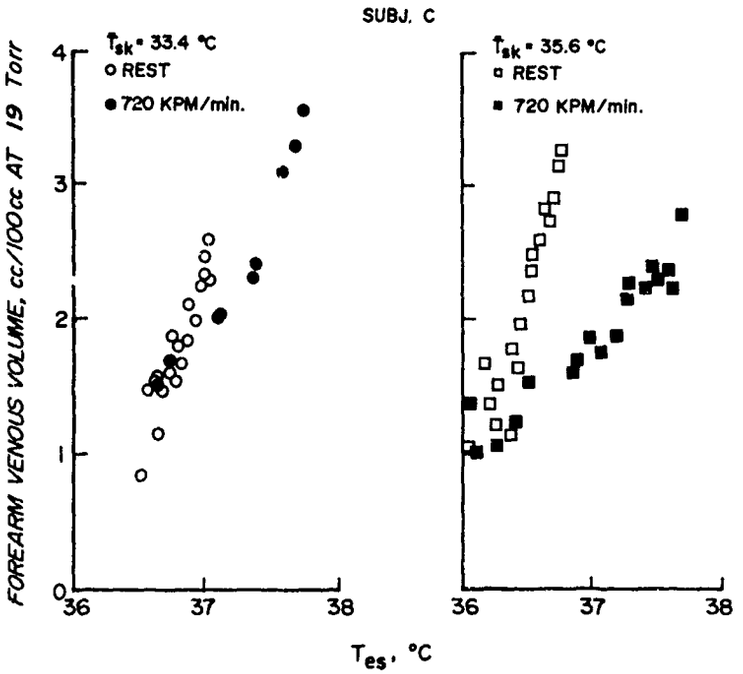

Figure 6. Effect of exercise at 40% of maximal oxygen consumption ($\dot{V}O_{2max}$) on the FVV:T_{es} relation in T_a of 25 °C (left panel) and 35 °C (right panel). During exercise, the slope of the FVV:T_{es} relation is lower at high $\bar{T}_{sk}$. Abbreviations are as in Fig. 5. Each experiment began with a state of near-maximal venoconstriction attained by eating ice. From Wenger and Roberts (1980), with permission of the American Physiological Society.

6 represents only the reflex effect on $\bar{T}_{sk}$. Thermal control of FVV is according to a weighted sum of T_{es} and $\bar{T}_{sk}$, as we saw above for the control of sweat rate and FBF. However, exercise markedly reduces FVV at any T_{es} (Fig. 6), whereas exercise has a much smaller effect on control of FBF and sweating. In fact, as we shall see below, during some protocols involving exercise, changes in FVV are dominated by non-thermal factors. Although we do not fully understand the afferent signals responsible for the effects of exercise on FVV, they seem to include both an effect related to cardiac filling and an effect related to the cardiovascular adjustments at the onset of exercise. Venoconstriction would, of course, tend to maintain cardiac filling by

limiting peripheral pooling of blood, and might also help to increase cardiac output at the beginning of exercise by moving blood toward the heart.

IMPAIRED CARDIAC FILLING DURING EXERCISE AND HEAT STRESS

Cardiac stroke volume (SV) is determined by cardiac contractility, aortic pressure, and cardiac filling pressure (Sagawa, *et al.*, 1975). Cardiac filling pressure in turn is largely determined by total blood volume and by the distribution of blood within the vascular compartment. Both the volume and the distribution of blood may change during exercise and heat stress, as plasma water is lost by sweating and by movement into the tissues, and as blood is redistributed away from the great veins and into dilated peripheral vessels. These changes may be substantial even during short-term exercise: plasma volume (PV) may fall as much as 20% during 20 min exercise (Nadel, *et al.*, 1979), and the effects of peripheral pooling of blood are likely to be at least as great as those of decreased PV, as will become clear below. As a consequence of these effects, SV frequently falls over the course of exercise, especially in the heat, as T_{es} and SkBF rise and PV falls (Fig. 7; Nadel, *et al.*, 1980; Fortney, *et al.*, 1981a) (We cannot exclude the effect on SV of a possible increase in aortic pressure, or reduction in cardiac contractility. However, such effects seem unlikely in these experiments, since most of the fall in SV typically occurred between the fifth and 15th min of exercise.) When heart rate is already nearly maximal, this reduction in SV will tend to limit cardiac output and oxygen delivery to active muscle, and thus exercise tolerance as well.

Peripheral venomotor responses may have a substantial effect on peripheral pooling of blood: for example, changes in FVV may be as much as 2% of forearm volume (Figs. 5, 6), an amount which -- for a forearm segment 10 cm in diameter, with skin 1 mm thick -- is equal to skin volume. However, since FVV is always measured with the same congesting pressure, it is an indication of the level of venous tone rather than a direct index itself of the amount of blood pooled in the veins. Since the veins are distensible and collapsible, they can assume various cross sections from flattened and nearly empty to round and engorged. The amount of blood which they contain thus depends not only on venous tone (i.e., the state of the smooth muscle in their walls, which determines their circumference at a particular congesting

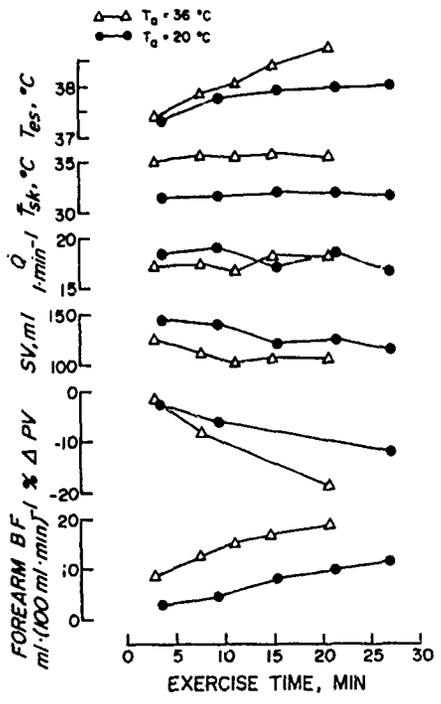

Figure 7. Circulatory responses of one subject during cycle exercise at 70% $\dot{V}O_{2max}$ in T_a of 20 and 36 °C, showing (from top) esophageal and mean skin temperatures, cardiac output, stroke volume, per cent change in plasma volume, and forearm blood flow. Redrawn from data presented in Nadel, *et al.* (1979).

pressure), but also on the pressure of the blood within them. In turn, the pressure within a venous bed depends on the rate of blood flow into it, its height with respect to the heart, and the effectiveness of the muscle pump in emptying the bed (Henry and Gauer, 1950). Thus, for example, during exercise in the supine posture, when most of the peripheral venous bed is near or above heart level, there is less peripheral pooling of blood and SV is greater than during exercise at the same intensity in the upright posture (Fig. 8).

The effect of increased SkBF on peripheral pooling and SV cannot be demonstrated in quite such a straightforward way,

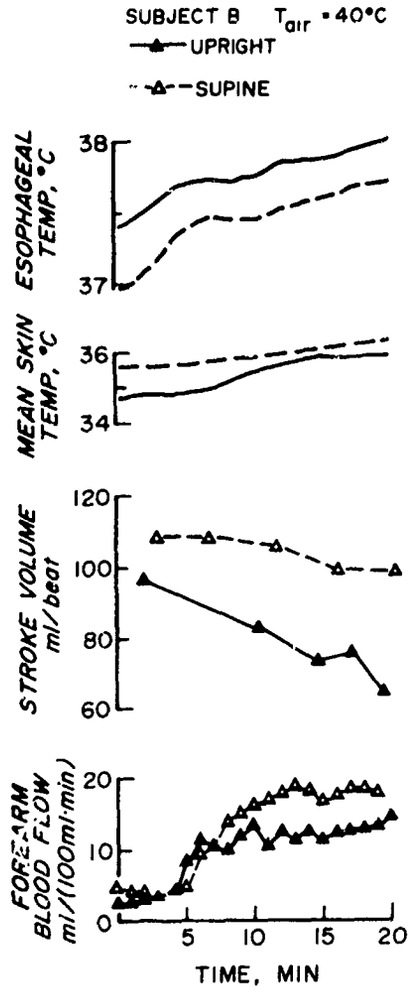

Figure 8. Time course of esophageal and mean skin temperatures, and circulatory responses during upright and supine cycle exercise at 40% $\dot{V}O_{2max}$. From Roberts and Wenger (1980), with permission of the American Physiological Society.

but probably accounts for much of the drop in SV which accompanies the increase in SkBF during exercise (cf. Figs. 7 and 9; Nadel, *et al.*, 1980; Fortney, *et al.*, 1981a). As we shall see below, this fall in SV may be several times as great as can be explained by changes in PV alone, so that much of the decrease in SV is left to be accounted for by

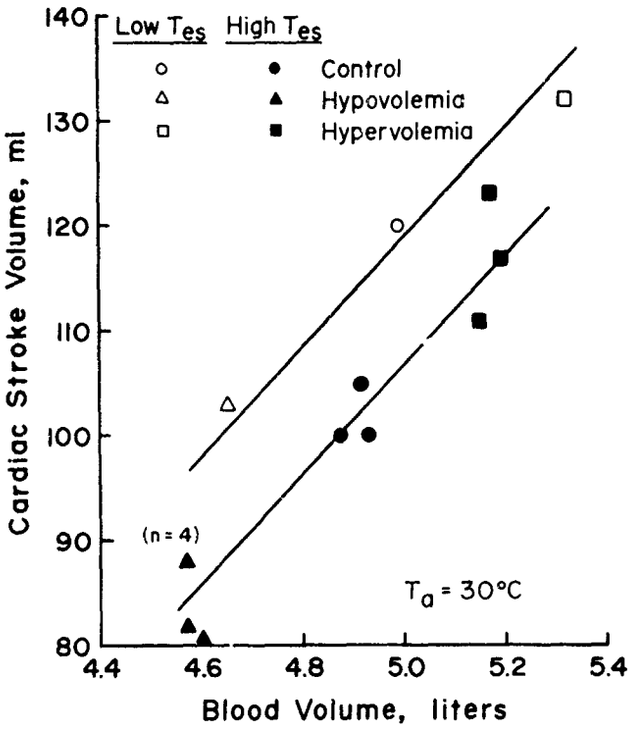

Figure 9. Relation of stroke volume (SV) to blood volume (BV) during cycle exercise at 65-70% $\dot{V}O_{2max}$ after 6 min of exercise (open symbols), when esophageal temperature (T_{es}) had risen only 35% of the way to its level at 30 min; and after 15, 20 and 30 min of exercise (filled symbols) when T_{es} was higher, and, presumably, peripheral pooling of blood was greater than at 6 min. Hypovolemia was produced by administering diuretics for four days preceding an experiment, and hypervolemia was produced by infusing a solution of albumin in saline immediately before an experiment. Except as noted, each point is the mean of data from five subjects.

increased peripheral pooling. Now, if a subject begins moderate exercise in a venodilated state, FVV may actually decrease over the course of exercise (cf. Fig. 10), so that the increase in peripheral pooling most probably owes to the accompanying increase in SkBF and consequent rise in venous pressure.

Quantification of the effects of peripheral pooling is complicated by the lack of a convenient means to measure

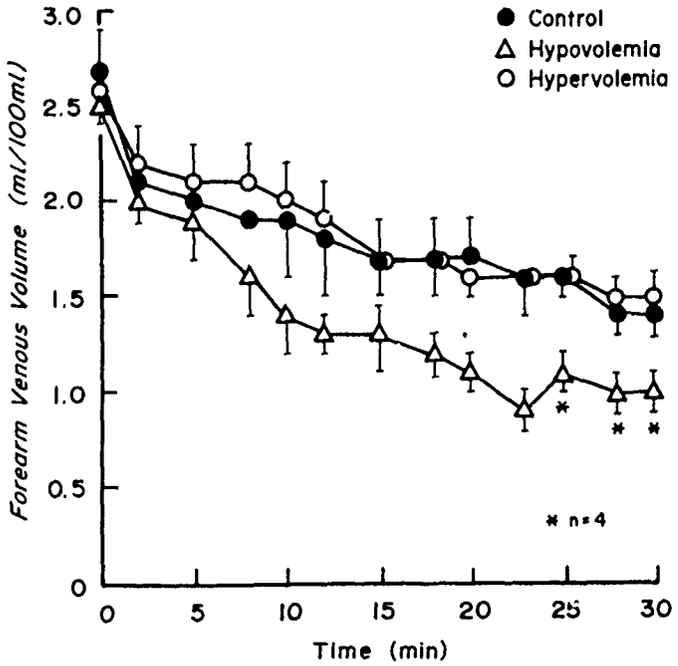

Figure 10. Time courses of forearm venous volume during cycle exercise at 65-70% $\dot{V}O_{2max}$ in air temperature of 30 °C, under three conditions of initial blood volume. Except as noted, each point is the mean of data from five subjects. These data are from the same experiments as those in Fig. 9.

peripheral pooling, and by the fact that peripheral pooling and loss of PV tend to occur together. However, there are a number of ways to manipulate peripheral pooling and PV independently, in order to evaluate the effect on SV of each variable separately. We have already seen how supine posture during exercise increases SV by reducing peripheral pooling (Fig. 8). Another approach is to give intravenous infusions or diuretics to alter the blood volume (BV) with which a subject begins exercise, so that comparisons of different experiments demonstrate the effect of BV on SV during exercise (Fig. 9). Although the increase in SkBF and peripheral pooling and the decreases in SV and BV occur more or less together during any one experiment, we can estimate the effect on SV of BV alone if we separate our measurements into two groups: those taken early in exercise, with relatively little peripheral pooling (open symbols), and those

taken later in exercise, with more peripheral pooling (filled symbols). Having thus controlled for the effect of peripheral pooling, we estimate the effect of BV on SV under these conditions as the average slope of the SV:BV relation, viz. 53 ml change in SV per liter change in BV. Now in Fig. 9, during the last 15 min of exercise, SV is, on the average, 17.7 ml less than at 6 min of exercise, and BV averages 0.1 liter less. This decrease in BV can account for only a 5.3 ml drop in SV, leaving 12.4 ml to be explained in terms of some other factor or factors, of which peripheral pooling of blood is likely to be the most important.

Although the foregoing analysis provides an estimate of the effect of peripheral pooling of blood on SV, it does not offer a means for computing the amount of blood pooled in peripheral vessels. We can, however, deduce that the volume of blood pooled must be smaller than the loss of blood volume necessary to reduce cardiac filling pressure by the same amount, since if e.g. 100 ml is lost from the vascular compartment, all the capacitance vessels of the body share the loss; if, however, 100 ml is pooled in the peripheral vessels, this loss must be borne by the vessels from which the 100 ml was displaced, so that these vessels experience a greater volume depletion that if the loss were shared by all the capacitance vessels.

DEFENSE OF CARDIAC FILLING PRESSURE DURING EXERCISE AND HEAT STRESS

As we have seen, all of the thermoregulatory responses to heat--sweating, increased SkBF, and venodilation--will tend to impair cardiac filling by reducing plasma volume or by favoring peripheral pooling of blood. At rest or during mild exercise, these effects may be fairly well compensated for by more forceful contraction of the heart or by increased heart rate. During more strenuous exercise, however, impaired cardiac filling will tend to limit cardiac output and exercise tolerance. When cardiac filling is reduced, all of the above thermoregulatory responses may be attenuated, so that the body accepts some impairment of thermoregulation in order to help defend cardiac filling against further reduction. These relationships will be discussed below, and are summarized in Fig. 11.

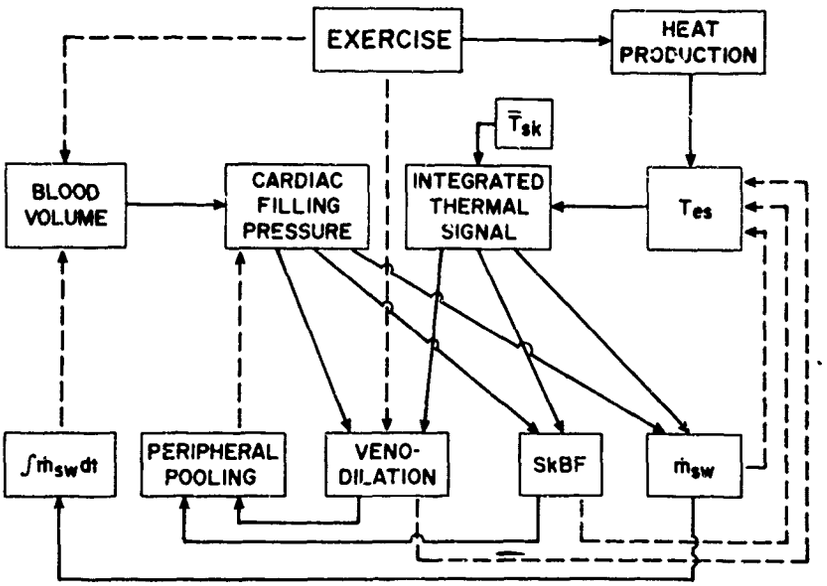

Figure 11. Diagram showing a) the effect of exercise on body temperature and blood volume, b) the thermoregulatory control and function of venodilation, skin blood flow (SkBF) and sweating ($\dot{m}_{sw}$) and c) the effects of venodilation, SkBF and $\dot{m}_{sw}$ on cardiac filling pressure, and their participation in responses which tend to maintain cardiac filling pressure. Solid arrow: an increase in the quantity at the tail of the arrow tends to increase the quantity at the head of the arrow. Dashed arrow: an increase in the quantity at the tail of the arrow tends to decrease the quantity at the head of the arrow. The effect of $\dot{m}_{sw}$ on blood volume is represented as an integral over time, to indicate that the effect is cumulative. For simplicity, effects of the thermoregulatory responses on T_{sk} are not shown. Also omitted are effects of exercise on SkBF and $\dot{m}_{sw}$, which have been reported under certain conditions.

Sweating

The temperature of the body core climbs during progressive exercise dehydration, and this effect has been ascribed to a reduction in sweating rate (Ekblom, *et al.*, 1970). Although some authors (e.g., Nielsen, *et al.*, 1971) have attributed the reduction in sweat rate to the increased plasma osmotic pressure which accompanies such dehydration,

recent work in our laboratory indicates that control of sweating is also sensitive to changes in plasma volume: following isotonic dehydration produced by diuretics, sweat rate during exercise was lower than at the same T_{es} during control experiments (Fortney, *et al.*, 1981b). This reduction in sweat rate took the form of a decrease in the slope of the sweat rate:T_{es} relation.

Peripheral Vasomotor Responses

Reduced cardiac filling also initiates several vasomotor and venomotor reflexes that tend to attenuate the reduction in central venous pressure. Vasoconstriction in the splanchnic area (Johnson, *et al.*, 1974b) and in skin and muscle (Rowell, *et al.*, 1973) are well documented responses to reductions in central venous pressure produced in resting subjects by lower body suction.* FBF at any T_{es} during leg exercise was reduced by isotonic dehydration produced by diuretics (Nadel, *et al.*, 1980). The reduction in FBF took the form of a higher T_{es} threshold for vasodilation and a lower maximum FBF (manifested as a plateau in the FBF:T_{es} relation) following dehydration than in control experiments. In other experiments, limiting the peripheral pooling of blood allowed a greater increase in SkBF during exercise: FBF in the supine posture was consistently higher than in the upright posture, even though T_{es} was lower (Fig. 8).

Peripheral Venomotor Responses

Constriction of the superficial veins might play a useful role in limiting the impairment of cardiac filling during exercise in the heat. In fact, many authors have reported constriction of superficial veins during short term (up to 5 min) static and dynamic exercise. This venoconstriction thereby resists the tendency toward venous pooling of blood. Bevegard and Shepherd (1965) found that forearm veins constricted in proportion to exercise intensity, and suggested

*Lower body suction is an experimental technique for causing blood to pool peripherally. The lower part of the subject's body, from about the waist down, is enclosed in a rigid, airtight chamber. Application of suction (e.g., 50 torr) to the box increases the transmural pressure across the walls of the blood vessels in the lower part of the body, causing these vessels to become engorged with blood.

that exercise-induced venoconstriction serves to improve cardiac filling and thus facilitate increases in cardiac output. This initial venoconstriction, which is sympathetically mediated and is considered to be part of the cardiovascular response at the onset of exercise (Merritt and Weissler, 1959; Shepherd, 1966; Zitnik, *et al.*, 1971), reportedly disappears as exercise continues if the exercise is not heavy (Rowell, *et al.*, 1971, Zitnik, *et al.*, 1971). It is unclear, however, whether this reduction in venomotor tone occurs because of rising internal temperature (Zitnik, *et al.*, 1971), or because the primary stimulus for the initial venoconstriction is transitory.

In contrast to their responses early in exercise, the response of peripheral veins to changes in cardiac filling (as during lower body suction) is still controversial, denied by some authors (Browse, *et al.*, 1966; Epstein, *et al.*, 1968; Hainsworth and Linden, 1979) but supported by the work of others (Ardill, *et al.*, 1967; Gilbert and Stevens, 1966; Newberry, 1970). The data in Fig. 10 give further support for such a response, since the venoconstriction reached during exercise in the hypovolemic condition is much more intense than that observed in control and hypervolemic conditions. However, the relation of venomotor responses to changes in cardiac filling is complicated by several features. In the first place, FVV at rest was virtually the same in all three conditions, suggesting that the venoconstrictor response is somehow sensitive to the heart's greater need for filling pressure sufficient to maintain stroke volume during exercise. In the second place, venomotor responses are virtually identical in the control and hypervolemic conditions, in spite of the differences in cardiac filling between these two conditions (Fig. 9). In the third place, the drop in BV during exercise is least in the hypovolemic condition (Fig. 9), and the degree of peripheral pooling is probably least also, because of both the venoconstriction (Fig. 10) and the smaller amount of vasodilation occurring during exercise in such conditions (Fortney, *et al.*, 1981a; Nadel, *et al.*, 1980). Yet the reduction in FVV during exercise was greatest in hypovolemia. Taken together, the second and third points indicate that the relation of FVV to cardiac filling -- or at least to BV and peripheral pooling -- is not linear, but that FVV is more sensitive to changes in BV and peripheral pooling when cardiac filling is reduced. The complexity of the peripheral venomotor response to changes in cardiac filling may explain much of the disagreement as to whether it occurs.

Such a peripheral venoconstrictor response would tend to limit the peripheral pooling associated with rising T_{es} and

SkBF during exercise, and would thus help to maintain cardiac filling and SV. It is likely that such a response accounts for much of the effect of exercise on FVV seen in Fig. 6. Although FVV increased as T_{es} rose during exercise in these experiments, FVV during exercise was always less than at the same T_{es} during rest. This difference in FVV became greater as exercise continued and, presumably, SkBF rose and PV fell. At higher exercise intensities, the demand for cardiac output is greater, yet cardiac filling is likely to be compromised even more, because of both a greater increase in SkBF and a greater fall in PV (Nadel, *et al.*, 1979). We might thus expect an even greater peripheral venoconstrictor response under such conditions. Indeed, FVV at the end of 30 min exercise was substantially lower at an exercise intensity of 65-70% of maximum oxygen consumption ($\dot{V}O_{2max}$) (Fig. 10) than at 40% $\dot{V}O_{2max}$ (Fig. 6). The fact that FVV rose during exercise in Fig. 6, but fell in Fig. 10 is explained by the low levels of T_{es} and FVV, produced by eating ice, with which the subject in Fig. 6 began exercise. By contrast, the subjects in Fig. 10 began exercise with much higher values of FVV, and control of FVV during exercise was so dominated by non-thermal factors that any relation of FVV to T_{es} during those experiments was completely obscured.

Most of the experimental work described in this chapter involved the use of exercise to heat the body core. The circulatory system must then respond in two ways: by supplying blood to the working muscles to meet their metabolic needs, and by carrying blood to the skin to remove heat from the body core. Like exercise, microwaves can heat the body core and evoke appropriate thermoregulatory responses (cf. Nielsen and Nielsen, 1965). However, since heating with microwaves does not impose the large metabolic demands that exercise does, we might expect the circulatory responses to increased body core temperature to occur in a "purer" form, because of the absence of competing metabolic demands for muscle blood flow. This potentially interesting problem seems, however, to have received relatively little experimental attention.

In summary, the three principal thermoregulatory responses in heat-stressed human subjects are venodilation, increased SkBF, and sweating. All of these may reduce cardiac filling and thus stroke volume, either through increased pooling of blood in peripheral vessels or through loss of plasma water. If cardiac filling is reduced sufficiently -- especially during exercise, when the demand for cardiac output is greatly increased -- these thermoregulatory responses may be attenuated, in order to minimize

further reductions in cardiac filling. Under the conditions which we have studied, the dependence of sweat rate or SkBF on internal body temperature is not obscured, even though the relationship may be altered. Under similar conditions, however, the control of the superficial veins may be so dominated by non-thermal factors that they will constrict in the face of rising internal body temperature.

ACKNOWLEDGMENTS

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REFERENCES

Ardill, B.L., Bhatnagar, V.M., Fentem, P.H., and Williams, R.L. (1967). Some observations on the nature of the stimulus to reflex constriction of forearm capacitance vessels during the suction manoeuvre. *J. Physiol., London* 191:123P.

Astrand, P.-O., Ekblom, B., Messin, R., Saltin, B., and Stenberg J. (1965). Intra-arterial blood pressure during exercise with different muscle groups. *J. Appl. Physiol.* 20:253.

Berenson, G.S., and Burch, G.E. (1952). The response of patients with congestive heart failure to a rapid elevation in atmospheric temperature and humidity. *Am. J. Med. Sci.* 223:45.

Bevegard, B.S., and Shepherd, J.T. (1965). Changes in tone of limb veins during supine exercise. *J. Appl. Physiol.* 20:1.

Browse, N.L., Shepherd, J.T., and Donald, D.E. (1966). Differences in response of veins and resistance vessels in limbs to same stimulus. *Am. J. Physiol.*211:1241.

Burch, G.E., and Miller, G.C. (1969). The effects of warm, humid environment on patients with congestive heart failure. *Southern Med. J.* 62:816.

Ekblom, B., Greenleaf, C.J., Greenleaf, J.E., and Hermansen, L. (1970). Temperature regulation during exercise dehydration in man. *Acta Physiol. Scand.* 79:475.

Epstein, S.E., Beiser, G.D., Stampfer, M., and Braunwald, E. (1968). Role of the venous system in baroreceptor-mediated reflexes in man. *J. Clin. Invest.* 47:139.

Fortney, S.M., Nadel, E.R., Wenger, C.B., and Bove, J.R. (1981a). Effect of acute alterations of blood volume on circulatory performance in humans. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 50:292.

Fortney, S.M., Nadel, E.R., Wenger, C.B., and Bove, J.R. (1981b). Effect of blood volume on sweating rate and body fluids in exercising humans. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 51:1594.

Fox, R.H., and Edholm, O.G. (1963). Nervous control of the cutaneous circulation. *Brit. Med. Bull.* 19:110.

Gilbert, C.A., and Stevens, P.M. (1966). Forearm vascular responses to lower body negative pressure and orthostatis. *J. Appl. Physiol.* 21:1265.

Goetz, R.H. (1950). Effect of changes in posture on peripheral circulation, with special reference to skin temperature readings and the plethysmogram. *Circulation* 1:56.

Hainsworth, R., and Linden, R.J. (1979). Reflex control of vascular capacitance. In *Cardiovascular Physiology III* (A.C. Guyton and D B. Young, eds.) Vol. 18. (Int. Rev. Physiol. Ser.), p. 67, University Park Press, Baltimore.

Henry, J.P., and Gauer, O.H. (1950). The influence of temperature upon venous pressure in the foot. *J. Clin. Invest.* 29:855.

Johnson, J.M., Rowell, L.B., and Brengelmann, G.L. (1974a). Modification of the skin blood flow body-temperature relationship by upright exercise. *J. Appl. Physiol.* 37:880.

Johnson, J.M., Rowell, L.B., Niederberger, M., and Eisman, M.M. (1974b). Human splanchnic and forearm vasoconstrictor responses to reductions of right atrial and aortic pressures. *Circulation Res.* 34:515.

Merritt, F.L., and Weissler, A.M. (1959). Reflex venomotor alterations during exercise and hyperventilation. *Am. Heart J.* 58:382.

Montagna, W., Ellis, R.A., and Silver, A.F. (Eds.) (1962). *Advances in Biology of Skin. Vol. 3. Eccrine Sweat Glands and Eccrine Sweating.* MacMillan, New York.

Nadel, E.R., Bullard, R.W., and Stolwijk, J.A.J. (1971a). Importance of skin temperature in the regulation of sweating. *J. Appl. Physiol.* 31:80.

Nadel, E.R., Mitchell, J.W., Saltin, B., and Stolwijk, J.A.J. (1971b). Peripheral modifications to the central drive for sweating. *J. Appl. Physiol.* 31.828.

Nadel, E.R., Cafarelli, E., Roberts, M.F., and Wenger, C.B. (1979). Circulatory regulation during exercise in different ambient temperatures. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 46:430.

Nadel, E.R., Fortney, S.M., and Wenger, C.B. (1980). Effect of hydration state on circulatory and thermal regulations. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 49:715.

Newberry, P.D. (1970). Effect of ambient temperature on venous reactivity to hydrostatic stress. *J. Appl. Physiol.* 29:54.

Nielsen, B., and Nielsen, M. (1965). Influence of passive and active heating on the temperature regulation of man. *Acta Physiol. Scand.* 64:323.

Nielsen, B., Hansen, G., Jorgensen, S.O., and Nielsen, E. (1971). Thermoregulation in exercising man during dehydration and hyperhydration with water and saline. *Int. J. Biometeorol.* 15:195.

Roberts, M.F., and Wenger, C.B. (1979). Control of skin blood flow during exercise: thermal and nonthermal factors. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 46:780.

Roberts, M.F., and Wenger, C.B. (1980). Control of skin blood flow during exercise by thermal reflexes and baroreflexes. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 48:717.

Rowell, L.B. (1977). Competition between skin and muscle for blood flow during exercise. In *Problems with Temperature Regulation during Exercise.* (E.R. Nadel, ed.), p. 49, Academic Press, New York.

Rowell, L.B., Brengelmann, G.L., Detry, J.-M.R., and Wyss, C. (1971). Venomotor responses to rapid changes in skin temperature in exercising man. *J. Appl. Physiol.* 30:64.

Rowell, L.B., Wyss, C.R., and Brengelmann, G.L. (1973). Sustained human skin and muscle vasoconstriction with reduced baroreceptor activity. *J. Appl. Physiol.* 34:639.

Sagawa, K., Kumada, M., and Schramm, L.P. (1975). Nervous control of the circulation. In *Cardiovascular Physiology I* (A.C. Guyton and C.E. Jones, eds.) Vol. 1. (Int. Rev. Physiol. Ser.), p. 197, University Park Press, Baltimore.

Shepherd, J.T. (1966). Role of the veins in the circulation. *Circulation* 33:484.

Stolwijk, J.A.J., and Nadel, E.R. (1973). Thermoregulation during positive and negative work exercise. *Federation Proc.* 32:1607.

Tam, H.-S., Darling, R.C., Cheh, H.-Y., and Downey, J.A. (1978). Sweating response: a means of evaluating the set-point theory during exercise. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 45:451.

Thauer, R. (1965). Circulatory adjustments to climatic requirements. In *Handbook of Physiology*. (W.F. Hamilton and P. Dow, eds.) sect. 2, vol. 3, chapt. 55. Am. Physiol. Soc., Washington, D.C.

Webb-Peploe, M.M., and Shepherd, J.T. (1968a). Responses of dogs' cutaneous veins to local and central temperature changes. *Circulation Res.* 23:693.

Webb-Peploe, M.M., and Shepherd, J.T. (1968b). Responses of large hindlimb veins of the dog to sympathetic nerve stimulation. *Am. J. Physiol.* 215:299.

Wenger, C.B. (1972). Heat of evaporation of sweat: thermodynamic considerations. *J. Appl. Physiol.* 32:456.

Wenger, C.B., and Roberts, M.F. (1980). Control of forearm venous volume during exercise and body heating. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 48:114.

Wenger, C.B., Roberts, M.F., Stolwijk, J.A.J., and Nadel, E.R. (1975). Forearm blood flow during body temperature transients produced by leg exercise. *J. Appl. Physiol.* 38:58.

Zitnik, R.S., Ambrosioni, E., and Shepherd, J.T. (1971). Effect of temperature on cutaneous venomotor reflexes in man. *J. Appl. Physiol.* 31:507.

ACCLIMATION TO HEAT AND SUGGESTIONS, BY INFERENCE, FOR MICROWAVE RADIATION

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Can man "acclimate" to microwave radiation? Using the definitions that were adopted for the *Glossary of Terms for Thermal Physiology* (Bligh and Johnson, 1973) where acclimation is identified as an active induction of an altered physiologic state resulting from intentional exposure of individuals to the environment, it seems certain that over the next decades we will not answer the question; intentional exposures of human beings to microwave fields of moderate strength are difficult to justify. In contrast, there may already be some evidence that man can "acclimatize" or "habituate" to microwave radiation; we have all been exposed to very low intensities of microwave radiation (Janes, 1979), and increasingly so over the last fifty years. Finally, it is unlikely that any member of genus *Homo* will survive long enough to learn whether man can "adapt" to microwave radiation.

Let me define the terms used above by referring to one of the experiments described in Dr. Justesen's paper (Chapter 10). A portion of the cage occupied by some mice over a 15-min session each day for six days, was exposed to microwave radiation and the length of time spent in the radiated and in the "safe" areas was recorded. Some of the survivors appear to have spent increasing time in the "safe" area during this experiment, which was actually an "acclimation" study because the exposures were planned to determine what changes could be induced in the mice. If the animals were moving to get into a safe zone because they sensed and responded behaviorally, or exhibited some physiological regulation to a naturally-occurring microwave stimulus, that would be "acclimatization". As suggested above, for the

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last fifty years man has been subjected to microwaves and thus given an unplanned opportunity to acclimatize. If that movement was a conscious attempt to get out of the microwave field, that would be "habituation"; an adjustment like putting on or taking off clothing. Finally, if the five mice who survived could transmit to their descendants, by genetic change, information on what to do when microwave radiation was sensed, that would be "adaptation", at least as those terms were defined for the *Glossary*.

Man is basically a sub-tropical animal. He has a wider range of more effective adjustments to heat than to cold. Many of the adjustments to heat (vasomotor, metabolic, and perhaps behavioral changes) are inverses of those to cold. However, a major adjustment to heat is the regulation of body temperature through sweating; this has no inverse for the cold, although shivering can be considered the parallel in the cold. Also, many of the changes that occur with heat acclimatization parallel those induced by exercise; in fact, a man who is in good physical condition is well along the road to heat acclimatization. It seems possible that an individual who is heat acclimatized *may* have some facet of microwave resistance.

Our knowledge of the processes involved in heat acclimatization is relatively new. Before World War II, Balfour (1923) suggested that "we have to overcome heat"; it was not something the body could adjust to, man had to exert conscious effort. It was believed that Caucasians had to have at least a solar Topee, "actinic" underwear and perhaps a spine pad to defeat the damaging rays of the sun; they also should wear a flannel cholera belt, should not eat meat, and should return to a cold climate at least every two or three years, if they were going to stay functional. Caucasians in the Tropics were viewed as sojourners, not as men capable of acclimatization to heat (Castellani, 1938). World War II, however, clearly indicated that man has a variety of physical, physiological and psychological adjustments to heat. There are a number of mechanisms involved; these mechanisms do not all develop at the same time or at identical rates, but are integrated as part of a complex picture. In the literature you will find that man has many ways to "acclimatize" to heat; for example, by drugs (Collins, *et al.*, 1965), taking a hot bath (Brebner, *et al.*, 1961), wearing vapor barrier suits in the heat (Fox, *et al.*, 1961), or resting in high humidity heat (Henane and Bittel, 1975) one can "acclimatize" the sweat glands. Man can "acclimatize to heat" by restricting sodium in the diet; that can increase the aldosterone levels, but that is only another of the changes (Ganong, *et al.*, 1966). The array of the physical,

physiological, and some of the psychological adjustments involved in the complex changes that occur in humans in response to heat exposure has been catalogued by Bass, *et al.* (1955).

Some of the physical adjustments would seem to fall into the category of true genetic adaptations that must have taken millenia to establish. It is difficult to prove. You can believe in creationism as having altered man for the tropics. You can believe in Lamarckian theories of acquired characteristics (updated with a reverse transcriptase to induce some of the acquired phenotypic changes and make them genotypic). Or you can believe in Darwinian evolution, where there is over-population, the struggle for survival, and random variations, some of which are beneficial in the heat and lead to survival of the fittest, (i.e., those who have those genetic adaptations). Alternatively, you may prefer gradualism and genetic drift. No matter which theory you adopt to explain such changes, it seems clear that there are adaptations to the heat that follow Bergman's Rule or Allan's Rule; i.e., "the warmer the environment the more linear the body structure", and "the greater the number of protuberances". It may be hard to prove cause-effect, but it is a fact that Blacks, as a population, have longer and thinner extremities in relation to their torso than do Caucasians. This is clearly an advantage in losing heat, and it can be considered as a genetic adaptation to a hot environment. Man's hairlessness is probably also in that category. The late Dr. Russell Newman (1970) wrote a very interesting paper ascribing why man is such a hairless, sweaty animal to the subtropical environment of his ancestral stock. Thus, it appears that the human race has adapted to tolerate heat.

Can man genotypically adapt to microwaves? He certainly has not yet had enough time to do so. The discussion in Chapter 23 suggests some longevity-altering effects of microwave exposure, but by that time man is usually well past the time for transmission of such changes by inheritance. It has recently been recognized that individual cells can adapt to heat; a single exposure to 45 °C induces a resistance to subsequent 45 °C exposures (Henle and Dethlefsen, 1978). This resistance peaks at about 48 hrs and then decays until, after about 72 hrs, the heat resistance of the cell is back to normal. So there can be cellular changes to heat, perhaps in protein metabolism or membrane structure. Can something similar occur in response to microwave radiation?

Turning to the psychological adjustments (not adaptations), my favorite definition of heat acclimatization is

Huxley's "getting used to not getting used to it". Ellsworth Huntington in 1915 made a great point about the stimulating effects of cold and the debilitating effects of heat and residence in heat. As late as 1947 authors wrote about tropical neurasthenia, fatigueability, anorexia, nausea, a drop in systolic blood pressure, and a vague malaise (Kark, *et al.*, 1947). These symptoms seem vaguely similar to some of the reported effects of exposure to microwave radiation. Adjustment of clothing, as for cold, is also an effective behavioral regulation against heat (Newburgh, 1949). There are at least two ways to adjust clothing against heat, and if we think that everybody is going to respond in a single way to microwave radiation, we're probably in trouble. The Arab living in a hot-dry climate adopts a very heavy clothing system, to reject the high radiant heat load and create convection currents close to the body; natives in the tropics wear a sarong, or lightweight clothing. In terms of behavioral regulation, there is one to heat that was not recognized when the ArabianAmerican Oil Company first went into Bahrain to open up the oil fields. They hired as many of the native population as possible, assuming that they would be well-acclimatized through their natural exposure over the years to heat; however, they experienced far more heat illness than expected. Kipling had the answer: "mad dogs and Englishmen go out in the mid-day sun" and work, but that smart native never did, he avoided work in the heat. We have an array of behavioral regulations and psychological adjustments to heat (See Chapter 17); we may have some similar ones to microwave exposure. We have heard of people being able to sense a certain microwave level and move away. What the ultimate extent of such psychological adjustments will be in response to microwave radiation of various types is unknown. Some conjectures in this regard are offered in Chapter 11.

Physiologically, there is a clear spectrum of changes that occurs upon heat exposure; these are all included in the term "heat acclimatization" (Nadel, *et al.*, 1974). How to induce it? With moderate work, because we're mimicking exercise; minimum clothing is best because we can work longer in the heat without clothing; in the shade is best since we can work longer; luxus water intake is best since, by avoiding dehydration we can work longer in the heat. We can induce different levels of acclimation (or acclimatization); we can induce hyper-acclimatization by working people harder, in hotter conditions than they will usually experience; or induce hypo-acclimatization by working people less hard or in less hot conditions (Lind and Bass, 1963; Nadel, *et al.*, 1974; Strydom, *et al.*, 1971; Wyndham, *et al.*,

1976). Man doesn't acclimatize to an environment; man acclimatizes to an overall heat load (Goldman, 1978). This fact is also probably germane to any microwave adjustments, if the body has such capacities. The adjustments won't be simply to a heat load produced by microwaves or to a heat load produced by the environment; they will be to some combination of the two, probably acting synergistically. It takes anywhere from two to four hours a day of work in the heat (Lind and Bass, 1963), for 5 to 7 or 9 days (Strydom, *et al.*, 1971) depending on ones fitness level, to get heat acclimated to about 95% of ones genetic capacity for such changes; 21 days seem required to reach a full 100% plateau, but the various components involved in heat acclimation reach full acclimation status (for a given level of heat, work, clothing, etc.) at different rates (Wyndham, *et al.*, 1976). Retention is anywhere from 3 to 4 weeks in the absence of intervening heat exposure (Pandolf, *et al.*, 1977) but retention can be maintained by as little as a once a week, two to four hour exposure to work in the heat. The intensity and duration of microwave exposure required to induce "microwave acclimation", if such changes are possible, are totally unexplored to date.

What physiological changes occur with heat acclimation (or acclimatization)? First there is a slight drop in metabolic heat production. This, of course, also occurs with "work acclimatization" (i.e., exercise) in association with a loss of body weight. In the heat, the drop in metabolic heat production is probably accounted for in part by a drop in body temperature for a given level of work in the heat From our modeling projections (Givoni and Goldman, 1973) there is a very marked drop in rectal temperature during work in the heat, amounting as a maximum to about 1.7 °C following full acclimation; i.e., up to 21 days of daily exposure for two to four hours a day to a given level of work, heat, clothing, etc. There is also a drop in skin temperature. There is a lower heart rate, associated with acclimatization; by about 40 b/min if we use the maximum suggested from our modeling projections (Givoni and Goldman, 1973). There is sometimes quite a change in sweat production depending on the initial state of the individual; that is a major manifestation, although a large part of the change is facilitated by the level of physical fitness attained from previous exercise. The "set-point" for sweating is also changed; one begins to sweat at a lower skin temperature, and produces more sweat per gland at a given internal body temperature level (Nadel,*et al.*, 1974). The gain change is very similar to the gain change induced by exercise itself. Nadel has suggested that, normally, we may

try to eliminate about 42% of our working heat production by sweating. In hot-dry environments, man may only have to increase his sweat production by about 15% as part of the acclimatization phenomenon to meet the demands for heat elimination. In a hot-wet environment man can increase sweat production by anywhere from 60 to as much as 100%, but the increase may not be beneficial. Unevaporated sweat is worse than useless, since excess sweating can lead to dehydration (Goldman, 1978). The 1.7 °C maximum decrease in rectal temperature with acclimatization, which occurs under the optimum set of conditions where acclimatization is beneficial, can drop to almost nothing in a hot-wet environment where one can not evaporate the sweat (Wyndham, *et al.*, 1976). For example, if you encapsulate a man in a vapor barrier suit, he is probably better off not being acclimatized; he will not dehydrate so rapidly and he is not able to get much benefit from any extra sweat production. There is usually an increase in blood volume, particularly plasma volume, with both exercise and heat acclimation; there is also a decrease in the sodium content of sweat. All these changes occur in parallel, but at different rates, probably with a substantial individual variability derived from both differences in genetic factors (morphology, heart size, etc.) and previous environmental-work history (Nadel, *et al.*, 1974; Pandolf, *et al.*, 1977; Strydom, *et al.*, 1971; Wyndham, *et al.*, 1976). The possible extent of any human potential for physiological acclimation to microwave radiation is unknown. Whether any of these physiological changes that occur in response to heat exposure would also be involved in microwave acclimation is speculative, but they should be among the first changes to be investigated.

In summary, human exposures to heat induce a variety of alterations: evolutionary changes over millenia of exposure; psychological/behavioral regulations which are adopted rapidly on initial exposure; and physiological acclimation responses induced at various rates, to varied degrees, over intermittent or continuous exposures of from 2 or 3 days to as many weeks. Animal models, while sometimes helpful in studying the changes that occur on exposure to heat can be confusing, or even misleading; the usual laboratory animals, such as the rat, mouse, dog, etc. are probably much less like man in their responses than the pig is. The extent to which parallels can be drawn from studies of human (or animal) exposures to heat and applied to the problems of adjustment to microwave exposures is unknown, but such studies are suggested as a good place to gain insight.

REFERENCES

Balfour, A. (1923). Sojourners in the tropics. *Lancet* 1:1329.

Bass, D.E., Kleeman, C.E., Quinn, M., Henschel, A. and Hegnauer, A.H. (1955). Mechanisms of acclimatization to heat. *Medicine* 34:323.

Bligh, J. and Johnson, K.G. (1973). Glossary of terms for thermal physiology. *J. Appl. Physiology* 35:941.

Brebner, D.F., Clifford, J.M., Kerslake, D. McK., Nelms, J.D. and Waddell, J.L. (1961). Rapid acclimatization to heat in man. *FPRC Memo Report 177*, R.A.F.Inst. Aviat. Med., Farnborough, Hants, 14 pp.

Castellani, A. (1938). *Climate and Acclimatization*. J. Bale, Sons and Curnow, London.

Collins, K.J., Crockford, G.W. and Weiner, J.S. (1965). Sweat gland training by drugs and thermal stress. *Arch. Environ. Health* 11:407.

Fox, R.H., Goldsmith, R., Kidd, D.J., and Lewis, H.E. (1961). Acclimatization of the sweating mechanism in man. *J. Physiol. (Lond.)* 157:56P.

Ganong, W.F., Biglier, E.G. and Mulrow, P.J. (1966). Mechanisms regulating adrenocortical secretions of aldosterone and glucocorticoids. *Recent Prog. Hormone Res.* 22:381.

Givoni, B. and Goldman, R.F. (1973). Predicting effects of heat acclimatization on heart rate and rectal temperature. *J. Appl. Physiol.* 35:875.

Goldman, R.F. (1978). Prediction of human heat tolerance. In *Environmental Stress* (L.J. Folinsbee, ed.) p. 53. Academic Press, N.Y.

Henane, R. and Bittel, J. (1975). Changes of thermal balance induced by passive heating in resting man. *J. Appl. Physiol.* 38:294.

Henle, K.J. and Dethlefsen, L.A. (1978). Heat fractionation and thermotolerance: a review. *Cancer Res.* 38:1843.

Huntington, E. (1915). *Civilization and Climate*. Yale Univ. Press, New Haven.

Kark, R.M., Aiton, H.F., Pease, E.D., Bean, W.B., Henderson, C.R., Johnson, R.E., and Richardson, L.M. (1947). Tropical deterioration and nutrition. *Medicine* 26:1.

Lind, A.R. and Bass, D.E. (1963). Optimal exposure time for development of acclimatization to heat. *Fed. Proc.* 22:704.

Nadel, E.R., Pandolf, K.B., Roberts, M.F. and Stolwijk, J.A.J. (1974). Mechanisms of thermal acclimation to heat. *J. Appl. Physiol.* 37:515.

Newburg, L.H. (1949). *The Physiology of Heat Regulation and the Science of Clothing*. W.B. Saunders, Philadelphia.

Newman, R. (1970). Why man is such a sweaty and thirsty naked animal. *Human Biology* 42:12.

Pandolf, K.B., Burse, R.L. and Goldman, R.F. (1977). Role of physical fitness in heat acclimatization, decay and reinduction. *Ergonomics* 20:399.

Strydom, N.B., Benade, A.J.S., Swanepoel, H.J.S. and Heyns, A.J.A. (1971). A comparison of the effectiveness of five-, seven-, eight-, and nine day acclimatization procedures. *J. So. African Inst. Mining and Metall*. Nov: 105.

Wyndham, C.H., Rogers, G.G., Senay, L.C., and Mitchell, D. (1976). Acclimatization in a hot, humid environment: cardiovascular adjustments. *J. Appl. Physiol*. 40:779.

THERMOREGULATION IN INTENSE MICROWAVE FIELDS

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INTRODUCTION

When an individual experiences a thermal burden, physiological and behavioral maneuvers will be initiated to increase heat loss, unless the set point for thermoregulation has been shifted (Hensel, 1981). If the thermal load can be dissipated by the host's physiological and behavioral responses, an increase in deep body temperature may not be detectable. Alternatively, if the host cannot completely compensate for heat gain, a temperature rise ensues. Thus, thermal stress may or may not be accompanied by detectable changes in core temperature. Although the colonic temperature reflects deep body (core) temperature under steady state conditions, it is slow to indicate changes in body temperature during thermal transients and does not indicate the quality of effective thermoregulatory responses (Nadel and Horvath, 1970).

Colonic temperature varies as a function of heat load and, within limits, is essentially independent of ambient air temperatures (Stolwijk, *et al.*, 1968). The "set point" temperature for mammals is maintained by physiological and behavioral processes that balance heat production or gain, and heat loss (Hammel, *et al.*, 1963; Kluger, 1979; Michaelson, 1974).

Integrative structures which presumably compare sensed temperature to "normal" temperature (the *set point* or *reference temperature*), determine whether existing body

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temperature is too high or too low, and activate the appropriate responses. Incidental changes in central temperature set in motion a sequence of events which eventually affect (or feed back upon) central temperature. A spontaneous deviation of central temperature in one direction sets into play mechanisms which tend to displace that temperature in the opposite (negative) direction; a rise in central temperature activates heat loss mechanisms, while a fall in central temperature activates heat conservation and heat production mechanisms. Clearly, homeothermy is the result of this negative feedback (Brengelmann, 1973). For a detailed discussion of relevant mechanisms, see Chapter 8.

Specific organ or tissue systems may "function" at significantly different rates if local thermal gradients are altered. Relatively large changes in circulation can be provoked by small deviations from neutral temperature--the temperature at which oxygen consumption in the resting state is at a minimum (Thauer 1965). Such circulatory changes are seen in exercise and work-related temperature increase (Saltin, 1970; Shepherd and Webb-Peploe, 1970). Neurophysiological responses to raised local tissue temperature may be elicited by direct effects on nervous tissue functions and/or reflex effects operating through sensors or transducers of these thermal changes and then through effector mechanisms in the central nervous system (Adey, 1981).

MICROWAVE-INDUCED THERMOREGULATION

Exposure of animals to microwave/radiofrequency (MW/RF) energy leads to body temperature elevation when the rate of energy absorption exceeds the rate of energy dissipation. Whether the resulting temperature elevation is diffuse or confined to specific anatomical sites, depends on: a) the electromagnetic field characteristics and distributions within the body, and b) the passive and active thermoregulatory mechanisms available to the individual. Most of the documented reactions to MW/RF energy absorption are explained by thermal energy conversion, almost exclusively as enthalpic energy phenomena.

Theoretical calculations of the rate of heating in model spheres and ellipsoids exposed to plane wave microwave fields have been carried out by Kritikos and Schwan (1972, 1975, 1976, 1979), Guy (1971), Johnson and Guy (1972), Shapiro, *et al.* (1971), and Weil (1975). Resonant absorption within the cranium may result in the focusing of energy and the production of electromagnetic "hot spots" in the

brain (cf. Chapters 1 and 5). Thus some observed effects may relate to higher absorption in such regions as the hypothalamus than in other loci.

To appreciate the thermoregulatory aspects of exposure to radiofrequency energies it is essential to integrate our understanding of the spatial distribution of the absorbed energy and the inherent thermoregulatory processes in the animal. The nonuniform, largely unpredictable, distribution of absorbed energy may result in temperature increases and rates of heating in local "hot spots" that could result in unique biological effects. It should be recognized, however, that the mammalian body normally is not a uniform incubator but does contain significant temperature gradients (Hardy, 1968) as well as diurnal temperature excursions (Aschoff, 1970; Hammel, *et al.*, 1963). Therefore, the uniqueness of the inhomogeneity of microwave-induced temperature distributions may be more apparent than real.

EXPERIMENTAL INVESTIGATION OF THERMOREGULATION IN INTENSE MICROWAVE FIELDS

Because of its large size and excellent thermoregulatory capacity we selected the dog as an animal model to assess the thermal characteristics and physiological consequences of microwave energy absorption. Thermoregulation was characterized in dogs exposed (whole-body) to 2880 MHz pulsed microwaves (Michaelson, 1971, 1974, 1977; Michaelson, *et al.*, 1961, 1967). The dogs were of mixed breed, 1-5 years old and weighed between 9 and 18 kg.

During horizontal microwave exposure, the dog was confined in a Plexiglas cage situated inside an anechoic chamber 7' x 7' x 15', lined with commercial microwave absorbing material. Generally, ambient conditions were 22 °C with 30 percent relative humidity. The source of microwaves was an AN/MPS-15 radar set operating at a frequency of 2880 MHz pulsed (360 pulses/sec, 2-3 microsec. pulse width with average power in excess of 2000 watts). The microwave horn antenna was situated six feet from the animal. The animals were exposed to 100 mW/cm^2 (est. specific absorption rate or SAR = 3.7 W/kg) or 165 mW/cm^2 (est. SAR = 6.1 W/kg) for various durations. Thermoregulatory responses were also measured while the animals were exposed to 100 mW/cm^2 or 165 mW/cm^2 at ambient temperatures (Ta) of 40.5 °C, or 11 °C in addition to 22 °C.

An electronic thermometer with a thermistor probe which

was shielded with Plexiglas and fixed in the rectum was used to monitor colonic temperature during exposure. The animal was placed in the Plexiglas cage for a 15-min. period prior to microwave exposure. When the colonic temperature stabilized, microwave exposure was begun. During exposure, the colonic temperature was read at 5-min. intervals.

In a separate series of experiments, dogs were exposed at a field intensity of 165 mW/cm^2 until colonic temperature reached 41.5 °C, at which time the microwave exposure was interrupted for a period of 20 minutes duration to allow cooling of the body. After this period, the exposure was resumed for an additional 20 minutes, followed by another 20-min. cooling period. Colonic temperature was monitored continuously. Hematocrit was determined at each heating and cooling period. Body weight was recorded initially and again at the conclusion of the exposure.

In another experiment, dogs were exposed at 165 mW/cm^2 until colonic temperature reached 41.5 °C, at which time, access to water was permitted. Two hundred to three hundred ml aliquots of water, at approximately 10 °C were delivered through tygon tubing into a Plexiglas cup positioned in a corner of the cage. At all times, approximately 100 ml of water were left in the cup. To improve palatability, as the water became warm, it was siphoned off and replaced with cool water.

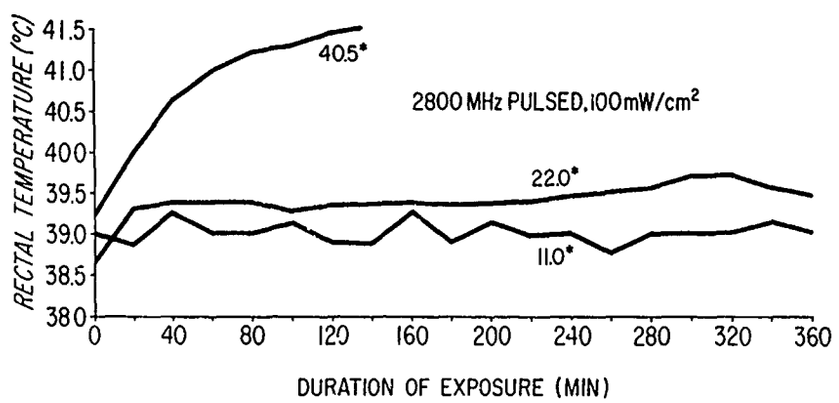

Figure 1. The change in rectal temperature (°C) exhibited by dogs exposed to 2800 MHz pulsed microwaves at various environmental temperatures 40.5, 22.0, and 11.0 °C as a function of exposure duration. Average power density was constant at 100 mW/cm^2.

EXPERIMENTAL RESULTS

In the absence of microwave exposure, colonic temperature decreased slightly over a 6-hour period when the ambient temperature (T_a) was 11 °C. At T_a = 22 °C, the body temperature variation over a 6-hour period was minimal. Dogs at T_a = 40.5 °C had minimal fluctuations of body temperature.

Microwaves - 100 mW/cm² (Estimated SAR = 3.7 W/kg)

Dogs at T_a = 11 °C or 22 °C tolerated 100 mW/cm² microwaves for 360 minutes as shown in Figure 1. At T_a = 11 °C, the colonic temperature response was negligible. At T_a = 22 °C, there was a moderate elevation of colonic temperature within 30 minutes after commencement of exposure. At T_a = 40.5 °C, a colonic temperature of 41 °C was reached in 60-135 minutes.

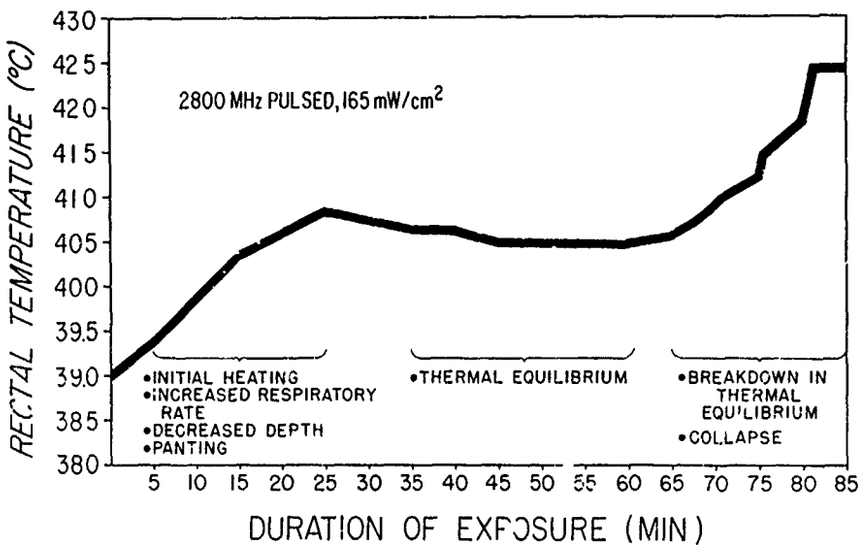

Figure 2. The triphasic response of the rectal temperature of dogs exposed to 2800 MHz pulsed microwaves at 165 mW/cm². Initial heating is followed by a period of thermal equilibrium and finally, if the exposure is continued, by thermoregulatory collapse.

Microwaves - 165 mW/cm² (Estimated SAR = 6.1 W/kg)

Whole-body exposure of dogs to 2880 MHz pulsed microwaves at 165 mW/cm² (T_a = 22 °C for 2-3 hours resulted in thermoregulatory responses characterized by three phases. These phases are illustrated in Figure 2 as : (1) initial temperature rise, (2) period of thermal equilibrium, and (3) thermoregulatory failure (Michaelson, *et al.*, 1961, 1967, 1974). In phase 1, (initial thermal response), colonic temperature increased by 2 °C during the half hour after the onset of exposure. In phase 2, (period of thermal equilibrium), colonic temperature stabilized for 1 hour, during which the temperature fluctuated between 40.6 and 41.1 °C. In phase 3, (period of thermal breakdown), the temperature rose above 41.1 °C, continued increasing rapidly until a critical temperature of 41.7 °C, or greater, was reached. If exposure was not stopped, death ensued.

