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FOREWORD

The authors wish to express their appreciation to A/1C David S. Belski and to Isaac F. Sheirbon for the preparation of the charts; to A/3C Thomas Fry and Cleo Cumberland, and to Telecomputing Services Inc., for the statistical treatment of the data; to the officers and technicians in the Astroecology Branch (Captains Simpson J. Roper, Rudolf A. Hoffman, William E. Ward; MSgt Edward Dittmer; A/1C Nicholas Skames, Robert Lockhart, George Pegram and James Mooney) for the monitoring of the subjects; to the Bioinstrumentation Branch for the services of SSgt Henry Fegley who also monitored the subjects; and to Lajuan Roberts for the typing of the drafts.

We appreciate the cooperative efforts of the Veterinary Services Branch, Comparative Psychology Branch, Bioinstrumentation Branch and Land-Air Inc., in making this study possible.

ABSTRACT

In a counterbalanced experiment four restrained, immature chimpanzees were subjected to a 100% oxygen environment at 14.7 psia for over 15 hours. During this period they were isolated in a chamber and performed various psychomotor tasks. These same animals served as subjects for the same period of time in a 20% oxygen environment. Relative humidity was maintained at 45 - 55%; temperature was maintained at 79 - 81°F.; environmental CO_2 was lower than 3.8 mm Hg. Heart rate, respiratory rate, and skin and rectal temperatures were monitored during the experiments. Clinical examinations, hematological and serum biochemical determinations, and urinalyses were performed before and following each test. The only significant findings were a relative bradycardia and tachypnea in the hyperoxygenated environment.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.

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Commander
6571st Aeromedical Research Laboratory

CARE AND HANDLING OF THE SUBJECTS

The animals used in this study were handled in accordance with the "Principles of Laboratory Animal Care" established by the National Society of Medical Research.

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CHIMPANZEE PHYSIOLOGICAL TOLERANCE TO BREATHING 100% OXYGEN AT 15 PSI

I. INTRODUCTION

Before a chimpanzee can be used to precede man in space experimentation, considerable ecological testing should be done. The separate and combined effects of many ecological variables of various artificial environments must be assessed. These variables range from physiological parameters to psychological aspects of prolonged isolation and confinement. One particular area needing investigation is the effect of breathing 100% oxygen at 760 mm Hg (14.7 psi) for limited periods of time. This is a gaseous environment to which a chimpanzee could be subjected during the countdown period prior to launch.

Many investigations into the biological effects of a high oxygen environment have been performed. The French investigator, Paul Bert (Ref. 1) was the first to show that a high oxygen concentration can kill many forms of living organisms. Since that time a large number of oxygen tolerance investigations on experimental animals and a few on humans have been conducted (Ref. 1, 2, 3, 4, 5, 6, 7 and 18), and the toxic effects of continuous exposure to high oxygen concentrations have been repeatedly confirmed. These investigations indicate that the primary toxic action of high concentrations of oxygen at ambient atmospheric pressure is irritation to the respiratory tract. The effects noted are believed to be due to the direct action of oxygen on lung tissue causing pulmonary edema, atelectasis, fibrosis of the alveolar walls, pleural effusions and eventually death.

Bean (Ref. 3) points out that the accumulation of much experimental data leaves little doubt that continuous exposure to oxygen in concentrations above 60 to 70% at normal atmospheric pressure for 12 to 14 hours or even less, results in pathological changes in the lung. Paine, Lynn and Keys (Ref. 8) in a series of experiments on 49 dogs found that pulmonary changes occurred while breathing oxygen in concentrations of 95 to 100% at atmospheric pressure for periods as short as 2 hours. One dog died after only 6 hours of exposure and at autopsy exhibited the typical pulmonary pathology; however, the average duration of life in such an oxygenated environment was 39 hours. Hulpieu and Cole found that increases in relative humidity combined with high temperature greatly increased the toxic effect of oxygen (Ref. 9).

The purpose of this study was to determine, as quantitatively as possible, whether a period of 15 hours, the potential countdown time in an actual launch, in this environment is toxic to the chimpanzee. A series of tests were conducted to identify any possible deleterious effects on restrained chimpanzees from an environment of 100% oxygen at 760 mm Hg (14.7 psi) over a 15 hour and 15 minute period by the evaluation of psychomotor performance, physiological response, clinical examinations, and hematological and biochemical data, before, during and following the testing period.

Physiological parameters monitored and recorded during these tests include rectal temperature, skin temperature, pulse rate, three-lead electrocardiogram, and respiratory rate (Ref. 13, 15 and 16). Environmental parameters controlled, monitored and recorded include oxygen and carbon dioxide content, temperature, relative humidity, and barometric pressure.

Metabolic profile studies were conducted on blood and urine samples to determine the chemical changes in the blood as a result of exposure to increased concentrations of oxygen.

Psychomotor performance, as measured by continuous and discrete avoidance tests, was studied to determine whether it was affected by increased concentrations of oxygen.

II. MATERIALS AND METHODS

A. Description of Apparatus

1. Restraint Devices

a. Restraint suits consisted of nylon webbing reinforced by nylon tape at the cuffs and other points of stress. They were developed by Aeromedical Research Laboratory personnel and fabricated by the Clothing Division, ASD, and they represent a modification of suits previously used in chimpanzee research (Ref. 10). Expansion of the suit to compensate for growth of the subject was provided for by adding inserts controlled by drawstrings.

b. The restraint chair was developed by Aeromedical Research Laboratory personnel for use with two to six year old chimpanzees, and was locally fabricated. The chair is designed for easy adjustment and when used with a suit will facilitate attachment of sensors for collection of

physiological data (Ref. 11), to various sized chimpanzee. The restraint chair used in this study was modified with a metal skirt (Fig. 1) to prevent the chimpanzee from removing the urinary catheter or physiological leads.

2. Test Chamber System

The environmental chamber utilized in these tests was a General Electric "closed environmental system for large primates" (Ref. 12). This system will maintain internal environmental conditions within the following extremes: temperature, 60°F to 100°F; pressure, 120 to 760 mm Hg absolute; relative humidity, 30% to 90%; and atmospheric composition, up to 100% oxygen.

The only outside sources of energy required to operate the system are 220 V AC 60-cycle single phase, 115 V AC 60-cycle single phase, and 28 V DC, unregulated power.

The system is comprised of four main mobile sub-assemblies. The first is the chamber proper (Fig. 2). Its internal dimensions are 30 inches deep by 48 inches high by 48 inches wide, giving it a basic volume of 40 cubic feet. All surfaces are fully water-jacketed and connected in parallel by manifolds for maintaining wall temperature at any desired level or for "heat pulsing" them from high to low extremes of temperature.

A plexiglass window (Fig. 3) is provided in one wall over the pneumatic control panel for viewing the subject. A second "overlay" may be affixed to it to provide either an opaque or "one-way" viewing surface.

Electrical interfaces are also provided for conducting electrical signals from internal test leads to outside monitoring instrumentation. Eight sampling outlets are also provided.

The pneumatic control console displays an absolute pressure gage, oxygen supply shutoff valves, "breathe-down" valves, bleed valves, a quick-vent valve, and a demand type precision oxygen regulator. Integral with the chamber sub-assembly is a vacuum pump which is used to evacuate the system to lowered pressures. A purge valve is also provided so that the desired atmosphere gas composition may be admitted and "air" expelled from the system.

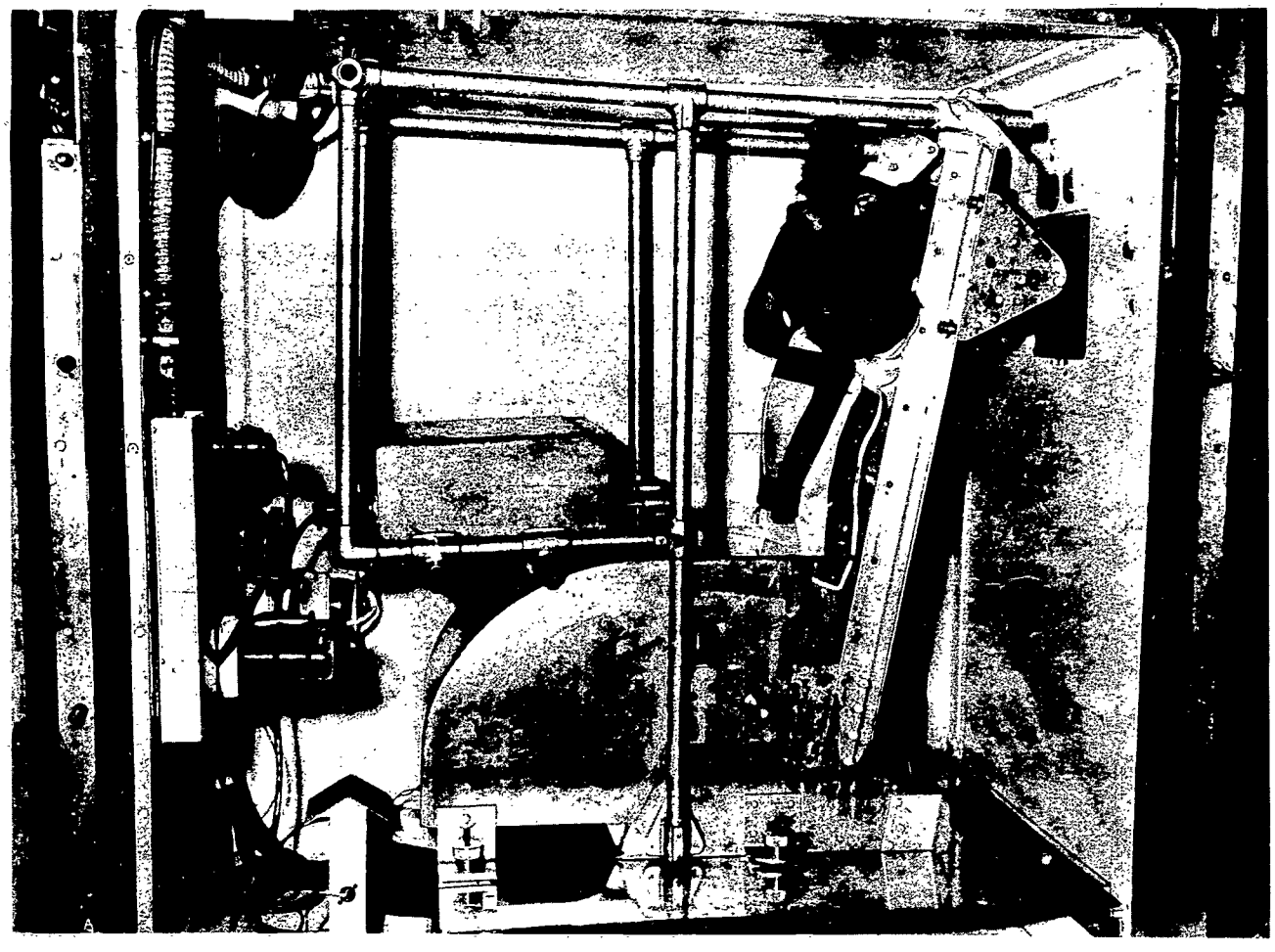

FIGURE 1. RESTRAINT CHAIR AND SUBJECT SEATED IN THE ENVIRONMENTAL TEST CHAMBER

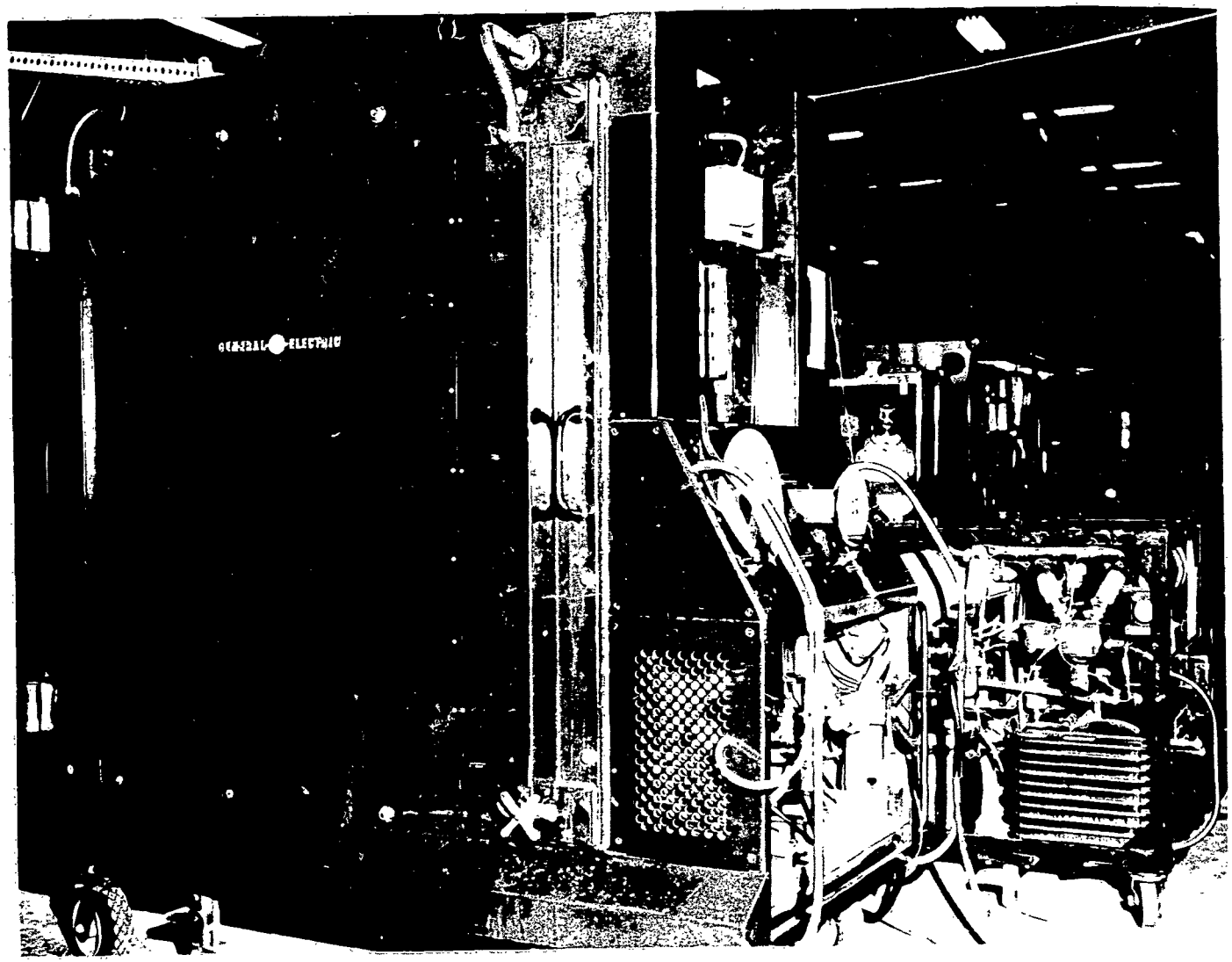

FIGURE 2. GENERAL ELECTRIC ENVIRONMENTAL TEST CHAMBER (END VIEW)

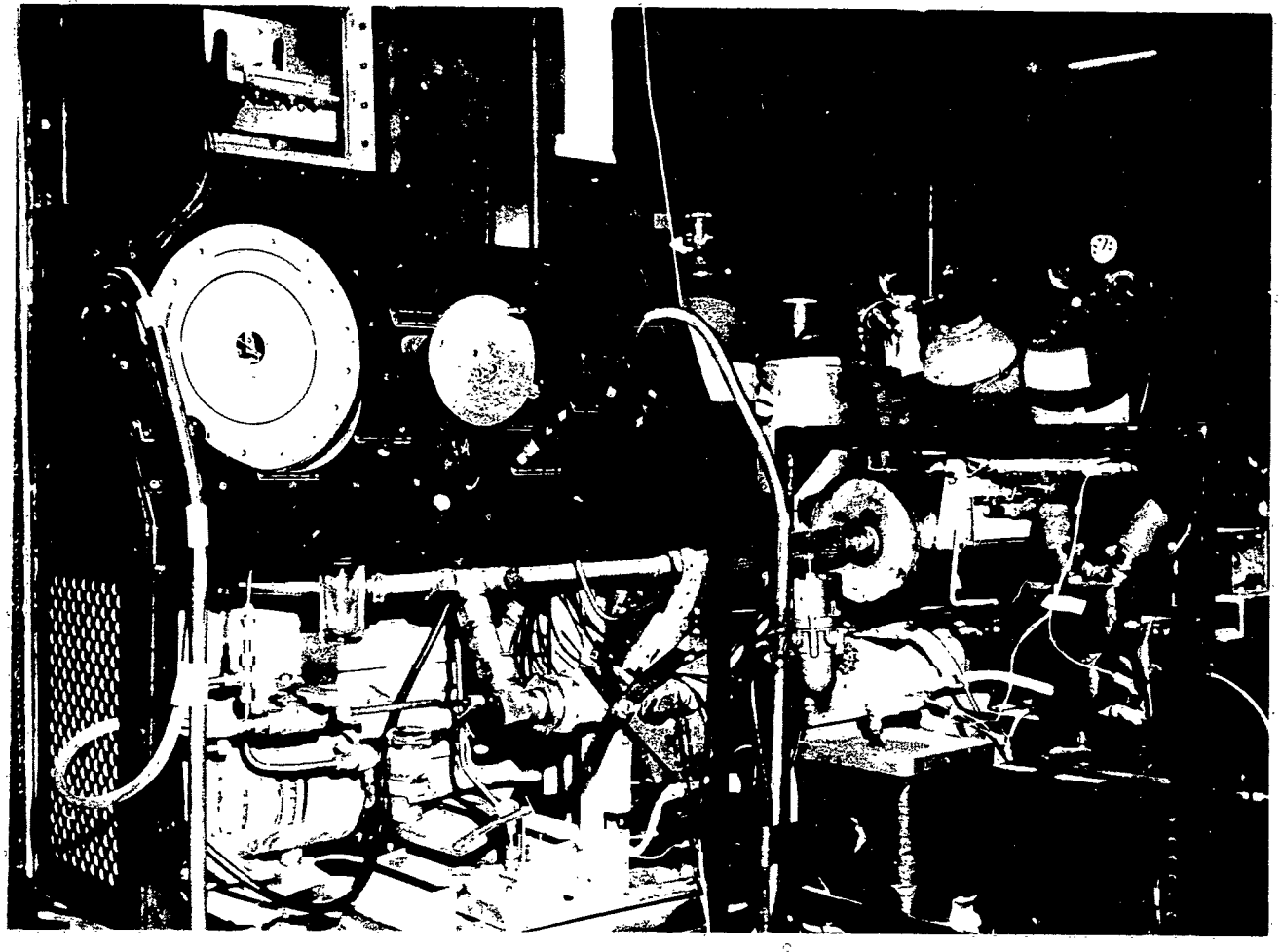

FIGURE 3. GENERAL ELECTRIC ENVIRONMENTAL TEST CHAMBER (FRONT VIEW)

The next sub-assembly to be described is the life support sub-system. It is entirely enclosed with easily removed sheet metal covers, as is the entire system. This sub-system has the function of maintaining a habitable environment within the chamber proper. The atmosphere from the chamber is recirculated through this system at a rate of approximately 15 cubic feet per minute by means of an axial flow blower. The "stale" air removed from the chamber is passed through a CO_2 absorber. This device is capable of maintaining the CO_2 partial pressure below two mm Hg. The air then enters one of two cold traps which "freezes-out" most of the water vapor in the air stream. Two cold traps are necessary since one must be alternately switched into the line to allow the other to defrost as it becomes saturated. Defrost heaters integral with the refrigerant coils perform this function. This freeze-out defrost cycle is programmed by an electro-mechanical timer which switches the flow path between cold traps by means of pneumatically actuated valves. The timer also determines refrigerant flow path sequence and defrost heater operation.

The cold air next enters the heater-humidifier where it is reheated and a controlled amount of moisture readmitted into the air-stream before re-entering the chamber by a manually operated micrometer valve.

The life support sub-system also houses the pick-ups for the CO_2 and O_2 analyzers which are an integral part of the system. The CO_2 analyzer is an infrared type and monitors the CO_2 level at the inlet to the CO_2 absorber. The O_2 analyzer operates on the para-magnetic principle and it continuously samples from the system atmosphere at the cold trap outlet. Hook-ups are provided to check the calibration of both of these instruments without shutting down during the course of a test.

The electrical control console is the third sub-assembly of the system (Fig. 4). This console displays all the chamber internal environmental parameters and provides means for controlling them. Indicator lights are provided to indicate operation of various important components within the system. The CO_2 analyzer display panel and the O_2 analyzer recorder-indicator are also in this assembly. An electrical interface is provided so that output from the environmental sensors may be fed to a continuous recorder if this is desired. An audible warning device is also provided which will indicate high or low extremes of either temperature or pressure. The console is connected to the other part of the system through a central junction box located on the life support sub-system.

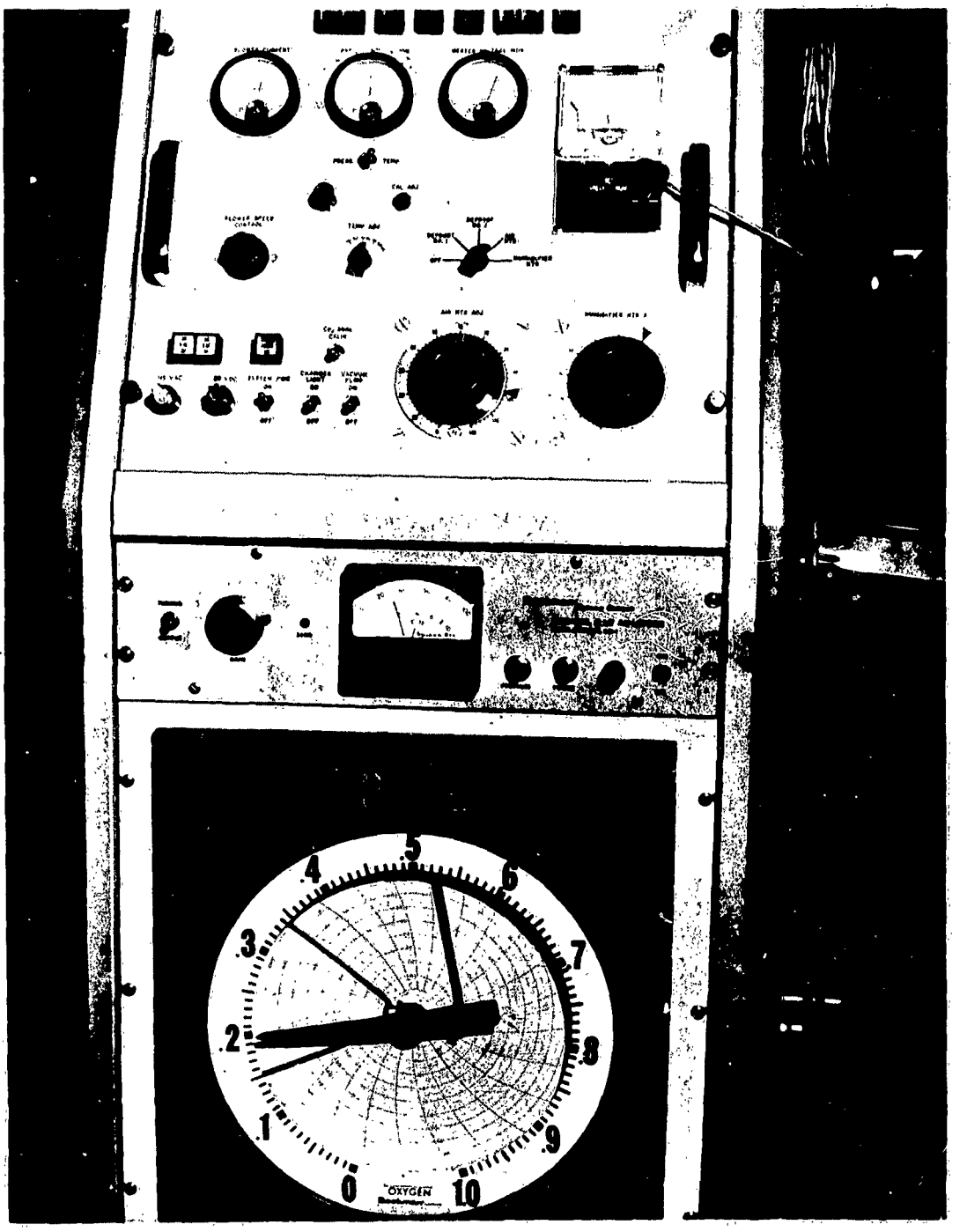

FIGURE 4. ELECTRICAL CONTROL CONSOLE DISPLAYING GENERAL ELECTRIC ENVIRONMENTAL TEST CHAMBER INTERNAL ENVIRONMENTAL PARAMETERS

The last part of the system to be described is the elevated wall temperature sub-system. This assembly provides the capability of heating the chamber walls to an elevated temperature and then cooling them back to ambient within a 10-minute period. The system contains two insulated 40-gallon tanks connected by three-way manual valves to an electrically driven centrifugal pump. The first tank contains thermostatically controlled immersion heater coils, and the second is the cold tank which is cooled by refrigeration coils connected to a one-third HP hermetic refrigeration unit. By manual regulation of the valves and pump, the desired temperature profile may be pulsed into the chamber walls. Additionally, this subsystem is used to maintain the chamber walls at the same temperature as the internal environment by means of a thermostatic temperature controller which cycles the water circulating pump to maintain a preset temperature. The chamber wall temperature may be independently raised from an ambient one to 150°F and then dropped back to ambient temperature within a 10-minute period.

3. Instrumentation

An FR-1100 tape recording system was used to record physiological and psychological information on magnetic tape and a Sanborn recorder provided a visual display of pertinent physiological functions (Fig. 5). The physiological parameters which were recorded on magnetic tape are as follows: ECG leads I, II and III, respiration, rectal and skin temperatures. The recorded psychological information was right lever, left lever, blue light, shock and program on. The physiological parameters recorded on the Sanborn recorder were: ECG leads I and III and respiration; the psychological information recorded was right lever, left lever, blue light and shock.

The following electronic equipment was used: Ampex FR-1100 tape recorder, Sanborn recorder, Tektronix amplifiers, Electro-Mechanical Research, Incorporated amplifiers, subcarrier oscillators, Electro-Mechanical Research, Incorporated discriminators and a Yellow Springs teletherm.

a. Electrocardiogram (ECG)

Four electrodes were used in the ECG system. The electrodes were made of four male and female snap fasteners and four steel sutures, .028 inch in diameter. The suture electrodes were attached to the left anterior chest, right anterior chest, left medial thigh, and right medial thigh. The

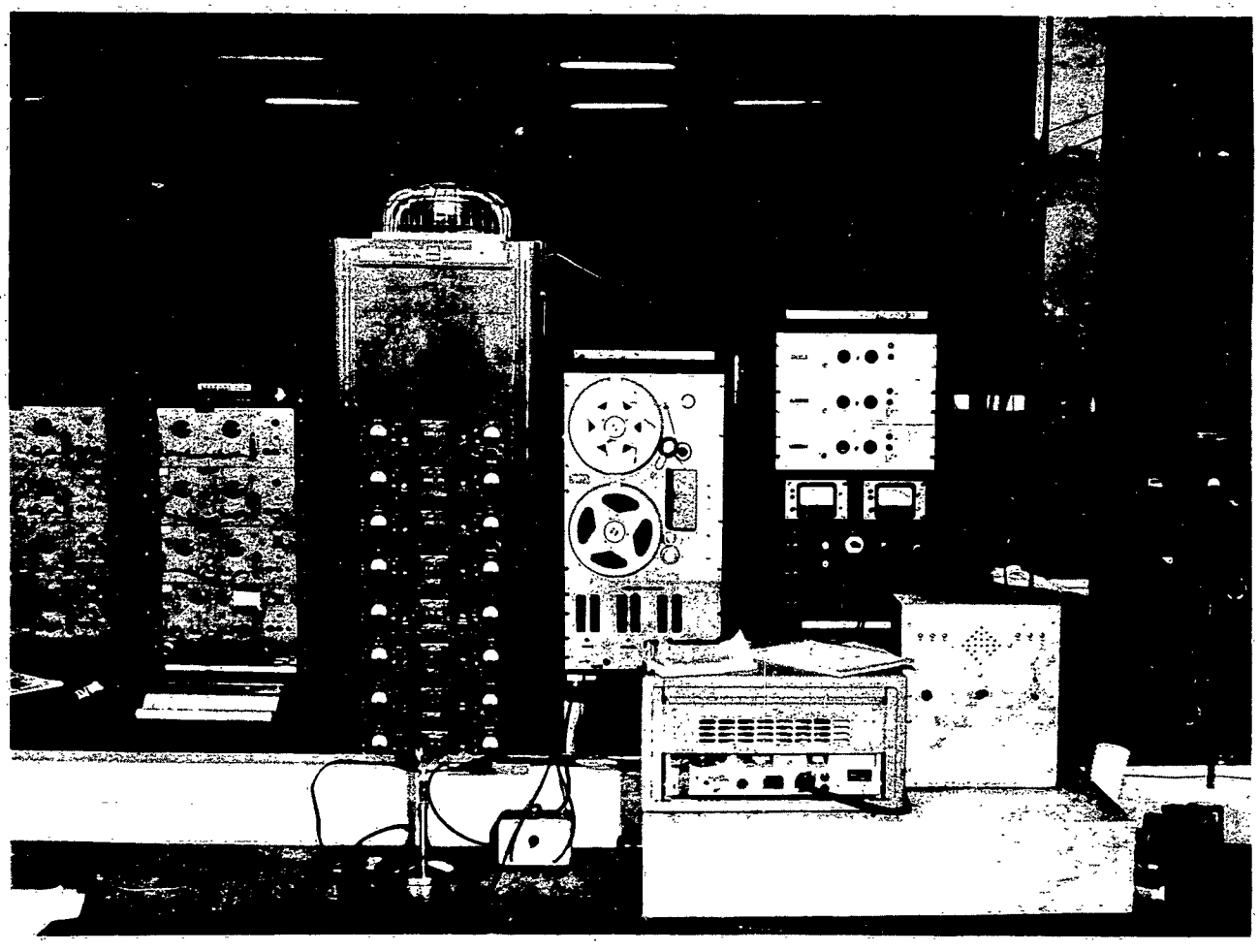

FIGURE 5. INSTRUMENTATION FOR RECORDING PHYSIOLOGICAL RESPONSE DURING O_2 TOLERANCE TEST (FR 1100 TAPE RECORDING SYSTEM AND SANBORN RECORDERS)

method of attachment was as follows: The suture was inserted subcutaneously and parallel to the surface of the skin for one-half inch. The end of the suture was then brought out of the skin through female snap fasteners. Male fasteners with electrical leads attached were snapped to the female fasteners at the point of suture entry. The appropriate connections were applied to and amplified by the Tektronix amplifiers, calibrated, amplified further by the Electro-Mechanical Research, Incorporated amplifiers, applied to the sub-carrier oscillator and recorded on the FR-1100 tape recorder. ECG leads I and III were then played back through Electro-Mechanical Research, Incorporated discriminators to the Sanborn recorder.

b. Respiration Sensor

The respiration sensor was a soft rubber tube one-eighth inch in diameter, approximately four inches long, filled with a 15% aqueous solution w/v of $CuSO_4$ with electrical connections on each end. The sensor was attached around the subject's chest at the level of the eleventh intercostal space. The change in electrical resistance of the tube as it was stretched with each chest expansion was applied through an amplifier (built by McDonnell Aircraft Co.) to a subcarrier oscillator, and recorded on magnetic tape and Sanborn paper.

c. Rectal Temperature

Rectal temperature was sensed by a Yellow Springs Instrument Company temperature probe which was inserted approximately nine inches into the rectum (Ref. 13). The resistance of the thermistor probe was measured by the bridge circuit of a Yellow Springs teletherm. After calibration the signal was amplified and recorded on magnetic tape. A visual readout could also be obtained for test time readout.

d. Skin Temperature

Skin temperature was sensed by a Yellow Springs Instrument Company thermistor skin temperature probe taped on the right medial thigh. Operation of this probe is the same as above.

e. Voice

Chimpanzee vocal reaction in the chamber was sensed by a microphone, amplified, and monitored for the detection of respiratory difficulties.

f. Time

A 99 hour coded clock provided time correlation, and was recorded on the tape as well as the Sanborn recorder. Also a 6.25 KC signal was inserted on the magnetic tape for computer correlation.

B. Description of Test

1. Preparation of Subject

Prior to the test, the subject was examined and declared in good health by the attending veterinarian. The subject was instrumented and restrained (Fig. 6).

ECG electrodes were secured with tape. The respiration sensor was placed one inch below the right chest ECG electrode. The skin temperature thermistor was taped to the medial thigh region. The rectal probe was inserted into the rectum and taped. The subject's urinary bladder was catherized and the urine collection begun. The subject's instrumentation was then checked (Fig. 7). The subject was placed in a restraint suit and transferred to the restraint chair. Instrumentation was again checked (Fig. 8). The subject was transferred to the chamber area and placed in the G.E. chamber (Fig. 1). The instrumentation readout was again checked for physiological presentation. The subject performed psychomotor tasks for five minutes to check psychomotor instrumentation.

2. Experimental Conditions

Each test had a duration of 15 hours and 15 minutes from the time the desired temperature, relative humidity, and atmospheric composition and pressure were reached. The pressure in the chamber was increased to that of sea level at approximately 1000 feet per minute. The subject received water ad lib and no food during this period. Upon completion of the test, the atmospheric pressure was decreased to field elevation of Holloman AFB (approximately 4200 ft) and the subject was removed from the chamber and transferred to the Vivarium and given a physical examination (Appendix II).