The effect of environmental temperature on the response of dogs to 165 mW/cm² microwaves is shown in Figure 3. Exposures lasting 360 minutes were possible when ambient temperature was 11 °C. During such exposures, there was a colonic temperature rise of 1.4 °C within two hours after

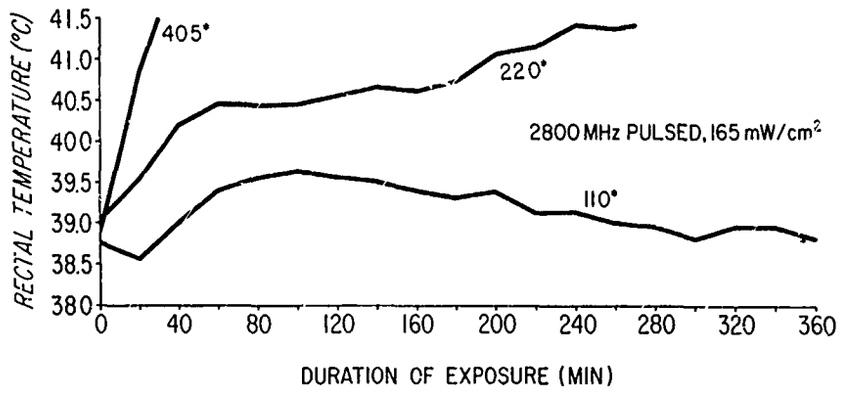

Figure 3. The change in rectal temperature (°C) exhibited by dogs exposed to 2800 MHz pulsed microwaves at various environmental temperatures 40.5, 22.0, and 11.0 °C as a function of exposure duration. Average power density was constant at 165 mW/cm².

the exposure began, but effective thermal compensation must have negated this response so that at the end of six hours of exposure, the colonic temperature change differed little from the initial value.

Thermal equilibrium was transient during microwave

exposure at 165 mW/cm^2 at T_a = 22 °C. The duration of exposure was limited to 180-300 minutes since continuation of exposure after the animal attained a colonic temperature of 41.5 °C could result in death. At a 40.5 °C ambient temperature, the increase in colonic temperature was rapid with no thermal equilibrium period. The critical level of colonic temperature (> 41.5 °C) was reached in 30-60 minutes at this ambient temperature.

We found that recovery of normal (neutral) body temperature was exponential. The pre-exposure level of colonic temperature was reached within an hour. Dogs exposed at 165 mW/cm^2 (T_a = 22 °C) showed a loss of body mass of 2.0 percent/hr. At 100 mW/cm^2, loss of body mass was 1.25 percent/hr. Reduction of body mass, no doubt a reflection of insensible water loss, was constant and linear with the duration of exposure to the microwave field. We also found that hematocrit alteration was biphasic. Shortly after exposure to 165 mW/cm^2 commenced, hemodilution occurred; after 1-1½ hours of exposure, hemoconcentration was evident. Hemodilution was again noted at approximately 2 hours followed by hemoconcentration. Apparently, the dog loses the ability to hemodilute when thermal equilibrium starts to break down. The animal is unable to maintain a normal body temperature or normally-stable hematocrit after a 5 percent loss of body mass. The change in body mass and change in hematocrit were correlated with the ambient temperature and the intensity of the microwave field. The highest field strength and T_a produced the maximum response. Hematocrit changes suggested varying degrees of hemodilution at T_a = 11 °C and T_a = 22 °C in the absence of microwaves. At T_a = 40.5 °C, hemoconcentration occurred. Hemodilution was observed in dogs that received 100 mW/cm^2 microwaves at T_a = 11 °C and 22 °C. At T_a = 40.5 °C there was apparent hemoconcentration. When microwaves were increased to 165 mW/cm^2, hemodilution occurred at T_a = 11 °C; whereas at T_a = 22 °C and 40.5 °C, hemoconcentration was evident.

Since these animals did not defecate or urinate while the microwave exposures were being conducted, loss of body mass was considered due largely to evaporative water loss through the oropharyngeal region (panting). The contribution of the differences between respired CO_2 and O_2 was negligible. Conversion of the loss of body mass to evaporative water loss under the various conditions of exposure allowed a comparison of the thermal burden imposed on the animal by microwaves at different ambient temperatures. Upon exposure to 100 mW/cm^2 at T_a = 22 °C, there was a three-fold increase in evaporative water loss and a 1.4 °C elevation in colonic temperature. When the field intensity was increased to

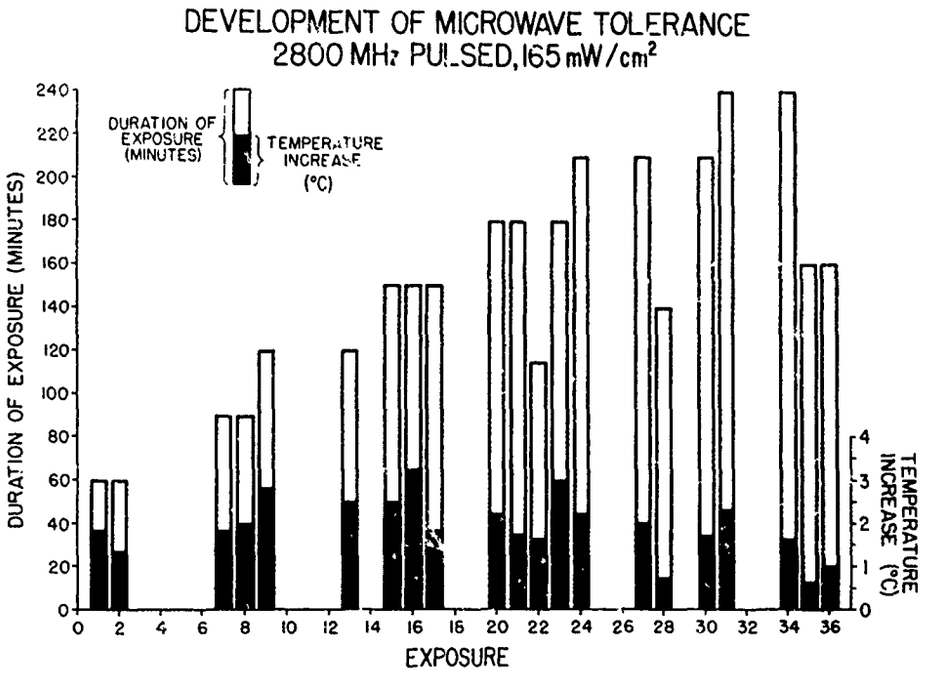

Figure 4. The development of tolerance to 2800 MHz pulsed microwaves, 165 mW/cm^2, as the number of microwave exposures increased. Solid bars indicate the increase of rectal temperature (right ordinate) at an exposure duration indicated by the open bars (left ordinate).

165 mW/cm^2, evaporative water loss was five times that which occurred in the absence of microwaves. Colonic temperature was increased 3 °C. The thermal burden from 100 mW/cm^2 exposures at T_a = 40.5 °C, or 165 mW/cm^2 at T_a = 22 °C or 40.5 °C incapacitated the animals and resulted in thermoregulatory failure.

When dogs were exposed on successive days, it became apparent that exposure duration could be prolonged from 1 to 4 hours without reaching thermal breakdown. This phenomenon is illustrated in Figure 4. Such prolonged exposures without significant temperature increase resembled accommodation, adaptation, or acclimatization (cf. Chapter 14).

The response to hydration, starting when colonic temperature reached 41 °C is shown in Figure 5. Hydration permitted an extension of the duration of microwave exposure by suppression of an increase in the body temperature. Maintenance of a normal body mass resulted from the consumption of water during the experiment as contrasted with a reduction in body mass among non-hydrated dogs. When the microwave exposures were interrupted for 20 minutes at 20 minute

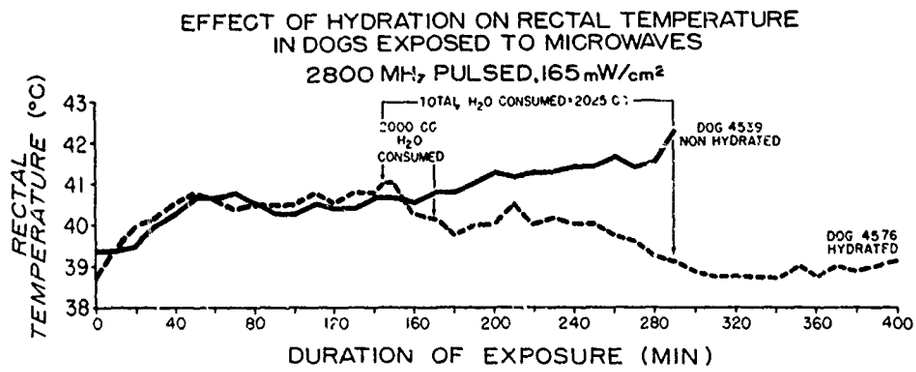

Figure 5. Effect of hydration on the rectal temperature of dogs exposed to 2800 MHz pulsed microwaves at an average power density of 165 mW/cm^2.

intervals, for each 0.5 °C rise in temperature, the hematocrit increased 2.5 percent. During the cooling phase, for each 0.5 °C decrease in colonic temperature, there was a 2.2 percent decrease in hematocrit, suggesting progressive hemodilution.

DISCUSSION

These studies clearly indicate the thermoregulatory capacity of the dog to withstand exposure to high microwave fields at specific absorption rates (SAR) of 3.7 and 6.1 W/kg. It appears that adequate thermoregulation takes place at an SAR of 3.7 W/kg but only transiently at 6.1 W/kg. These values, compared with the standardized resting metabolic rate of 3.29 $W/kg^{(0.75)}$, provide a basis for assessing the relationship of the thermal burden and thermoregulatory disruption by microwaves in the dog. To elucidate the thermal potential of microwave exposure, it was helpful to conduct these exposures at various ambient temperatures in which the normal body temperature remained stable, thus permitting comparison of heat production and dissipation with or without microwaves. The "zone of thermal neutrality" or thermoneutral zone of vasomotor activity, 22-26.5 °C, where body temperature is regulated by changes in vasomotor tonus, fulfilled this requirement.

Other ambient temperatures selected for these studies produce different autonomic responses: (a) increased metabolic heat production with no evaporative water loss at T_a = 11-12.5 °C, (b) increased heat dissipation with some increase in metabolism to be expected, mainly by evaporative water loss to counter-balance an ambient temperature of 40.5 °C.

An early manifestation of acute heat stress for the dog in these experiments was hemodilution, which occurred during the first 30 minutes of exposure and before body temperature increased. Upon prolonged exposure, hemodilution was reversed as a result of dehydration and hemoconcentration occurred. Early hemodilution is no doubt due to an influx of extravascular fluid as a result of the peripheral vasodilation which had taken place.

Exposure of dogs to 165 mW/cm^2 (est. SAR = 6.1 W/kg) resulted in a loss of body mass which was related to the duration of exposure. Exposure at this power density until 41-41.5 °C colonic temperature was reached, resulted in a loss of body mass equivalent to 10 percent of the extravascular fluid. In general, among hydrated dogs, 12 percent (6-20 percent) or less of ingested water was retained and body weight increased by approximately 3 percent.

The influence of environmental temperature on the thermoregulatory response to microwaves can be seen in terms of evaporative water loss at the various environmental temperatures and microwave energy levels utilized. Dogs in ambient temperatures of 11-40.5 °C can maintain body temperature within physiologic limits. The imposition of microwave energy results in an increased thermal burden when the animal is unable to cope with the environmental thermal burden; colonic temperature increases in an uncontrolled manner. This of course is influenced by the prevailing environmental temperature.

Respiratory water loss in the dog paralleled the level of microwave energy to which the animal was exposed. At 165 mW/cm^2 (SAR = 6.1 W/kg), approximately 1.4 times more water was lost than at 100 mW/cm^2 (SAR = 3.7 W/kg), and 2.5 times more than at T_a = 40.5 °C. Upon hydration during exposure to 165 mW/cm^2, the respiratory excretion of water was 1.7 times greater than that seen in the non-hydrated dog similarly exposed.

Exposure of various species of animals to whole-body microwaves, at levels of 100 mW/cm^2 or more, is characterized by a temperature rise, which is a function of the absorbed energy, the thermoregulatory processes involved, and active adaptation of the animal. The end result is either a reversible or irreversible change in body

temperature, depending on the conditions of exposure and the physiologic state of the animal. The thermal response induced by whole-body, high-level (> 100 mW/cm^2) microwave exposure in an animal such as the dog is characterized by an initial colonic temperature increase of 1-2 °C above normal followed by a period of thermal equilibrium and, if exposure is not terminated, a period of thermal breakdown. In regions of the body in which relatively little blood circulates, the temperature may rise more rapidly than in more vascular parts of the body since there is little means for the interchange of heat. Consequently, tissue damage is more likely to occur in those areas where proportionately, a greater rise in temperature can occur.

The pattern of temperature response in the dog, as a consequence of whole-body exposure to microwave energy, follows that of normal physiologic regulation. When the aggregate heat loss balances heat gain, regulation proceeds. If, on the other hand, the aggregate heating exceeds the aggregate loss, heat exchange can become positive and the body temperature may rise to the lethal temperature for the animal.

These studies clearly indicate that when a homeotherm is exposed to a thermal stress, whether it be elevated ambient temperature or exposure to microwaves, if the heat gain from the environment plus metabolic heat exceeds the animal's capacity for heat dissipation, there will be an increase in body temperature. Since the metabolic rate of a homeotherm is influenced by ambient temperature, the response to microwaves is also dependent on environmental temperature.

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REFERENCES

Adey, W. R. (1981). Tissue interactions with nonionizing electromagnetic fields. *Physiol. Rev.* 61:435.

Aschoff, J. (1970). Circadian rhythm of activity and of body temperature. In *Physiological and Behavioral*

Temperature Regulation (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 905, C.C. Thomas, Springfield, Illinois.

Brengelmann, G. (1973). Temperature regulation. Chapter 5. In *Physiology and Biophysics* (T.C. Ruch and H.D. Patton, eds.), p. 105, Saunders, Philadelphia, PA.

Guy, A.W. (1971). Electromagnetic fields and relative heating patterns due to a rectangular aperture source in direct contact with bilayered biological tissue. *IEEE Trans. Microwave Theory Tech.* 19:214.

Hammel, H.T., Jackson, D.C., Stolwijk, J.A.J., Hardy, J.D., and Strømme, S.B. (1963). Temperature regulation by hypothalamic proportional control with an adjustable set point. *J. Appl. Physiol.* 18:1146.

Hardy, J.D. (1968). Thermal comfort: skin temperature and physiological thermoregulation. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 856, C.C. Thomas, Springfield, Illinois.

Hensel, H. (1981). *Thermoreception and Temperature Regulation*. Academic Press, New York.

Johnson, C.C. and Guy, A.W. (1972). Nonionizing electromagnetic wave effects in biological materials and systems. *Proc. IEEE* 60:692.

Kluger, M.J. (1979). *Fever: Its Biology, Evolution, and Function*. Princeton University Press: Princeton, New Jersey.

Kritikos, H.N. and Schwan, H.P. (1972). Hot spots generated in conducting spheres by electromagnetic waves and biological implications. *IEEE Trans. Biomed. Eng.* 19:53.

Kritikos, H.N. and Schwan, H.P. (1975). The distribution of heating potential inside lossy spheres. *IEEE Trans. Biomed. Eng.* 22:457.

Kritikos, H.N. and Schwan, H.P. (1976). Formation of hot spots in multilayer spheres. *IEEE Trans. Biomed. Eng.* 23:168.

Kritikos, H.N. and Schwan, H.P. (1979). Potential temperature rise induced by electromagnetic field in brain tissues. *IEEE Trans. Biomed. Eng.* 26:29.

Michaelson, S.M. (1974). Thermal effects of single and repeated exposures to microwaves - a review. In *Biologic Effects and Health Hazards of Microwave Radiation* (P. Czerski, *et al.*, eds.), p. 1, Polish Medical Publishers, Warsaw.

Michaelson, S.M. (1977). Central nervous system responses to microwave-induced heating. *Neurosci. Res. Progr. Bull.*, 15:98.

Michaelson, S.M., Thomson, R.A.E., and Howland, J.W. (1961). Physiologic aspects of microwave irradiation of mammals. *Am. J. Physiol.* 201:351.

Michaelson, S.M., Thomson, R.A.E., and Howland, J.W. (1967). *Biologic Effects of Microwave Exposure*. RADC: ASTIA Doc No AD 824-242, Griffis AFB, also United States Senate, Ninetieth Congress, second session on S 2067, S 3211 and HR 10790, 1968: Radiation Control for Health and Safety Act of 1967. p. 1443.

Nadel, E.R. and Horvath, S.M. (1970). Comparison of tympanic membrane and deep body temperatures in man. *Life Sci.* 9:869.

Saltin, B. (1970). Circulatory adjustments and body temperature regulation during exercise. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 316, C.C. Thomas, Springfield, Illinois.

Shapiro, A.R., Lutomirski, R.F., and Yura, H.T. (1971). Induced fields and heating within a cranial structure irradiated by an electromagnetic plane wave. *IEEE Trans. Microwave Theory Tech.* 19:187.

Shepherd, J.T. and Webb-Peploe, M.M. (1970). Cardiac output and blood flow distribution during work in heat. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 237, C.C. Thomas, Springfield, Illinois.

Stolwijk, J.A.J., Saltin, B., and Gagge, A.P. (1968). Physiological factors associated with sweating during exercise. *J. Aerospace Med.* 39:1101.

Thauer, R. (1965). Circulatory adjustments to climatic requirements. In *Handbook of Physiology* (W.F. Hamilton, ed.), p. 1921, Waverly Press, Baltimore, Maryland

Weil, C.M. (1975). Absorption characteristics of multilayered sphere models exposed to UHF/microwave radiation. *IEEE Trans. Biomed. Eng.* BME-22:468.

EVALUATION OF THERMOREGULATORY RESPONSE TO MICROWAVE POWER DEPOSITION

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INTRODUCTION

All animals exhibit a considerable response to changes in body temperature, and are characterized by a preferred level of body temperature at which their functioning and well-being is optimal. In cold-blooded (poikilothermic) animals these preferred temperatures are achieved by a choice of their immediate micro-climate through voluntary behavioral preferences. Cold-blooded animals tolerate a relatively wide range of body temperatures. In warm-blooded (homeothermic) animals an involuntary physiological system is added to the behavioral system of cold-blooded animals. Although the physiological thermoregulation maintains a much narrower range of body temperature, even homeothermic animals rely to a considerable extent on behavioral thermoregulation. In the absence of effective behavioral thermoregulation, which includes the thermostatic control of the immediate micro-environment, the body temperature in homeotherms will be regulated by physiological mechanisms which control heat production, the distribution of heat in the body, and the avenues and the rate of heat loss from the body to the environment. The mechanisms the human body uses to maintain a nearly-constant body temperature are well-described and are understood in a quantitative sense as well. Since the thermal characteristics of the human body are reasonably well known it is possible to develop mathematical simulation models of physiological thermoregulation

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in reasonable detail and validate them in a generally acceptable manner (Stolwijk and Hardy, 1966; Stolwijk and Hardy, 1977). A number of such models have been developed for a variety of purposes, and in some cases such models have been adapted for purposes other than the original one for which it was formulated (see e.g. Montgomery, 1972). Because heat production and body heat loss can occur and be described in a wide variety of specific circumstances there is a special usefulness in evaluating such specific conditions through simulation. The deposition of electromagnetic energy as heat in all of the human body, or in specific parts of it is one of the specific conditions which lend themselves uniquely to a preliminary evaluation through simulation modeling.

CHARACTERISTICS OF MODELS OF HUMAN THERMOREGULATION

As in any simulation model, models of human thermoregulation are based on simplifications of the actual system. The simplifications are applied to less relevant parts of the system which are not considered critical for the understanding or the prediction of the responses which are to be modeled.

For purposes of understanding the simplifications, it is useful to recognize the separation of the system into two major components: the regulated or passive system, and the regulatory or control system. In all models both of these systems are simplified. The passive system usually could be described in more detail than it actually is, and the choice of the degree of detail is up to the user or formulator. The controlling system is incorporated with a degree of simplification which is determined by our lack of more precise knowledge about the details of the regulatory system.

The controlling or the regulatory part of the model to be discussed here consists of the sensory structures which sense body temperatures and their response characteristics, the central neural integration, the neural effector pathways and the effector mechanisms themselves such as shivering muscles, secreting sweat glands, and the tone of peripheral blood vessels in the skin and elsewhere which control the convective heat transfer between different organs and structures of the body.

The controlled system consists of the simplified representation of the thermal characteristics of all the body tissues including metabolic heat production, heat

capacitance, local temperature, heat transfer by conduction and convection inside the body and via evaporation, conduction, convection and radiation between the skin and the external environment.

Normally the events which are to be evaluated by models of human thermoregulation are heat production by exercise, and modification of normal heat loss patterns by unusual environmental temperatures, water vapor pressure, clothing characteristics, etc.

The Controlled System

In the model to be discussed the human body is represented by six cylindrical elements, each consisting of four concentric cylinders, and a central blood compartment. The exact details of the specification and validation of the controlled system have been presented elsewhere (Stolwijk and Hardy, 1977) and the reader is referred to the more complete description for such details. The concentric cylinders in each element are made to correspond to the mass of skin, subcutaneous fat, muscle, and core tissues of the head, trunk, arms, hands, legs and feet. Together with a central blood compartment, which exchanges blood and heat with each of the tissue compartments, there are then a total of 25 tissue compartments. Each of these compartments is characterized by a heat capacitance, a basal and exercise-related heat production rate, a blood flow rate indicating its convective connection to the central blood compartment, a heat conductance to adjacent compartments, and for the skin, evaporative, radiant, convective, and conductive heat exchange with the environment.

The simulation model provides for each of these 25 compartments the temperature based on the initial condition and the integrated flows of heat into and out of the compartment.

The Controlling System

The controlling system receives from the controlled system the instantaneous temperature of each of the 25 compartments. These temperatures are compared with reference or set point temperatures and summed with a relative weighting based on physiological measurements. In the current version of the thermoregulatory model, as described in more detail by Stolwijk and Hardy (1977), the thermal sensors feeding into the integrating structure are located in

the skin according to an experimentally determined distribution, and in the core of the head element which represents the temperature of the hypothalamus. Although other organs and structures also contain thermosensitive nervous structures, it is not known whether and how these contribute to human thermoregulation. The skin receptor signals and the head core signals are integrated with a relative weight of about 0.1 for the skin and 0.9 for the core, and converted into efferent commands to the sweat glands, to the peripheral muscles or to the peripheral blood vessels controlling skin blood flow. These effector actions will then produce changes in heat production, heat loss and heat transfer which will counteract the effects of internal or external loads which would otherwise change body temperatures away from the preferred and regulated levels.

APPLICATION OF SIMULATION MODELS TO SPECIAL CASES OF THERMAL STRESS

It is natural and appropriate to use thermoregulatory simulation models for the evaluation of special conditions of thermal stress. Especially, conditions which are difficult to evaluate experimentally such as the effects of technical failures in life support mechanisms during extravehicular activities in space, or in deep diving activities should be evaluated first in appropriately adapted simulation models. Typically, this requires some re-specification of such models because of the special demands such applications make. When Montgomery (1979) used our model to evaluate deep sea divers and their thermal conditions he had to modify the controlled system by dividing the concentric compartments into additional layers to improve the precision of the conductive heat transfer description within the body. Under other applications it may become necessary to extend the temperature ranges or the heat production or the heat loss rates beyond the levels which were used in the design and validation of the original simulation model. Such extensions and the evaluations which they produce should be regarded with considerable caution and interpreted with great care. Simulation models of human thermoregulation have been developed with varying levels of detail (Hwang and Konz, 1977) but all are based on experimental observations involving exposure of human subjects to thermal stress of high or low temperature environments and increased internal stress of high or low temperature environments and increased internal heat production due to controlled levels of

exercise. As a result, all these models are based on data obtained at body temperatures not very far away from regulated levels. Experimental data on tissue responses and whole body responses to body temperatures in excess of 40°C and below 34°C are almost nonexistent for humans and are relatively scarce for animals. Extension of thermoregulatory simulation models beyond these temperatures should be carried out with a great deal of caution, and whenever possible at least partial experimental verification should be obtained.

APPLICATION OF SIMULATION MODELS OF HUMAN THERMOREGULATORY SYSTEM TO DEPOSITION OF RADIOFREQUENCY POWER WITHIN THE BODY

The evaluation of the thermal effects of the absorption of radiofrequency electromagnetic radiation in the human body is receiving increasing attention. Animal studies can provide useful insights and guidance, but there are inevitable problems in transferring such insights to the evaluation of possible effects in the human body. The concern over the effect of relatively low levels of electromagnetic radiation which might be absorbed by the general population is only one important area. In recent years there is an increased interest in the controlled delivery of substantial amounts of electromagnetic radiation in the radiofrequency range to specific tissues such as neoplastic growths, as one facet in the treatment of cancer patients. In recent years a considerable amount of progress has been made in the quantification of the absorption of electromagnetic radiation in animal and human tissues (Guy, *et al.*, 1974; Kritikos and Schwan, 1979; Gandhi, 1982) so that mathematical models are now available to simulate the deposition of electromagnetic energy in the radiofrequency area into fairly well detailed mathematical representations of the human body. It is then logical to combine such models of radiofrequency power deposition with models of thermoregulatory response to evaluate physiological responses to such power deposition (Way, *et al.*, 1981; Stolwijk, 1980). The interweaving of two simulation models which were developed for different purposes using different rationales and objectives poses particular problems. Different types of prior assumptions and simplifications have been incorporated in the two models and these may lead to internal incompatibilities which may not immediately become apparent.

The formulation of the power deposition model in general

will be designed to accommodate the mathematical treatment of power deposition which is sensitive to shape and dimensions, electrical conductivity and dielectric constant. The formulation of the thermoregulatory model will be designed to accommodate the location of sensory modalities and the location of effector mechanisms as well as that of metabolic heat sources and of blood flow patterns. Unless one deals with rather specialized forms and locations of power deposition such as was done by Way, *et al.* (1981) and Stolwijk (1980) it may be difficult for the energy deposition model to function within the spatial definition of the thermoregulatory model, or for the thermoregulatory model to function within the spatial definition of the energy deposition model.

In special, or conceptional situations as outlined by Stolwijk (1980) the combined simulation will provide useful insights. If 100 watts of radiofrequency energy were deposited in the human brain, the pure thermal effect would create consequences which might not be necessarily anticipated. Figure 1 shows some of the relevant outcomes from such an exposure for 30 minutes. The first result of this simulation is that the brain temperature is raised, but by an amount which is much lower than one might expect. One important reason for this small rise in brain temperature is the relatively high rate of blood flow in the brain, of the order of 50 ml of blood for every 100 grams of brain every minute. Because the brain is an important site of thermoreceptors the thermoregulatory system reacts very strongly to even the limited rise in brain temperature and causes a rate of body heat loss through sweating which exceeds even the total radiofrequency energy input. As a result all body temperatures fall, and the drop in temperature of the blood being supplied to the brain causes the brain temperature to fall as well. Figure 2 shows the result of a similar simulation in which 500 watts of radiofrequency power was deposited into the core of the trunk for 30 minutes. It will be seen that the trunk core rises somewhat more rapidly in temperature than other compartments. The sweating response is disabled in this simulation and the thermoregulatory system is overwhelmed by this rate of power deposition, and all body temperatures rise throughout the exposure.

Even without any tissues reaching temperatures above 41 or 42 °C it is also evident from these two examples, as well as from the examples in Way, *et al.* (1981), that the amount of thermal mixing and thermal averaging over all body tissues through the convective heat transfer via blood flow results in the protection of individual tissues. This in

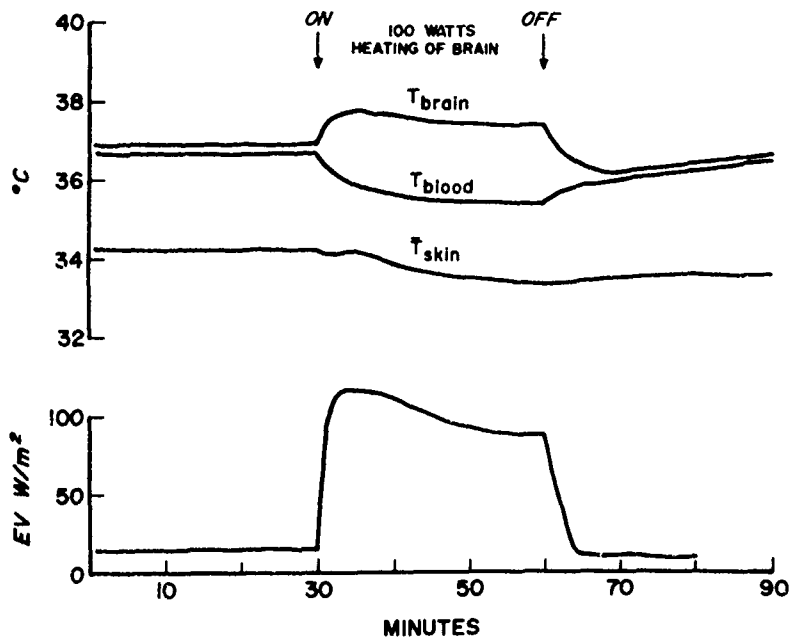

Figure 1. Simulation of the deposition of 100 watts of electromagnetic energy into the head core for 30 minutes in a thermoneutral environment. The exposure causes an amount of sweating which exceeds the energy gain, and causes a net loss of body heat during the exposure. (EV is evaporative heat loss, T_{BRAIN} is head core temperature, T_{BLOOD} is the central blood temperature, $\bar{T}_{SKIN}$ is the mean skin temperature).

effect makes it rather difficult to raise the temperature of a small amount of tissue to a high level, without the deposited energy being dissipated over the heat capacitance of the whole body.

It is, of course, theoretically possible that a tissue with very poor perfusion such as resting muscle, or the lens of the eye will increase in temperature if high specific energy deposition rates are applied. In such cases there is, for many of these tissues, in especially well vascularized tissues such as muscle a tremendous increase in blood flow as soon as temperatures of 40-42 °C are exceeded. Such increases in blood flow have been recorded by Cunningham (1970) and by other authors as well.

In cases in which the results of energy-deposition modeling need to be incorporated into thermoregulation

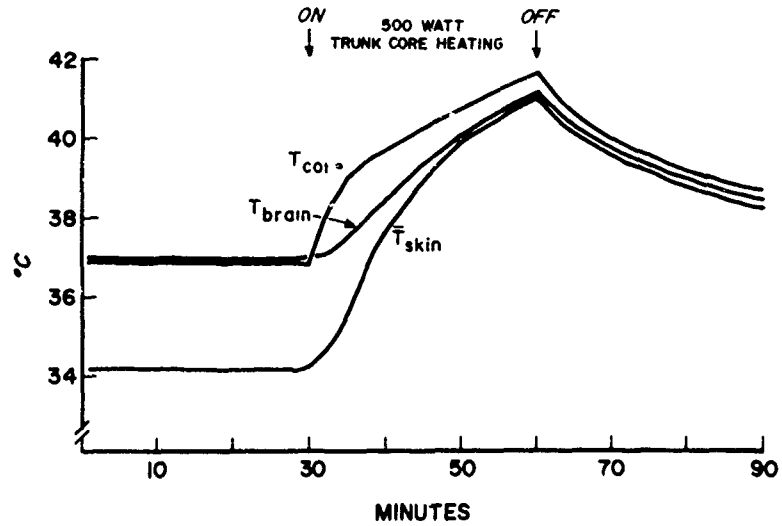

Figure 2. Simulation of the deposition of 500 watts for 30 minutes into the trunk core, in a thermoneutral environment which does not permit the evaporation of sweat (T_{CORE} is the temperature of the core of the trunk, T_{BRAIN} is the temperature of the core of the head, $\bar{T}_{SKIN}$ is the mean temperature of the skin.

models, the most effective way of coupling such systems may be to leave both systems as originally developed but transfer the energy deposition rates from the compartments of the deposition model to the differently formulated compartments of the thermoregulation model which can then predict the thermal and thermoregulatory responses.

In any case, predicted local temperatures in excess of 42 °C should be interpreted very carefully, and specifically evaluated for the presence or absence of an increased blood perfusion response.

In general the use of one of the widely accepted models of thermoregulation to evaluate the thermal effects of exposure to radiofrequency electromagnetic radiation should be seen as a useful tool which should be interpreted with reasonable caution.

REFERENCES

Cunningham, D.J. (1970) An evaluation of heat transfer through the skin in the human extremity. In: *Physiological and Behavioral Temperature Regulation.* (J.D. Hardy, A.P. Gagge and J.A.J. Stolwijk, eds.) p. 302. Charles C. Thomas: Springfield.

Gandhi, O.P. (1982) Electromagnetic absorption in an inhomogeneous model of man for realistic exposure conditions. *Bioelectromagnetics* 3:81.

Guy, A.W., Webb, M.D., and Sorensen, C.C. (1974) Determination of power absorption in man exposed to high frequency electromagnetic fields by thermographic measurements in scale models. *IEEE Trans. Biomed. Eng.* 23:361.

Hwang, C.-L. and Konz, S.A. (1977) Engineering models of the human thermoregulatory system - A review. *IEEE Trans. Biomed. Eng.* BME 24:309.

Kritikos, H. and Schwan, H.P. (1979) Potential temperature rise induced by electromagnetic field in brain tissues. *IEEE Trans. Biomed. Eng.* 26:29.

Montgomery, L.D. (1972) Simulation of heat transfer in man under immersed conditions. Ph.D. Dissertation, University of California at Los Angeles.

Stolwijk, Jan A.J. (1980) Mathematical models of thermal regulation. *Ann. N.Y. Acad. Sci.* 33:98.

Stolwijk, J.A.J. and Hardy, J.D., (1955) Temperature regulation in man - a theoretical study. *Pflügers Archiv.* 291:129.

Stolwijk, J.A.J. and Hardy, J.D. (1977) Control of body temperature. In: *Handbook of Physiology. Reactions to Environmental Agents.* (D.H.K. Lee, ed.) p. 45 American Physiological Society: Bethesda, MD.

Way, W.I., Kritikos, H., and Schwan, H. (1981) Thermoregulatory physiologic responses in the human body exposed to microwave radiation. *Bioelectromagnetics* 2:341.

THERMOREGULATORY BEHAVIORAL RESPONSES

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INTRODUCTION

Behaviors that limit or facilitate heat gain or heat loss are displayed by all animals as soon as locomotion is possible. Although these behaviors may be quite simple, they may also be quite sophisticated, especially in humans. They result in an improved constancy of body temperature. However, due to human artifacts, some experimental situations can be devised to fool nature, as for example when animals are allowed to self cool or warm their deep nervous centers directly and thus bypass the normal thermal flow. Exposure of the body to microwaves is comparable since in that case heat may be produced directly in the core of the body, i.e. below the bypassed skin thermodetectors. In this review of thermoregulatory behaviors we shall first list behaviors where the responses modify the subject's thermal environment; we shall start with the simplest behaviors and follow with behaviors of increasing complexity. Then we shall look at behaviors where the responses modify the subject's internal state directly. Each behavior should be compared to its homologous autonomic response (see Chapter 7) to judge its efficacity.

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MODIFICATION OF THE THERMAL ENVIRONMENT

Postural Adjustments

Postural changes influence heat exchange between the body and the environment in various ways according to the species considered. The result is always a modification of the relative surface of the organism. Expanded postures increase heat exchange by increasing the surface/volume ratio. Retracted postures decrease heat exchange. Positioning the body *vis-à-vis* solar radiation is the same type of behavior.

Behaviors of this type that facilitate either heat loss or heat gain have been reported in scorpions (Alexander and Ewer, 1958) and many insects: orthoptera (Fraenkel, 1929), lepidoptera (Clench, 1966), odonata (Tracy, *et al.*, 1979).

The elytrons of a desert coleopter *Onymacris plana*, and probably of other species as well, reflect solar radiation with a wavelength shorter than 700 nm, but absorb longer waves. This insect basks in the sun in morning and evening when the sun is low in the sky. Then 60 percent of solar radiation is 700 nm and above. At midday, on the other hand, it does need heat and is better protected since solar radiation contains no more than 50 percent radiation with a wavelength longer than 700 nm (Henwood, 1975).

Use of solar heat and postural adjustments relative to solar radiation have also been described in amphibians (Brattstrom, 1963), reptiles (whose behavior means basking in the French language), (Saint Girons, 1956; Bartholomew, 1966; De Witt, 1971; Cruce, 1972; Cloudsey-Thompson, 1972), albatrosses and gulls (Bartholomew, 1964; Lustick, *et al.*, 1978), kangaroos (Dawson, 1972), lagomorpha (Schmidt-Nielsen, *et al.*, 1965; MacArthur and Wang, 1974), rodents (McEwen and Heath, 1973), pinnipedes (Fay and Ray, 1968; Ray and Smith, 1968; Odell, 1974), and in dromedaries (Pilters-Gauthier, 1961). To resist cold, these animals raise their bodies, spread their limbs and place themselves perpendicular to the sun's rays; to resist heat they squat, crouch and face the sun. In the gull *Larus argentatus* this position minimizes heat gain because the bird thus exposes only white surfaces (Lustick, *et al.*, 1978).

These very simple postural adaptations can be extremely efficient, not only for a butterfly whose surface becomes almost virtual when its wings are parallel to the sun's rays, but also in bigger and more globular animals. For example the area of projection of a dog varies from 1 to 3 between face and profile. A steer receiving the sun at a 30° angle can double the amount of heat gained by changing

its position from parallel to perpendicular to the rays (Ingram and Mount, 1975). In the same way the pattern of the human body varies by a factor of 5 or 6 when the person changes from crouched with the limbs close to the body to "spread eagle" (Vaughan, *et al.*, 1977). The efficiency of this very simple behavior is extremely impressive.

Postural adjustments are also quite efficient for controlling heat loss. Piglets spread their limbs in warm environments and hold them close to the body in cool environments (Mount, 1968). The monkey *Aotus trivirgatus* doubles its rate of water evaporation at ambient temperatures above 30 °C just by spreading its limbs; below 30 °C it tends to hold its limbs close to its body (Le Maho, *et al.*, 1981). The rabbit has been observed to adopt three fundamental positions: spread out in a warm environment, relaxed at tepid temperatures and ball-like in a cold environment. Thus it is able to keep its metabolism constant at ambient temperatures ranging from 30 °C to 0 °C (McEwen and Heath, 1973). Sled dogs adopt the same variety of postures and remain at resting metabolism in ambient temperatures as low as -30 °C (Scholander, *et al.*, 1950).

Postural changes also control heat exchange with water efficiently. The survival time of human subjects in cold water is approximately doubled if they adopt a crouched position rather than swim. It is therefore advisable not to try to swim to the shore if a shipwreck takes place more than 1.4 km out at sea (Hayward, *et al.*, 1975).

Avoidance of Noxious Environments and Search for Favorable Environments

As soon as locomotion is present, animals respond to ambient temperature by displacement. This is easy to observe in domestic animals which frequently sleep by the stove or the fireplace. Close observation shows that all species are able to display comparable behaviors. It is impossible to cite a complete list of all the studies of this behavior. The following list is limited to a few examples. Arachnids (Alexander and Ewer, 1958; Abushama, 1964; Seymour and Vinegar, 1973; Carrel, 1977), insects (Heath, *et al.*, 1971; Casey, 1976), molluscs (Rising and Armitage, 1969; Edney, 1957; Jaremovic and Rollo, 1979), crustacea (Miller and Vernberg, 1968), amphibians (Brattstrom, 1963; Cunningham, 1963; Tester and Breckenridge, 1964; Licht and Brown, 1967) bask in the sun, seek shade or bury themselves to obtain heat or to avoid it or to avoid

frost. Many studies focus on reptiles, mostly lizards (Saint Girons and Saint Girons, 1956; Mayew, 1963; Heath, 1964; Bartholomew, 1966; McGinnis and Dickson, 1967; De Witt, 1971; CloudsleyThompson, 1972; Cruce, 1972; Johnson, 1972; Spelleberg, 1972; Barber and Crawford, 1977; Huey, *et al.*, 1977; Fitzpatrick, *et al.*, 1978), but also tortoises (Boyer, 1965) and snakes (Saint Girons and Saint Girons, 1956; Stewart, 1964; Cloudsley-Thompson, 1972). These animals too alternate their stays in the shade and in the sun and bury themselves. The efficiency of this behavior is of course a function of the available environment. Endotherms also use it: during the hottest part of the day, Arizona Jack rabbits (SchmidtNielsen, *et al.*, 1965) as well as steers (Adeyemo, *et al.*, 1979) rest in the shade where they radiate heat toward the clear sky. Sparrows choose warm irradiation or cool breezes according to the prevailing ambient temperature (Dejong, 1979).

A special case of this behavior consists in alternating air and water environments. Humans by the millions behave this way on sea shores without knowing they thermoregulate thereby. This behavior is common in semi-aquatic animals such as the marine iguana (Bartholomews, 1966), the alligator (Smith, 1975), and the hippopotamus (Cena, 1964). The rat will bathe in water when necessary, if a tub is available (Stricker, *et al.*, 1968). Domestic animals will frequently demonstrate this behavior.

Another form of this behavior is gregarism (huddling) displayed by many species including bees (Heinrich, 1981). It is used most often in cold environments but also in hot environments. Dromedaries tend to stay close to each other in order to avoid hot environmental radiation (Pilters-Gauthier, 1961). Sheep adopt the same behavior. However, most often individual subjects tend to disperse in a warm environment and to gather together in a cold environment, as was reported in rat pups (Cosnier, 1965), in adult bats (Licht and Leitner, 1967) and in piglets (Mount, 1968). This behavior is frequent in new borns of species with a late maturity. It permits noticeable metabolic savings: 20 day old rat pups reduced their thermogenesis by 32 percent at 21 °C ambient temperature (Cosnier, *et al.*, 1965; Alberts, 1978). The reduction amounted to 50 percent in 7 and 18 day old mouse pups (Stanier, 1975). Young hamsters until the age of 8 days (Leonard, 1978), field mice (Tertil, 1972), naked rats (Withers and Jarvis, 1980), and even some snakes (Aleksius, 1977) have been reported to behave similarly. Paradoxically, gregarism may increase oxygen consumption of mouse pups because it is accompanied by agitation (Bryant and Hails, 1975). Huddling is as efficacious

as crouching in humans after a wreck at sea (Hayward, *et al.*, 1975). In the Antarctic, emperor penguins are thus able to remain at their resting metabolism even at ambient temperatures as low as -10 °C (Le Maho and Delclite, 1974; Le Maho, *et al.*, 1976; Le Maho, 1977).

In the laboratory, avoidance of noxious temperatures and search for favorable temperatures is usually studied with a temperature gradient also designated a thermocline or multiple-compartment shuttlebox. In such a device, after a period of time for exploration, the animal sojourns in its preferred temperature, or thermopreferendum (Viaud, 1955). Probably the oldest such experiment, historically as well as phylogenetically, was reported by Mendelssohn (1895) who observed a population of paramecia moving toward their thermopreferendum of 24-28 °C in a water gradient extending from 12 to 36 °C.

This method has been used with many species. Table I gives a non-exhaustive list. More information will be found elsewhere (see Prosser, 1973; Whittow, 1970). The temperature gradient and the shuttlebox, complex or simple with only two or three boxes, are advantageous because they resemble the natural environment. The few field studies quoted above show that the natural preferendum is the same as that determined in the laboratory. This behavior can be considered as fundamental, i.e., it is efficacious in response to the animal's thermal needs. However it has two disadvantages. The first one for the experimenter: the animal's locomotion may hamper the measurement and recording of various physiological parameters. This problem is usually solved by using instrumental conditioning (s below). The second disadvantage is for the animal: the locomotion implies that all the animal's activity is devoted to environmental improvement or thermoregulation. This behavior is therefore competitive with other behaviors. Only a handful of studies have been devoted to this problem.

Specific Behaviors

We saw above that animals of all species will, when necessary, improve or limit their heat loss by using their posture or by moving. Each species possesses one or several preferred postures, as we saw in the case of the rabbit (McEwen and Heath, 1973). This is especially evident in rodents: rat, mouse, gerbil, hamster, and guinea pig use body extension, locomotion, and grooming preferentially (Roberts, *et al.*, 1974). In addition, some species use behaviors made possible by an anatomical or ecological

Table I. Experimental Studies in Thermal Gradient

Group		Species	Thermopreferendum °C	References
Unicellulars		*Paramecium aurelia*	25-26	Mendelssohn (1895)
		Human spermatozoa	33-34	Jeddi, *et al* (1977)
Worms		*Enchytraeus albidus*	40	McCue & Thorson (1964)
Molluscs		*Philomus carolianus*	20-24	Rising & Armitage (1969)
		Limax maximus		
Crustacean decapods		*Arconestes immunis*	18-22 day night	Crawshaw (1974)
		Cambarus bartoni	22.1	Casterlin & Reynolds (1977a, 1978, 1980)
		Homarus americanus	16	Casterlin & Reynolds
		Penaeus duoraum	31	(1979d)
Arachnids	Scorpions	*Opisthophtalmus latimanus*	32-38	Alexander & Ewer (1958)
		Leiurus quinquestriatus	25-26	Abushama (1964)
		Scorpio maurus fuscus	24	Warburg &
		Nebo hierochonticus	21-23	Ben-Horin

		Buthotus judaicus	26	(1981)
		Buthus occitanus	24-25	Cabanac & Le Guelte(1980)
		Androctonus australis		
	Spiders	*Agelana consociata*	22.7	Kraft (1967)
Insects	Orthoptera	*Acheta domestica*	27-23	Herter (1923)
			day night	
		Gryllulus domesticus	25-30	Cachen (1948)
			26-30	Villardebo (1948)
			28-29	Chauvin (1948)
	Coleoptera	*Tribolium castaneum*	17-22	
		Cadra cautella	laying 28	Amos *et al.* (1968)
			17-20(laying)	
	Hymenoptera	*Formica rufa*	22-32	Herter (1923)
		Apis mellifica	31.7-33.8	Heran (1952)
Cyclostoma		*Petromyzon marinus*	14.3	Mc Cauley, *et al.*(1977)
Fishes	Elamobranchs	*Heterodontus francisci*	27.1	Crawshaw & Hammel(1973)
		Mustelus canis	25.9-28	Casterlin & Reynolds (1979a)
	Holostean	*Amia calva*	31.3-29.6	Reynolds, *et al.*(1978a)
			day night	
	Teleostean	*Oligocottus maculosus*		
		Clupea pallasii		Shelford & Powers (1915)
		Lepidopsetta bilineata		

Table I continued.

Group	Species	Thermopreferendum °C	References
Fishes (cont.) Teleostean	*Myoxocephalus sp.*	5	Hammel, *et al.* (1969) Strømme, *et al.* (1971)
	Chromis chromis	20	Cabanac & Jeddi (1971)
	Scorpena scorfa	20	Green & Lomax (1976)
	Notothenia coriiceps	1.5-3	
	Chaenocephalus aceratus	1.5-3	Crawshaw & Hammel (1971)
	Perca flavescens	24.2	Ross *et al.* (1977)
	Ictalurus nebulosus	26	Crawshaw & Hammel (1974)
		25-26	Crawshaw (1975 a, b)
	Ictalurus natalis	28.4	Reynolds & Casterlin (1978b)
	Ictalurus punctatus	28-30	Cheetham, *et al.* (1976)
	Lepomis cyanellus	28.2	Beitinger, *et al.* (1975)
		10-25 (depending on acclimation)	Nelson & Prosser (1979)
	Lepomis macrochirus	28-32	Neill, *et al.* (1972)
		25-26	Crawshaw (1975b)
		30.5	Reynolds, *et al.* (1976a, 1977)

Salmo salar	19	Fryer & Ogilvie (1978)
Micropterus salmoides	30.1-29.9	Reynolds, *et al.* (1976ab)
	30--25-29 day night	Reynolds (1977)
Carassius auratus		Fry (1964)
	28	Covert & Reynolds (1977)
	26-30	Reynolds, *et al.* (1978b,c)
	10-25 (depending on acclimation)	Nelson & Prosser (1979)
Fundulus heteroclitus	25-30	Garside & Morrison (1977)
Fundulus diaphanus	15	
Ambloplites rupestris	29.4	Reynolds & Casterlin (1978c)
Enneacanthus gloriosus	28.5	Casterlin & Reynolds (1979b)
Catostomus commersoni	23-26	Reynolds & Casterlin (1978a)
Poecilia reticulata	29	Ogilvie & Fryer (1971)
	21.9	Fryer & Ogilvie (1978)
Notropis cornutus	15-20, spring	Ulvestad & Zar (1977)
	11-19, fall	
Esox masquinongy	22-27	Reynolds & Casterlin (1979)

Table I continued.

Group		Species	Thermopreferendum °C	References
Amphibians	Urodeles	*Taricha rivularis*	20-26 (tadpoles)	Licht & Brown (1967)
		Plethodon cinereus	16-20	Feder & Pough (1975)
		Necturus maculosus	13-15	Hutchison, *et al.* (1979)
	Anouran	*Rana esculenta*	25	Cabanac & Jeddi (1971) Duclaux, *et al.* (1973) Myhre, *et al.* (1977)
		Rana catesbeiana	adults	Lillywhite (1971)
			25.5 (tadpoles)	Casterlin & Reynolds (1977b)
		Rana pipiens	20.7	Hutchinson & Hill (1978)
				Casterlin & Reynolds (1979c)
			27.9 (tadpoles)	
			(tadpoles)	Casterlin & Reynolds
			28.5 (tadpoles)	(1977b)
		Ascophus truei	2-22	
		Hyla regilla	25	Claussen (1973)
		Hyla cinerea	25.5	Kluger (1977)

Reptiles	Lizards*	*Dipsausaurus dorsalis*	38.5	De Witt (1967)
			37-41	Vaughn, *et al.* (1974)
		Tiliqua scincoides	37-41	Kluger, *et al.* (1973)
			30-37	Hammel, *et al.* (1967)
			29.3	Myhre & Hammel (1969)
				Cabanac & Hammel (1971 a, b)
		Cnemidophorus ceralbensis	40.7	Soulé (1963)
		Klauberina riversiana	27-32	
		Phrynosoma cornutum	32-33	Regal (1967)
		Uma notata	28-33	
		Uma sp. Holbrookia sp.	38.5	Soulé (1963)
		Urosaurus ornatus	37.5	
		Sceloporus grociosus	35.4	Licht (1965)
		Sceloporus virgatus	36.3	
		Sceloporus olivaceus	32-33	Fitzpatrick, *et al.* (1978)
		Sceloporus sp	34.9	Soulé (1963)
		Uromastix acanthinurus	33-34	Grenot & Loirat (1973)
		Lacerta vivipara	29-33	Patterson & Davies (1978)
	Snakes	*Constrictor constrictor*	40 in digestion 23 out of digestion	Regal (1966)

Table I continued.

Group		Species	Thermopreferendum °C	References
Reptiles(cont.)	Snakes	*Vipera aspis*	32.5-35.5	Naulleau & Marques (1973)
		Morelia spilotes variegata	31.3	Johnson (1972)
Birds	Partridge	*Lagopus lagopus*(chick)	37.6 hatchling 33.4 8 days	Myhre, *et al.* (1975)
		Alectoris chukar	25-32	Laudenslager & Hammel (1977)
	Quail	*Coturnix coturnix japonica*	31	Spiers, *et al.* (1974)
Mammals	Pig	*Sus sus domesticus* (young)	32-30	Mount (1963)
	Rats	*Rattus norvegicus*	29-30	Rudiger & Seyer (1965) Edwards & Roberts (1972) Yehuda & Wurtman (1974) Fowler & Kelloy (1975) Cox, *et al.* (1975) Johanson (1979)
		Sigmodon hispidus	24-29	Kirksey, *et al.* (1975)

Mammals (cont.)	Mice	*Mus musculus*	32	Ogilvie & Stinson (1966)
			31-36	Lynch, *et al.* (1976)
			<30	Murakami & Kinoshita (1977)
		Peromyscus leucopus	32	
		Peromyscus maniculatus	26-29	Ogilvie & Stinson (1966)
	Vole	*Microtus arvalis*	34 newborn	
			24 adult	Bashenina & Borovskaja (1963)
	Hamster	*Cricetus cricetus*	36	
			37 newborn	Leonard (1974)
		Cricetus auratus		Leonard (1978)
	Guinea pig	*Cavia cobaya*	29	Blatteis & Smith (1980)
	Rabbit	*Oryctolagus cuniculus*	immature	Jeddi (1970)
				Satinoff, *et al.* (1976)
				Kleitman & Satinoff (1981)
	Dog	*Canis familiaris*	38.5	
			12-16	Cabanac, *et al.* (1965)
				Cabanac, *et al.* (1966)
			(pup)	Jeddi (1970)

*A bibliography in Huey & Slatkin (1976).

characteristic of the species or made necessary to compensate for a given deficit of the species, as shown in the following examples.

Penguins ingest ice (Hammel, 1971); beavers tend to keep their tail immersed in water during heat waves (Steen and Steen, 1965); alligators keep their mouth open and thus accelerate the relative warming of the head compared to the rest of the body (Spotila, *et al*, 1977). Many animals fan themselves and thus increase their convective heat loss: seals with their flippers (Bartholomew and Wilke, 1956), elephants with their ears, sea birds with their palmed feet (Bartholomew, 1964), and ostriches with their wings (Helmendach, *et al.*, 1965). In addition, ostriches erect their feathers in order to shade their glabrous skin areas. It was even proposed that the fossil lizard *Dimetrodon grandis* used its dorsal sail for the behavioral control of heat loss in the shade and heat gain in the sun (Bramwell and Felgett, 1975). Some species lacking autonomic evaporative heat loss capability use an expensive behavior: they spread saliva on their glabrous skin areas in their fur and thus compensate for the absence of sweat. This has also been described in marsupials (Martin, 1903; Bartholomew, 1956) although they also can pant. Although this behavior seems not to be totally specific to heat defense (Feyereisen and Blondiau, 1978), it is the main response to hyperthermia in the rat (Hainsworth, 1967). Desalivation of rats placed in a hot environment is followed by hyperthermia that is potentially lethal (Hainsworth and Stricker, 1969; Lipton and Marotto, 1969; Stricker and Hainsworth, 1970; Toth, 1973; Cabanac, *et al.*, 1976). Storks adopt a somewhat comparable behavior since they defecate their liquid feces on their vasodilated legs and thus improve their evaporative heat loss when ambient temperature increases (Kahl, 1963). Nocturnal activity is probably a thermoregulatory adaptation to desert life enabling the animal to avoid day heat. While the periodic disappearance of food is probably the main cause of bird migrations (Blondel and Frochot, 1972), it is nevertheless possible that ambient temperature participates in its determinism.

The above enumeration does not pretend to be exhaustive; however it casts some light on the innumerable solutions found by various species to solve their common problem, thermoregulation.

Building Micro-Environments

This activity is not reserved to humans.

1. In Animals. Many species are able to control their environment by building nests, burrows, or dens. In very ancient species such as scorpions (Alexander and Ewer, 1958; Hadley, 1970, 1974) or lice (Edney, 1957) the burrow offers a good thermal protection. This protection increases in social insects. They produce behaviorally a practically constant temperature for the colony throughout the year. This constancy has been reported in termites, bees, and wasps. When the outside temperature drops, the imagos increase their activity and their thermogenesis (Lindauer, 1951; Stussi, 1967); at the same time they increase the ventilation of the hive to provide enough oxygen (Stussi, 1967). Thermogenesis and nest temperature are functions of the amount of sugar stored (Roland, 1969). During hot weather, active ventilation of the hive is also increased to improve convective and evaporative heat loss (Hazelhoff, 1954). Occasionally, bees (Lindauer, 1954) and wasps (Roland, 1969) carry water from outside to the combs to let it evaporate.

Building sophisticated microclimates is displayed by vertebrates as well as social insects. However, it is usually limited to the protection of immature offsprings. We shall therefore discuss it below, under parental behavior.

2. In Humans. For purposes of thermoregulation, humans use clothing and build houses that are heated or cooled. Weather prediction is also partly thermoregulatory in its purpose. There is practically no limit to the efficiency of these behaviors which allow humans and commensal species to live permanently with improving technology, in favorable environments even when external conditions are extremely aggressive such as at the poles, under the sea, and on the moon (Stolwijk, 1970).

However, milleniums before humankind was able to accomplish such prowess, humans lived in all climates with the help of some simple but efficacious techniques. A campfire produces enough heat to permit naked subjects to remain at their resting metabolism and sleep at night while ambient temperature approaches 0 °C (Scholander, *et al.*, 1958). Under their clothes, Sams (Lapps) live in a subtropical climate, in terms of temperature and humidity (Scholander, *et al.*, 1957). This is also true for the bed (Goldsmith and

Hampton, 1968; Candas, *et al.*, 1978; Muzet, *et al.*, 1978). A mere sleeping bag made of down with a hood maintains skin temperature at 32 °C while ambient temperature drops to -33 °C; however the occupants may complain of feeling cold (Buguet, *et al.*, 1976). During long term sojourns in antarctic climes, a negative proportionality was found between outside temperature down to -50 °C and the number of clothing layers worn by human subjects (Rogers, 1973). Such quantitative adjustment shows both the adaptability and the efficiency of this behavior (Goldman, 1974; Shkolnik, *et al.*, 1980). The adaptability and insulating power of clothing was quantitatively defined by Gagge, *et al.* (1941) who defined a new unit, the clo:

$$1 \text{ clo} = 0.155 \text{ °C} \cdot \text{m}^2 \cdot \text{W}^{-1}.$$

One clo is approximately the amount of insulation provided by one layer of light cotton clothes (See Chapter 2).

Homes and buildings fulfill the same function as clothes with regard to microclimate. Their efficacy is also infinite. After empirical investigations that span millenia, engineers and physiologists can quantify with precision human heat balance under a wide variety of conditions (Gagge, *et al.*, 1967; Hardy, 1971; Fanger, 1970; Gagge, *et al.*, 1971; Oleson, *et al.*, 1972, 1973; Thompson, 1972; Rohles, 1974; Nishi and Gagge, 1974, 1977; Gonzalez and Nishi, 1976; Vogt, *et al.*, 1977). It is now possible to predict with great precision the conditions and limits of thermal comfort. Heat balance is the only relevant dimension since, contrary to common belief, neither color nor noise influence the perception of thermal comfort (Fanger, *et al.*, 1977). The result of building a microclimate, whether by clothing or housing, is the freeing of behavior for other purposes.

Parental Behavior

Thermoregulatory behavior can also be a social activity when parents defend their offsprings before and after birth or hatching, against noxious ambient temperatures, most often against the cold. In many species, newborns are immature and would not survive without their parents protection (Ginglinger and Kayser, 1929; Blix and Steen, 1979).

Such thermal protection is quite frequent since it is displayed even by insects. For example, by quasi-shivering imago wasps (Ishay, 1972) and bees (Heinrich, 1972) rewarm the nymphae up to 32 °C, the temperature favorable to their

development. The same behavior is adopted by the female python which broods when ambient temperature falls below 33 °C (Hutchison, *et al.*, 1966). Brooding birds maintain their eggs at a constant temperature (White and Kinney, 1974). The female beluga seeks warm waters to deliver her calf (Sergent, 1973).

After birth or hatching, brooding is still intense especially in polar species, and is a prerequisite of survival (Le Maho, 1977). Parents provide both heat and thermal insulation. Chicks can spend up to 90 percent of their time under their parents' wings if the weather is cold (Theberge and West, 1973; Boggs, *et al.*, 1977; Sherry, 1981); as a result, the chicks cloacal temperature remains 8 to 10 °C higher than that of unprotected chickens (Barth, 1949). Brooding of the cub was also reported in the polar bear (Kost'Yan, 1954), a species whose newborns are especially immature. In both hot and cold environments, birds also shade their chicks under their wings (Bartholomew, 1964).