3. Design

Four chimpanzees were divided into two groups to accomplish a crossover design so that each animal acted as his own control. Group I subjects were exposed first to 20% oxygen, 14.7 psi and later to 100% oxygen, 14.7 psi. Group II

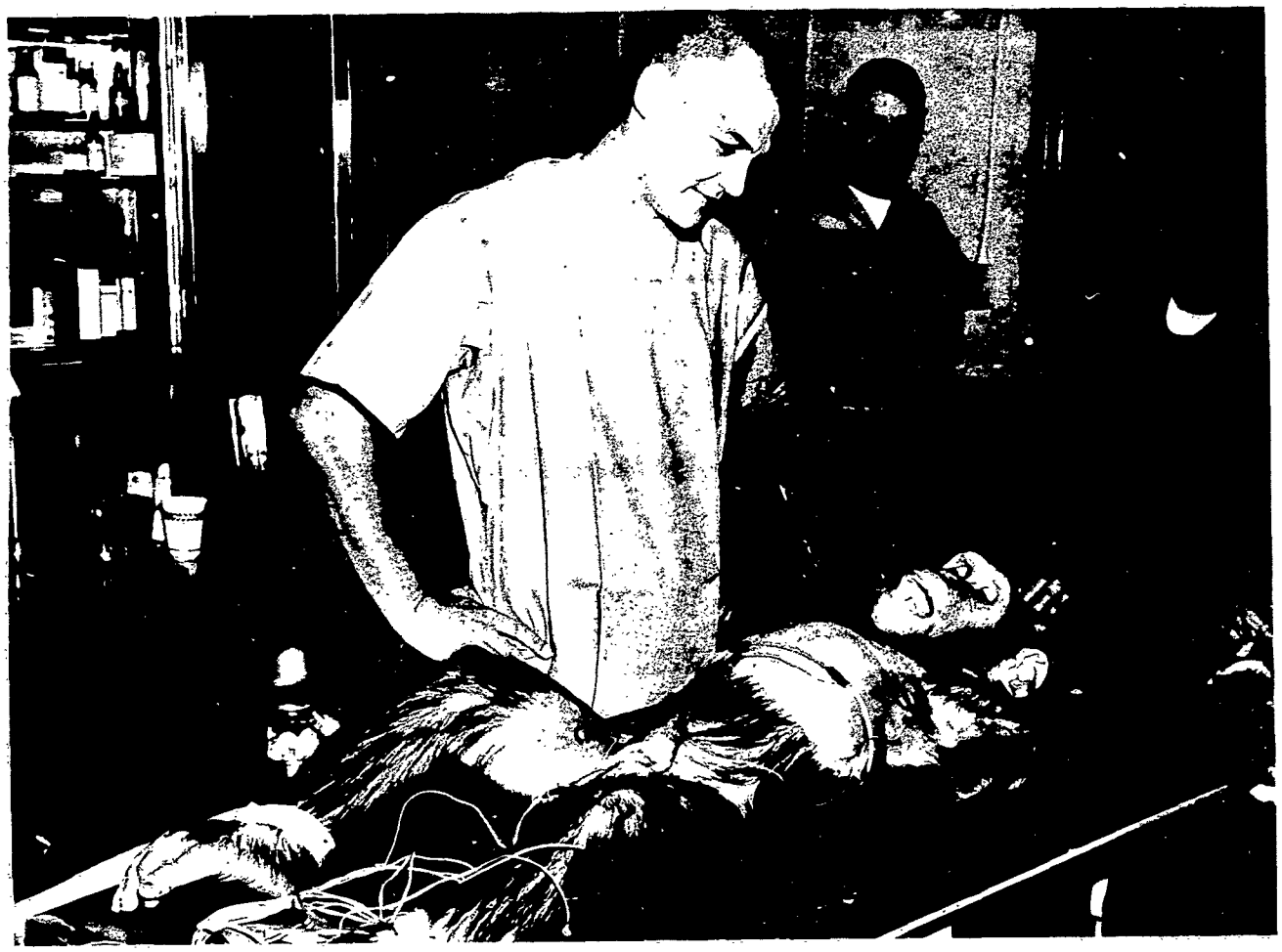

FIGURE 6. SUBJECT INSTRUMENTATION USED TO RECORD PHYSIOLOGICAL PARAMETERS (ECG, RESPIRATION, RECTAL AND SKIN THERMISTORS)

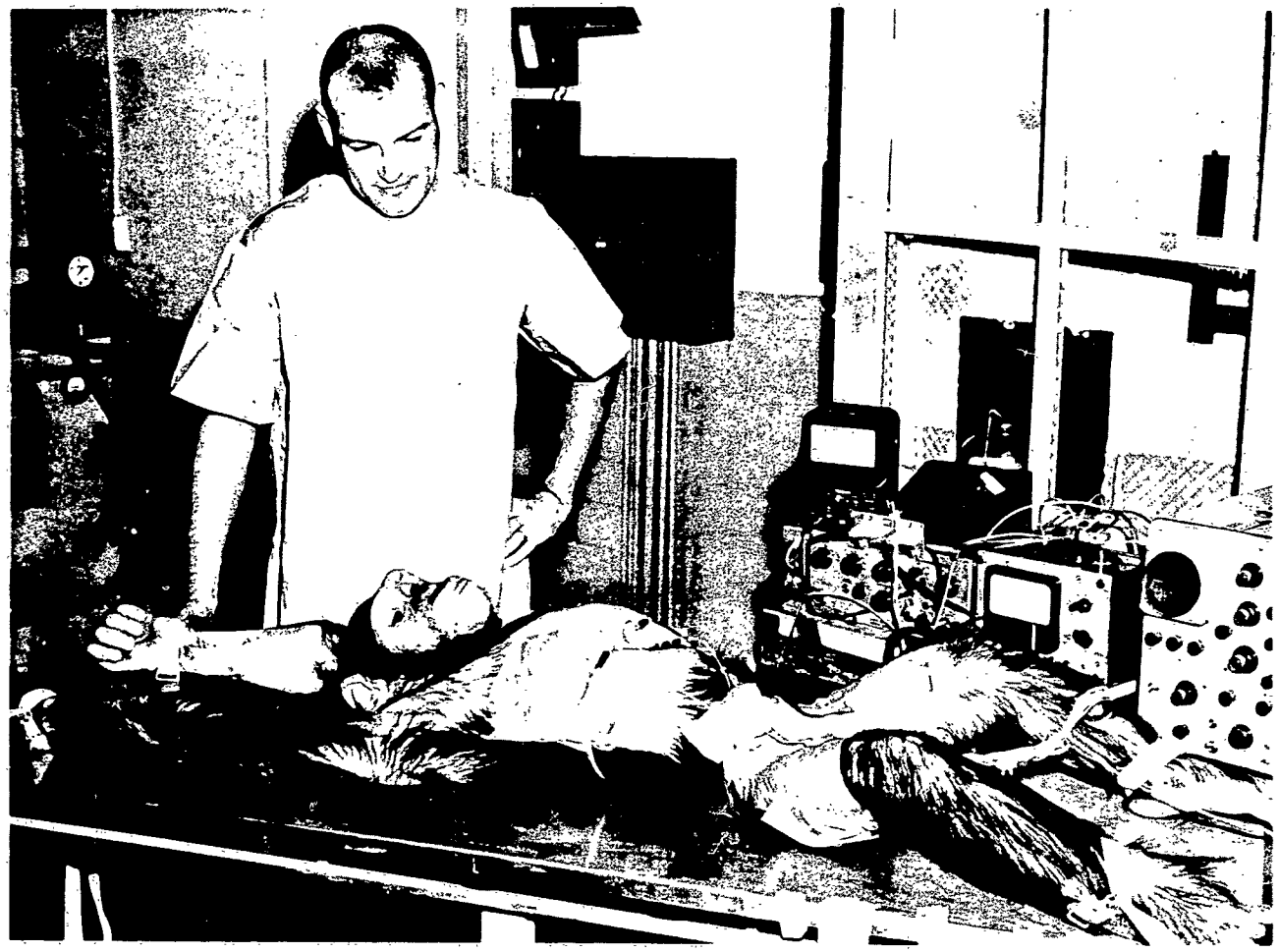

FIGURE 7. SUBJECT'S INSTRUMENTATION CHECK

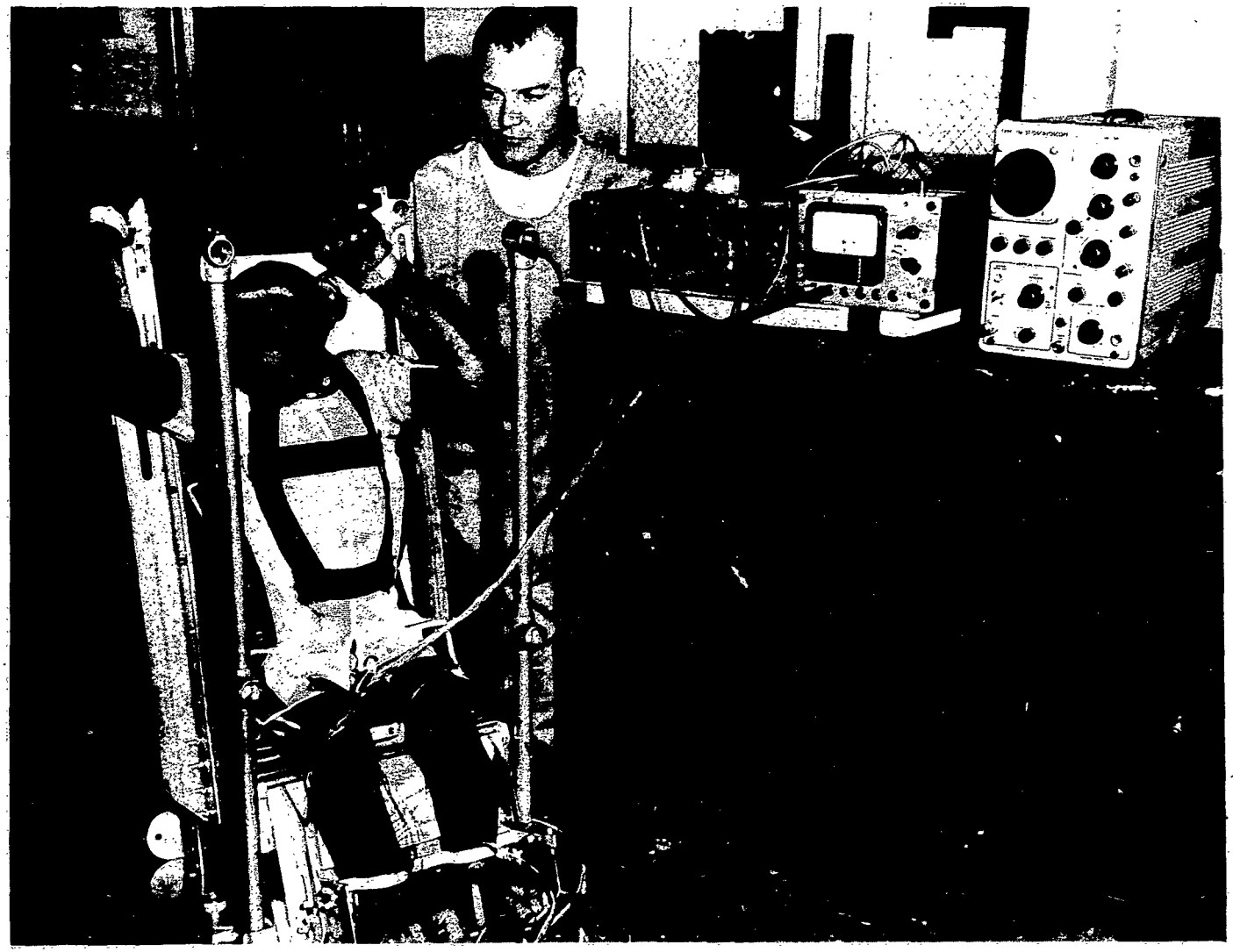

FIGURE 8. SUBJECT SEATED IN RESTRAINT CHAIR DURING INSTRUMENTATION CHECK

animals were exposed to 100% oxygen, 14.7 psi prior to 20% oxygen, 14.7 psi environment. This technique obviated possible sequential effects which might have occurred in the usual test-retest situation.

Heart rate and respiration rate were determined by manually counting from Sanborn paper the QRS complex for heart rate and the respiration wave form for respiration. Rectal and skin temperature were recorded from telethermometer (teletherm). These readings were recorded for 1 minute at 15-minute intervals. During the 15-hour test session for each animal, the behavioral tasks were presented for 15 minutes at 3-hour intervals. The results of the behavioral tests are reported by Farrer (Ref. 14). Physiological parameters were recorded every minute for 15 minutes: (1) prior to the work period (pre-work period), (2) during the work period (behavioral test), and (3) after each work period (post-work period). Thus physiological information was collected once every 15 minutes of the test and for 45 consecutive minutes during each of five pre-work, work and post-work periods.

4. Subjects

Healthy chimpanzees approximately four years nine months, to six years 11 months of age were used as test subjects. Of the four animals, two were male and two female.

C. Blood and Urine Analyses

Venous blood samples were taken from each subject immediately before and immediately after each 15-hour test period. Urine specimens for urinalysis were also taken immediately before, and during the first post-test hour after, the experiment. Urine was collected during the 15-hour period by means of an indwelling catheter. Urine and blood samples were analyzed by conventional methods.

1. Hematology

White blood cell count and differential, red blood cell count, esinophile count, hemoglobin content, hematocrit, platelet count, sedimentation rate, and reticulocyte percentage.

2. Venous Blood Serum

Sodium, potassium, chloride, CO_2, pH, O_2 content, oxygen capacity, urea nitrogen, total protein, creatinine, calcium and inorganic phosphorus concentrations.

3. Urine

Specific gravity, pH, sugar, albumin, examination of sediment, and 17-hydroxy-corticosteroids. The latter determination was performed only on the 15-hour test sample and was done by a modification of the Porter-Silber technique.

III. RESULTS

It will be noted from Table I that the subjects withstood the test in good physical condition, with the exception of edema of the penis due to suit stricture in one subject in both the 20% and 100% O_2 tests, and foot edema in three subjects caused apparently by the ankle restraint bar. It is interesting that the greatest body weight loss occurred during test Number 8 when 4.68% of total body weight was lost during the 15 hour and 15 minute test. All subjects consumed approximately one liter of water during the test with the exception of subject Number 32 in test Number 1.

The ranges, means, and standard deviations of the physiological measures were computed for the 20% O_2 and 100% O_2 environments and are presented in Tables II and III, respectively. These means were computed by averaging only that recorded vital sign data collected every 15 minutes (N) during each test. It will be noted that there is consistently a marked decrease in the mean heart rate in 100% O_2 as compared to the control test condition in 20% O_2.

Two of the subjects (No. 35 and No. 46) exhibited no significant change in average respiratory rate over that of the 20% oxygen environment when subjected to pure oxygen. Two other subjects (No. 32 and 42) exhibited relative tachypnea when subjected to the pure oxygen environment. This tachypneic response would appear significant even though the overall average respiratory rate showed no significant increase in 100% oxygen (see Tables V and VI).

The average skin temperatures exhibited a slight rise in 100% oxygen experiments, but neither this nor the average rectal temperatures should be considered to have changed significantly in the 100% oxygen environment (Tables V and VI). This lack of significance is due to approximately equal fluctuation in both directions in the two different environments.

Table IV lists the mean difference, 20% O_2 vs. 100% O_2, standard error of mean for 20% O_2 and 100% O_2 and the results of "t" tests of these intra-animal analyses of the physiological measures. All measures were statistically significant at the .01 or .05 level with the exception of respiration in tests 2, 3, 6 and 7.

TABLE I

SUMMARY OF PHYSICAL EXAMINATION DATA

Test No.	Subject No.	Physical Condition Pre-Test	Physical Condition Post-Test	Body Weight Loss	Condition Test
1	32	Good	Good Marked edema of penis due to stricture of suit	2.4%	20% O_2
2	35	Good	Good	4.34%	20% O_2
3	42	Good	Good Moderate edema of both feet	0.98%	100% O_2
4	46	Good	Good Slight edema of feet	3.19%	100% O_2
5	32	Good	Good Marked edema of penis due to stricture of suit, edema of feet	2.4%	100% O_2
6	35	Good	Good	4.34%	100% O_2
7	42	Good	Good	1.85%	20% O_2
8	46	Good	Good	4.68%	20% O_2

TABLE II

ANALYSIS OF PHYSIOLOGICAL DATA
(20% Oxygen, 14.7 psi, 80°F, 50% RH)

Measure	Test No.	Subject No.	Sex	N	Range	Mean	SD
Heart Rate Beats/Min	1	32	M	62	75-189	113.0	30.12
	2	35	F	62	84-174	106.5	21.12
	7	42	M	61	77-132	108.3	11.86
	8	46	F	62	63-117	80.9	14.70
Respiration Breaths/Min.	1	32	M	62	18-62	33.0	13.42
	2	35	F	62	24-48	32.7	5.72
	7	42	M	59	16-32	26.9	2.31
	8	46	F	62	12-45	24.7	7.66
Skin Temp. Degree F.	1	32	M	62	94.8-101.3	97.0	1.84
	2	35	F	62	95.4-98.8	96.6	.843
	7	42	M	61	96.5-100.0	98.1	1.17
	8	46	F	62	97.4-100.2	98.2	.670
Rectal Temp. Degrees F.	1	32	M	11	99.6-100.6	99.9	.249
	2	35	F	62	98.6-100.6	99.4	.633
	7	42	M	62	98.3-101.0	99.5	.918
	8	46	F	62	98.6-100.3	99.4	.612

TABLE III

ANALYSIS OF PHYSIOLOGICAL DATA
(100% Oxygen, 14.7 psi, 80°F, 50% RH)

Measure	Test No.	Subject No.	Sex	N	Range	Mean	SD
Heart Rate Beats/Min.	5	32	M	61	72-147	97.4	20.57
	6	35	F	62	71-137	88.2	13.27
	3	42	M	62	60-129	81.8	12.00
	4	46	F	61	62-135	76.2	13.42
Respiration Breaths/Min.	5	32	M	62	21-78	37.0	15.18
	6	35	F	62	24-49	31.9	5.10
	3	42	M	62	21-56	30.6	7.55
	4	46	F	62	16-48	23.3	5.49
Skin Temp. Degrees F.	5	32	M	62	96.9-101.8	98.6	1.50
	6	35	F	62	97.8-100.1	98.5	.621
	3	42	M	62	96.1-98.6	97.2	.881
	4	46	F	62	96.6-99.0	97.4	.728
Rectal Temp. Degrees F.	5	32	M	10	98.6-99.5	98.9	.230
	6	35	F	62	98.0-100.0	98.8	.642
	3	42	M	62	99.9-101.3	99.9	.741
	4	46	F	62	99.4-101.8	100.0	.743

TABLE IV

RESULTS OF t TEST ON PHYSIOLOGICAL MEASURES
(14.7 psi, 80°F, 50% RH)

Measure	Subject No.	Tests No.	Mean Difference 20% vs. 100% O_2	SE m[1] 20%	SE m 100%	t
Heart Rate Beats/Min	32	1-5	15.6	3.827	2.633	3.53**
	35	2-6	18.3	2.683	1.686	3.317**
	42	7-3	26.5	1.518	1.524	2.223*
	46	8-4	4.7	1.867	1.718	4.757**
Respiration Breaths/Min.	32	1-5	-4.0	1.705	1.928	3.38**
	35	2-6	0.8	.726	.648	1.46
	42	7-3	-3.7	.300	.959	1.12
	46	8-4	1.4	.973	.9302	1.91*
Skin Temp. Degrees F.	32	1-5	-1.6	.233	.190	21.47**
	35	2-6	-1.9	.1071	.789	10.80**
	42	7-3	0.9	.149	.1119	14.14**
	46	8-4	0.8	.085	.925	11.5**
Rectal Temp. Degrees F.	32	1-5	1.0	.075	.0727	2.16*
	35	2-6	0.6	.0804	.8157	13.52**
	42	7-3	-0.4	.1166	.0941	6.07**
	46	8-4	-0.6	.0777	.0601	10.24**

* $P < .05$

** $P < .01$

1 - SE m (Standard Error of Mean) = $\frac{\sigma}{\sqrt{N-1}}$

Appendix III contains graphs of the physiological and environmental data for each of the tests. The environmental parameters plotted concurrently with the physiological ones were chamber temperature, $\%CO_2$, and $\%O_2$. Pressure and relative humidity remained within established limits (760 mm Hg ± 1 mm Hg, 50% relative humidity ± 5%).

Figure 9 presents a composite graph of physiological data derived from the four control tests, i.e., at 760 mm Hg, 20% O_2. Figure 10 presents a composite graph of physiological data derived from the four experimental tests, i.e., at 760 mm Hg, 100% O_2. The solid curves connect points which are the arithmetic mean for comparable successive 15 minute readings for each chimpanzee for its respective 15 hour and 15 minute test periods. Since it was not possible to start all tests at precisely the same time of day, it was necessary to plot the composite data in terms of hypothetical starting time of 1000 hours.

It is apparent from the rectal temperature curves of Figures 9 and 10 that a diurnal cycle in the chimpanzee is evident. The skin temperatures of the chimpanzees in these tests average approximately 1 to 2°F below that of the rectal temperatures.

Tables V and VI contain statistical summaries of the average physiological measures obtained from the four animals in 20% O_2 control conditions and the same four animals in 100% O_2 test conditions. It will be noted that the mean heart rate is higher in the 20% O_2 vs. 100% O_2. Respiration and rectal and skin temperatures are slightly higher in the 100% O_2 condition.

TABLE V

SUMMARY OF PHYSIOLOGICAL MEASURES

(20% Oxygen, 14.7 psi, 80°F, 50% RH)

Measure	N	Range	Mean	SD
Heart Rate Beats/Min.	247	63-189	102.1	24.2
Respiration Breaths/Min	245	12-62	29.4	8.96
Skin Temp. Degrees F.	247	94.8-101.3	97.47	1.549
Rectal Temp. Degrees F.	197	98.3-101.0	99.50	.774

TABLE VI

SUMMARY OF PHYSIOLOGICAL MEASURES
(100% Oxygen, 14.7 psi, 80°F, 50% RH)

Measure	N	Range	Mean	SD
Heart Rate Beats/Min	246	60-147	86.0	16.537
Respiration Breaths/Min.	248	16-48	30.7	10.48
Skin Temp. Degrees F.	248	96.1-101.8	97.90	1.216
Rectal Temp. Degrees F.	196	98.6-101.8	99.53	1.1

Page 86, Appendix III, provides an overall summary of the tests conducted in 20% vs. 100% O_2 and summarizes the mean difference of 20% vs. 100% O_2, standard error of mean difference, and the results of "t" testing on the inter-animal analyses of the physiological measures. Only the heart and respiration rates exhibit statistically significant differences (0.001 level) in the two environments.

Figure 11 presents composite graphs of physiological data obtained from the means of the fifteen minute pre- during, and post- "work periods" for the five "work sessions" from each of the four control tests and four experimental tests in 100% O_2. With the exception of the first session, the mean heart rate was higher in the 20% oxygen environment. In the fifth session in the 20% oxygen environment the heart rate was the greatest during the post "work period," while all other heart rates both in the 20% and 100% oxygen environment were highest during the work period. Respiration rates averaged higher in 20% oxygen during the first session, but in all other sessions they were higher in 100% oxygen. Rectal temperature remained consistently higher in the 100% oxygen environment. Average skin

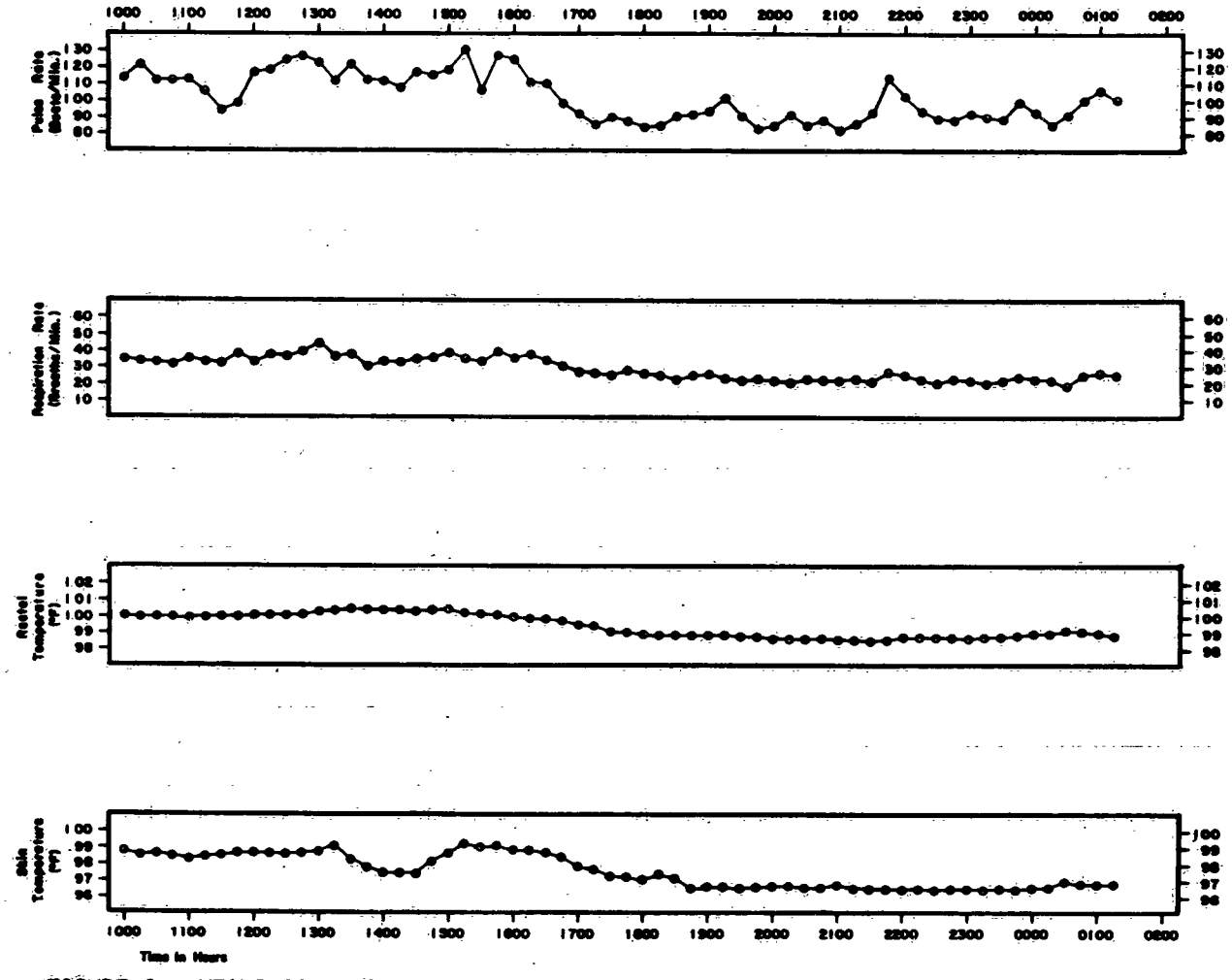

FIGURE 9. MEANS OF PHYSIOLOGICAL DATA, FOUR CONTROL TESTS AT 760 MM HG, 80°F, 50% RELATIVE HUMIDITY, 20% OXYGEN

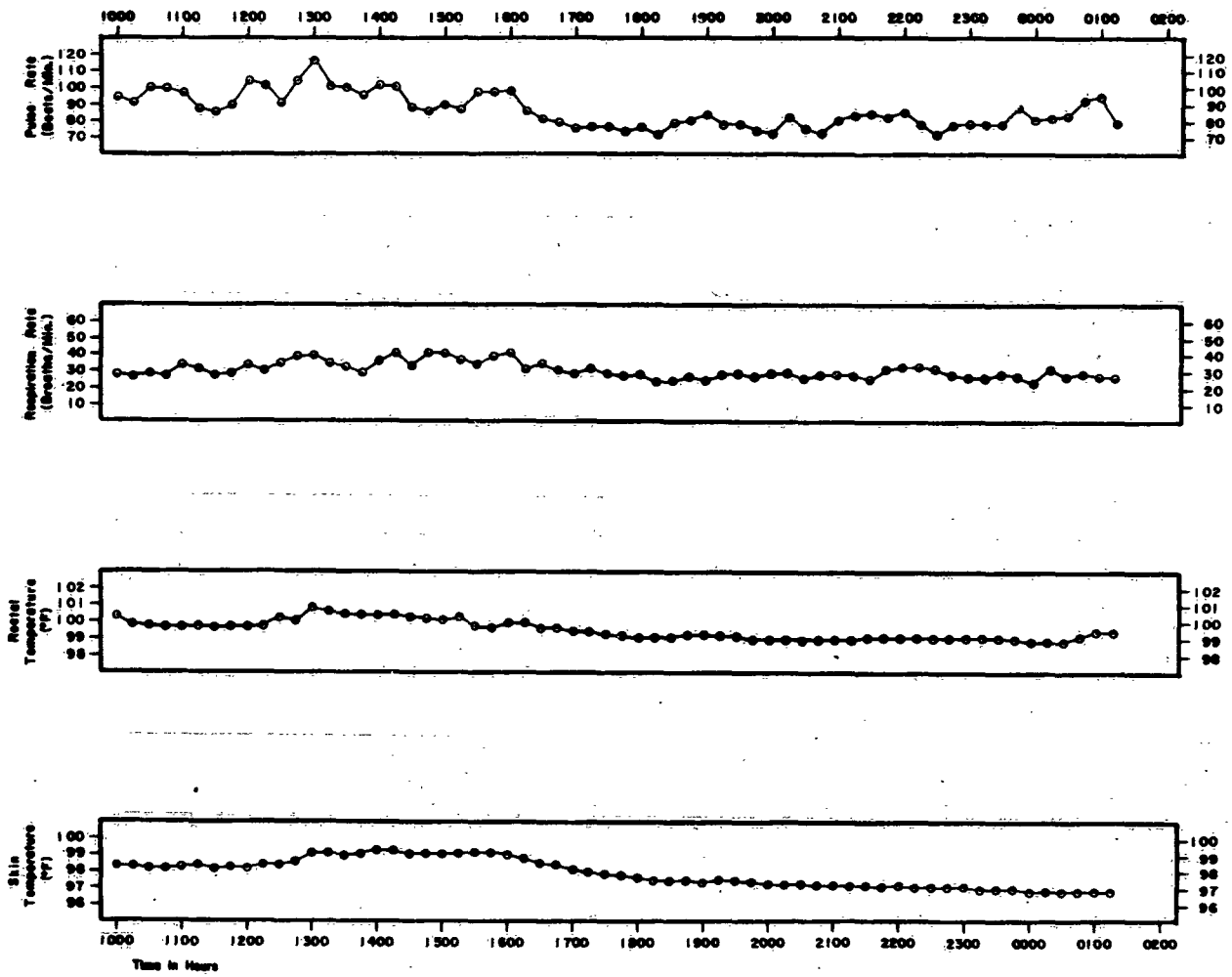

FIGURE 10. MEANS OF PHYSIOLOGICAL DATA, FOUR TESTS AT 760 MM HG, 80°F, 50% RELATIVE HUMIDITY, 100% OXYGEN

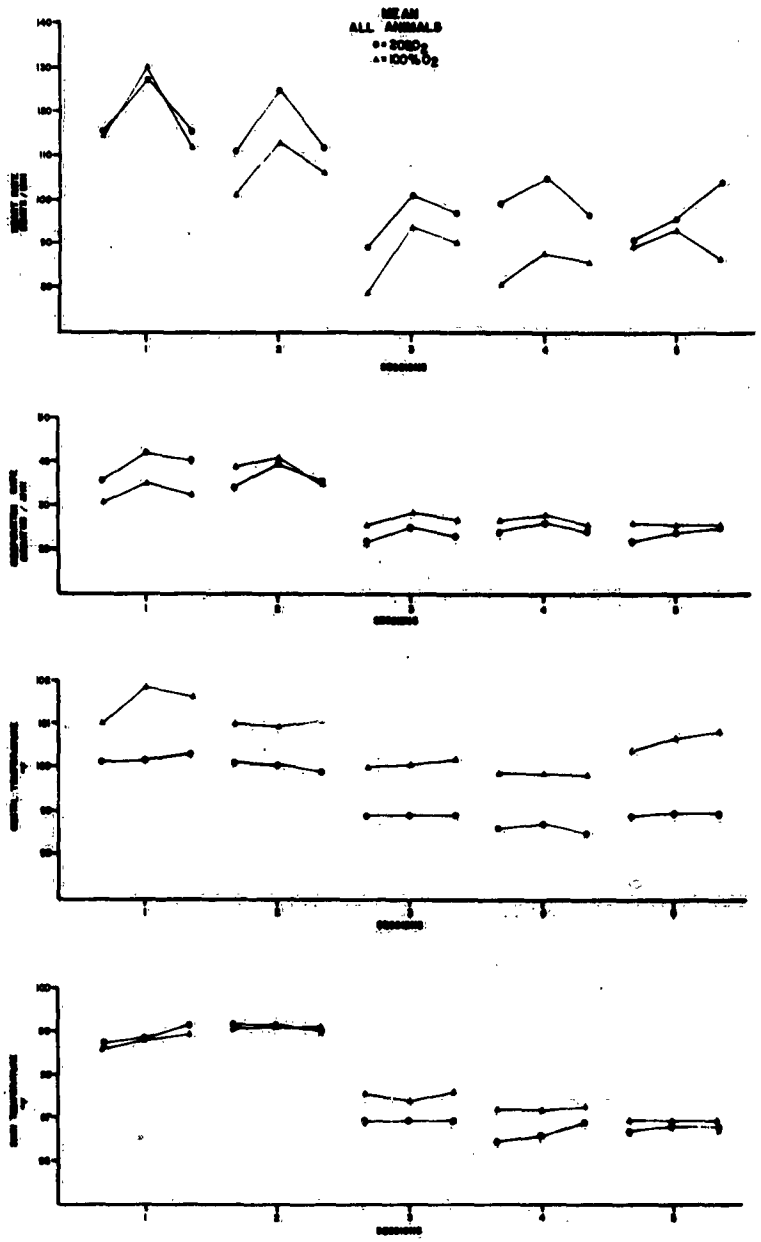

FIGURE 11. MEANS OF PHYSIOLOGICAL DATA, "PRE, DURING, POST" FOR EACH WORK SESSION: FOUR TESTS AT 760 MM HG, 80°F, 50% RELATIVE HUMIDITY, 20% O_2; FOUR TESTS 760 MM HG, 80°F, 50% RELATIVE HUMIDITY, 100% O_2

temperatures during the 20% O_2 test exhibited very little difference from the 100% O_2 test during session one and two but higher readings were maintained in 100% O_2 for the remaining three sessions.

Appendix V contains graphs of the physiological data from both 20% and 100% O_2 tests for each animal showing the means for the five "work sessions" (pre, during, post). On animal No. 46, during the first session, the 15 minute post-mean for respiration is absent. This was due to the respiration tracing being illegible. Rectal temperatures were not recorded in the test period in 100% oxygen for animal No. 32. The probe was inadvertently expelled from the rectum prior to the first session in 100% oxygen. Appendix IV contains graphs of the physiological data for each of the five "work periods" for each test.

Tables VII and VIII depict hematological and urinalysis data. Absolute polymorphonuclear leukocyte and "mononuclear" concentrations were determined by percentage calculation, as observed on 200 counted white blood cells on a Wright's stained smear. Lymphocytes are often difficult or impossible to distinguish from monocytes in chimpanzee blood. They have thus been lumped together as "mononuclears" for our purposes. The hematological data obtained from subject No. 42 is essentially worthless due to clotting of the pre-run oxalated blood sample prior to this subject's 100% oxygen test period. Only that data which would be considered abnormal is tabulated from each pre- and post-test urinalysis.

Immediate pre- and post-test serum biochemical levels are recorded in Table IX. Table X exhibits the 17-hydroxy corticosteroid excretion during each 15 hour and 15 minute test calculated on a 24-hour basis.

Hematological and serum biochemical values from each of the four chimpanzee subjects for a period of 12 months prior to, and 6 months following their use as subjects for these chamber tests were analyzed. The ranges and medians of these values are recorded in Appendix VI. Only those values obtained from blood samples taken for routine hematological and serum biochemical determinations were used in these analyses. Results from those blood studies done because the animal was clinically ill or when that particular animal was used as a subject for other experiments were not incorporated into this data. "N" signifies the number of values from which each individual range and median were calculated.

TABLE VII

HEMATOLOGY

Venous Blood

Subject No. Environment	RBC Mil/mm^3	Hemo-globin gm %	Hcrit %	Retics % RBC	O_2 Content Vol %	O_2 Capacity Vol %
No. 32						
20% O_2						
Pre	5.82	15.2*	48*	0.1	14.1	20.4
Post	4.70	14.1	45	1.3	7.9	21.0
100% O_2						
Pre	5.50	13.0	43	0.7	16.0	21.5
Post	4.20	14.1	45	0.1	14.9	22.4
No. 25						
20% O_2						
Pre	3.13**	12.6	40	0.35	10.6	19.3
Post	4.16	11.9	39	-	5.5	17.3
100% O_2						
Pre	3.84*	13.0	41	0.15	clotted	clotted
Post	4.90	13.0	41	0.3	8.0	21.8
No. 42						
20% O_2						
Pre	4.00*	14.1	45	0.3	11.0	19.0
Post	4.69	14.1	44	-	8.6	20.3
100% O_2						
Pre	clotted	clotted	clotted	clotted	clotted	clotted
Post	5.24	14.4	46	0.05	-	-
No. 46						
20% O_2						
Pre	3.77*	13.0*	41	0.3	13.6	21.2
Post	3.64*	13.0*	41	0.15	clotted	19.6
100% O_2						
Pre	6.31	15.2	48	1.05	19.8	27.4
Post	5.62	13.7	43	-	7.4	20.0

* Concentration above or below the usual range of this particular animal.

** The reliability of this value, although duplicated, is doubtful because of suspected partial clotting of the specimen.

TABLE VIII

HEMATALOGY (CONTINUED) AND URINALYSES

Subject No. Environment	WBC /mm^3	Polys /mm^3	Immature Polys /mm^3	Mono-nuclears /mm^3	Eosin /mm^3	Sed Rate mm/hr	Urine
No. 32							
20% O_2							
Pre	22400*	14907*	1347*	5459	38*	6*	WBC: 1-3
Post	11625	6452	291	4883*	57*	6	Negative
100% O_2							
Pre	12400	6014	124	6138	231	12	WBC: rare
Post	16055	6904	482	8670	143	6	WBC: occ., RBC: many
No. 35							
20% O_2							
Pre	41700*	30034*	5004*	6047	1043*	45*	Casts: occ
Post	21800	16132*	654	4796	48*	44*	WBC: 1-2, RBC: occ.
100% O_2							
Pre	18800	5828	2444*	10152*	55	7*	WBC: occ RBC: occ
Post	7150*	1180*	1287*	4612	-	-	WBC: 20-30 Alb: 1+
No. 42							
20% O_2							
Pre	15300	6579	1454*	7268	613	8	WBC: occ
Post	12080	5798	1087	5132	-	1*	WBC: 15-20 RBC: 5-6 Casts: occ
100% O_2							
Pre	Clotted	Clotted	Clotted	Clotted	Clotted	Clotted	Negative
Post	8150	1712	41	5909	-	12	WBC: occ RBC: occ Casts: rare Alb: 1+
No. 46							
20% O_2							
Pre	23075*	18229*	1500*	2423*	28*	34*	WBC: 15-20 Alb: 1+
Post	18450	10516	185	7288	680*	25*	WBC: 15-20
100% O_2							
Pre	23750*	18525*	2256*	2850	230	11	WBC: rare Casts: rare
Post	29550*	19946*	2660*	6944	55*	10	No specimen

*Concentration above or below the usual range of this particular animal.

TABLE IX

SERUM BIOCHEMICAL LEVELS - VENOUS BLOOD

Subject No. Environment	CO_2 Vol %	K mEq/L	Na mEq/L	Cl mEq/L	pH	Urea N mg %	Total Protein gm %	Creatinine mg %	Ca mg %	P mg %
No. 32										
20% O_2										
Pre	68.8	4.7	147	100.5	7.25*	9.3	7.9*	1.3*	11.5*	3.5*
Post	62.0	5.54*	155*	101.0	7.31*	10.7	8.2*	1.5*	11.3*	3.7*
100% O_2										
Pre	56.2	5.0*	142	101.5	7.40	9.1	7.8*	1.5*	11.9*	3.6*
Post	63.0	5.1*	145	100.0	7.32*	9.2	7.2	1.4*	11.8*	-
No. 35										
20% O_2										
Pre	62.7*	4.7*	148*	101.0	7.24*	13.0	8.0	1.5*	10.9	3.9
Post	69.2*	4.7*	144	100.0	7.40*	12.6	8.1	1.6*	11.1*	3.7
100% O_2										
Pre	59.8*	9.3**	141	101.0	7.37*	12.0	7.7	1.4	10.9	3.4
Post	63.0*	20.2**	145*	99.7	7.40*	10.8	8.3	1.2	10.8	3.5
No. 42										
20% O_2										
Pre	48.8	5.0	149*	102.0	7.26*	8.6*	7.5	1.9*	10.1	4.0
Post	60.7	5.0	146	103.0	7.35	9.0*	7.6*	1.8*	9.9	4.2*
100% O_2										
Pre	54.2	5.0	146	100.5	7.35	7.5*	7.4	1.8*	10.1	4.0
Post	59.2	5.1*	147	102.0	7.41	8.4*	7.5	1.9*	10.1	4.1
No. 46										
20% O_2										
Pre	69.2*	4.5	142	100.0	7.46	8.5	7.2	1.8*	10.5	3.7
Post	68.1*	5.0	142	101.2	7.34*	9.2	7.3	1.7*	10.3	3.7
100% O_2										
Pre	61.0	4.5	139	94.5	7.47	8.3	7.5	1.5	10.7	3.7
Post	52.2	5.1*	144	96.0	7.27*	9.2	7.5	1.7*	10.2	3.5

* Concentration or level above or below the usual range of this particular animal

**These values were duplicated several times and, no doubt, represent contamination. On the day following the test, a serum sample from this animal exhibited a potassium of 3.9 mEq/L.

TABLE X

17-HYDROXY CORTICOSTEROID EXCRETION

Subject No.	17-OH Corticosteroids Excretion/24 Hours*	Remarks
No. 32		
20% O_2	2.1 mg/24 hrs	Urine volume: 150 ml (feces present) Edema of penis post-test Urinated "copiously" 1 hr post-test
100% O_2	7.4 mg/24 hrs	Urine volume: 700 ml Edema of penis post-test
No. 35		
20% O_2	11.4 mg/24 hrs	Urine volume: 1000 ml collected but unable to catheterize
100% O_2	4.4 mg/24 hrs	Urine volume: 550 ml but some urine loss due to leakage around catheter
No. 42		
20% O_2	9.0 mg/24 hrs	Urine volume: 1000 ml
100% O_2	6.8 mg/24 hrs	Urine volume: 1000 ml
No. 46		
20% O_2	2.1 mg/24 hrs	Urine volume: 150 ml
100% O_2	3.3 mg/24 hrs	Urine volume: 300 ml Subject lacerated finger during test

* Calculated from 15-hour and 15-minute collections and extrapolated to a 24-hour value.

IV. DISCUSSION

The effects of breathing high concentrations of oxygen for prolonged periods of time have been studied by many investigators with a variety of animals including frogs, turtles, pigeons, mice, rats, guinea pigs, cats, dogs and monkeys (Ref. 3). Practically all of these investigations have reported the occurrence of irritation, congestion, edema of the lungs, and even death following long exposures. The time at which symptoms appear varies considerably from one species to another, and there is also a wide variation of susceptibility from one individual of a species to another (Ref. 8, 16, 18). Hence it was of interest to conduct a series of experiments with the chimpanzee to determine as quantitatively as possible whether breathing 100% oxygen at 760 mm Hg for 15 hours is deleterious, since this could conceivably be the environment and time period of the count-down prior to the chimpanzee's being launched into space.

A. Environmental Parameters

Environmental conditions were maintained throughout the test with minor deviations from the parameters defined in the experimental protocol (Appendix I). The following ranges were closely adhered to in the chamber: 80°F ± 1°F, 50% RH ± 5%, CO_2 not greater than .05%, O_2 ± 1% of desired concentration, and pressure ± 1 mm Hg. Although instrumentation was not provided to measure oxygen consumption, it appears that oxygen consumption from the oxygen bottle pressure changes was from 1 to 1.5 cubic feet per hour. Leakage from the chamber's system was insignificant.

B. Instrumentation

Minor instrumentation difficulties were encountered during the test series. Between 1345 hours and 1400 hours of the first test, the skin temperature teletherm unit became erratic and had to be changed (chart No. 1, Appendix III). This explains the decrease in skin temperature.

During Test No. 4, 28 minutes of information was lost on magnetic tape caused by a defective direct record amplifier. However, data were recorded on Sanborn paper. This loss of information in no way hindered the outcome of the test. During Test No. 7, ECG leads II and III were disconnected since they were interfering with the tracing from lead I.

This test was interrupted after 13 hours and 41 minutes when the respiration readout was lost. It was discovered on opening the chamber door that the subject had disconnected wires inside the chamber. Repairs were made and the test was resumed to completion.

C. Physiological Parameters

1. Clinical Examination

None of the toxic signs of breathing 100% O_2 were detected in the four subjects. No lung changes could be detected either on auscultation or with X-ray. Two subjects, No. 35 and No. 46, were coughing when the chamber door was opened, but breath sounds and X-rays remained unremarkable on follow-up examinations. Comroe et al. point out that roentgenograms would not detect minor pneumonic lesions (Ref. 6).

2. Heart Rate

Heart rate data indicated that a significant slowing of the heart occurred in the 100% O_2 environment as compared to an air environment. Bean (Ref. 3) and Stadie et al. (Ref. 2) conclude from extensive search of the literature that the evidence leaves little doubt that breathing O_2 or hyperoxygenated air at atmospheric pressure predisposes to a bradycardia.

3. Respiration

Respiration data indicated that a slight increase in respiration rate occurred in the 100% O_2 environment. Neither dyspnea nor hyperpnea was noted by observers during the tests. Bean points out (Ref. 3) that the lack of unanimity among the various reports concerning the effects of O_2 administration on breathing may, perhaps, be attributable to various influences which make comparison of the reported effects and final conclusion difficult, if not impossible. The more reliable evidence indicates these changes are not marked and may be readily masked by techniques employed in administration and measurement. Becker-Freyseng and Clamann, serving as their own experimental subjects, could detect no consistent change in respiration in 0.9 atmospheres of oxygen for 60 hours (Ref. 15). Stadie et al. concluded that oxygen appears to be less irritating to the respiratory system of man than that of other species (Ref. 2).

4. Rectal and Medial Thigh Skin Temperatures

There was no difference noted from the overall inter-animal statistical evaluation of rectal and skin temperatures in the 100% O_2 environment. Tables V and VI show that the slight increases in mean rectal and skin temperatures in 100% O_2, when compared with 20% O_2, was not statistically significant. Thus, this fails to confirm the findings of other workers. Bert found that animals exposed to pressures of oxygen at one atmosphere exhibited a fall in body temperature (Ref. 1). Hill and Macleod observed that oxygen at or above one atmosphere lowered the body temperature in mice, rats, and young rabbits (Ref. 16). Becker-Freyseng and Clamann observed a lowering of their body temperature during the first 24 hours of exposure to 90% O_2 at atmospheric pressure (Ref. 15). Ohlsson observed that the body temperature of human subjects showed no change that could be interpreted as due to exposure to oxygen after continuous exposure for 53-57 hours to 78-88% oxygen (Ref. 4).

Archibald and Ward noted in their temperature-humidity tolerance studies that the high point of the diurnal temperature cycle in chimpanzees occurs around noon and the low point at about midnight (Ref. 13). The result from these tests show that the high point of the measured cycles occurs around 1545 hours for skin temperature and 1400 hours for rectal temperature; and the low point occurred around 2200 hours for both rectal and skin temperature. The difference between skin and rectal temperature at the high points may possibly be explained by the erratic readings from the defective teletherm used in test one. Since the animals were required to perform psychomotor tasks during these tests, the true diurnal cycle was possibly masked.

5. Body Weight

Three out of four animals lost an essentially equal proportion of their body weights in the two environments (see Table I). Subject No. 46 lost the most weight in the 20% O_2 environment. It was interesting to note that subject No. 32 lost equal amounts of body weight in both tests. In one test he ingested no water while in the other he consumed approximately one liter. This acute loss of body weight is due to dehydration. Adolph states that a loss of 1% of the body water of man causes a noticeable disturbance and that a 5% loss in body weight indicates serious dehydration (Ref. 17). The results from this test did not agree with Adolph in that the chimpansee was in good physical condition upon post-physical examination.

6. Work Session

Although not in tabular form, the grand mean heart rate of all work sessions in 100% O_2 shows a marked decrease from that in 20% O_2 tests. There was a slight increase in respiration rate and in rectal and skin temperatures in the 100% O_2 tests. This was comparable to the overall evaluation of the 15 minute readings in both environments (Tables V and VI).

a. Heart Rate

From the overall analysis of the means during each session (Fig. 11), heart rate was the highest during the work period with the exception of the fifth session in 20% O_2, when it was highest during the 15 minute post-work period. Two animals, No. 32 and No. 42 (Appendix V), exhibited the highest reading during the post-work period (20% O_2), accounting for the elevated mean value. There was a relative bradycardia in 100% oxygen.

b. Respiration

The respiration rate was slightly higher during work sessions except for the first session where respiration was higher in the 100% O_2 environment.

c. Rectal Temperature

With the exception of the first session, rectal temperature increased slightly in most instances during the post-work period, and it was the highest in the 100% O_2 environment.

d. Skin Temperature

Skin temperature from three of the five sessions was higher in 100% O_2 environment.

D. Blood and Urine Analyses

The hematological response to breathing high concentrations of oxygen at sea level pressures has been thoroughly documented. It would seem that Ohlsson's (Ref. 4) conception of these blood changes occurring in three successive and well defined stages has some merit. His review cites investigations with both human and animal subjects that exhibited a rapid decrease in erythrocyte concentration after exposure to pure

oxygen. This first stage is reflected by a fall in the hemoglobin concentration within 15 minutes of breathing oxygen and persists for up to a few hours. This stage is followed by one lasting up to 48 hours, during which the formed elements of the blood return to and remain at normal levels. The third stage coincides with the development of demonstrable lung pathology and consists of a hemoconcentration which persists throughout the terminal period until death ensues. The increase in the oxygen-carrying capacity of blood described (Ref. 8) in dogs respiring high concentrations of oxygen until lung pathology becomes evident, probably reflects this hemoconcentration. This hemoconcentration does not occur in a 100% oxygen environment if the total gaseous pressure approximates that of the partial pressure of oxygen at sea level; this same environment produces no pathology over long periods of time in man (Ref. 24) or in rats (Ref. 25).

Probably the most comparable study to this one is that of Comroe et al. (Ref. 6) who did hematological studies on many healthy, young men before and following 24-hour exposures to 100% oxygen at one atmosphere. They were unable to find any significant changes in the hematocrit or in hemoglobin, erythrocyte, and leukocyte concentrations (Ohlsson's second stage). Behnke et al. (Ref. 21) did record a definite trend toward a leukocytosis in human subjects in a similar atmosphere, but their experiments were of much shorter duration and there was no attempt towards establishing controls.

Karsner (Ref. 19) described no consistent alteration in the peripheral blood concentrations of erythrocytes, leukocytes, and hemoglobin of rabbits exposed to 80-96% oxygen at one atmosphere, even in those animals which had reached the pathology-demonstrable, terminal stage. Campbell (Ref. 20) observed a significant and sustained drop in hemoglobin and erythrocyte concentrations in rabbits, but in his experiments the oxygen content of the inspired air was not sufficient to cause any lung pathology, even after several days. Ohlsson (Ref. 4) could demonstrate no consistent hematological change in human subjects breathing 82-84% oxygen at one atmosphere for 53 hours.

Chemical studies of tissues of animals subjected to increased tensions of oxygen have been limited. There is a definite tendency toward retention of CO_2 and O_2 in tissues including the venous blood of such subjects (Ref. 4, 20, 22, 23). Probably a concomitant result of the hemoconcentration is the slight rise (Ref. 4, 8) in blood non-protein nitrogen and serum proteins coincident with a high oxygen environment. Ohlsson recorded (Ref. 4) a rather marked increase in serum total base concentration in two human subjects after two days in 82-84% oxygen at atmospheric pressures.

Rather marked alterations in both the hematological and serum biochemical values are evident on cursory examination of Tables VII, VIII, and IX. Thus it would appear that a 20% oxygen environment invariably was accompanied by a decrease in total circulating leukocyte concentrations, whereas a 100% oxygen environment usually caused the opposite. Closer scrutiny of the values, especially when compared to the median and range of white blood cell concentrations (see Appendix VI), revealed that the total white blood cell counts were abnormally increased at the beginning of most of the experiments. In fact, hematological and serum biochemical values were more often outside of the recorded ranges (Appendix VI) for each individual chimpanzee (see figures marked with an asterisk in Tables VII, VIII, and IX) prior to the 15 hour and 15 minutes experiments than immediately upon removal from the chamber environment. Less significance is in this way attached to the several apparent reverse tendencies in the two environments, e.g., that of the beginning leukocytosis returning towards normal levels, as reflected mainly in mature and immature polymorphonuclear leukocytes, in the 20% oxygen, and the tendency in the 100% oxygen for the animals to exhibit a lymphocytosis. Similar statements can be made concerning some apparent tendencies in serum biochemical changes.

Probably a better means of illustrating how these many apparently significant tendencies really amount to nothing is a chart included within Appendix VI. This chart exhibits all directions of possibly significant changes between pre- and post-test blood samples of the hematological and serum biochemical values. Since those directional changes from pre-test levels outside of the recorded range for each individual animal (suggesting much pre-test stress) could be attributed as well to a healthy environment as an unhealthy one causing blood alterations, these changes must not be considered. These changes are thus given no more weight in the Appendix VI chart than those values which evidenced no essential change during the 15 hour and 15 minute restraint period. It can be readily appreciated from this chart that no consistent hematological or serum biochemical change was demonstrated with restraint in either a 100% or 20% oxygen environment at 14.7 psi.

Table VII exhibits data on percent (of total red blood cells) reticulocytes as well as oxygen content and capacity (determined by manometric means) of venous blood samples; there is not enough information on these variables to speak of their normal ranges in these particular animals. However, no tendency in either direction occurred with these variables in either oxygen environment.

The same may be said for the urinalysis data recorded in Table VIII. There would occasionally appear to be more cells in the post-experiment sample, but this could very well have resulted from urinary bladder catheterization.

Excretion of 17-OH corticosteroids exhibited rather marked changes in the two oxygen environments; however, the directional change in excretion varied. The quantitative excretions of these steroids were well within the normal limits established in our laboratories for restrained chimpanzees.

It can be appreciated that the unfortunate limitation of numbers of experiments on a limited number of chimpanzee subjects might readily lend insignificance to many measurable changes which, were greater numbers of subjects used in the design of this study, may have proved significant. Unlike the evaluation of continuous recordings of physiological data, this is particularly the situation in evaluating hematological and serum biochemical changes, since these evaluations perforce must be made from the analysis of a restricted number of specimens. Moreover, the characters of the formed and chemical constituents of blood at any one time are determined not only by the effects of any particular controlled variable in the animal's environment, but are subject to many subtle and more difficultly controlled variables such as the conditions and time of animal restraint prior to the drawing of the sample, incalculable anxiety of the subject at the time the specimen is obtained, etc.

Further, it must be stressed that many poorly controlled factors are at work from the time the blood samples are taken until the specific determinations are performed on them. These factors are notorious for going unnoticed in all studies similar to this one and include difficulty in obtaining sufficient blood samples, requiring, occasionally, several independent venipunctures, changeable concentrations of elements in venous blood samples secondary to variabilities in time of tourniquet compression, variable conditions and time in transport of blood samples to the laboratory, and the variations inherent in the technical determinations themselves.

Every means was used to control these and other variables. Thus, all hematological and biochemical determinations were duplicated, and all values, even the apparently aberrant ones, were reproduced closely. Sera were separated from their clot exactly 45 minutes following the venipuncture. Those determinations which have been shown to change rapidly

with time, such as platelet counts, serum pH, serum CO_2, and blood O_2, were performed within two hours after the receipt of the specimen in the laboratory.

It can be stated, however, that the most poorly controlled variable and the one most reflected in the total blood picture was that of the invariably prolonged preparation to which each animal was subjected prior to each experiment. If no other significance has been shown in these blood studies, they do serve to point up how liable these chimpanzee blood values are to the effects of handling and instrumentation procedures. These pre-experiment factors might very well be borne in mind in assessing the physiological measures as well.

V. CONCLUSIONS

Restraint and isolation of immature chimpanzees in a 100% oxygen environment caused a relative bradycardia and tachypnea compared to those rates in the same animals in a 20% oxygen environment. Changes in the other physiological parameters measured, varied inconsistently in the two environments; however, body temperature exhibited a diurnal variation.

Appreciation of many other possible subtle differences in physiological alterations within the two oxygen environments was made difficult by the fact that the subjects in many of the tests evidenced much greater indications of stress at the beginning of the experiments than toward its termination. The physical and psychological traumas associated with the one or more hours necessary for instrumentation, suiting, and final restraining of each animal subject were no doubt the cause of many of the abnormal physiological, hematological, and serum biochemical values at the beginning of the experiments. It is fair to state, however, that an immature chimpanzee can tolerate well a 100% oxygen environment physiologically, hematologically, and biochemically for 15 hours and 15 minutes.

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APPENDIX I

Experimental Protocol*

*Experimental Protocol, Chimpanzee Tolerance Studies of Breathing 100% Oxygen at 15 PSI. Project 6892 - Bio-Medical Test and Techniques for Advanced Vehicles. Task 689202 - Altered Environments for Biological Specimens. Report dated August 1961 by Thomas L. Gleason, III, Captain, USAF, MSC.

I. INTRODUCTION

Based on the existing commitment of Aeromedical Field Laboratory to support Project ABC, an investigation is requested to determine the effects of chimpanzee breathing 100% oxygen at 760 mm Hg (15 psi) for 15 hours. This will simulate the environment that the chimpanzee will be subjected to during the countdown time before the orbital shot.

II. TEST OBJECTIVES

The objective of this series of tests is to determine the deleterious effect of 100% oxygen on the chimpanzee at 760 mm Hg (15 psi) by the evaluation of physiological and psychomotor performance data.

III. REQUIREMENTS

Instrumentation Support

A. Instrumentation will be provided to sense, monitor, and record the following parameters from chimpanzee subjects:

1. On magnetic tape
   - a. ECG I, II, and III
   - b. Respiration - copper sulfate sensor
   - c. Skin temperature
   - d. Rectal temperature
   - e. Four channels psychomotor
   - f. Programmer
   - g. Time
   - h. Voice
2. On Sanborn
   - a. ECG I and III
   - b. Respiration - copper sulfate sensor
   - c. Four channels of psychomotor
   - d. Time

3. Rectal and skin temperatures teletherm (manual readout)

B. Chamber temperature and relative humidity (RH), oxygen, carbon dioxide values will be sensed, recorded, and controlled within the following limits:

1. Temperature: 80°F ± 1°F

2. Relative humidity: 50% ± 5%

3. Pressure: 760 mm Hg ± 1 mm Hg

4. Atmosphere: 20% O_2 ± 1%, 100% O_2 ± 1%

5. CO_2: 0.5% ± .05%

C. A block diagram of the instrumentation to be used in these tests is shown in Figure 1.

IV. RESPONSIBILITIES

A. Captain Gleason will have responsibility for overall supervision and conducting of the tests. He will be assisted by Captain Roper. Evaluation of physiological data, psychomotor data and the preparation of reports will be the joint responsibility of the Physiology Section and Comparative Psychology Branch. Data reduction for the physiological data will be accomplished by Computation Division (MDRGC). The type of instrumentation to be used will be determined jointly by the Chiefs of Astroecology, Bioinstrumentation and Comparative Psychology Branches.

B. Land-Air, Inc.

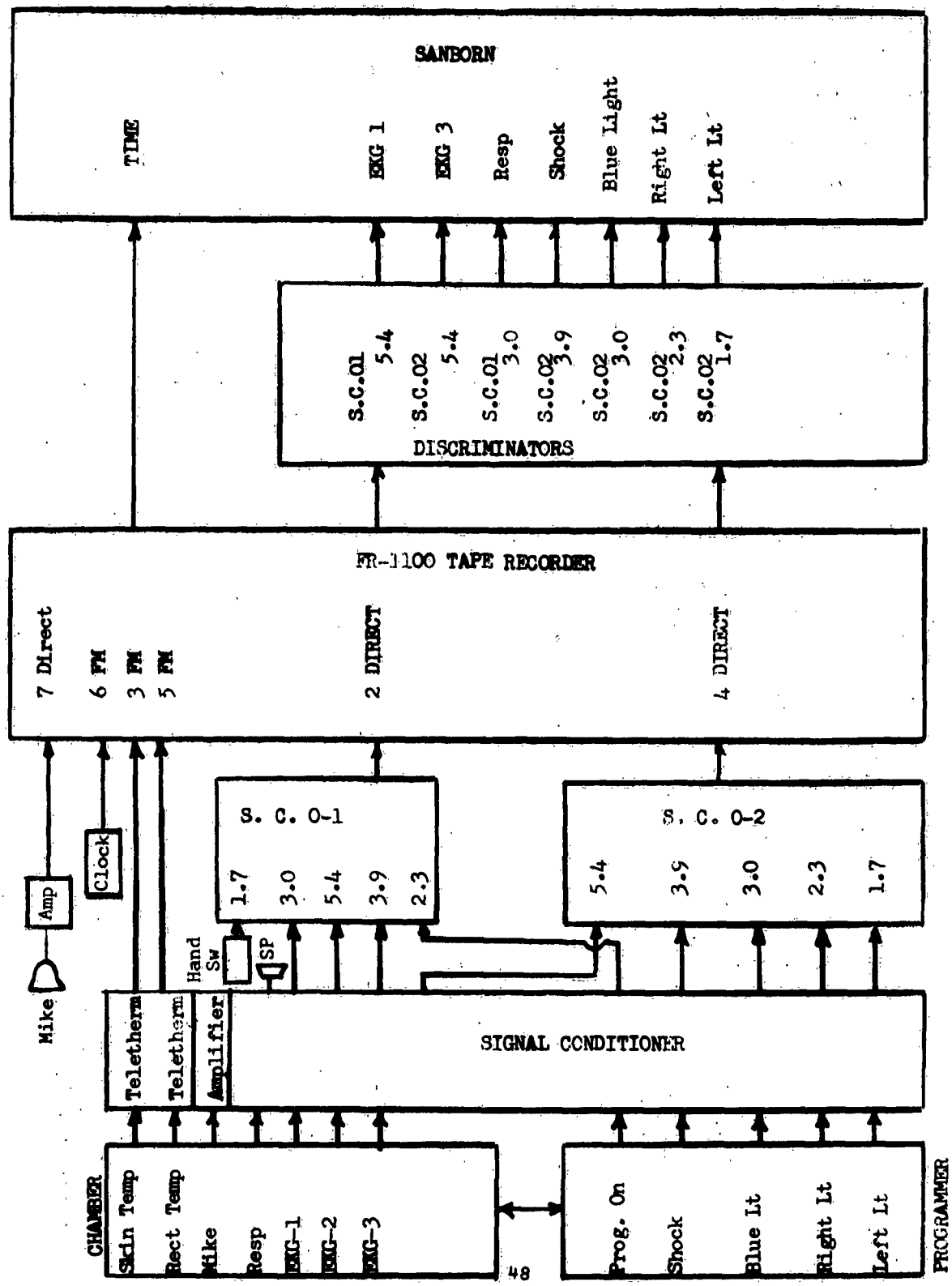
1. Land-Air will be utilized to install, calibrate, check out, monitor and maintain physiological monitoring instrumentation. They will furnish the necessary personnel to provide this service.

2. Still and Cine photographic coverage, both black and white and color, will be required to document any malfunction of equipment and to provide a visual record of chimpanzee behavior.

C. Environmental Test Section

1. Furnish G. E. chamber program, and maintain the following environmental parameters:

FIGURE 1 - FR-1100 RECORDING SYSTEM BLOCK DIAGRAM



a. Temperature-humidity 80°F - 50% RH

b. 760 mm Hg (15 psi)

c. Gaseous environment: Four tests at 20% O_2; four tests at 100% O_2.

d. Monitor CO_2 level and record O_2 level.

D. Veterinary Services Branch will:

1. Perform subject pre- and post-test physical examinations. Attach physiological sensors and aid in restraint of the subjects. Physical examinations will include chest x-rays (pre and post). One veterinarian will be on call during each flight for immediate consultation. A veterinary technician will be on duty for duration of test. The Veterinary Services Branch has sole responsibility for the well-being of the animal subject.

2. Collect, process and perform preliminary analyses of blood and urine samples in accordance with the following instructions.

a. Instructions for collection schedule for metabolic profile urine samples: Collect the following urine samples and deposit them in Clinical Laboratory in Building 1200:

(1) Pre-run urine, obtained at preliminary catheterization one hour pre-test. This sample will be collected in a clean, dry container and labelled "Pre-test Sample for Urinalysis," and with the subject's number, time and date. A urinalysis will be performed on this specimen.

(2) Experimental sample, obtained via an indwelling catheter following collection of the "Pre-test Urinary Sample" to include the entire 15-hour experimental urinary excretion. This sample will be collected in a glass or polyethylene container (of at least 600 cc capacity) to which has been added 50 cc's of 1 N HCL. This sample will be removed as soon as the experiment is over and transferred to a clean, dry polyethylene container labelled, "Experimental Sample for Steroids" and with the subject's number, the exact time period of collection and date. The catheter will be left indwelling. Quantitative steroid determinations will be performed on this specimen.

(3) Post-run sample, obtained during the one hour period following the collection of the "Experimental Sample."

This sample will be collected in a clean, dry container labelled "Post-test Sample for Urinalysis" and with the subject's number, time period of collection and date. A urinalysis will be performed on this specimen. The urinary catheter will now be removed.

b. Collect the following blood samples and deposit them in the Clinical Laboratory in Building 1200:

(1) Pre-test samples. These samples of blood will be collected immediately prior to closing the chamber before the experiment. There will be three pre-test blood samples:

(a) Three cc's of oxalated venous blood with which a complete blood count will be performed.

(b) Five cc's of venous blood will be collected and allowed to clot under oil. Biochemical analyses will be performed on the serum of this sample.

(c) Four cover-slip smears will be made from non oxalated venous blood. Blood morphology will be studied from these smears.

(d) Five cc's of oxalated venous blood will be drawn in an oiled syringe and transferred to a tube containing oil. Blood oxygen will be performed on this specimen.

(2) Post-test samples. These samples of blood will be collected immediately following the opening of the chamber after the experiment. There will be four post-test blood samples collected as outlined under b, (1)(a), (b), (c), and (d) above.

(3) All blood samples will be labelled with the subject's number, time and date of collection.

3. Obtain chest x-rays 24 hours post-test. A 24-hour post-test follow-up venous blood specimen should be obtained for analyses in all subjects exhibiting 24-hour persistence or formation of any shadows suggestive of pathology on chest x-ray in accordance with 2, b, (1)(a) - (c).

E. Comparative Psychology Branch

1. This branch will furnish one project officer and two psychology aides per test.

2. Furnish normal chimpanzees (see Figure 2) that are restraint adapted to sit quietly for periods up to 24 hours, and are trained for continuous and discrete avoidance test.

3. Collection and evaluation of psychomotor data (continuous and discrete avoidance test) will be the responsibility of this branch.

DAY	G.E. CHAMBER 100% O_2	G.E. CHAMBER 20% O_2
23 October		Paleface
25 October		Elvis
27 October	Roscoe	
30 October	Minnie	
1 November	Paleface	
3 November	Elvis	
6 November		Roscoe
8 November		Minnie

Figure 2. Test Schedule (Conditions)

V. TEST SCHEDULE GENERAL

One chimpanzee subject will be used on each chamber flight. One 15-hour chamber flight will be conducted per day, in accordance with schedule listed in Figure 2. Subject will be used in the G. E. chamber at 760 mm Hg (80°F - 50% R.H.), breathing ambient air (20%) and 100% oxygen in accordance with schedule listed in Figure 2.

VI. DETAILED TEST PROCEDURE

A. Pre-test

1. Completed physical examination of each subject.

2. X-rays of lungs. AP and lateral

3. Restraint and sensor attachments

a. ECG electrodes (ECG reading: 3 standard leads)

b. Respiration sensor

c. Thermal sensors

(1) Rectal temperature thermistor

(2) Skin temperature thermistors (one medial thigh)

4. Preparation of animal: The day prior to each test, the subject should be shaved in a band 15 cm wide from the armpits downward, completely around his body. The left thigh should be completely shaved from the groin downward for 10 cm.

5. Check continuity and function of instrumentation at chamber.

B. Test

1. Catheterization of bladder. Save obtained specimen. Connect catheter to collection container.

2. Install subject into G. E. chamber.

3. Connect all instrumentation leads and check-out of physiological sensors and psychomotor apparatus.

4. Subject will perform psychomotor task for five minutes.

5. Obtain blood samples.

6. Chamber door will be sealed.

7. G. E. chamber will be flushed with 100% O_2 and pressure will be increased to 760 mm Hg (15 psi).

8. Record physiological data at 15-minute intervals in task record book.

9. Animals will perform psychomotor task (continuous and discrete avoidance) according to the following schedule:

0 - 2-3/4 hrs	rest
2-3/4 - 3 hrs	first work period
3 - 5-3/4 hrs	rest
5-3/4 - 6 hrs	second work period
6 - 8-3/4 hrs	rest
8-3/4 - 9 hrs	third work period
9 - 11-3/4 hrs	rest
11-3/4 - 12 hrs	fourth work period
12 - 14-3/4 hrs	rest
14-3/4 - 15 hrs	fifth work period
15 hrs	termination of test.

10. Chamber will return to ambient altitude.

11. Obtain test sample of urine. Leave urinary catheter indwelling.

C. Post-test

1. Obtain blood samples
2. ECG (3 standard)
3. Obtain one-hour post-urine sample
4. Complete post-test physical examination of subject
5. Chest X-ray
6. Evaluate data and prepare preliminary test report

D. 24-Hours Post-test

1. Chest X-rays
2. Blood samples*

*Only in those subjects exhibiting post 24-hour disease.

E. 48-Hours Post-test*

1. X-rays

2. Blood samples

F. Conditions Warranting the Cancellation of Test

1. ECG - Heart rate higher than 220 beats per minute or lower than 60 beats per minute.

2. Respiration Rate - Respiration higher than 90 breaths per minute or lower than 12 breaths per minute.

3. Rectal Temperature - Temperature above 105°F or lower than 96.0°F (any sudden rise in temperature should be carefully monitored).

4. Skin Temperature - Temperature above 103°F or lower than 88.5°F (any sudden rise in temperature should be carefully monitored).

5. CO_2 Concentrations 1.0 - 1.5%. Whenever concentration reaches 0.5% or more, the chamber will be flushed with 100% O_2 /atmospheric air.

6. Any other relatively sharp deviation from the monitor record (i.e.) any trend from the record of the test in progress, which in the opinion of the veterinarian on call is a serious hazard to the health of the animal or indicates that the test has become invalid.

7. Instrumentation difficulties that require opening chamber while in 100% O_2 environment.

8. If animal ceases to perform behavioral program which in the opinion of the project officer (Comparative Psychology Branch) indicates that the test has become invalid.

9. After notifying the veterinarian on call, notify one of the following in the order below:

a. Captain Gleason GR 3-6252

b. Captain Roper GR 3-2323

*Only in those subjects exhibiting post 24-hour disease.

E. 48-Hours Post-test*

1. X-rays

2. Blood samples

F. Conditions Warranting the Cancellation of Test

1. ECG - Heart rate higher than 220 beats per minute or lower than 60 beats per minute.

2. Respiration Rate - Respiration higher than 90 breaths per minute or lower than 12 breaths per minute.

3. Rectal Temperature - Temperature above 105°F or lower than 96.0°F (any sudden rise in temperature should be carefully monitored).

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5. CO_2 Concentrations 1.0 - 1.5%. Whenever concentration reaches 0.5% or more, the chamber will be flushed with 100% O_2 /atmospheric air.

6. Any other relatively sharp deviation from the monitor record (i.e.) any trend from the record of the test in progress, which in the opinion of the veterinarian on call is a serious hazard to the health of the animal or indicates that the test has become invalid.