Burrows and dens, in addition to defending occupants against predators, maintain a temperature favorable to the offspring. The mere presence of the mother polar bear is sufficient to maintain the ice den near 0 °C while external temperature is -30 °C (Blix and Lentfer, 1979). The mother rat keeps the ambient temperature in the nest between 14 and 18.5 °C. If the nest temperature tends to rise above 18.5 °C she moves the nest to another place; if the temperature drops below 14 °C she increases its insulation (Gelineo and Gelineo, 1952). Hummingbirds (Horvath, 1964) and terns (Howell and Bartholomew, 1962) also move and orient their nests to keep a constant temperature therein. As a result, the offspring's metabolism remains low: there is no need for autonomic thermogenesis to increase (Bryant and Hails, 1975; Alberts, 1978). The resulting nest temperature is then not favorable for the mother, whose neutral temperature is lower than that of the pups, and she must leave the nest (Croskerry, *et al.*, 1978). In fact the thermal protection of the pups is controlled by the mother's body temperature: when her body temperature increases, bouts of nest building tend to become less frequent (Leon, *et al.*, 1978). Nest building in mice seems to be related to progesterone concentration (Lynch and Possidente, 1978).

Human newborns are also quite immature, in that their autonomic responses are able to make them independent of temperature only at the age where their motor and verbal development makes them behaviorally independent. Parents must therefore take care of their baby's temperature regulation. Adults frequently underestimate both the excessive insulation that they provide and the baby's high thermolysis

due to a small volume/surface area ratio (Motil and Blackburn, 1973). Even trained hospital staff make the same mistake (Chance, *et al.*, 1973). Fortunately the new born "closes the loop" and alerts its parents by crying when thermally uncomfortable (Brück, *et al.*, 1972; Brück, 1968).

Operant Behavior

Weiss (1957) and Carlton and Marks (1958) first modified the operant conditioning paradigm to study thermoregulatory behavior; they allowed rats to press a bar and to thus obtain, not the classical alimentary reward, but a thermal reward. In general, each press on the lever provides a puff of cold air or a few seconds of infrared heat. In other situations the press removes noxious infrared heat for few seconds. As soon as the animal has learned how to use the device at its disposal the experimenter is able to obtain a quantitative measurement of behavior, either bar pressing frequency or a more informative measure, total time spent pressing the lever (Hamilton, 1959). The latter permits measurement of both the animal's motivation and the heat gained - or lost - through behavior.

After its introduction, this method was widely adopted and extensively used principally with rats as subjects, but also with many other kinds of animals. A tentative list is given in Table II. In deriving experimental results with this method, one should keep in mind an important limitation: bar pressing, or non pressing, can also be a non-specific behavior resulting from general excitation or apraxia. A response should be considered thermoregulatory only if it fulfills at least one of the following three conditions:

- the response must be accompanied by its symmetrical response, e.g. augmented pressing for heat and diminished pressing for a cold stimulus;
- the response is a quantitative function of ambient temperature and/or of the animal's body temperature. The most likely function is direct proportionality;
- the response magnitude is a function of the stimulus intensity.

Several empirical trials are required to select the optimal rewarding stimulus. When the intensity of the stimulus is varied the animal tends to decrease its behavior with both weak and strong stimuli. When the optimal stimulus intensity is found empirically, it is then necessary to check that accompanying stimuli such as noise or light are not also rewarding or aversive (Sabourin, *et al.*, 1973).

Table II. Thermoregulatory Behavior Measured by Operant Conditioning

Molluscs

Aplysia
Downey & Jahan-Parwar (1972).

Fishes

Carassius auratus
Rozin & Mayer (1961).

Lizards

Dipsausaurus dorsalis
Kemp (1969).
Klauberina riversiana
Regal (1971).
Tupinambus teguixen
Yori (1978).

Birds

Streptopelia risoria
Budgell (1971).
Coturnix coturnix
Spiers, *et al.* (1974).
Columbia livia
Schmidt & Rautenberg (1975); Schmidt (1976, 1978a, b); Schmidt & Simon (1979); Rautenberg, *et al.* (1980).

Gallus domesticus
Horowitz, *et al.* (1978); Wasserman, *et al.* (1975).

Mammals

Mus musculus
(Mouse)
Revusky (1966); Baldwin (1968); Baldwin & Ingram (1968a).
Rattus norvegicus
(Rats)
Weiss (1957); Weiss & Laties (1960, 1961); Laties & Weiss (1959), 1960); Yeh & Weiss (1963); Stern, *et al.* (1979); Carlton & Marks (1958); Hamilton (1959, 1963); Hamilton & Sheriff (1959); Panuska & Popovic (1963); Satinoff (1964, 1977); Satinoff & Rutstein (1970); Satinoff &

Table II continued.

Mammals (cont)

Shan (1971); Satinoff & Cantor (1975); Jakubczak (1966); Carlisle (1966a, b; 1968a, b; 1969a, b; 1970); Beckman & Carlisle (1969); Carlisle & Snyder (1970); Crawshaw & Carlisle (1974); Carlisle & Laudenslager (1979); Rudiger & Seyer (1968); Epstein & Milestone (1968); Leeming & Crowder (1968); Lipton (1968, 1969, 1971); Lipton & Marotto (1969); Lipton, *et al.* (1970); Clark & Lipton (1974); Polk & Lipton (1975); Corbit (1969, 1970); Corbit & Ernits (1974); Beckman (1970); Blass (1969, 1971); Murgatroyd & Hardy (1971); Wakeman, *et al.* (1970); Avery (1970); Avery & Penn (1973); Rapaport (1971, 1972); Crawshaw (1972); Sabourin & Ducharme (1973); Sabourin, *et al.* (1973); Scott & Blackwood (1973); Toth (1973); Wagener (1973); Yehuda & Wurtman (1974); Morhardt & Molt (1975); Cabanac, *et al.* (1976a); Cabanac & Serres (1976); Cormarèche-Leydier, *et al.* (1977); Dib, *et al.* (1982); Humphreys, *et al.* (1976); Van Zoeren & Stricker (1977).

Spermophilus beldingi
(Spermophile)
Morhardt & Molt (1975).

Sus sus domesticus
(Pig)
Baldwin & Ingram (1967a, b, 1968a, b); Carlisle & Ingram (1973); Ingram, *et al.* (1975); Ingram (1975); Heath (1980).

Ovis aries
(Sheep)
Baldwin (1975); Baldwin & Yates (1977).

Canis familiaris
(Dog)
Robinson & Hammel (1967); Cabanac, *et al.* (1970); Duclaux & Cabanac (1971); Cormarèche-Leydier & Cabanac (1973, 1976).

Felix domesticus
(Cat)
Weiss, *et al.* (1967); Clark & Lipton (1974).

Papio papio
(Baboon)
Pister, *et al.* (1967); Gale, *et al.* (1970).

Saimiri sciureus
(Squirrel monkey)
Carlisle (1966b, 1969a); Adair, *et al.* (1970); Adair (1971, 1974, 1976a, b, 1977a, b): Adair & Stitt (1971); Adair & Rawson (1974); Adair & Wright (1976); Stitt *et al.* (1971); Crawshaw & Stitt

Table II continued.

Mammals(cont)
(1975); Laudenslager (1976a, b).
Humans
Homo sapiens sapiens
Paul, *et al.* (1962);
Cabanac, *et al.* (1971, 1972, 1976b);
Cabanac & Massonnet (1974); Olesen &
Fanger (1971); Olesen, *et al.* (1972);
Fanger, *et al.* (1974, 1977); Shitzer,
et al. (1978); Bleichert, *et al.* (1973);
Scarperi, *et al.* (1975, 1976); Behling,
et al. (1976); Wever (1974); Wilmore,
et al. (1975); Grivel & Fraise (1979).

When these precautions are observed, operant or instrumental behavior is a precise tool for the experimental analysis of thermal motivation.

MODIFICATIONS OF THE DEEP BODY TEMPERATURE OF THE SUBJECT

Sometimes behavior can result in a change of the subject's internal temperature, without any stimulation of skin thermoreceptors. This situation can be natural in some circumstances; it can also be purposely devised by a (Machievellian) experimenter to test the capacity of the stimulated tissue to arouse a perceived sensation. Examples of this kind of behavior are of course not numerous: ingestion, muscular work, and operant behavior.

Food and Water Intake

All endotherms increase their food intake during prolonged cold exposure. Inversely food intake decreases during prolonged heat exposure. The amount of food consumed is proportional to the environmental cold (Gasnier and Mayer, 1939) but exceptions to this rule may exist (Hamilton, 1971). In the same way subjects increase their water intake in warm environments (Adolph, 1947). These behavioral adjustments are logical from the point of view of energy and water balance, they may nevertheless not be thermoregulatory.

In cold environments, endotherms lose more heat and therefore must increase their metabolism. In warm environments, they lose more water via evaporative heat loss; they therefore ingest more in order to compensate for their expenditure. When a 10 kg body ingests food, its body temperature can theoretically increase by 1 °C by eating and catabolizing 2 g carbohydrate, a frequent energy source in the environment. The same 10 kg homeotherm is able to lower its body temperature by the same amount by drinking and evaporating 14 g water. Eating and drinking is therefore remarkably efficient if the subject can wait the time necessary to produce autonomic responses. Over the short term however, before metabolism or evaporation takes place, ingestion is of little utility in changing body temperature. For example, if we simplify by approximating all specific heats to 1, the 10 kg homeotherm should, in order to raise its body temperature by 1 °C, ingest 1/10 of its body mass

of a food 10 °C warmer than its own body. In the case of a cold ingestion, the tolerated difference from body temperature can be as much as 40 °C without harm; a 1 °C drop of body temperature would be provided by at least 250 g ingestion of 0 °C water. The efficacy is sufficient and can be improved with the heat of fusion of the ice. Indeed emperor penguins ingest ice when they are overheated (Hammel, 1971).

Controversial results have been obtained in studies of the relations between temperature and water intake during short-term warm exposures (McFarland and Budgell, 1970; Box, *et al.*, 1973; Grace and Stevenson, 1971; Nelson, *et al.*, 1975; Kechil, *et al.*, 1981), or brain heating (Andersson, *et al.*, 1963; Hamilton and Ciaccia, 1971; Ingram and Stephens, 1979), and spinal cord heating (Ingram and Stephens, 1979). Usually heating the skin or the brain results in water intake. However, this is more likely to be an anticipatory response to future dehydration than a thermoregulatory behavior aimed at short-term cooling of the body. Indeed there are some reasons to think that increased water intake in a warm environment is mainly a response to dehydration (Carlisle, 1971; Carlisle and Laudenslager, 1976). In addition cold water inhibits intake (Fregly, *et al.*, 1979; Deaux and Engstrom, 1973; Gold, *et al.*, 1973, 1977). If animals were aiming at cooling their body core they would drink more.

Therefore although the ambient temperatures that arouse thermoregulatory behaviors also trigger food and water intake, and although these responses are favorable to heat balance, their immediate influence can be considered negligible. Food and water intake should not be considered as thermoregulatory behaviors *sensu stricto*, unless ingestion leads to a change of deep body temperature as with ice or cold water taken in large quantity. Temperature may be a signal for satiety or for food intake with the special case of hematophageous parasites (Hocking, 1971; Bernard, 1974), but as a rule food and water intake serves not temperature regulation but long term energy balance.

Internal Heat Production

Heat, a natural by-product of metabolic processes is generated in large quantity within the body. This heat is not under the control of the subject's volition. However two behaviors result in internal heat production and may contribute to the general heat balance: muscular work and exposure to microwave irradiation. Can these sources of heat be used to pay heat deficits in cold environments?

Will subjects behave to produce heat from muscular work or from microwaves? In other words are these behaviors thermoregulatory? Experimental data are scarce in both cases.

Muscular Work. Empirical evidence tells that humans on occasion choose to exercise in order to warm themselves. This evidence was confirmed when subjects placed in a cool environment pedalled on a bicycle ergometer with an intensity negatively proportional to their own temperature (Caputa and Cabanac, 1980). However it is not known whether subhuman species will choose to exercise themselves rather than shiver in a cold environment.

Microwave Exposure. Rats exposed to microwaves in a cold environment requested less infrared heating than controls (Stern, *et al.*, 1979). Thus microwaves affected behavior in a specific manner. In the same way when squirrel monkeys, trained to select for themselves a preferred ambient temperature, were exposed to microwave heating, they chose to reduce ambient temperature significantly (Adair and Adams, 1980). It is not yet sure that animals, or uninstructed humans, will bar press or otherwise work to obtain microwave heating (See Chapters 9 and 18). Thus animals and humans are able to integrate the heat produced in their deep thermal core and behave accordingly. Because there is a lag, due to inertia of heat transfer, between this heat production and the stimulation of deep thermal sensors, (or peripheral sensors in the case of microwaves) it is likely that it takes some time before a subject learns to use endogenous heat (See Chapter 10). However both muscular work and microwave exposure produce heat that is integrated in the behavioral heat balance and should be considered as thermoregulatory behavior.

Thermal Self Stimulation of Nervous Centers

Animals can be trained to press a lever that actuates an electrical stimulus delivered directly in their own brain. This experiment has been replicated with temperature stimuli. Thus rats (Corbit, 1969; Corbit and Ernits, 1974) self-cooled their hypothalamus when it was heated experimentally. This result is difficult to replicate due to the importance of experimental conditions. It is likely that ambient temperature is important; there may also be a warm

but not a cold "sensation" from the brain (Baldwin and Ingram, 1967). However it is certain that animals placed under optimal conditions may behaviorally warm or cool their CNS thermoregulatory centers (Adair, 1977; Cormarèche-Leydier and Cabanac, 1976; Dib, *et al.*, 1982). Should this kind of behavior be considered thermoregulatory? Strictly speaking it is the opposite of regulatory since the animal's very behavior, in changing the temperature of the center, produces an open loop deviation of mean body temperature. However the open loop situation is an artifact created by the experimenter and the regulation inherent in the nervous system works well with its behavioral response. Although the net result is opposite to a stable deep body temperature, the response is a regulatory one aimed at preserving a constant thermodetectors' temperature.

CONCLUSION

The list of natural and artifactual behaviors ~~sketched above is of course incomplete.~~ Its purpose is simply to demonstrate that animals have developed and/or can learn various behavioral ways to control heat exchange between their own body and the environment.

Most behaviors tend to modify the immediate environment of the subject or of its offspring, modifying heat exchange thereby. The main result is survival in good condition for ectotherms and, for endotherms, economy of their autonomic thermoregulatory responses. Food and water intake should not be considered as thermoregulatory behavior, but the search for heat from muscular work or microwave exposure can be considered thermoregulatory behavior. A thermoregulatory behavior is therefore not only modification of the microclimate, but rather a propositional modification of external and/or internal temperatures.

Various thermoregulatory behavioral responses are used by different species according to environmental, ethological, or physiological constraints, as different solutions to the same problem. Any thermoregulatory behavior could be measured to study temperature regulation and motivation; any law described with one behavior would apply to other responses. They are all equivalent but two are specially convenient for the experimenter: temperature gradients and operant conditioning. Tables I and II show that these have been widely used.

The multitude of behavioral responses shows that all animals display thermoregulatory behaviors, thus underscoring

the importance of the problem they face.

REFERENCES

Abushama, F.T. (1964). On the behaviour and physiology of the scorpion *Leiurus quinquestriatus*. *Animal Behav.* 12: 140.

Adair, E.R. (1971). Displacements of rectal temperature modify behavioral thermoregulation. *Physiol. Behav.* 7: 21.

Adair, E.R. (1974). Hypothalamic control of thermoregulatory behavior. In *Recent Studies of Hypothalamic Function* (K. Lederis and K.E. Cooper, eds.), p. 341. Karger, Basel.

Adair, E.R. (1976a). Autonomic thermoregulation in squirrel monkey when behavioral regulation is limited. *J. Appl. Physiol* 40: 694.

Adair, E.R. (1976b). Behavioral temperature regulation in the squirrel monkey: unilateral versus bilateral preoptic thermal stimulation. *Israel J. Med. Sc.* 12: 1033.

Adair, E.R. (1977a). Skin, preoptic and core temperatures influence behavioral thermoregulation. *J. Appl. Physiol.* 42: 559.

Adair, E.R. (1977b). Preference for skin cooling during hypothalamic heating. *Proc. IUPS.* 13: 8.

Adair, E.R. and Adams, B.W. (1980). Microwaves modify thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics.* 1: 1.

Adair, E.R., Casby, J.U. and Stolwijk, J.A.J. (1970). Behavioral temperature regulation in the squirrel monkey: changes induced by shifts in hypothalamic temperature. *J. comp. physiol. Psychol.* 72: 17.

Adair, E.R. and Stitt, J.T. (1971). Behavioral temperature regulation in the squirrel monkey: effects of midbrain temperature displacements. *J. Physiol. (Paris)* 63: 191.

Adair, E.R. and Rawson, R.O. (1974). Autonomic and behavioral temperature regulation. Unilateral vs bilateral preoptic thermal stimulation. *Pflügers Arch.* 352: 91.

Adair, E.R. and Wright, B.A. (1976). Behavioral thermoregulation in the squirrel monkey when response effort is varied. *J. comp. physiol. Psychol.* 90: 179.

Adeyemo, O., Heath, E., Adadevoh, B.K., Steinbach, J. and Olaloku, E.A. (1979). Some physiological and behavioral responses in *Bos indicus* and *Bos taurus* heifers, acclimated to the hot humid seasonal equatorial climate. *Int. J. Biometeor.* 23: 231.

Adolph, E.F. (1969). *Physiology of Man in the Desert.* Hafner Publ. Co., New York.

Alberts, Jr. (1979). Huddling by rat pups: group behavioral mechanisms of temperature regulation and energy conservation. *J. comp. physiol. Psychol.* 92: 231.

Aleksiuk, M. (1977). Cold induced aggregative behavior in the red-sided garter snake (*Thamnopis sirtalis parietalis*). *Herpetologica.* 33: 98.

Alexander, A.J. and Ewer, D.W. (1958). Temperature adaptative behaviour in the scorpion *Opisthophthalmus latimanus* (Koch). *J. Exp. Biol.* 35: 349.

Amos, T.G., Waterhouse, F.L., and Chetham, N.A. (1968). Temporal distribution of *Tribolium castaneum* (Herbst) and *Cadra cautella* (Walker) on temperature gradients. *Experientia* 24: 96.

Andersson, B., Gale, C.C., and Sundsten, J.W. (1963). The relationship between body temperature and food and water intake. In *Olfaction and Taste. Proc. First Intern. Sympos.* (Y. Zotterman, ed.), p. 361 Pergamon Press, Oxford.

Avery, D.D. (1971). Intrahypothalamic adrenergic and cholinergic injection effects on temperature and ingestive behavior in the rat. *Neuropharmacol.* 10: 753.

Avery, D.D. and Penn, P.E. (1973). Effects of intrahypothalamic injections of adrenergic and cholinergic substances on behavioral thermoregulation and associated skin temperature levels in rats. *Pharmacol. Biochem. Behav.* 1: 159.

Baldwin, B.A. (1968). Behavioural thermoregulation in mice. *Physiol. Behav.* 3: 401.

Baldwin, B.A. (1975). The effects of intra-ruminal loading with cold water on thermoregulatory behaviour in sheep. *J. Physiol. (London).* 249: 139.

Baldwin, B.A. and Ingram, D.L. (1967a). Behavioural thermoregulation in pigs. *Physiol. Behav.* 2: 15.

Baldwin, B.A. and Ingram, D.L. (1967b). Effect of heating and cooling the hypothalamus on behavioural thermoregulation in the pig. *J. Physiol. (London).* 191: 375.

Baldwin, B.A. and Ingram, D.L. (1968a). The effects of food intake and acclimatization to temperature on behavioural thermoregulation in pigs and mice. *Physiol. Behav.* 3: 395.

Baldwin, B.A. and Ingram, D.L. (1968b). Factors influencing behavioural thermoregulation in the pig. *Physiol. Behav.* 3: 409.

Baldwin, B.A. and Yates, J.O. (1977). The effects of hypothalamic temperature variation and intracarotid cooling on behavioural thermoregulation in sheep. *J. Physiol. (London)* 265: 705.

Barber, B.J., and Crawford, E.C. Jr. (1977). A stochastic dual-limit hypothesis for behavioral thermoregulation in lizards. *Physiol. Zool.* 50: 53.

Barth, E.K. (1949). Kroppstemperatur hos maakeunger. *Nytt Mag. Naturvidenkapr.* 163: 177.

Bartholomew, G.A. (1956). Temperature regulation in the macropod marsupial *Satonix brachyrus*. *Physiol. Zool.* 29: 26.

Bartholomew, G.A. (1964). The roles of physiology and behaviour in the maintenance of homeostasis in the desert environment. In: *Homeostasis and Feedback Mechanisms. Soc. Exp. Biol.* (Cambridge Univ. Press), 18: 7.

Bartholomew, G.A. (1966). A field study of temperature relations in the Galapagos marine iguana. *Copeia*. 2: 241.

Bartholomew, G.A. and Dawson, W.R. (1979). Thermoregulatory behavior during incubation in Hermann's gulls. *Physiol. Zool.* 52: 422.

Bartholomew, G.A. and Wilke, F. (1956). Body temperature of the northern fur seal. *J. Mammal.* 37: 327.

Bashenina, N.V. and Borovskaja, E.M. (1963). The peculiarity of development of heat regulation in vole during the first month after birth. *Jpyatal Prirody. Otd. Biol.* 68: 34.

Beckman, A.L. (1970). Effect of intrahypothalamic norepinephrine on thermoregulatory responses in the rat. *Am. J. Physiol.* 127: 164.

Beckman, A.L. and Carlisle, H.J. (1969). Intrahypothalamic infusion of acetylcholine in the rat. *Nature*. 221: 561.

Behling, K., Bleichert, A. and Scarperi, M. (1976). Transient responses in behavioral thermoregulation of man. *Israël J. Med. Sci.*12: 1068.

Beitinger, T.L., Magnuson, J.J., Neill, W.H., and Shaffer, W.R. (1975). Behavioural thermoregulation and activity pattern in the green sunfish *Lepomis cyanellus*. *Anim. Behav.* 23: 222.

Bernard, J. (1974). Etude électrophysiologique de récepteurs impliqués dans l'orientation vers l'hôte et dans l'acte hématophage chez un hémiptère: *Triatoma infestans*. Thèse Doct. Sci. Univ. Rennes. 287 p.

Blass, E.M. (1969). Thermoregulatory adjustments in rats after removal of the frontal poles of the brain. *J. comp. physiol. Psychol.* 69: 83.

Blass, E.M. (1971). Effects of frontal pole-area ablation on temperature regulation in the rat. *J. comp. physiol. Psychol.* 74: 233.

Blatteis, C.M. and Smith, K.A. (1979). Hypothalamic sensitivity to leucocytic pyrogen of adult and new-born guinea pigs. *J. Physiol.* 296: 177.

Blatteis, C.M. and Smith, K.A. (1980). Behavioral fever induced in guinea pigs by intrapreoptic pyrogen. *Experientia* 36: 1086.

Bleichert, A., Behling, K., Scarperi, M., and Scarperi, S. (1973). Thermoregulatory behavior of man during rest and exercise. *Pflüg. Arch.* 338: 303.

Blix, A.S. and Lentfer, J.W. (1979). Modes of thermal protection in polar bear cubs - at birth and on emergence from the den. *Am. J. Physiol.* 236: R67.

Blix, A.S. and Steen, J.P. (1979). Temperature regulation in newborn polar homeotherms. *Physiol. Rev.* 59: 285.

Blondel, J. and Frochot, B. (1972). Pourquoi les oiseaux migrent? *La Recherche.* 3: 621.

Boggs, C., Norris, E. and Steen, J.B. (1977). Behavioural and physiological temperature regulation in young chicks of the willow grouse (*Lagopus lagopus*). *Comp. Biochem. Physiol.* 58: 371.

Box, B.M., Montis, F., Yeomans, C. and Stevenson, J.A.F. (1973). Thermogenic drinking in cold acclimated rats. *Am. J. Physiol.* 225: 162.

Boyer, D.R. (1965). Ecology of the basking habit in turtles. *Ecology.* 46: 99.

Bramwell, C.D. and Fellgett, P.B. (1973). Thermal regulation in sail lizards. *Nature.* 242: 203.

Brattstrom, B.H. (1963). A preliminary review of the thermal requirements of amphibians. *Ecology (USA).* 44: 238.

Brück, K. (1968). Which environmental temperature does the premature infant prefer? *Pediatrics.* 41: 27.

Brück, K., Parmelee, A.H. Jr. and Brück, M. (1962). Neutral temperature range and range of thermal comfort in premature infants. *Biol. Neonat. Suisse.* 4: 32.

Bryant, D.M. and Hails, C.J. (1975). Mechanisms of heat conservation in the litters of mice. *Comp. Biochem. Physiol.* 50: 99.

Budgell, P. (1971). Behavioral thermoregulation in the barbary dove (*Streptopelia risoria*). *Anim. Behav.* 19: 524.

Buguet, A.G.C., Livingstone, S.D., Reed, L.D., and Limmer, R.E. (1976). Cold induced shivering in man with thermoneutral skin temperatures. *J. Appl. Physiol.* 41: 142.

Cabanac, H.P. and Hammel, H.T. (1971a). Peripheral sensitivity and temperature regulation in *Tiliqua scincoides*. *Int. J. Biometeor.* 15: 239.

Cabanac, H.P. and Hammel H.T. (1971b). Comportement thermorégulateur du lézard *Tiliqua scincoides*: réponses au froid. *J. Physiol. (Paris)*. 63: 222.

Cabanac, M., Cormarèche-Leydier, M. and Poirier, L.J. (1976a). The effect of capsaicin on temperature regulation of the rat. Pflüg Arch. 366: 217.

Cabanac, M., Chatonnet, J. and Duclaux, R. (1965). Influence de la température centrale sur le choix de l'ambiance thermique chez le chien. *J. Physiol.* 57: 574.

Cabanac, M., Cunningham, D.J. and Stolwijk, J.A.J. (1971). Thermoregulatory set point during exercise: a behavioral approach. *J. comp. physiol. Psychol.* 76: 94.

Cabanac, M., Duclaux, R. and Chatonnet, J. (1966). Influence d'une élévation passive de la température interne sur le comportement thermorégulateur du chien. *J. Physiol. (Paris)*. 58: 214.

Cabanac, M., Duclaux, R. and Gillet, A. (1970). Thermorégulation comportementale chez le chien. Effet de la fièvre et de la thyroxine. *Physiol. Behav.* 5(6): 697.

Cabanac, M., Hildebrandt, G., Massonnet, B. and Strempel, H. (1976b). A study of the nycthemeral cycle of behavioural temperature regulation in man. *J. Physiol. (London)*. 257: 275.

Cabanac, M. and Jeddi, E. (1971). Thermopreferendum et thermorégulation comportementale chez trois poïkilothermes. *Physiol. Behav.* 7: 375.

Cabanac, M. and Le Guelte, L. (1980). Temperature regulation and prostaglandin E_1 fever in scorpions. *J. Physiol. (London)*. 303: 365.

Cabanac, M. and Massonnet, B. (1974). Temperature regulation during fever: change of set point or change of gain? A tentative answer from a behavioural study in man. *J. Physiol. (London)*. 238: 561.

Cabanac, M., Massonnet, B. and Belaiche, R. (1972). Preferred skin temperature as a function of internal and mean skin temperatures. *J. Appl. Physiol.* 33: 699.

Cabanac, M. and Serres, P. (1976). Peripheral heat as a reward for heart rate response in the curarized rat. *J. comp. physiol. Psychol.* 90: 435.

Cachan, P. (1948). Sur le preferendum thermique des insectes. II. Le thermopreferendum du grillon. *Physiol. Comp. Oecol.* 1: 83.

Candas, V., Libert, J.P., Vogt, J.J., Ehrhart, J. and Muzet, A. (1978). Body temperature during sleep under different conditions. In *Proc. Int. Indoor Climate Sympos.* (O. Fanger, ed.) København.

Caputa, M. and Cabanac, M. (1980). Muscular work as thermal behavior in humans. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 48: 1020.

Carlisle, H.J. (1966a). Behavioural significance of hypothalamic temperature sensitive cells. *Nature* 209: 1324.

Carlisle, H.J. (1966b). Heat intake and hypothalamic temperature during behavioral temperature regulation. *J. comp. physiol. Psychol.* 61: 388.

Carlisle, H.J. (1968a). Initiation of behavioral responding for heat in cold environment. *Physiol. Behav.* 3: 827.

Carlisle, H.J. (1968b). Peripheral thermal stimulation and thermoregulatory behavior. *J. comp. physiol. Psychol.* 66: 507.

Carlisle, H.J. (1969a). Effect of fixed ratio thermal reinforcement on thermoregulatory behavior. *Physiol. Behav.* 4: 23.

Carlisle, H.J. (1969b). Effect of preoptic and anterior hypothalamic lesions on behavioral thermoregulation in the cold. *J. comp. physiol. Psychol.* 69(2): 391.

Carlisle, H.J. (1970). Intermittent heat as a reinforcer for rats in the cold. *Physiol. Behav.*5: 581.

Carlisle, H.J. (1971). Fixed ratio polydipsia: thermal effects of drinking pausing and responding. *J. comp. physiol. Psychol.* 75: 10.

Carlisle, H.J. and Ingram, D.L. (1973). The effects of heating and cooling the spinal cord and hypothalamus on thermoregulatory behaviour in the pig. *J. Physiol. (London).* 231: 353.

Carlisle, H.J. and Laudenslager, M.L. (1976). Separation of water and ambient temperature effects on polydipsia. *Physiol. Behav.* 16: 121.

Carlisle, H.J. and Laudenslager, M.L. (1979). Observations on the thermoregulatory effects of preoptic warming in rats. *Physiol. Behav.* 23: 723.

Carlisle, H.J. and Snyder, E. (1970). The interaction of hypothalamic self-stimulation and temperature regulation. *Experientia.* 26: 1092.

Carlton, P.L. and Marks, R.A. (1958). Cold exposure and heat reinforced operant behavior. *Science* 128: 1344.

Carrell, J.E. (1977). Behavioral thermoregulation in an orb-weaving spider. In *Proc. I.U.P.S. XIII*, p. 341.

Casey, T.M. (1976). Activity patterns, body temperature and thermal ecology in two desert caterpillars (Lepidoptera: Sphingidae). *Ecology.* 57: 485.

Casterlin, M.E. and Reynolds, W.W. (1977a). Behavioral fever in crayfish. *Hydrobiologia*. 56: 99.

Casterlin, M.E. and Reynolds, W.W. (1977b). Behavioral fever in anuran amphibian larvae. *Life Sci.* 20: 593.

Casterlin, M.E. and Reynolds, W.W. (1977c). Behavioral thermoregulation in *Rana pipiens* tadpoles. *J. Thermal Biol.* 3: 143.

Casterlin, M.E. and Reynolds, W.W. (1978). Prostaglandin E_1 fever in the crayfish *Cambarus bartoni*. *Pharmacol. Biochem. Behav.* 9: 593.

Casterlin, E.M. and Reynolds, W.W. (1979a). Shark thermoregulation. *Comp. Biochem. Physiol.* 64: 451.

Casterlin, M.E. and Reynolds, W.W. (1979b). Thermoregulatory behavior of the bluespotted sunfish, *Enneacanthus gloriosus*. *Hydrobiologia* 64: 3.

Casterlin, M.E. and Reynolds, W.W. (1979c). Fever induced in marine arthropods by prostaglandin-E_1. *Life Sci.* 25: 1601.

Casterlin, M.E. and Reynolds, W.W. (1980). Fever and antipyresis in the crayfish *Cambarus bartoni*. *J. Physiol. (London)*. 303: 417.

Cena, K. (1964). Thermoregulation in the hippopotamus. *Internat. J. Biometeor.* 8: 57.

Chance, G.W., O'Brien, M.J. and Sawyer, P.R. (1973). Transport of sick neonates, 1972: an unsatisfactory aspect of medical care. *Can. Med. Assoc. J.* 109: 847.

Chauvin, R. (1948). Sur le preferendum thermique des insectes. *Physiol. Comp. Eocol.* 1: 76.

Cheetham, J.L., Garten, C.T., Jr., King, C.L. and Smith, M.H. (1976). Temperature tolerance and preference of immature channel catfish (*Ictalurus punctatus*). *Copeia*. 3: 609.

Clark, W.G. and Lipton, J.H. (1974). Complementary lowering of the behavioral and physiological thermoregulatory set points by tetradotoxin and saxitoxin in the rat. *J. Physiol. (London)*. 238: 81.

Claussen, D.L. (1973). The thermal relations of the tailed frog, *Ascophus truei*, and the Pacific treefrog, *Thyla refilla*. *Comp. Biochem. Physiol.* 44: 137.

Clench, H.K. (1966). Behavioral thermoregulation in butterflies. *Ecology*. 47: 1021.

Cloudsley-Thompson, J.L. (1972). Temperature regulation in desert reptiles. In *Symp. Zool. Soc. London*, London 31: 39.

Corbit, J.D. (1969). Behavioral regulation of hypothalamic temperature. *Science*. 166: 256.

Corbit, J.D. (1970). Behavioral regulation of body temperature. In *Physiological and behavioral temperature regulation* (J.D. Hardy, A.P. Gagge and J.A.J. Stolwijk, eds.), p. 124 Charles C. Thomas, Springfield, IL.

Corbit, J.D. and Ernits, T. (1974). Specific preference for hypothalamic cooling. *J. comp. physiol. Psychol.* 86: 24.

Cormarèche-Leydier, M., Banet, M., Hensel, H. and Cabanac, M. (1977). Thermoregulatory behaviour after repetitive cooling of the preoptic area and the spinal cord in the rat. *Pflüg Arch.* 369: 17.

Cormarèche-Leydier, M. and Cabanac, M. (1973). Influence de stimulations thermiques de la moelle épinière sur le comportement thermorégulateur du chien. *Pflüg Arch.* 341: 313.

Cormarèche-Leydier, M. and Cabanac, M. (1976). Dog behaviour as related to spinal cord temperature. *Experientia.* 32: 66.

Cosnier, J. (1965). Le comportement grégaire du rat d'élevage - Etude éthologique. Thèse Doct. Sci. Univ. Lyon, no. 348.

Cosnier, J., Duveau, A. and Chanel, J. (1965). Consommation d'oxygène et grégarisme chez le rat nouveau-né. *C. R. Soc. Biol.* 159: 1579.

Covert, J B. and Reynolds, W.W. (1977). Survival value of fever in fish. *Nature.* 267: 43.

Cox, B., Green, M.D. and Lomax, P. (1975). Behavioral thermoregulation in the study of drugs affecting body temperature. *Pharmacol. Biochem. Behav.* 3: 1051.

Crawshaw, L.I. (1972). Effects of intracerebral 5-hydroxytryptamine injection on thermoregulation in rat. *Physiol. Behav.* 9: 133.

Crawshaw, L.I. (1974). Temperature selection and activity in the crayfish *Arconectes immunis*. *J. Comp. Physiol.* 95: 315.

Crawshaw, L.I. (1975a). Attainment of the final thermal preferendum in brown bullheads acclimated to different temperatures. *Comp. Biochem. Physiol.* 52A: 171.

Crawshaw, L.I. (1975b). Twenty-four hour records of body temperature and activity in bluegill sunfish (*Lepomis macrochirus*) and brown bullheads (*Ictalurus nebulosus*). *Comp. Biochem. Physiol.* 51A: 11.

Crawshaw, L.I. and Carlisle, J. (1974). Thermo-regulatory effects of electrical brain stimulation. *J. comp. physiol. Psychol.* 87: 440.

Crawshaw, L.I. and Hammel, H.T. (1971). Behavioral thermoregulation in two species of antarctic fish. *Life Sci.* 10: 1009.

Crawshaw, L.I. and Hammel, H.T. (1973). Behavioral temperature regulation in the California Horn Shark *Heterodontus francisci*. *Brain Behav. Evol.* 7: 447.

Crawshaw, L.I. and Hammel, H.T. (1974). Behavioural regulation of internal temperature in the brown bullhead - *Ictalurus nebulosus*. *Comp. Biochem. Physiol.* 47A: 51.

Crawshaw, L.I. and Stitt, J.T. (1975). Behavioural and autonomic induction of prostaglandin E_1 fever in squirrel monkeys. *J. Physiol. (London).* 244: 197.

Croskerry, P.G., Smith, G.K. and Leon, M. (1978). Thermoregulation and the maternal behaviour in the rat. *Nature.* 273: 299.

Cruce, M. (1972). L'influence de la température sur le comportement du lézard *Lacerta taurica* Pall., 1831. *Rev. roumaine. Biol. Zool.* 17: 361.

Cunningham, J.D. (1963). Additional observations on the ecology of the Yosemite Toad *Bufo canorus*. *Herpetologica.* 19: 56.

Dawson, T. (1792). Likely effects of standing and lying on the radiation heat load experienced by a resting kangaroo on a summer day. *Austral. J. Zool.* 20: 17.

Deaux, E. and Engstrom, R. (1973). The temperature of ingested water, its effects on body temperature. *Physiol. Psychol.* 1: 152.

Dejong, A.A. (1979). Thermal irradiation preferences of white-crowned sparrows in relation to ambient temperature. *Physiol. Behav.* 22: 157.

De Witt, C.B. (1967). Precision of thermoregulation and its relation to environmental factors in the desert iguana *Dipsausaurus dorsalis*. *Physiol. Zool.* 40: 49.

De Witt, C.B. (1971). Postural mechanisms in the behavioral thermoregulation of a desert lizard, *Dipsausaurus dorsalis*. *J. Physiol. (Paris).* 63: 242.

Dib, B., Cormarèche-Leydier, M. and Cabanac, M. (1982). Behavioral self warming and cooling of spinal canal by rats. *Physiol. Behav.* 28: 489.

Downey, P., Jahan-Parwar, B. (1972). Cooling as reinforcing stimulus in Aplysia. *Am. Zoologist.* 12: 507.

Duclaux, R. and Cabanac, M. (1971). Effets de la noradrénaline intracérébrale sur le comportement thermorégulateur chez le chien. *J. Physiol. (Paris).* 63: 246.

Duclaux, R., Fantino, M. and Cabanac, M. (1973). Comportement thermorégulateur chez *Rana esculenta*: influence du réchauffement spinal. *Pflüg. Arch.* 342: 347.

Edney, E.B. (1957). *The Survival of Animals in Hot Deserts.* Oxford Univ. Press.

Edwards, D.A., and Roberts, R.L. (1972). Olfactory bulb removal produces a selective deficit in behavioral thermoregulation. *Physiol. Behav.* 9: 747.

Epstein, A.N., and Milestone, R. (1968). Showering as a coolant for rats exposed to heat. *Science.* 160: 895.

Fanger, P.O. (1970). *Thermal Comfort, Analysis and Applications in Environmental Engineering.* p. 244 Danish Technical Press, København.

Fanger, P.O. Højbjerre, J., and Thomsen, J.O.B. (1974). Thermal comfort conditions in the morning and in the evening. *Int. J. Biometeor.* 18: 16.

Fanger, P.O., Breum, N.O., and Jerking, E. (1977). Can colour and noise influence man's thermal comfort? *Ergonomics.* 20: 11.

Fay, F.H. and Ray, C. (1968). Influence of climate on the distribution of Walruses *Odobenus rosmarus L.* I. Evidence for thermoregulatory behavior. *Zoologica.* 53: 1.

Feder, M.E. and Pough, F.H. (1975). Temperature selection by the red-backed salamander *Plethodon c. cinereus* (Green). *Comp. Biochem. Physiol.* 50: 91.

Feyerreisen, P. and Blondiau, C. (1978). Comportements de toilettage et activation chez le rat blanc. *Behaviour.* 65: 99.

Fitzpatrick, L.C., Hughes, J.L. and Venables, B.J. (1978). Relations between preferred body temperatures and metabolic compensation in the rusty lizard *Sceloporus olivaceus. Comp. Biochem. Physiol.* 59: 13.

Fowler, S.J. and Kellog, C. (1975). Ontogeny of thermoregulatory mechanisms in the rat. *J. comp. physiol. Psychol.* 89: 738.

Fraenkel, G. (1929). Untersuchungen über lebensgewohneiten, Sinnesphysiologie und Sozialpsychologie der wandernden Larven der afrikanischen Wanderheuschrecke *Schistocerca gregaria F. Biol. Zentralblatt.* 49: 657.

Fregly, M.J., Barney, C.C., Katovich, M.J. and Miller, E.A. (1979). Effect of water temperature on isoproterenol-induced water intake. *Proc. Soc. Exp. Med.* 160: 359.

Fry, F.E.J. (1964). Animals in aquatic environments: fishes. In *Handbook of physiology sect. IV* (D.B. Dill, ed.) Amer. Physiol. Soc., Washington.

Fryer, J.N. and Ogilvie, D.M. (1978). Alteration of thermoregulatory behavior in fish by 5-hydroxytryptamine. *Pharmac. Biochem. Behav.* 8: 129.

Gagge, A.P., Burton, A.C. and Bazett, H.C. (1941). A practical system of units for the description of the heat exchange of man with his environment. *Science.* 94: 428.

Gagge, A.P., Stolwijk, J.A.J. and Hardy, S.D. (1967). Comfort and thermal sensations and associated physiological responses at various ambient temperatures. *J. Environ. Res.* 1: 1.

Gagge, A.P., Stolwijk, J.A.J. and Nishi, Y. (1971). An effective temperature scale based on a simple model of human physiological regulatory response. *Ashrae Transactions.* 77(part I): 247.

Gale, C.C., Mathews, M. and Young, J. (1970). Behavioral thermoregulatory responses to hypothalamic cooling and warming in baboons. *Physiol. Behav.* 5: 1.

Garrick, L.D. (1979). Lizard thermoregulation: operant responses for heat at different thermal intensities. *Copeia.* 2: 258.

Garside, E.T. and Morrison, G.C. (1977). Thermal preferences of mummichog *Fundulus heteroclitus*, and banded killifish, *F. diaphanus* (Le Sueur), (Cyprinodantidae) in relation to thermal acclimation and salinity. *Can. J. Zool.* 55: 1190.

Gasnier, A. and Mayer, A.R. (1939). Recherches sur la régulation de la nutrition. III. Mécanismes régulateurs de la nutrition et intensité du métabolisme. *Ann. Physiol. (Physiochim. Biol.)* 15: 186.

Gelineo, S. and Gelineo, A. (1952). La température du nid du rat et sa signification biologique. *Bull. Acad. Serbe Sci. IV. Sc. naturelles* 2: 197.

Gingliner, A. and Kayser, C. (1929). Etablissement de la thermorégulation chez les homéothermes au cours du développement. *Ann. Physiol. (Physiochim. Biol.)* 5: 710.

Gold, R.M., Kapatos, G., Prowse, J., Quackenbush, P.M. and Oxford, T.W. (1973). Role of water temperature in the regulation of water intake. *J. comp. physiol. Psychol.* 85: 52.

Gold, R.M., Laforge, R.C., Sawchenko, P.E., Fraser, J.C. and Pytko, D. (1977). Cool water's suppression of water intake: persistence across deprivation conditions, ages, sexes and osmolarities. *Physiol. Behav.* 18: 1047.

Goldman, R.F. (1974). Clothing design for comfort and work performance in extreme thermal environments. *Trans. N.Y. Acad. Sci. Series II.* 36: 531.

Goldsmith, R. and Hampton, I.F.G. (1968). Nocturnal microclimate of man. *J. Physiol. (London).* 194: 32.

Gonzales, R.R. and Nishi, Y. (1976). Effect of cool environments on local thermal sensation, discomfort and clothing selection. *A.S.H.R.A.E. Trans.* 82: 76.

Grace, J.E. and Stevenson, J.A.F. (1971). Thermogenic drinking in the rat. *Am. J. Physiol.* 220: 1009.

Green, M.D. and Lomax, P. (1976). Behavioural thermoregulation and neuroamines in fish. (*Chromus chromus*). *J. Thermal Biol.* 1: 237.

Grenot, C. and Loirat, F. (1973). L'activité et le comportement thermorégulateur du lézard saharien *Uromastix acanthinurus* B. *La Terre et la Vie, Rev. Ecol. Appl.* 27: 435.

Grivel, F. and Fraise, J.P. (1979). Self-adjustment of preferred temperature: "confort thermique." I.N.S.E.R.M., Paris, 75: 79.

Hadley, N.F. (1970). Micrometeorology and energy exchange in two desert arthropods. *Ecology.* 51: 434.

Hadley, N.F. (1974). Adaptational biology of desert scoprions. *J. Arachnology.* 2: 11.

Hainsworth, F.R. (1967). Saliva spreading, activity and body temperature regulation in the rat. *Am. J. Physiol.* 212: 1288.

Hainsworth, F.R. and Stricker, E.N. (1969). Evaporative cooling in the rat: effect of partial desalivation. *Am. J. Physiol.* 217: 494.

Hamilton, C.L. (1959). Effect of food deprivation on thermal behaviour of the rat. *Proc. Soc. Exp. Biol. Med.* 100: 354.

Hamilton, C.L. (1971). Food intake and temperature stress in the monkey. *Proc. Soc. Exper. Biol.* 136: 207.

Hamilton, C.L. and Ciaccia, P.J. (1971). Hypothalamus, temperature regulation and feeding in the rat. *Am. J. Physiol.* 221: 800.

Hamilton, C.L. and Sheriff, J.R. (1959). Thermal behavior of the rat before and after feeding. *Proc. Soc. Exp. Biol. Med.* 102: 746.

Hammel, H.T. (1971). Antarctica's nearer side, cited by Matthews, S.W. and Curtsinger. *Nat. Geo.* 140: 622.

Hammel, H.T., Caldwell, F.T. and Abrams, R.M. (1967). Regulation of body temperature in the blue-tongued lizard. *Science.* 156: 1260.

Hammel, H.T., Strømme, S.B., and Myhre, K. (1969). Forebrain temperature activates behavioral thermoregulatory response in arctic Sculpins. *Science.* 165: 83.

Hardy, J.D. (1971). Thermal comfort and health. *A.S.H.R.A.E. J.* Feb.: 43.

Hayward, J.S., Eckerson, J.D. and Collis, M.L. (1975). Thermal balance and survival time prediction of man in cold water. *Can. Physiol. Pharmacol.* 53: 21.

Hazelhoff, E.H. (1954). Ventilation in a beehive during summer. *Physiol. comp. oecol.* 3: 343.

Heath, J.E. (1964). Head body temperature differences in horned lizards. *Physiol. Zool.* 37: 273.

Heath, J.E., Hanegan, J.L., Wilkin, P.J., and Heath, M.S. (1971). Thermoregulation by heat production and behavior in insects. *J. Physiol. (Paris)*. 63: 267.

Heath, M.E. (1980). Effect of nearing-temperature on the thermoregulatory behavior of pigs. *Behav. Neural Biol.* 28: 193.

Heinrich, B. (1972). Patterns of endothermy in bumblebee queens, drones and workers. *J. Comp. Physiol.* 77: 49.

Heinrich, B. (1981). The regulation of temperature in the honeybee swarm. *Sc. Amer.* 244: 146.

Helmendach, R.H., Dent, H.D. and Brown, E.P. (1965). Observations concerning temperature regulatory mechanisms in the ostrich *Struthio camelus*. *The Physiologist*. 8: 190.

Henwood, K. (1975). Infrared transmittance as an alternative thermal strategy in the desert beetle *Onymacris plana*. *Science*. 189: 993.

Heran, H. (1952). Untersuchungen über den temperatursinn der Honigbiene (*Apis mellifica*) unter gesonderer Berücksichtiqung der Wahrnehmung Strahlender Wärme. *Z. vergl. Physiol.* 34: 179.

Herter, K. (1923). Untersuchungen über den Temperatursinn der Hausgrille (*Achetadomestica L*) und der roten Waldameise (*Formica rufa L*). *Biol. Zentbl.* 43: 282.

Hocking, B. (1971). Blood-sucking behavior of terrestial Arthropods. *Ann. Rev. Ent.* 16: 1.

Horowitz, K.A., Scott, N.R., Hillman, P.E., and Van Tienhoven, A. (1978). Effect of feathers on instrumental thermoregulatory behavior in chickens. *Physiol. Behav.* 21: 233.

Horvath, O. (1964). Seasonal differences in rufous hummingbird nest height and their relation to nest climate. *Ecology*. 45: 235.

Howell, T.R. and Bartholomew, G.A. (1962). Temperature regulation in the sooty tern *Sterna fuscata*. *Ibis*. 104: 98.

Huey, R.B., Pianka, E.R. and Hoffman, J.A. (1977). Seasonal variation in thermoregulatory behavior and body temperature of diurnal Kalahari lizards. *Ecology*. 58: 1066.

Humphreys, R.B., Hawkins, M. and Lipton, J.M. (1976). Effects of anesthetic injected into brainstem sites on body temperature and behavioral thermoregulation. *Physiol. Behav.* 17: 667.

Hutchison, V.H., Black, J.J. and Erskine, O. (1979). Metatonin and chlorpromazine - thermal selection in the mud puppy, *Necturus maculosus*. *Life Sci.* 25: 527.

Hutchinson, V.H., Dowling, H.G. and Vinegar, A. (1966). Thermoregulation in a brooding female Indian python, *Python morulus bivittatus*. *Science* 151: 694.

Hutchison, V.H. and Hill, L.G. (1978). Thermal selection of bullfrog tadpoles (*Rana catesbeiana*) at different stages of development and acclimation temperatures. *J. Therm. Biol.* 3: 57.

Ingram, D.L. (1975). The efficiency of operant thermoregulatory behaviour in pigs as determined from the rate of oxygen consumption. *Pflügers. Arch.* 353: 139.

Ingram, D.L., and Legge, K.F. (1970). The thermoregulatory behavior of young pigs in a natural environment. *Physiol. Behav.* 5: 981.

Ingram, D.L. and Mount, L.E. (1975). *Man and animals in hot environments*, p. 185. Springer-Verlag, Berlin, Heidelberg, New York.

Ingram, D.L. and Stephens, D.B. (1979). The relative importance of thermal, osmotic and hypovolaemic factors in the control of drinking in the pig. *J. Physiol. (London).* 293: 501.

Ingram, D.L., Walters, D.E. and Legge, K.F. (1975). Variations in behavioral thermoregulation in the young pig over 24 hour periods. *Physiol. Behav.* 14: 689.

Ishay, J. (1972). Thermoregulatory pheromones in wasps. *Experientia*. 28: 1185.

Jakubczak, L.F. (1966). Behavioral thermoregulation in young and old rats. *J. Appl. Physiol.* 21: 19.

Jaremovic, R. and Rollo, C.D. (1979). Tree climbing by the snail "*Cepaea nemoralis* (L)": a possible method for regulating temperature and hydration. *Can. J. Zool.* 57: 1010.

Jeddi, E. (1970). Confort du contact et thermorégulation comportementale. *Physiol. Behav.* 5: 1487.

Jeddi, E., Guerin, J.F. and Czyba, J.C. (1977). Have human spermatozoa a thermopreferendum? *Biol. Reproduction.* 16: 561.

Johanson, I.B. (1979). Thermotaxis in neonatal rat pups. *Physiol. Behav.* 23: 871.

Johnson, C.R. (1972). Thermoregulation in pythons I. Effect of shelter, substrate type and posture on body temperature of the Australian carpet python, *Morelia spilotes variegata*. *Comp. Biochem. Physiol.* 43: 271.

Kahl, M.P. (1963). Thermoregulation in the wood stork with special reference to the role of the legs. *Physiol. Zool.* 36: 141.

Kechil, A.A., Richards, S.A. and Sykes, A.H. (1981). An acute drinking response in hens induced by thermal stimuli. *Physiol. Behav.* 27: 73.

Kemp, F.D. (1969). Thermal reinforcement and thermoregulatory behavior in the lizard *Dipsausaurus dorsalis*. *Anim. Behav.* 17: 446.

Kirksey, E.R., Pagels, J.F. and Blem, C.R. (1975). The role of the tail in temperature regulation of the cotton rat, *Sigmodon hispidus*. *Comp. Biochem. Physiol.* 52: 707.

Kleitman, N. and Satinoff, E. (1981). Behavioral responses to pyrogen in cold stressed and starved newborn rabbits. *Am. J. Physiol.* 241: R167.

Kluger, M.J. (1977). Fever in the frog *Hyla cinerea*. *J. Thermal Biol.* 2: 79.

Kluger, M., Tarr, R.S. and Heath, J.E. (1973). Posterior hypothalamic lesions and disturbances in behavioral thermoregulation in the lizard *Dipsausaurus dorsalis*. *Physiol. Zool.* 46: 79.

Kost'Yan, E.Y. (1954). New data on the reproduction of the polar bears. *Zool. Zh.* 33: 207.

Kraft, B. (1967). Thermopreferendum de l'araignée sociale *Agelena Consociata* (Denis). *Insectes Sociaux (Paris)*. 14: 161.

Laties, V.G. and Weiss, B. (1959). Thyroid state and working for heat in the cold. *Am. J. Physiol.* 197: 1028.

Laties, V.G. and Weiss, B. (1960). Behavior in the cold after acclimatization. *Science*. 131: 1891.

Laudenslager, M.L. (1976a). Proportional hypothalamic control of behavioral thermoregulation in the squirrel monkey. *Physiol. Behav.* 17: 383.

Laudenslager, M.L. (1976b). The influence of hypothalamic temperature on some thermoregulatory effects of hypothalamic injections of norepinephrine. *Pharmacol. Biochem. Behav.* 5: 713.

Laudenslager, M.L. and Hammel, H.T. (1977). Environmental temperature selection by the Chukar partridge *Alectoris chukar*. *Physiol. Behav.* 19: 543.

Leeming, E.C. and Crowder, W.F. (1968). Response rate as a function of magnitude and schedule of heat reinforcement. *J. Exper. Psychol.* 76: 74.

Le Maho, Y. (1977). The emperor penguin: a strategy to live and breed in the cold. *Am. Scientist*. 65: 680.

Le Maho, Y., and Delclitte, P. (1974). Evaluation de la dépense énergétique chez le manchot empereur (*Aptenodytes forsteri* G) d'après la décroissance pondérale au cours du jeûne. *C.R. Acad. Sci.* 278: 2189.

Le Maho, Y., Delclitte, P. and Chatonnet, J. (1976). Thermoregulation in fasting emperor penguins under natural conditions. *Am. J. Physiol.* 23: 913.

Le Maho, Y., Goffart, M., Rochas, A., Felbabel, H., and Chatonnet, J. (1981). Thermoregulation in the only nocturnal simian: the night monkey *Aotus trivirgatus*. *Am. J. Physiol.* 240: R156.

Leon, M., Croskerry, P.G. and Smith, G.K. (1978). Thermal control of mother-young contact in rats. *Physiol. Behav.* 21: 793.

Leonard, C.M. (1974). Thermotaxis in golden hamster pups. *J. comp. physiol. Psychol.* 86: 458.

Leonard, C.M. (1978). Maturational loss of thermotaxis prevented by olfactory lesions in golden hamster pups (*Mesocricetus auratus*). *J. comp. physiol. Psychol.* 92: 1084.

Licht, P. (1965). The relation between preferred body temperatures and testicular heat sensitivity in lizards. *Copeia* 4: 428.

Licht, P. and Brown, A.G. (1967). Behavioral thermoregulation and its role in the ecology of the red-bellied newt, *Taricha rivularis*. *Ecology* 48: 598.

Licht, P. and Leitner, P. (1967). Behavioral responses to high temperatures in three species of california bats. *J. Mammology*. 48: 52.

Lillywhite, M.B. (1971). Temperature selection by the bullfrog *Rana catesbeiana*. *Comp. Biochem. Physiol.* 40: 213.

Lindauer, M. (1951). Die temperaturregulierung der Biener bei Stocküberhitzung. *Naturwissenschaften* 38: 308.

Lindauer, M. (1954). Temperaturregulierung and Wasserhaushalt im Bienenstaat. *Z. vergleish. Physiol.* 36: 391.

Lipton, J.M. (1968). Effect of preoptic lesions on heat escape responding and colonic temperature in the rat. *Physiol. Behav.* 3: 165.

Lipton, J.M. (1969). Effects of high fat diets on caloric intake, body weight, and heat-escape responses in normal and hyperphagic rats. *J. comp. physiol. Psychol.* 68: 507.

Lipton, J.M. (1971). Behavioral temperature regulation in the rat: effect of thermal stimulation of the medulla. *J. Physiol. (Paris)*. 63: 325.

Lipton, J.M., Avery, D.D. and Marotto, D.R. (1970). Determinants of behavioral thermoregulation against heat: thermal intensity and skin temperature levels. *Physiol. Behav.* 5: 1083.

Lipton, J.R. and Marotto, D.R. (1969). Effects of desalivation on behavioral thermoregulation against heat. *Physiol. Behav.* 4: 723.

Lustick, S., Battersby, B. and Kelty, M. (1978). Behavioral thermoregulation: orientation toward the sun in herring gulls. *Science*. 200: 81.

Lynch, G.R., Lynch, C.B., Dube, M., and Allen, C. (1976). Early cold exposure: effects on behavioral and physiological thermoregulation in the house mouse, *Mus musculus*. *Physiol. Zool.* 49: 191.

Lynch, C.B. and Possidente, B.P. (1978). Relationships of material nesting to thermoregulatory nesting in house mice (*Mus musculus*) at warm and cold temperatures. *Anim. Behav.* 26: 1136.

Mac Arthur, R.A. and Wang, L.C.H. (1974). Behavioral thermoregulation in the pika *Ochotona princeps*: a field study using radiotelemetry. *Can. J. Zool.* 52: 353.

Martin, C.J. (1903). Thermal adjustment and respiratory exchange in monotremes and marsupials. A study in the development of homeothermism. *Phil. Trans. Roy. Soc. (London)*. B195: 1.

Mayew, W.W. (1963). Temperature preferences of *Sceloporus orcutti*. *Herpetologica*. 19: 217.

McCauley, R.W., Reynolds, W.W. and Huggins, N.J. (1977). Photokinesis and behavioral thermoregulation in adult sea lampreys (*Petromyzon marinus*). *J. Exper. Zool.* 202: 431.

McCue, J.F. and Thorson, R.F. (1964). Behavior of parasitic helminth in thermal gradient. *J. Parasitol.* 50: 67.

McEwen, G.N. and Heath, J.E. (1973). Resting metabolism and thermoregulation in the unrestrained rabbit. *J. Appl. Physiol.* 35: 884.

McFarland, D.J. and Budgell, P.W. (1970). Determination of a behavioural transfer functions by frequency analysis. *Nature*. 226: 966.

McGinnis, S.M. and Dickson, L.L. (1967). Thermoregulation in the desert iguana *Dipsausaurus dorsalis*. *Science*. 156: 1757.

Mendelssohn, M. (1895). Ueber den Thermotropismus einzelliger Organismen. *Arch. ges Physiol.* 60: 1.

Miller, D.C. and Vernberg, F.J. (1968). Some thermal requirements of Fiddler Crabs of temperate and tropical zones and their influence on geographic distribution. *Amer. Zool.* 8: 459.

Morhardt, J.E. and Molt, P. (1975). Body temperatures and heart rates of laboratory rats and belding squirrels (*Spermophilus beldingi*) during behavioral thermoregulation. *Comp. Biochem. Physiol.* 52: 701.

Motil, K.J. and Blackburn, M.G. (1973). Temperature regulation in the neonate - A survey of the pathophysiology of thermal dynamics and of the principles of environmental control. *Clin. Pediatr.* 12: 634.

Mount, L.E. (1963). Environmental temperature preferred by the young pig. *Nature.* 199: 1212.

Mount, L.E. (1968). *The climatic physiology of the pig.* Edward Arnold, London.

Murakami, H. and Kinoshita, K. (1977). Spontaneous activity and heat avoidance of mice. *J. Appl. Physiol.* 43: 573.

Murgatroyd, D. and Hardy, J.D. (1970). Central and peripheral temperatures in behavioral thermoregulation of the rat. In *Physiological and Behavioral Temperature Regulation.* (J.D. Hardy, A.P. Gagge and J.A.J. Stolwijk, eds.) p. 874. Chas. C. Thomas, Springfield, Illinois.

Muzet, K., Ehrhart, J., Libert, J.P. and Candas, V. (1978). The effect of thermal environment on sleep stages. In *Proc. Int. Indood Climate Sympos.* (O. Fanger, ed.) København, Denmark.

Myhre, K., Cabanac, M. and Myhre, G. (1975). Thermoregulatory behavior and body temperature in chicks of willow grouse (*Lagopus lagopus lagopus) Poultry Sci.* 5: 1174.

Myhre, K., Cabanac, M. and Myhre, G. (1977). Fever and behavioural temperature regulation in the frog *Rana esculenta. Acta Physiol. Scand.* 101: 219.

Myhre, K. and Hammel, H.T. (1969). Behavioral regulation of internal temperature in the lizard *Tiliqua scincoides. Am. J. Physiol.* 217: 1490.

Naulleau, G. and Marques, M. (1973). Etude biotélémétrique préliminaire de la thermorégulation de la digestion chez *Vipera aspis. C.R. Acad. Sc. (Paris).* 276D: 3433.

Neill, W.H., Magnuson, I.J. and Chipman, G.G. (1972). Behavioral thermoregulation by fishes: a new experimental approach. *Science* 176: 1443.

Nelson, D.O. and Prosser, C.L. (1979). Effect of preoptic lesions on behavioral thermoregulation of green sunfish, *Lepomis cyanellus* and of goldfish, *Carassius auratus. J. Comp. Physiol.* 129: 193.

Nelson, E.L., Fregly, M.J., and Tyler, P.E. (1975). Peripheral body temperature and thermogenic drinking in cold treated rats. *J. Appl. Physiol.* 39: 965.

Nishi, Y. and Gagge, A.P. (1974). A psychrometric chart for graphical prediction of comfort and heat tolerance. *A.S.H.R.A.E. Trans.* 80: 115.

Nishi, Y. and Gagge, A.P. (1977). Effective temperature scale useful for hypo and hyperbaric environments. *Aviat. Space Environment. Med.* 48: 97.

Odell, D.K. (1974). Behavioral thermoregulation in the California sea lion. *Behav. Biol.* 10: 231.

Ogilvie, D.M. and Fryer, J.N. (1971). Effect of sodium pentobarbital on the temperature selection response of guppies (*Poecilia reticulata*). *Can. J. Zool.* 49: 949.

Ogilvie, D.M. and Stinson, R.H. (1966). Temperature selection in *Peromyscus* and laboratory mice *Mus musculus*. *J. Mammal.* 47: 655.

Olesen, S., Bassing, J.J. and Fanger, P.O. (1972). Physiological comfort conditions at sixteen combinations of activity, clothing, air velocity and ambient temperature. *A.S.H.R.A.E. Trans.* 78 Part II: 2254.

Olesen, S. and Fanger, P.O. (1971). Can man be adapted to prefer a lower ambient temperature? In *Proc. 5th. Internat. Congress for Heating Ventilating and Air Condition* København 1: 27.

Panuska, J.A. and Popovic V. (1963). Learning in hypothermic rats. *J. Appl. Physiol.* 18: 1016.

Patterson, J.W. and Davis, P.M.C. (1978). Preferred body temperature; seasonal and sexual differences in the lizard *Lacerta vivipara*. *J. Thermal Biol.* 3: 39.

Paul, G.L., Eriksen, C.W. and Humphreys, L.G. (1962). Use of temperature stress with cool air reinforcement for human operant conditioning. *J. Exp. Psychol.* 64: 329.

Pilters-Gauthier, H. (1961). Observations sur l'écologie du dromadaire dans le Sahara nord occidental. *Mammalia* 25: 195.

Pister, J.D., Jobin, M. and Gale, C.C. (1967). Behavioral responses to anterior hypothalamic cooling in unanesthetized baboon. *Physiologist* 10: 279.

Polk, D.L. and Lipton, J.M. (1975). Effects of sodium salicylate, aminopyrine and chlorpromazine on behavioral temperature regulation. *Pharmacol. Biochem. Behav.* 3: 167.

Prosser, C.L. (1973). Temperature. In *Comparative Animal Physiology* 3rd Edition (C.L. Prosser, ed.) Chap. 9, Saunders, Philadelphia, London, Toronto.

Rapaport, A. (1971). Utilisation du conditionnement instrumental dans la boîte de Skinner comme test d'adaptation à l'hyperthermie ambiance chez le jeune rat. *C. R. Soc. Biol. Fr.* 165: 2272.

Rapaport, A. (1972). Du conditionnement instrumental à l'adaptation en milieu hyperthermique chez le rat. *J. Physiol. (Paris).* 65: 291.

Rautenberg, W., May, B. and Arabin, G. (1980). Behavioral and autonomic temperature regulation in competition with food intake and water balance of pigeons. *Pflügers Arch.* 384: 253.

Ray, C. and Smith, M.S.R. (1968). Thermoregulation of the pup and adult Weddell seal, *Leptonychotes wedelli* (Lesson), in antarctica. *Zool.* 33: 53.

Regal, P.J. (1966). Thermophilic response following feeding in certain reptiles. *Copeia* 3: 588.

Regal, P.J. (1967). Voluntary hypothermia in reptiles. *Science.* 155: 1551.

Regal, P.J. (1971). Long term studies with operant conditioning techniques of temperature regulation patterns in reptiles. *J. Physiol.* (Paris) 63: 403.

Revusky, S.H. (1966). Cold acclimatization in hairless mice measured by behavioural thermoregulation. *Psychonom. Sci.* 6: 209.

Reynolds, W.W. (1977). Fish orientation behavior: an electronic device for studying simultaneous responses to two variables. *J. Fish. Res. Board. Can.* 34: 300.

Reynolds, W.W. and Casterlin, M.E. (1978a). Behavioral thermoregulation and diel activity in white sucker (*Catostomus commersoni*). *Comp. Biochem. Physiol.* 49: 261.

Reynolds, W.W. and Casterlin, M.E. (1978b). Ontogenetic change in preferred temperature and diel activity of the yellow bullhead, *Ictalurus natalis. Comp. Biochem. Physiol.* 59: 409.

Reynolds, W.W. and M.E. Casterlin. (1978c). Behavioral thermoregulation in the rock bass, *Ambloplites rupestris. Comp. Biochem. Physiol.* 60: 263.

Reynolds, W.W. and Casterlin, M.E. (1979). Thermoregulatory rhythm in juvenile muskellunge *Esox masquinongy*: evidence of a diel shift in the lower set-point. *Comp. Biochem. Physiol.* PTA. 63: 523.

Reynolds, W.W., Casterlin, M.E. and Covert, J.B. (1976a). Behavioural fever in teleost fishes. *Nature* 259: 41.

Reynolds, W.W., Casterlin, M.M. and Covert, J.B. (1977). Febrile responses of bluegill (*Lepomis macrochirus*) to bacterial pyrogens. *J. Thermal Biol.* 3: 129.

Reynolds, W.W., Casterlin, M.E. and Millington, S.T. (1978a). Circadian rhythm of preferred temperature in the bowfin *Amia calva*, a primitive holostean fish. *Comp. Biochem. Physiol.* 60: 107.

Reynolds, W.W., Casterlin, M.E., Matthey, J.K., Millington, S.T. and Ostrowskia, C. (1978b). Diel patterns of preferred temperature and locomotor activity in the goldfish *Carassius auratus*. *Comp. Biochem. Physiol.* 59: 225.

Reynolds, W.W., Covert, J.B. and Casterlin, M.E. (1978c). Febrile responses of goldfish *Carassius auratus* (L.) to *Aeromona hydrophila* and to *Escherichia coli* endotoxin. *J. Fish Diseases*. 1: 271.

Reynolds, W.W., McCauley, R.W., Casterlin, M.E. and Crawshaw, L.I. (1976b). Body temperatures of behaviorally thermoregulating largemouth black bass (*Micropterus salmoides*). *Comp. Biochem. Physiol.* 54A: 467.

Rising, J.D. and Armitage, K.B. (1969). Acclimation to temperature by the terrestrial gastropods, *Limax maximus* and *Philomycus carolianus*: oxygen consumption and temperature preference. *Comp. Biochem. Physiol.* 30: 1091.

Roberts, W.W., Mooney, R.D. and Martin, J.R. (1974). Thermoregulatory behaviors of laboratory rodents. *J. comp. physiol. Psychol.* 86: 693.

Robinson, J.J. and Hammel, H.T. (1967). Behavioral thermoregulation in response to heating and cooling of the hypothalamic preoptic area of the dog. Report AMRL - TR -67-144., Wright Patterson A.F.B., Ohio.

Rogers, A.F. (1973). Antarctic climate, clothing and acclimatization. In *Polar Human Biology* (O.G. Edholm and E.K.E. Gunderson, eds.). p. 265. William Heinemann Medical Books Ltd.

Rohles, F.H. Jr. (1974). The measurement and prediction of thermal comfort. *A.S.H.R.A.E. Trans.* 80: 98.

Roland, C. (1969). Rôle de l'involucre et du nourissement au sucre dans la régulation thermique a l'intérieur d'un nid de Vespides. *C. R. Acad. Sc. Paris)*. 269(Série D): 914.

Ross, J., Powles, P.M. and Berrill, M. (1977). Thermal selection and related behavior in larval yellow perch (*Perca flavescens*). *Canad. Field Naturalist*. 91: 406.

Rozin, P.N. and Mayer, J. (1961). Thermal reinforcement and thermoregulatory behavior in the Goldfish, *Carassius auratus*. *Science*. 134: 942.

Rudiger, W. and Seyer, G. (1965). Lateralisation of cortico-hypothalamic relations as revealed by thermosensitive behaviour in the rat. *Physiol. Biochem.* 14: 515.

Rudiger, W. and Seyer, G. (1968). Thermosensitive barpressing behavior of the rat with unilateral lesion in the hypothalamus and during cortical spreading depression. *Acta Biol. Exp (Varsovie)* 28: 375.

Sabourin, M., Deschambault, A. and Ducharme, R. (1973). Effect of light on thermal reinforcement in behavioral thermoregulation. Perceptual and Motor Skills. 37: 611.

Sabourin, M. and Ducharme, R. (1973). L'activité instrumentale de thermorégulation et le rythme cardiaque du rat albino. *Can. J. Psychol.* 27: 103.

Satinoff, E. (1964). Behavioral thermoregulation in response to local cooling of the rat brain. *Am. J. Physiol.* 206: 1389.

Satinoff, E. (1977). Quinine induced hypothermia in cold exposed rats. *Pharmacol. Biochem. Behav.* 6: 539.

Satinoff, E. and Cantor, A. (1975). Intraventricular norepinephrine and thermoregulation in rats. In *Temperature regulation and drug action* (J. Lomax, E. Schönbaum and J. Jacob, eds.). p. 103. Karger, Basel.

Satinoff, E., McEwen, G.N. Jr. and Williams, B.A. (1976). Behavioral fever in newborn rabbits. *Science.* 193: 1139.

Satinoff, E. and Rutstein, J. (1970). Behavioral thermoregulation in rats with anterior hypothalamic lesions. *J. comp. physiol. Psychol.* 71: 77.

Satinoff, E. and Shan, S.S.Y. (1971). Loss of behavioral thermoregulation after lateral hypothalamic lesions in rats. *J. comp. physiol. Psychol.* 77: 302.

Saint-Girons, H. and Saint-Girons, M.C. (1956). Cycle d'activité et thermorégulation chez les reptiles (lézards et serpents). *Vie et milieu* 7: 133.

Scarperi, M., Behling, K. and Bleichert, A. (1975). Investigation on the possible role of a work factor in thermoregulatory behavior of man. *Pflüg Arch.* 357: 267.

Scarperi, M., Behling, K. and Bleichert, A. (1976). Investigation on the possible role of a work factor in human behavioral thermoregulation. *Isr. J. Med. Sci.* 12: 1065.

Schmidt, I. (1976). Effect of central thermal stimulation on the thermoregulatory behavior of the pigeon. *Pflügers Arch.* 363: 271.

Schmidt, I. (1978). Behavioral and autonomic thermoregulation in heat stressed pigeons modified by central thermal stimulation. *J. Comp. Physiol.* 127: 75.

Schmidt, I. (1978). Interactions of behavioral and autonomic thermoregulation in heat stressed pigeons. *Pflügers Arch.* 374: 47.

Schmidt, I. and Rautenburg, W. (1975). Instrumental thermoregulatory behavior in pigeons. *J. Comp. Physiol. A.* 101: 225.

Schmidt, I. and Simon E. (1979). Interaction of behavioral and autonomic thermoregulation in cold exposed pigeons. *J. Comp. Physiol. A.* 133: 151.

Schmidt-Nielsen, K., Dawson, T.J., Hammel, H.T., Hinds, D. and Jackson, D.C. (1965). The Jack Rabbit - a study in its desert survival. *Hvalraadet: Skrift.* 48: 125.

Scholander, P.F., Andersen, K.L., Krog, J., Lorentzen, F.V. and Steen, J. (1957). Critical temperature in Lapps. *J. Appl. Physiol.* 10: 231.

Scholander, P.F., Hammel, H.T., Hart, J.S., LeMesurier, D.H. and Steen, J. (1958). Cold adaptation in Australian Aborigines. *J. Appl. Physiol.* 13: 211.

Scholander, P.F., Hock, R., Walters, V. and Irving, L. (1950). Heat regulation in some arctic and tropical mammals and birds. *Biol. Bull.* 99: 237.

Scott, D.M. and Blackwood, V. (1973). Response latencies of rats during behavioral thermoregulation. *Percept. Psychophys.* 14: 531.

Sergeant, D.E. (1973). Biology of the white whales in Western Hudson Bay. *J. Fish. Res. Board Can.* 30: 1065.

Seymour, R.S. and Vinegar, A. (1973). Thermal relation water loss and oxygen consumption of a North American tarantula. *Comp. Biochem. Physiol.* 4A: 83.

Shelford, V.E. and Powers, E.B. (1915). An experimental study of the movements of herring and other marine fishes. *Biol. Bull.* 28: 315.

Sherry, D.F. (1981). Parental care and the development of thermoregulation in Red Junglefowl. *Behaviour* 76: 250.

Shitzer, A., Rasmussen, E.G. and Fanger, P.O. (1978). Human responses during recovery from heat stress with relation to comfort. *Ergonomics.* 21: 21.

Shkolnik, A., Taylor, C.R., Finch, V. and Borut, A. (1980). Why do Bedouins wear black robes in hot deserts? *Nature* 283: 373.

Smith, E.N. (1975). Thermoregulation of the American Alligator, *Alligator mississippiensis. Physiol. Zool.* 48: 177.

Soulé, M. (1963). Aspects of thermoregulation in nine species of lizards from Baja California. *Copeia* 1: 107.

Spellerberg, I.F. (1972). Thermal ecology of allopatric lizards (*Sphenomorphus*) in Southeast Australia. III. Behavioural aspects of thermoregulation. *Oecologia. Allem.* 11: 1.

Spiers, D.E., McNabb, R.A. and McNabb, F.M.A. (1974). The development of thermoregulatory ability, heat seeking activities and thyroid function in hatching Japanese quail (*Coturnix coturnix japonica*). *J. Comp. Physiol.* 89: 159.

Spotila, J.R., Terpin, K.M. and Dodson, P. (1977). Mouth gaping as an effective thermoregulatory device in alligators. *Nature.* 265: 235.

Stanier, M.W. (1975). Effect of body weight, ambient temperature and huddling on oxygen consumption and body temperature in young mice. *Comp. Biochem. Physiol.* 51: 79.

Steen, I. and Steen, J.B. (1965). Thermoregulatory importance of the beaver's tail. *Comp. Biochem. Physiol.* 15: 267.

Stern, S., Margolin, L., Weiss, B., Lu, S.-T. and Michaelson, S.M. (1979). Microwaves: effect on thermoregulatory behavior in rats. *Science* 206: 1198.

Stewart, G.R. (1964). Thermal ecology of the garter snakes (*Thamnophis sirtalis consinnus* (Hallowell) and *Thamnophis ordinoides*). Dissert. Abstr. 25(3): 2116.

Stitt, J.T., Adair, E.R., Nadel, E.R. and Stolwijk, J.A.J. (1971). The relation between behavior and physiology in the thermoregulatory response of the squirrel monkey. *J. Physiol.* (Paris). 63: 424.

Stolwijk, J.A.J. (1970). Thermal loads in lunar ambulation. *Aerospace Med.* 41: 1266.

Stricker, E.M., Everett, J.C. and Porter, R.E.A. (1968). The regulation of body temperature by rats and mice in the heat: Effects of desalivation and the presence of a water bath. *Comm. Behav. Biol.* 2:113.

Stricker, E.M. and Hainsworth, F.R. (1970). Evaporative cooling in the rat: Effects of hypothalamic lesions and chorda tympani damage. *Can. J. Physiol. Pharmacol.* 48: 11.

Strømme, S.B., Myhre, K. and Hammel, H.T. (1971). Forebrain temperature activates behavioral thermoregulatory response in arctic sculpins. *J. Physiol. (Paris).* 63: 433.

Stussi, T. (1967). Thermogénèse de l'abeille et ses rapports avec le niveau thermique de la ruche. Thèse Doctorat Etat. Lyon 378p.

Tertil, R. (1972). The effect of behavioural thermoregulation on the daily metabolism of *Apodemus agravius*. *Acta Theriol. Pologne* 17: 295.

Tester, J.R. and Breckenridge, W.J. (1964). Winter behaviour patterns of the Manitoba toad *Bufo hemiophrys*, in northwestern Minnesota. Ann. *Acad. Sci. Fennicae.* 71(Series A): 423.

Theberge, J.B. and West, G.C. (1973). Significance of brooding to the energy demands of Alaskan rock ptarmigan chicks. *Arctoc* 26: 138.

Thompson, A.B. (1972). A time-sharing computer program for defining human thermal comfort conditions in any atmosphere. In *Environ. control life support syst. conf., San Francisco.* A.S.M.E., New York, 33: 1.

Toth, D. (1973). Temperature regulation and salivation following preoptic lesions in the rat. *J. comp. physiol. Psychol.* 82: 480.

Tracy, C.R., Tracy, B.J. and Dobkin, D.S. (1979). The role of posturing in behavioral thermoregulation by black dragons (*Hageruis brevistylus* Selys, Ordonata). *Physiol. Zool.* 52: 565.

Ulvestad, D.A. and Zar, J.H. (1977). Preferred temperature of the common shiner, *Notropis cornutus*, in relation of age, size, season, and nutritional state. *Ohio J. Sci.* 77: 170.

Van Zoeren, J.G. and Stricker, E.M. (1977). Effects of preoptic, lateral hypothalamic, or dopamine depleting lesions on behavioral thermoregulation in rats exposed to the cold. *J. comp. physiol. Psychol.* 91: 989.

Vaughan, J.M., Stewart, J.M., Van Rensburg, A.J. (1977). Surface areas for calculating heat transfer from nude and clothed men. *Proc. Int. Union Physiol. Sci.* 13: 782.

Vaughn, L., Bernheim, H.A. and Kluger, M.J. (1974). Fever in the lizard *Dipsausaurus dorsalis*. *Nature.* 252: 473.

Viaud, G. (1955). Le thermopreferendum et les thermotropismes. In *Le Comportement des Homéothermes vis-à-vis du Stimulus Froid*. p. 35 Coll. Nat. CNRS Strasbourg.

Villardebo, A. (1948). Sur le preferendum thermique des insectes. II Sur l'évaluation de l'activité du grillon (*Grylluluus domesticus* L.) en fonction de la température, à l'aide du thermoactographe. *Physiol. Comp. Oecol.* 1: 86.

Vogt, J.J., Foehr, R., Kuntzinger, E., Seywert, L., Libert, J.P., Candas, V. and Van Peteghem, T. (1977). Improvement of the working conditions at blast-furnaces. *Ergonomics* 20: 167.

Wagener, J.W. (1973). Self stimulation of preoptic and lateral hypothalamus during behavioral thermoregulation in the albino rat. *J. comp. physiol. Psychol.* 84: 652.

Wakeman, K.A., Donovick, P.J. and Burright, R.G. (1970). Septal lesions increase bar pressing for heat in animals maintained in the cold. *Physiol. Behav.* 5: 1193.

Warburg, M.R. and Ben-Horin, A. (1981). The response to temperature gradients of scorpions from mesic and xeric habitats. *Comp. Biochem. Physiol. A. Comp. Physiol.* 68: 277.

Wasserman, E.A., Hunter, N.B., Gutowski, K.A. and Bader, S.A. (1975). Autoshaping chicks with heat reinforcement: the role of stimulus-reinforcer and response-reinforcer relations. *J. Exp. Psychol.* 104: 158.

Weiss, B. (1957). Thermal behaviour of the subnourished and pantothenic acid-deprived rat. *J. comp. physiol. Psychol.* 50: 481.

Weiss, B. and Laties, V.G. (1960). Magnitude of reinforcement as a variable in thermoregulatory behavior. *J. comp. physiol. Psychol.* 53: 603.

Weiss, B. and Laties, V.G. (1961). Behavioral thermoregulation. *Science* 133: 1338.

Weiss, B., Laties, V.G. and Weiss, A. B. (1967). Behavioral thermoregulation by cats with pyrogen-induced fever. *Arch. Int. Pharmacodyn.* 165: 467.

Wever, R. (1974). The influence of self controlled changes in ambient temperature on autonomous circadian rhythms in man. *Pflügers Arch.* 352: 257.

White, F.N. and Kinney, J.L. (1974). Avian incubation. *Science* 186: 107.

Whittow, G.C. (1970). *Comparative physiology of thermoregulation. Vol. I Invertebrates and nonmammalian vertebrates.* Academic Press, New York and London.

Wilmore, D.W., Orcutt, T.W., Mason, A.D. and Pruitt, B.A. (1975). Alterations in hypothalamic function following thermal injury. *J. Trauma* 15: 697.

Withers, P.C. and Jarvis, J.U.M. (1980). The effect of huddling on thermoregulation and oxygen consumption for the naked mole-rat. *Comp. Biochem. Physiol.* 66: 245.

Yeh, S.D.J. and Weiss, B. (1963). Behavioral thermoregulation during vitamin B_6 deficiency. *Am. J. Physiol.* 205: 857.

Yehuda, S. and Wurtman, R.J. (1974). Paradoxical effects of d-amphetamine on behavioral thermoregulation: possible mediation by brain dopamine. *J. Pharmacol. Exper. Therap.* 190: 118.

Yori, J.G. (1978). Active one-way avoidance to a heat aversive stimulus in tegu lizards (*Tupinambus teguixen*). *Behav. Biol.* 23: 100.

CHANGES IN THERMOREGULATORY BEHAVIOR DURING MICROWAVE IRRADIATION

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Voluntary behavioral action is an organism's first defense against exogenous thermal challenge. Endotherms and ectotherms alike use behavioral strategies whenever possible to counteract inhospitable alterations in the exchange of thermal energy between their bodies and the environment. Ordinarily, temperature sensors in the skin are activated when environmental temperature changes, and information from these sensors is relayed to the central integrator or controller, thereby providing an error signal that initiates a behavioral thermoregulatory response. As demonstrated in Chapter 17, responses as diverse as the thermotropisms of unicellular organisms and the complex behavior-plus-technology of man's lunar walk share a common purpose--that of providing a hospitable microclimate so that the internal body temperature may be regulated with precision at a characteristic (neutral) level. For ectothermic species, these behaviors represent most of the thermoregulatory response available to the organism. For endothermic species, these behaviors ensure minimal involvement of innate mechanisms of heat production and heat loss during thermoregulation, thus conserving the body's energy stores and water.

Exposure to nonionizing electromagnetic radiation at microwave frequencies (30-30,000 MHz), and at power densities well above natural background levels, may provide an unusual condition that the thermoregulatory system (*cf.* Chapter 7) is poorly designed to handle. Frequencies at or near whole-body resonance for a particular biological target would provide a "worst case" wherein thermalizing energy could be deposited directly in deep body tissues, bypassing the peripheral thermodetectors. Meager or delayed activity

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in the peripheral sensory apparatus could lead to impaired appreciation of potentially-inhospitable thermal conditions and delayed or inappropriate thermoregulatory behavior. Such conditions have been likened (cf. Chapters 11 and 17) to those that obtained in experiments by Corbit and his collaborators (1969; 1974) and others (Adair, 1977a & b; Cormarèche-Leydier and Cabanac, 1976; Dib, *et al.*, 1982) that were designed to probe thermal sensations arising in hypothalamic and other thermosensitive tissue. It is interesting to note that formidable difficulties were encountered by some of these investigators as they attempted to train experimental animals to regulate hypothalamic temperature directly. These difficulties imply that even though a particular neural tissue may contain thermodetectors (i.e., be thermosensitive), temperature changes in that tissue will not necessarily be sensed or appreciated directly by the animal.

Against this background, what do we know of changes in various thermoregulatory behaviors when a source of nonionizing radiation is introduced into the organism's environment? What we know depends upon the specific question we ask, or, more accurately, the specific thermoregulatory behavior paradigm we consider. Table I shows two basic paradigms, designated 1 and 2. In case 1, the animal is engaged in some behavior, either an instinctive behavior or a learned operant response, by which it manipulates conventional radiant or convective climate-conditioning sources. This activity provides a thermally-comfortable environment and allows the animal to maintain thermal balance. At some point in time, a microwave field intrudes upon this ongoing behavior. Under the assumption that the microwave field is of sufficient duration and intensity to disturb the thermal balance of the animal, what are the rules that govern the changes in the animal's behavior?

In the second case, the microwave field is made available to the animal for its direct manipulation, i.e., it may be utilized by the animal as a heat source to achieve thermal balance. Either the field exists as part of the complex thermal environment and the animal orients around it, or the animal learns to control the field directly, i.e., turn it on and off. Once again, what are the rules that govern changes in the animal's behavior? In all cases, while collecting data to derive these rules, the animal itself is used as a null instrument; an absence of change in internal body temperature in the presence of a microwave field indicates that changes in the animal's behavior have maintained thermal homeostasis.

TABLE I. BEHAVIOR PARADIGMS

1. MICROWAVE FIELD INTRUDES UPON ONGOING BEHAVIOR, DISTURBING THERMAL BALANCE.
A. Instinctive escape and avoidance behavior (Thermoregulatory?)
B. Learned operant control of environmental temperature.
2. MICROWAVE FIELD UTILIZED DIRECTLY AS HEAT SOURCE TO ACHIEVE THERMAL BALANCE.
A. Instinctive approach behavior in thermal gradiant incorporating microwave source.
B. Learned operant control of microwave source.

It is important to note that under both basic paradigms in Table I there can be both instinctive and learned behaviors. The instinctive behaviors are in fact extremes on an approach-avoidance continuum. If the environment is cold and the microwave source is strategically located, an experimental animal may well bask in the radiation. On the other hand, escape from and avoidance of a microwave field, particularly a field of high intensity, are also instinctive behaviors, as discussed in Chapter 10. While the basis for such escape responses may be a desire to maintain thermal homeostasis, specific thermoregulatory responses (e.g., sweating, panting, saliva spreading, or even body temperatures) have not as a rule been monitored during experimental investigations of escape behavior. Thus, it is difficult to classify these behaviors as thermoregulatory in the traditional sense. With the exception of one recent pilot study (see below), investigations of instinctive escape behaviors will not be discussed further in the present chapter. However, those who undertake study of such behavior in the future are urged to make every effort to assess the total thermal environment impinging upon the animal and the thermoregulatory consequences of the response under scrutiny. Only with such data in hand will it be possible to quantify the thermal basis for escape and avoidance responses, or lack of same as the case may be.

The first paradigm in Table I is the one about which we know the most; i.e., the animal learns to control conventional sources of thermal energy to provide an acceptable microclimate for itself, and then is exposed to a microwave

source. The animal's behavior will change in predictable ways that are directly related to the intensity and duration of the microwave exposure.

Stern and his colleagues (1979) were among the first to probe some of these fundamental relationships. They trained shaved rats in a 5 °C environment to press a lever for 2-sec bursts of heat from an infrared lamp. The animal worked inside a Styrofoam compartment that was located under a horn antenna inside an electrically anechoic chamber. After behavioral training, each rat was exposed for 15-min periods to 2450 MHz (12.3 cm wavelength) continuous-wave (CW) microwaves at power densities of 5, 10, and 20 mW/cm^2. Both ascending and descending power density series were presented, with individual microwave exposures separated by a 15-min. control period with no microwaves present.

Stern, *et al.* found that the presence of the microwave field stimulated the rats to work for less infrared heat, even at the lowest power density. A reliable reduction in bar pressing rate appeared quickly whenever the microwaves were turned on, reversed when the microwaves were extinguished. Further, the higher the power density, the less infrared heat was demanded by the rats. A summary of the results of this experiment appears in Figure 1, which shows for all animals the ratio of bar presses for infrared heating during microwave exposure to the bar presses in the control period immediately preceding that microwave exposure. This metric, designated the "infrared-selection ratio", varies in linear fashion with power density. In other words, as more thermalizing energy is supplied by the microwave field, less infrared heat is required for thermal comfort in a cold environment. Although Stern did not monitor the rats' body temperatures during his experiments, he assumed from a few spot checks of rectal temperature that the animals were achieving thermal balance by appropriate adjustments in thermoregulatory behavior. Use of only three power densities did not permit Stern to determine a precise threshold for a change in thermoregulatory behavior; however, the results showed that a rate of energy deposition (SAR) equivalent to 15 to 20% of the resting heat production of the rat interrupted ongoing thermoregulatory behavior reliably.

A somewhat different approach to the study of similar problems has been taken in the author's laboratory. In the belief that the environmental temperature selected by the animal and the skin and deep body temperatures achieved thereby are vital supporting data to any study of thermoregulatory behavior, we designed experiments to measure these variables. The subjects were adult male squirrel

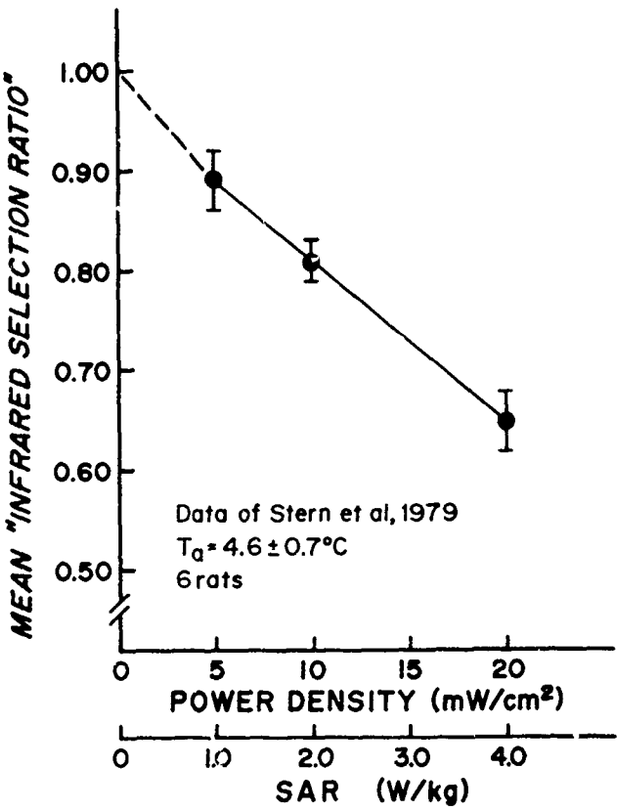

Figure 1. Mean reduction in operant responding for infrared heat exhibited by 6 rats exposed for 15-min periods to 2450 MHz CW microwaves relative to a 15-min control (no microwaves) period immediately preceding that exposure. Data (± 1 SE) are plotted as a function of microwave power density (mW/cm^2) and specific absorption rate (W/kg). T_a = ambient temperature (°C). Data adapted from Stern, *et al.* (1979).

monkeys, each highly trained to regulate the temperature of the environment behaviorally. During the experiments an animal was chair-restrained in the far field of a horn antenna inside an anechoic chamber. The space occupied by the monkey was heated and cooled by forced convection; the animal controlled the temperature of the circulating air by pulling a response cord to select between two preset air temperatures, one cold (10-15 °C) and one hot (50-55 °C). Usually, the monkey was exposed to air at one of these

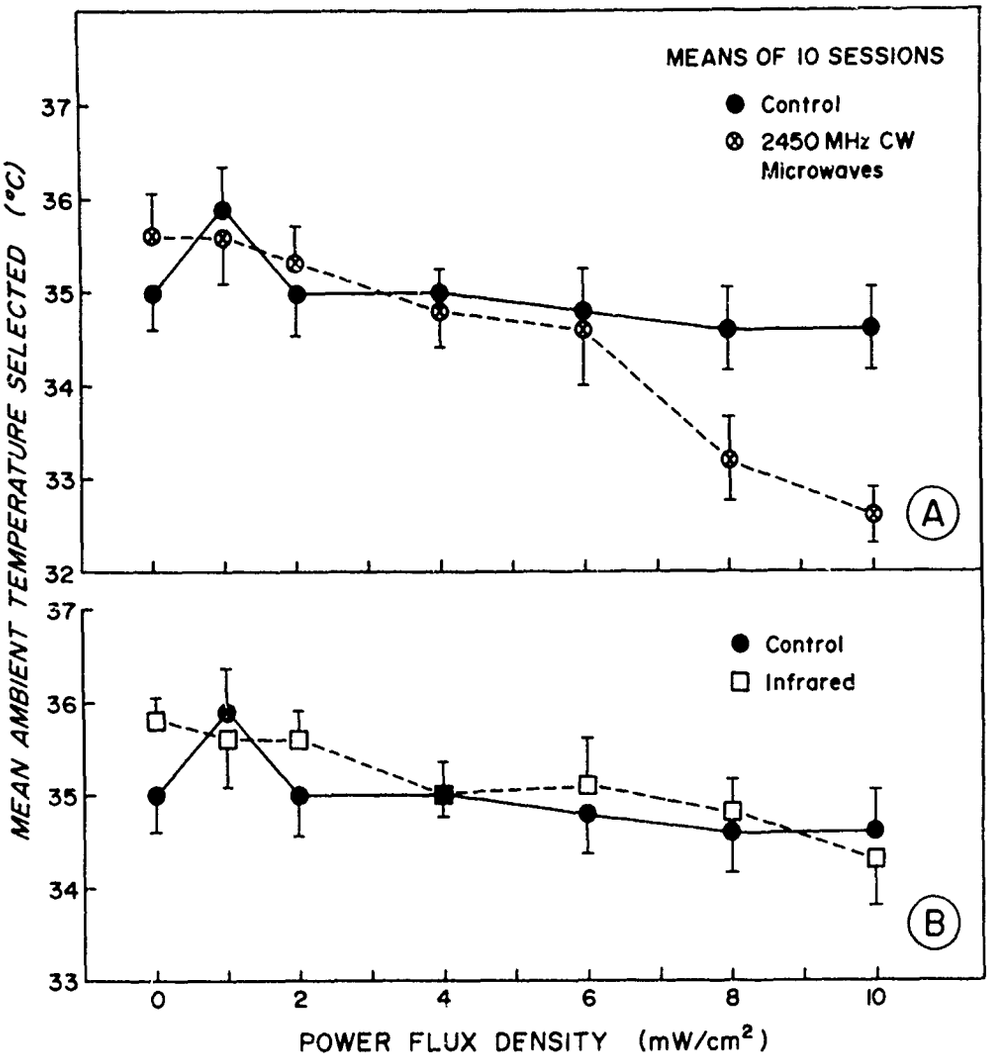

Figure 2. Mean (± 1 SE) ambient temperature (°C) selected by two squirrel monkeys, during 5 sessions each, as a function of the power flux density (mW/cm^2) of 10-min microwave exposure (Panel A) or infrared exposure (Panel B) compared with comparable time period in control (no microwave) experiments. Monkeys selected between 15 and 55 °C air sources to achieve preferred ambient temperature. A significantly cooler environment was selected when microwave power density exceeded 6 mW/cm^2.

temperatures and worked for 15-s. reinforcements of the other. Well-trained animals respond at a rate that produces a preferred average air temperature of 35-36 °C. During all experiments, rectal temperature and four representative skin temperatures (abdomen, tail, leg, and foot) were measured continuously using fine copper-constantan thermocouples that were carefully shielded from the microwave field. (Technical details of the exposure arrangement, dosimetry, and response measures are given in Adair and Adams, 1980).

Our initial experiments determined the microwave power density that would reliably alter the thermoregulatory behavior described above. Monkeys were exposed for 10-min periods to 2450 MHz CW microwaves at discrete power densities that ranged from 1 to 10 mW/cm^2. Individual exposures were separated by like periods with microwaves absent. In a second series of experiments, the same animals were exposed to 10-min periods of infrared radiation (produced by two T-3 quartz lamps) at comparable power densities. A third series of experiments (control) assessed the temporal variations of normal thermoregulatory behavior in the absence of microwave or infrared radiation.

Figure 2 shows the average environmental temperature selected by two monkeys (five sessions each) as a function of the power density of microwaves (panel A) or infrared radiation (panel B) to which they were exposed. In each case, the data are evaluated against comparable time periods in control experiments in which no radiation was present. Microwave power densities above 6 mW/cm^2 reliably stimulated the animals to select a cooler environment, whereas comparable intensities of infrared radiation had no such effect. Thus, the behavioral change resulted primarily from activation of thermodetectors located deep in the body rather than in the skin. Under these conditions, microwave irradiation at a power density of 6 to 8 mW/cm^2 may be considered a threshold intensity for the alteration of normal thermoregulatory behavior. The rate of energy absorption at this intensity is about 1.1 W/kg and represents 20% of the resting metabolic rate of the squirrel monkey. This SAR is similar to that found by Stern, *et al.* (1979) for the rat.

How well do the animals succeed in regulating their internal body temperature when they cool down their environment in the presence of a microwave field? They succeed admirably as shown in Figure 3. The figure shows the rectal temperature (T_{re}), weighted mean skin temperature ($\bar{T}_{sk}$), and ambient temperature (T_a) selected by one monkey as a function of experimental time. The points represent means calculated across five experiments in which the animal underwent 10-minute microwave exposures at increasing power

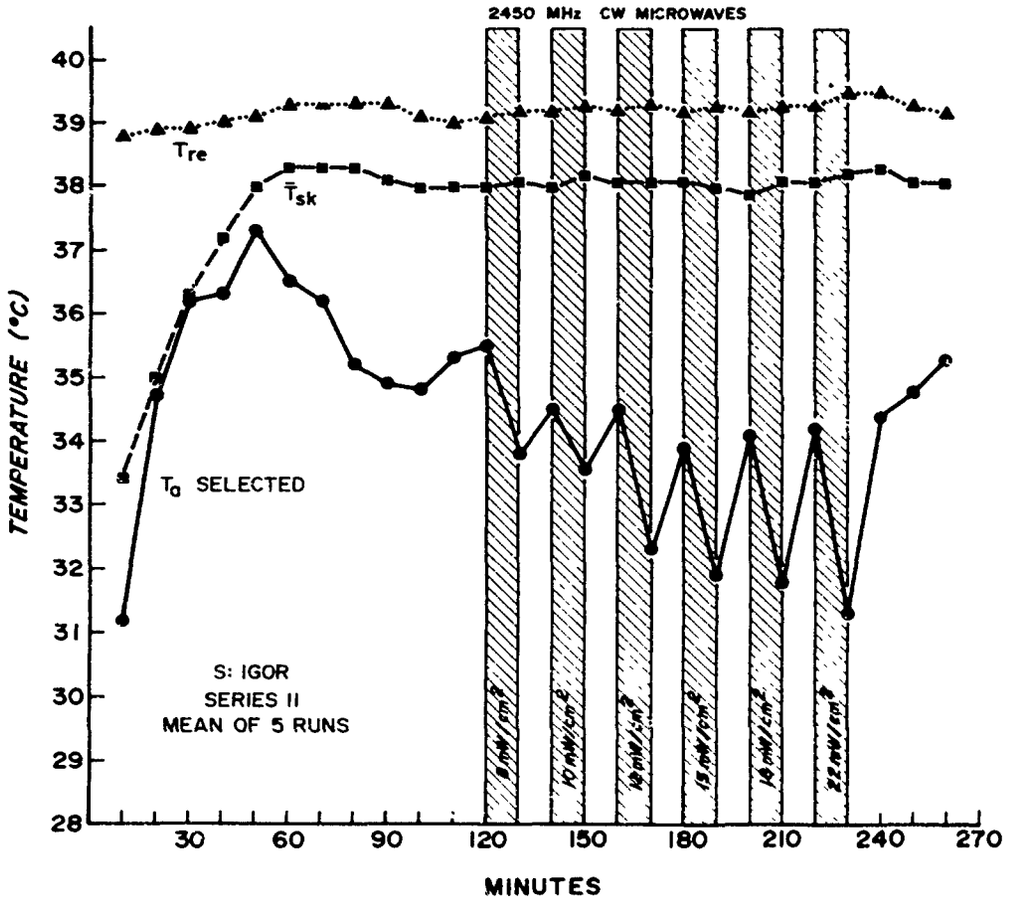

Figure 3. Rectal temperature (T_{re}), mean skin temperature ($\bar{T}_{sk}$), and ambient temperature (T_a) selected by one monkey (taken in 10-min time blocks) as a function of experimental time. Points represent means of 5 experiments in which the animal was exposed to 10-min periods (shaded) of 2450 MHz CW microwaves of increasing power density (8, 10, 12, 15, 18, and 22 mW/cm^2). The monkey worked in 55 °C air for 15-sec reinforcements of 15 °C air. Reprinted from *Bioelectromagnetics* 1:16 (1980) by permission of Alan R. Liss, Inc.

densities (8, 10, 12, 15, 18, and 22 mW/cm^2). There is no evidence of significant changes in either skin or deep body temperatures during the exposures, even at a power density of 22 mW/cm^2. By lowering the air temperature behaviorally, by an amount linearly related to microwave intensity, the animal regulated its body temperatures accurately at the normal levels. These results confirm and extend those obtained for the rat by Stern, *et al.* (1979).

These findings are illustrated even more clearly in Figure 4 where data from two series of experiments are combined. The figure shows the environmental temperature selected by one monkey when no microwaves were present (control) and in the presence of 2450 MHz microwaves at power densities ranging from 1 to 22 mW/cm^2. At the "threshold" power density of 6-8 mW/cm^2, the animal selected a significantly cooler environment than during control experiments. It seems reasonable to assume that these animals could deal with irradiation at power densities substantially in excess of those studied here, without a significant increase in body temperature, provided sufficient environmental cooling was available to them. To date, the upper limit of behavioral thermoregulatory capability under microwave exposure has not been determined experimentally for any species.

The findings described above pertain to 10- to 15-min. microwave exposures but shed no light on behavioral adjustments during longer exposure durations. Will a behaviorally-selected cooler environment persist unchanged throughout a long microwave exposure, or is the behavioral adjustment only transitory, exhibiting modification over time? The answer to this question, illustrated in Figure 5, is that an experimental animal will continue to select a cooler environment, appropriate to the power density imposed, so long as the microwave field is present (Adair and Adams, in press). The figure shows results of experiments in which microwaves at a power density of 20 mW/cm^2 (SAR = 3 W/kg) were presented for 2½ hours. The squirrel monkey's initial response was to lower the environmental temperature by 3 °C and keep it lowered for the duration of the exposure. Once again, the skin and deep body temperatures were regulated precisely at the normal level throughout the exposure. A clear tradeoff has thus been delineated in this experiment: a 3 °C reduction in air temperature is equivalent to a specific absorption rate of 3 W/kg (60% of the resting metabolic heat production of the animal under study). Presumably, similar tradeoffs will obtain for other species, including man (cf. Pound, 1980, and also Chapter 2 of this volume).

To summarize, we know a great deal about *what* an animal

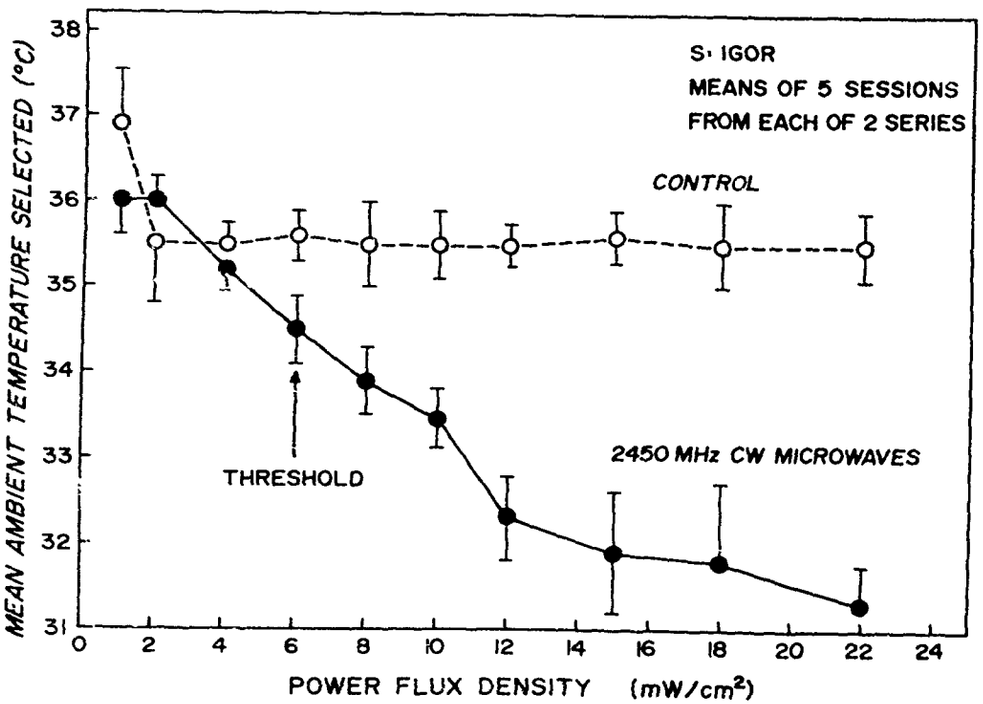

Figure 4. Mean ambient temperature (°C) selected by one monkey as a function of the power flux density (mW/cm2) of 10-min exposures to 2450 MHz CW microwaves compared with comparable time periods in control (no microwave) experiments. Data from 2 experimental series, 5 sessions each, are combined in this graph. The monkey worked in 55 °C air for 15-sec reinforcements of 15 °C air.

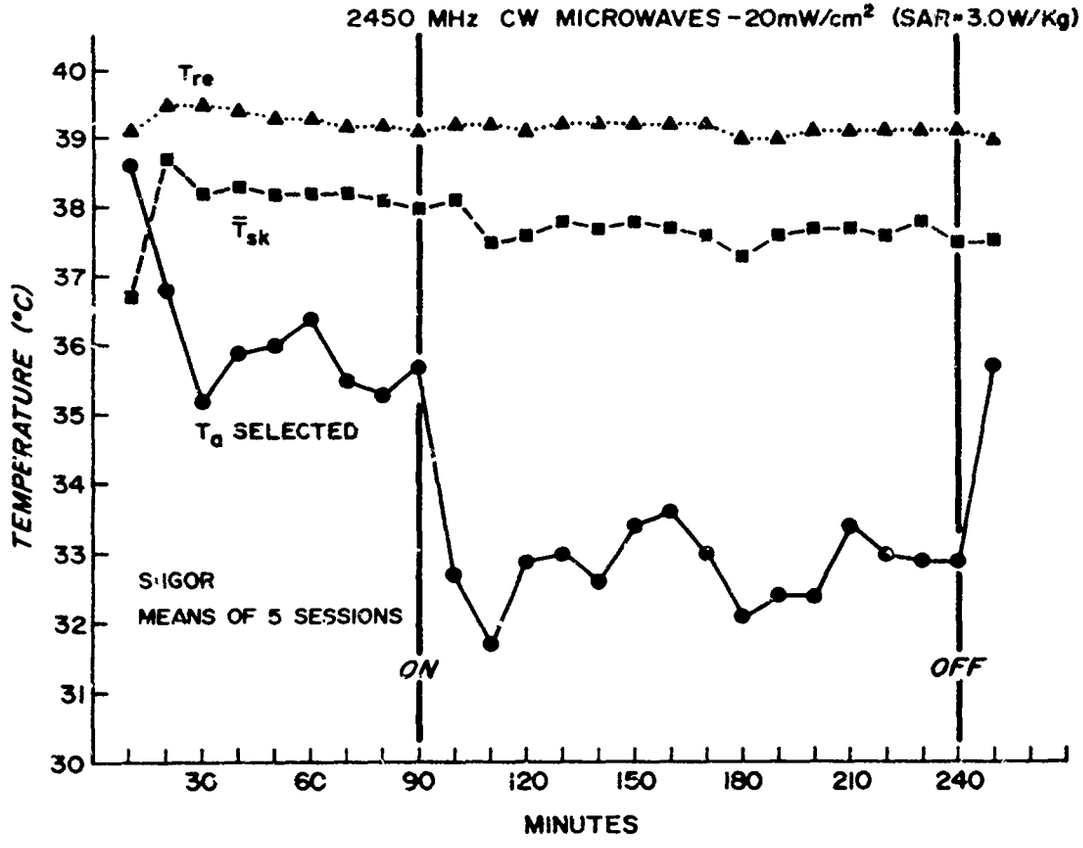

Figure 5. Mean ambient temperature (T_a) selected by one monkey exposed to 2450 MHz CW microwaves for 2½ hours at a power density of 20 mW/cm^2 (SAR = 3.0 W/kg). Skin (—■—) and rectal (···▲···) temperatures are also shown.

will do when a low intensity microwave field intrudes upon ongoing thermoregulatory behavior. If the field strength equals or surpasses a threshold level, the organism will select a cooler environment than normally preferred. The reduction in preferred environmental temperature is a linear function of field strength, at least for moderate levels, and ensures that the internal body temperature will be regulated at the norm l level. Finally, this altered behavior appears to persist unchanged so long as the field is present.

Let us turn now to the second behavioral paradigm (cf. Table I), the one involving the direct utilization or manipulation of a microwave source in order to achieve thermal balance. A story has been told (Bem and Trzaska, 1976) of a pair of sparrows that nested and raised their young at the feedpoint of a powerful transmitting antenna in the Polish city of Constantinov. For safety, the Polish Broadcasting Company had relocated all families residing within a 10 km radius of the antenna tower and yet the sparrows prospered in the center of this two-megawatt source. The heat provided by the field must have been, as Professor Schwan observed," . . . just enough to keep a tiny bird warm on a cold day" (D. R. Justesen, personal munication).

The first study designed to quantify this kind of instinctive thermoregulatory behavior was undertaken by D'Andrea and his associates at the University of Utah (D'Andrea, *et al.*, 1978). Their subjects, 6 whiptail lizards (*Cnemidophorus tigris*) from the Lake Powell desert, were first housed on sand in a glass terrarium and observed for one week. Every day from 7 AM to 9 PM, an infrared heat lamp was turned on over one corner of the terrarium. Five times a day, for ½-hour periods, the lizards' activity was recorded and then the cloacal temperature of each was measured. The following week, the lizards moved to new housing, a Styrofoam and Plexiglas terrarium inside an anechoic chamber in full view of an antenna radiating 2450 MHz CW microwaves. The orientation of the terrarium was such that an effective "microwave gradient" was created inside, the field strength varying from $\sim$90 mW/cm^2 in the corner nearest the antenna to $\sim$2 mW/cm^2 in the opposite corner. Again the lizards' activity was observed five times a day, over a closed-circuit TV monitor, and the cloacal temperature was measured at the end of each observation period, as before.

A summary of D'Andrea's results appears in Figure 6, which shows the percentage of each half-hour observation period the lizards spent basking (or inactive), and the mean cloacal temperature achieved. Since the average ambient

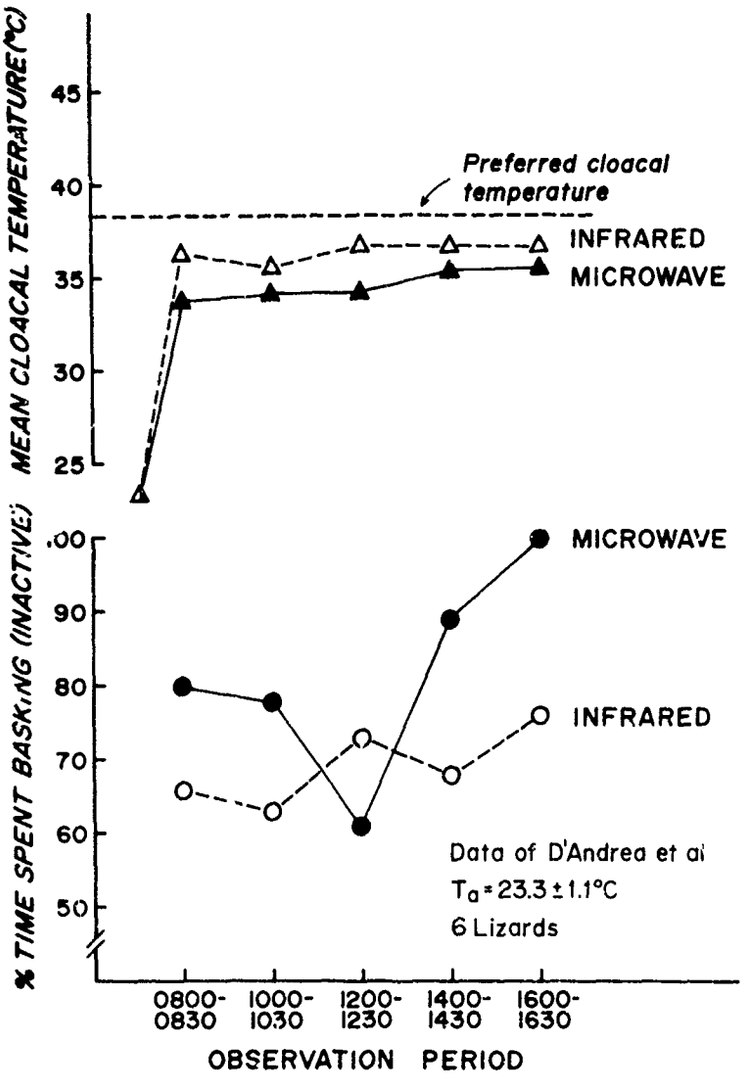

Figure 6. Mean percentage of six 30-min observation periods that 6 whiptail lizards spent inactive in the presence of infrared radiation (- -○- -) or 2450 MHz CW microwaves (—●—) and the mean cloacal temperature (°C) achieved thereby. Data adapted from D'Andrea, *et al.* (1978).

temperature was 23 °C, this was the initial body temperature of these ectotherms each morning before the radiation (either infrared or microwaves) was turned on. It is clear that the lizards utilized the environmental energy source efficiently in both cases, quickly raising their internal temperatures close to that normally preferred (i.e., measured in the natural habitat) and keeping it there throughout the day. In the microwave gradient, the lizards moved gradually toward the microwave source so that at the end of each day they were piled up in the 90 mW/cm^2 corner of the terrarium. While this behavior complicated dosimetric measurements, it illustrated clearly that these animals were able to sense and utilize the microwave field nearly as efficiently as the source of infrared radiation to regulate their body temperatures behaviorally.

Corroborative evidence from a similar experiment on a mammal, is reported by Justesen in this volume (Chapter 10, data of Riffle). Four Long-Evans rats, with a history of cavity exposure to an intense 2450 MHz field, learned to escape the radiation by moving to a "safe" region within the exposure cavity. The reinforcement (extinction of the microwave field) was cued by a 2900 Hz tone for two of the animals, uncued for the other two. Dose rates of 30, 60, and 120 mW/g were investigated. Four daily 10-min sessions at a given dose rate were preceded by one baseline session and followed by one extinction session in which no radiation was present; this constituted one set. Four such sets of sessions were conducted in the following order: 60, 30, 120, and 60 mW/g. Set one is regarded by the author of Chapter 10 as a "tutorial" for the rats and is so treated here.

The mean data from the final 3 sets of sessions are summarized in Figure 7 as a function of microwave dose rate. Both the percentage of time the animals spent in the safe (non-irradiated) area and the postsession rectal temperature achieved support the conclusion that the rats were behaving in a purposeful manner relative to the thermalization produced by the field. As the dose rate increased, so did the time they spent in the safe area. Further, the postsession colonic temperature was remarkably stable, the variability (cf. Chapter 10, Table II) suggesting no significant alteration from thermoneutrality as a function of dose rate. Even though the experiment is characterized by Justesen in Chapter 10 as a pilot study, the results indicate a) that instinctive escape behaviors in the presence of an intense microwave field are indeed thermoregulatory in nature and b) that experience and/or training aids the appreciation of the potential lethality of such fields.

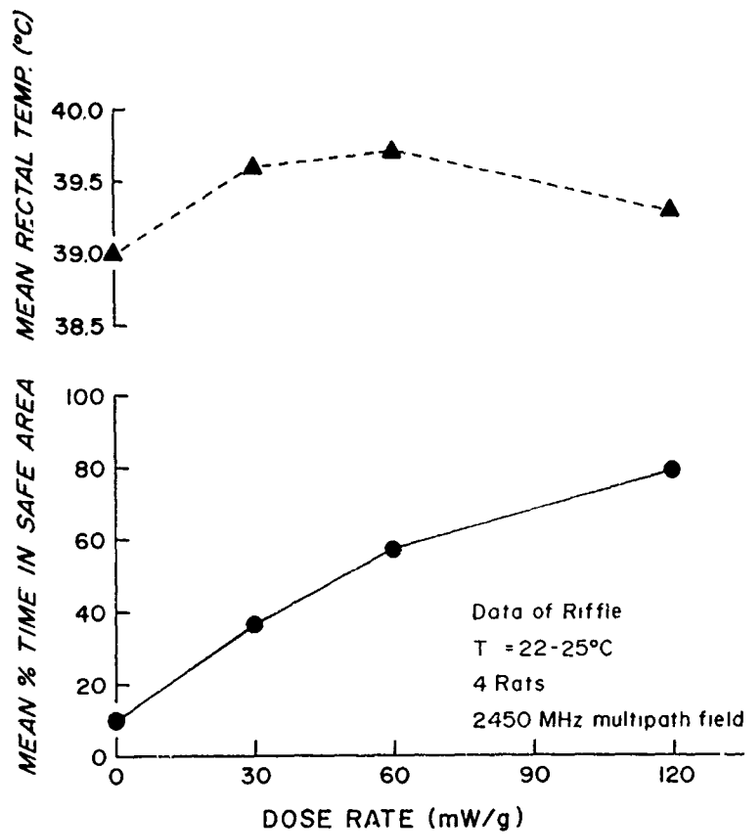

Figure 7. Mean percentage of time during four 10-min sessions spent by four "educated" rats (see text) in a demarcated safe area of a 2450 MHz multipath cavity as a function of the available dose rate (mW/g). The mean rectal temperature (°C) recorded immediately post-session is also shown. Unpublished data of Riffle as described by Justesen in Chapter 10.