7. Instrumentation difficulties that require opening chamber while in 100% O_2 environment.

8. If animal ceases to perform behavioral program which in the opinion of the project officer (Comparative Psychology Branch) indicates that the test has become invalid.

9. After notifying the veterinarian on call, notify one of the following in the order below:

a. Captain Gleason GR 3-6252

b. Captain Roper GR 3-2323

*Only in those subjects exhibiting post 24-hour disease.

c. Captain Ward GR 3-2866

d. Major Corkhill GR 3-2986

G. Personnel Requirements Based on 24-Hour Shifts

Three project officers - Physiology Section

Six scientific aides (restraint) - Physiology Section

Electronic technicians as needed - Land-Air, Inc

Chamber operators as needed - Environmental Test Section

Veterinary officers as needed - Veterinary Services Branch

Project officers as needed - Comparative Psychology Branch

Three psychologist aides as needed - Comparative Psychology Branch

ADDENDUM TO EXPERIMENTAL PROTOCOL

Automatic Reduction and Analysis of Physiological and Psychomotor Data

I. PHYSIOLOGY

Six physiological measurements will be recorded: EKG I, EKG II, EKG III, respiration, rectal temperature, and skin temperature. EKG II and respiration signals will be conditioned by rectifying the respective physiological cycles into square wave, unit pulses which are counted and averaged into continuous rate functions. The counting interval is a 15-second sliding window. EKG I and EKG III have proven to be less reliable as a source of heart rate but are recorded to provide the cardiologist with a complete visual record of each experiment, and to serve as a back-up in case EKG II is lost.

Condensed time plots of heart rate, respiration rate, skin temperature, and rectal temperature will be made during the analog phase of processing. These four functions will be serially transmitted into the Event Time Reader (ETR), tabulated, and re-recorded in digital form on 1103A Univac tape. The Biological ETR Program (Prichard) compensates for any tape speed ratio other than 1:1 and assigns an item number to each sample and thus maintains a real time sensing. Each item number corresponds to 15 seconds of real time. After all physical tapes associated with a single test are digitized, the data will be merged (Rane) and stacked (Lotz) so that one tape contains all of the data from a given test. This final tape is processed through the Physiological Intra-Animal Analysis Program (Dennis) which computes the following items for each function during a given test segment: sample size, range, mean, standard deviation, standard error of the mean, 1% and 5% confidence limits. The mean and confidence limits are hand drawn on the time condensed plots to provide a quick look summary of the entire test. Any part of the test that proves to be of unusual interest may be recalled and subjected to the same analysis using smaller segments of time.

II. PSYCHOMOTOR

Four channels of psychomotor will be recorded. Only the Continuous and Discrete Avoidance are used in this test series. From the original recording, the data will be transmitted through the ETR at tape speed ratios of up to 128:1, and written on Univac tape by the Standard ETR Program (Bliss). To uncover timing errors, the data are immediately subjected to the Flag Edit Program (Coffin): and if errors are detected they

are corrected by the ERT Time Correction routine (Coffin) or the General Data Edit Program (Coffin). The data are then processed through the Psychomotor Analysis Program (Dennis and Neill), which counts pulses, identifies responses and lists the activity of each work period. The output will include basic statistics appropriate to each tabulation.

APPENDIX II

Pre- and Post-Test Physical Examination Data

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #1	6892/689201	Paleface #32	M	23 October 1961

PAST CLINICAL HISTORY

Subject is approximately 6 years, 11 months of age. Last quarterly physical accomplished 25 September 1961. Utilized as subject for data acquisition flight #40 on 14 September 1961. No serious illnesses in past six months.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	61.25	59.75
RECTAL TEMP	100.00°	100.20°
BLOOD PRESSURE	178/132	160/100
PULSE/MIN	106	108
RESPIRATION/MIN	32	28
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None	None
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	AP & lateral - normal	AP & lateral - normal

MEASUREMENTS PERTINENT TO TEST

N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General appearance - very good Ears, eyes, nose and throat - normal Chest (auscultation) Heart - systolic murmur Lungs - normal Abdomen (palpation) - normal Extremities - normal Mental Status - quiet	Findings same as pre-test except: Extremities - Penis - marked edema due to stricture caused by suit

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LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
  (a) 5cc clotted in oil
  (b) 5cc oxalated in oil
  (c) 5cc oxalated without oil
  (d) Slides for Differential Count
(2) Post Test (as soon as the chamber door was opened)
  (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

Post-Test Itinerary:

0200 hrs - chamber opened, subject calm.
0208 hrs - blood samples drawn.
0230 hrs - arrived at Vivarium.
0235 hrs - de-instrumentation-catheter out at time of post test physical.
0240 hrs - urine in pan filtered through gauze into bottle #2.
0245 hrs - second catheterization produced no additional urine.
0305 hrs - urinated copiously. Sample obtained for purpose of 1 hr post run test.

/s/
JERRY FINEG
Captain, USAF, VC
61 Chief, Project Support Section
(Signature of Veterinarian/Assistant)
WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #2	6892/689201	Elvis #35	F	25 October 1961

PAST CLINICAL HISTORY

Last quarterly physical on 18 October 1961. No illnesses since that time. Used by Comparative Psychology on 19 October 1961.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	57½	55
RECTAL TEMP F°	98.8	100.0
BLOOD PRESSURE	148/128	185/150
PULSE/MIN	92	120
RESPIRATION/MIN	28	22
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None	None
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	AP & Lateral - normal	AP & Lateral - normal

MEASUREMENTS PERTINENT TO TEST

N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General appearance - good	General appearance - good
Mental status - normal	Mental status - normal
Eyes, ears, nose, throat - normal	Eyes, ears, nose, throat - normal
Lungs - clear	Lungs - normal
Heart - normal	Heart - normal
Abdomen - normal	Abdomen - constipated
Extremities - normal	Extremities - normal
Vagina - normal	Vagina - normal

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
   (a) 5cc clotted in oil
   (b) 5cc oxalated in oil
   (c) 5cc oxalated without oil
   (d) Slides for Differential Count
(2) Post Test (as soon as the chamber door was opened)
   (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 0^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

Pre and Post Run Itinerary:

1. Pre-Run
   a. Unable to effectively place indwelling catheter.
      (1) Urine to be collected in pan under chair
      (2) Hcl placed in collection pan
      (3) Pan placed at 0900 hrs
   b. Pre-run urine sample collected 0830 hrs.
   c. Restraint devices carefully checked to prevent strictures.
   d. Instrumentation functional except for foreign noise in ECG; not resolvable by instrumentation technician.
   e. Hard foam rubber padding has been added to the seat of the chair since the 23 October run. This will not interfere with urine collection.
   f. Capt Reynolds has provided water on this run in an attempt to induce increased urine output.
   g. 0955: Bleeding of subject accomplished with no complications.
   h. 0956: Chamber closed.

2. Post-Run

   a. 0137: Chamber opened.
   b. 0145: Blood samples drawn.
   c. 0200: Animal returned to Vivarium.

/s/

JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #3	6892/689201	Roscoe #42	M	28 October 1961

PAST CLINICAL HISTORY

Last quarterly physical examination 14 June 1961. Subject was returned from MDRBC 8 September in very poor condition. He had lost 12 pounds in 36 days. Subject has been convalescing at MDRBL with occasional daily issue to MDRBC since that time and he has gained 7 pounds.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	51	50½
RECTAL TEMP F°	99.0	100.3
BLOOD PRESSURE	292/180 (wild)	184/145 (quiet)
PULSE/MIN	124	132
RESPIRATION/MIN	36	22
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None required	
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	AP & Lateral - normal	AP & Lateral - normal

MEASUREMENTS PERTINENT TO TEST

N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General appearance - good Mental Status - wild, fighting Eyes, ears, nose, throat - normal Chest (auscultation) Heart - systolic murmur Lungs - normal Abdomen (palpation) - normal Extremities - normal	Findings same as pre-test except: Mental Status - much quieter on examination table Extremities - moderate edema of both feet

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
  (a) 5cc clotted in oil
  (b) 5cc oxalated in oil
  (c) 5cc oxalated without oil
  (d) Slides for Differential Count
(2) Post Test (as soon as the chamber door was opened)
  (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

Pre-Test:

Subject catheterized during the entire test for urine collection - #8 Fr Folley catheter.

/s/

JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #4	6892/689201	Minnie #46	F	30 October 1961

PAST CLINICAL HISTORY

Last quarterly physical examination - 12 September 1961. No serious illnesses since last quarter. Subject's age: 4 years and 9 months (approximately).

DATA	PRE TEST	POST TEST
WEIGHT/LBS	47	45½
RECTAL TEMP F°	99°	100.5°
BLOOD PRESSURE	145/115	150/110
PULSE/MIN	88	100
RESPIRATION/MIN	36	33
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None required	
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	AP & Lateral - normal	AP & Lateral - normal

MEASUREMENTS PERTINENT TO TEST

N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General appearance - good	Findings same as pre-test except:
Ears, eyes, nose and throat - normal	Extremities - slight edema of feet
Chest (auscultation) Heart - systolic murmur (loud) Lungs - normal	Subject was coughing when door was opened; however, lung sounds were normal during the physical examination.
Mental Status - straining. Occasionally against restraint	A deep laceration was observed on the subject's 2nd finger of the right hand. Cause unknown.
Abdomen - normal	
Extremities - normal	

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
  (a) 5cc clotted in oil
  (b) 5cc oxalated in oil
  (c) 5cc oxalated without oil
  (d) Slides for differential count
(2) Post Test (as soon as the chamber door was opened)
  (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

Pre-test: Subject catheterized during test for urine collection - #6 Fr. Folley catheter.

Post-test:

0200 hrs - Blood drawn for laboratory analysis.
0210 hrs - Arrived at Vivarium Section and started de-instrumentation procedures.
0230 hrs - Accomplished physical examination.
0300 hrs - Attempted to collect urine samples, but failed.

/s/

JERRY FINNG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #5	6892/689201	Paleface #32	M	1 November 1961

PAST CLINICAL HISTORY

Subject's age - 6 years and 11 months (approximately).
Last quarterly physical examination 25 September 1961. No serious illnesses since that time.
Experimental subject for the following since last physical:
MDRBC - 9 and 10 Oct 61 - training.
Oxygen Toxicity Study - Test #1 on 23 Oct 61. No serious after effects.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	62½	61
RECTAL TEMP F°	100.0	98.4
BLOOD PRESSURE	240/110 (Diastolic-3rd sound)	204/160
PULSE/MIN	112	136
RESPIRATION/MIN	24	32
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None required	
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	AP & Lateral - normal	AP & Lateral - normal

MEASUREMENTS PERTINENT TO TEST

N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General Appearance - very good Mental Status - straining Eyes, ears, nose, throat - normal Chest (auscultation) Heart - systolic murmur Lungs - clear, normal Abdomen (palpation) - normal Extremities - normal	All findings same as pre-test except: Extremities - Penis revealed marked edema due to stricture of suit. Feet - edema due to restraint band.

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
- (a) 5cc clotted in oil
- (b) 5cc oxalated in oil
- (c) 5cc oxalated without oil
- (d) Slides for differential count

(2) Post Test (as soon as the chamber door was opened)
- (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

Subject consumed a full container of water during the test. One hour post test u sample collected from 0200 - 0245 hrs. Urinary catheter came out at 0245 hrs whe the animal strained while lying on the examination table.

/s/

JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #6	6892/689201	Elvis #35	F	3 November 1961

PAST CLINICAL HISTORY

Last quarterly physical on 18 October 1961. No illnesses since that time. Used by Comparative Psychology on 19 October 1961. Subject for Oxygen Toxicity Study #2 on 25 October 1961. No serious illnesses noted following tests.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	57½	55
RECTAL TEMP F°	98.2	100.0
BLOOD PRESSURE	190/155	210/130
PULSE/MIN	88	128
RESPIRATION/MIN	24	36
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None	None
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	(AP & Lateral - normal) (Pre-test #2)	(AP & Lateral - normal) (Chest 36 hrs post-test)
MEASUREMENTS PERTINENT TO TEST	N/A	N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General Appearance - very good Mental status - Vocalizing, but fairly quiet Eyes, ears, nose, throat - nasal discharge, very slight. Others normal. Chest (auscultation) Heart - normal Lungs - Clear, normal Abdomen (palpation) - normal Extremities - normal	All findings are same as pre-test except: Coughing but lungs sound normal.

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
- (a) 5cc clotted in oil
- (b) 5cc oxalated in oil
- (c) 5cc oxalated without oil
- (d) Slides for differential count

(2) Post Test (as soon as the chamber door was opened)
- (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

- -

Pre-Test: Subject catheterized with #8 Fr Folley catheter for urine collection during the test.

Post-Test: Catheter in place until diaper removed, leaking did occur however.

/s/

JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #7	6892/689201	Roscoe #42	M	6 November 1961

PAST CLINICAL HISTORY

Last quarterly physical examination 14 June 1961. Subject was returned from MDRBC 8 September 1961 in very poor condition. He had lost 12 pounds in 36 days. Subject has been convalescing at MDRBL with occasional daily issue to MDRBC since that time and he has gained 7 pounds. Experimental test subject for Oxygen Toxicity Study #3 on 27 October 1961. No serious effects noted following test.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	54	53
RECTAL TEMP F°	100.8	98.8
BLOOD PRESSURE	168/132	145/118
PULSE/MIN	116	120
RESPIRATION/MIN	32	24
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None	None
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation intact
X-RAY 400 MA 64 KVP 1/60 sec. 48"	Pre-test Chest - dtd 26 Oct	36 hour post - Chest
MEASUREMENTS PERTINENT TO TEST	N/A	N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General Appearance - good Mental Status - fairly quiet Eyes, ears, nose, throat - normal Chest (auscultation) Heart - systolic murmur Lungs - normal Abdomen (palpation) - normal Extremities - normal	All findings same as Pre-Test. Subject very quiet during Post-Test physical examination. Subject catheterized with #8 Fr Folley catheter during test.

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
  (a) 5cc clotted in oil
  (b) 5cc oxalated in oil
  (c) 5cc oxalated without oil
  (d) Slides for differential count
(2) Post Test (as soon as the chamber door was opened)
  (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

- -

Subject destroyed a portion of the wiring inside the chamber, causing a loss of 2 channels ECG. This also delayed the test end point by approximately 45 minutes during repair.

0215 hrs - End of test - chamber opened, subject calm, post-test blood samples drawn.

0215 - 0300 hrs - Post-Test urine collection period. Catheter was still in place at the end of the test, but it was accidentally pulled out during de-suiting. However the subject did not urinate voluntarily until 0300 hrs. This was considered adequate for the post-test sample, making catheterization at 0315 hrs unnecessary.

/s/

JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)

WILLIAM E. BRITZ, JR
Captain, USAF, VC

PHYSICAL EXAMINATION PRE AND POST TEST

TEST	PROJECT/TASK NR	ANIMAL IDENTIFICATION	SEX	DATE
Oxygen Toxicity Study #8	6892/689201	Minnie #46	F	8 November 1961

PAST CLINICAL HISTORY

Last quarterly physical examination - 12 September 1961. No serious illnesses since last quarter. Subject's age: 4 years and 9 months (approximately). Experimental subject for Oxygen Toxicity Study #4 on 30 October 1961. No serious after effects.

DATA	PRE TEST	POST TEST
WEIGHT/LBS	48	45 3/4
RECTAL TEMP F°	98	100.0
BLOOD PRESSURE	180/150	164/125
PULSE/MIN	120	88
RESPIRATION/MIN	32	24
ANESTHESIA/RESTRAINT	IF USED AMOUNT, TYPE AND TIME None	None
E. C. G.	OBSERVATIONS: Instrumented for ECG	OBSERVATIONS: Instrumentation
X-RAY	Chest - Pre study #4	36 hr post - Test - Chest

MEASUREMENTS PERTINENT TO TEST

N/A	N/A

REMARKS

[General appearance and mental status, eye, ear, nose and throat, chest (lungs and heart sounds), abdomen (palpation), extremities]

PRE	POST
General Appearance - good Mental Status - straining against restraint constantly Eyes, ears, nose and throat - normal Chest (auscultation) Lungs - normal Heart - systolic murmur Abdomen (palpation) - normal Extremities - normal, except post healing, laceration 2nd finger right hand. (See physical exam O_2 toxicity study #4) 74	All findings same as pre-test

AFMDC FORM FEB 60 0-252 (MDWML-2)

LABRATORY REQUIREMENTS

HEMATOLOGY *(Number of samples, times to be collected, type and amounts)*

(1) Pre Test (just prior to closing the chamber door)
- (a) 5cc clotted in oil
- (b) 5cc oxalated in oil
- (c) 5cc oxalated without oil
- (d) Slides for differential count

(2) Post Test (as soon as the chamber door was opened)
- (a) Same as Pre Test

URINALYSIS *(Number of samples, times to be collected, type and amounts)*

Subject was catheterized with an indwelling Folley catheter for continuous urine collection during the test. For 17 O^H corticosteroid determinations. Also, Pre and Post Test urine samples were collected for urinalyses.

- -

Pre-Test: Subject catheterized with #8 Fr Folley catheter.

Post-Test:

0200 hrs - Chamber opened - subject calm.
0205 hrs - Post test blood samples taken.
0210 hrs - One hour post test urine sample collection begun.
0245 hrs - Catheter in at time of de-instrumentation but came out soon after - retention bladder contained no air to hold it in?
0310 hrs - Urinated on table - small sample collected - catheterized - no more urine available.

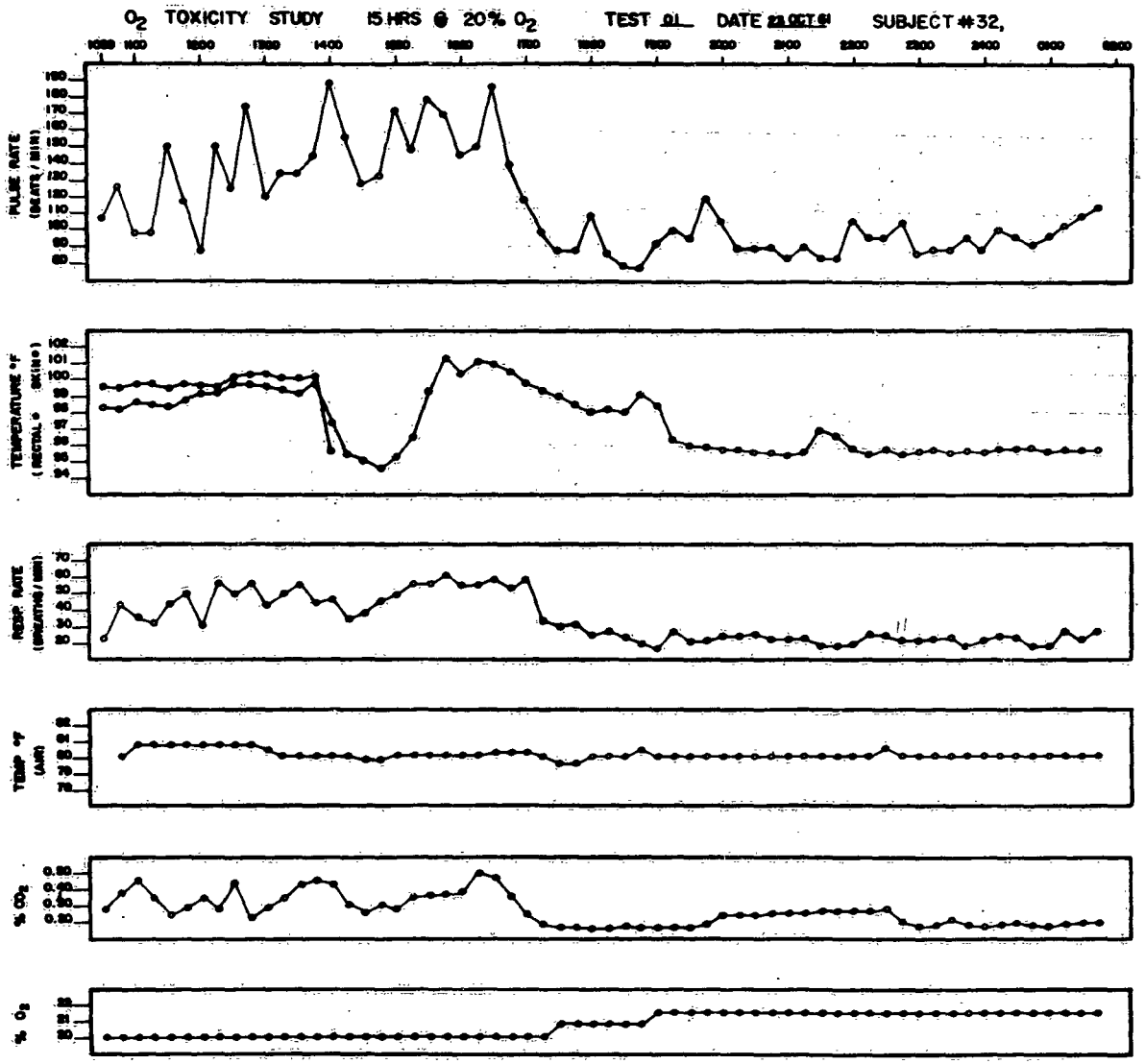
/s/
JERRY FINEG, Captain, USAF, VC
Chief, Project Support Section
Veterinary Services Branch

(Signature of Veterinarian/Assistant)
WILLIAM E. BRITZ, JR
Captain, USAF, VC

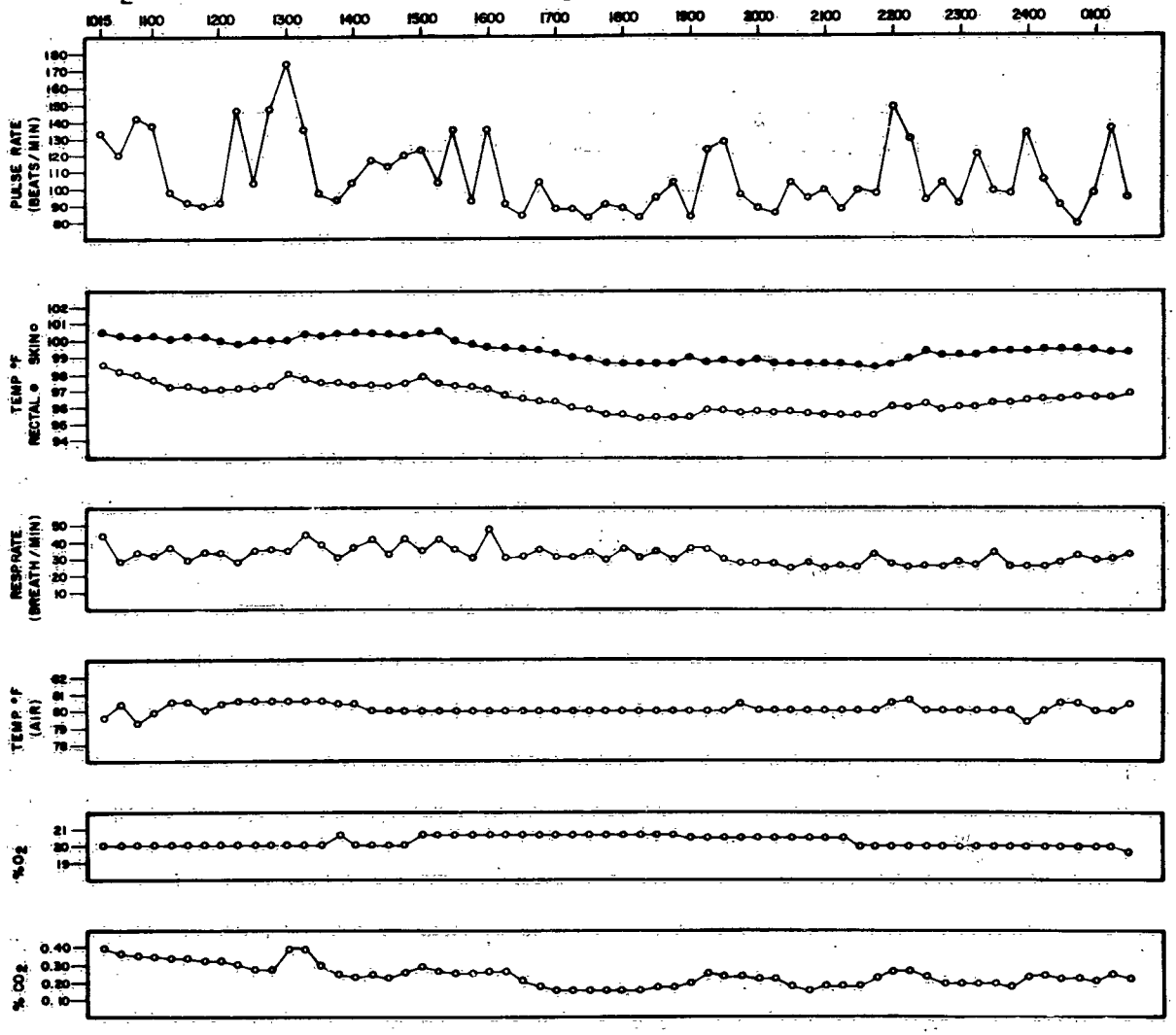
APPENDIX III

Individual Oxygen Tolerance Tests
Number 1, 2, 3, 4, 5, 6, 7 and 8

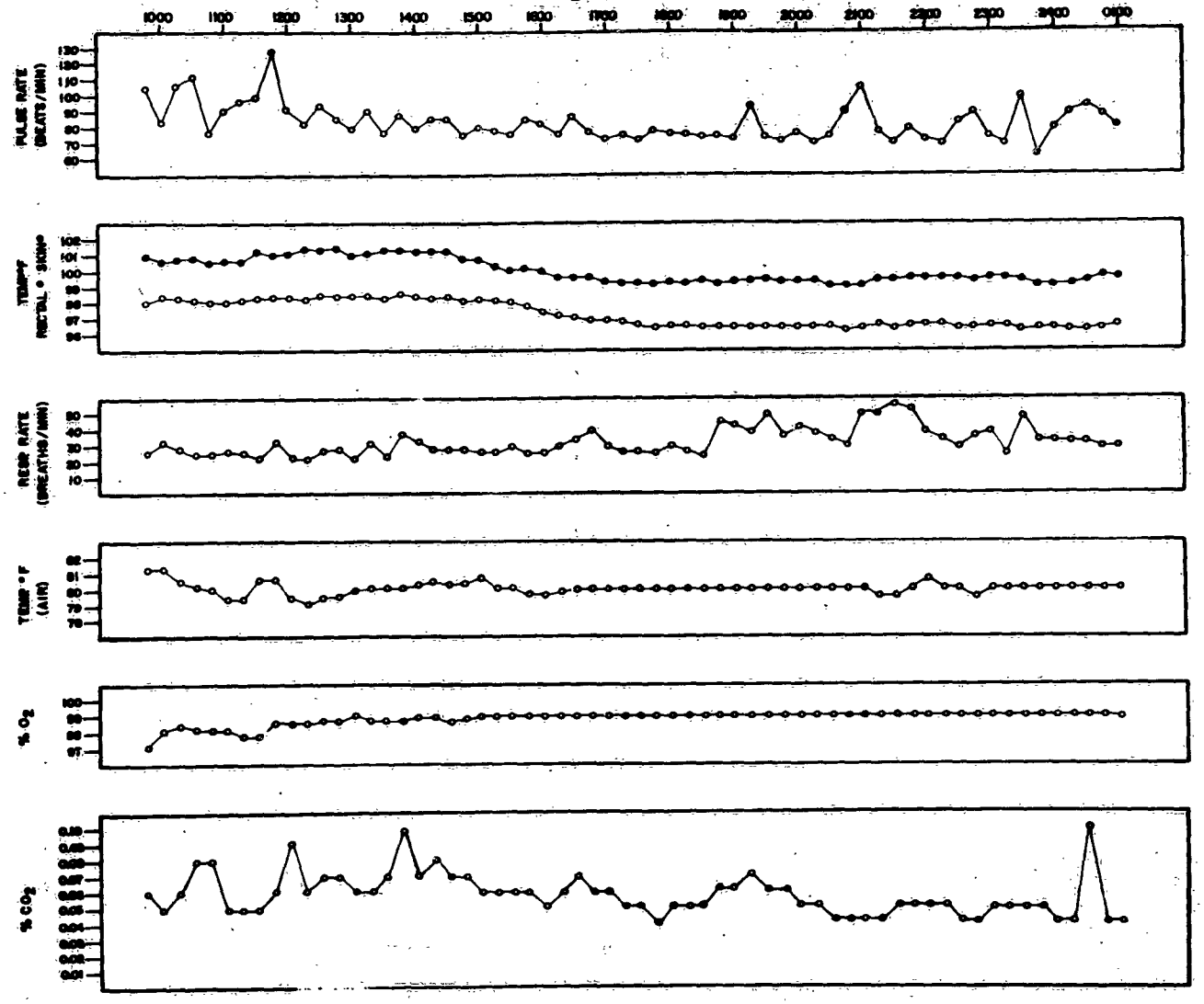
(Physiological and Environmental Data)


O_2 TOXICITY STUDY 15 HRS @ 20% O_2 TEST 01 DATE 29 OCT 64 SUBJECT #32,
PULSE RATE (BEATS / MIN)
TEMPERATURE °F (RECTAL & SKIN)
RESP RATE (BREATHS / MIN)
TEMP °F (AIR)
% CO_2
% O_2

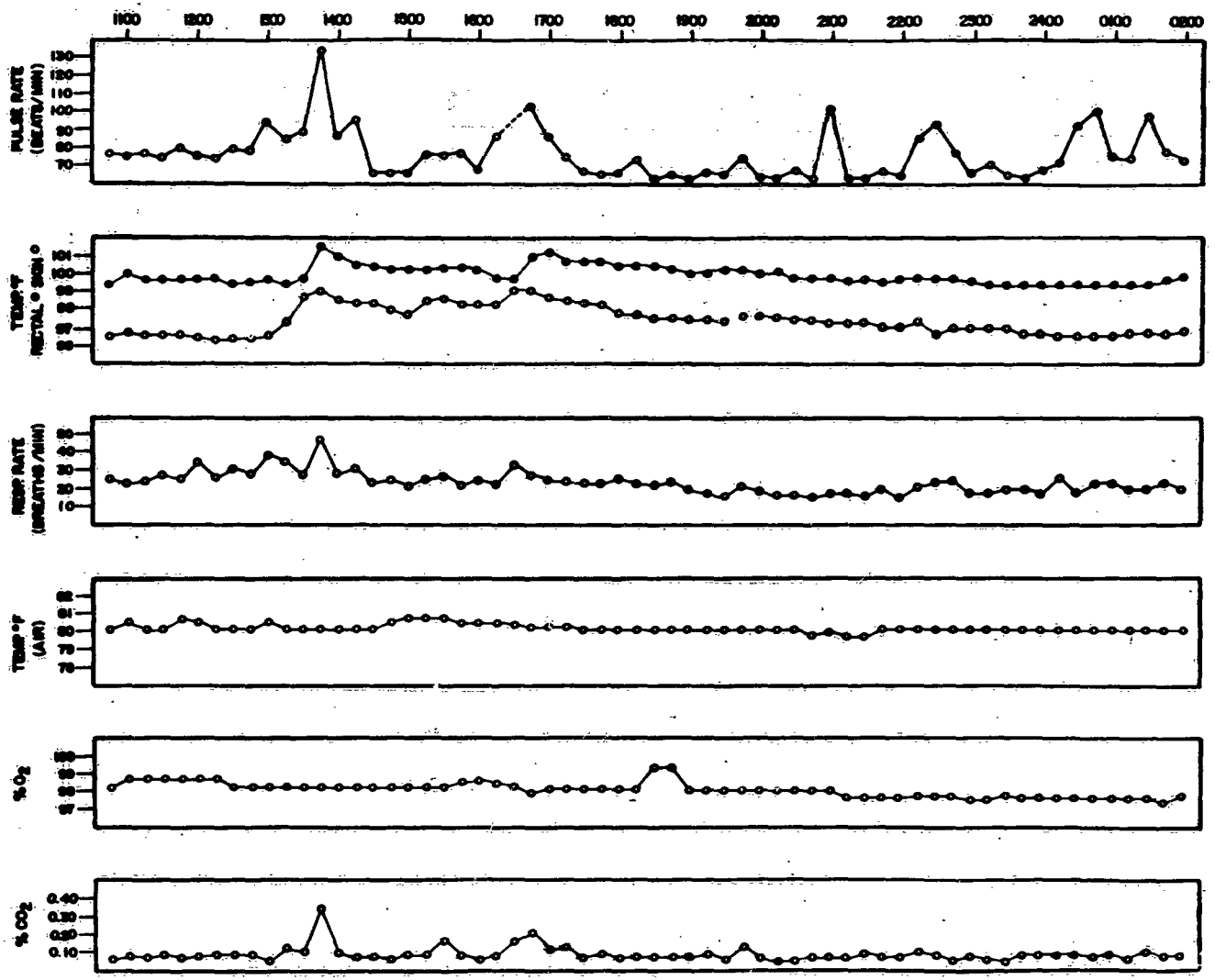
O_2 TOXICITY STUDY 15 HRS 20% O_2 TEST 02 DATE 25 OCT 61 SUBJECT # 35