The results described above have been confirmed in a similar study by Bruce-Wolfe who successfully trained three squirrel monkeys to operate a source of 2450 MHz CW microwaves (Bruce-Wolfe and Adair, 1981). These experiments were conducted in the anechoic test chamber described by Adair and Adams (1980). Individual animals were restrained in a chair inside an air-conditioned Styrofoam box that was located in the far field of the horn antenna. Initially,

each monkey was trained to select appropriate amounts of circulating hot (50 °C) and cold (10 °C) air to provide an acceptable thermal environment inside the box. Whenever the animal pulled the response cord, the incoming air temperature changed: if it had been cold, it became hot or vice versa. A visual cue that was correlated with air source temperature (450 nm "blue" accompanying 10 °C air, 600 nm "red" accompanying 50 °C air) was provided for one of the animals. Rectal temperature, four representative skin temperatures, and the air temperature selected by the animal were monitored continuously during 2 hour experimental sessions.

After the monkeys were well trained, 2450 MHz CW microwaves accompanied by thermoneutral (30 °C) air replaced the 50 °C air, but all other experimental conditions remained the same. In other words, the monkeys now had a choice between cold air and microwaves instead of between cold air and hot air. Three 2-hour experimental sessions were conducted on each animal at each of three microwave power densities, 20, 25, and 30 mW/cm^2 (SAR = 0.15 [W/kg]/[mW/cm^2]).

A summary of the major results of this study appears in Figure 8. For the three microwave power densities, together with the 50 °C air available during training sessions, the figure shows (for the final 30 minutes of all experiments) the mean percentage of time the animals selected the source of heating. The ambient temperature produced by this behavior and relevant measurements of the body temperature are also shown. The most striking finding is that the animals somehow discerned the endogenous consequences of the available sources of thermalizing energy and altered their behavioral strategies accordingly. Normal thermoregulatory behavior in this apparatus results in a 70% selection of 50 °C air over 10 °C air. When microwaves at 20 mW/cm^2 replaced the hot air, this percentage shifted to a 90% selection of the heat source. As a consequence of this behavioral change, mean ambient temperature fell to the level (30 °C) of the circulating air that accompanied the microwave field (a necessary control for air movement) but relatively minor reductions in skin temperature occurred. At the highest power density (30 mW/cm^2), the monkeys turned on the microwaves significantly less often than at the two lower power densities, demonstrating a remarkable sensitivity to the strength of the field. It is clear that these behavioral adjustments were not only purposive and appropriate but also efficient, since they always produced precise regulation of the internal body temperature at the physiologically neutral level. Whether or not such precise thermoregulatory behavior would be exhibited by a naive (un-

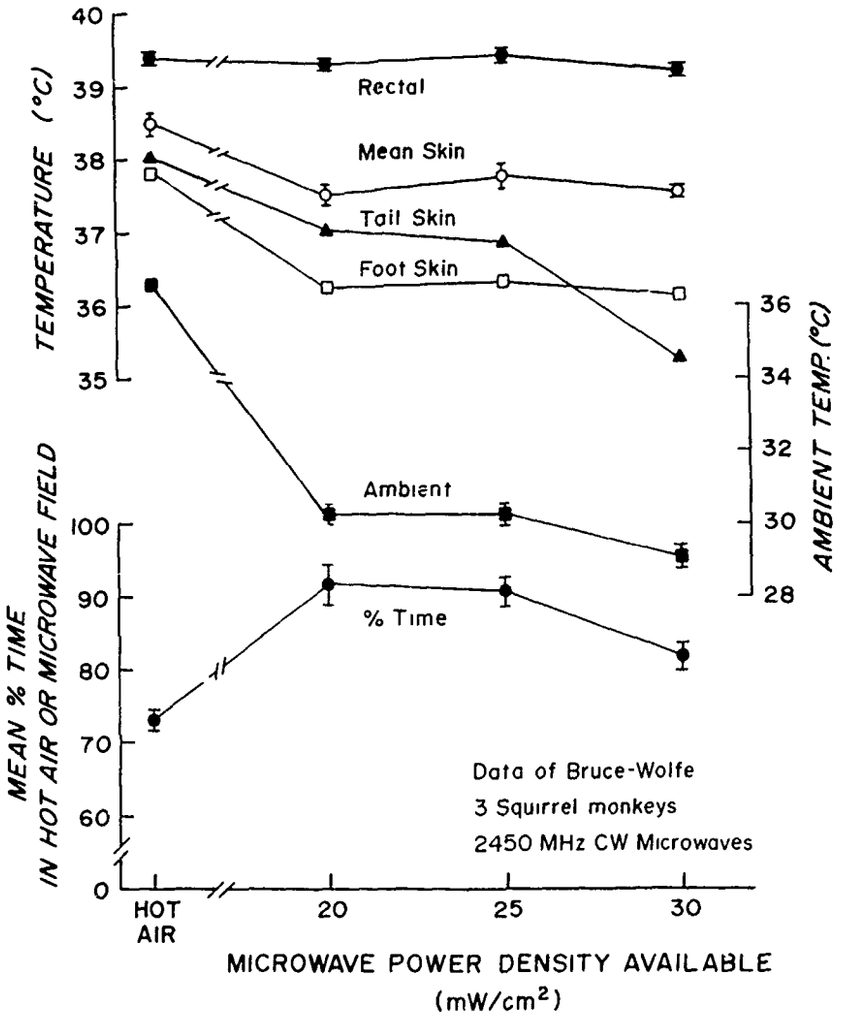

Figure 8. Mean percentage of time (during final 30 min of three 2-hr experimental sessions) 2450 MHz CW microwaves were chosen over 10 °C air by 3 squirrel monkeys as a function of the microwave power density available (mW/cm^2), and the ambient and body temperatures achieved thereby. Comparable measures from 3 training sessions (in which 50 °C air was chosen over 10 °C air) are also shown. Error bars represent ± 1 SE. Unpublished data of Bruce-Wolfe.

trained) animal, or whether it would be exhibited in a cool surround of invariant temperature, is not addressed by this study. These are among the many questions yet to be answered.

The literature dealing with changes in thermoregulatory behavior in the presence of microwave fields has been reviewed in this paper. Most of the studies cited are preliminary in nature and much work remains to be done. So far, we have learned that in most situations, especially with subjects trained to manipulate environmental thermal stimuli, microwave exposure at moderate intensities will be compensated by appropriate behavioral adjustments so that no significant change occurs in the regulated internal body temperature. Furthermore, while we know that irradiation at a minimal power density must be exceeded before overt changes in thermoregulatory behavior can be measured, we have no inkling of the maximal power density that can be dealt with effectively. Surely the behavioral response to intense microwave fields will be governed in large measure by the prevailing ambient temperature.

On another note, what is the import of frequencies other than the 2450 MHz utilized in all studies reported to date? Recent evidence (Lotz, 1982; Krupp, Chapter 5) indicates that exposure to frequencies near whole-body resonance may pose special problems for a behaving animal because of greatly enhanced rates of energy absorption that may overwhelm the thermoregulatory system.

There are other critical questions. For example, how may efficient thermoregulatory behavior be compromised by alterations in the thermoregulatory set point such as may occur during febrile states or under the action of certain drugs? Also, what might be the import of defective neurophysiological control of the thermoregulatory effector system as would be produced by lesions in certain CNS thermosensitive sites (e.g., anterior hypothalamus, medulla). Such sites are surely heated, to a greater or lesser extent (Kritikos and Schwan, 1979; Burr and Krupp, 1980) during microwave exposure. Answers to these and other questions will begin to provide insight into the basic mechanisms that underlie detection of a source of radiofrequency electromagnetic energy and translate that detection into effective behavioral action, whether the source upsets the organism's thermal balance or is utilized by the organism to achieve it.

ACKNOWLEDGMENTS

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REFERENCES

Adair, E.R. (1977a) Studies on the behavioral regulation of preoptic temperature. In: *Drugs, Biogenic Amines and Body Temperature*. p. 84 Karger: Basel.

Adair, E.R. (1977b) Preference for skin cooling during hypothalamic heating. *Proc. IUPS* 13:8.

Adair, E.R. and Adams, B.W. (1980) Microwaves modify thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics* 1:1.

Adair, E.R. and Adams, B.W. Behavioral thermoregulation: Adaptation processes during prolonged microwave exposure. *J. comp. physiol. Psychol.* (in press)

Bem, D.J. and Trzaska, H. (1976) The insouciant sparrows of Constantinov: A case study of electromagnetic ethology. In *Biological Effects of Electromagnetic Waves*. (C.C. Johnson and M.L. Shore, Eds.) HEW Publication (FDA) 77-8010, 284.

Bruce-Wolfe, V. and Adair, E.R. (1981) Operant control of microwave radiation by squirrel monkeys. In: *Bioelectromagnetics Society*, 3rd Annual Conference Abstracts. p. 42.

Burr, J.G. and Krupp, J.H. (1980) Real-time measurement of RFR energy distribution in the *Macaca mulatta* head. *Bioelectromagnetics* 1:21.

Corbit, J.D. (1969) Behavioral regulation of preoptic temperature. *Science* 166:256.

Corbit, J.D. and Ernits, T. (1974) Specific preference for hypothalamic cooling. *J. comp. physiol. Psychol.* 86:24.

Cormarèche-Leydier, M. and Cabanac, M. (1976) Dog behavior as related to spinal cord temperature. *Experientia* 32:66.

D'Andrea, J.A., Cuellar, O., Gandhi, O.P., Lords, J.L., and Nielson, H.C. (1978) Behavioral thermoregulation in the whiptail lizard (*Cnemidophorus tigris*) under 2450 MHz CW microwaves. In *Biological Effects of Electromagnetic Waves*. Abstracts URSI General Assembly. p. 88 Helsinki.

Dib, B., Cormarèche-Leydier, M. and Cabanac, M. Behavioral self warming and cooling of spinal canal by rats. *Physiol. Behav.* (in press)

Kritikos, H.N. and Schwan, H.P. (1979) Potential temperature rise induced by electromagnetic field in brain tissues. *IEEE Trans. Biomed. Engr.* BME-26:29.

Lotz, W.G. (1982) Hyperthermia in rhesus monkeys exposed to a frequency (225 MHz) near whole-body resonance. *NAMRL Tech. Report No. 1284*, Pensacola, FL 32508: Naval Aerospace Medical Research Laboratory.

Pound, R.V. (1980) Radiant heat for energy conservation. *Science* 208:494-495.

Stern, S., Margolin, L., Weiss, B., Lu, S.-T., and Michaelson, S. (1979) Microwaves: Effect on thermoregulatory behavior in rats. *Science* 206:1198.

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THE THERMAL BASIS FOR DISRUPTION OF OPERANT BEHAVIOR BY MICROWAVES IN THREE ANIMAL SPECIES

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INTRODUCTION

Several years ago research on the behavioral effects of microwave exposure was initiated in our laboratory. The original work (de Lorge, 1976) used rhesus monkeys because their thermoregulatory responses are similar to man's (Kenshalo and Hall, 1974; Smiles, *et al.* 1976) and because few investigators in this research area had studied the responses of primates. The overriding interest in using primates was caused by attempts to generalize data derived from animal research to man. As our research effort continued it became obvious that animals of different sizes exposed to different microwave frequencies would need to be examined if generalizations regarding larger animals were to be drawn. This realization resulted in selecting rats and squirrel monkeys and three different microwave frequencies, all above the resonant frequency for these animals. The microwave frequencies, 1.3, 2.45 and 5.7 GHz, were chosen primarily because of availability and secondarily because they represented frequencies in use by the Navy.

Another key aspect of the program has been to choose a behavioral task on which all three species could be trained and that would generalize to human behavior without serious qualifications. An observing response task was chosen wherein an animal engages in operant behavior and obtains positive reinforcement (Holland, 1957). The task is similar to vigilance behavior and requires the sustained attention of the animal. For various reasons some of this work has utilized data from animals on other operant tasks (Sanza and

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de Lorge, 1977; Nelson, 1978), but the primary data have been taken from a series of experiments measuring observing-response performance (de Lorge, 1976; 1980; de Lorge and Ezell, 1980).

The behavioral literature reveals no unique behavior associated with microwaves other than the auditory phenomenon (Frey and Messenger, 1973). Thus, the present approach has attempted to examine changes in operant behavior as a consequence of exposure to microwaves. Disruption of ongoing behavior is the effect on which this study was focused because it is the effect most commonly reported in the literature (Justesen and King, 1970). Disruption of stable performance baselines typically is seen as a decreased rate of responding, although an increase in response rate has also been observed as a consequence of microwave irradiation (de Lorge, 1979). The present studies were not designed to evaluate an animal's detection of the microwaves nor were reinforcement contingencies associated with the presence of microwaves. Instead, the studies were designed to establish the lowest power density of microwaves that would disrupt ongoing behavior. On the observing-response task reinforcement was scheduled so that response-rate-changes normally did not increase or decrease its frequency; that is, either random interval or variable interval schedules of reinforcement were used (Catania, 1968).

The approach is one of seeing how well an operant response can be maintained when the animal is confronted with a biophysical agent as pervasive as microwaves. This approach demonstrated that a well-controlled operant response was unassailable or immune to microwave disruption as long as the animal's body temperature did not rise at least 1 °C above its baseline level.

METHOD

Subjects

The subjects were rats either of the Long Evans strain (de Lorge and Ezell, 1980), or the Sprague-Dawley strain (Sanza and de Lorge, 1977) obtained from the Charles River Colonies; squirrel monkeys, *Saimiri sciureus*, obtained from Colombia, South America; and rhesus monkeys, *Macaca mulatta*, produced in our own breeding colony. All of the subjects were males. The average body masses of the animals were 300-400g for rats, 700g for squirrel monkeys and 4.7-5.1 kg for the rhesus.

All of the subjects were trained while food deprived and maintained at approximately 85 to 95% of their free-feeding body mass. In the long duration studies with the rhesus the animals were periodically placed on free-feeding schedules for several weeks to establish new 100% free-feeding values.

Apparatus

The microwave exposures typically occurred in chambers anechoic to the microwave energy. The chambers differed only in basic dimensions that depended upon the direction and frequency of the irradiation. A schematic of a chamber instrumented for a rat experiment is illustrated in Figure 1. The chambers have been previously described in detail in the various experiments providing material for the present report (de Lorge, 1976; Sanza and de Lorge, 1977; de Lorge and Ezell, 1980). In brief, each chamber was constructed of copper faced wood and lined with microwave radiation absorber. The chambers were cooled with air conditioners and ventilation fans and each was equipped with a closed circuit television camera and a white-noise auditory masking source of approximately 75 dB SPL. Equipment for presenting either visual or auditory stimuli was located in the chambers along with transducers for recording ambient relative humidity and temperature.

Various military and commercial radar sets were used to generate the microwaves at three different frequencies: 1.3, 2.45 and 5.7 GHz. The frequency of 5.7 GHz is an average value based upon the 5.62 GHz microwaves used for irradiating the rats and squirrel monkeys and the 5.8 GHz microwaves used in the rhesus monkey experiment. Incident power density and its distribution in the chamber were determined in each experiment in the absence of the subject, and the value measured at the location of the center of an animal's head was the value referred to as the power density to which the animal was exposed.

All of the experiments used Styrofoam restraint devices in the form of either a chair (Reno and de Lorge, 1977) or an operant conditioning box (Sanza and de Lorge, 1977). Manipulanda and food apertures were placed in one wall of these devices. The primate chairs allowed continuous monitoring of the colonic temperatures of the monkeys. Reference air temperature probes, external to the animals, were located near the colonic probes.

Colonic temperatures were not obtained from the rats used in these experiments but from animals of the same size and strain that had been previously exposed in the same or

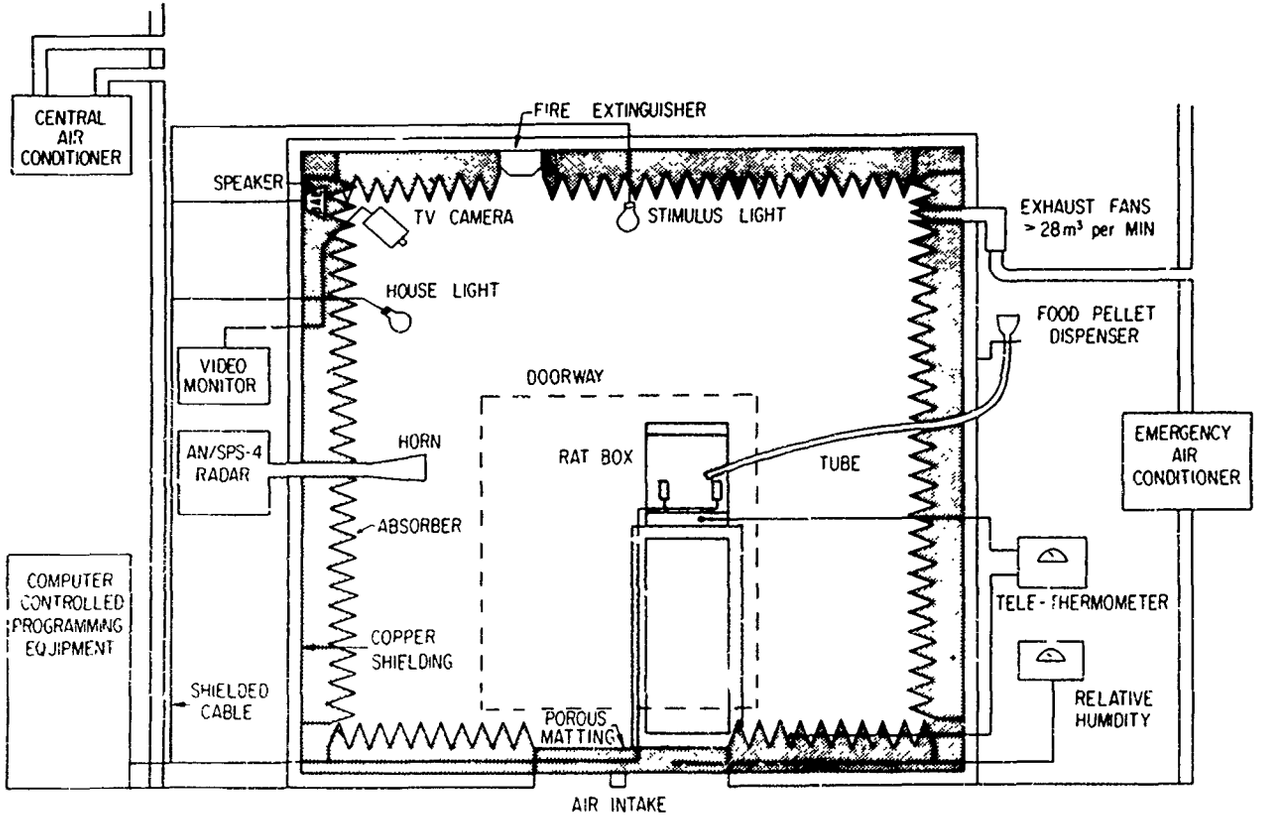

Figure 1. Diagram of an exposure chamber in which experiments at 5.67 to 5.8 GHz were conducted.

similar chambers (Houk and Michaelson, 1974; Lotz and Michaelson, 1978). No colonic temperature data were available on rats exposed at 1.3 or 5.7 GHz. An estimate of the temperatures of rats exposed to 1.3 GHz was obtained from dosimetry data of de Lorge and Ezell (1980) and a study by Merritt, *et al.* (1977) that used smaller rats at 1.6 GHz.

Procedure

The general approach of the entire study is summarized in Table I. At the left side of the table are indicated the three subject groups and at the top are the three microwave frequencies. The P refers to pulsed energy and CW refers to continuous wave. The operant task is shown in each cell as either an observing response with two levers, B1; a fixed interval schedule with one lever, B2; or a repeated acquisition task with three levers, B3. The upper-case T indicates that colonic temperature was continuously measured during the behavioral sessions and the lower-case t indicates that the colonic temperature was estimated. The orientation of the long axis of the subject to the electric field vector of the plane wave is denoted by X, Y, and Z and whether the animal is facing the horn, frontal; below the horn, dorsal; or has its right side towards the horn, lateral.

Several variations in approach are evident in the Table I matrix. Squirrel monkeys were not irradiated at 1.3 GHz and all exposures were not oriented to the same polarization. Nevertheless, it will be shown that the distinctiveness and general lack of ambiguity in the overall results of these experiments question the relevance of these inconsistencies.

The specific procedure in each of these experiments was to train an animal on an operant task. The operant task most frequently used was an observing-response task; details of the procedure are provided in the experiment by de Lorge and Ezell (1980). Details of the fixed-interval schedule experiment are found in Sanza and de Lorge (1977), and similar information regarding the repeated acquisition task is found in Nelson (1978) and de Lorge (1980). Most of the daily food allotment was obtained during experimental sessions, and no water was available during the session.

The primary method of monitoring performance was with cumulative response recording. Response rate was the major index of performance, although other measures such as reaction time, errors of omission and commission, post-reinforcement pause and response latency were also obtained. After within-session and between-session stable performance

TABLE I. Characteristics of Contributing Experiments

	MICROWAVE FREQUENCY[a]		
Subject	1.3, P	2.45, CW	5.7, P
RAT	B_1 t X+Y, lateral	B_2 t X+Y, dorsal	B_1 X+Y, lateral
SS		B_1 T Z+Y, dorsal	B_3 T Y, frontal
RH	B_1 T Y, frontal	B_1 T Y, frontal	B_1 T Y, frontal

[a]Symbol identification:

B_1 = Observing Response

B_2 = Fixed Interval

B_3 = Repeated Acquisition

X,Y,Z = Long Axis Orientation to E Field

T = Colonic Temperature Measured

t = Colonic Temperature Estimated

P = Pulsed

CW = Continuous Wave

had developed (as determined by response-rate equivalency) the animal was exposed to the microwave field while performing the task. Typically, sham-exposure sessions (all of the radar equipment energized except the magnetron) preceded and followed exposure sessions by one day except that Friday sessions were followed by two days of no sessions and a sham-exposure session on Monday. With very few exceptions, each subject was exposed at least three times to each power density in every experiment and three to eight subjects participated in each experiment. The animals were trained on a specific operant task to manipulate one or more levers to obtain food. Exposure sessions were from 40 to 60 min. A power density threshold was determined by assessing the level where stable performance was disrupted. Disruption was most often seen as a response rate decrement. Simultaneously, in those studies where colonic temperature was measured, a body temperature was determined corresponding to the behavioral disruption threshold.

RESULTS

The response rate decrement as a consequence of microwave exposure is illustrated in Figure 2. This figure contains examples of cumulative observing-response records for a rat (R9) exposed at 5.62 GHz to power densities ranging from 0 to 48.5 mW/cm^2 (de Lorge and Ezell, 1980). Only selected power densities are shown in the figure because of space limitations. The numbers at the upper left of each record denote the power density (mW/cm^2) and C denotes a sham or control session. Each recording is from an entire 40-min session and each record for an exposure session is preceded by the sham session record. Sessions begin at the left with time increasing to the right. Each observing-response steps the record upwards. Hash marks on the response lines indicate the occurrence of a food lever response and hence reinforcement. The response pen resets after 280 responses or at the end of a session. At 26 mW/cm^2 this record shows a slight rate difference in the latter part of the session, at 31.5 mW/cm^2 a larger rate change with extensive pauses and at 42 mW/cm^2 the rate change was greater and the pauses longer. These effects are typical of those observed throughout the study with all of the animals at all frequencies although exceptions did occur as illustrated in the behavior of a squirrel monkey in one experiment (de Lorge, 1979).

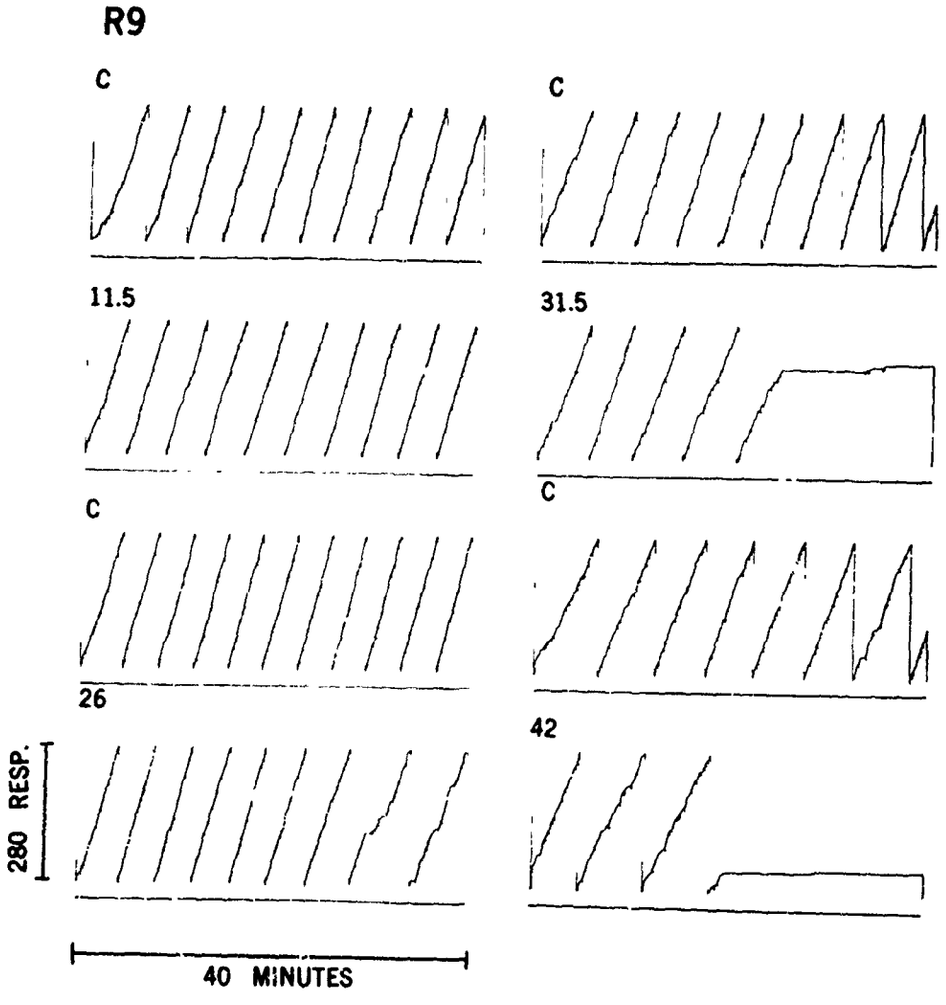

Figure 2. Cumulative records of observing-responses for a rat (R9) for sham (C) and exposures at 5.62 GHz. Power densities are indicated at the upper left of each record. An exposure session followed the sham session immediately above it. Responses are shown on the left and time is indicated at the bottom.

A similar record of observing-responses is shown in Figure 3 for a squirrel monkey. In addition, the colonic temperature of this animal is shown for the same exposure session (bottom record) as denoted on the left. Time is indicated at the bottom in consecutive minutes. The horizontal line below the cumulative response record indicates when the food available signal was present. In this experiment (de Lorge, 1979) the microwave exposure began 30 min (first arrow) into the session and lasted for 1 h (second arrow). A slight rise in temperature occurred during the initial half hour followed by a more rapid rise during the exposure period. A decrement in response rate gradually developed during the microwave exposure. Several pauses occurred as irradiation continued and temperature increased. At the termination of irradiation the monkey stopped responding for several minutes and then gradually resumed pre-irradiation response rates. The rapid fall in colonic temperature after the microwaves were removed and the other characteristics of temperature and response changes were typical of this and similar experiments in the present report.

The cumulative records provided an excellent method of assessing a microwave effect in action, but a quantitative assessment of this effect was achieved by comparing response rates in sham sessions with response rates during exposure sessions. An example of these ratios is illustrated in Figure 4. This figure summarizes the results of experiments on 5 rhesus monkeys exposed to 1.3 GHz microwaves during 1-h observing-response sessions. The circles indicate the mean ratio as shown on the left and each mean is bracketed by the standard error of the mean. The horizontal line at a ratio of 1.0 denotes the same response rates during sham and exposure sessions. No large differences in responding at the various power densities were observed below 63 mW/cm^2. The slight increase at 45 mW/cm^2 was caused by an exceptionally high rate of responding by one animal. Omission of that animal's data produces a mean ratio of 1.01 and a corresponding smaller standard error. Ordinarily the decrement in response rate was correlated with increases in power density. An absolute threshold of 56 mW/cm^2 was chosen here. Similar graphs were plotted for all of the experiments and thresholds were determined by choosing a level midway between the power density where an obvious effect was reliably observed and the one where no effect was seen.

The body temperature of the animals as indexed by colonic temperature is shown in Figure 5. A linear regression was calculated with these temperature data and 42 mW/cm^2 was

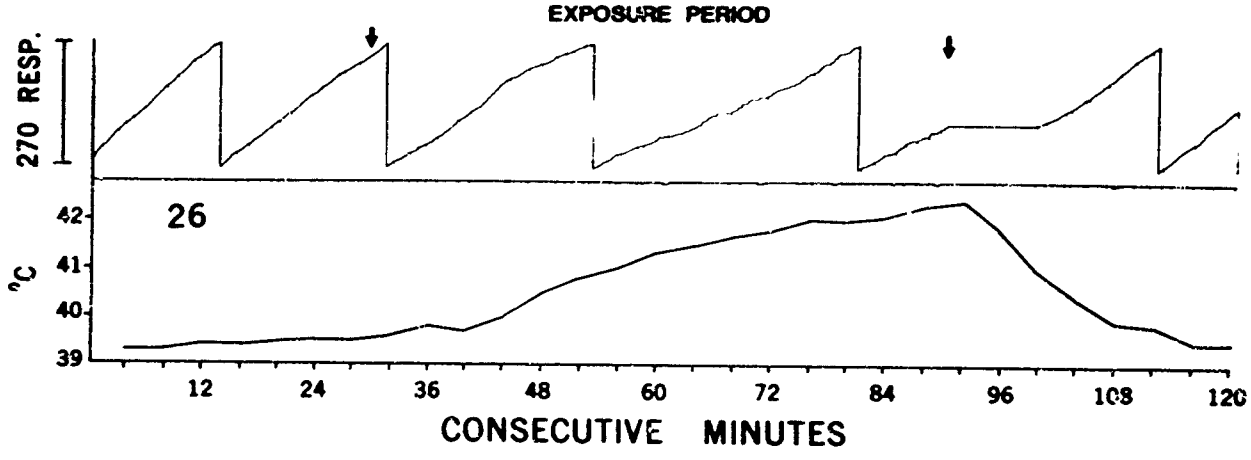

Figure 3. A cumulative record of observing-responses and rectal temperature for a squirrel monkey (26) exposed to 2.45 GHz microwaves. The response record is above and the temperature record is below. Irradiation began at 30 minutes and ended at 90 minutes as denoted by the arrows.

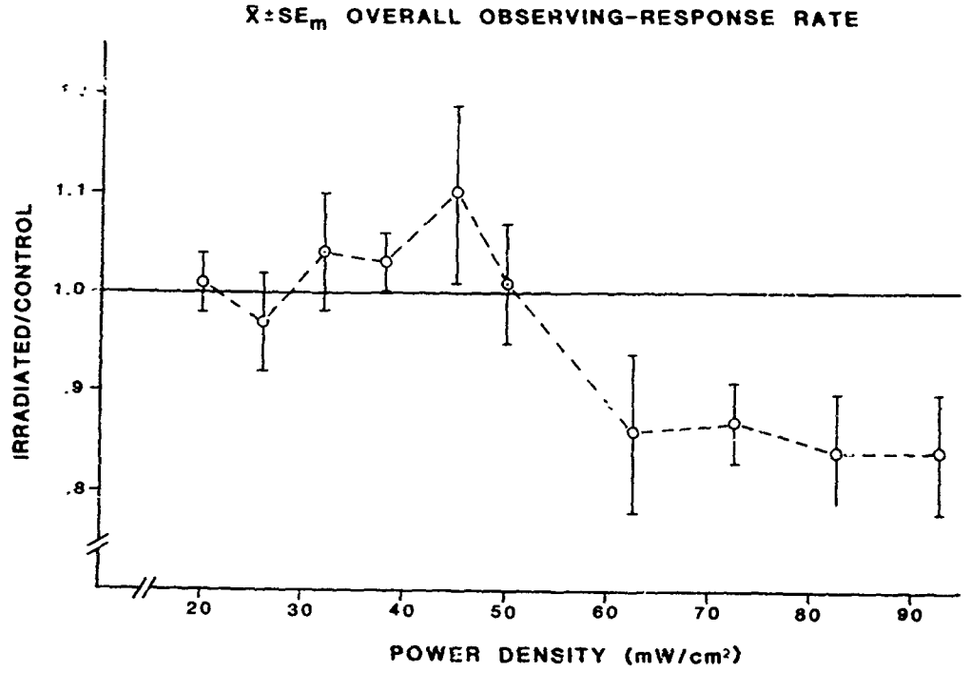

Figure 4. Observing-response rate plotted as a ratio of irradiated session means to sham (control) session means (including ± standard error of these ratios). Each point represents the mean of 5 animals (except at 93 mW/cm^2 when n = 4).

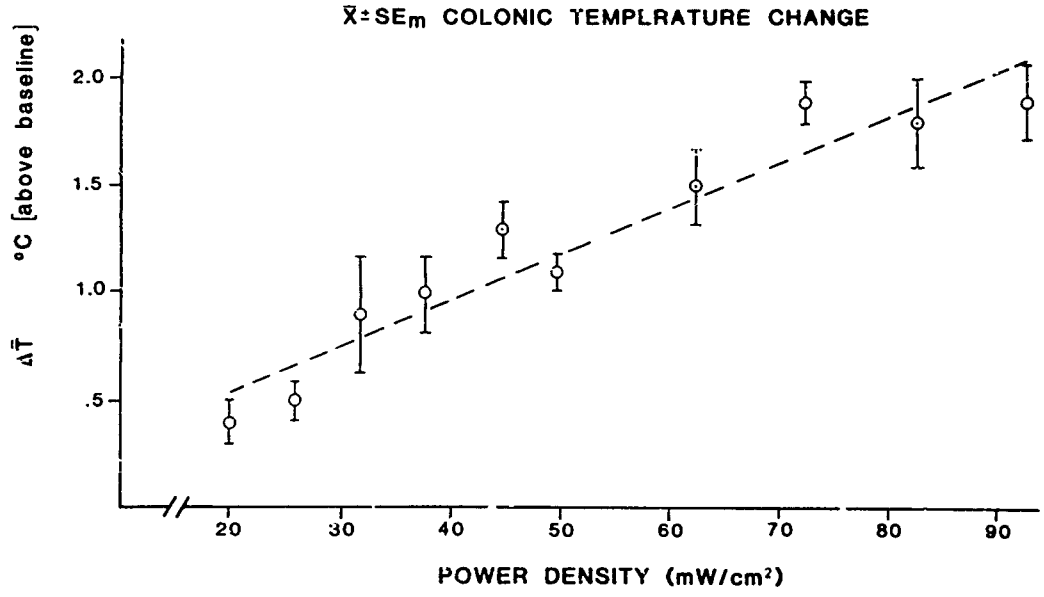

Figure 5. The mean ΔT in rectal temperature of five rhesus monkeys (n=4 at 93 mW/cm^2) exposed to microwaves at 1.3 GHz for 60 min. The rectal temperatures of the preceding sham session for each monkey served as a baseline at each power density.

estimated to be the power density at which a 1 °C body temperature increase above baseline would occur.

DISCUSSION AND CONCLUSIONS

After analyzing the empirical records to determine the power density thresholds necessary to produce a significant change in behavior, these data were used to generate three families of curve sets that show relationships among microwave field parameters and various anatomical indices. The first set is shown in Figure 6 which shows the behavioral thresholds as a function of body mass. Mass is plotted on the abscissa on a logarithmic scale and each curve corresponds to a specific microwave frequency. The ordinate is power density in mW/cm^2 at threshold. The three points corresponding to the heavier animals, the rhesus monkeys, are grouped at the right, the three data points derived from rats are at the left and the two data points derived from squirrel monkeys are at the center of the figure. The plotted values are the means for all animals in the same species that were used to establish the thresholds. It is apparent that an increase in power density sufficient to cause an effect occurs as the microwave frequency and body mass increase. The relative increase in threshold power density at the high frequency for the rhesus is about the same as that for the other animals except that 2.45 GHz is the frequency requiring most energy for an effect in the smaller animals.

An animal's ability to generate or maintain body heat is often given as specific metabolic rate or metabolic heat production per unit body mass; therefore, the curves of Figure 6 might provide a basis for extrapolation to other sized animals and thus predict power densities where similar behavior would be disrupted. However, it is also likely that an animal's body surface area would be an important index for extrapolation. Body mass and body surface area are directly correlated (McMahon, 1973) and curves based on one resemble curves based on the other. The same is true of body length and body mass (Liu and Higbee, 1976). For example, in Figure 7 the same behavioral thresholds of power density that were previously shown are now plotted as a function of one half of the body surface area of the animals. This measure was used as a liberal estimate of the surface exposed to the microwave field.

Instead of whole-body heat deposition as a predictive index of an animal's reaction to microwave irradiation, one

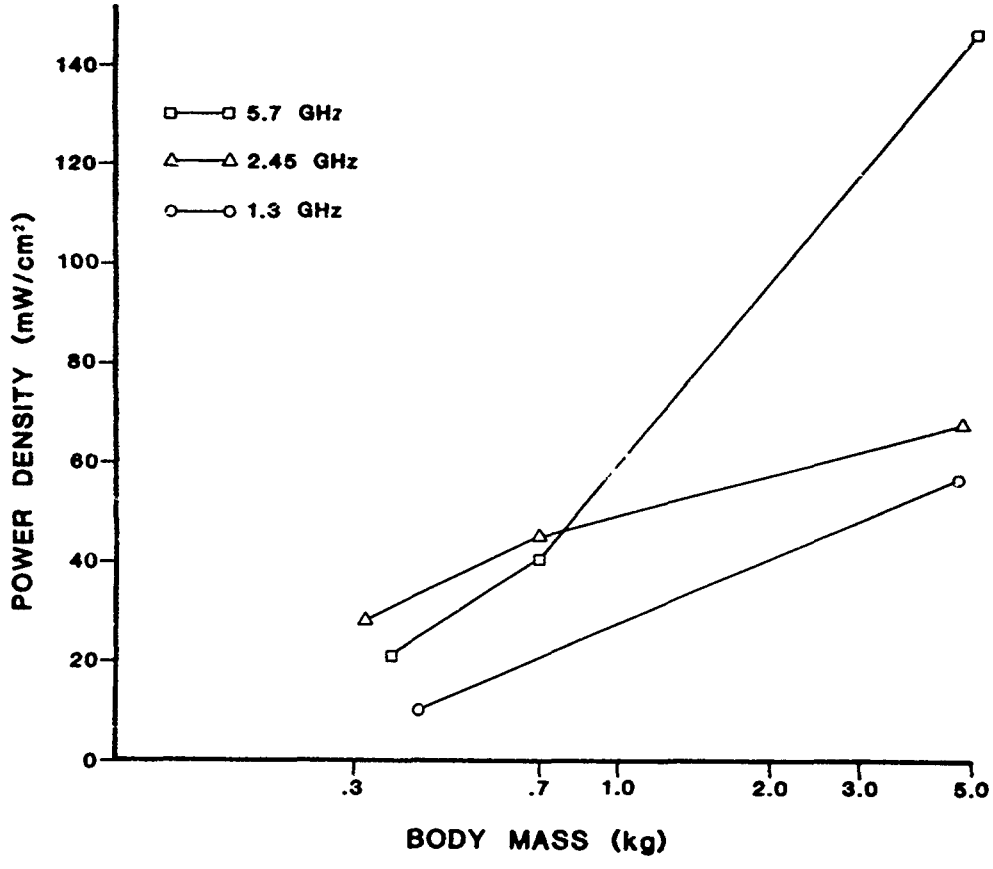

Figure 6. The thresholds of behavioral disruption on operant tasks for different sized animals as a function of power density (ordinate) and body mass (abscissa). The body mass is plotted on a logarithmic scale and the different curves correspond to different frequencies as shown in the upper left.

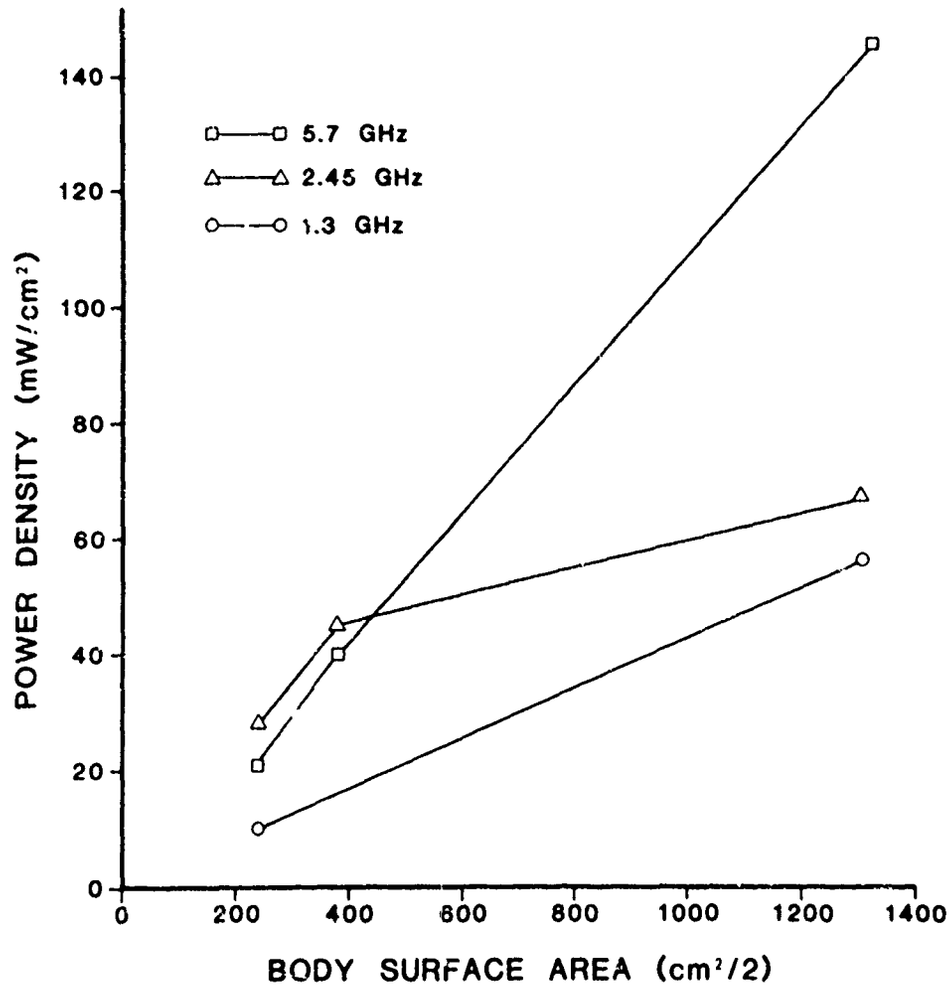

Figure 7. The thresholds of behavioral disruption on operant tasks at three frequencies shown as a function of estimated exposed body surface area (abscissa).

might consider local heat deposition in specific anatomical structures. For example, the three species of animals in the present study all have different sized cranial cavities that may have unique relationships to the wavelengths of the three different microwave frequencies. In Figure 8 the behavioral thresholds shown in previous figures are illustrated as a function of the anterior-posterior length of the cranial cavity for a representative animal of each group of subjects. With the exception of the rhesus monkey at 5.7 GHz, this particular relationship is more linear than the previous relationships and might be a better index for predicting behavioral effects in animals with cranial cavities

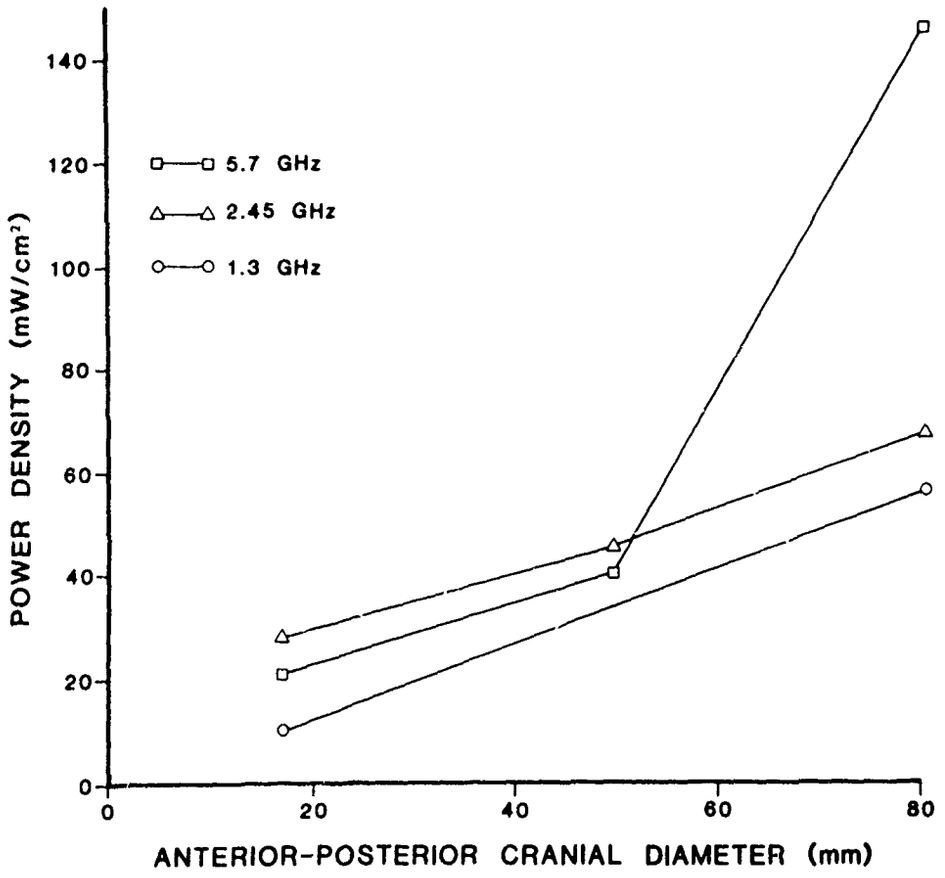

Figure 8. The thresholds of behavioral disruption at three frequencies shown as a function of the anterior-posterior cranial cavity diameter (abscissa).

smaller than that of the rhesus.

Similar correlations to those shown in Figures 6, 7 and 8 could be constructed by using power density levels required for a 1 °C colonic temperature rise instead of the behavior disruption thresholds. The coincidence between these relationships is strikingly illustrated in Figure 9. This figure shows the power density required for a 1 °C change in temperature and the power density threshold for a behavioral change, both plotted as a function of microwave frequency. Each group of subjects is represented by a set of connected lines. The triangles denote the levels where temperature increases of 1 °C occurred and the circles represent the levels where behavior was affected. Several conclusions can be drawn from Figure 9. The smaller the animal the greater

the relative effect at all frequencies, although this is only a guess for the squirrel monkey at 1.3 GHz. Behavioral changes will probably occur with the 1 °C colonic temperature change or at slightly higher temperature changes in the rhesus monkey. As the animal size increases higher power densities are required to affect either behavior or colonic temperature at the chosen frequencies. At the frequency of whole-body resonance it is expected that all of these animals will display greater sensitivity. It is also possible that some of these values for the squirrel monkeys and rats differ more because of body orientation with respect to the microwave field vectors than from the change in wavelength. For example, lateral irradiation of the rat

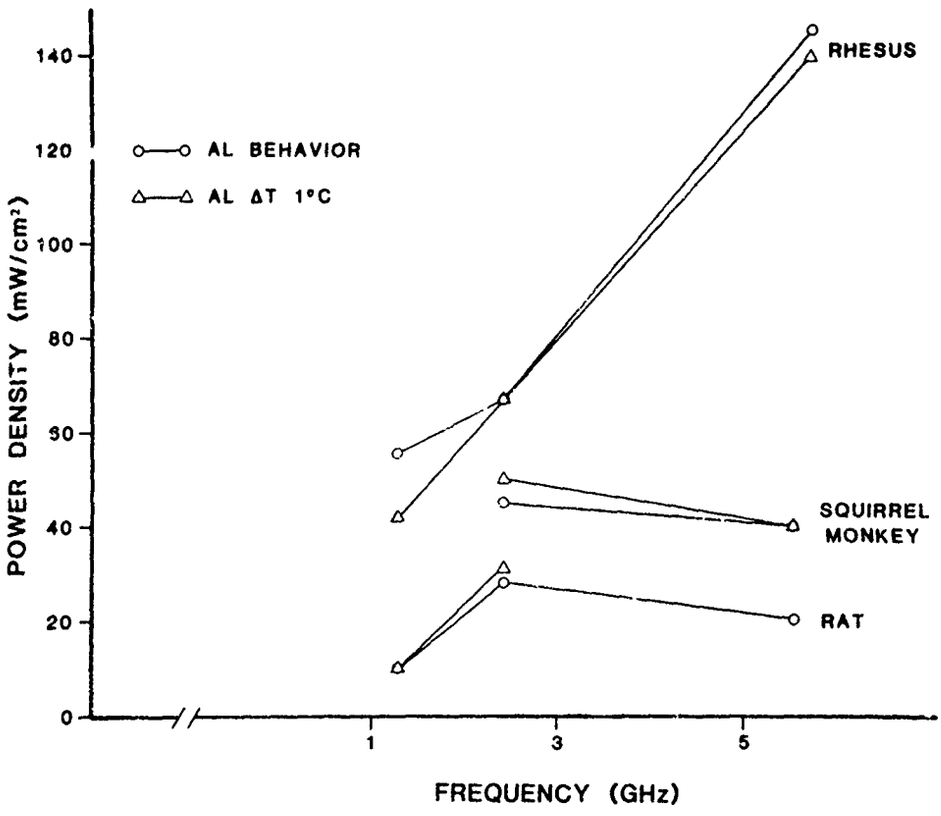

Figure 9 Thresholds (AL) of behavioral disruption of an operant task and of a 1 °C temperature increase above baseline for three different sized animals as a function of power density (ordinate) and frequency (abscissa).

may deposit more energy than dorsal irradiation at 2.45 GHz, and frontal irradiation of the sitting squirrel monkey may deposit more energy than dorsal irradiation at the same frequency.

In contrast to the relationships of earlier figures, Figure 9 suggests that data obtained from one animal species do not lend themselves very well to generalizations about other species. The results of the rat studies might lead one to draw completely different conclusions than those derived from the rhesus data. Only with several different species at very different body sizes as in the present study can one begin to gain a realistic assessment of microwave effects.

The general shape of these curves might be predicted from the specific absorption rate curves for these animals as described in Durney, *et al.* (1978). One major exception to this was the high power required at 5.8 GHz for the rhesus monkey. Much less power to produce effects at this frequency was predicted. The cause of this exception may lie in the fact that, at this frequency, it was necessary to position the animal at about 60 percent of the far-field distance from the horn to achieve high power densities in the area of the animal's head. This proximity to the horn resulted in a highly nonuniform distribution of power density across the ventral surface of the animal.

Specific absorption rates calculated or measured in saline models at the various threshold values for different species showed no consistencies except at 2.45 GHz. At this frequency the SAR's tended to average between 4 and 5 W/kg. The rat at 5.7 GHz and the rhesus at 1.3 GHz also absorbed between 4 and 5 W/kg at the behavioral thresholds. However, the squirrel and rhesus monkeys at 5.7 GHz absorbed higher levels of energy and the rat at 1.3 GHz absorbed less energy. Consequently, whole body estimates of energy absorption may not be the best data for predicting behavioral effects across frequencies. Other aspects of microwave energy deposition such as distribution or local resonance might be more consistent parameters for predicting behavioral effects. Although the correlation between behavioral change and a 1 °C temperature rise is very useful for estimating disruption of behavior, the argument that the response is caused merely by a core temperature change is not very convincing. As indicated in Figure 8 the causal agent could be energy deposition in the brain or head area.

It might be that at certain frequencies surface irradiation literally causes the animal to move away from a location so that another surface is illuminated or causes him to become less active and reduce metabolic rate

(Roberts, *et al.*, 1974). Such responses, compatible with reduced energy capture but incompatible with ongoing responding, could explain the results of several studies using both restrained and unrestrained animals. In addition, other characteristics of microwaves such as novel stimulation, affective tone, auditory stimulation, and even the body temperature decrease that occurs with the removal of microwave irradiation, should not be dismissed.

Our experiments only raise questions relating to the behavioral effects of microwaves at frequencies above resonance for these specific animals. A different set of relationships may exist at resonant and below resonant frequencies although this investigator would hazard a guess that the power density threshold would continue to decrease for all three animal sizes at resonant frequencies and then increase again at frequencies below resonance. The utility of any of the specific relationships, e.g., that in Figure 8, at any range of frequencies will have to be empirically determined. To help resolve the issue a study should be conducted with a single behavioral task in a species of animals where a large variation in body size occurs in adults of that species (the canine, for example). Microwave parameters could be determined that would allow a representative series of wavelengths below resonance, at resonance, and above resonance for each body size. Holding constant the species variable while allowing body and brain sizes to vary should provide definitive answers to many questions elicited by the present study.

ACKNOWLEDGMENTS

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REFERENCES

Catania, A.C. (1968). *Contemporary Research in Operant Behavior*. Scott, Foresman and Company. New York.

de Lorge, J.O. (1976). The effects of microwave radiation on behavior and temperature in rhesus monkeys. In "Biological Effects of Electromagnetic Waves. Selected papers of the USNC/URSI annual meeting." Vol. 1, U. S. Dept. of Health, Education and Welfare, Public Health Service, FDA, Bureau of Radiological Health. Washington, DC: DHEW Publication No (FDA) 77-8010.

de Lorge, J.O. (1979). Operant behavior and colonic temperature of squirrel monkeys during microwave irradiation. *Radio Sci* 14: 217.

de Lorge, J.O. (1980). The effects of microwaves on animal behavior. In *Ondes Electromagnetique et Biologie*. (A. I. Berteaud and B. Servantie, eds.), p. 171 URSI, CNFRS, Jouy en Josas, France.

de Lorge, J.O. and Ezell, C.S. (1980). Observing-responses of rats exposed to 1.28- and 5.62-GHz microwaves. *Bioelectromagnetics* 1:183.

Durney, C.H., Johnson, C.C., Barber, P.W., Massoudi, H., Iskander, M.F., Lords, J.L., Ryser, D.K., Allen, S.J., and Mitchell, J.C. (1978). *Radio-frequency Radiation Dosimetry Handbook*. 2nd edition, SAM-TR-78-22. Brooks Air Force Base, TX 78235: USAF School of Aerospace Medicine. NTIS Springfield, VA.

Frey, A.H., and Messenger, R. Jr. (1973). Human perception of illumination with pulsed ultra-high frequency electromagnetic energy. *Science* 181: 356.

Holland, J.G. (1957). Technique for behavioral analysis of human observing. *Science* 125: 348.

Houk, W.M. and Michaelson, S.M. (1974). Metabolic and thermoregulatory responses to microwave radiation in young male rats. In "Preprints of 1974 Scientific Program Aerospace Medical Association, 45th Annual Scientific Meeting," p. 174 Washington, DC, May 6-9.

Justesen, D.R. and King, N.W. (1970). Behavioral effects of low level microwave irradiation in the closed space situation. In *Biological Effects and Health Implications of Microwaves* Report BRH/DBE 70-2. (S.F. Cleary, ed.), p. 154 Bureau of Radiological Health., Washington, DC.

Kenshalo, D.R., and Hall, E.C. (1974). Thermal thresholds of the rhesus monkey. *J. comp. physiol. Psychol.* 86: 902.

Liu, C.T. and Higbee, G.A. (1976). Determination of body surface area in the rhesus monkey. *J. Appl. Physiol.* 40:101.

Lotz, W.G. and Michaelson, S.M. (1978). Temperature and corticosterone relationships in microwave-exposed rats. *J. Appl. Physiol.* 44:438.

McMahon, T. (1973). Size and shape in biology. *Science* 179: 1201.

Merritt, J.H., Chamness, A.F., Hartzell, R.H., and Allen, S.J. (1977). Orientation effects on microwave-induced hyperthermia and neurochemical correlates. *J. Microwave Power* 12: 167.

Nelson, T.D. Behavioral effects of microwave irradiation on squirrel monkeys (*Saimiri sciureus*) performance of a repeated acquisition task (1978). NAMRL-1245 Pensacola, FL 32508: Naval Aerospace Medical Research Laboratory.

Reno, V.R. and de Lorge, J.O. (1977). A primate restraint device for use in microwave biological research. *IEEE Trans. Biomed. Eng.*, BME-24: 201.

Roberts, W.W., Mooney, R.D., and Martin, J.R. (1974). Thermoregulatory behaviors of laboratory rodents. *J. comp. physiol. Psychol.* 86: 693.

Sanza, J.N., and de Lorge, J. (1977). Fixed interval behavior of rats exposed to microwaves at low power densities. *Radio Sci.* 12: 173.

Smiles, K.A., Elizondo, R.S., and Barney, C.C. (1976). Sweating responses during changes of hypothalamic temperature in the rhesus monkey. *J. Appl. Physiol.* 40:653.

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SUBTLE CONSEQUENCES OF EXPOSURE TO WEAK MICROWAVE FIELDS: ARE THERE NONTHERMAL EFFECTS?

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I. INTRODUCTION

Several studies have examined responses of the central nervous system, including behavior, to short-term (acute) microwave exposure. Comprehensive reviews have been prepared by Adey (1980), Justesen (1980), and Lovely (1982). Thermoregulatory response changes (Adair and Adams, 1980; Stern, *et al.*, 1979) are but one subset of such exposure effects. Few studies however, outside of those conducted in the Soviet Union, have examined effects of long-term (subchronic) exposure to microwaves at low levels of incident energy (less than 10 mW/cm^2). Thus, we know little about the effects of long-term exposure on behavior *per se* and

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other functions of the central nervous system including thermoregulation.

One reason for the paucity of research on the biological consequences of subchronic microwave exposure is the inherent difficulty in exposing a laboratory animal to microwave fields for long periods of time. For example, the introduction of life-support facilities (e.g., a source of drinking water) can compromise the exposure regimen densitometrically and dosimetrically by an order of magnitude or more (Guy and Korbel, 1972).

Recently, Guy and Chou (1976) developed an exposure system, the circularly polarized waveguide system, that could be used for the long-term exposure of a laboratory animal while maintaining relatively constant, and minimally unperturbed, field densitometry and correlated dosimetry. The studies reported here examined some mammalian responses to subchronic microwave exposure in this exposure system.

When we speak of "subtle consequences of exposure" we mean only that the effects were observed in the absence of changes in core temperature due to microwave exposure. When we measure + ΔT (°C) in core temperature consequent to microwave exposure, we are witnessing a breakdown of thermoregulatory mechanisms. Short of this event, the exposed subject makes a number of thermoregulatory *and metabolic* accommodations to maintain a constant body temperature and to deal effectively with the energy being deposited in its tissues. These latter changes should interest us for they *are* the subtle consequences of exposure to weak microwave fields. The long-term accommodations, which accompany subchronic exposure, can lead to a number of interesting effects some of which are described below.

II. MATERIALS AND METHODS

A. Exposure Protocols

Two fundamentally different types of experimental protocol were employed. In Experiment IA, independent groups of male rats were either exposed or sham-exposed to 915-MHz microwaves for 10 hr/night for up to 4 mo. In Experiment IB, independent groups of rats were similarly exposed, or sham-exposed, to 2450-MHz microwaves for 10 hr/ night for 4 mo. In Experiment II, using a different type of protocol, pregnant female rats were exposed for 20 hr/day for 19 days of gestation. Control groups were either sham-exposed or served as caged controls. The main focus of the study

attended to assessment of various functions and the developmental status of the gravid rats' progeny.

B. Microwave Exposure System

The exposure system illustrated in Figure 1 shows the Plexiglas cages in which the rats resided. Each rat could move freely within the 20 x 17 x 12 cm Plexiglas cage, which was centered inside the waveguide. Also shown is the non-field-perturbing water source (A), the food magazine (B), and the collecting tray (C) which catches and funnels excreta out of the exposure system. The exposure chamber consists of a cylindrical waveguide excited with circularly polarized guided waves. Eight waveguides were energized from a single power source via an eight-way power splitter

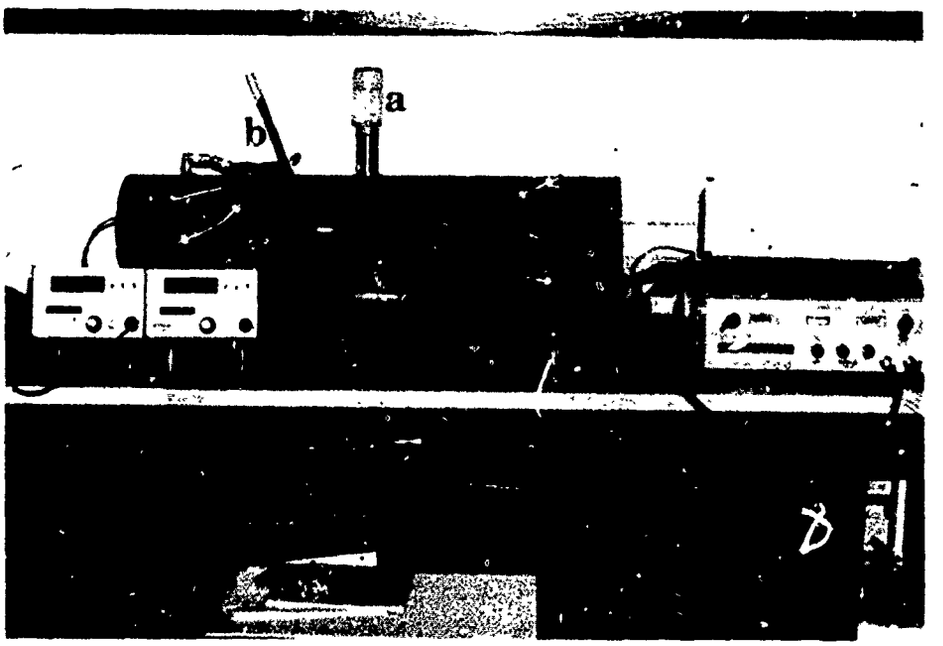


Figure 1. Side view of circular waveguide exposure system with rat in Plexiglas hutch. Water source (a) provides isolated drop of water that is electrically decoupled from microwave field by two quarter-wave concentric chokes. Food magazine (b) holds 15 to 20 chow pellets. Waste and excreta is funnelled to collecting tray (c). In the left foreground are power meters providing for measuring forward and reflected power which, in turn, can be used for numerical solution of energy capture by the rat to determine specific absorption rate (SAR).

(915-MHz) or four network-dividers with directional couplers (2450-MHz). The waveguide system allows for easy quantification of fields, in terms of specific absorption rate (SAR; i.e., the mass-normalized rate of energy absorption) and of spatially-averaged power density of energy incident on the animal. Eight similar sham-exposure units (i.e., not energized) were distributed proximal to the exposure units; all units were kept in the same room in which the hanging metal rat cages were maintained. Further details on the exposure system, as well as dosimetric evaluations, have been described by Guy and Chou (1976) for the 915-MHz system and by Guy and McDougall (1979) for the 2450-MHz system.

C. Exposures of Adult Male Rats (Experiment I)

In Experiments IA and IB, the subjects were independent groups of 16 naive Wistar-derived male rats (obtained from Simonsen Laboratories, Gilroy, CA) approximately 75 days of age on arrival at our laboratory. They were adapted to the laboratory environment for 2 weeks during which they lived in standard hanging metal laboratory cages (24 x 18 x 18 cm) on a diet of Purina chow and tap water *ad libitum*. Four 40-W red light bulbs illuminated the room continuously while banks of fluorescent ceiling lights were cycled on at 0700 hr and cycled off at 1900 hr. The room temperature averaged 22 ± 1 °C (range) and relative humidity was 50 ± 5% (range).

The general procedure has been described in detail elsewhere (Moe, *et al.*, 1976). Briefly, after the rats had been adapted to the hanging metal cages for 2 wk, they were allowed to adapt to the waveguide exposure system Plexiglas cages for 2 additional wk. At 1700 hr daily, each rat was placed in the Plexiglas cage, which was then inserted into the waveguide, where the rat remained until 0800 hr the next day. Exposure to microwaves was from 2200 hr to 0800 hr the next day, 7 days/wk for 16 wk. At 0800 hr, each rat was removed from the exposure system cage and returned to its hanging cage until 1700 hr, at which time the daily procedure was repeated. In addition to body mass, consumption of food and of water in the exposure system was determined each morning as were similar consumption measures for the home cage residence time at 1700 hr daily. In determining food consumption we included all chow that was spilled and that remained dry. This usually accounted for more than 80 percent of the rats daily spillage. Colonic temperature measurements were made as rapidly as possible (within 2 min) after termination of an exposure session. These measurements were made with a Bailey (BAT-8) digital display

thermistor thermometer. On a day scheduled for colonic temperature measurements one exposed rat and one sham exposed rat were removed from their exposure system cage immediately after the microwave source was turned off (0800 hr). The rat was gently cradled in one arm and the Bailey thermometer probe was inserted approximately 5 cm beyond the anal sphincter. Asymptotic temperature measurements were obtained in 7-10 sec. The procedure was then repeated the next morning at 0800 hr on a second pair of rats until all rats had been through the procedure. These determinations were made during the second, sixth and tenth week of exposure. In addition to these determinations, 2 cc intracardial blood samples were obtained, under light Penthrane anesthesia at 4, 8, 12 and 16 wk of exposure, for the determination of serum electrolytes, glucose, urea nitrogen, and carbon dioxide. At 13 wk of exposure, 2 cc blood samples were similarly obtained under ether anesthesia to determine basal and ether-stress-induced levels of corticosterone. When blood was sampled (0900-1100 hr), the rats were quickly and quietly removed from their home cage and placed in a dessicator jar filled with cotton soaked in anesthesia. Any blood sample not obtained within 2.5 min following removal of the rat from the home cage was discarded.

At the beginning of the 2 wk period of adaptation to the exposure system, the rats were matched for body mass and randomly assigned to either the exposed group (N = 8) or to the sham-exposed group (N = 8). If the groups were significantly different in mean body mass at the end of adaptation, they were matched again and reassigned to new groups before the start of exposure.

For Experiment IA, the 915-MHz waveguides were energized to produce a spatially-averaged power density of 5 mW/cm^2 (maximum of 10 mW/cm^2 on the center axis of the waveguide), representing a whole-body SAR of approximately 2.0 W/kg. For Experiment IB, the 2450-MHz waveguides were energized to produce a spatially-averaged power density of 5 mW/cm^2, which corresponded to a whole-body SAR of approximately 3.2 W/kg.

D. Exposures of Gravid Female Rats (Experiment II)

Thirty-eight naive, Wistar-derived, female rats obtained from the vivarium in the Psychology Department at the University of Washington (Simonsen Laboratories breeding stock, Gilroy, CA) were approximately 85 days of age on arrival at our laboratory. The next day they were allowed to adapt to

the laboratory for 5 days while residing in standard hanging metal cages (24 x 18 x 18 cm) with free access to Purina chow and tap water. The room temperature was 21 ± 1 °C; relative humidity and room lighting were the same as that described previously.

The 2450-MHz exposure system was the same as that employed in Experiment IB, except that it was energized to provide a spatially averaged power density of 500 $\mu W/cm^2$, corresponding to an SAR of approximately 0.3 W/kg in the *adult* rat.

After a 5-day period of adaptation to the laboratory, eight females (four smallest and four largest) were discarded to provide a more homogenous group of subjects. The remaining 30 females were then matched for body mass and randomly assigned to the exposed, sham-exposed, or non-handled caged control groups.

The 30 females were then allowed to adapt to the waveguide housing and exposure system for 2 wk. At 1200 hr daily, each rat was placed in the Plexiglas cage, which was then inserted into the waveguide, where the rat remained until 0800 hr the next day. At 0800 hr, each rat was removed from the exposure system and returned to it's home cage until 1200 hr, at which time the daily procedure was repeated. During this period, body mass, consumption of food and of water in the exposure system and in the home cage were determined each morning at 0800 hr and 1200 hr respectively.

At the end of the 2-wk period of adaptation to the exposure system, each female was randomly assigned to and individually housed with a male rat experienced as a breeder (obtained from the same Wistar stock as the female). Mating was determined by the presence of a sperm plug beneath the cage. The first eight of ten rats in each group to conceive were included in the three treatment groups described below (N = 8/group). At 1200 hr following mating, the female rat was returned to its exposure system cage or home cage, depending on treatment group.

1. Exposed Group. The pregnant rats were exposed for the first 19 days of gestation from 1200 hr to 0800 hr the following day. The rats were housed in their home cages from 0800 hr to 1200 hr each day. Body mass, consumption of food and of water in the exposure system and in the home cage were determined each morning at 0800 hr and 1200 hr respectively.

2. Sham-Exposed Group. The females were subjected to the same procedures as the exposed group, except that their waveguides were never energized.

3. Non-Handled Caged-Control Group. The females of this group were not handled through 19 days of gestation and were housed in hanging metal cages.

At 1200 hr, after the 19th exposure period, or the 19th day of gestation for caged controls, all gravid females were placed in individual opaque polyvinyl breeder bins (25 x 32 x 15 cm) with hardware cloth lids. These were filled with corn cob litter material; Purina chow and tap water were available continuously. At parturition (day 1), individual birth weights and the number of live and stillbirths, and obvious physical abnormalities were recorded. On day 4, each litter was culled to four females and four males, which were left with their natural mothers (N-pups). The prenatally exposed or sham-exposed pups, which were culled *out* of the above litters, were given to naive foster mothers (F-pups) of the same postpartum status, which were obtained from the same colony in the vivarium. They were housed in lucite breeder bins with stainless steel wire lids filled with corn cob litter material. The foster mothers had access to Purina chow and tap water *ad libitum*. Each F-pup was either exposed or sham-exposed to 500 $\mu W/cm^2$, 2450-MHz microwaves, 2 hr/day from day 4 through day 11 of life During exposure, the F-pups were placed on a Styrofoam platform. This constrained movement of the pups to a 25-cm^2 area in the center of the Plexiglas cage which was inserted into the exposure system as shown in Figure 2. Determinations of the temperature of thoracic skin were made before and after each exposure period for all F-pups. All temperature measurements were made with a Bailey (BAT-8) digital display thermistor thermometer. As each foster pup was removed from its breeder bin, or 2 hr later from the exposure system, the Bailey surface sensor was placed firmly against the pups rib cage. The sensor was attached to a sturdy wire lead so that only pressure on the wire distal from the sensor was necessary to achieve a firm contact with the thoracic skin over an area of approximately 1 cm. Asymptotic temperature readings were obtained within 7-10 sec. Body mass on day 7 and day 11 of life was also measured.

A summary of the partial fostering design of the experiment and the N's involved is shown in Table I.

On day 7 of life, and weekly thereafter, the body mass of each N-pup was determined. All pups were weaned at 28 days

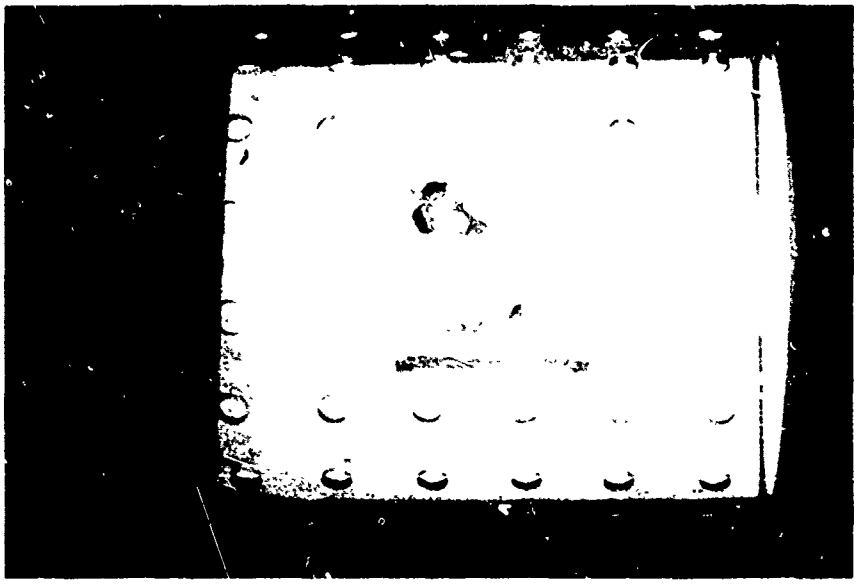


Figure 2. Plexiglas rat hutch with Styrofoam support pad inserted to hold neonatal rat pup for postnatal microwave exposure. The center square was made with Styrofoam walls to constrain neonatal movement during exposure.

of age. At 98 days of age, all F-pups were subjected to an 8-hr (maximum time) cold stress test at 5 ± 0.5 °C. During the cold stress test, the rats were restrained in a Plexiglas rodent holder. The colonic temperature of each rat was monitored continuously using the Bailey thermistor thermometer. The probe was inserted approximately 5 cm beyond the anal sphincter and was left in this position throughout the cold stress test with the wire lead terminal left outside the test chamber. These in turn were plugged into the Bailey thermometer and core temperature was recorded at half hour intervals. We did not carry out this assessment, or continue with the postnatal microwave exposure, in the N-pups because other tests (not described here) had been scheduled for these main groups (e.g., day of eye openings, shuttlebox-avoidance conditioning, circadian period of deep colonic temperature, etc.).

Table I. Number of F-Pups/Treatment Condition and Experimental Design

Prenatal Condition/Postnatal Condition	Code	N Females	N Males
Exposed/Exposed	E/E	3	4[a]
Exposed/Sham-Exposed	E/S	3	4
Sham-Exposed/Exposed	S/E	4	4
Sham-Exposed/Sham-Exposed	S/S	4[a]	4

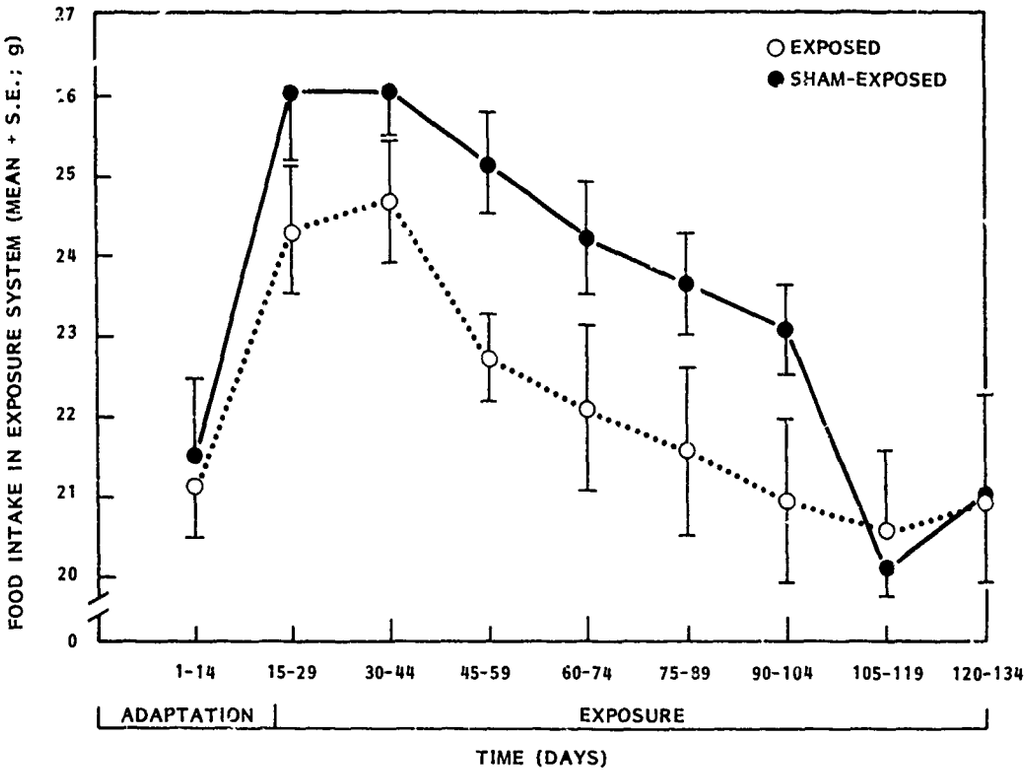
[a] N = 3 for adult assessment

III. RESULTS AND DISCUSSION

A. Exposures of Adult Male Rats (Experiment I)

The effect of exposure to 915 MHz microwaves on food consumption and body mass is shown in Figure 3. In Figures 3A and 3C, it is clear that there was a dramatic drop in total food consumption and food consumption in the exposure system for the sham-exposed rats at the end of the 14th wk of exposure. This occurred because exposure logistics necessitated employing a new water bottle which failed to operate properly when it was initially installed (in the 13th wk). This reduction in food consumption (contingent upon availability of water) was offset, in part, by an increased consumption of food in the home cage (Figure 3B). Nevertheless, total food consumption by the sham-exposed control group was reduced during the 13th and 14th wk (Figure 3C). Because food consumption was compromised by apparatus malfunction, we analyzed the data presented in Figure 3 only through 12th wk of exposure.

The food consumption and body mass data shown in Figure 3 were analyzed by a repeated-measures analysis of variance (Edwards, 1978). Food consumption in the exposure system was not significantly different for the two groups, F (1, 14) = 3.61, $0.05 < p < 0.10$, although there was a significant source of variance attributable to repeated measures,



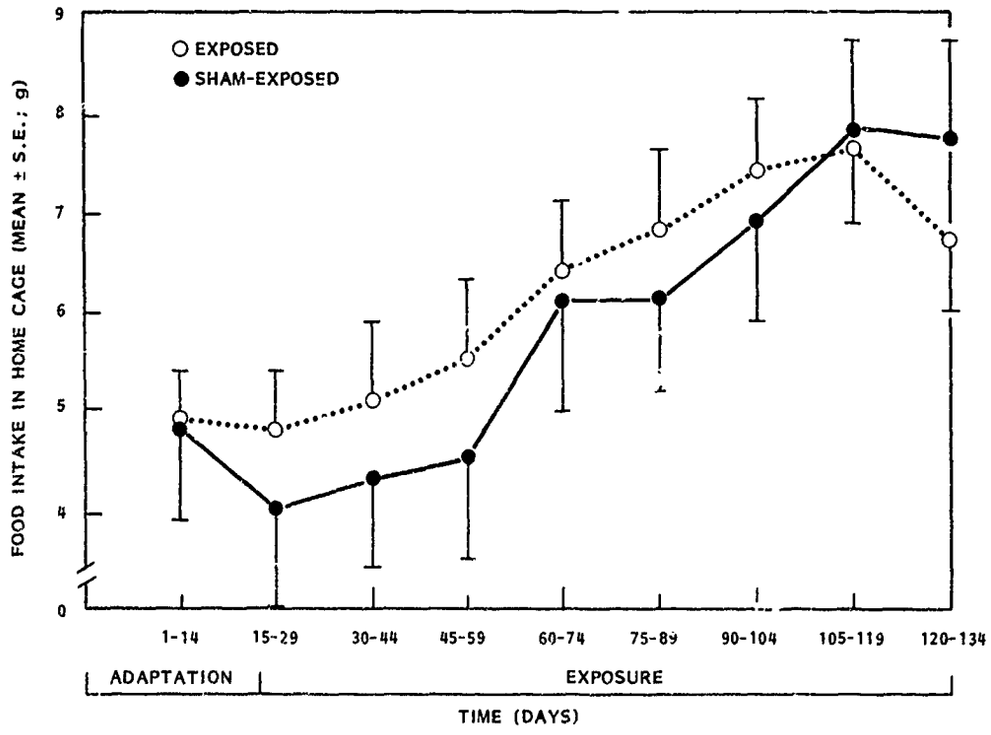
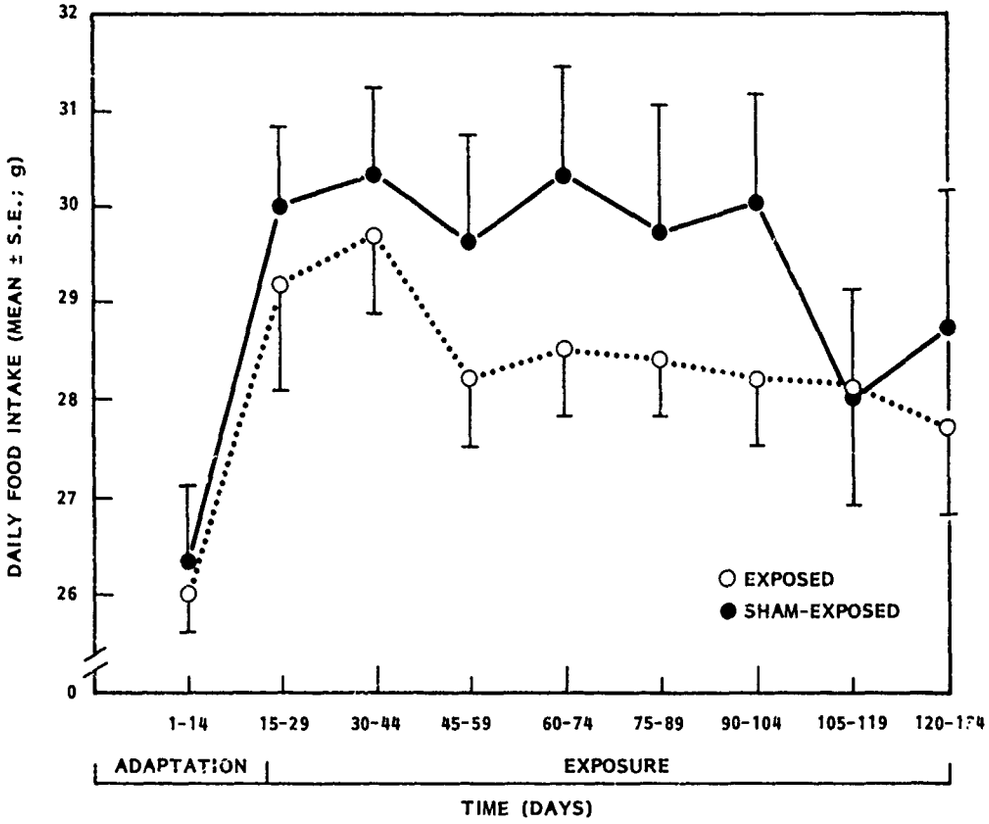
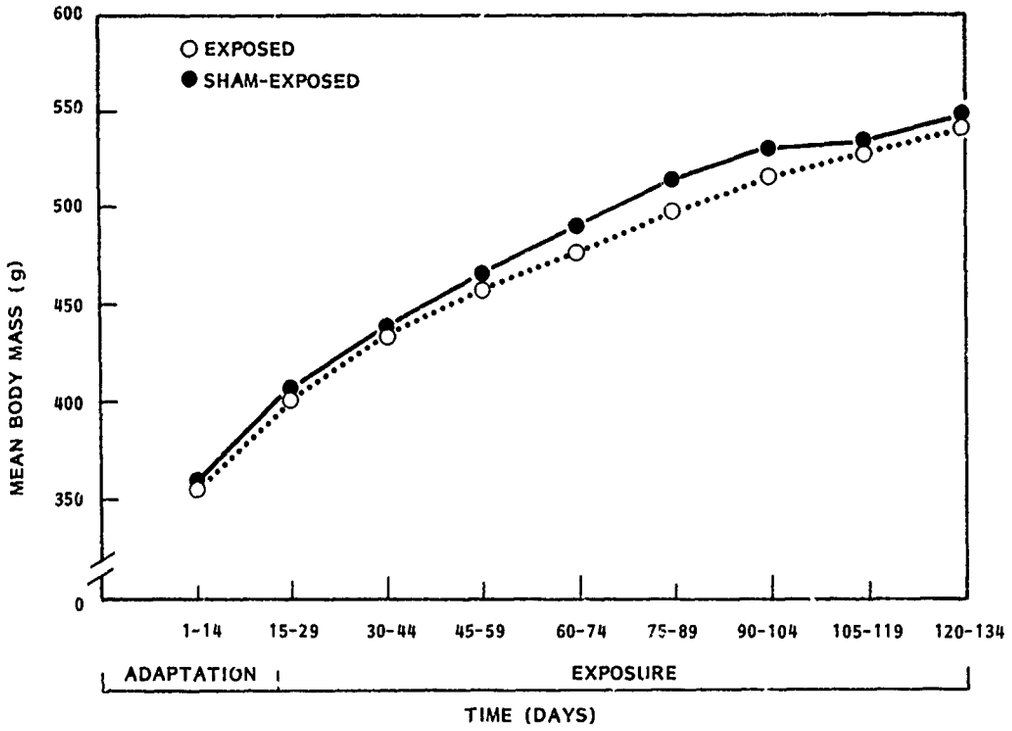


Figure 3A and B





Figures 3C and D (Legend on following page.)

F (5, 70) = 31.76, $p < 0.001$. The interaction term was not significant, F (5, 70) < 1.0. Similarly, food consumption in the home cage failed to differentiate groups with regard to treatment, F (1, 14) < 1.0, although a significant effect of repeated measures was found, F (5, 70) = 30.83, $p < 0.001$, while the interaction term was not significant, F (5, 70) < 1.0. As for total daily food consumption, no significant differences were found due to treatments, F (1, 14) = 1.01, repeated measures, F (5, 70) = 1.75, nor was there a significant interaction, F (5, 70) < 1.0. As Figure 3D suggests, microwave exposure failed to alter body mass, F (1, 14) < 1.0. There was, however, a significant effect of repeated measures, indicating that rats in both groups increased body mass with age, F (5, 70) = 174.78, $p < 0.001$. As with the other analyses, the interaction term was not significant, F (5, 70) < 1.0.

Turning to Experiment IB at 2450-MHz, the food consumption in the exposure system, food consumption in the home cage, total daily food consumption, and body mass are illustrated in Figures 4A, B, C and D (respectively) and were analyzed in the same manner as the 915-MHz data, with two exceptions: 1) The analysis of variance evaluated the data over the entire experiment (16 wk), as opposed to the 12-wk analysis of Experiment IA; 2) Since one rat in each condition died during the 4th wk of exposure from complications of the blood drawing procedure, all data analyses involved N = 7 sham-exposed rats and N = 7 exposed rats.

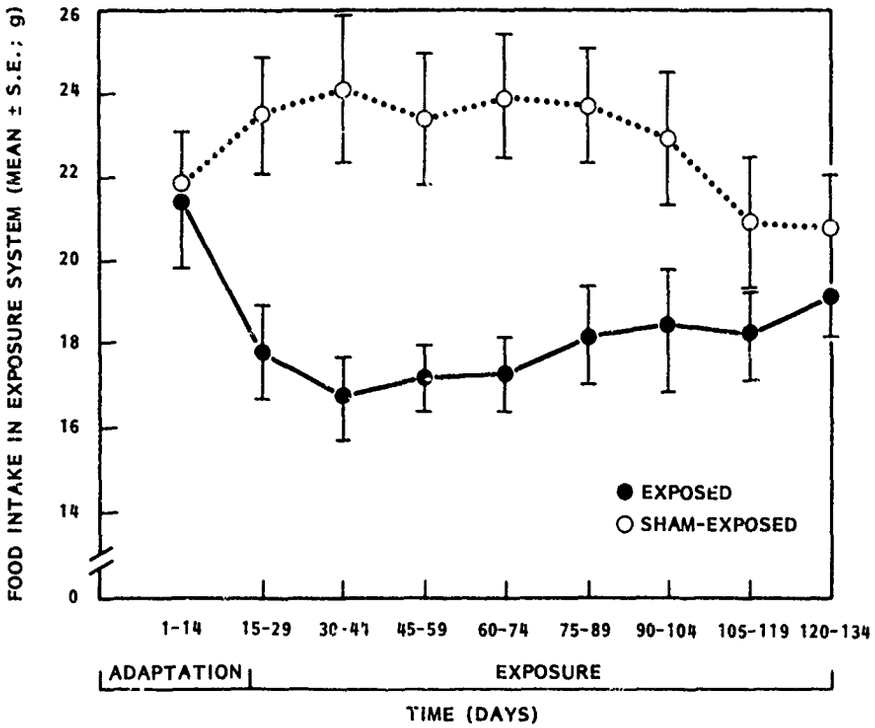
A repeated measures analysis of variance on food consumption in the exposure system revealed a significant source of variation for treatments, F (1,12) = 8.21, $p < 0.025$. Significant sources of variation were also found for repeated

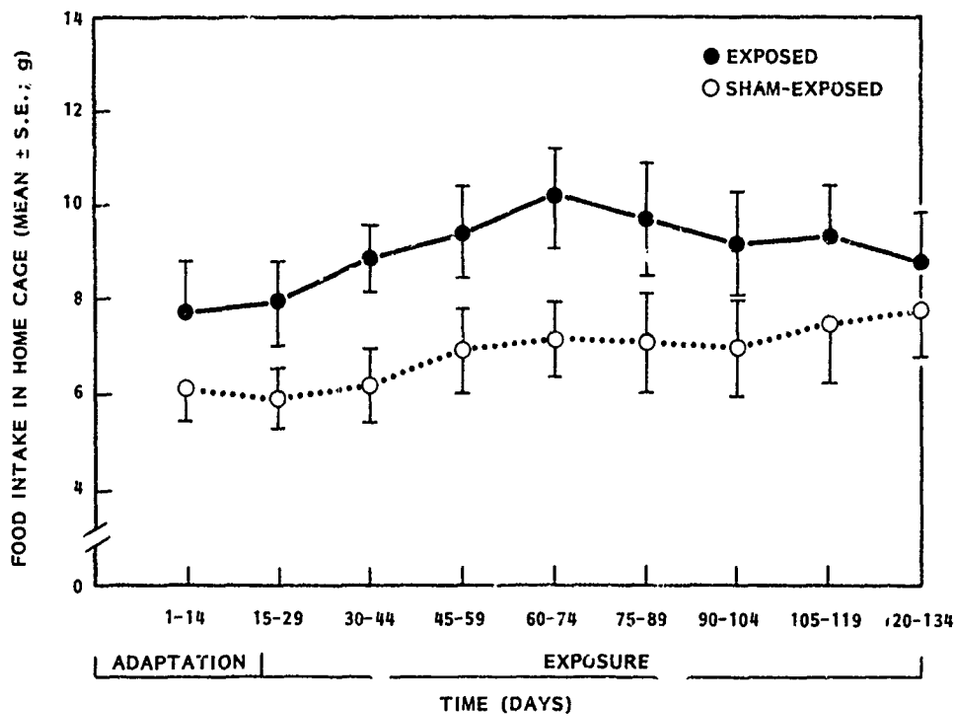
Figure 3. Summary of food consumption data and correlated body mass for sham-exposed rats and for rats exposed to 5 mW/cm^2, 915-MHz microwaves 10 hr/night, 7 days/wk for 16 wk. Panel A shows the exposure system food intake in g/day plotted by 14-day blocks. The precipitous drop in sham-exposure food consumption in the 7th block (day 105) was caused by a failure in the watering system. Panel B shows complimentary home cage food intake in g/day by 14-day blocks. Panel C shows the total daily food intake for exposed and sham-exposed rats over the course of the experiment. Means are plotted in 14-day blocks (± SE). Panel D shows the body mass in g for the two groups of rats studied (mean ± SE). Data were similarly plotted by 14-day blocks.

measures, F (7, 84) = 6.39 $p < 0.05$, and the treatment by repeated measures interaction term, F (7, 84) = 4.59 $p < 0.001$, as might be expected from inspection of the functions in Figure 4A. Figure 4B suggests that, in the home cage, exposed rats compensated for some of the reduction in exposure system food intake, however, analysis of variance failed to reveal significant treatment effects, F (1, 12) = 2.91. There was a significant effect of repeated measures because both groups increased food consumption in the home cage by 1 to 2 g over the course of the experiment, F (7, 84) = 6.05, $p < 0.001$. The interaction term was not significant, F (7, 84) = 1.33. Total daily food consumption as a function of time is shown in Figure 4C. While the exposed rats consumed less food throughout most of the experiment, the overall analysis of variance failed to reveal a significant effect of exposure, F (1, 12) = 2.74. Both groups increased food consumption, on the average, over the course of the study, as was reflected in a significant effect of repeated measures, F (7, 84) = 2.92, $p < 0.025$. As the functions in Figure 4C suggest, there was also a significant interaction term, F (7, 84) = 4.31, $p < 0.001$. Despite the fact that the exposed group consumed less food, there was no significant difference in body mass between the two groups, F (1, 12) < 1.0 (Figure 4D). The same analysis did reveal a significant effect of repeated measures, F (7, 84) = 10.45, $p < 0.001$, reflecting normal growth. The interaction term was not significant, F (7, 84) < 1.0.

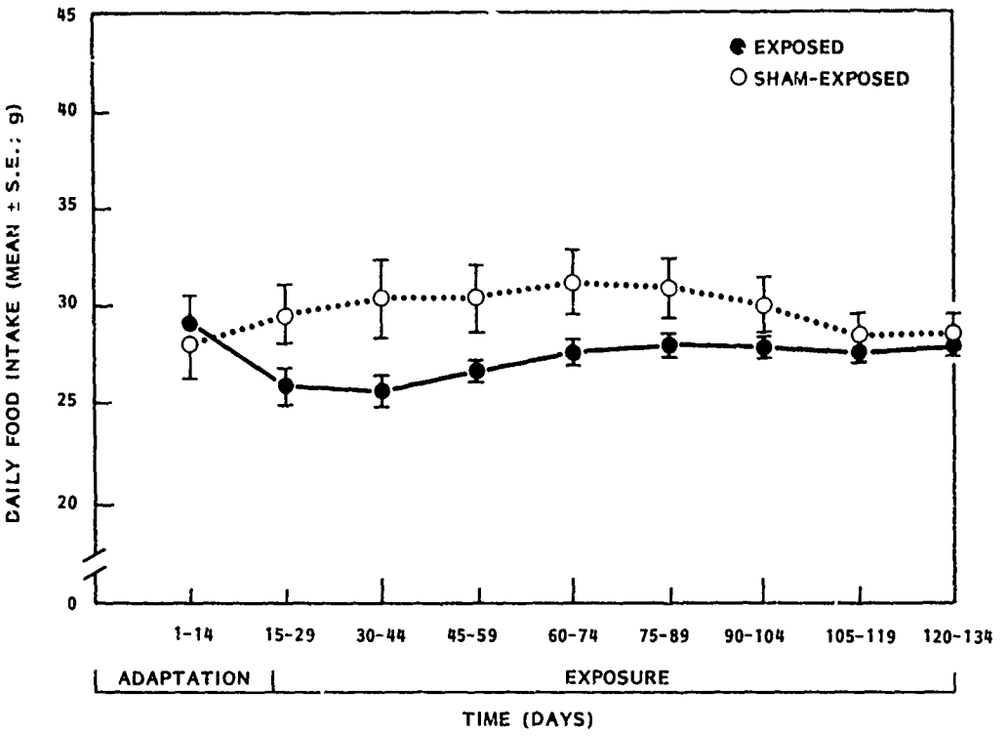
Figures 3 and 4 suggest that rats exposed to microwave energy reduce food intake during exposure and compensate (but not completely) by increasing food consumption in the home cage such that there is a net reduction in food intake that occurs without a correlated reduction in body mass. Despite the variability in the data reported, and the fact that changes in baseline food consumption in home cage versus exposure system often occur (Figures 3A and 3B), reduction in food intake is the most robust and dose-dependent effect we have observed in response to subchronic microwave exposure.

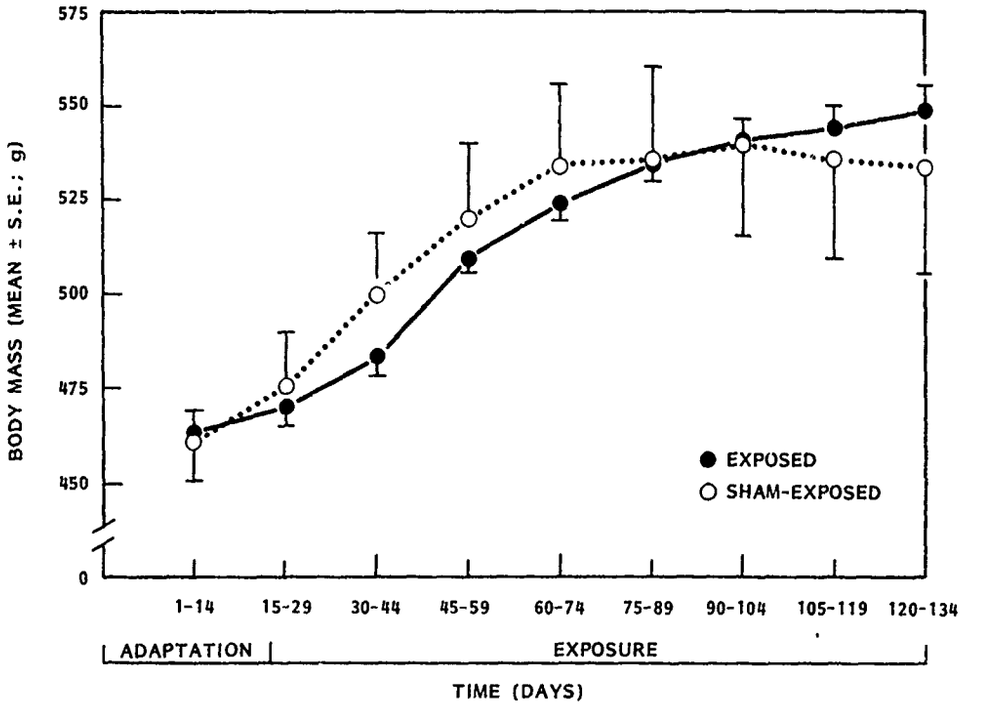
In an earlier study (Moe, *et al.*, 1976), we exposed rats to 915-MHz microwaves at 10 mW/cm^2 (SAR = 3.6 W/kg). At that dose, we observed an average reduction in food intake, relative to controls, that was about twice as large as that observed here at 5 mW/cm^2. Similarly, Lovely, *et al.* (1977) reported a reduction in food intake for 915-MHz subchronic exposures at 2.5 mW/cm^2 (SAR = 0.9 W/kg) which was about half the amount observed in the 915-MHz study reported here. These values are summarized in Figure 5. The overall average reduction in food intake obtained at 2450-MHz, incident





Figures 4A and B





Figures 4C and D (Legend on following page.)

at 5 mW/cm^2, reported here also appears in Figure 5. It is clear that the 915-MHz dose-response function is a rather good predictor of the reduction in food intake during subchronic exposure to 2450-MHz microwaves.

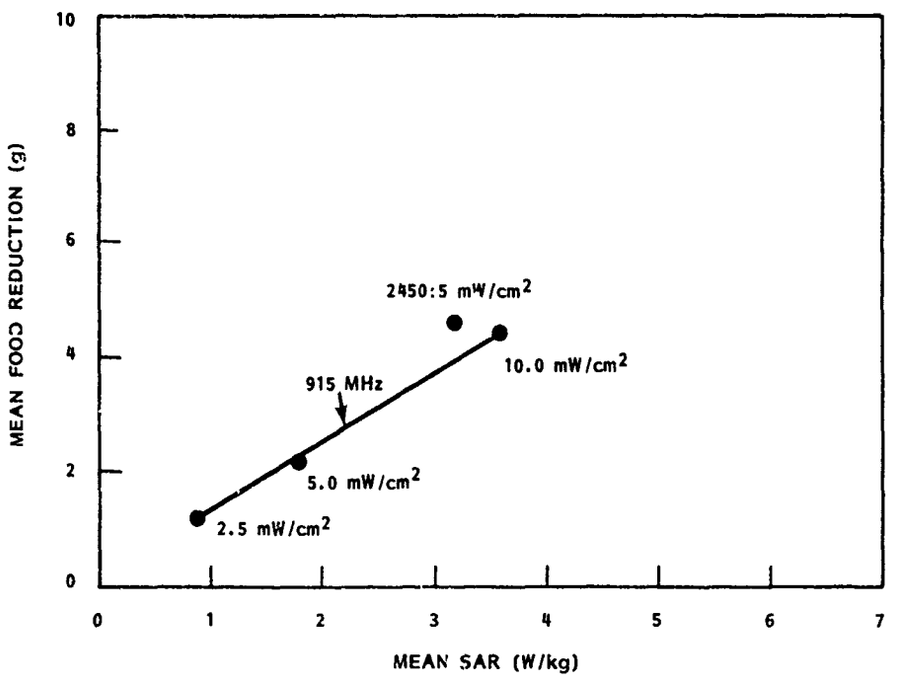


Figure 5. Summary of the average food reduction by rats exposed to 915-MHz microwaves as a function of mean specific absorption rate (SAR). The values plotted represent overall mean difference scores from the sham-exposed rats tested in the same experiment (see text). The result of the 2450-MHz study reported here is also plotted and is close to the value that would be predicted from the 915-MHz function.

Figure 4. Summary of food consumption data and correlated body mass for sham-exposed rats and for rats exposed to 5 mW/cm^2, 2450-MHz microwaves 10 hr/night, 7 days/wk for 16 wk. Panels A, B and C show the exposure system food intake, home cage food intake and total daily food intake plotted in 14-day blocks. Panel D shows the correlated body mass in g for the two groups of rats studied. All values are mean ± SE.

The most parsimonious explanation for the effects summarized in Figure 5 would seem to be that the exposed rats make a metabolic accommodation as a consequence of the energy being deposited in their tissues. We can think of no other explanation since exposed rats maintain the same body mass as their sham-exposed counterparts. Since we were not prepared to assess oxygen consumption or carbon dioxide production *during* exposure, we are not able to confirm or negate our hypothesis of metabolic accommodation. Nevertheless, we believe our interpretation of the data most likely accounts for the dose-dependent difference in total food consumption of the exposed and sham-exposed rats. In all of these studies, we have carried out a number of behavioral assessments at the end of subchronic exposure (e.g., shuttlebox avoidance learning, open field performance, and reactivity to ac electric foot shock) but we have failed to see consistent effects which differentiated groups by treatment condition or dose rate. Similarly, the blood analyses we performed did not produce consistent findings related to exposure. Small and evanescent changes occurred in such blood parameters as hematocrit, glutathione, blood cholinesterase, and serum sodium. However, such changes typically occurred once, were not replicated in subsequent studies and appeared on a haphazard basis throughout the 4 mo of exposure and blood sampling. We are inclined to dismiss such effects as false positives in light of the large number of parameters we have assessed. Additionally, basal and ether-stress-induced corticosterone levels have consistently failed to differentiate between treatment groups. Therefore, reduced food consumption remains the one parameter we consistently observed to be a consequence of subchronic microwave exposure. This finding can be generalized across microwave frequencies and is both reliable and predictable. We should not be surprised that the rodent profits from subchronic exposure to microwave energy and that its reduced energy needs are manifested by a reduction in daily food consumption.

B. Exposures of Gravid Female Rats (Experiment II)

Observation for sperm plugs proved to be at least 80% efficient in detecting conception. Seven out of eight female rats in each treatment group came to term. Table II summarizes food and water intake for the exposed and sham-exposed groups throughout gestation. As in the exposures of adult male rats, it appears that total food intake was less

for the exposed than for the sham-exposed rats, however the effect is not statistically significant. Unlike the results from adult male rats this led to a reduced increase in body mass for the exposed dams relative to the sham-exposed dams as shown in Figure 6 (see inset). However, this effect was not significant (see Table II).

Despite the fact that the exposed dams ate less food and gained less weight, there was not a statistical difference in the mean body mass at birth of the three groups' progeny, suggesting that all viable fetuses were healthy at birth. These data are shown in Table III, together with other data bearing on litter viability. There were no obvious physical

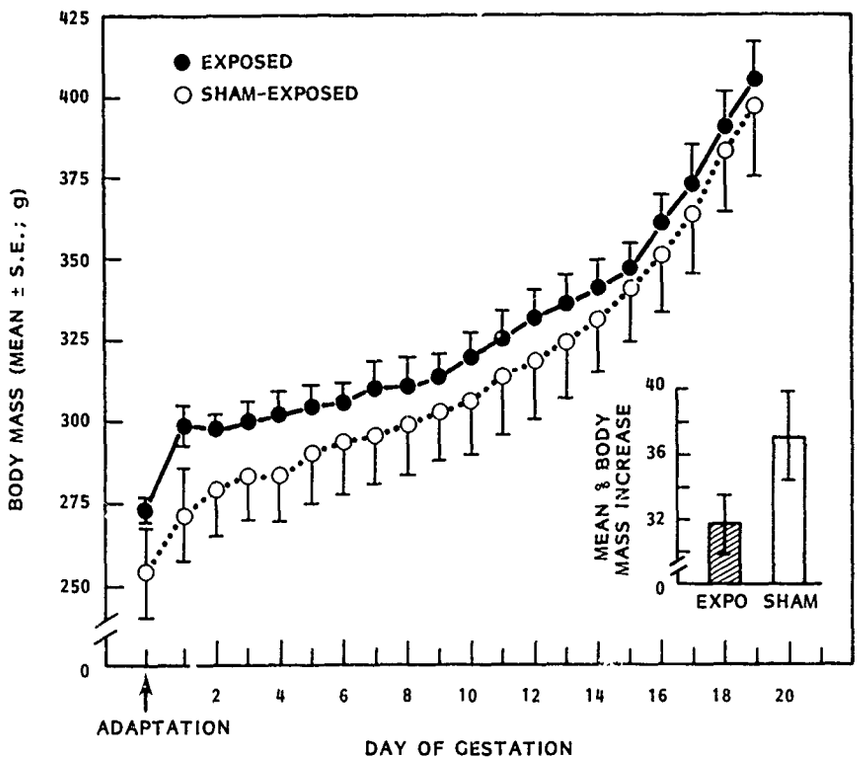


Figure 6. Body mass (Mean ± SE) and growth curves for the gravid female rats exposed or sham-exposed to 500 $\mu W/cm^2$ 2450-MHz microwaves. Inset shows mean increase in body mass for the two groups of gravid rats as a percentage increase from days 1-3 of gestation to days 17-19 of gestation.

abnormalities among the live pups of each dam, although there was a six-fold increase in neonatal deaths in the microwave-exposed group relative to the sham-exposed and caged control groups that occurred within the first week of life (p = 0.13, Fishers Exact, Segal, 1956).

Table II. Maternal Food and Water Intake Through Gestation and Associated Changes in Body Mass

	Mean Increase (%)[a]		
	Exposed	Sham-Exposed	P Value[b] (One-Tail)
Body Mass (BM)	+31.81	+37.11	$p < 0.10$
Waveguide Food Intake/100 g BM	-1.109	-0.459	$p < 0.10$
Home Cage Food Intake/100 g BM	+0.550	+0.357	NS[c]
Total Food Intake/100 g BM	-0.556	-0.090	NS
Waveguide Water Intake/100 g BM	-0.206	+1.059	$p < 0.10$
Home Cage Water Intake/100 g BW	+1.1419	+0.358	$p < 0.025$
Total Water Intake/100 g BM	+1.064	+1.453	NS

[a]Value obtained by subtracting mean value for days 1-3 from the mean value for days 17-19

[b]t-test, df = 12

[c]NS = not significant; $p > 0.05$

Body mass determinations of the N-pups on day 7 of life revealed significantly lower values for the prenatally-exposed pups relative to controls, both for female progeny, F (2, 82) = 5.41, $p < 0.01$, and for male progeny, F = 3.17 (2, 80), $p < 0.05$. By day 14, body mass no longer differentiated prenatal treatment groups. However, we observed apparent differences in body mass that began to emerge in

Table III. Litter Viability and Summary of Neonatal Status (Mean ± SEM)

Prenatal Condition	Mean Number Live Births	Mean Number Stillbirths	Mean Litter Weights (g)[a]	Mean Birth Weight (g)	Total Neonatal Deaths[b]
Exposed	13.14 ± 0.77	0.143 ± 0.143	85.06 ± 5.56	6.40 ± 0.08	6/92
Sham-Exposed	12.71 ± 1.15	0.143 ± 0.143	82.33 ± 5.88	6.40 ± 0.06	1/89
Caged Controls	13.43 ± 0.92	0	87.06 ± 3.26	6.48 ± 0.08	1/94

[a]Value includes live and stillbirths
[b]Value does not include F-pups

young adult female progeny of the exposed dams, which we failed to see in the male progeny of these dams. Further, the effect appeared to occur in both the female N-pups (Figure 7) and in the F-pups (Figure 8). A repeated-measures analysis of variance on the data from N-pups revealed that although the growth curve for the prenatally exposed rats was higher than that for controls, no significant source of variation could be attributed to treatment conditions, F (2, 42) = 1.20. There was a significant effect of repeated measures, as expected, F (13, 546) = 388.58, $p < 0.001$, while the interaction term was not significant, F (26, 546) = 1.18. A similar analysis on the functions for the body mass of F-pups did reveal a significant treatment effect, F (1, 12) = 9.15, $P < 0.025$, and an effect of repeated measures, F (7, 84) = 227.7, $p < 0.001$. The interaction term was not significant, F (7, 84) < 1.0.

The thermoregulatory tests showed that during the postnatal exposure period (days 4 through 11 of life), the prenatally exposed females that were postnatally sham-exposed

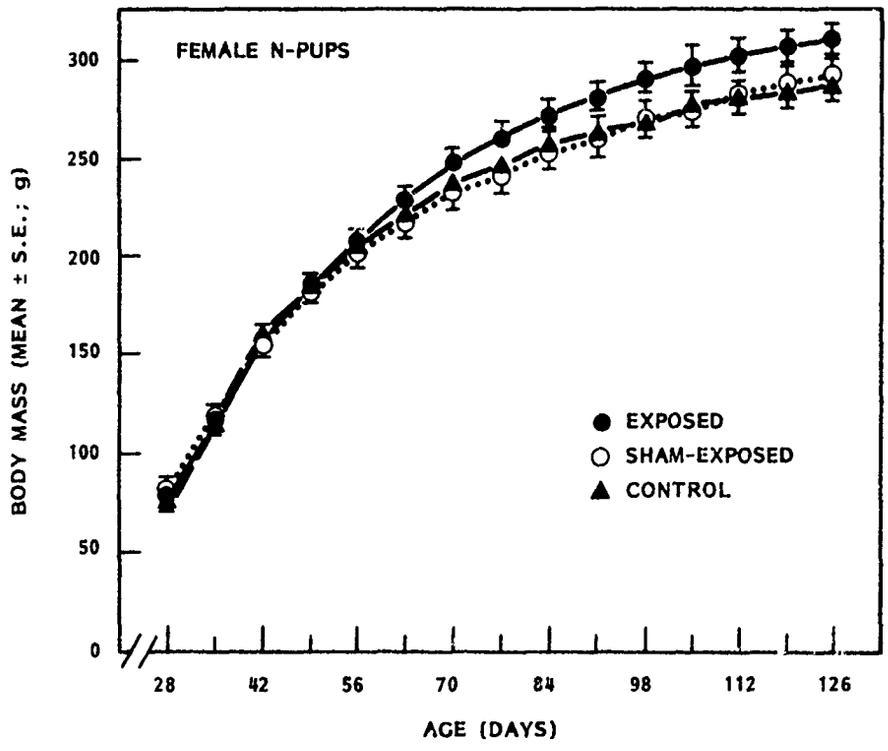


Figure 7. Body mass (Mean ± SE) and growth function for the female progeny of microwave-exposed, sham-exposed and caged-control dams that were left with their natural mothers i.e., N-pups.

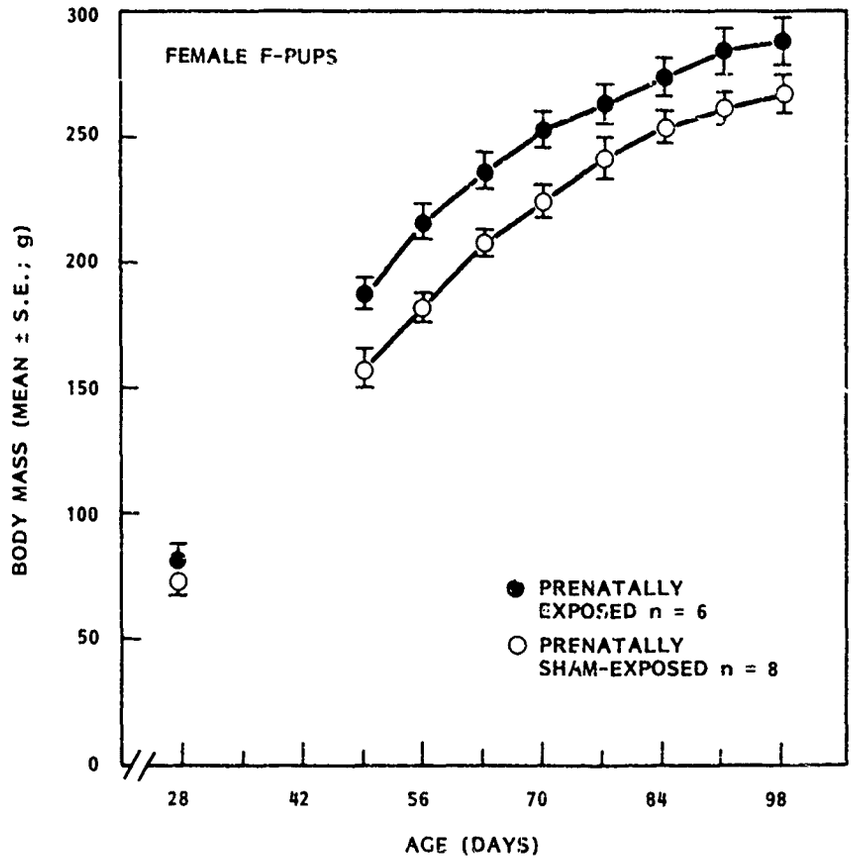


Figure 8. Body mass (Mean ± SE) and partial growth function for the female progeny that came from exposed or sham-exposed rat dams and then fostered (F-pups) to naive dams at 4 days of age to continue exposure or sham-exposure for one week of postnatal life. The above functions are resolved only by plotting data as a function of prenatal condition. Evaluation of the data by postnatal treatment or combined pre- and postnatal condition failed to produce different body mass functions.

(group E/S) sustained a greater reduction in surface temperature than did the other foster groups. This difference was only observed on the last 3 days of treatment (days 9-11, Figure 9). A repeated-measures analysis of variance on the scores of the females revealed a significant effect of treatments, F (3, 10) = 10.27, $p < 0.005$. The effect of repeated measures and the interaction term were not significant, F (2, 20) = 3.09, F (6, 20) < 1.0, respectively. As

the left side of Figure 9 suggests, the E/S group was significantly different ($p < 0.001$) from the other three groups, while the latter were not significantly different from one another as determined by *t*-tests using the pooled error term from the analysis of variance. A similar analysis of the scores of the males failed to resolve differential effects of treatment, F (3, 12) < 1.0, or a significant interaction, F (6, 24) < 1.0. There was, however, a significant effect of repeated measures, F (2, 24) = 4.39, $p < 0.025$. This was due to a linear increase in change of

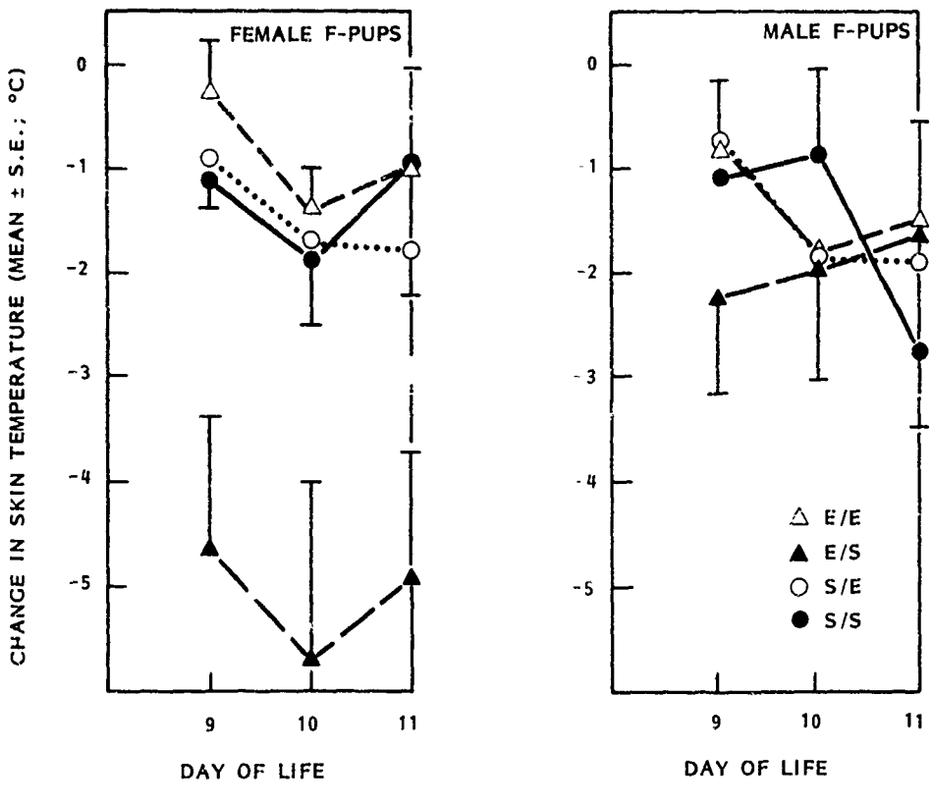


Figure 9. Change in thoracic skin temperature (Mean ± SE) during the last 3 days of postnatal microwave exposure or sham-exposure for 2 hr daily. Values represent temperature changes (°C) from time pup was taken from dam to the time it was removed from the waveguide to be returned to the dam. Abbreviations represent fostering code as follows: E/E - prenatally exposed to microwave/postnatally exposed to microwaves, E/S - prenatally exposed to microwaves and postnatally sham-exposed, S/E - prenatally sham-exposed and postnatally exposed to microwaves, S/S - prenatally and postnatally sham-exposed.

temperature over the last 3 days of testing (about 0.4 °C/day) taken over *all* groups.

The results of the cold-stress test are shown in Figure 10. Deep colonic temperatures are plotted from the time that the rats reached their peak colonic temperature in response to the combination of insertion of the thermistor probe, restraint in a rodent holder and placement in the 5 °C environment. The test was scheduled for up to 8 hr, but some of the male F-pups became severely hypothermic (e.g., to 33 °C in 4 hr) and had to be removed prematurely from the test environment. Thus, the data are presented and analyzed only through the first 4 hr of testing so that data from all of the F-pups tested could be included in the analysis. The mean colonic temperatures are plotted at half hour intervals and were analyzed by repeated-measures analysis of variance.