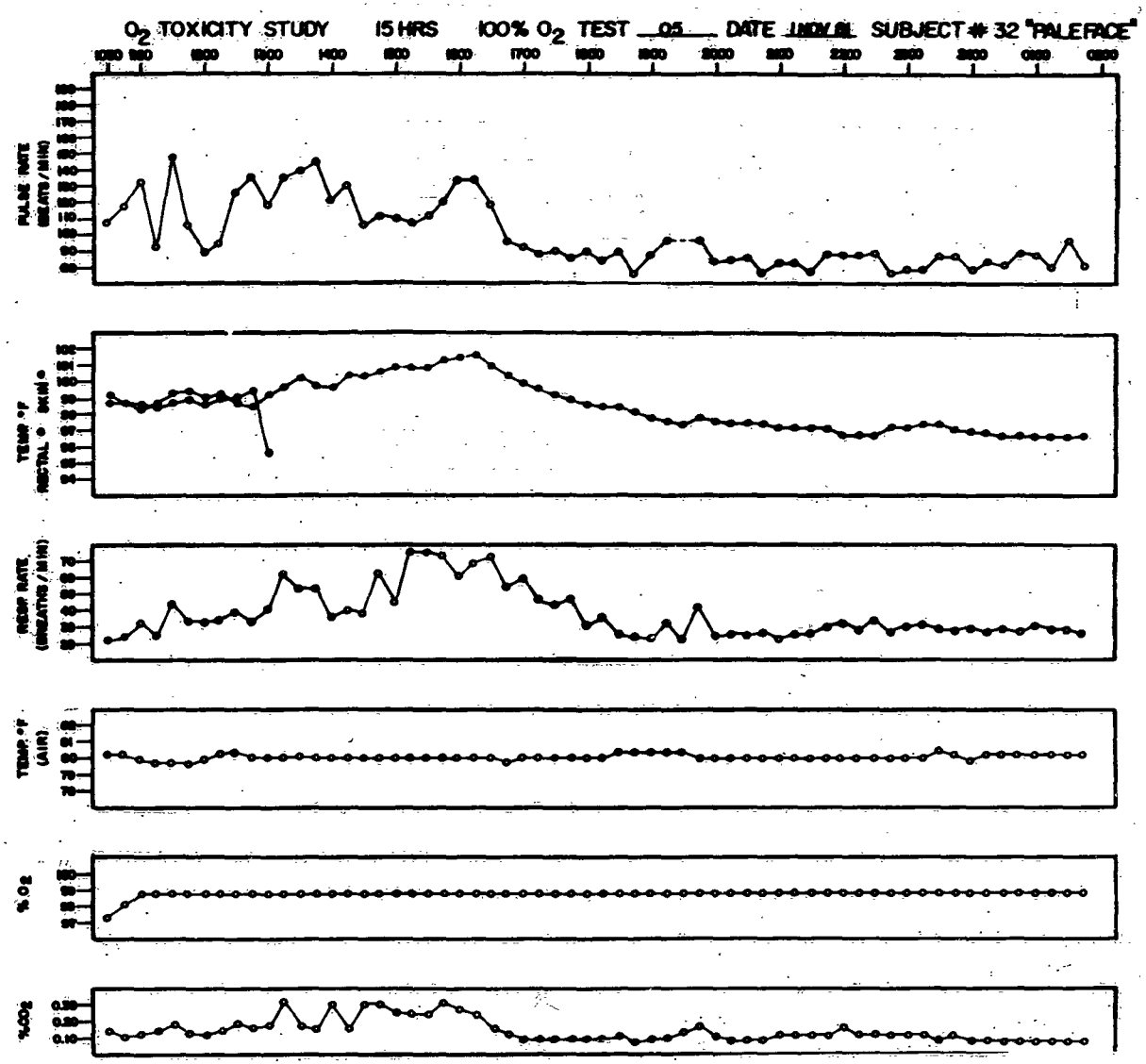


O_2 TOXICITY STUDY 15 HRS 100% O_2 TEST 03 DATE 27 OCT 61 SUBJECT # 42

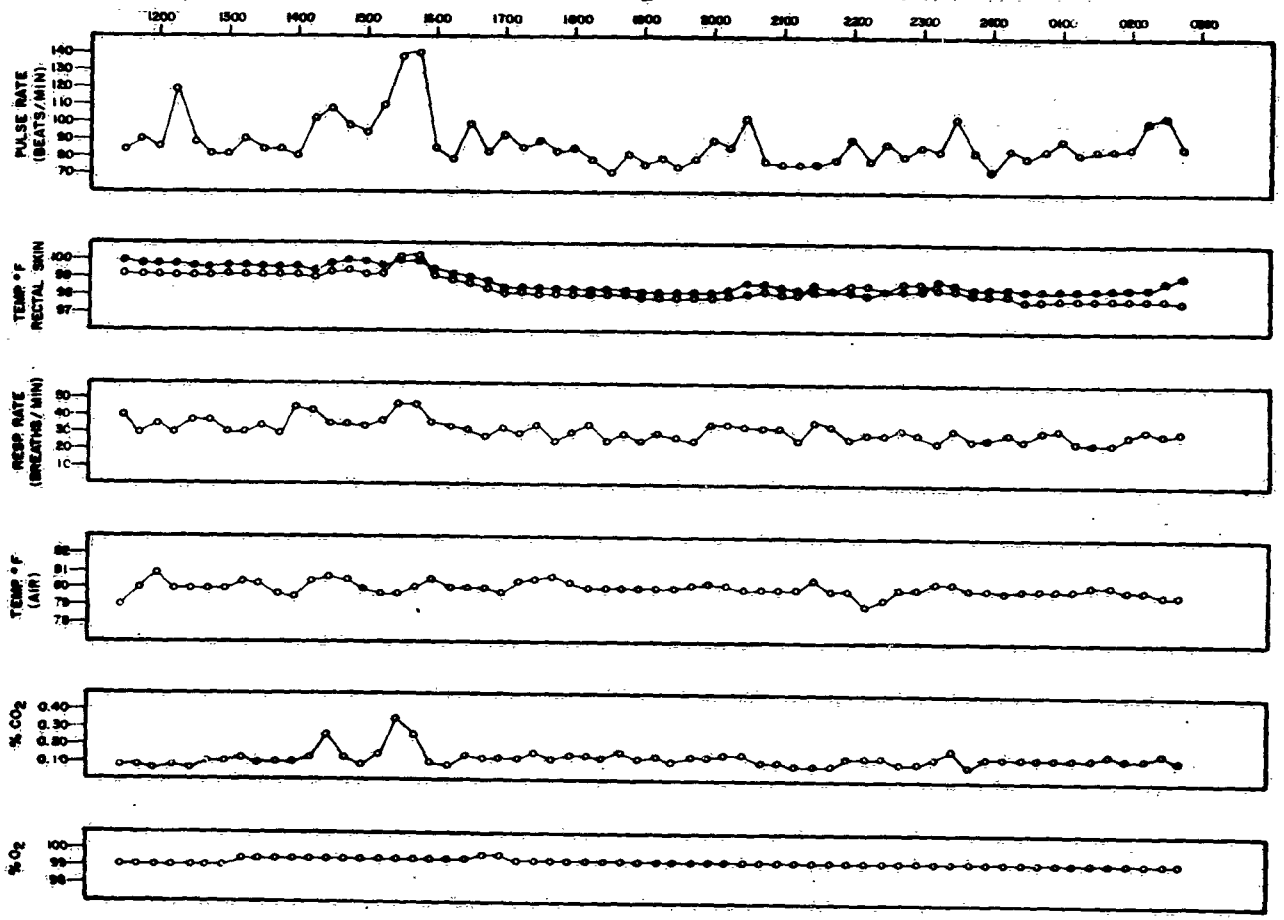


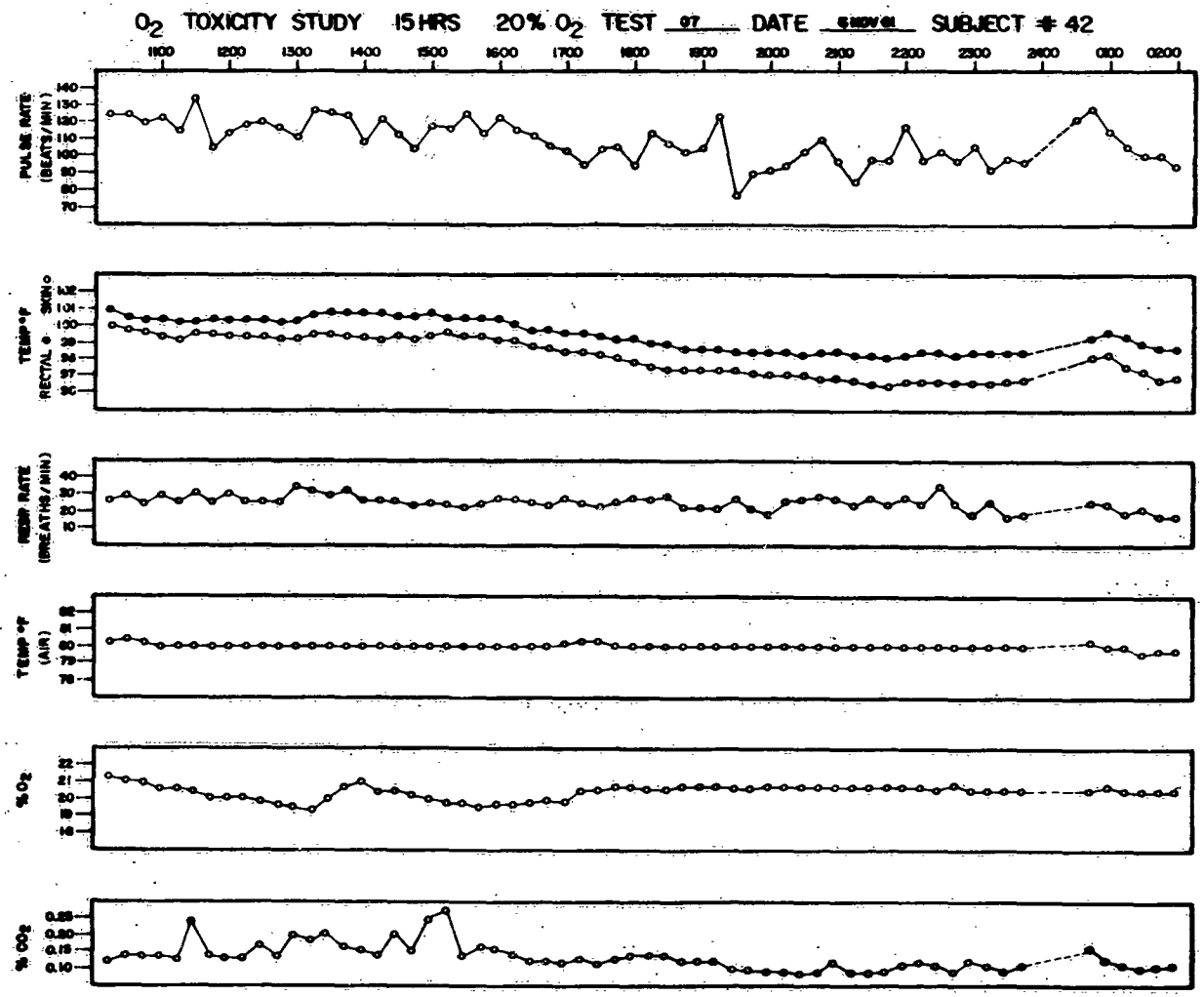
O_2 TOXICITY STUDY 15 HRS 100% O_2 TEST 04 DATE 30 OCT 61 SUBJECT # 46



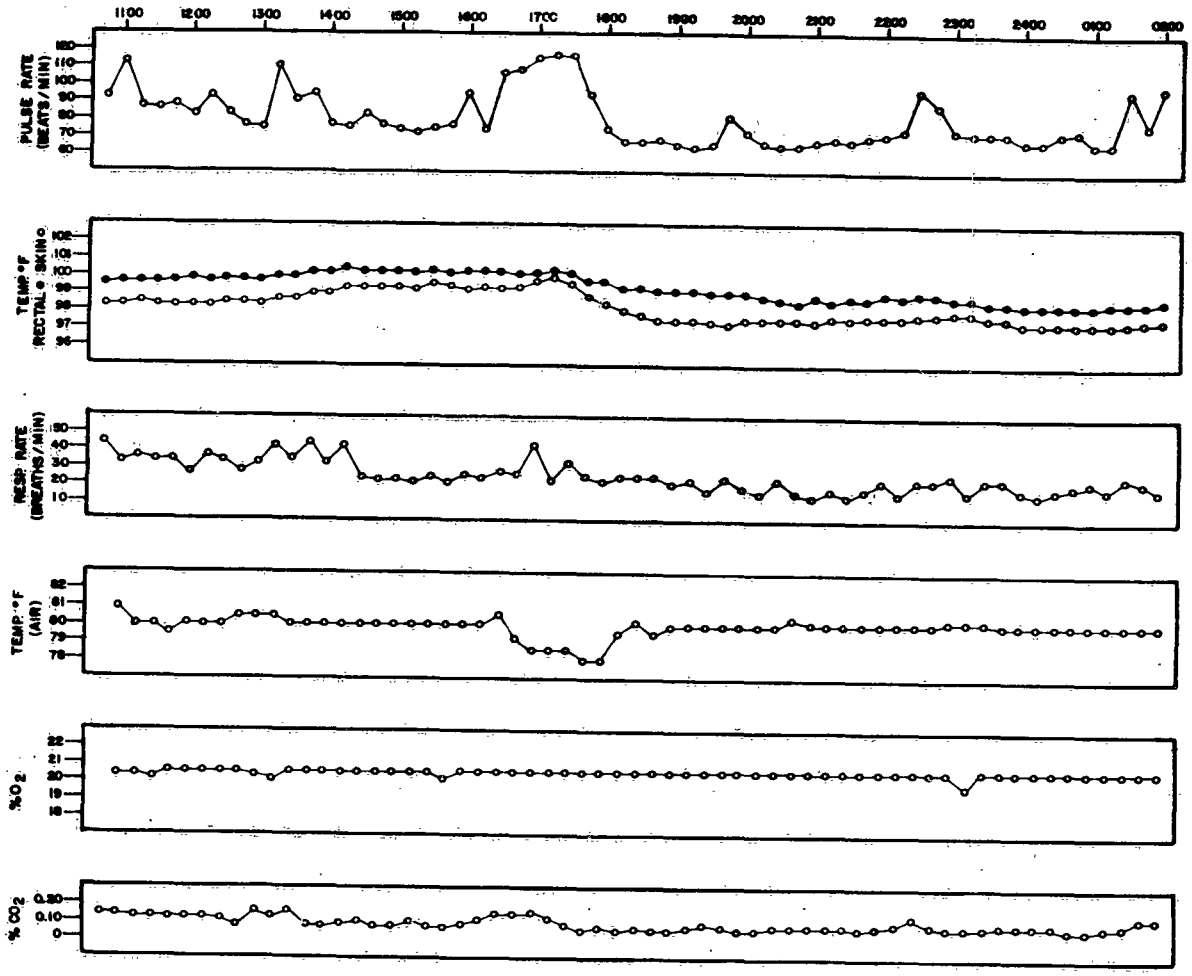

O_2 TOXICITY STUDY 15 HRS 100% O_2 TEST 05 DATE NOV 81 SUBJECT # 32 "PALEFACE"
PULSE RATE (BEATS/MIN)
TEMP °F RECTAL ° SKIN
RESP RATE (BREATHS/MIN)
TEMP °F (AIR)
% O_2
% CO_2

O_2 TOXICITY STUDY 15 HRS 100% O_2 TEST 06 DATE 3 NOV 61 SUBJECT #35




O_2 TOXICITY STUDY 15 HRS 20% O_2 TEST 97 DATE 6 NOV 61 SUBJECT # 42
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
2100
2200
2300
2400
0100
0200
PULSE RATE (BEATS/MIN)
TEMP °F RECTAL ● SKIN ○
RESP. RATE (BREATHS/MIN)
TEMP °F (AIR)
% O_2
% CO_2

O_2 TOXICITY STUDY 15 HRS 20% O_2 TEST 08 DATE 8NOV61 SUBJECT # 48



SUMMARY OF PHYSIOLOGICAL MEASURES
(14.7 psi, 80°F., 50% RH)

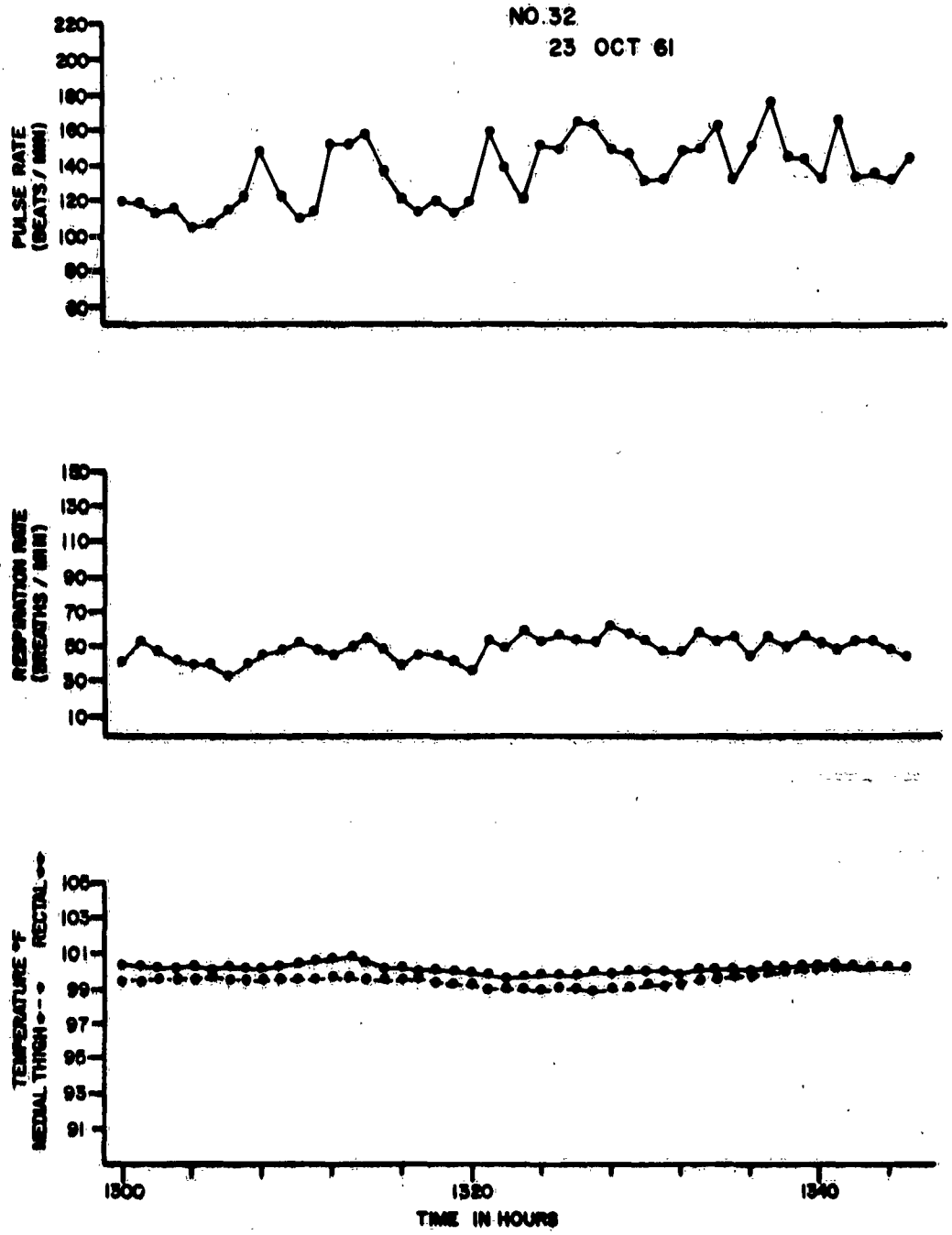
	N	Mean Difference 20% vs. 100% O_2	SE md	t Ratio
Heart Rate	245	16.28	1.54	10.57**
Respiration	245	-2.35	0.251	-9.36**
Skin Temp.	247	-0.75	0.502	-1.49
Rectal Temp.	196	-0.08	1.01	.092

** $P < .001$

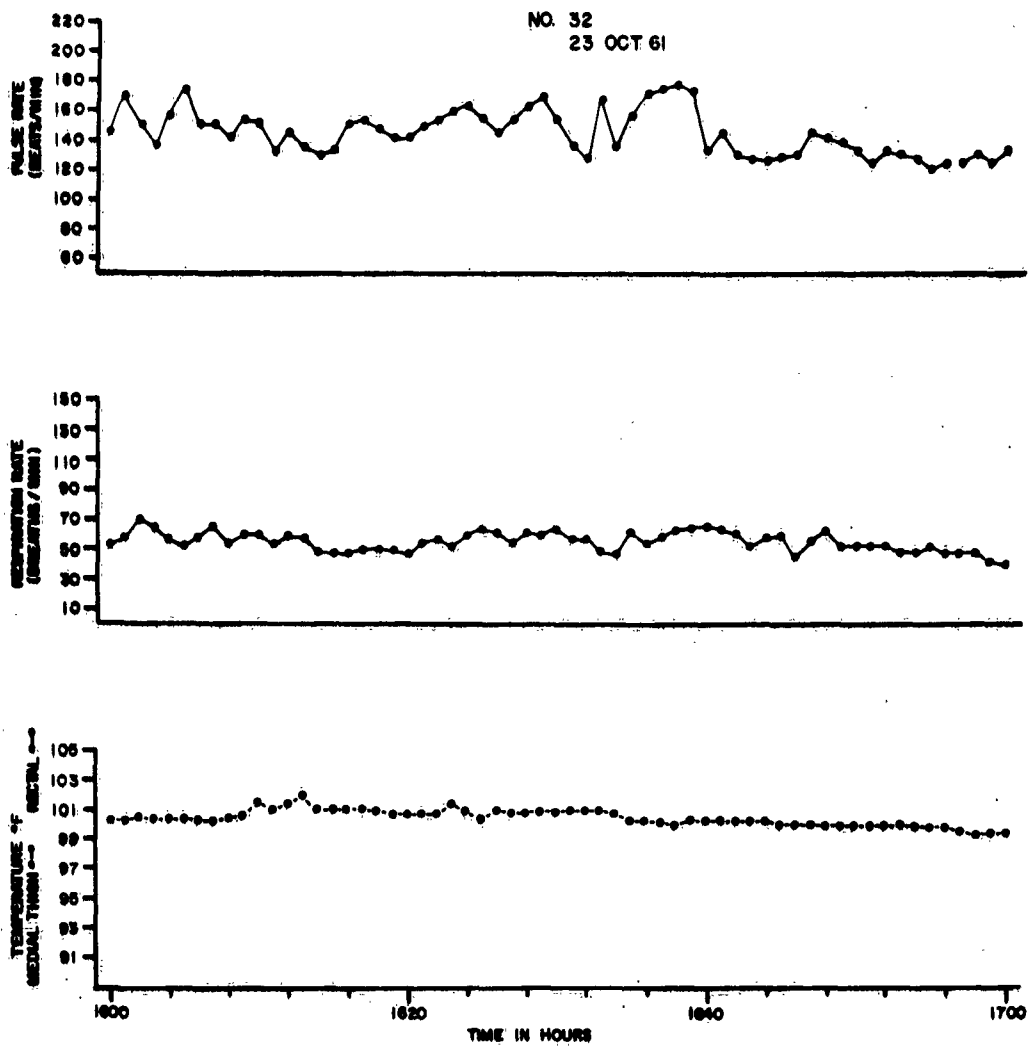
APPENDIX IV

Charts of Individual Oxygen Tolerance Tests
Number 1, 2, 3, 4, 5, 6, 7, 8

(Physiological Data for Five "Work Sessions")



Physiological Data Oxygen Tolerance Test 01, First "Work Session"



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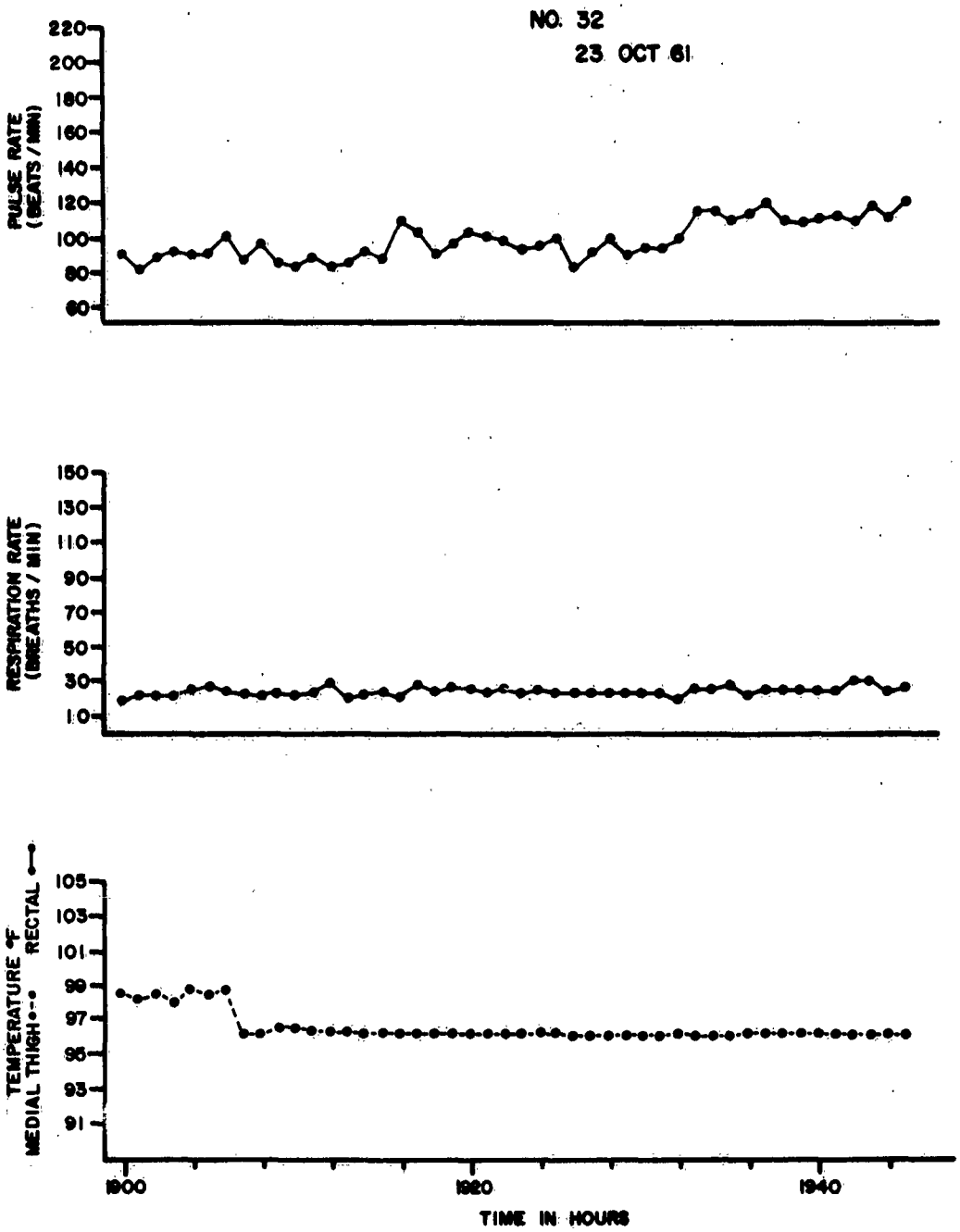
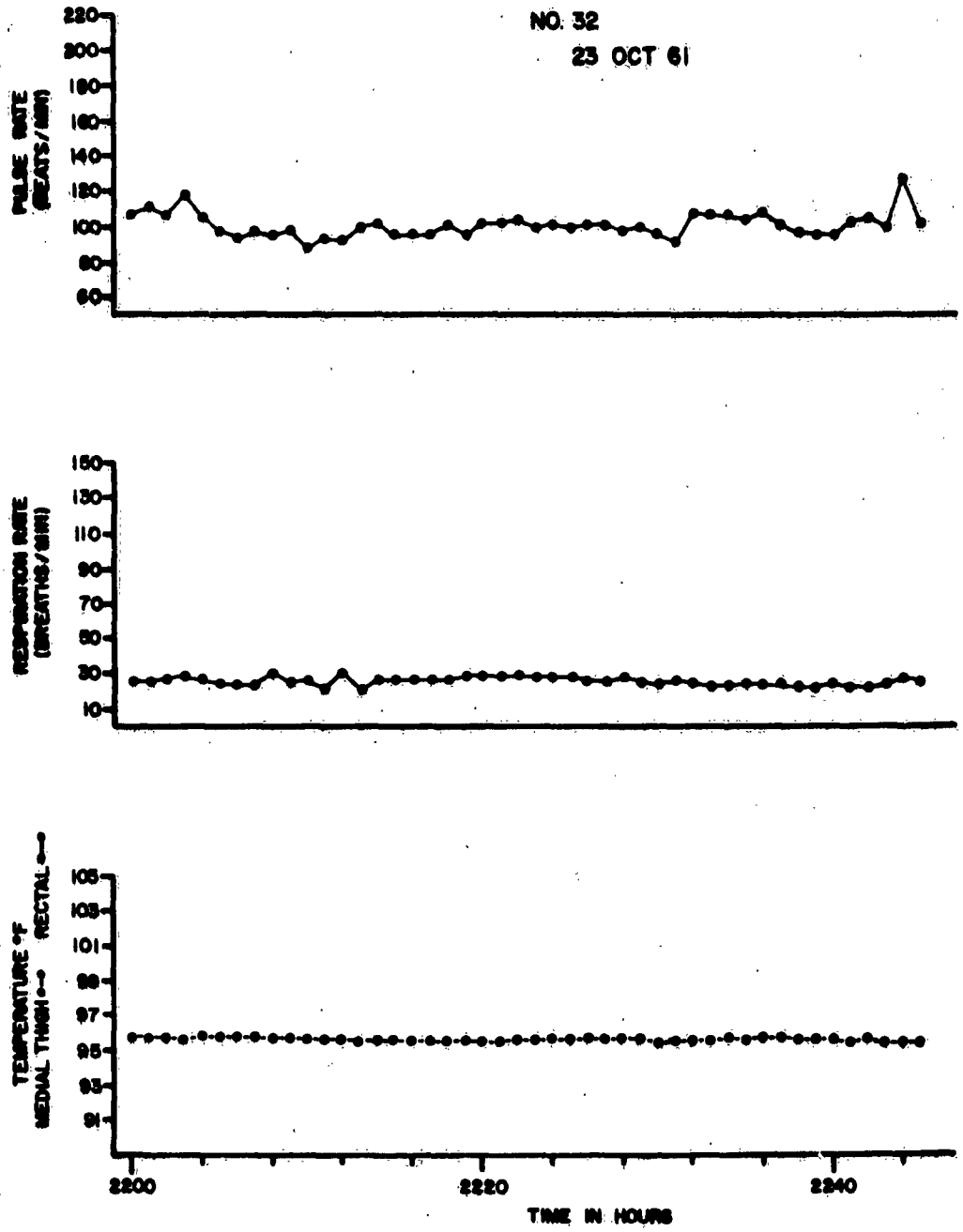
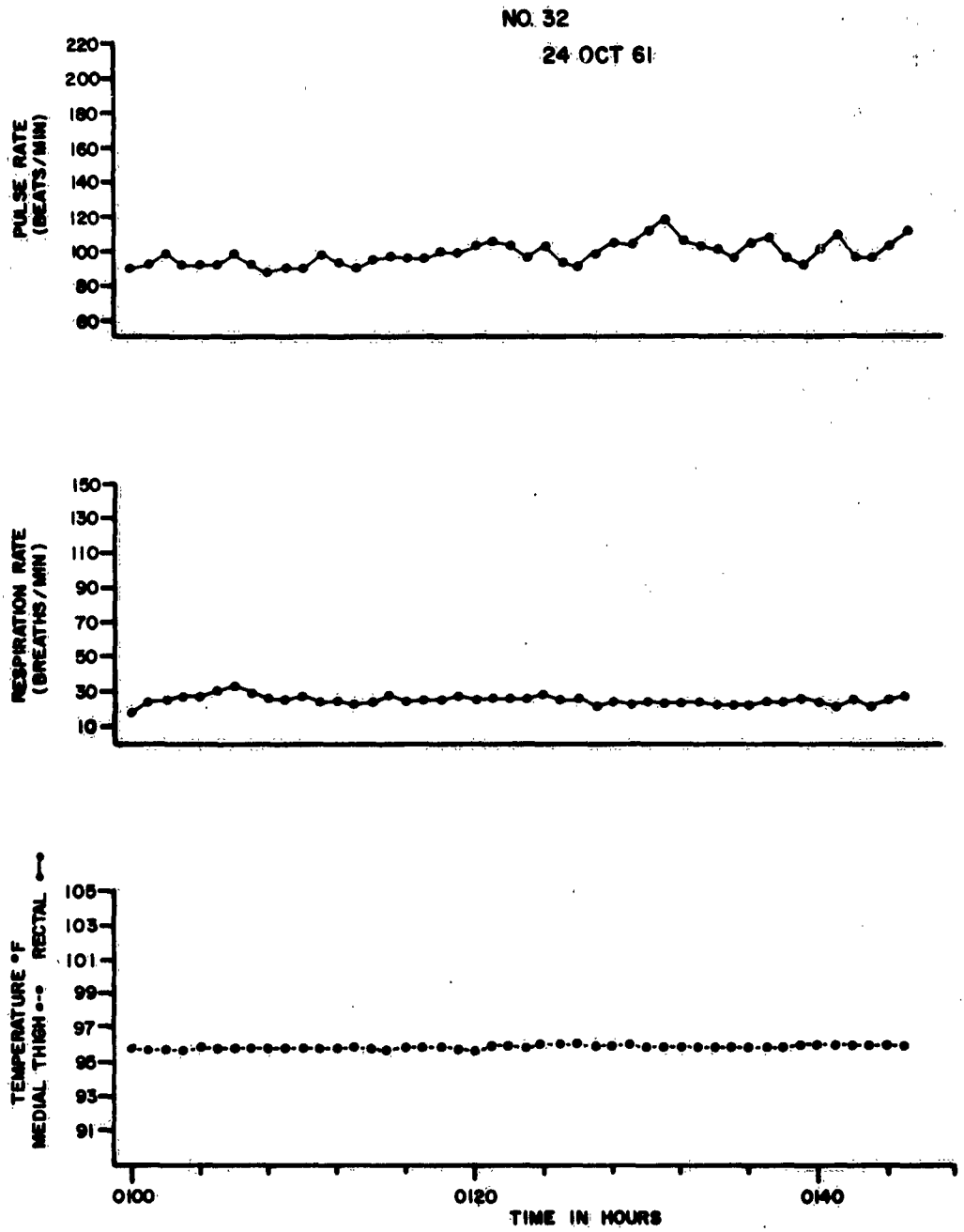


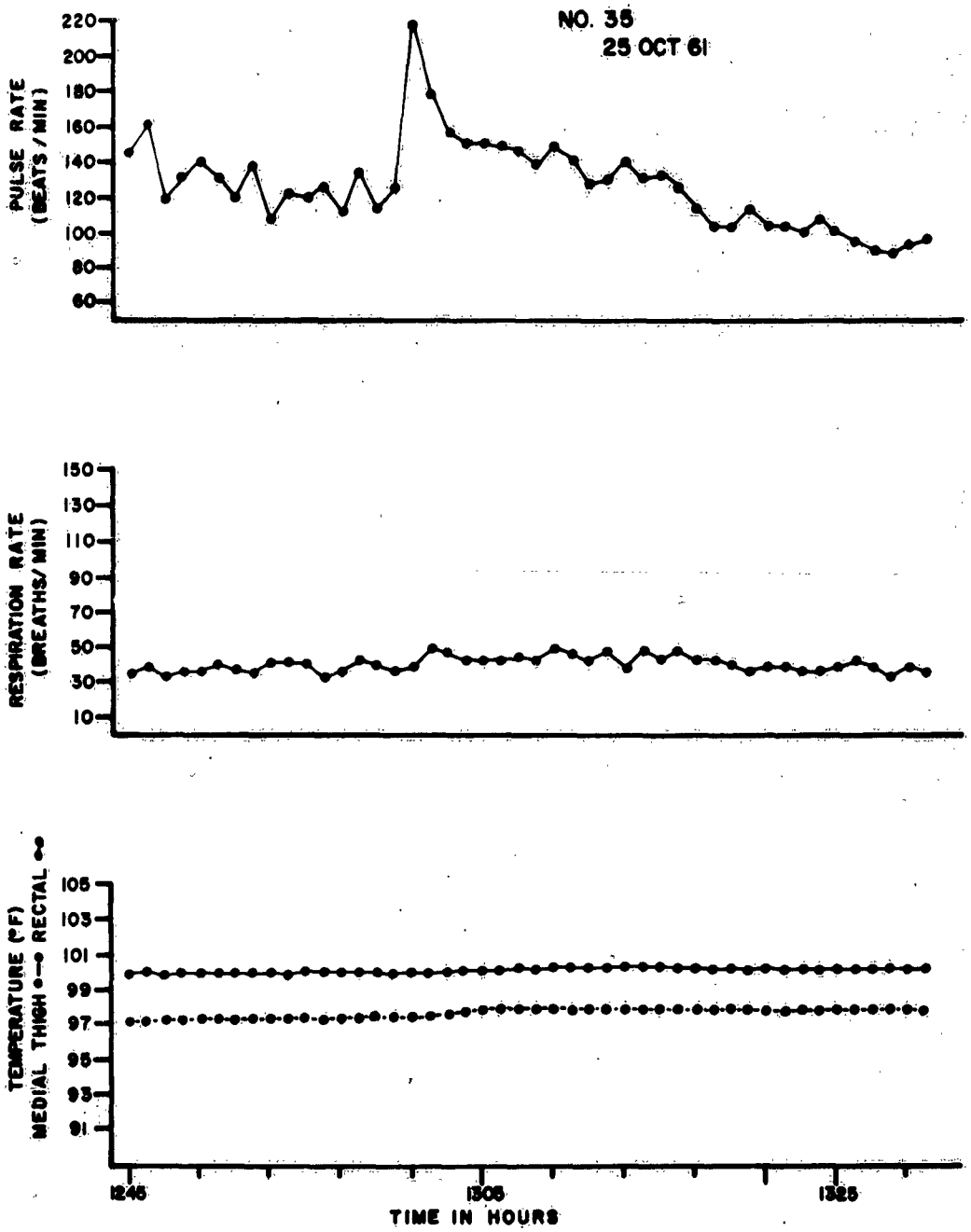
Physiological Data Oxygen Tolerance Test 01, Third "Work Session"



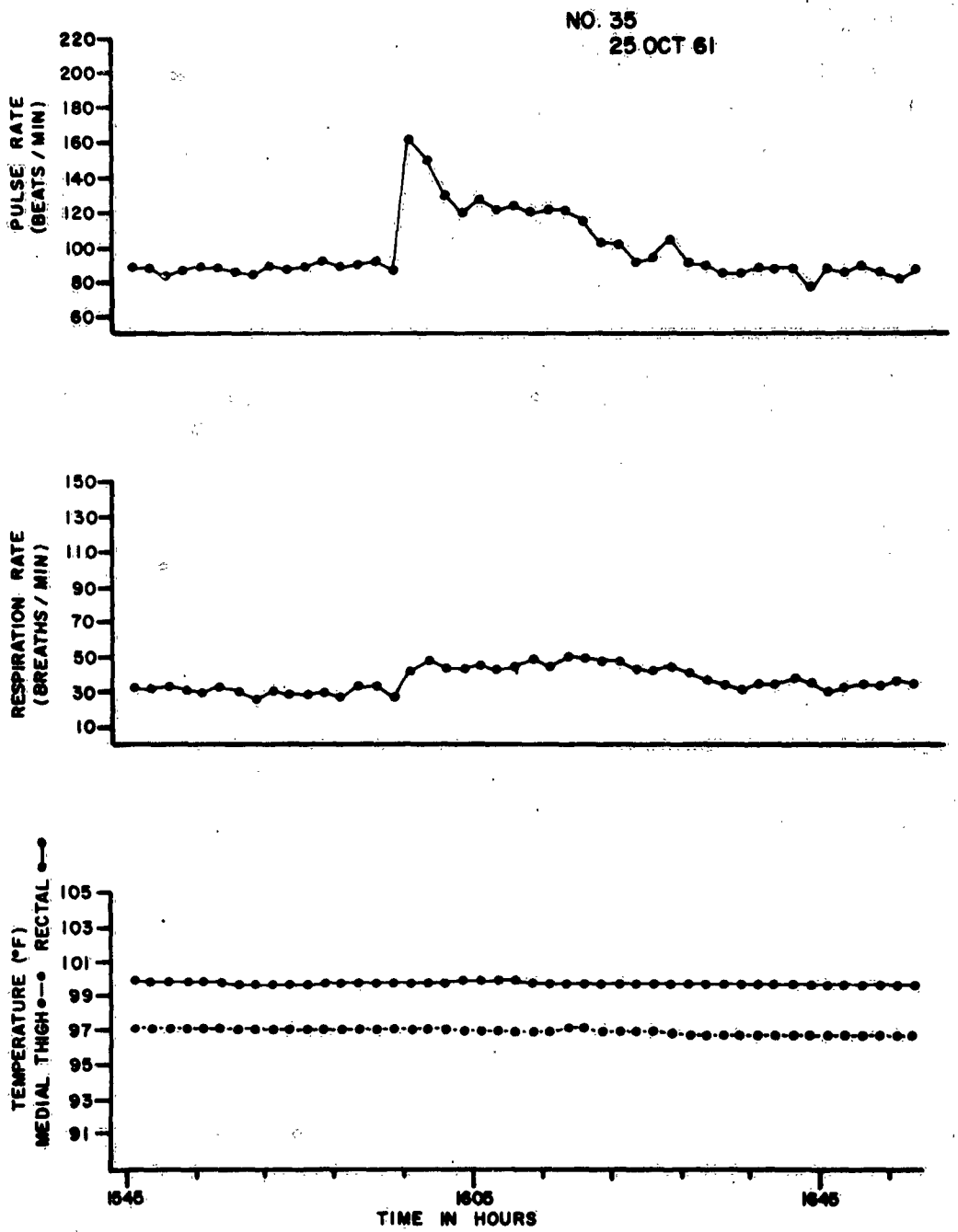
Physiological Data Oxygen Tolerance Test 01, Fourth "Work Session"



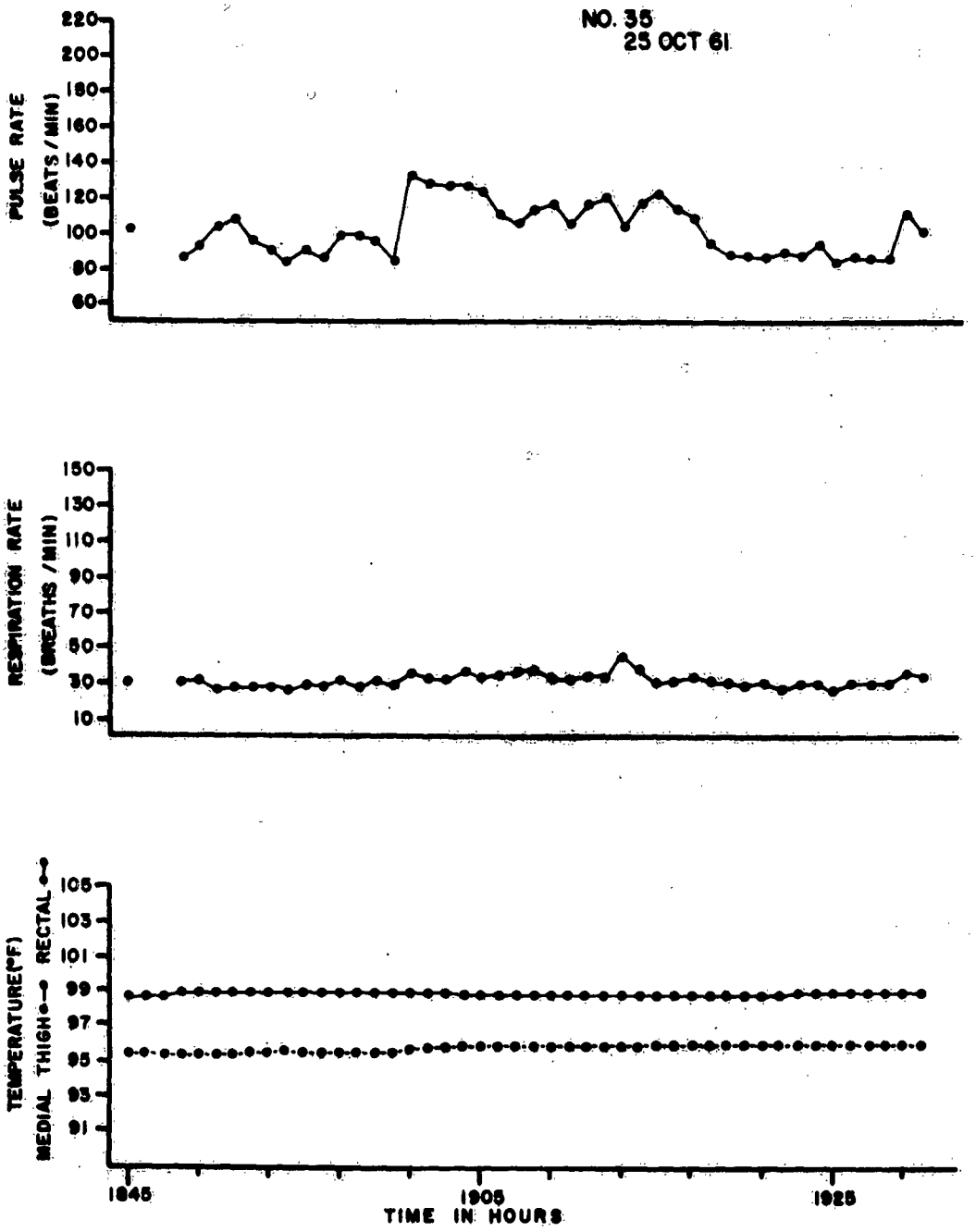
Physiological Data Oxygen Tolerance Test 01, Fifth "Work Session"



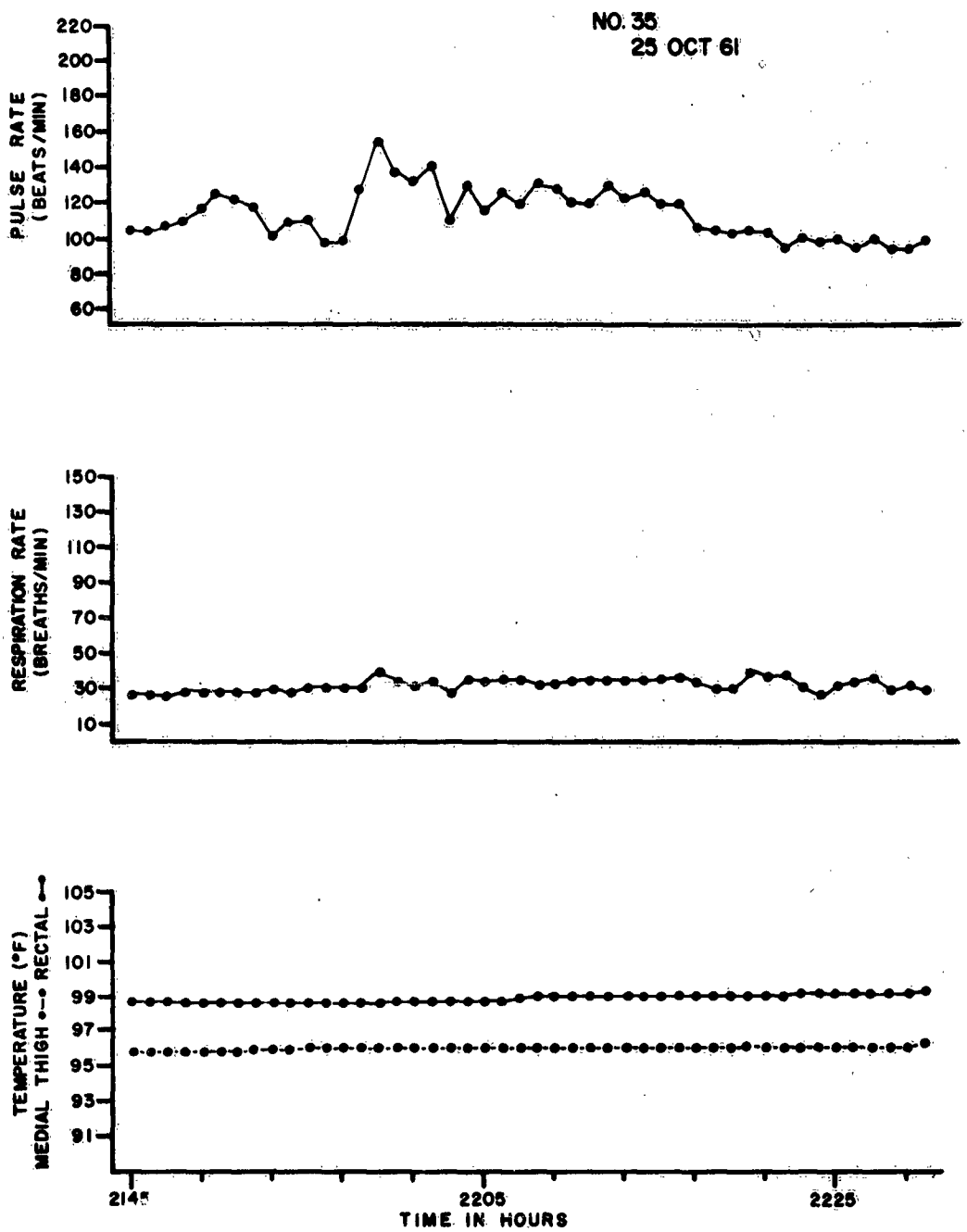
Physiological Data Oxygen Tolerance Test 02, First "Work Session"



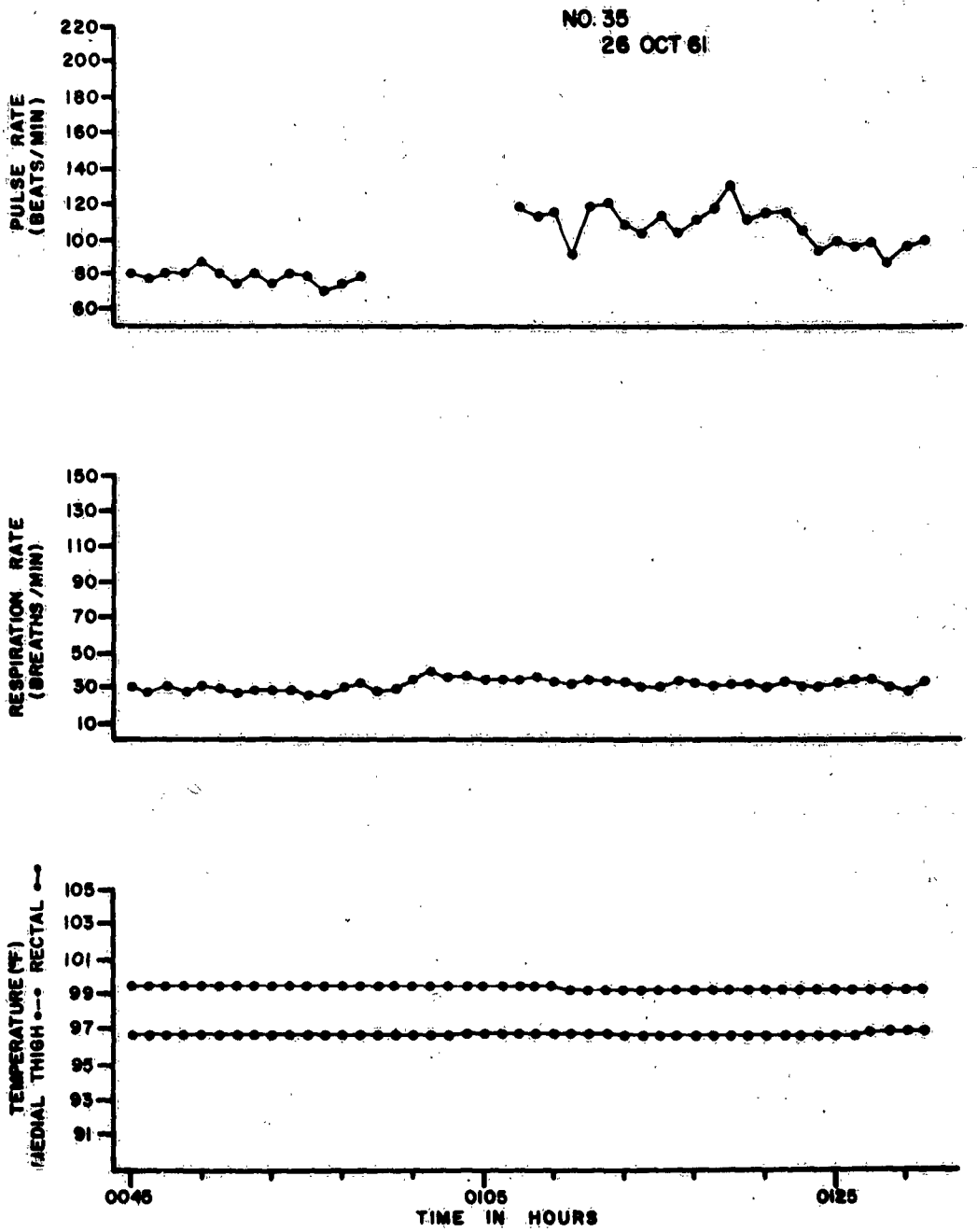
Physiological Data Oxygen Tolerance Test 02, Second "Work Session"



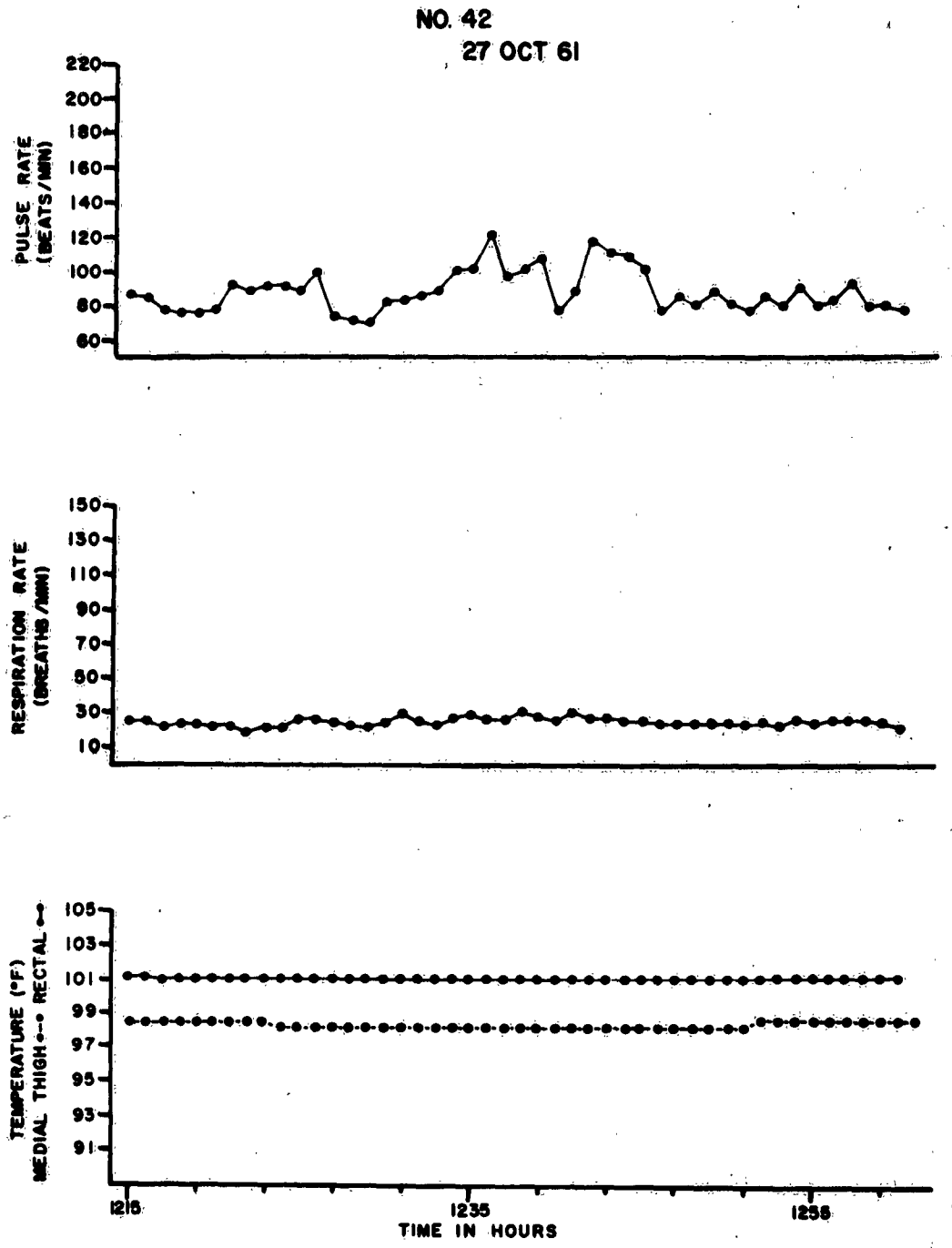
Physiological Data Oxygen Tolerance Test 02, Third "Work Session"



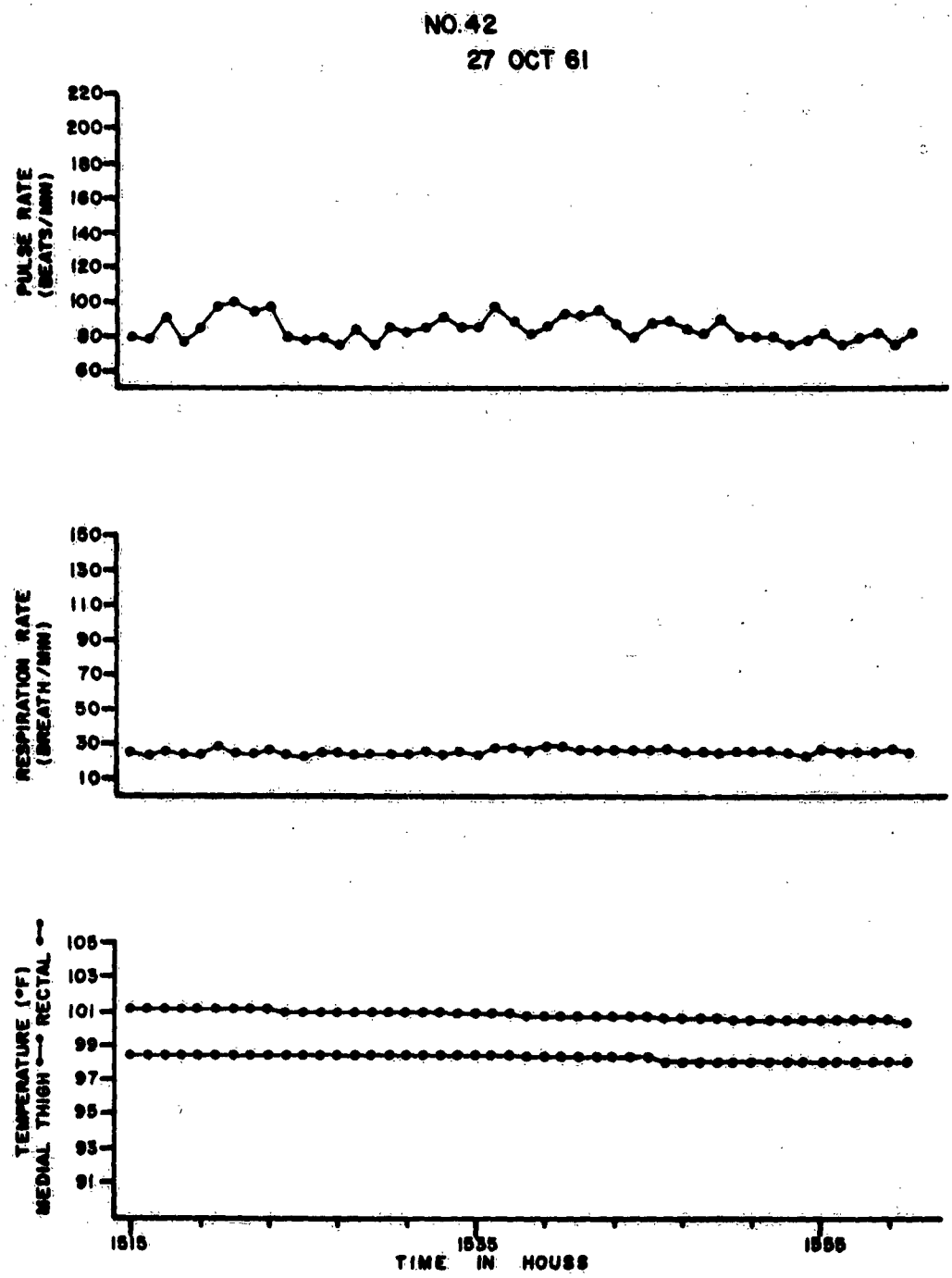
Physiological Data Oxygen Tolerance Test 02, Fourth "Work Session"



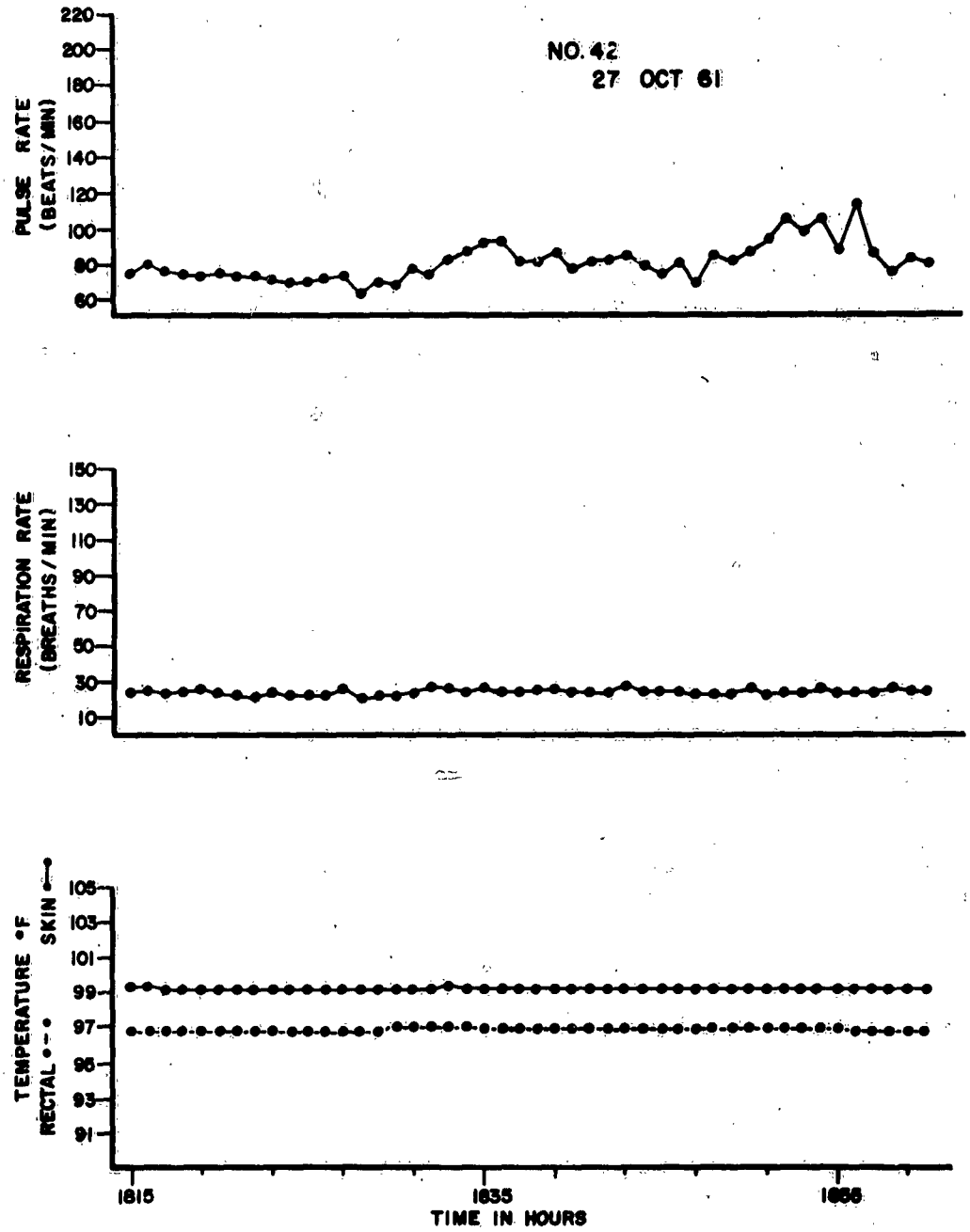
Physiological Data Oxygen Tolerance Test 02, Fifth "Work Session"



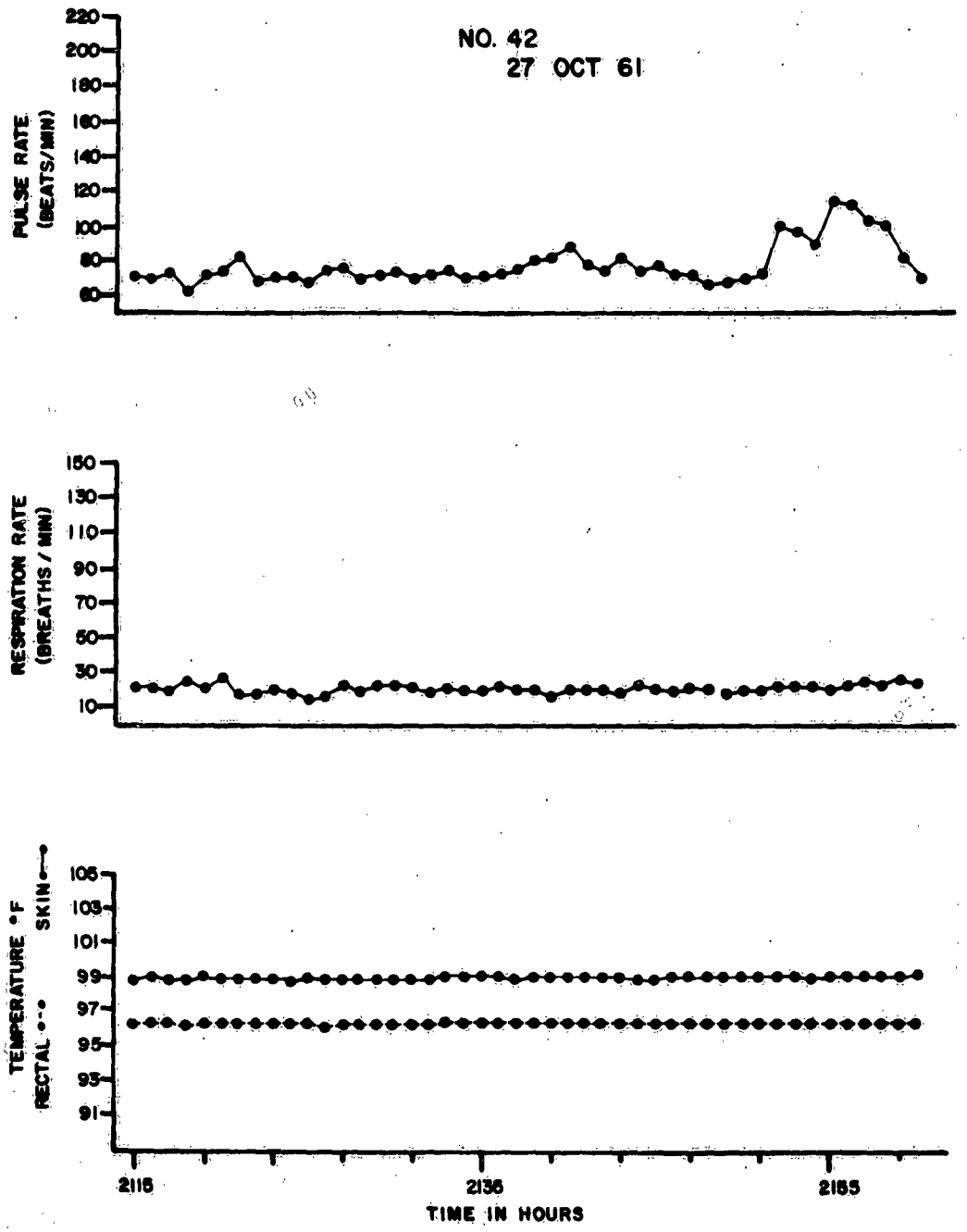
Physiological Data Oxygen Tolerance Test 03, First "Work Session"



Physiological Data Oxygen Tolerance Test 03, Second "Work Session"



Physiological Data Oxygen Tolerance Test 03, Third "Work Session"



Physiological Data Oxygen Tolerance Test 03, Fourth "Work Session"

SUBJECT NO. 42
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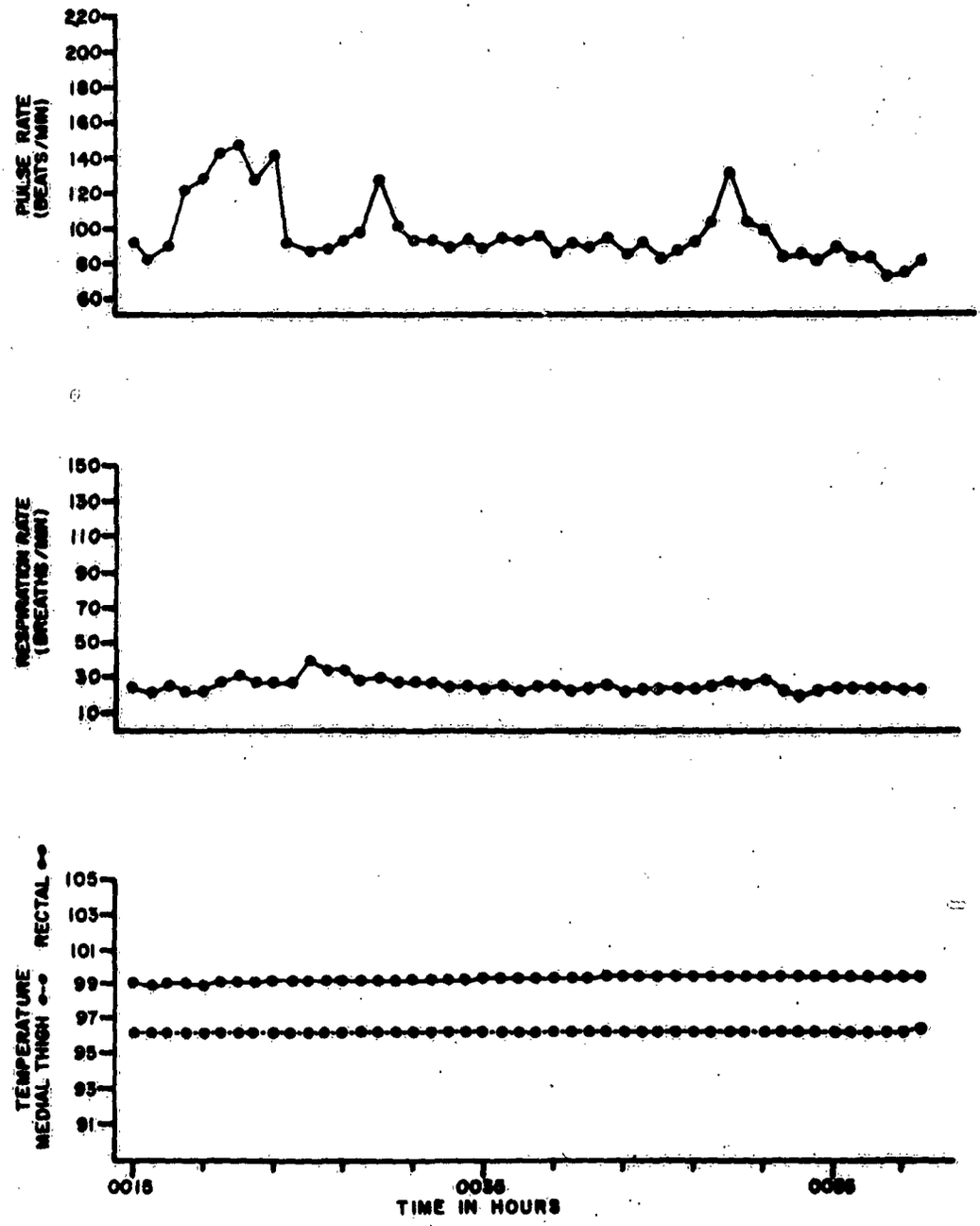