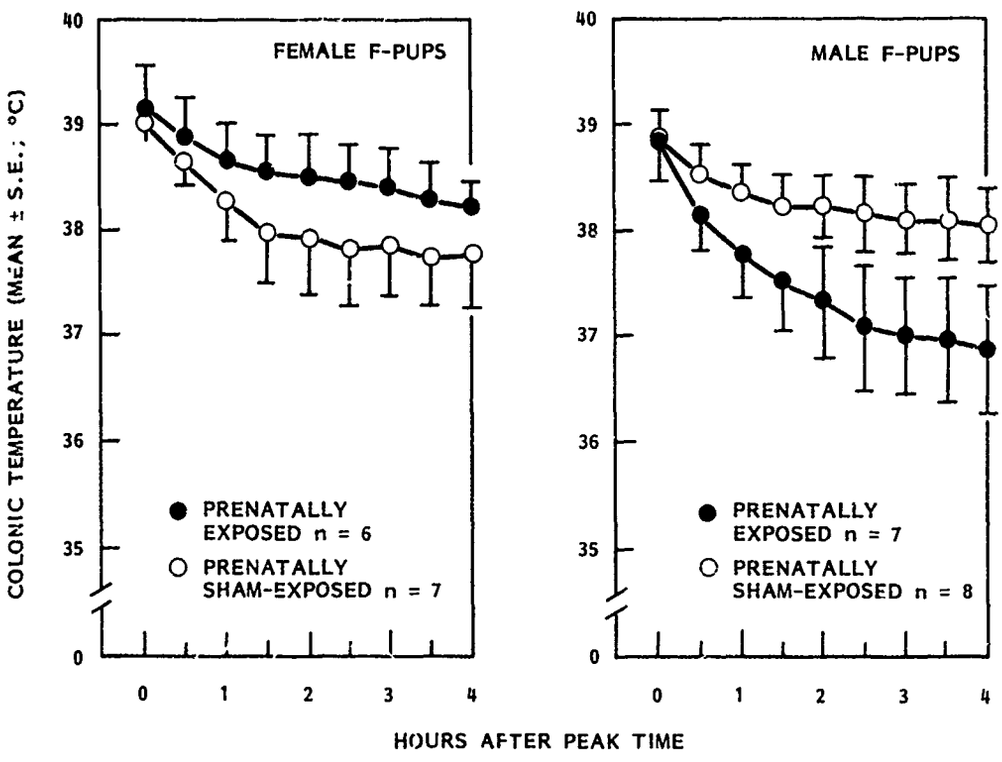


Figure 10. Colonic temperature functions for female and male F-pups tested at approximately 90 days of age. Peak time refers to the highest temperature recorded resulting from insertion of colonic probe, restraint and subsequent cold stress and is plotted at t = 0. Mean (± SE) values are plotted at half hr epochs through the 4 hr following t = 0.

As the left half of Figure 10 suggests (females), there was no significant source of variation due to treatments, F (1, 14) = 1.10. Neither was the interaction term significant, F (12, 144) < 1.0. The colonic temperature of all rats fell over time, as reflected in a significant effect of repeated measures, F (12, 144) = 32.44, $p < 0.001$. The right half of Figure 10 shows the comparable temperature functions for the male F-pups. A repeated-measures analysis of variance failed to reveal a significant treatment effect, F (1, 14) = 1.71, but did identify significant sources of variation due the temporal variable (repeated measures) and a significant treatment by trials interaction reflecting the differential rate of heat loss in the prenatally exposed male F-pup adults, F (8, 112) = 19.22, $p < 0.001$, and F (8, 112) = 3.20, $p < 0.005$, respectively.

In summary, prenatal exposure to 2450-MHz microwaves at 500 $\mu W/cm^2$ produced no discernible physical birth defects or difference in body mass at birth relative to the two control groups. However, male and female progeny of exposed dams had smaller body masses at the end of 1 wk of life relative to controls. Female progeny exposed prenatally and fostered on day 4 of life had greater changes in skin temperature when taken from their foster mothers 2 hr/day for postnatal sham-exposure while other fostered groups had no such difficulty. As young adults, and later in life, female rats exposed prenatally developed greater body mass than female rats comprising groups of control progeny. While male progeny exposed prenatally could not be differentiated from the control groups on these parameters they were different in their ability to retain core heat in a 4 hr cold stress test. For this last test, however, prenatally-exposed females maintained core temperature relative to the female rats of the sham-exposed control group. Thus, other than body mass at 7 days of age the various effects of prenatal microwave exposure appear to be specific to one sex or the other depending on the parameter assessed.

The diversity of observed effects resulting from prenatal microwave exposure are worthy of several comments. First, in any developmental study that allows the pups of the experimental dam to come to term, there is the possibility that any effects observed may be due to residual or proactive treatment effects on the dam which cause her to engage in abnormal postnatal mothering. We are inclined to dismiss this as an explanation for the effects reported here because of the partial fostering design employed. For example, female progeny showed increased body mass whether they were fostered or left with their natural mothers. Further, the partial fostering design had four treatment conditions,

but the data analysis showed that the prenatal treatment condition accounted for the effects observed. The one exception to this generalization was the reduced surface skin temperature seen during the week of postnatal microwave exposure (Figure 9) where the E/S females sustained greater temperature reductions over 2 hr than the other three groups. However, their prenatal female counterparts, the E/E group, were exposed to microwaves during the same 2-hr period so that the post-exposure skin temperature measurements on the E/E progeny may only reflect microwave heating that offsets potential skin temperature change. Thus, we believe the effects reported here are due solely to the prenatal microwave exposure.

A second major comment relates to dosimetry. At first blush it was difficult for us to accept the reported effects of treatment as a product of a 0.3 W/kg SAR. However, this value represents a whole-body average for the dam. We have no estimate of the energy distribution within the dam's body, but it is not unlikely that there could be hot spots in the region of the uterus given the differential fluid volume at that locus due to constant placental perfusion and the presence of amniotic fluid. Thus, we do not know the actual dose to the neonate, nor do we know to what degree the neonatal dose, the maternal dose or both caused the functional alterations observed. It is quite possible that there are as many causes, and thus doses, as there were observed effects.

The issue of dose distribution is an important one and could well explain why prenatal exposure to low levels of microwave energy appear to lead to frequency-specific effects. For example, Johnson, *et al.* (1978) used a design similar to that reported here to expose gravid female rats to 5 mW/cm^2 918-MHz microwaves for the first 19 days of gestation. They found that exposed dams increased food consumption (whereas ours decreased food consumption) and that the progeny of exposed dams weighed more at birth than did those of the sham-exposed (whereas we found no differences in birthweight). They also found more rapid development (i.e., date of eye opening) in the exposed progeny relative to the sham-exposed. In our study we found that the eye-opening response was retarded by about 36 hr. That frequency, and not microwave power density, may be the basis for the difference in findings is supported by the work of Shore, *et al.* (1977). They also exposed gravid female rats to 2450-MHz microwaves at 5 mW/cm^2 from day 3 to day 19 of gestation, and found that, depending on orientation relative to the electric field, progeny of the exposed rats had lower body mass through the first week of life. Although we

observed a reduced body mass only for progeny between the first and second week of life, our data are more consistent with the data of Shore, *et al.* than with those of the Johnson, *et al.* study. Shore, *et al* also observed increased postnatal mortality in the progeny of microwave-exposed dams.

We have discussed at length the issues of frequency and dose distribution because we believe that it would be premature and speculative to suggest causation for our observations and a rigid interpretation of the findings of the prenatal microwave exposure study reported here. Rather, we hope the data reported here serve as an impetus for further research which relates measured effects to precise descriptions of dose distribution and frequency. Within this framework, our data indicate that it would be most profitable to concentrate on those parameters which reflect the functional integrity of metabolic accommodation and thermoregulatory processes in response to in-utero microwave exposure.

IV. SUMMARY

We report here a number of subtle consequences of exposure to weak microwave fields. In Experiment IA and IB, exposure to microwaves for 10 hr/night caused rats to reduce their total food intake relative to sham-exposed controls. The effect is robust, dose-dependent and generalizeable across at least two microwave frequencies. In contrast to this finding, we have not been able to identify other behavioral or physiological effects of subchronic exposure to microwaves that are as robust and replicable in nature. In Experiment II, it was found that exposure of gravid female rats to microwaves for 20 hr/day through nineteen days of gestation caused the progeny to have a number of postnatal functional alterations relative to the progeny of pregnant rats that were either sham-exposed or served as caged controls. The alterations observed were, in most cases, sex-specific. However, they were similar in nature and they related to changes in thermoregulatory capability and changes in neonatal and adult body mass. In both Experiment I and II we did not observe changes in core temperature as a consequence of subchronic exposure to microwaves. However, this should not lead the reader to conclude that the effects reported are non-thermal in nature. Labeling the effects as non-thermal or athermal would be semantic folly because when microwave energy is deposited in tissues

the mechanics of energy transfer will create heat. Rather, the metabolic and thermoregulatory accommodations made were quite effective at precluding $+\Delta T$ (°C) as a result of subchronic exposure to microwaves. The "costs", however, of making these accommodations on a long-term basis are significant as born out by the data reported here.

ACKNOWLEDGMENTS

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REFERENCES

Adair, E.R. and Adams, B.W. (1980). Microwaves alter thermoregulatory behavior in squirrel monkey. *Bioelectromagnetics* 1:1.

Adey, W.R. (1980). Neurophysiologic effects of radiofrequency and microwave radiation. *Bull. NY Acad. Med.* 55:1079.

Edwards, A.L. (1978). *Experimental Design in Psychological Research*. Holt, Rhinehart and Winston, New York.

Guy, A.W. and Chou, C.K. (1976). System for quantitative chronic exposure of a population of rodents to UHF fields. In *Biological Effects of Electromagnetic Waves*, Volume II (C.C. Johnson and M.L. Shore, eds.), pp. 389-422, Selected Papers of the USNC/URSI Annual Meeting, October 20-23, 1975, Boulder, CO. HEW publ. (FDA) 77-8011, U.S. Government Printing Office, Washington, DC.

Guy, A.W. and Korbel, S.F. (1972). Dosimetry studies on a UHF cavity exposure chamber for rodents. In *Proceedings of the Microwave Power Symposium*, p. 180. International Microwave Power Institute.

Guy, A.W. and McDougall, J.A. (1979). Circularly polarized 2450-MHz waveguide system for the chronic exposure of small animals to microwaves. *Radio Science* 14:63.

Johnson, R.B., Mizumori, S. and Lovely, R.H. (1978). Adult behavioral deficit in rats exposed prenatally to 918-MHz microwaves. In *Developmental Toxicology of Energy-Related Pollutants*, (D.D. Mahlum, M.R. Sikov, P.L. Hackett, and F.D. Andrew, eds.), p. 281. Seventeenth Hanford Biology Symposium, October 17-19, 1977, Richland, WA. CONF-771017, NTIS, Springfield, Virginia.

Justesen, D.R. (1980). Behavioral and psychological effects of microwave radiation. *Bull. NY Acad. Med.* 55:1058.

Lovely, R.H. Neurobehavioral responsivity from exposure to electromagnetic fields (0 - 300 GHz): Sensitivity of assessment methods. *Environ. Health Perspec.* (in press).

Lovely, R.H., Myers, D.E., and Guy, A.W. (1977). Irradiation of rats by 915-MHz microwaves at 2.5 mW/cm^2: Delineating the dose-response relationship. *Radio Science* 12: 139.

Moe, K.E., Lovely, R.H., Myers, D.E., and Guy, A.W. (1976). Physiological and behavioral effects of chronic low level microwave radiation in rats. In *Biological Effects of Electromagnetic Waves*, Volume I (C.C. Johnson and M.L. Shore, eds.), p. 238, Selected Papers of the USNC/URSI Annual Meeting, October 20-23, 1975, Boulder, CO. HEW Pub. (FDA) 77-8011, U.S. Government Printing Office, Washington, DC.

Segal, S. (1956). *Nonparametric Statistics for the Behavioral Sciences*. McGraw-Hill, New York.

Shore, M., Felton, R.P., and Lamanna, A. (1977). The effects of repetitive prenatal low-level microwave exposure on development in the rat. In *Symposium on Biological Effects and Measurements of Radio Frequency/Microwaves*, p. 280. DHEW 78-5807, U.S. Government Printing Office, Washington, DC.

Stern, S.S., Margolin, L., Weiss, B., Lu, S-T, and Michaelson, S.M. (1979). Microwaves: Effect on thermoregulatory behavior in rats. *Science* 206:1198.

DETECTION OF RADIOFREQUENCY RADIATION - INDUCED WHOLE BODY HEATING FOLLOWING CHEMICAL IMPAIRMENT OF THERMOREGULATION

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I. INTRODUCTION

Heating by radiofrequency (RF) radiation at high intensities can cause biological changes by whole body hyperthermia or by altered thermal gradients within the body (Johnson and Guy, 1972). However, there have been reports of effects, such as on the reproductive, immunologic, neuroendocrine and nervous systems of experimental animals, at low intensities of RF radiation without evidence of increased body temperature (Baranski and Czerski, 1976). Over the years, there has been considerable controversy concerning the potential for RF radiation to cause various biological effects in experimental animals in the absence of detectable increases in body or tissue temperature. In many instances, the effects produced by RF radiation have been attributed to direct interactions (i.e., athermal or field-specific) unrelated to any detectable temperature change in the biological specimen. We have been particularly interested in attempting to interpret the many studies that report RF radiation-induced effects on the immune system of exposed animals in the absence of a colonic temperature increase (Smialowicz, 1979). To this end studies were undertaken to determine if subtle heating by RF radiation at low power densities ($\leq$1 mW/cm^2) might be detectable in

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animals whose thermoregulatory response was compromised.

In earlier work, Stern, *et al.* (1979) and Adair and Adams (1980), using techniques to assess behavioral and physiological thermoregulatory responses, demonstrated that animals would respond to RF radiation by selecting less infrared heat or by initiating peripheral vasodilation respectively when placed in a cool environment at power densities below 20 mW/cm^2. Putthoff, *et al.* (1977) showed increases in the core temperature of rats made hypothermic with cortisone and then exposed to RF radiation at a dose rate of approximately 40 W/kg. These results indicate that animals in which normal thermoregulatory responses are compromised by drugs or animals in which individual thermoregulatory responses are measured in cool environments may be sensitive models for the detection of subtle RF-induced heating.

To further examine this hypothesis, two agents were used to compromise the thermoregulatory response of rodents. Lipopolysaccharide (LPS) or endotoxin from Gram-negative bacteria was used in rats and 5-hydroxytryptamine (5-HT) was used in mice. LPS induces a febrile response in man and several other species; however, rats, mice and guinea pigs injected with LPS and held in a cool (22 °C) environment develop hypothermia (Feldberg and Saxena, 1975). Likewise, mice injected with 5-HT, which are held in a cool (22 °C) environment, develop a hypothermia in a matter of minutes (Dooley and Quock, 1976). Impairment of thermoregulation by endotoxin in the rat and 5-HT in the mouse in these studies allowed us to detect subtle whole body heating by RF radiation at a power density (1 mW/cm^2) heretofore considered to be nonthermogenic.

II. METHODS

The methods employed have been reported previously (Smialowicz, *et al.*, 1980, 1981a). Unless stated otherwise, experimentally naive young adult rats and mice were used once and then killed after several days of observation. Rats were injected intravenously with a single dose of Salmonella typhimuriun LPS (100 µg/kg) and mice intraperitoneally with a single dose of 5-HT creatine sulfate complex (20 mg/kg) in a volume of 0.2 ml. These agents render the animals hypothermic when they are maintained at a cool ambient temperature of 22 °C. Control animals were injected with an equal volume of pyrogen-free saline. In preliminary studies it was found that LPS was more effective in

producing hypothermia in rats than in mice where a great deal of variability in response was observed. The opposite was found with 5-HT-induced hypothermia in which mice responded better than rats.

Immediately following injection, individual rats were placed in perforated acrylic restrainers and mice were placed in perforated polycarbonate boxes. The restrained rats were positioned with their long axis oriented parallel to the H-field vector. The mice had freedom of movement in the boxes and their orientation in the field was random. Four such animals were then placed each in one of four positions of a diamond-shaped array in an environmentally controlled exposure chamber which was positioned beneath a 10-db-gain pyramidal horn antenna in the far field. The exposure chamber was confined in an anechoic chamber. The animals were then exposed to fields generated by a Varian Model PPS-2.5 AS industrial heating unit at a frequency of 2450 MHz in a continuous-wave mode (Smialowicz, *et al.*, 1980). Rats were exposed for 90 min and mice for 15 min. Species-, strain- and age-matched LPS- or 5-HT-injected animals were positioned in a similar array in a sham-irradiation chamber located outside of the anechoic chamber. A common environmental control for the RF exposure and sham-irradiation chambers permitted regulation of the temperature and humidity, unless stated otherwise, at 22 ± 0.5 °C and 50 ± 10%, with an air flow of 4.3 m^3/min.

Power density was determined using an E-field dipole probe in the absence of animals and containers at the four positions. Measurements were also made at positions with the other three occupied by water loads or animals. The specific absorption rate (SAR) was determined by twin-well calorimetry (Kinn, 1977). Briefly, an irradiated carcass and an unirradiated control of equal mass were each placed in the wells of a colorimeter and a strip chart recording was made as the calorimeter returned to equilibrium. The area under the curve of equilibrium was calculated and converted to energy absorbed by the carcass with the SAR determined from the animal's mass.

Prior to the injection of LPS or 5-HT and immediately following exposure to RF radiation, the colonic temperature of each animal was measured with a Model 520 YSI (Yellow Springs Instrument Co., Yellow Springs, Ohio) thermistor probe inserted 2.5 cm beyond the anal sphincter in mice and with a Model 401 thermistor probe inserted 8.0 cm beyond the anal sphincter in rats. Colonic temperatures were read to an accuracy of 0.1 °C from a YSI Model 46 telethermometer.

III. RESULTS

A. Detection of RF Heating in Rats

The time-dependent colonic temperature response of non-irradiated rats injected with 100 µg/kg LPS and maintained at an ambient temperature of 22 °C and relative humidity of 50% is shown in Figure 1. Under these conditions the maximal hypothermic response occurred approximately 90 minutes following injection. Colonic temperatures returned to normal after 3-4 hours. One hundred µg/kg of LPS per rat is well below the LD_{50} of 1.6 mg/kg (Smialowicz, *et al.*, 1980). Since the nadir of the hypothermic response of rats to LPS occurred at 90 minutes post-injection, subsequent experiments with RF radiation were conducted for this length of time.

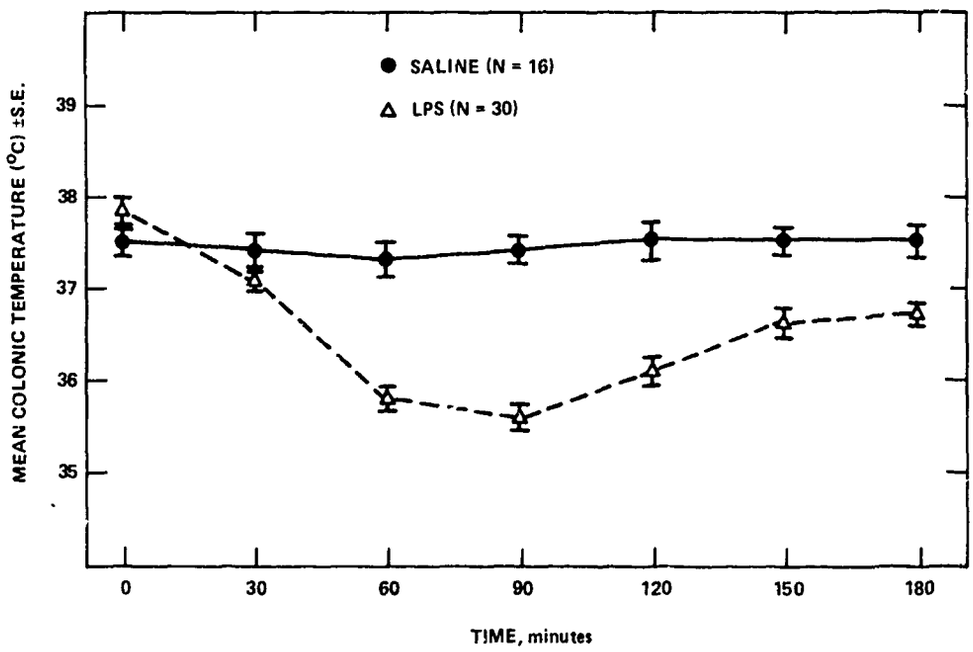

Figure 1. Time-dependent colonic temperature response to endotoxin 100 µg/kg and saline of rats held at T_a = 22 °C (Smialowicz, *et al.*, 1980. Reproduced by permission of Alan R. Liss.)

In a series of exposures to 2450 MHz radiation at different power densities (1, 5, and 10 mW/cm^2), an increase in the colonic temperature of LPS-injected rats was observed to be related to an increase in power density (Figure 2). At each power density, the mean colonic temperature was significantly greater ($P < 0.05$, Dunnett's t-test) than that of LPS-injected, sham-irradiated rats (plotted at a power density of 0 in the figure). The specific absorption rate (SAR) for rats in this study was approximately 0.2 $(W/kg)/(mW/cm^2)$. This SAR value was obtained by the method of twin-well calorimetry and has been reported by Kinn (1977) and Smialowicz, *et al.* (1979a).

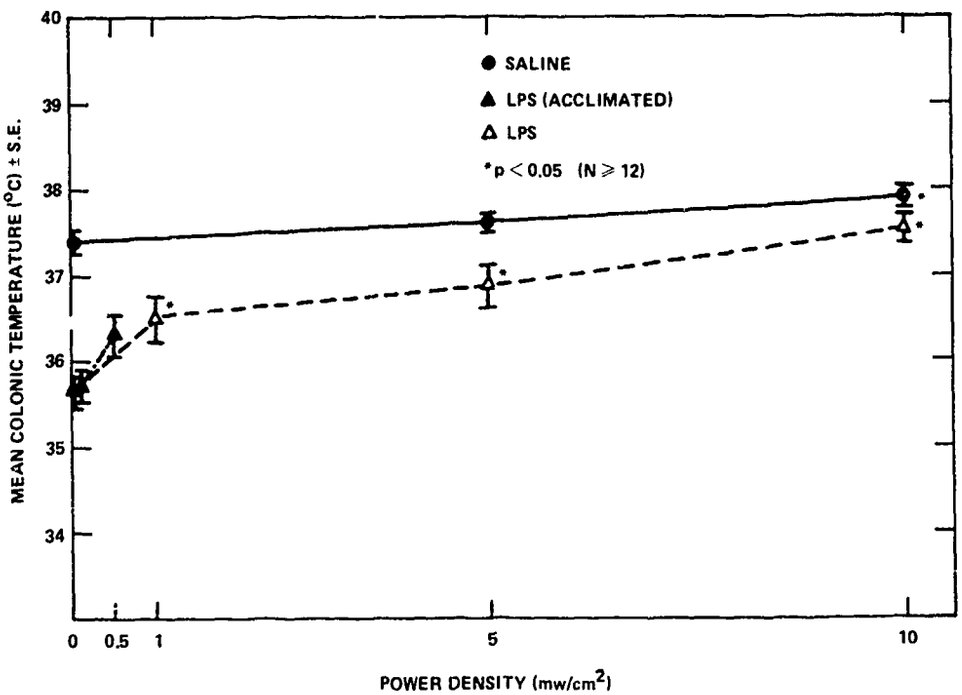

Figure 2. The effect of 90 minutes radiofrequency irradiation on endotoxin-induced hypothermia in rats. (Smialowicz, *et al.*, 1980. Reproduced by permission of Alan R. Liss.)

Rats injected with pyrogen-free saline and exposed for 90-minutes at an average power density of 5 mW/cm^2 did not show a significant increase in colonic temperature compared with saline-injected, sham-irradiated controls (Figure 2). A statistically significant difference ($P < 0.05$, Student's t-test) was observed in the colonic temperature of saline-injected rats exposed at 10 mW/cm^2, relative to saline-injected, sham-irradiated controls.

In another experiment, the effects of procedural acclimatization on the response to RF radiation was examined. Two groups of rats were acclimated to handling procedures for two weeks prior to LPS injection and RF radiation exposure. Figure 2 shows that when these rats were irradiated with 2450 MHz RF radiation at 0.5 mW/cm^2 their mean colonic temperature was 0.6 °C higher than sham-irradiated LPS-injected rats, although this difference was not significant. These results suggest that rats which are appropriately acclimated to handling and then made hypothermic with LPS may serve as an even more sensitive model than naive rats for detection of RF-induced heating.

The effect of ambient temperature alone on the magnitude of endotoxin-induced hypothermia is shown in Figure 3. In this experiment naive rats were injected with LPS (100 µg/kg), placed in restrainers and held at ambient temperatures ranging from 18 to 34 °C and at a relative humidity of 50%. Ninety minutes after LPS injection, the colonic temperature was measured. The colonic temperature of LPS-injected rats after 90 minutes depended on the ambient temperature at which the animal was held. Only when the ambient temperature exceeded 30 °C, which is at the upper limit of the thermoneutral zone for the rat, was the colonic temperature of LPS-induced hypothermic rats significantly greater than saline-injected rats held at 22 °C.

B. Detection of RF Heating in Mice

The time-dependent hypothermic response of non-irradiated BALB/C mice to 5-HT at 22 °C and 50% humidity is shown in Figure 4. The nadir of body temperature of mice treated with 5-HT occurred approximately 15 min following injection. A similar response was observed with CBA/J mice. Colonic temperature returned to normal within 90 minutes. On the basis of these data, mice were exposed to RF radiation during the first 15 min following 5-HT injection.

Table 1 shows the colonic temperature response of 5-HT injected mice exposed to 2450 MHz RF radiation at several power densities. Two strains of mice were studied, male

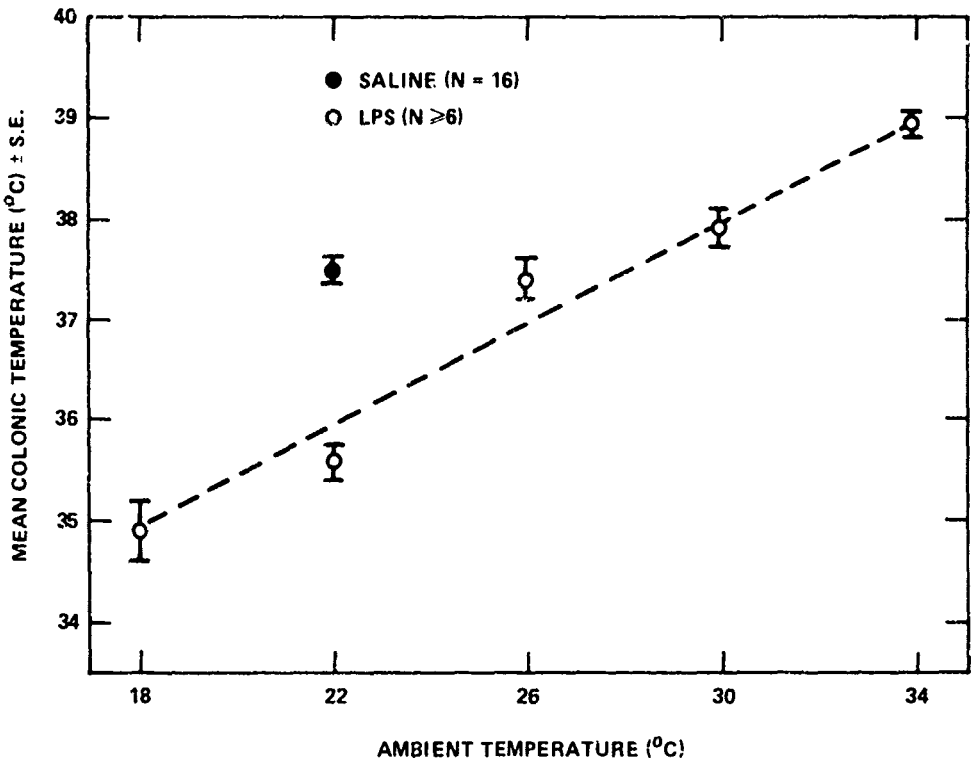

Figure 3. The effect of ambient temperature on colonic temperature of rats 90 minutes after injection of endotoxin (100 µg/kg) or saline. (Smialowicz, *et al.*, 1980. Reproduced by permission of Alan R. Liss.)

CBA/J and female BALB/C mice. These two strains were used because of our work with these mice in assessing the immunologic effects of RF radiation (Smialowicz, *et al.*, 1979b, Smialowicz, *et al.*, 1981b, and Riddle, *et al.*, 1982). The mice were maintained in an environment at 22 °C, 50% relative humidity with an air flow at 4.3 m^3/min during irradiation. Significant ($P \leq 0.05$, Student's t-test) increases in the colonic temperature of 5-HT treated BALB/C mice were observed at 10, 5 and 1 mW/cm^2 compared with 5-HT treated sham-irradiated mice. CBA/J mice irradiated at 10 and 5 mW/cm^2 also showed significantly ($P < 0.05$) higher colonic temperatures compared with their sham-irradiated controls. At 1 mW/cm^2, 5-HT treated CBA/J mice had higher colonic

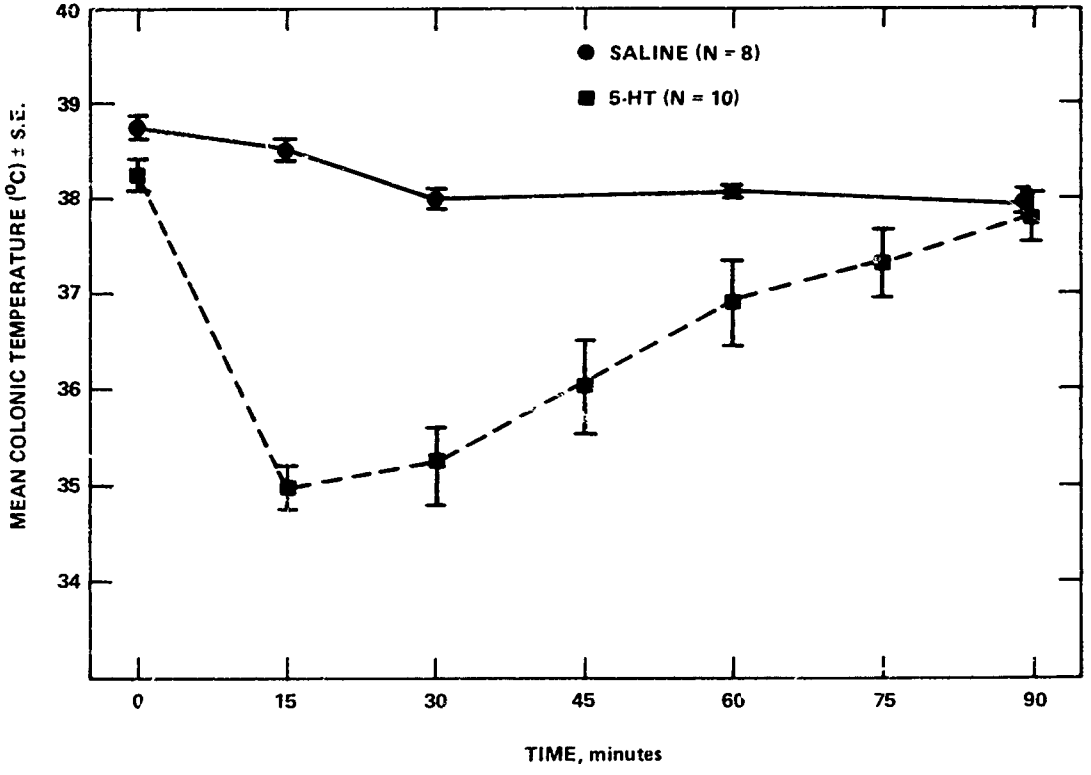

Figure 4. Time-dependent colonic temperature response of BALB/C mice held at T_a = 22 °C to 5-hydroxytryptamine (20 mg/kg) and saline (Smialowicz, *et al.*, 1981a. Reproduced by permission of Academic Press.)

Table 1. EFFECT OF 2450 MHz RADIOFREQUENCY RADIATION ON COLONIC TEMPERATURE OF 5-HYDROXYTRYPTAMINE-INDUCED HYPOTHERMIC MICE

STRAIN	TREATMENT	POWER DENSITY (mw/cm^2)	MEAN COLONIC TEMPERATURE (°C) ± SE SHAM[a]	IRRADIATED	P
BALB/C	5-HT	1	34.3 ± 0.1	34.8 ± 0.1	< 0.05
		5	34.8 ± 0.1	35.7 ± 0.1	< 0.01
		10	34.5 ± 0.2	36.5 ± 0.2	< 0.01
	SALINE	10	38.5 ± 0.1	38.7 ± 0.1	N.S.
CBA/J	5-HT	0.5	34.2 ± 0.3	34.7 ± 0.2	N.S.
		1	34.5 ± 0.2	35.0 ± 0.2	0.051
		5	34.4 ± 0.2	35.6 ± 0.2	< 0.01
		10	34.7 ± 0.2	36.3 ± 0.3	< 0.01
	SALINE	10	37.6 ± 0.2	37.7 ± 0.1	N.S.

[a]EIGHT TO TWELVE MICE AT EACH POWER DENSITY.

Table 1. Colonic Temperature Response of Mice Injected with either Saline or 5-Hydroxytryptamine (20 mg/kg) to 2450 MHz Radiofrequency Radiation. (Smialowicz, *et al.*, 1981a. Reproduced by permission of Academic Press.)

temperatures than shams, although this difference was not significant. Saline-injected BALB/C or CBA/J mice irradiated at 10 mW/cm^2 showed no significant increase in colonic temperature compared with saline-injected sham-irradiated mice. The SAR for mice in this study was approximately 0.7 $(W/kg)/mW/cm^2$). This value was obtained by the method of twin-well calorimetry (Smialowicz, *et al.*, 1979b).

The effect of ambient temperature on the hypothermic response of 5-HT-treated CBA/J mice is shown in Figure 5. Experimentally naive mice were injected with 5-HT (20 mg/kg), placed in perforated boxes and held at ambient temperatures ranging from 18 to 34 °C and at a relative humidity of 50%. Fifteen minutes after 5-HT injection, the colonic temperature was measured. Colonic temperature increased linearly with increasing ambient temperature. Even at an ambient temperature of 34 °C, the hypothermic effect of 5-HT was still evident.

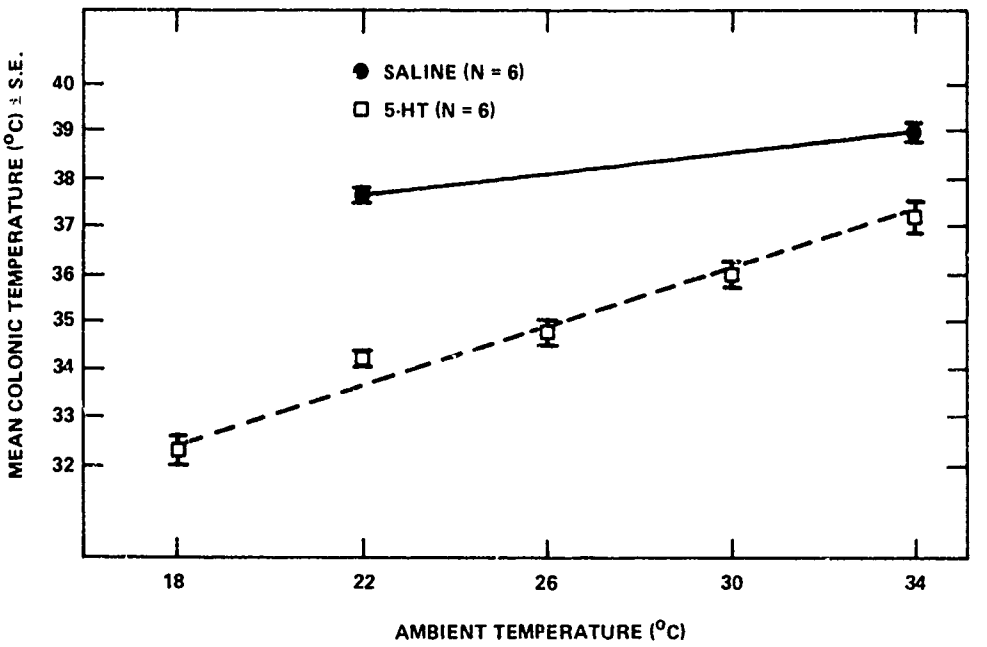

Figure 5. The effect of ambient temperature on colonic temperature of CBA/J mice 15 minutes after injection of 5-hydroxytryptamine (20 mg/kg) or saline. (Smialowicz, *et al.*, 1981a. Reproduced by permission of Academic Press.)

IV. DISCUSSION

These results demonstrate that RF heating once thought to be undetectable can be detected in rats whose normal thermoregulation was impaired by LPS and in mice whose normal thermoregulation was impaired by 5-HT at power densities heretofore considered to be nonthermogenic. Significantly higher colonic temperatures in hypothermic rats and mice compared with saline-injected animals were measured at SARs of 0.2 W/kg and 0.7 W/kg respectively. By acclimating test animals to handling procedures, the detectability of temperature increases in hypothermic rats was increased, although not significantly. These results suggest that acclimation of animals to handling procedures may reduce some of the variability observed in non-habituated LPS-injected rats and 5-HT-injected mice and increase the sensitivity of these hypothermia models for detecting subtle thermogenesis by

low-level RF radiation.

The rat, unlike other species, exhibits a decreased body temperature following intravenous injection of endotoxin. The absence of a rise in body temperature in rats following endotoxin treatment is believed to be due to a high rate of heat loss in these animals. This response may be a consequence of a reduction in insulation during shivering in the rat, which has a large body surface area to mass ratio (Bligh, 1973). Ambient temperature plays a critical role in this response to endotoxin; at temperatures above thermal neutrality, endotoxin-treated rats respond with a typical biphasic febrile response (Szekely and Szelenyi, 1979).

The systemic administration of 5-HT produces a dose-related decrease in body temperature of rats exposed to environmental temperatures below the thermoneutral point (Winter, 1971). It is believed that 5-HT hypothermia is mediated via peripheral mechanisms because systemically administered 5-HT does not cross the blood-brain barrier (Underfriend, *et al.*, 1957; Carter and Leander, 1980). The degree and direction of the change in body temperature induced by 5-HT has been shown to be a function of the ambient temperature employed and has been characterized as a poikilothermic response (Shemano and Nickerson, 1958). The exact mechanism by which 5-HT induces hypothermia is not known. It has been postulated that 5-HT acts peripherally resulting in changes in cardiovascular and/or respiratory function or may act by depressing general activity (Myers and Waller, 1977).

The colonic temperature increase in LPS-injected rats induced by RF radiation was found to be dependent on the power density at which the animals were exposed just as it was found to be dependent on ambient temperature. A similar response was observed in 5-HT-injected mice. No significant increase in the colonic temperature of rats or mice injected with saline and irradiated at 5 mW/cm^2 was observed compared with sham-irradiated saline-injected animals. These data indicate that the increase in colonic temperature in LPS-injected rats and 5-HT-injected mice exposed to RF radiation was due to the thermalizing energy of this radiation.

These results indicate that small doses of thermalizing energy from low-intensity (SAR $\leq$ 1 W/kg) RF radiation are detectable as significant increases in colonic temperature. In normal rats and mice (saline-injected), the thermalization by RF radiation at these low intensities may be compensated for by an increase in the rate of heat loss. This compensatory heat loss may then be exceeded when animals are irradiated at higher intensities, as evidence by a significant increase in the colonic temperature of saline-injected

rats exposed at 10 mW/cm^2 (Figure 2).

A re-evaluation of the literature on RF radiation-induced biological effects, particularly effects on the immune system, is indicated by these studies. More prudent assessment of claims for "nonthermal" (i.e., absence of measurable elevation of tissue or body temperature) RF-induced biological effects is needed, with consideration of the thermogenic potential of RF radiation as a cause for changes in biological responses.

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DISCLAIMER

This report has been reviewed by the Office of Research and Development, EPA, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

REFERENCES

Adair, E.R. and Adams, B.W. (1980). Microwaves induce peripheral vasodilation in squirrel monkeys. *Science* 207:1381.

Baranski, S. and Czerski, P. (1976). *Biological Effects of Microwaves*. p. 78. Dowden, Hutchinson and Ross, Stroudsburg, PA.

Bligh, J. (1973)., *Temperature Regulation in Mammals and Other Vertebrates*, p. 228. American Elsevier, New York.

Carter, R.B. and Leander, J.D. (1980). Evidence for a peripheral effect of serotonin or metabolites in 5-hydroxytryptophan-induced hypothermia. *Neurophysiol.* 19:777.

Dooley, D.J. and Quock, R.M. (1976). Tryptamine and 5-hydroxytryptamine-induced hypothermia in mice. *J. Pharm. Pharmacol.* 28:775.

Feldberg, W. and Saxena, P.N. (1975). Prostaglandins, endotoxin and lipid A on body temperature in rats. *J. Physiol. (London)* 249:601.

Johnson, C.C. and Guy, A.W. (1972). Nonionizing electromagnetic wave effects in biological materials and systems. *Proc IEEE* 60:692.

Kinn, J.B. (1977). Whole-body dosimetry of microwave radiation in small animals: The effect of body mass and exposure geometry. *Radio Sci.* 12(6S):61.

Myers, R.D. and Waller, M.B. (1977). Thermoregulation and Serotonin. In: *Serotonin in Health and Disease, Vol II. Physiological Regulation and Pharmacological Action* (W.B. Essman, ed.), Spectrum, New York.

Putthoff, D.L., Justesen, D.R., Ward, L.B., and Levinson, D.M. (1977). Drug-induced ectothermia in small mammals: The quest for a biological microwave dosimeter. *Radio Sci.*12(6S):73.

Riddle, M.M., Smialowicz, R.J. and Rogers, R.R. (1982). Microwave radiation (2450 MHz) potentiates the lethal effect of endotoxin in mice. *Health Physics* 42:335.

Shemano, I. and Nickerson, M. (1958). Effect of ambient temperature on thermal responses to drugs. *Can. J. Biochem. Physiol.* 36:1243.

Smialowicz, R.J. (1979). Hematologic and immunologic effects of nonionizing electromagnetic radiation. *Bull. N.Y. Acad. Med.* 55:1094.

Smialowicz, R.J., Kinn, J.B. and Elder, J.A. (1979a). Perinatal exposure of rats to 2450 MHz CW microwave radiation: Effects on lymphocytes. *Radio Sci.* 14(6S):147.

Smialowicz, R.J., Riddle, M.M., Brugnolotti, P.L., Sperrazza, J.M. and Kinn, J.B. (1979b). Evaluation of lymphocyte function in mice exposed to 2450-MHz (CW) microwaves. In *Proceedings of the 1978 Symposium on Electromagnetic Fields in Biological Systems* (S.S. Stuchly, ed.) p. 122, International Microwave Power Institute, Edmonton, Canada.

Smialowicz, R.J., Compton, K.L., Riddle, M.M., Rogers, R.R., and Brugnolotti, P.L. (1980). Microwave radiation (2450 MHz) alters the endotoxin-induced hypothermic response of rats. *Bioelectromagnetics* 1:353.

Smialowicz, R.J., Riddle, M.M., Brugnolotti, P.L., Rogers, R.R., and Compton, K.L. (1981a). Detection of microwave heating in 5-hydroxytryptamine-induced hypothermic mice. *Radiat. Res.* 88:108.

Smialowicz, R.J., Brugnolotti, P.L. and Riddle, M.M. (1981b). Complement receptor positive spleen cells in microwave (2450 MHz) irradiated mice. *J. Microwave Power* 16:73.

Stern, S., Margolin, L., Weiss, B., Lu, S.-T. and Michaelson, S.M. (1979). Microwaves: Effects on thermoregulatory behavior in rats. *Science* 206:1198.

Szekely, M. and Szelenyi, Z. (1979). Endotoxin fever in rats. *Acta Physiol. Acad. Sci. Hung.* 53:265.

Underfriend, S., Weissbach, H. and Bodanski, D.F. (1957). Biochemical findings related to the action of serotonin. *Ann. N.Y. Acad. Sci.* 6:602.

Winter, J.C. (1971). Interaction of serotonin antagonists with harmaline-induced changes in operant behavior and body temperature in the rat. *Arch. Int. Pharmacodyn. Ther.* 191:120.

INFLUENCE OF THE CIRCADIAN RHYTHM OF BODY TEMPERATURE ON THE PHYSIOLOGICAL RESPONSE TO MICROWAVES: DAY VS NIGHT EXPOSURE

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I. INTRODUCTION

Previous studies have demonstrated the existence of an adrenocortical response to acute microwave exposure in rats and rhesus monkeys (Lotz and Michaelson, 1978; Lu, *et al.*, 1980a; Lotz and Podgorski, 1982). The adrenal response was observed only during exposures to a power density that was greater than a threshold power density required to cause a rectal temperature increase greater than 1.5 °C. In the rat, exposures to intensities greater than this threshold caused additional increases in both rectal temperature and circulating corticosterone levels. The dose-response curve for the rhesus monkey was not evaluated with multiple exposure intensities above the threshold for adrenocortical response, but corticosterone levels in the rat were strongly correlated with body temperature above this threshold such that the more the rise in body temperature exceeded 1.5 °C, the greater was the increase in corticosterone levels. The adrenal response was also similar in character and mechanism to the nonspecific adrenocortical "stress" response that has been associated with many environmental stimuli (Lu, *et al.*, 1980b). The earlier experiments with monkeys were conducted with a 24-h experimental protocol that was designed to look for persistent or delayed effects of exposure, including those that might involve the known circadian rhythms in these parameters. However, no delayed or persistent effects of this type were noted. Because the overall response of

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the pituitary-adrenal axis to stress has been reported to have a diurnal variation (Gibbs, 1970; Engeland, *et al.*, 1977), and because diurnal variations have also been shown in the sensitivity of different levels of the axis to specific controlling hormones (Kaneko, *et al.*, 1980), this study was designed to compare the effects of identical microwave exposures carried out at two different phases of the circadian cycle on body temperature and circulating cortisol levels of the rhesus monkey. Rectal temperature increases during 8-h microwave exposures were virtually identical for both day and night exposures even though sham and exposed absolute temperatures were substantially lower at night due to the normal circadian rhythm of body temperatures. However, the marked increase in circulating cortisol levels that was observed during the day exposures to 38 mW/cm^2 was completely absent during the night exposures. The absence of a cortisol response during the night exposures may be simply related to the absolute body temperature reached, although more complex circadian influences cannot be ruled out by these data.

II. MATERIALS AND METHODS

A. Animals

Six male rhesus monkeys (*Macaca mulatta*, 6 to 10 kg) were used in these experiments. These animals were normally housed individually in standard metal primate cages and were maintained on a diet of Wayne Monkey Chow (Allied Mills, Inc., Chicago IL) supplemented with fresh fruit. The illumination in both the normal housing room and the experimental chamber was on a 16:8 light/dark cycle with lights on from 0600-2200. Animals were provided water *ad libitum* throughout the experiment. Prior to use in this study, the monkeys had been conditioned to prolonged restraint (up to 42 h) in a foamed polystyrene (Styrofoam) restraint chair and had had an indwelling venous catheter surgically implanted in the jugular vein using techniques adapted from those of Herd, *et al.* (1969) as previously described (Lotz, 1979).

B. Microwave Equipment and Exposure Protocol

The microwave exposures were conducted in a microwave anechoic chamber according to a 24-h protocol. Both the

chamber and the protocol have been described in detail previously (Lotz and Podgorski, 1982). Briefly, the microwave source provided 1.29 GHz pulsed radiation (3 μsec pulse width, pulse repetition rate 337 sec^{-1}) and the animals were irradiated in the far-field zone of a horn antenna while seated in a Styrofoam restraint chair. Power density measurements were averaged over the region occupied by the monkey (crown to rump) and the specific absorption rate was estimated on the basis of previous data (Olsen, *et al.*, 1980) to be 0.107 (W/kg)/(mW/cm^2) or 4.1 W/kg for 38 mW/cm^2 exposures. The resting metabolic rate (RMR) of a rhesus monkey is reported to be about 2.4 W/kg (Bourne, 1975). Exposures were eight hours in length and were conducted from either 1200-2000 (day) or 2200-0600 (night). Hourly blood samples were collected before, during, and after the exposure for a total period of 24-h from 0800 to 0800 the following morning. The samples were drawn remotely (from outside the chamber) via the catheter and were promptly centrifuged. The plasma was separated and stored frozen at -25 °C for later analysis. Body temperature was continuously monitored and recorded hourly using a YSI 402 thermistor probe (Yellow Springs Instrument Co., Inc., Yellow Springs, OH) inserted 10 cm into the rectum of the monkey. Although this probe is not designed for noninterference in microwave fields, no temperature artifacts were observed in measurements accurate to 0.1 °C. These checks were made by cycling the microwave power on and off at each of the power densities used in this study, with the probe in the normal position in the monkey. The chamber was ventilated with room air, with air flow from the back to the front of the chamber with respect to the monkey. Over 30 m^3 of air were exchanged each minute, a sufficient rate for an exchange of the chamber volume once per minute, and the velocity of air movement around the animal in the chair was 15 to 30 m/min. The restraint chair covered the back surface of the monkey's body from the waist down to just above the knee, effectively blocking air flow from the pelvic and upper leg surface areas. The neck was also covered by the upper part of the restraint chair. Ambient temperature was maintained at 24 ± 2 °C (range) and relative humidity averaged 55 ± 17% (mean ± SD) during all experiments.

C. Hormone Analysis

Plasma samples were later thawed and analyzed for levels of cortisol by a competitive protein binding method (Murphy, 1967) and for thyroxine by a radioimmunoassay method

(Clinical Assays, Inc., Cambridge, MA).

D. Data

Four monkeys were each exposed three times to each condition (sham-day, exposed-day, sham-night, exposed-night). Corresponding values from these three sessions were then averaged to obtain representative values for each subject. The data presented are the means of the values for the four subjects.

III. RESULTS

The effects of microwave exposure on the rectal temperature of these animals for day or night exposures are shown in Figure 1. For the shams, the normal circadian rhythm in deep body temperature is clearly apparent, with the lowest mean temperature occurring at 0100 hours. The pattern of response and magnitude of the temperature increase is virtually identical for both exposure situations, with an average increase of 1.7 and 1.6 °C, respectively, for day and night exposures (Table I). In both cases, the temperature increased steadily for the first two hours of exposure, then stabilized at an elevated level for the remaining six hours of exposure, before returning to sham exposure levels within one to two hours after the exposure ended.

Comparisons of mean rectal temperatures for the sham and exposure conditions for three time intervals are shown in Table I. Values for daytime exposures at 28 mW/cm^2 from another paper (Lotz and Podgorski, 1982) are included here for comparison purposes. No change in plasma cortisol levels occurred during these day exposures to 28 mW/cm^2. The three time periods represent the pre-exposure period for day exposures (0800-1200), the period during the day exposure when body temperature was elevated and stable (1500-2000, representing exposure hours three through eight), and the corresponding period during the night exposure when body temperature was elevated and stable (0100-0600). Note that the mean temperature during day exposure to 28 mW/cm^2 (1500-2000) is exactly the same as the mean temperature during night exposure to 38 mW/cm^2 (0100-0600). The increase in temperature (ΔT) is, however, quite different for those two periods. In contrast to that

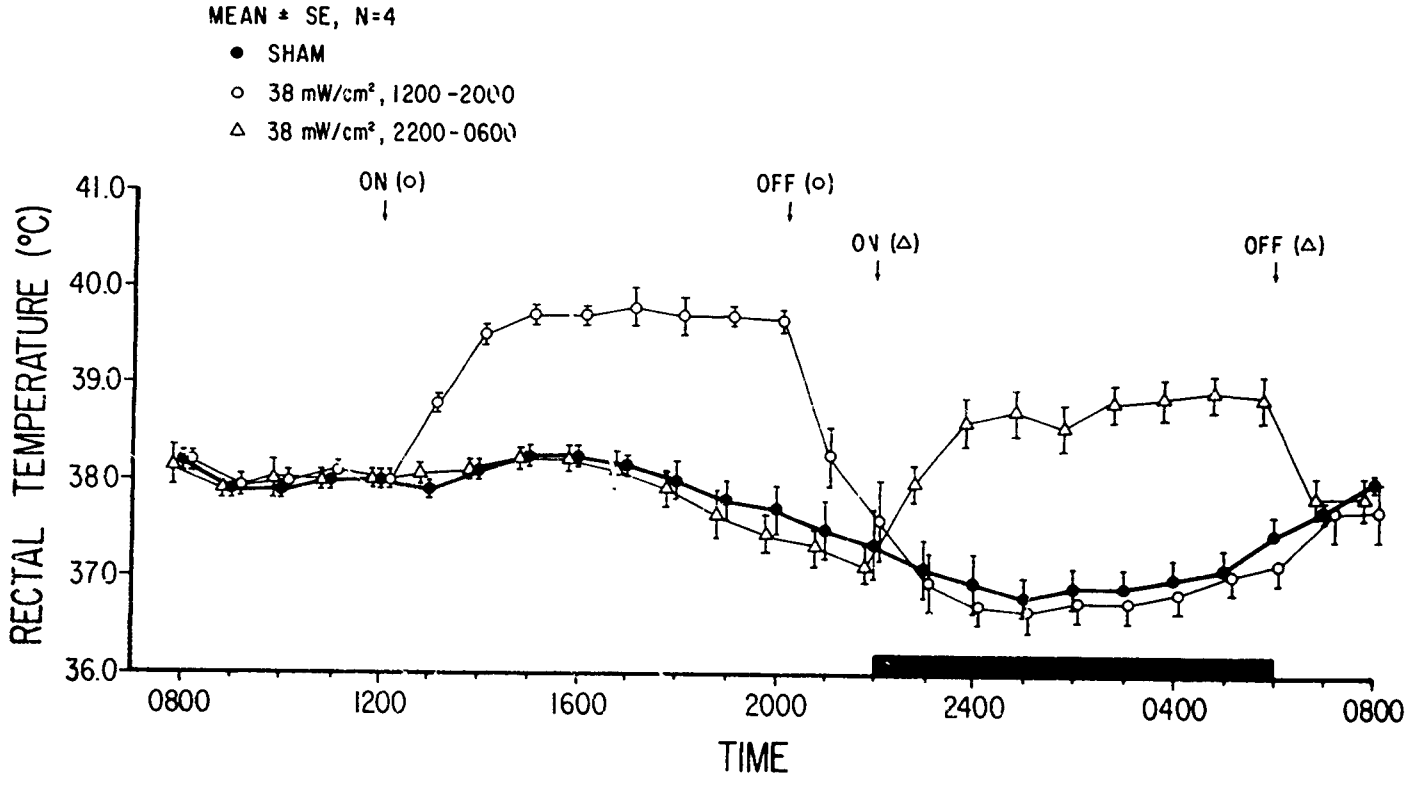


Figure 1. Rectal temperature of rhesus monkeys sham-exposed or exposed to microwaves during the day (1200-2000) or at night (2200-0600). Arrows indicate the beginning and end of the exposure period. The dark bar on the abscissa indicates the dark period of the light cycle.

situation, the temperature increase for both the day and night exposures to 38 mW/cm^2 is practically identical even though the absolute temperature means differ by 0.9 °C.

Table I. Rectal Temperature Comparisons

Type of Exposure	Rectal temperature (mean ± SE)[a]		
	0800-1200	1500-2000	0100-0600
SHAM	38.0 ± 0.1	38.0 ± 0.1	37.2 ± 0.1
28 mW/cm^2 (DAY)[b]	38.0 ± 0.1	38.8 ± 0.1	37.2 ± 0.1
38 mW/cm^2 (DAY)	38.1 ± 0.1	39.7 ± 0.1*	36.9 ± 0.1
38 mW/cm^2 (NIGHT)	38.0 ± 0.1	37.9 ± 0.1	38.8 ± 0.1

[a]Values are the mean of hourly measurements for 4 monkeys for times included in the intervals shown.

[b]These data are taken from another study (Lotz and Podgorski, 1982).

*Circulating cortisol levels were significantly altered from sham levels ($p < .05$).

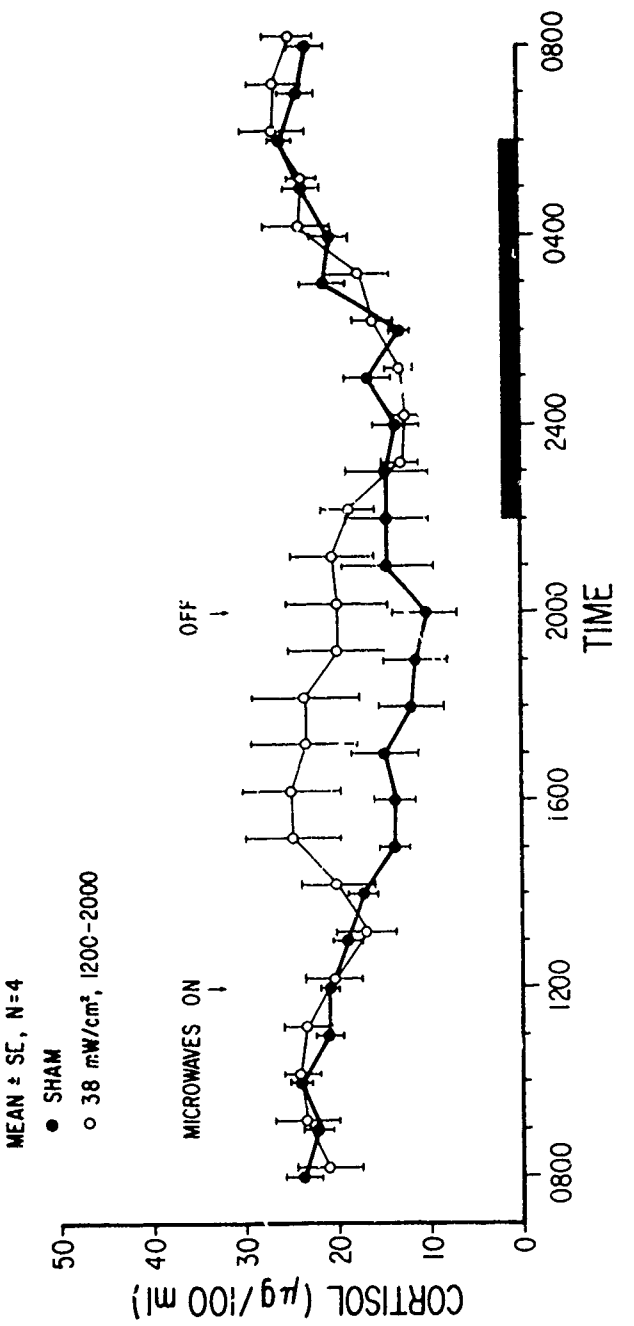
Circulating cortisol levels in the monkeys are shown in Figures 2A and 2B for day and night exposure sessions, respectively. For day exposures, a clear increase in cortisol levels exists, beginning two to three hours after the onset of exposure. It is readily apparent from Figure 2B that no difference between cortisol levels of sham or exposed monkeys existed during the night sessions.

No differences in thyroxine levels existed between sham and exposed conditions for either day or night sessions.

IV. DISCUSSION

These results indicate that the effects of microwave exposure on body temperature and plasma cortisol levels of the rhesus monkey were influenced by the circadian rhythm in these parameters. The increase in body temperature (ΔT) caused by identical exposures conducted either in the day or at night was the same, but the peak level of that temperature was almost 1 °C lower at night. This comparable ΔT suggests that the thermoregulatory response to this microwave exposure was comparable for both day and night exposures, and that this response is consistent with the concepts that have been established from studies of thermoregulatory control mechanisms. The concept of a sustained error signal has been developed to explain body temperature and thermoregulatory responses during a sustained heat load associated with exercise (Stitt, 1979). The work of Nielsen and Nielsen (1965) suggests that the thermoregulatory response to a microwave heat load is essentially equivalent to an exercise heat load. The nocturnal drop in body temperature is thought to be due to a drop in the regulatory set-point at night in animals that are active during the day (Hensel, 1973). Wenger, *et al.* (1976) demonstrated that the nocturnal lowering of the thermoregulatory set point is accompanied by a lowering of thresholds for sweating and vasodilation in man. The increments in body temperature we observed during microwave exposure, virtually the same whatever the time of day, reflect the constant error signal produced by identical exposures, while the different levels of body temperature reached during irradiation at different times of day reflect the fact that the error signal is added onto a different level of thermoregulatory set point. There is no indication that the microwave exposure has any effect on the control of the basic circadian rhythm of body temperature.

One aspect of this temperature response that is not consistent with the analogy to exercise-induced hyperthermia is the fact that a ΔT in rectal temperature of about 1.6 °C is caused by a rate of microwave heating that is less than twice the resting metabolic rate of the animal. In exercising humans, the degree of hyperthermia is proportional to the relative work load, i.e. to the percentage of the maximum aerobic capacity. Rectal temperatures do not normally exceed 1.5 °C in humans engaged in sustained exercise unless the metabolic rate is more than 5 times the RMR (Saltin and Hermansen, 1966). Although there are few data in the literature on metabolic rates of exercising monkeys, it appears


A
MEAN ± SE, N=4
● SHAM
○ 38 mW/cm², 1200-2000
MICROWAVES ON
OFF
CORTISOL (μg/100 ml)
50
40
30
20
10
0
0800
1200
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TIME

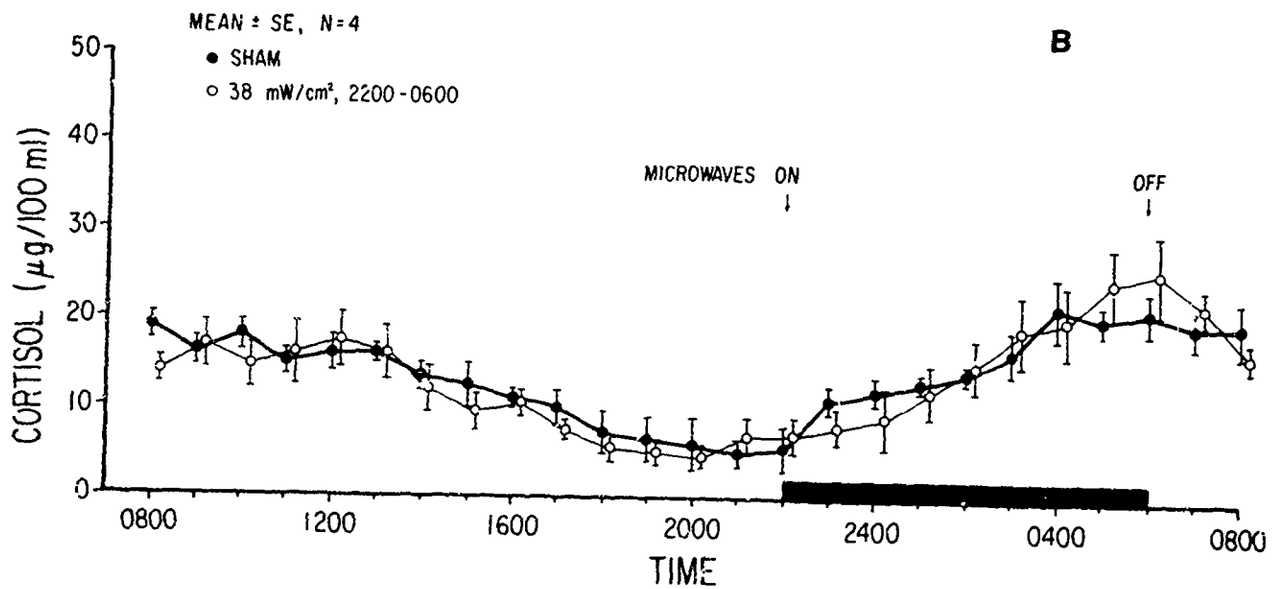

Figure 2. Plasma cortisol levels in rhesus monkeys sham-exposed or exposed to microwaves. Arrows indicate the beginning and end of the exposure period. The dark bar on the abscissa indicates the dark period of the light cycle.

A. Cortisol levels for exposure during the day (1200-2000).

B. Cortisol levels for exposure during the night (2200-0600).

that rhesus monkeys can exercise vigorously at metabolic rates several times the RMR without causing more than a 1.5 °C rise in rectal temperature (Myers, *et al.*, 1977). An important question, then, is how can a monkey dissipate heat more effectively when exercising than when heat is being generated in his tissues passively by exposure to microwave radiation? It may be that the rhesus monkey is not a good model for humans with which to study thermoregulation during exercise, even though the rhesus monkey is a good model for man with respect to thermoregulation at rest (Johnson and Elizondo, 1979). On the other hand, the rhesus monkey may be a suitable model for exercise-induced hyperthermia, but have a maximum aerobic capacity that is relatively low when compared to the RMR. In the case of a relatively low aerobic capacity, a microwave-induced heat load equivalent to twice the RMR might be predicted to cause a significant increase in body temperature, according to the principle that the degree of hyperthermia is proportional to the relative work load. However, based on the available information, this explanation seems unlikely. If the rhesus monkey is a good model of man for thermoregulation in the exercising or microwave-exposed subject, then other possible explanations for the relative inability to dissipate microwave heat must be considered.

Muscle blood flow may be an important part of the answer to this question, because the initial stimuli to which the blood flow responds is different for the two situations under consideration. Muscle blood flow in the active muscles increases rapidly within seconds of the onset of exercise. This increased blood flow is in response to the increased metabolic demands of the muscle, but the enhanced blood flow also transfers the metabolic heat to the body core where it provides information for the prompt and proportional control of thermoregulatory responses by the hypothalamus. However, at 1.29 GHz, the limbs of the monkey are heated at a rate as much as 5 to 7 times the rate of heating of the body core (Olsen, *et al.*, 1980; Olsen and Griner, 1982). Much of this energy would be deposited in the muscles of the limbs, where blood flow is quite low in the resting animal. This heat could go virtually undetected by either the superficial cutaneous warmth sensors or by the hypothalamus, until muscle temperature had increased sufficiently to cause increased blood flow in the muscles. Based on studies with diathermy, blood flow in a passive muscle does not increase until local temperature reaches about 41 °C (Guy, *et al.*, 1974). Thus, until muscle blood flow increases, the peripheral muscles may be storing a considerable amount of heat. Prior to that transfer, the

thermoregulatory response would be based on incomplete information while the amount of stored heat in the body increased. Once the muscle blood flow increased, the thermoregulatory response would increase in proportion to the additional heat load transferred to the body core, but the legs would probably remain relatively hot throughout the exposure in order to keep their blood flow high enough to carry off enough heat to avoid getting even hotter. It is possible that this extra heat transferred from the legs by the pelvic veins influenced rectal temperature, in a manner similar to that observed by Mead and Bonmarito (1949) in man, to make rectal temperature a biased index of deep body temperature in these microwave-exposed animals. The influence of microwave heating of the peripheral muscles might also explain the difference between the level of heating observed in this study and the level observed by Nielsen and Nielsen (1965), in which the diathermy exposure was limited to the body torso. The whole-body exposed monkeys had a rectal temperature increase of 1.7 °C at a microwave-heat production rate of about twice the RMR, while the human subjects of Nielsen and Nielsen had a rectal temperature increase of only $\sim$ 1 °C at an electromagnetic-heat production rate of $\sim$ 5 times the RMR. Obviously, some information on the temperature or blood flow in the leg muscles and on other deep body temperatures during microwave exposure is needed to test this hypothesis. If this idea holds up to such tests, a given rate of heat production and radiant energy absorption should not warm the leg muscles of exercising monkeys nearly as much as those of irradiated monkeys, because of the much higher blood flow in the exercising muscle.

The surprising result of these experiments was the complete absence of an adrenocortical response during the night exposures, in spite of the equivalent increase in rectal temperature. Earlier reports of both adrenocortical and behavioral effects of microwaves suggested the hypothesis that the interaction of these effects with body temperature was closely correlated with a threshold ΔT during microwave exposure (Lotz and Podgorski, 1982; de Lorge, 1979). The results of these experiments do not support the "critical ΔT" concept, however. These results are more compatible with the idea that the adrenocortical response was only stimulated in the rhesus monkey if the body temperature exceeded a particular critical level between 38.8 °C and 39.7 °C. Cortisol levels were not affected during exposures that raised rectal temperature to 38.8 °C, whether those exposures were to 28 mW/cm^2 during the day (Lotz and Podgorski, 1982) or to 38 mW/cm^2 at night, but cortisol

levels were increased during 38 mW/cm^2 day exposures that raised rectal temperature to 39.7 °C. The results do not, however, exclude the possibility that the absence of an adrenocortical response during the night exposure was due to complex mechanisms in the CNS control of the rhythmic neuroendocrine system that were unrelated to the body temperature. Even if a higher exposure intensity had been used to increase the rectal temperature to 39.7 ° at night, it is possible that the cortisol response would still not have occurred as it did during day exposures that raised rectal temperature to that absolute level.

The circadian rhythm of glucocorticoid secretion is well defined in most mammals, including man (Gallagher, *et al.*, 1973) and the rhesus monkey (Holaday, *et al.*, 1977). Kaneko, *et al.* (1980) have described a number of variations in the frequency and amplitude modulation of different levels of the adrenocortical system with respect to the circadian cycle of the rat. The observations of Kaneko, *et al.* may help to clarify a complex picture in which the adrenocortical response to stress has been reported to be either dependent or independent of the circadian cycle (Gibbs, 1970; Allen, *et al.*, 1975). In those reports that indicate an adrenocortical response that is dependent upon the circadian rhythm, an enhanced response during the peak phase of the cycle has been observed in the rat. For the monkey, the corresponding time of greatest adrenocortical response would be in the morning, when cortisol levels are high. In the study reported here, the "day" microwave stimulus was actually delivered after the morning peak of cortisol levels had begun to decline, but while the levels were still near that peak. The "night" exposure was begun at or near the nadir of circulating cortisol levels and was continued through the period of increasing cortisol secretion to the time of early morning peak levels of cortisol. In actuality, these two periods are contrasted by changes in cortisol secretory rates (Holaday, *et al.*, 1977) as well as cortisol levels in that the secretory rate is low in the early afternoon and high in the early morning. Furthermore, the plasma cortisol in monkeys irradiated during the day rose to, but not above, the early morning peak seen in sham experiments. Thus, these data could be interpreted to mean that small stimuli can increase the cortisol secretory rate up to its highest level in the normal daily range, but much larger stimuli are needed to increase it beyond this range. As shown in Figure 2A, irradiation during the day returned cortisol release to its highest normal daily level, reversing the drop in circulating cortisol, but the mild stimulus of irradiation (Figure 2B) did not alter the cortisol secretory rate at

night when it was already at its normal daily high, and hence produced no change in circulating cortisol levels. This interpretation might be tested in protocols in which the circadian rhythm of body temperature is separated from the pattern of plasma cortisol by infusing ACTH.

Only one other report has been found in which the effects of microwave exposure at different times of the circadian cycle have been studied. Lu, *et al.* (1980a) observed a suppression of the normal afternoon circadian rise in plasma corticosterone levels of rats exposed to 20 mW/cm^2 for eight hours. The colonic temperature of the rats was 1.35 °C higher after the exposure than after a sham exposure. The timing of their experiment was comparable, in its phase relationship to the circadian cycle, to the night exposures of rhesus monkeys in this study. However, the expected rise in plasma cortisol was unaffected in our study, but was suppressed during irradiation in the study of Lu, *et al.*

The hypothesis that the adrenocortical response observed in the day exposures depends on a body temperature in excess of a particular level might be tested by altering the ambient temperature in conjunction with microwave exposure. Other effects of microwave exposure have been shown to be altered by varying environmental temperature during exposure (Deichmann, *et al.*, 1959). Thus, the cortisol response might be stimulated by lower intensity microwave exposure with higher ambient temperature or, conversely, might be negated by lowering the ambient temperature during the exposure that caused the observed effect. More complex experiments of this type using thermodes to alter hypothalamic temperature during exposure could also help clarify this question.

V. CONCLUSIONS

In summary, the results of this study demonstrate an influence of the circadian rhythm on the effects of microwave exposure on plasma cortisol and rectal temperature. The lower rectal temperature during night exposures was presumably due to the lower sham-condition temperature at night, since the temperature increase over sham levels was similar for either day or night exposures. The absence of a cortisol response during night exposures may be simply related to the absolute body temperature reached, although more complex circadian influences cannot be eliminated by these data. Although the results were insufficient to provide a clear understanding of the mechanisms involved, it

was shown conclusively that the responses studied depended not only on the independent variables of microwave exposure selected, but also on the baseline levels of the normal physiological state that existed at the time of exposure.

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REFERENCES

Allen, C.F., Allen, J.P., and Greer, M.A. (1975). Absence of nycthemeral variation in stress-induced ACTH secretion in the rat. *Aviat. Space Environ. Med.* 46:296.

Bourne, G.H. (1975). Collected anatomical and physiological data from the rhesus monkey. In *The Rhesus Monkey* (G.H. Bourne, ed.), Vol. 1, p. 55, Academic Press, New York.

de Lorge, J. (1979). Disruption of behavior in mammals at three different sizes exposed to microwaves: extrapolation to larger mammals. In *Electromagnetic Fields in Biological Systems* (S.S. Stuchly, ed.), Proceedings of the 1978 Symposium in Ottawa Canada, June 28-30, p. 215, IMPI Ltd, Edmonton.

Deichmann, W.B., Bernal, E., and Keplinger, M. (1959). Effect of environmental temperature and air volume exchange on survival of rats exposed to microwave radiation of 24,000 megacycles. In *Proceedings of Third Annual Tri-Service Conference on Biological Effects of Microwave Radiating Equipments* (C. Susskind, ed.), p. 62, U. of California Printing Dept, Berkeley.

Engeland, W.C., Shinsako, J., Winget, C.M., Vernikos-Danellis, J., and Dallman, M.F. (1977). Circadian patterns of stress-induced ACTH secretion are modified by corticosterone responses. *Endocrinology* 100:138.

Gallagher, T.F., Yoshida, K., Roffwarg, H.D., Fukushima, D.K., Weitzman, E.D., and Hellman, L. (1973). ACTH and cortisol secretory patterns in man. *J. Clin. Endocrinol. Metab.* 36: 1058.

Gibbs, F.P. (1970). Circadian variation of ether-induced corticosterone secretion in the rat. *Am. J. Physiol.* 219: 288.

Guy, A.W., Lehmann, J.F., and Stonebridge, J.B. (1974). Therapeutic applications of electromagnetic power. *Proc. IEEE* 62: 55.

Hensel, H. (1973). Neural processes in thermoregulation. *Physiol. Rev.* 53: 948.

Herd, J.A., Morse, R.T., Kelleher, R.T., and Jones, L.G. (1969). Arterial hypertension in the squirrel monkey during behavioral experiments. *Am. J. Physiol.* 217: 24.

Holaday, J.W., Meyerhoff, J.L., and Natelson, B.H. (1977). Cortisol secretion and clearance in the rhesus monkey. *Endocrinology* 100: 1178.

Johnson, G.S. and Elizondo, R.S. (1979). Thermoregulation in *macaca mulatta*: a thermal balance study. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 46: 268.

Kaneko, M., Hiroshige, T., Shinsako, J., and Dallman, M.F. (1980). Diurnal changes in amplification of hormone rhythms in the adrenocortical system. *Am. J. Physiol.* 239 (Regulatory Integrative Comp. Physiol. 8): R309.

Lotz, W.G. (1979). Endocrine function in rhesus monkeys exposed to pulsed microwave radiation. In *Electromagnetic Fields in Biological Systems* (S.S. Stuchly, ed.), Proceedings of the 1978 Symposium in Ottawa, Canada, June 28-30, p. 32, IMPI Ltd, Edmonton.

Lotz, W.G. and Podgorski, R.P. (1982). Temperature and adrenocortical responses in rhesus monkeys exposed to microwaves. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* (In Press).

Lotz, W.G. and Michaelson, S.M. (1978). Temperature and corticosterone relationships in microwave exposed rats. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 44:438.

Lu, S.-T., Lebda, N., Pettit, S., and Michaelson, S.M. (1980a). Delineating acute neuroendocrine responses in microwave-exposed rats. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 48: 927.

Lu, S.-T., Lotz, W.G., and Michaelson, S.M. (1980b). Advances in microwave-induced neuroendocrine effects: the concept of stress. *Proc. IEEE* 68: 73.

Mead, J. and Bonmarito, C.L. (1949). Reliability of rectal temperatures as an index of internal body temperature. *J. Appl. Physiol* 2: 97.

Murphy, B.E.P. (1967). Some studies of the protein-binding of steroids and their application to the routine micro and ultramicro measurement of various steroids in body fluids by competitive protein-binding radioassay. *J. Clin. Endocrinol. Metab.* 27: 973.

Myers, R.D., Gisolfi, C.V., and Mora, F. (1977). Role of brain Ca^{2+} in central control of body temperature during exercise in the monkey. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 43: 689.

Nielsen, B. and Nielsen, M. (1965). Influence of passive and active heating on the temperature regulation of man. *Acta Physiol. Scand.* 64: 323.

Olsen, R.G., Griner, T.A., and Prettyman, G.D. (1980). Far-field microwave dosimetry in a rhesus monkey model. *Bioelectromagnetics* 1: 149.

Olsen, R.G. and Griner, T.A. (1982). Partial-body absorption resonances in a sitting rhesus model at 1.29 GHz. *Radiat. Environ. Biophysics* (In Press).

Saltin, B. and Hermansen, L. (1966). Esophogeal, rectal, and muscle temperature during exercise. *Am. J. Physiol.* 21: 1757.

Stitt, J.T. (1979). Fever versus hyperthermia. *Federation Proc.* 38: 39.

Wenger, C.B., Roberts, M.F., Stolwijk, J.A.J., and Nadel, E.R. (1976). Nocturnal lowering of thresholds for sweating and vasodilation. *J. Appl. Physiol.* 41: 15.

"THE BRAIN IS THE ORGAN OF LONGEVITY": INTRODUCTION TO G. A. SACHER'S FREE-ENERGY HYPOTHESIS OF LIFE-SPAN ENHANCEMENT

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INTRODUCTION

The explosion of scientific knowledge during the 20th Century and the subsequent thrust toward hyperspecialization have all but extinguished Renaissance Man. Isaac Asimov and Carl Sagan are among the few, well-known contemporaries that evince a broad grasp of physical and biological theory and data, but neither has achieved the critical criterion of innovativeness--of the bold stroke of insightful synthesis --that moves the corpus of scientific knowledge toward new frontiers. George Alban Sacher was encyclopedic of grasp; he was highly productive as a practicing, publishing scientist; and he was innovative of concept and theory. He easily qualified as a Man for all Scientific Seasons.

I shall leave it to other, more competent biographers to present in detail Sacher's personal and educational background, and his long and productive labors in the domain where biology intersects the ionizing radiations. Suffice to say that he was born in 1917 a native of the United States, that he moved horizontally as an undergraduate through a labyrinth of university disciplines--experimental psychology, physiology, genetics, biometrics, mathematics, and physics--and that he never seriously aspired to seek a graduate degree after award of the baccalaureate from the University of Chicago in 1943. A long and distinguished association with the Argonne National Laboratories followed, as did a large number of important publications related to the biology of aging. He died in January of 1981, victim of an accident.

I shall touch on some contents of Sacher's publications but for the greater part will emphasize a side of his thinking that until now has not been reflected in archival print. He nourished during his last decade the hope of establishing a microwave-instrumented biological laboratory in which he could verify--or infirm--certain implications of his belief that the central nervous system might play a major role in determining longevity. Always a cautious scientist, Sacher's keen analytical skills were ever constrained by a tenacious desire for empirical substantiation: An hypothesis is a propositional ladder that must rest firmly on the fundament of fact before one ascends it in the search for additional facts. It was Sacher's intent to perform certain experiments before unveiling in the open literature what I term his *free-energy* hypothesis.

In the pages that follow, I shall sketch the free-energy concept in terms of antecedents and implicat ons, and also examine it in the light of pertinent findings.

METABOLISM AND LONGEVITY

My introduction to Sacher's works occurred in the late 1960s when I chanced on an essay by Roland Fischer (1966), who portrayed metabolic rate as a fundamental constraint on longevity and cited empirical support in investigations reported by Sacher (e.g., 1958; 1959). Sacher's datum, which was based on studies of life tables, allometric data, and metabolic measures of hundreds of species and which was earlier hypothesized by Rubner (1908) and Pearl (1928), was given poetic expression by Fischer: *The length of our lives is inversely proportional to the height of our metabolic flames.*

Intrigued by this seeming affirmation of mother wit--that burning of the human candle at both ends exacts a toll of mortal time--I sought means to perform model experiments on murine species in which the second flame, so to speak, was to be ignited in the microwave field of a multi-mode cavity. The intent was chronically to dose mice and rats with sufficient microwave energy to match their resting metabolic rates, thereby forcing them into a "faster rate of living" (Pearl, 1928). To accomplish this and other work, a request for grant support was submitted to the National Institutes of Health in the early 1970s. A project-site visit by NIH officials and consultants to my laboratory followed. Appropriately enough, Sacher was the chairman of the site-visiting team.

My recollection of the visit is spotty, but one exchange with Sacher remains vivid in memory. To his question: What would one expect to find if mice or rats were continuously or intermittently exposed during the term of life to a moderately thermalizing microwave field? I answered, without hesitating, that life span would be truncated. Sacher responded, also without hesitating, that life span might be extended. Thence followed my introduction by Sacher to his free-energy hypothesis, which he incorporated in a short but masterful lecture that began with a review of four established *actuarial* correlates of longevity (*cf.* Sacher, 1974; 1978):

ACTUARIAL AND CONSTITUTIONAL CORRELATES OF LONGEVITY

1. *Core temperature.* The weakest correlate, one that accounts for less than five percent of life-span variation,

but one that is highly reliable in the statistical sense, is core temperature. A *higher* core temperature, in general, is associated with *greater* longevity.

2. *Body mass.* More massive animals generally live longer than smaller animals. The factor of body mass accounts for about 15 to 20 percent of the variation of longevity.

3. *Metabolic rate.* Metabolic rate is inversely related to longevity, accounting for about 25 percent of the variance.

4. *Brain mass.* The mass of the brain is the strongest correlate of longevity, accounting for about 35 percent of the variance.

Sacher illustrated the relation of brain mass and metabolic rate to life span by comparing two species, *Peromyscus leucopus* (the white-footed field mouse) and *Mus musculus* (the house mouse, which is the progenitor of all common laboratory strains). To the eye, adults of both species are remarkably similar as regards coloration, form, and size. Yet, under optimal conditions, the field mouse survives nearly eight years, while the house mouse seldom lives longer than three years. Physiologically and anatomically, the animals are highly similar but for two compelling differences: The mean of the metabolic rate of the longer-lived mouse is about 20 percent lower, and its brain is half again more massive than that of its shorter-lived cousin.

Sacher next indicated that two of the actuarial predictors--body mass and core temperature--are redundant to and subsume under the constitutional factors of, respectively, the degree of encephalization (as indexed by the brain-to-body-mass ratio) and the efficiency of energy conservation, i.e., the specific metabolic rate will be lower and the mean of core temperature will be higher when thermodynamic efficiency is maximized--when entropy is minimized (*cf.* Sacher, 1967).

The role of genetics as a controlling factor in longevity was in no wise minimized by Sacher. Indeed, he remarked on several occasions that degree of encephalization and longevity might be largely independent, each primarily driven in the causal sense by a species' genes. More, he carefully differentiated between genetic and ontogenetic factors as determinants of life span, although he recognized the difficulty of parceling the contribution of each. When *Homo sapiens*' optimal life span is compared with that of other primates of comparable body mass, the difference favoring man is reckoned in several decades. But does the larger, more complex brain of man enable him significantly to effect more efficient expenditure of energy within the *milieu*

intérieur, thereby prolonging life? In short, is the advanced brain a metabolic modulator? The same questions could be asked of *Mus* and *Peromyscus*.

Sacher definitely subscribed to the possibility that the more advanced brain of the more highly evolved species is not only correlated with but might be causally related to its greater life span, hence his expression, "*The brain is the organ of longevity*" (see Mackay, 1977, p. 131). It was also Sacher's belief that the brain of the mammal--even the dimunitive organ of the murine animal--might be sufficiently advanced that a chronic infusion of mildly thermalizing microwave energy into the body would result in neurally and humorally mediated reduction of expenditures of endogenous energy. Free energy imparted by the field might spare to some extent the endogenous store, the while being used to energize the machinery of the body.

A question comes immediately to mind regarding the specificity of microwave energy as a free-energy source. Why should 10-cm microwaves differ from the less-than-1-mm far-infrared waves in sparing the endogenous calories of, say, a mouse? Sacher never directly addressed this question in our exchanges but I conjecture two possibilities, both based on the limited depth of penetration of submillimeter waves. One, these waves do not significantly invest the deeper tissues in which the bulk of the body's metabolic activity takes place. Electromagnetic energy might be used more efficiently by organelles and cells if it is coupled directly to them. And two, psychological and physiological factors come into play. The phylogenetically advanced (endothermic) species are creatures whose comfort and survival depend on an environment at a temperature well below that of the body (see, e.g., Hardy, 1970). The implication of this provision is that the environment is a sink of thermal energy, and that energy drawn from the metabolic well is being dissipated continuously to maintain comfort and adaptive physiological function. Electromagnetic fields at the longer wavelengths of the microwaves and the shorter wavelengths of the shortwaves might present the only practical means of coupling significant quantities of thermalizing energy to the deeper reaches of the mammalian body while preserving a moderate temperature of the skin, in which reside receptors that mediate comfort and thermoregulation.

Electromagnetic energy at shorter wavelengths ($<<1$mm) is readily absorbed by molecules of air. It follows that the sizable infrared fluxes of sun and other conventional sources of heating are indiscriminate energizers of the gaseous environment as well as its inhabitants. Thermalization of air that is incident on the surface of the body

can narrow or even obliterate the vital gradient of temperature between the immediate surround and the body. Survival of the species has therefore depended on evolutionary adaptations by which the organism either maintains a safe thermal distance between itself and environment (by behavioral thermoregulation) or invokes evaporative cooling (via autonomic regulation), both of which exact a toll of endogenous energy. The radio waves in consequence of their longer wavelengths can warm the body without directly warming the surrounding air, which selectivity affords a means of introducing energy to the deeper reaches of the body while preserving a cool surround--and the cooler surface temperatures that could augur for comfort and reduced metabolic demand. *If* comfort can be maintained in a field that lessens the metabolic burden of internal warming, endogenous energy to some extent will be conserved.

If not a wholesale convert to Sacher's unorthodox views, I did note the splendid competition of his hypothesis and mine--greater versus decreased longevity of the chronically microwave-irradiated mammal--and agreed with him that the implications of the free-energy concept, if valid, are profound as regards an understanding of the role of the central nervous system in metabolic, endocrinological, and immunological function and adaptation. We agreed, too, that the instrumentation required chronically to house, feed, water, and irradiate large numbers of animals under dose-determinate, environmentally controlled conditions was beyond economic reach if not beyond the engineering state-of-the art. Only later, with the creation and introduction of the multiple-unit guided-wave exposure systems of Arthur W. Guy (Guy and Chou, 1977; Guy, *et al.*, 1979; see Lovely, Chapter 20 of this volume) would the requisite instrumentation become affordable and accessible. It is one of the ironies of Sacher's career that he had been a leading candidate to direct the Institute On Aging at the University of Washington in Seattle, where collaboration with Guy had been assured and would have enabled rigorous testing of the free-energy hypothesis, when his own life came to an untimely end.

SUMMARY OF PERTINENT FINDINGS

What, now, do the data say about the free-energy hypothesis? No experiment reported to date constitutes an adequate test in the sense of supplying comprehensive information on survival time, metabolic rate, food consumption

and utilization, body mass, anatomical integrity (especially that of the skeletal and nervous systems), status of the immune and endocrine systems, and physiological and behavioral competence in the wake of chronic exposure to a moderately thermalizing radio field. Some reports do provide data on one or more of the important end points, usually in association with a single exposure or a limited number of brief exposures. These reports receive cursory review, but all must be addressed in the light of a caveat often sounded by Sacher (e.g., 1974, 1978): One must distinguish between prolongation of life in senescence and enhancement of longevity based on actual retardation of the rate of aging. More, retardation of aging, if sorely taxed at the expense of quality of living, is no bargain. Some hibernators live relatively long lives, but the torpor of hibernation--a prolonged period of somnolence and greatly reduced metabolic activity--is hardly the stuff of a vibrant psychological existence.

Longevity of Microwave Irradiated Animals

The first report of direct pertinence to the free-energy hypothesis was published by Prausnitz and Süsskind in 1962. Mature mice were exposed (n = 200) or sham-exposed (n = 100) to a 9270-MHz field 4.5 minutes a day, five days a week, until 50 percent of the controls expired, which embraced a period of 59 weeks. The composite strength of the incident field, 100 mW/cm^2, was of sufficient duration to elevate core temperature by slightly more than 3 °C; I estimate the dose rate was at a level near 50 mW/g. At termination of the experiment, 64 percent of the irradiated mice survived (Fig. 1). A two-by-two χ^2-test of the 64-50 difference yields a two-sided *P* value that is less than .02 at 1 *df*. The quantity of microwave energy imparted to the mice, about 70 J/g per weekly exposure, approximates a value that is one percent of the mouse's weekly metabolic energy production, based on a time-averaged specific metabolic rate (SMR) of 8 mW/g (see Durney, *et al.*, 1978). Relative to the SMR, the small proportion of free microwave energy available to the mice is associated with a 14 percent increase in median number of survivors, which extrapolates to a three-month augmentation of median survival time, indicating a marked nonlinearity in the energy-dose survival-time function. The association is statistical, not necessarily causal, but certainly does no violence to the direction of Sacher's thesis.

Preskorn, *et al.* (1978) exposed or sham-exposed mice *in*

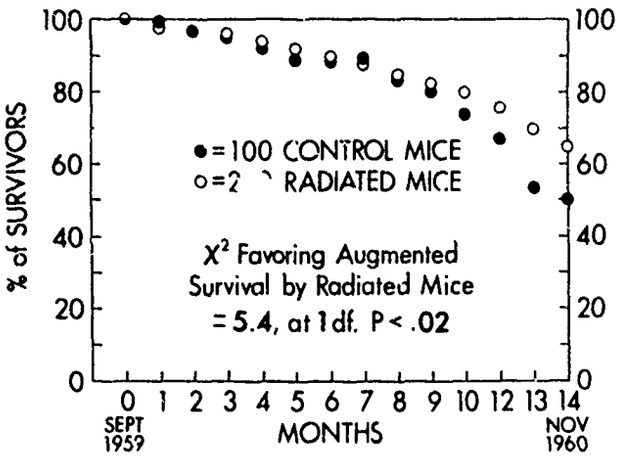

Figure 1. Survival curves of microwave-irradiated and sham-irradiated mice. Irradiated animals were exposed to 9270-MHz microwaves in the far field at 100 mW/cm^2. The animals were exposed 4.5 minutes a day, five days a week for 59 weeks, at which time 50 percent of the controls had expired. Sixty-four percent of the exposed mice survived the 295 periods of irradiation. The estimated energy dose per exposure is 13.5 J/g. (Redrawn, with permission, from Prausnitz and Süsskind, 1962.)

utero to 2450-MHz microwaves a total of four times for a period of 20 minutes during each exposure. The average dose rate was 35 mW/g, and the average energy dose per radiation treatment was 42 J/g. During the 16th day *post partum*, all of the pups were injected subcutaneously with an homogenate of a reticular-cell sarcoma. Subsequently, the animals were assorted into one of two groups on the basis of whether tumor growth occurred, then were observed for survival times through the full term of life. At the point in time--97 weeks *post partum*--when 50 percent of 36 non-tumor-bearing controls had expired, 67 percent of 45 irradiated non-tumor-bearing mice survived. Although the differential in survival rate of irradiated animals at the controls' median closely approximates that observed by Prausnitz and Süsskind (1962), the contribution of "free" microwave energy during the gestational exposures, ∿170 J/g, is only a miruscule proportion of the estimated production of endogenous energy, ∿500 kJ/g, through the 97th *post partum* week. One suspects that enhanced immunocompetence was a contributing factor since other data found in a companion study by Preskorn, *et*

al. (1978) revealed retarded rates of tumor growth and histological evidence of anti-tumor activity in mice irradiated both *in utero* and *post partum*. The tumor-bearing mice, as expected, exhibited severely truncated survival times. The mice that had been irradiated *in utero* did exhibit a longer median survival time than did tumor-bearing controls, and the difference is reliable ($P < .05$).

Only one additional paper has appeared in the archival literature on microwave irradiation in which longevity of a genetically hardy mammal was observed (Spaulding, *et al.*, 1971). Mice were exposed 2-h daily, 5 days a week, for 35 weeks to 800-MHz microwaves at a power density of 43 mW/cm^2, which would result in dose rates (depending on an animal's orientation in the field) ranging approximately from 1 to 10 mW/g. Microwave-irradiated mice lived longer on the average than did controls (664 vs. 645 days) but small samples (n = 24) and the high variability of mammalian life span summon the null hypothesis.

A study recently completed in my laboratory (Reeves, *et al.*, 1981), which has yet to appear in archival print, involved highly intense irradiation of mouse dams in a 2450-MHz field a total of three times during the fetal period (duration of each treatment, 10 min.; dose rate, 46 mW/g). A large percentage of pups (17% *vs.* 6% of controls; $P < .05$) expired shortly following birth, ostensible victims of cannibalism by their dams. Thereafter, survival curves from time of weaning until expiration first were parallel, then converged, i.e., the mortality curve of control mice after the 18th month was steeper (Fig. 2). The total dose of microwave energy imparted to irradiated fetuses was ∿80 J/g--once again a minuscule contribution to the total production of endogenous energy.

The studies of Preskorn, *et al.* (1978) and Reeves, *et al.* (1981) yielded quite different outcomes in mice of the same (CFW) strain during initial *post-partum* periods of observation; pre-weaning loss of pups did not differ among controls and irradiated animals in the studies of Preskorn, *et al.*, but Reeves, *et al.* observed a threefold increase over controls in percentage of deaths of fetally irradiated pups. Although the energy dose per exposure was lower in the Reeves, *et al.* study, the dose rate was considerably higher and led to larger ΔTs of dams' colonic temperature (respective means of elevation are 2.24 and 2.76 °C),* which may

*Measurements of temperature immediately before and after irradiation were made with sensors of relatively large thermal time constants (∿10 s). Recent comparisons of ΔTs of

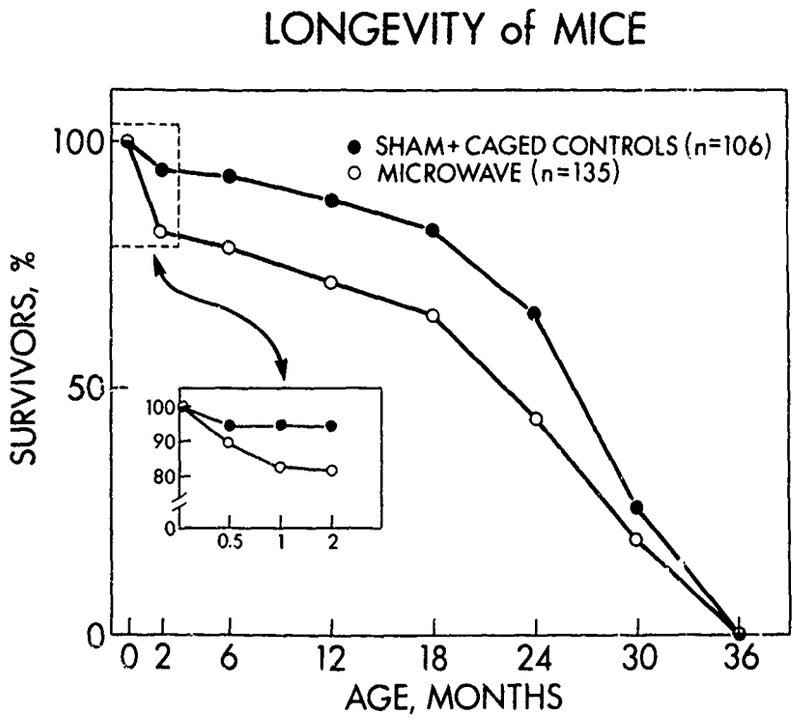

Figure 2. Survival curves of 135 CFW mice that were irradiated three times *in utero* (11th, 13th, and 15th day of gestation) for 10-min. periods in a multi-mode cavity (2450-MHz microwaves; dose rate 46 mW/g). Sham-irradiated mice and reference (continuously caged) controls (total n = 106) differed negligibly in survival times; their data were pooled. Seventeen percent of the irradiated mice (vs. 6% of controls) died before weaning ($P < .05$), victims of cannibalism. Thereafter, survival curves were parallel through the 18th month, then declined more steeply for controls. The calculated energy dose per exposure is ∿28 J/g, which is near the lethal threshold for brief (<20-min.) periods of irradiation (Reeves, *et al.*, unpublished).

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irradiated mice in the author's laboratory based on the same sensors and on microwire thermocouples (time constant<<1 s) have revealed that elevated body temperatures of mice decline so rapidly after cessation of irradiation that nonlethal maxima are undervalued by as much as 3 °C when conventional sensors are used. A critical factor in the comparison of studies of Preskorn, *et al.* and Reeves, *et al.* is the difference in measured ΔTs, not their absolute values.

have played a role in the selectively high incidence of demise. Of obvious import for future studies of longevity of animals irradiated *in utero* is the need to avoid excessive temperature elevations of dams and their concepti.

Effects of Microwave Irradiation on Other End Points of Aging

Many markers have been used in classical studies of the rate of mammalian (including human) aging; among them: bone growth and development, density of CNS neurons, body mass, immunocompetence, food consumption, and metabolic rate (Sacher, 1974; Shock, 1974). Studies typically involving brief periods of microwave irradiation of mice and rats at moderate to intense levels (i.e., dose rates ranging from 1 to 20 mW/g, and total durations of exposure ranging from a few tens of minutes to a few days) have revealed with respect to controls that bone growth of fetuses is delayed (Berman, *et al.*, 1982; see Fig. 3); that body mass of fetuses is smaller (Chernovetz, *et al.*, 1979; O'Connor, 1980; Berman, *et al.*, 1982; see Fig. 4); that food consumption of adults is reduced, even though normal body mass is maintained (Lovely, Chapter 20 of this volume); that immunocompetence of adults is enhanced (Szmigielski, *et al.*, 1979; Roszkowski, *et al.*, 1980); and that density of neocortical neurons of adults is higher (Brizzee, *et al.*, 1971). The most frequently confirmed finding of direct pertinence to the free-energy hypothesis is reduction of metabolic rate during periods of microwave irradiation, which has been reported in the adult rat by Phillips, *et al.* (1975), in the adult mouse by Ho and Edwards (1977*a*, *b*), and in the adult primate--the squirrel monkey--by Adair and Adams (1982). Most of the irradiation-induced changes in end points related to age-markers and to metabolism are of a direction that comports with Sacher's free-energy hypothesis.

Caveats

To avoid any supposition that mine is a special plea --that data favorable to the free-energy concept have been cited selectively--I hasten to repeat my earlier cautionary about the lack of *any* published experiment that suffices an adequate test. The studies cited qualify only as heuristic examples, and any of them might have yielded results by means quite removed from the organism's utilization of free

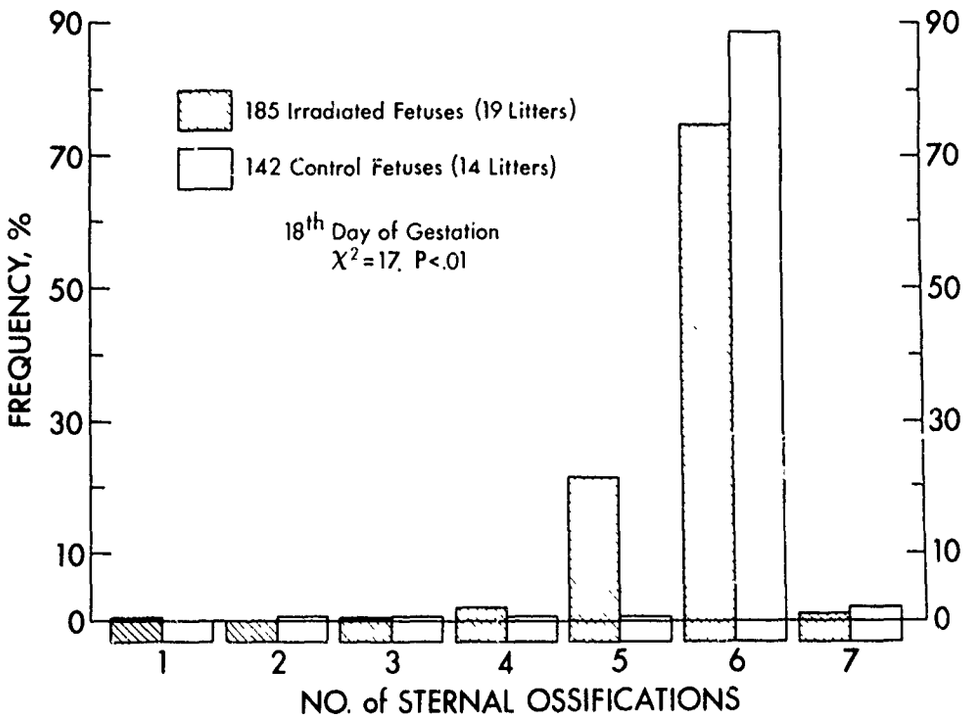

Figure 3. Percentages are shown for observed frequencies of sternal ossifications, a measure of skeletal development, in mouse fetuses of the CD-1 strain. Their dams were sham irradiated or were irradiated 100 minutes daily in the far field by 2450-MHz microwaves at 28 mW/cm^2 from the 6th through the 17th day of gestation (estimated mean of dose rate, 16.5 mW/g). (The data were provided in a personal communication, 1981, from Ezra Berman and represent a detailed breakdown of findings in the 1982 report of Berman, *et al.*).

energy. For example, Berman, *et al.*'s finding of retarded development of skeletal structure in fetally irradiated mice might represent toxic stunting, not a delay in rate of maturation. Only long-term studies that provided comparative data on asymptotes of body mass of mature controls and of mature mice after fetal irradiation could shed definitive light on the mechanism of retarded development. A predicted outcome of the free-energy hypothesis is that fetally irradiated animals would reach the normal limits of body mass at a later-than-normal time; cf an hypothesis based on toxi-

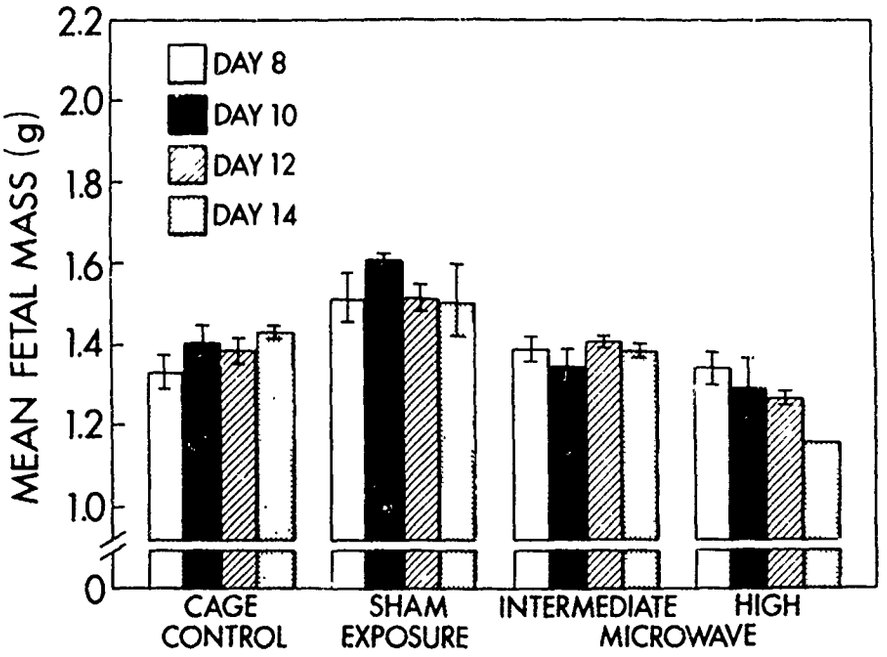

Figure 4. Means of body mass (±SE) are shown for rat fetuses (Sprague-Dawley strain): 52 reference (continuously-caged) controls, 50 sham-exposed animals; 123 dosed with 2450-MHz energy at ∿17 mW/g, and 73 dosed at ∿30 mW/g. Dams of 16 independent groups were irradiated once in a multimode cavity for 20 minutes during the 8th, 10th, 12th, or 14th day of gestation. All measurements of body mass were made during the 18th day immediately after Caesarian section. The calculated energy doses are ∿20 and ∿36 J/g; the incidence of lethality exceeded 20 percent in dams dosed at 36 J/g. Only live fetuses from surviving dams yielded data shown in the figure (Chernovetz, *et al.*, unpublished).

cation, a persistent arrest of growth.

The datum of reduced body mass at term of embryonically or fetally irradiated mice and rats might itself be considered at variance to the free-energy hypothesis. If there were a linear, one-for-one trade-off of endogenous for exogenous energy *in utero*, one would expect no differences in body mass between irradiated and control preparations. However, the dependence of embryo or fetus on maternal metabolic events might conspire for conditions in which

reduced rate in the dam's utilization of endogenous energy is reflected in a disproportionately reduced flux of metabolites to the placenta. Conversely, both dam and conceptus during irradiation might be exhibiting the same, reduced rate of living (aging). The former possibility likely would be associated with a normal period of gestation but smaller fetuses, while the latter possibility would be associated with a longer-than-normal period of gestation and with neonates of normal body mass at time of parturition.

Another possibility at variance to the free-energy hypothesis may lie in the microwave-irradiation-augmented immunocompetence observed by Szmigielski, *et al.* (1977) and by Roszkowski (1980). This augmentation might be an acute response that is lost or even reversed in animals during a prolonged exposure or after manifoldly repeated exposures to a mildly thermalizing field. Indeed, in recent work involving mice with genetically disposed or experimentally induced malignancies, Szmigielski, *et al.* (1982) reported reliable truncation of life span of animals exposed 2-h daily, 6 days a week for 1 to 6 months to 2450-MHz fields that resulted in dose rates between 2 and 8 mW/g. This finding, which contrasts with those of Prausnitz and Süsskind (1962) and of Preskorn, *et al.* (1978), who found evidence of enhanced survival times in mice intensely irradiated, respectively, as adults and fetuses, raises an interesting question. Are some animals constitutionally disposed to profit from the free energy of the microwave field while others face a loss? This question is both scientifically intriguing and hygienically important--and begs for answers from the laboratory.

VALIDATION OF THE FREE-ENERGY HYPOTHESIS

Sacher and I communicated frequently during the late 1970s, the recurrent topics being the ideal--but probably un-doable "crucial"--experiment for attacking the free energy hypothesis, and the doable experiments that would permit one, step-by-step, to cleave between or among competing hypotheses. The problem of securing a valid biological model was of much concern to Sacher, not only in the sense of selecting the appropriate species or strain of animal but also in implementing a living environment that is as compatible with the animal's natural *modus vivendi* as it is with the accoutrements of the laboratory. The widespread practice of isolating, even of physically restraining

animals during irradiation treatments invokes sources of stress that are demonstrably injurious (Justesen and King, 1970; Justesen, *et al.*, 1971). The elegantly designed experiments of Szmigielski, *et al.* (1980, 1982) have revealed, for example, that a regimen involving chronic social isolation and confinement of mice is as potent or more so in augmenting growth of spontaneous and induced neoplasms and in decreasing life span as is chronic microwave irradiation that results in dose rates of 2 to 3 mW/g. More, there is an as yet unassayed possibility that isolation and confinement, even if adapted below thresholds of manifest stress in sham-irradiated controls, might complex with relatively low levels of irradiation to trigger a suprathreshold stress reaction in the experimental animal. One hears the argument that isolation and confinement are necessary to control energy dosing of the animal in a free field, which gives one pause to wonder whether the quest for dosimetric accuracy and control has too often exacted an incommensurate cost by way of socio-biological confounding.

Sacher's theoretical focus on the mammalian brain as an ontogenetic instrument of long-term survival led me to suggest that measures of cerebral metabolism and neuroelectric activity are highly appropriate to the study of the aging animal. Edward C. Beck and colleagues at the Veterans Administration Medical Center and the University of Utah in Salt Lake City have published numerous reports on human subjects that reveal highly characteristic, age-related changes in the waveforms and latencies of components of sensorily evoked, computer-summed electrocortical potentials (Beck, 1975; Beck, *et al.*, 1980; Dustman and Beck, 1969; Dustman, *et al.*, 1977). Typically, component amplitudes decrease and latencies increase monotonically as the individual advances from maturity to senescence, yielding as it were indices of the biological age of the central nervous system. Since chemical stress in the form of excessive, chronic intake of ethanol accelerates the electrophysiologically-indexed rate of aging (Beck, *et al.*, 1979), there is precedent for the supposition that other factors that augment (or delay) the aging process in mammals can be detected by the evoked-response measure. Accordingly, a first doable experiment might involve chronic, intermittent irradiation of animals in a low-stress environment in which one performs longitudinal studies of brain temperature (as an index of cerebral metabolism) and of sensorily evoked responses.

The imaginative reader will certainly conjure other experiments that bear on Sacher's free-energy hypothesis. One that has tantalized me is implicit in R.V. Pound's recent proposal (1980) to remake the human home in the form of a

capacious multi-mode cavity, thence selectively to warm its inhabitants with microwave energy. Pound's motive is economic--why waste energy on the inert materials of the domicile when you can invest it directly in its lively inhabitants?--but I suspect that Sacher would look beyond the dollar to the possibility that the inhabitants might enjoy a longer sojourn during the trek to senescence.

Hardly evangelical in his belief of the possibility of free-energy utilization, Sacher was nonetheless committed to the view that the possibility has implications worthy of intensive exploration and evaluation in the laboratory. I lament the untimely demise that prevented him from culturing his brain child but would do his memory honor by unveiling his conceptus and by urging other scientists with the requisite means to determine its viability.

George Sacher was a creative explorer, a brilliant navigator of many scientific seas. If the free-energy hypothesis is validated, he will in time be regarded as a latter-day Ponce de Leon whose fountain of youth lay not in magic waters but in a beneficent stream of electromagnetic energy.

APOLOGIA

George Sacher's command of scientific knowledge was awesomely broad and deep. Were I numbered among that rare species of which he was member and exemplar, my task as expositor would have been easy. The task was not easy, and whatever errors and voids in translation of his views appear in my exposition should be charged solely to me. The largest voids in gauging the implications of the free-energy hypothesis lie in the realms of biological physics and chemistry--in the goings on of enzyme kinetics, in the distribution of high-energy phosphates, in the traffickings of the mitochondria, in the balance of anabolic and catabolic events, etc. I leave it to scientists who are gifted with the requisite knowledge to assess Sacher's hypothesis for its goodness of fit with what is known--and to specify means of testing its validity--in the domain of molecular biology.

Another void lies at the other end of the biological spectrum in what might be labeled the intersection of mind and medicine. A glance at the life tables of the years 1900 and 1980 reveals that the average longevity of *Homo sapiens* in the environs of North America has nearly doubled. From the fertile minds and facile hands of Pasteur, Koch, Ehrlich, Flemming, Halsted, and others have flowed discoveries and advances that have added remarkably to the life span of

man. In this socio-biological sense Sacher is doubtless vindicated in championing the brain as the organ of longevity.

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REFERENCES

Adair, E.R. and Adams, B.W. (1982). Adjustments in metabolic heat production by squirrel monkeys exposed to microwaves. *J. Appl. Physiol.* 52: 1049.

Beck, E.C. (1975). Electrophysiology and behavior. *Ann. Rev. Psychol.* 26: 233.

Beck, E.C., Dustman, R.E., Blueswicz, M.J., and Cannon, W.G. (1979). Cerebral evoked potentials and correlated neuropsychological changes in the human brain during aging: A comparison of alcoholism and aging. In *Aging, Sensory Systems, and Communication in the Elderly* (J.M. Ordy and K.R. Brizzee, eds.), p. 203. Raven Press, New York.

Beck, E.C., Swanson, C., and Dustman, R.E. (1980). Long latency components of the visually evoked potential in man: Effects of aging. *Exp. Aging Res.* 6: 523.

Berman, E., Carter, H.B., and House, D. (1982). Reduced weight in mice offspring after *in utero* exposure to 2450-MHz (CW) microwaves. *Bioelectromagnetics* 3: 285.

Brizzee, K.R., Justesen, D.R., and King, N.W. (1971). Microwaves and density of brain cells. In *Proceedings: Department of Defense Electromagnetic Workshop* (P.E. Tyler, ed.), p. 353. U.S. Navy Bureau of Medicine and Surgery: Washington, D.C.

Chernovetz, M.E., Reeves, D.L., and Justesen, D.R. (1979). Teratology in rats exposed to 2450-MHz microwaves at intense and intermediate dose rates. *Abstracts, 1979*

National Radio Science Symposium, p. 407. National Academy of Sciences: Washington, D.C.

Durney, C.H., Johnson, C.C., Barber, P.W., Massoudi, H., Iskander, M.F., Lords, J.L., Ryser, D.K., Allen, S.J., and Mitchell, J.C. (1978). *Radio-Frequency Radiation Dosimetry Handbook* (Second Edition). USAF School of Aerospace Medicine Publication SAM-TR-78-22: Brooks Air Force Base, Texas.

Dustman, R.E. and Beck, E.C. (1969). The effects of maturation and aging on the waveform of visually evoked potentials. *Electroenceph. Clin. Neurophysiol.* 26:2.

Dustman, R.E., Schenkenberg, T., Lewis, E.G., and Beck, E.C. (1977). In *The cerebral evoked potential: Life span changes and twin studies* (J.E. Desmedt, ed.), p. 363. Clarendon: Oxford.

Fischer, R. (1966). Biological time. In *The Voices of Time* (J.T. Fraser, ed.), p. 357. George Braziller: New York.

Guy, A.W. and Chou, C.-K. (1977). System for quantitative exposure of a population of rodents to UHF fields. In *International Symposium on Biological Effects of Electromagnetic Waves* (C.C. Johnson and M.L. Shore, eds.), p. 389. HEW Publication 77-8011. U.S. Government Printing Office: Washington, D.C.

Guy, A.W., Wallace, J., and McDougal, J.A. (1979). Circularly polarized 2450-MHz waveguide system for chronic exposure of small animals to microwaves. *Radio Sci.* 14/6S:63.

Hardy, J.D. (1970). Thermal comfort: Skin temperature and physiological thermoregulation. In *Physiological and Behavioral Temperature Regulation* (J.D. Hardy, A.P. Gagge, and J.A.J. Stolwijk, eds.), p. 856. Chas. C. Thomas: Springfield.

Ho, H.S. and Edwards, W.P. (1977a). Oxygen-consumption rate of mice under differing dose rates of microwave radiation. *Radio Sci.* 12/6S:131.

Ho, H.S. and Edwards, W.P. (1977b). Absorbed dose rate and oxygen consumption rate in mice confined in a small holder during exposure to 2450 MHz microwave radiation. *Rad. Env. Biophys.* 14: 251.

Justesen, D.R. and King, N.W. (1970). Behavioral effects of low-level microwave irradiation in the closed-space situation. In *Symposium Proceedings: Biological Effects and Health Implications of Microwave Radiation* (S.F. Cleary, ed.), p. 154. BRH/DBD 70-2. USPHS: Rockville, Maryland.

Justesen, D.R., Levinson, D.M., Clarke, R.L., and King, N.W. (1971). A microwave oven for behavioural and biological research: Electrical and structural modifications, calorimetric dosimetry, and functional evaluation. *J. Microwave Power* 6:237.

MacKay, A.L. (1977). *The Harvest of a Quiet Eye: A Selection of Scientific Quotations*, p. 131. The Institute of Physics: London.

O'Connor, M.E. (1980). Mammalian teratogenesis and radiofrequency fields. *Proc. IEEE* 68: 56.

Pearl, R. (1928). *The Rate of Living*. A.A. Knopf, Inc.: New York.

Phillips, R.D., Hunt, E.L., and King, N.W. (1975). Field measurements, absorbed dose, and biological dosimetry of microwaves. *Ann. N.Y. Acad. Sci.* 247: 499.

Pound, R.V. (1980). Radiant heat for energy conservation *Science* 208: 494.

Prausnitz, S. and Süsskind, C. (1962). Effects of chronic microwave radiation on mice. *IRE Trans. Biomed. Elec.* BME-9: 104.

Preskorn, S.H., Edwards, W.D., and Justesen, D.R. (1978). Retarded tumor growth and augmented longevity in mice after fetal irradiation by 2450-MHz microwaves. *J. Surg. Oncol.* 10: 483.

Reeves, D.L., Levinson, D.M.., O'Connor, M.E., and Justesen, D.R. (1981). Longevity in mice after acute exposures in utero to 2450-MHz microwaves. *Abstracts, 3rd Annual Conference*, p. 39. Bioelectromagnetics: Gaithersburg, Maryland.

Roszkowski, W., Wrembel, J.K., Roszkowski, K., Janiak, M., and Szmigielski, S. (1980). Does whole body microwave hyperthermia therapy involve participation by the immune system? *Int. J. Cancer* 25: 289.

Rubner, M. (1980). *Das problem der Lebensdauer and Seine Beziehungren zurn Wachstum und Ernahrung*. Oldenbourg: Munich.

Sacher, G.A. (1958). Entropic contributions to mortality and aging. In *Symposium on Information Theory in Biology* (H. Yockey, *et al.*, eds.), p. 317. Pergamon Press: New York.

Sacher, G.A. (1959). Relation of lifespan to brain weight and body weight in mammals. In *Ciba Foundation Colloquia on Aging* (G.E.W. Wolstenholme and M. O'Connor, eds.), The Lifespan of Animals, 4: 115. Churchill: London.

Sacher, G.A. (1967). The complementarity of entropy terms for the temperature dependence of development and aging. *Ann. N.Y. Acad. Sci.* 138: 680.

Sacher, G.A. (1974). Aging. In *The New Encyclopaedia Britannica (15th Ed.) Macropaedia Vol. I*, p. 299. Benton: Chicago.

Sacher, G.A. (1978). Longevity and aging in vertebrate evolution. *Bioscience* 28: 49.

Shock, N. (1974). Human aging. In *The New Encyclopaedia Britannica (15th Ed.) Macropaedia Vol. I*, p. 305. Benton: Chicago.

Spaulding, J.F., Freyman, R.W., and Holland, L.M. (1971). Effects of 800-MHz electromagnetic radiation on body weight, activity, hematopoiesis and life span in mice. *Health Phys.* 20: 421.

Szmigielski, S., Pulverer, G., Hyrniewicz, W., and Janiak, M. (1977). Inhibition of tumor growth in mice by microwave hyperthermia. *Radio Sci.* 12/6S: 185.

Szmigielski, S., Szudzinski, A., Pietrazek, A., and Bielec, M. (1980). Acceleration of cancer development in mice by long-term exposition to 2450 MHz microwave fields. In *Proceedings of the International Symposium on Electromagnetic Waves and Biology*, (A.J. Berteaud and B. Servantie, eds.) p. 165. International Union of Radio Science: Paris.

Szmigielski, S., Szudzinski, A., Pietrazek, A., Bielec, M., Janiak, M., and Wrembel, J.K. (1982). Accelerated development of spontaneous and benzopyrene-induced skin cancer in mice exposed to 2450-MHz microwave irradiation. *Bioelectromagnetics* 3: 179.

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