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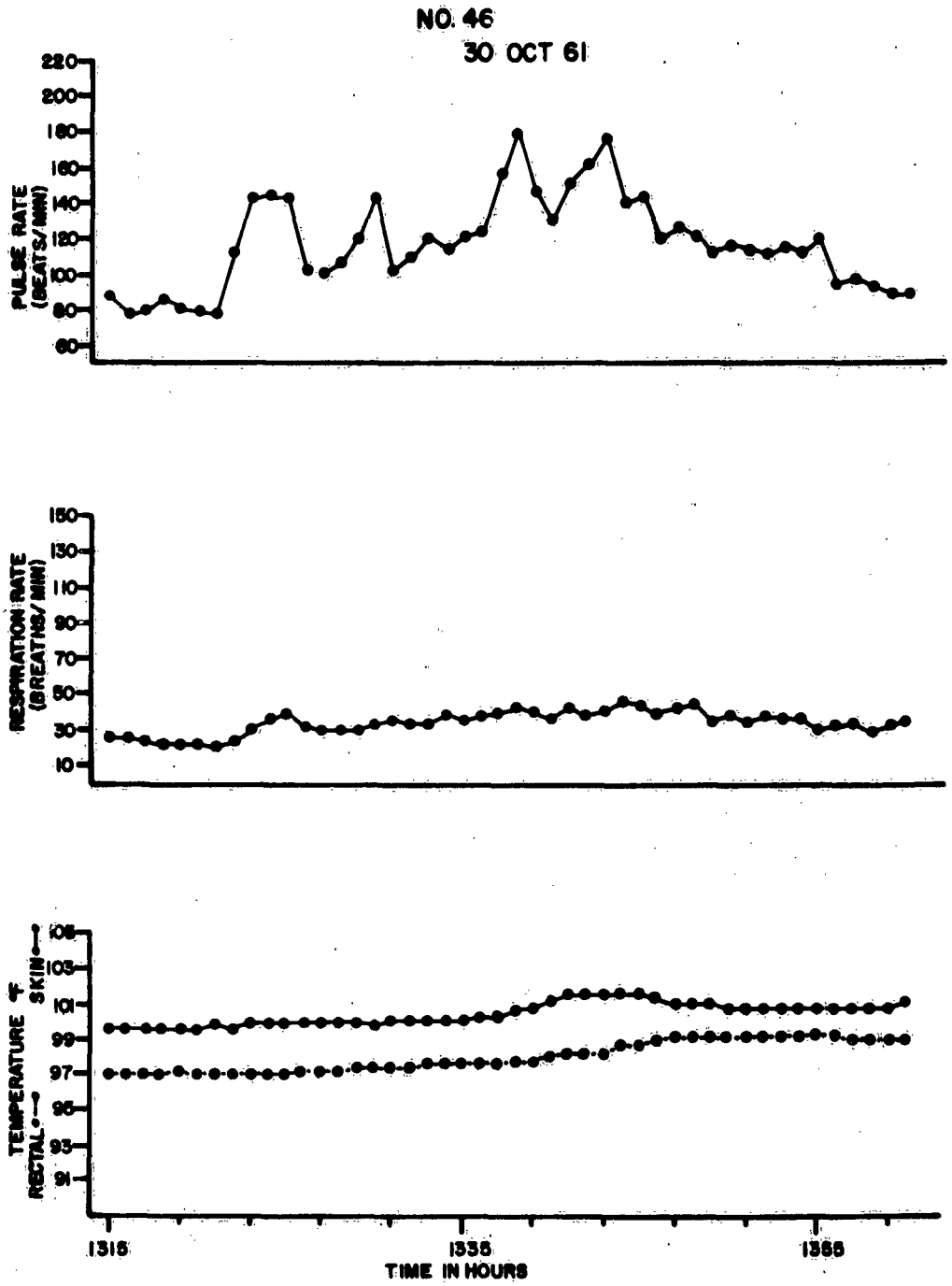

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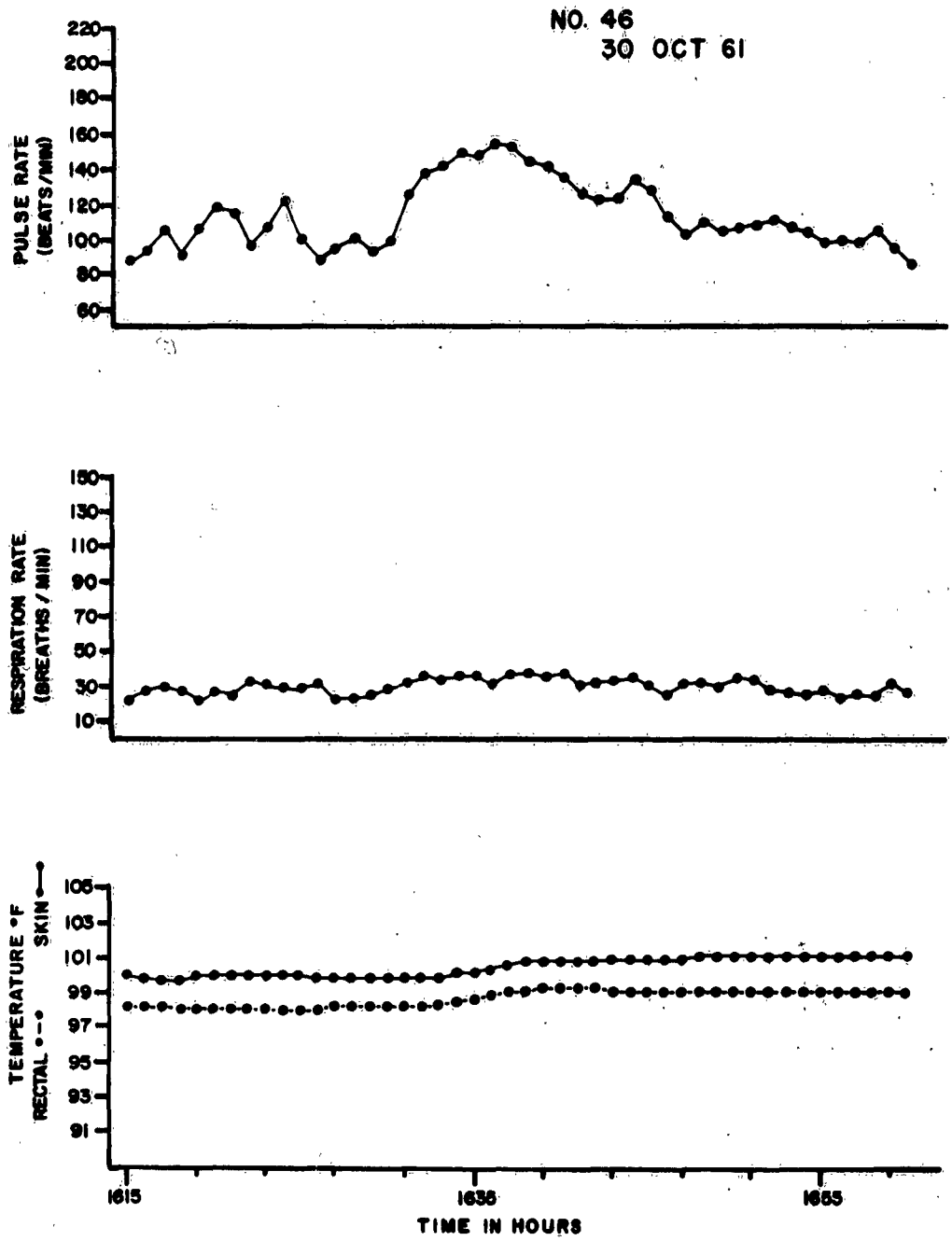

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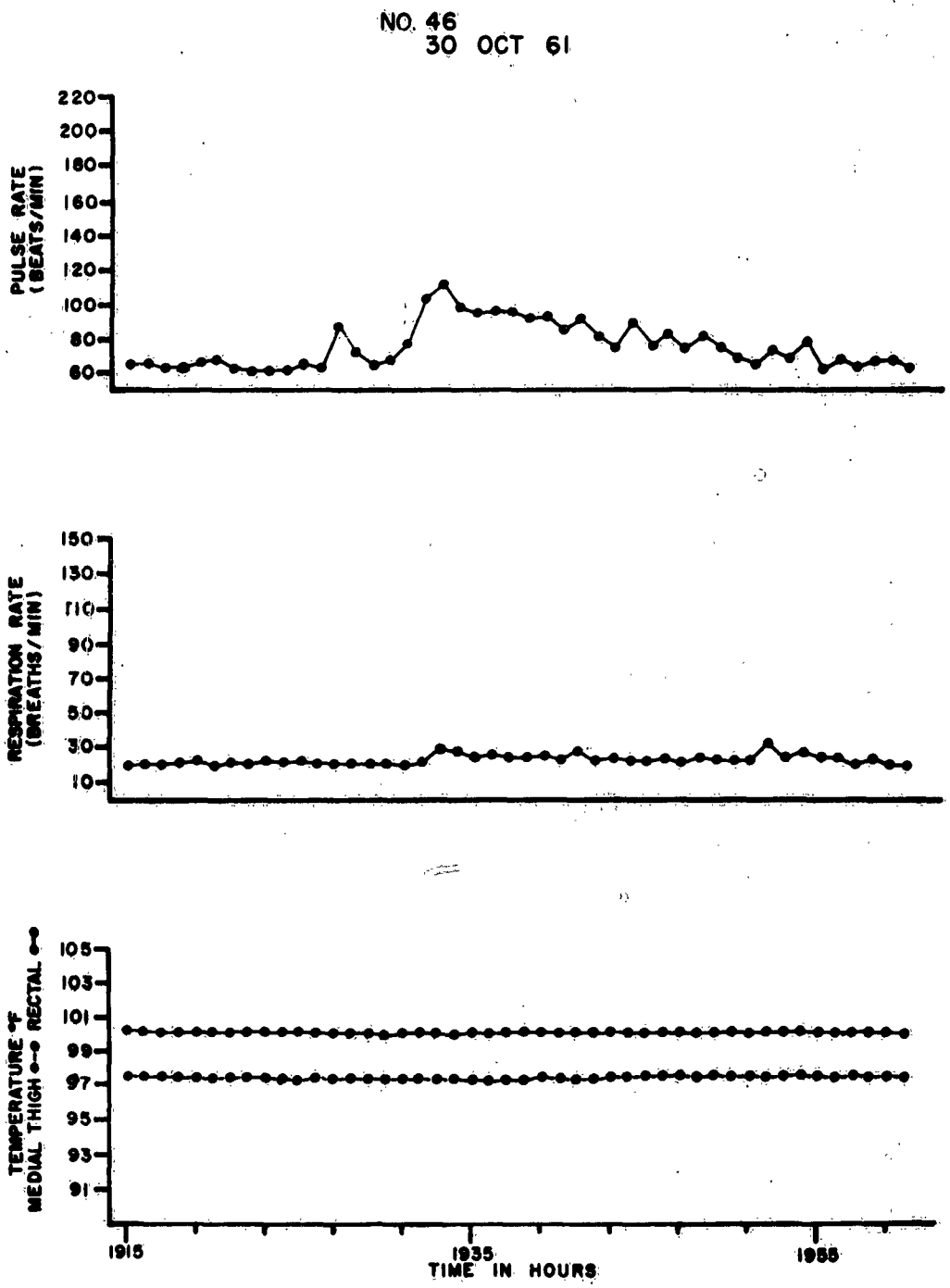

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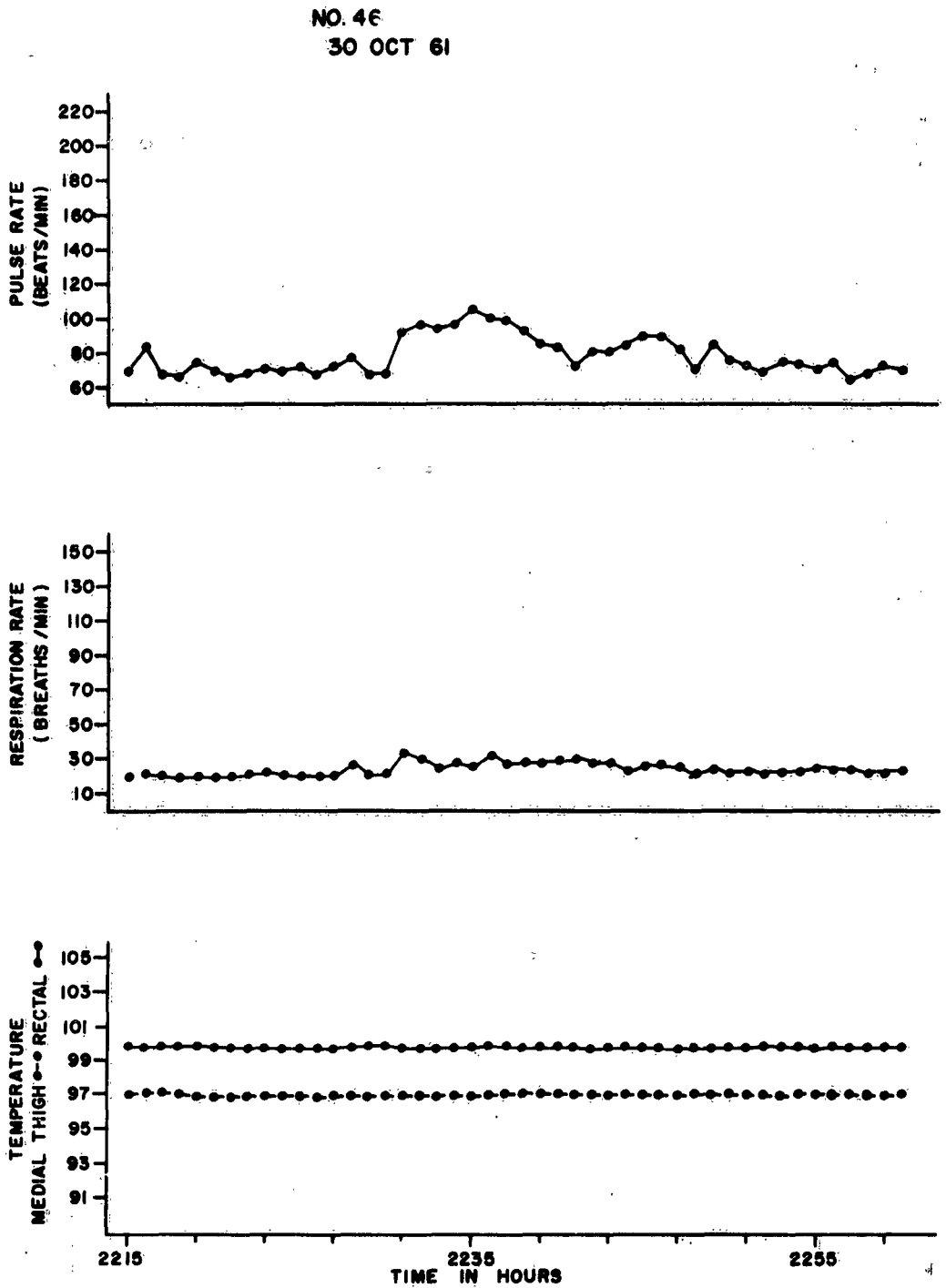

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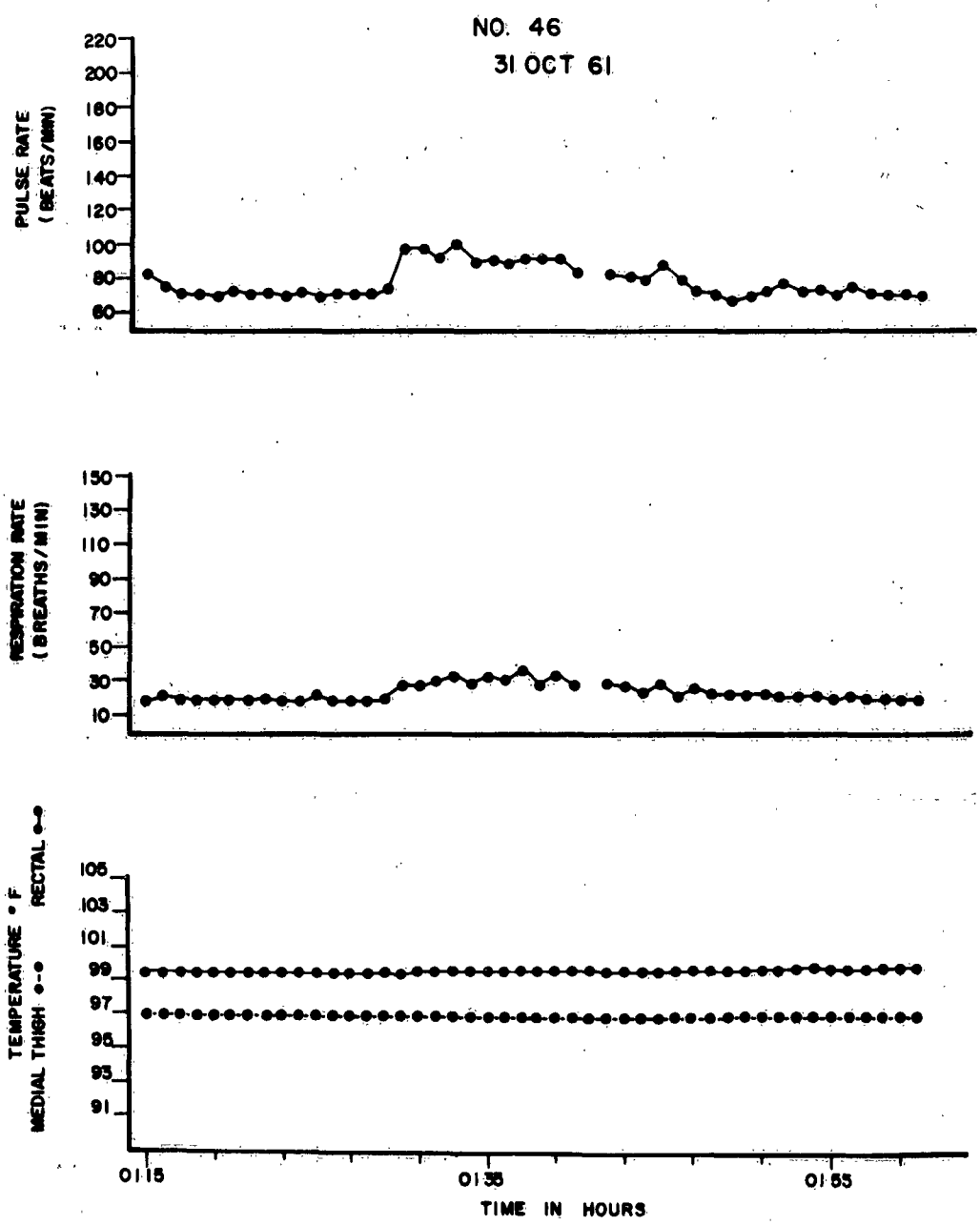

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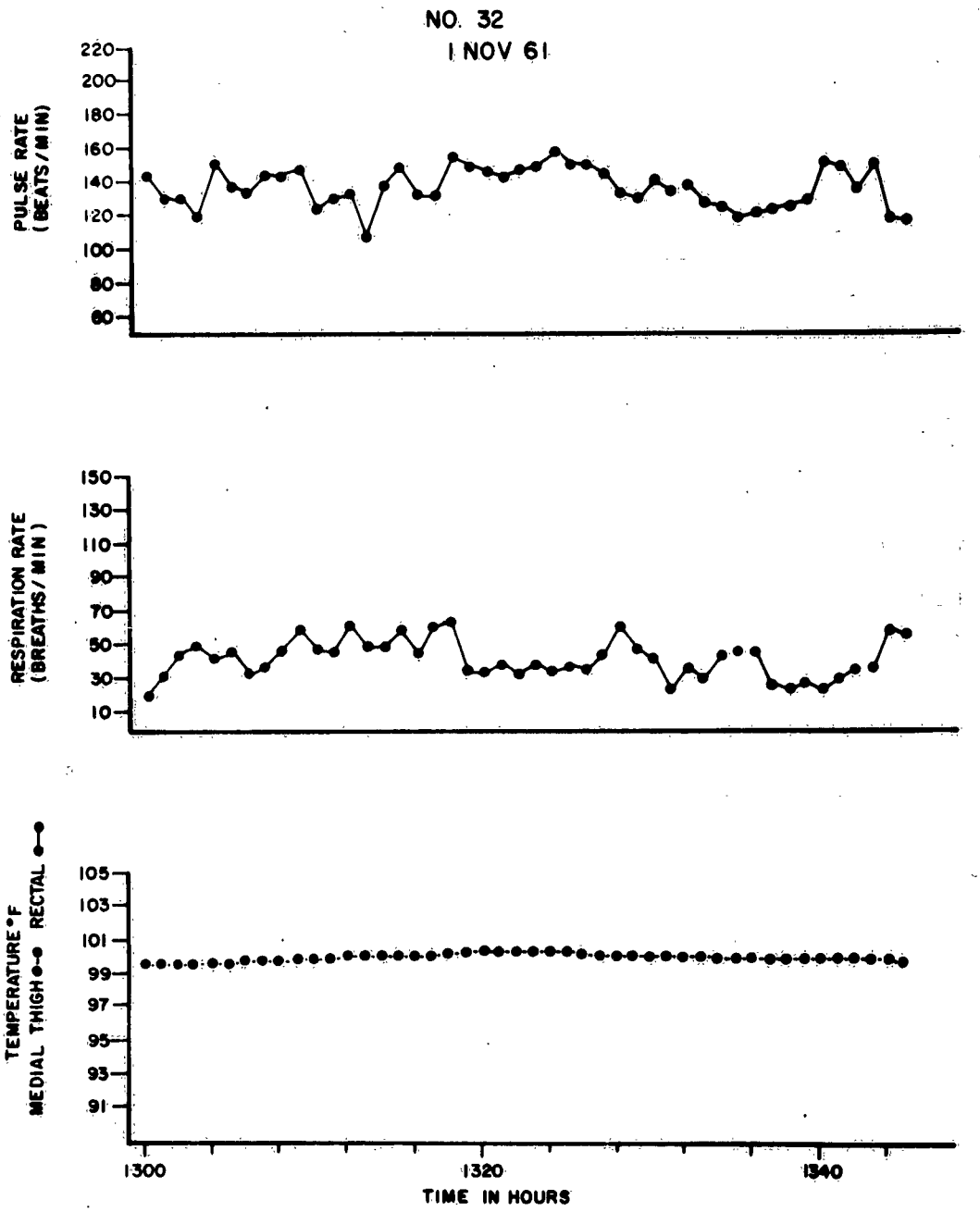

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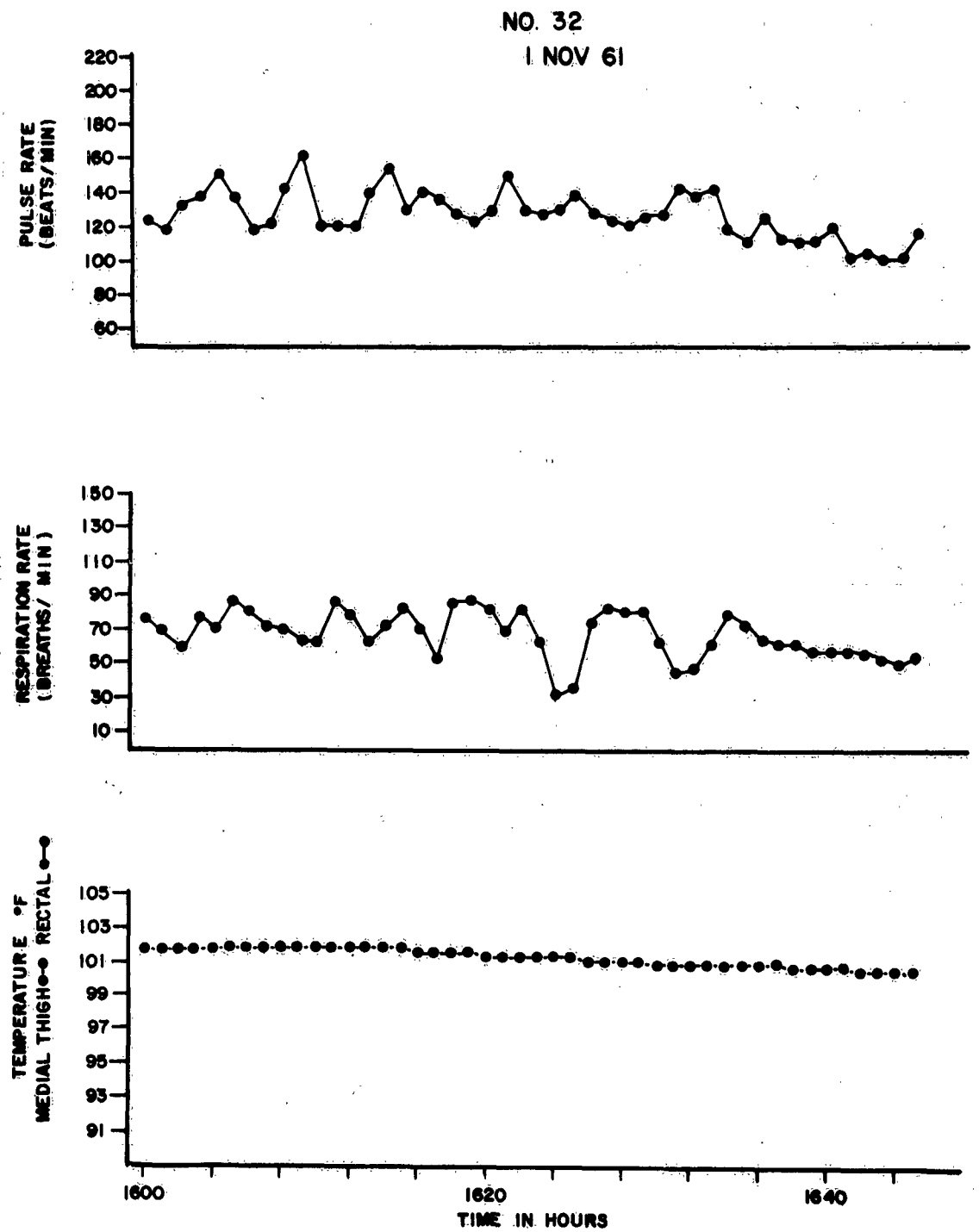

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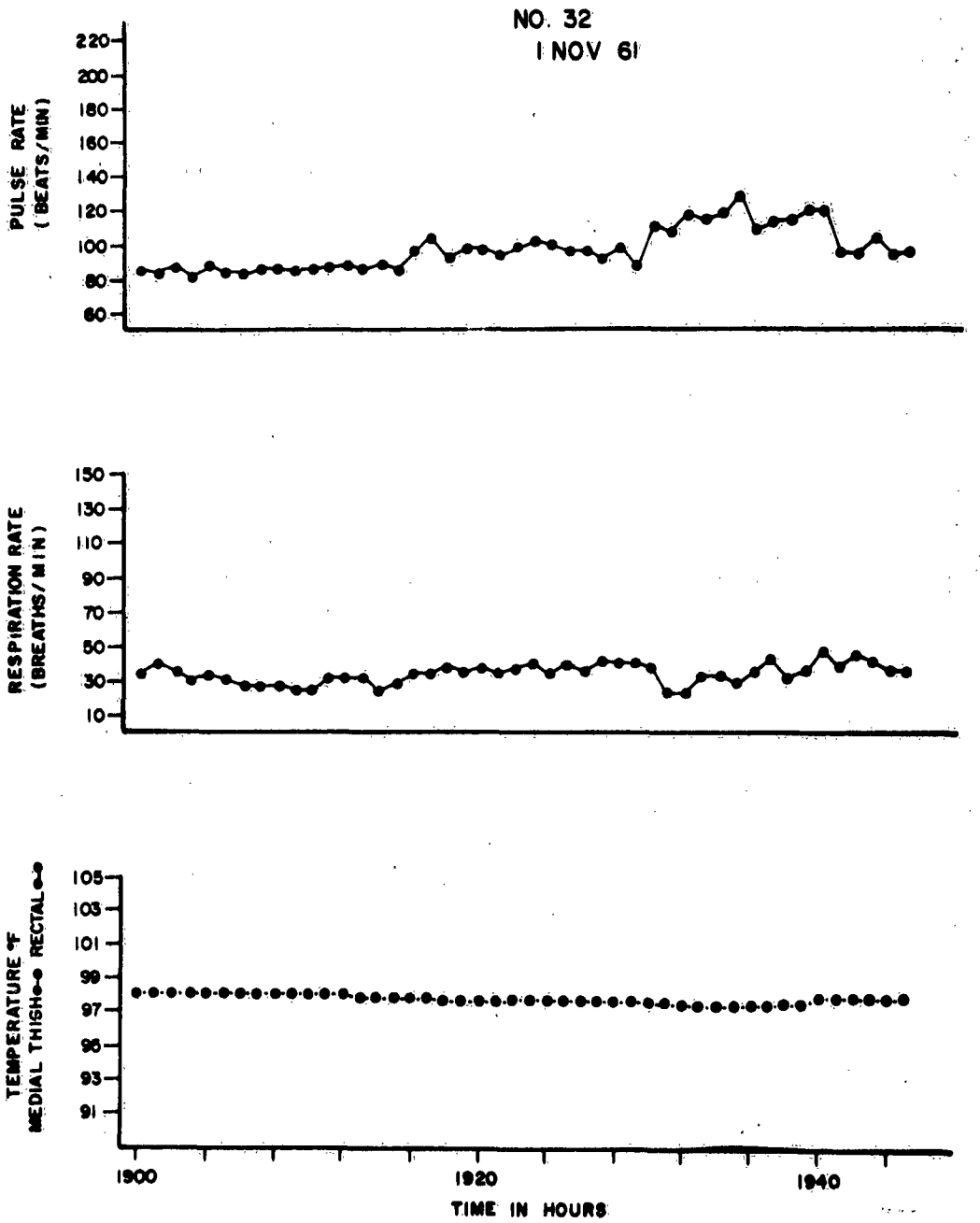

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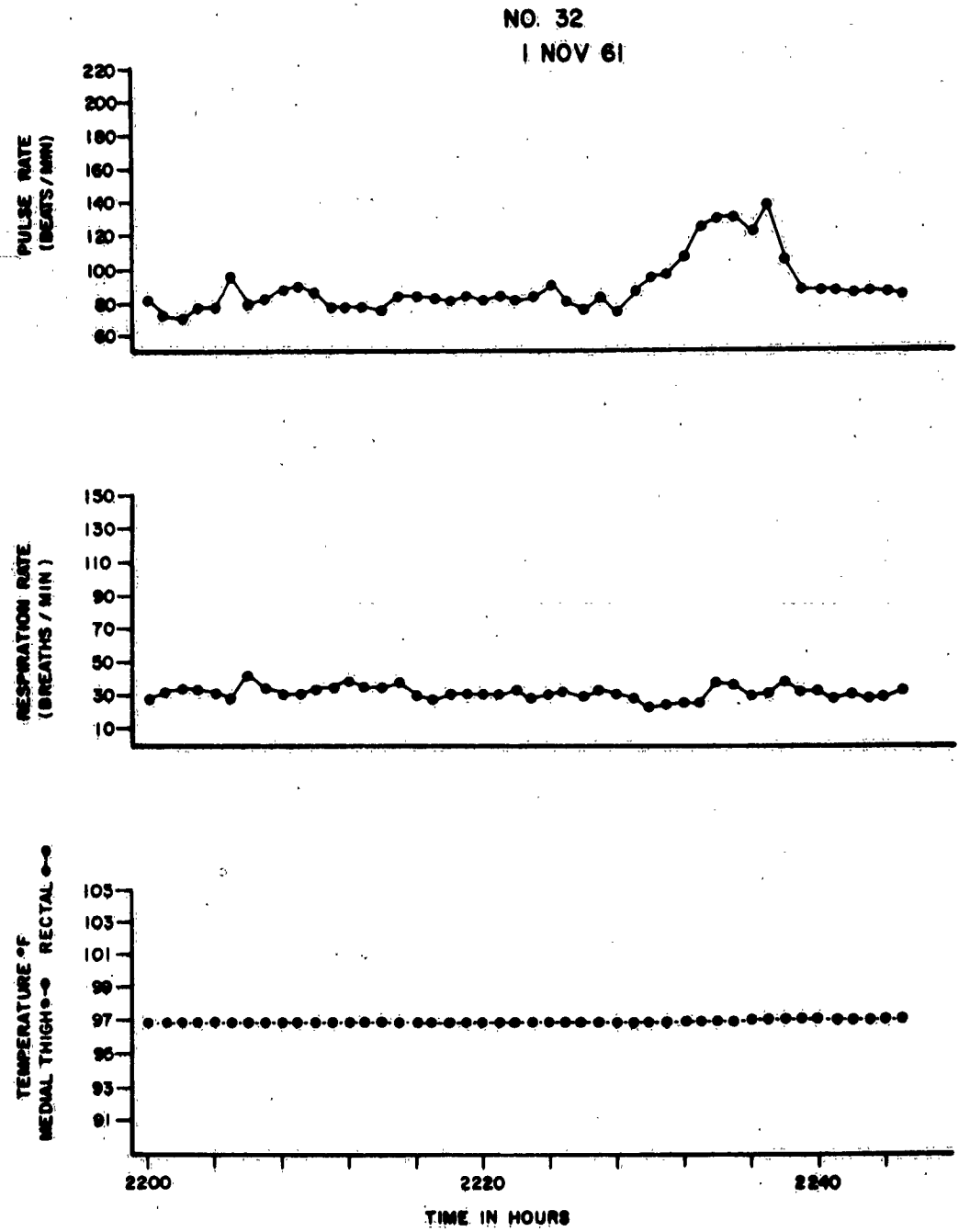

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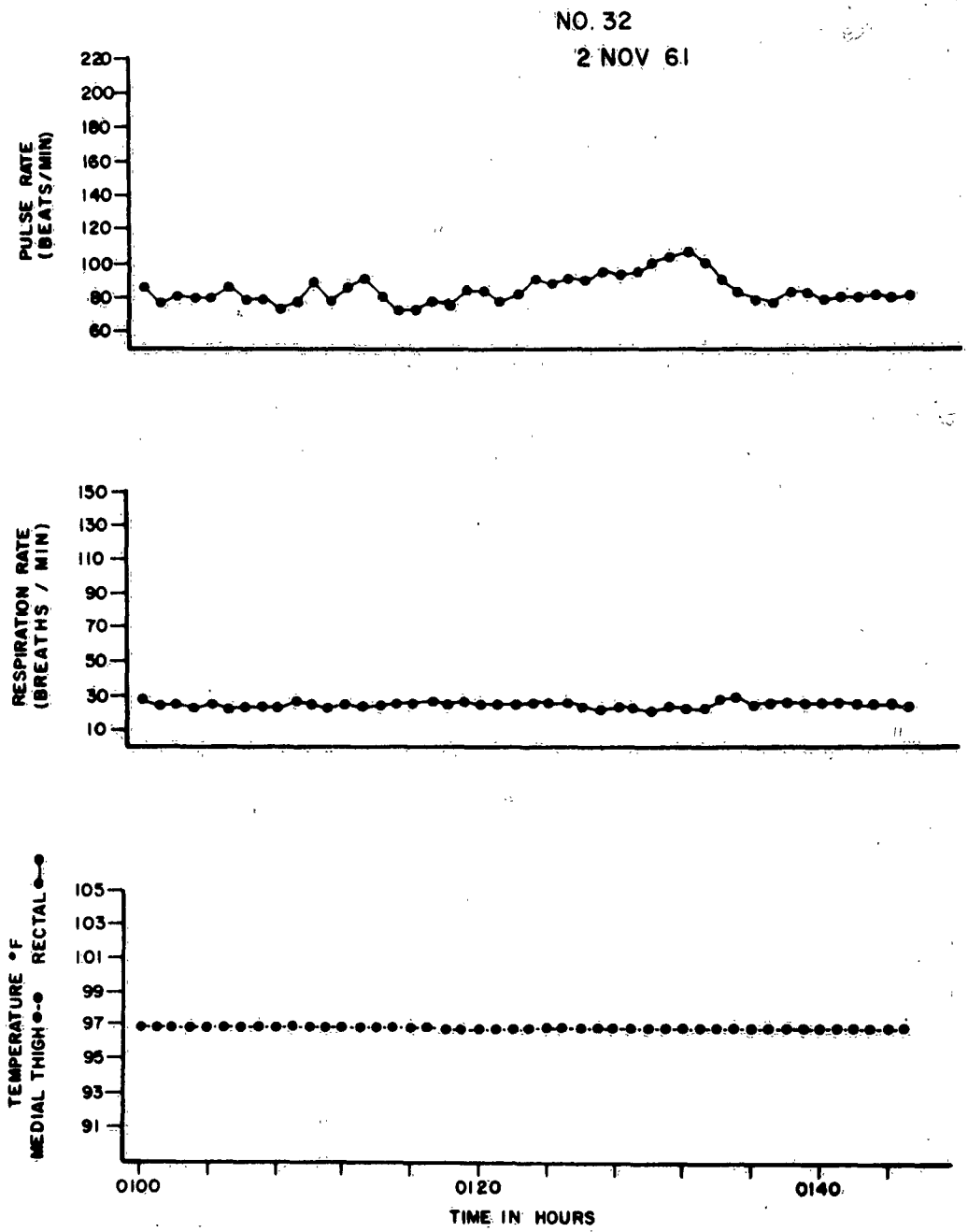

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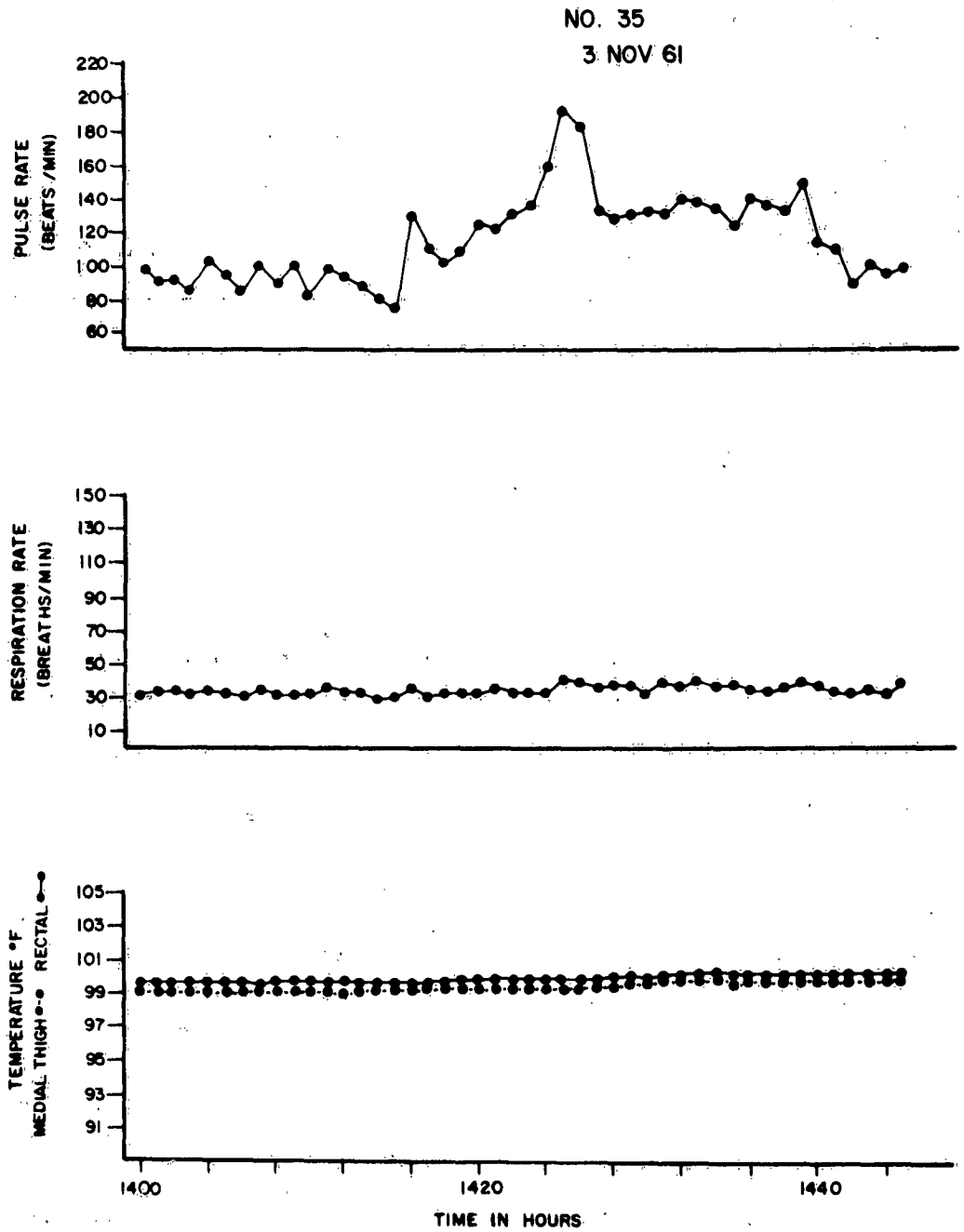

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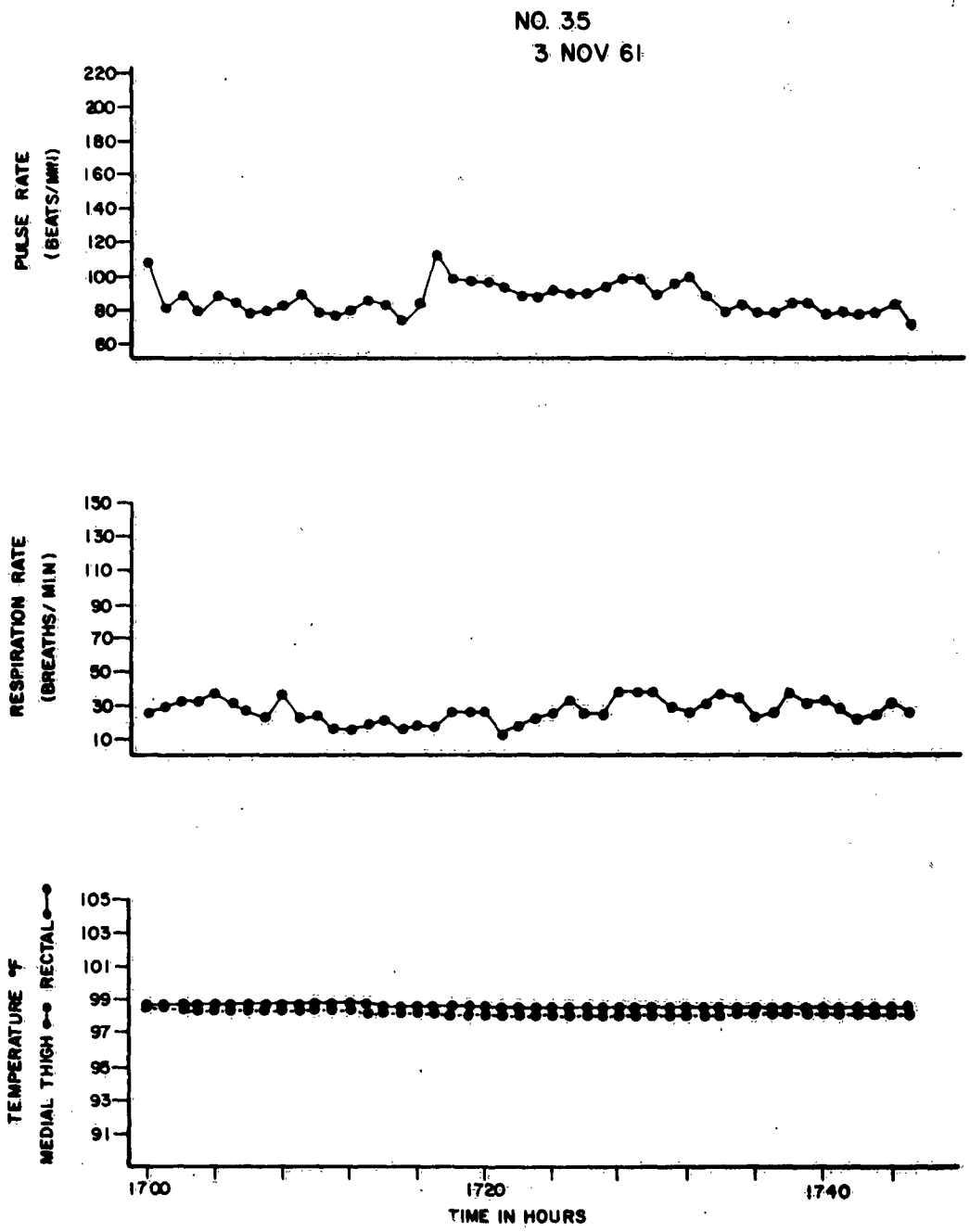

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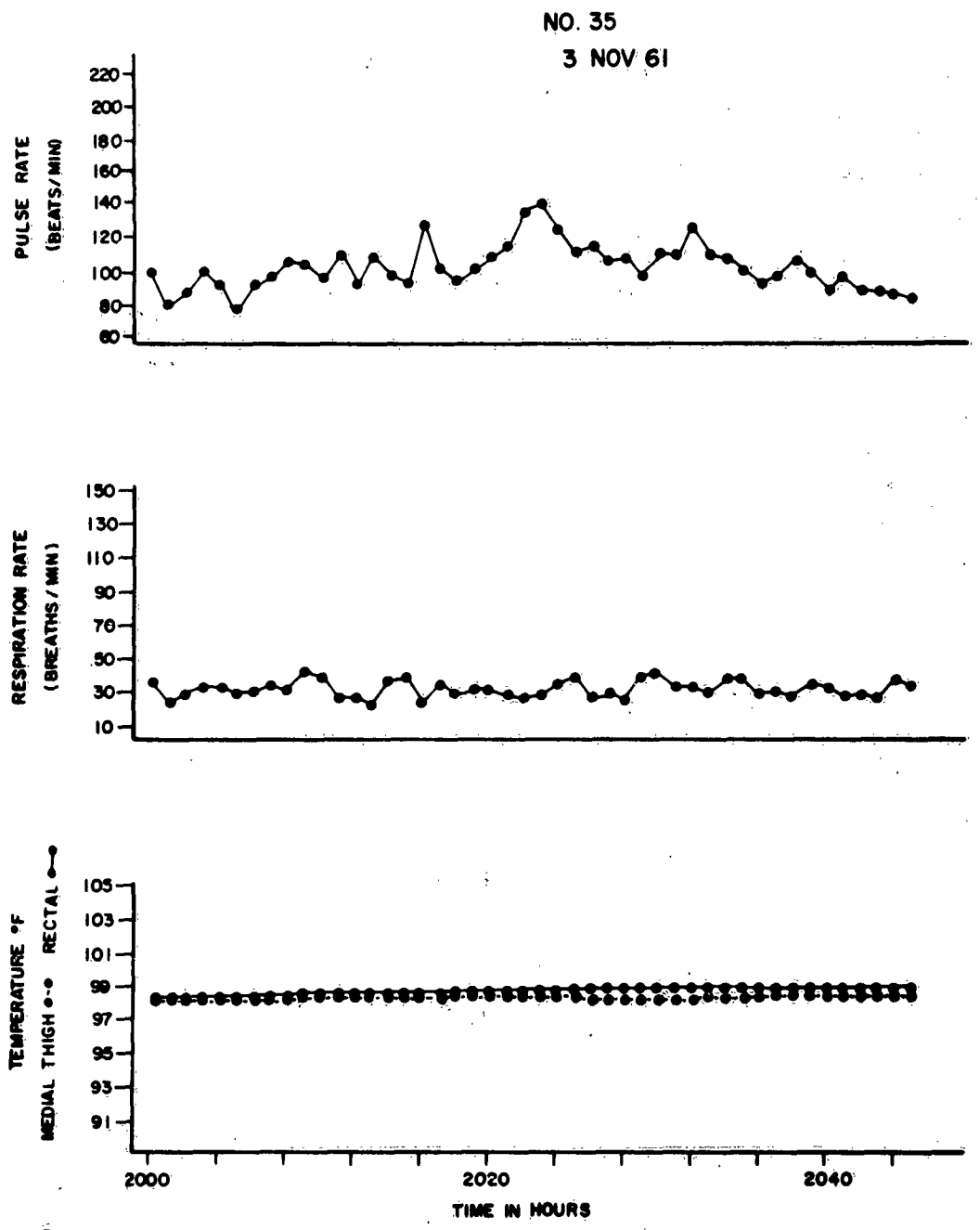

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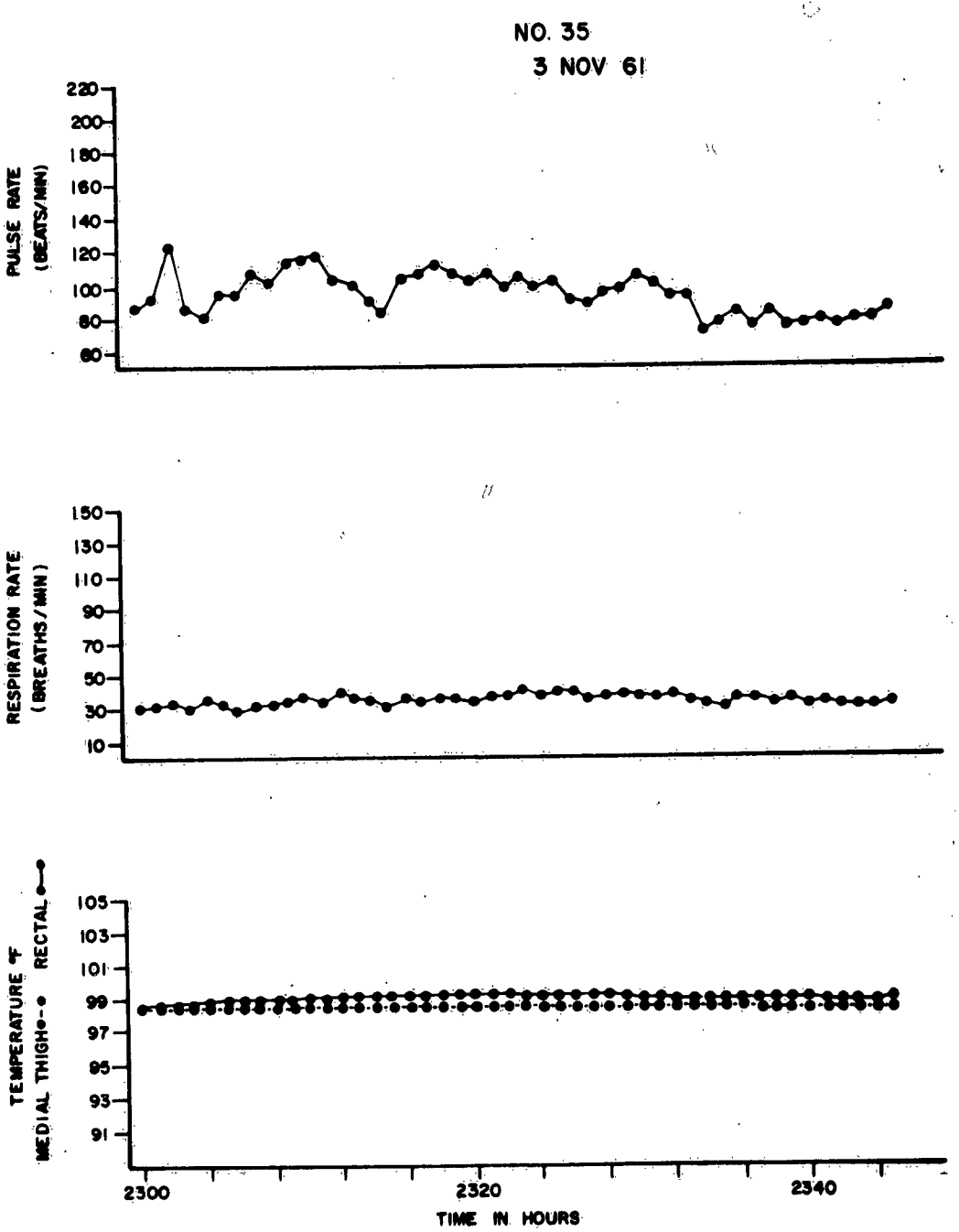

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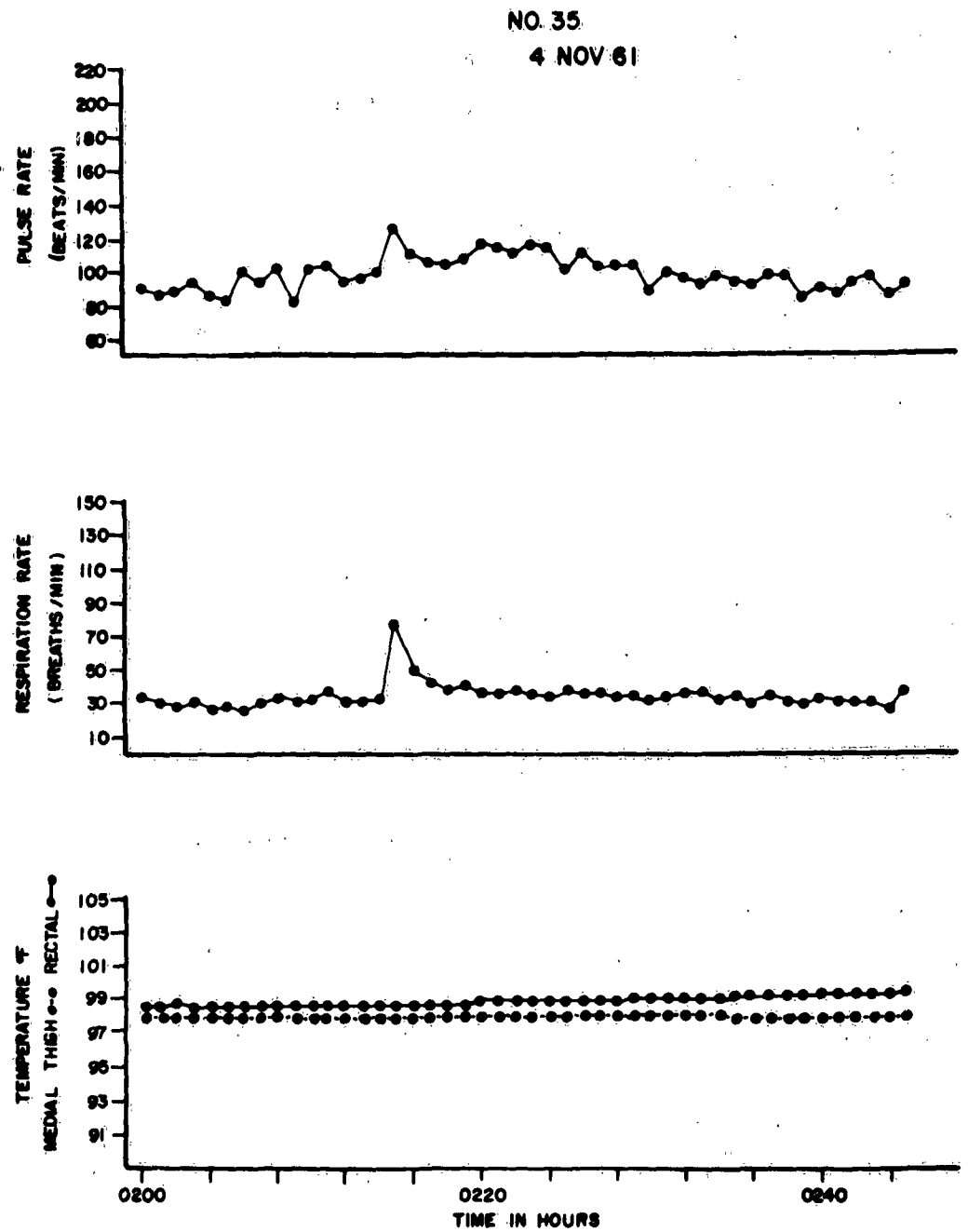
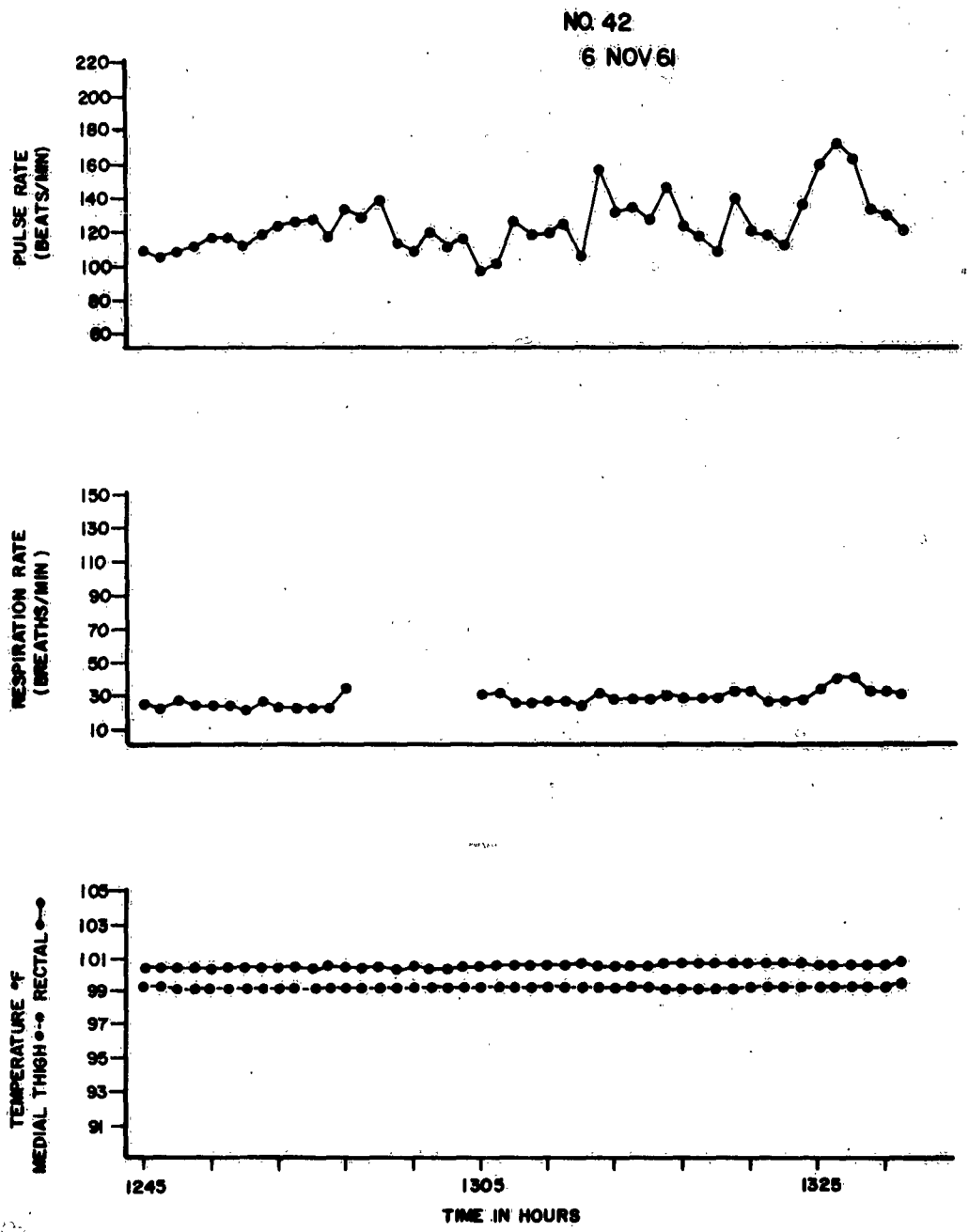


Physiological Data Oxygen Tolerance Test 06, Fifth "Work Session"



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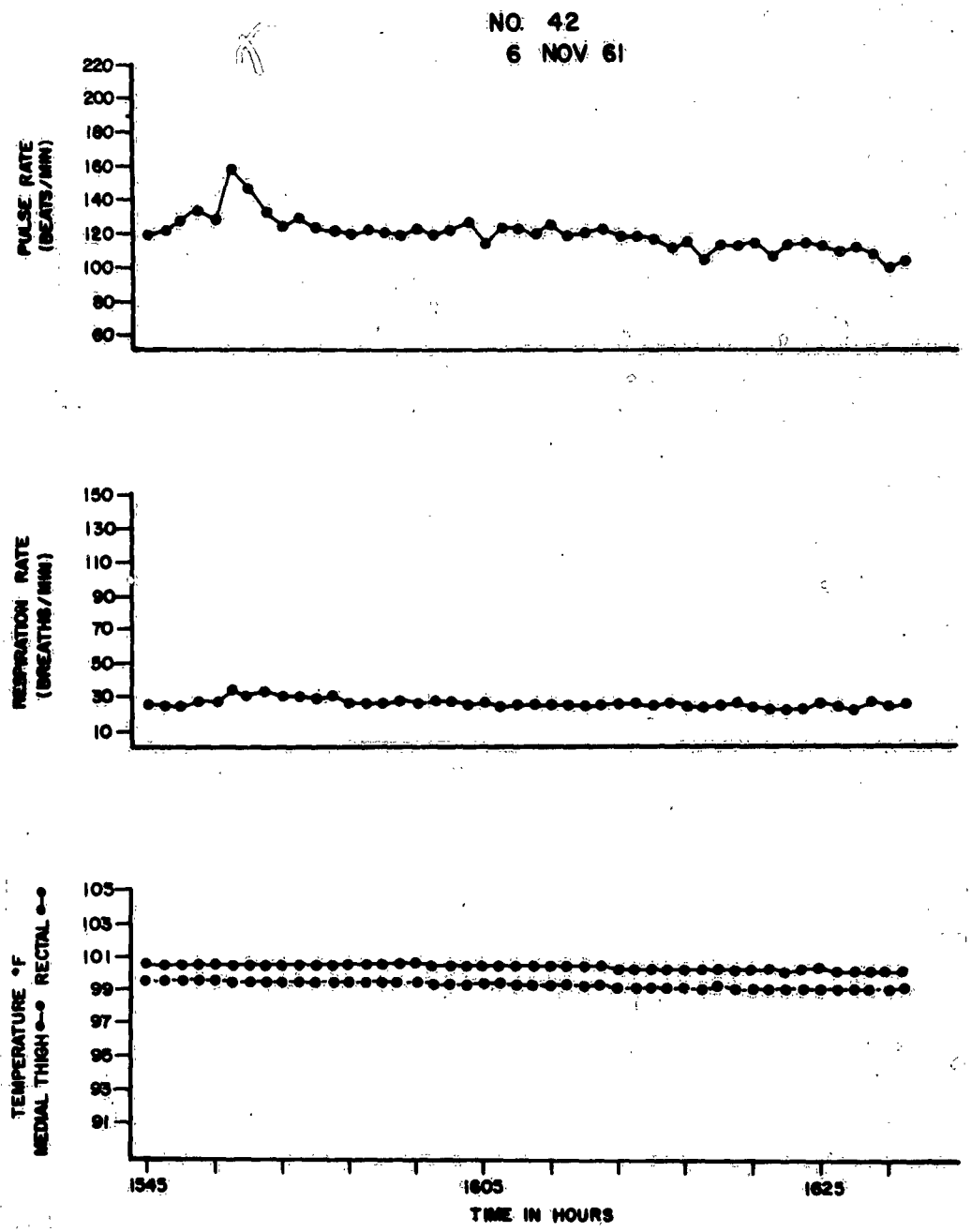

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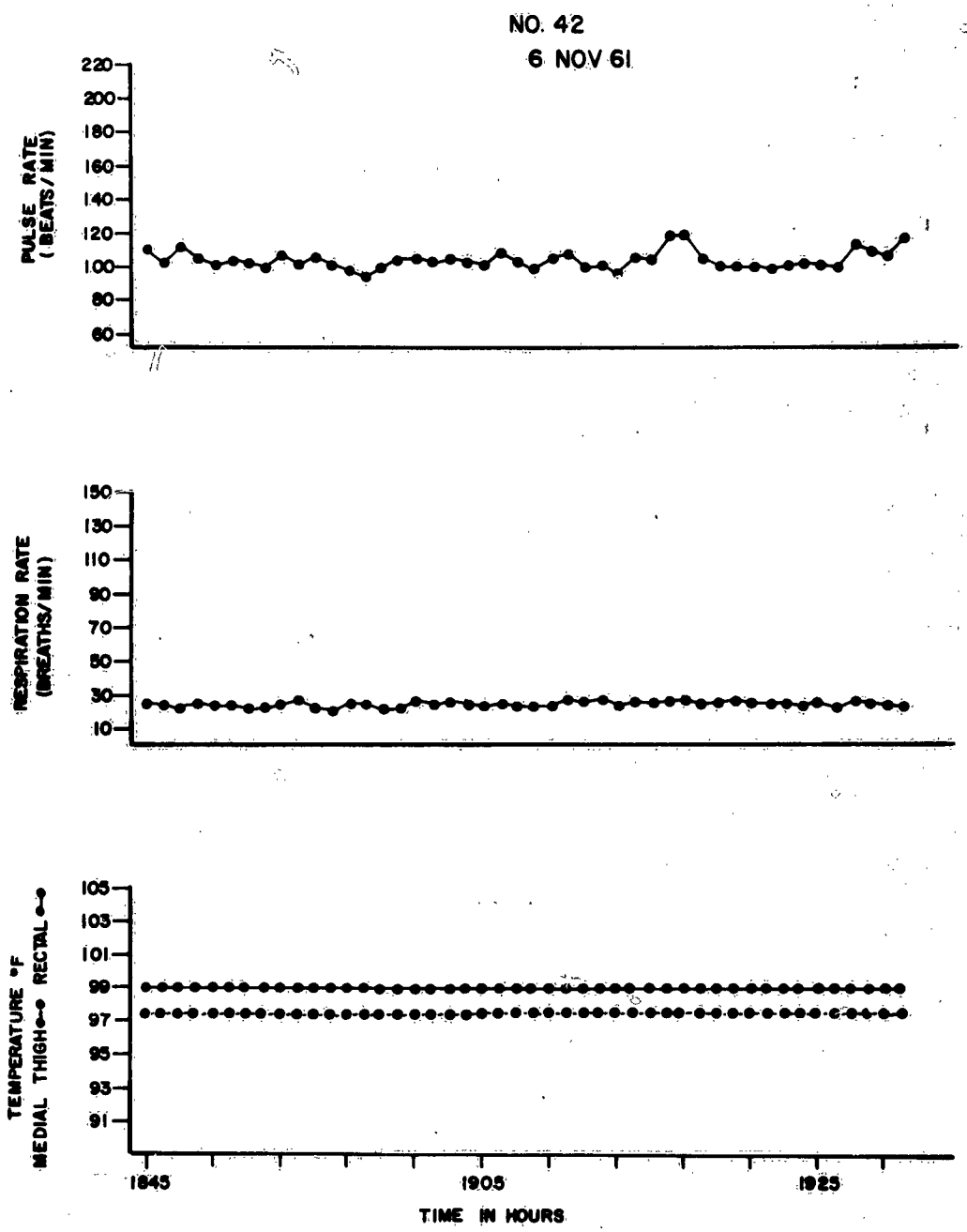

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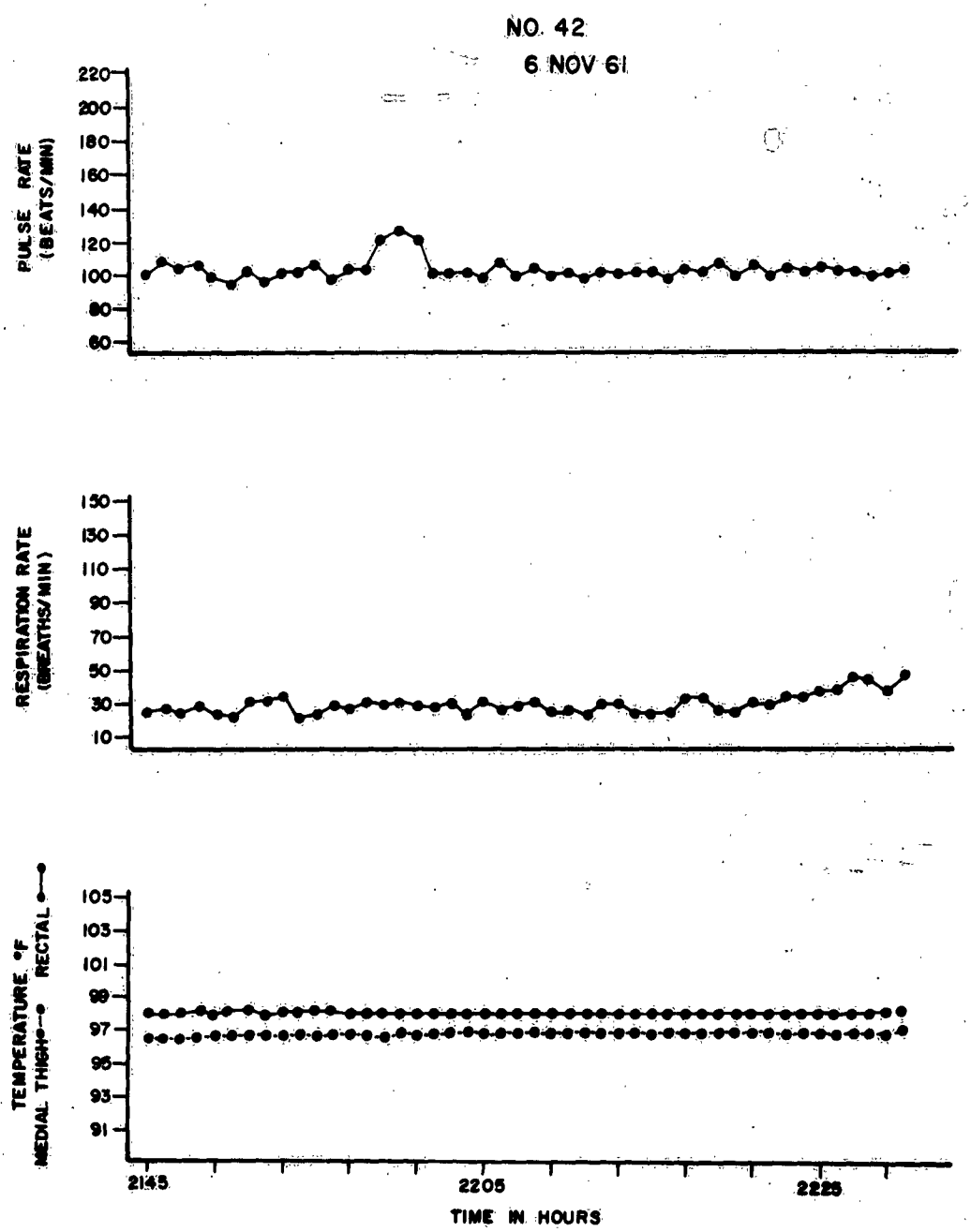

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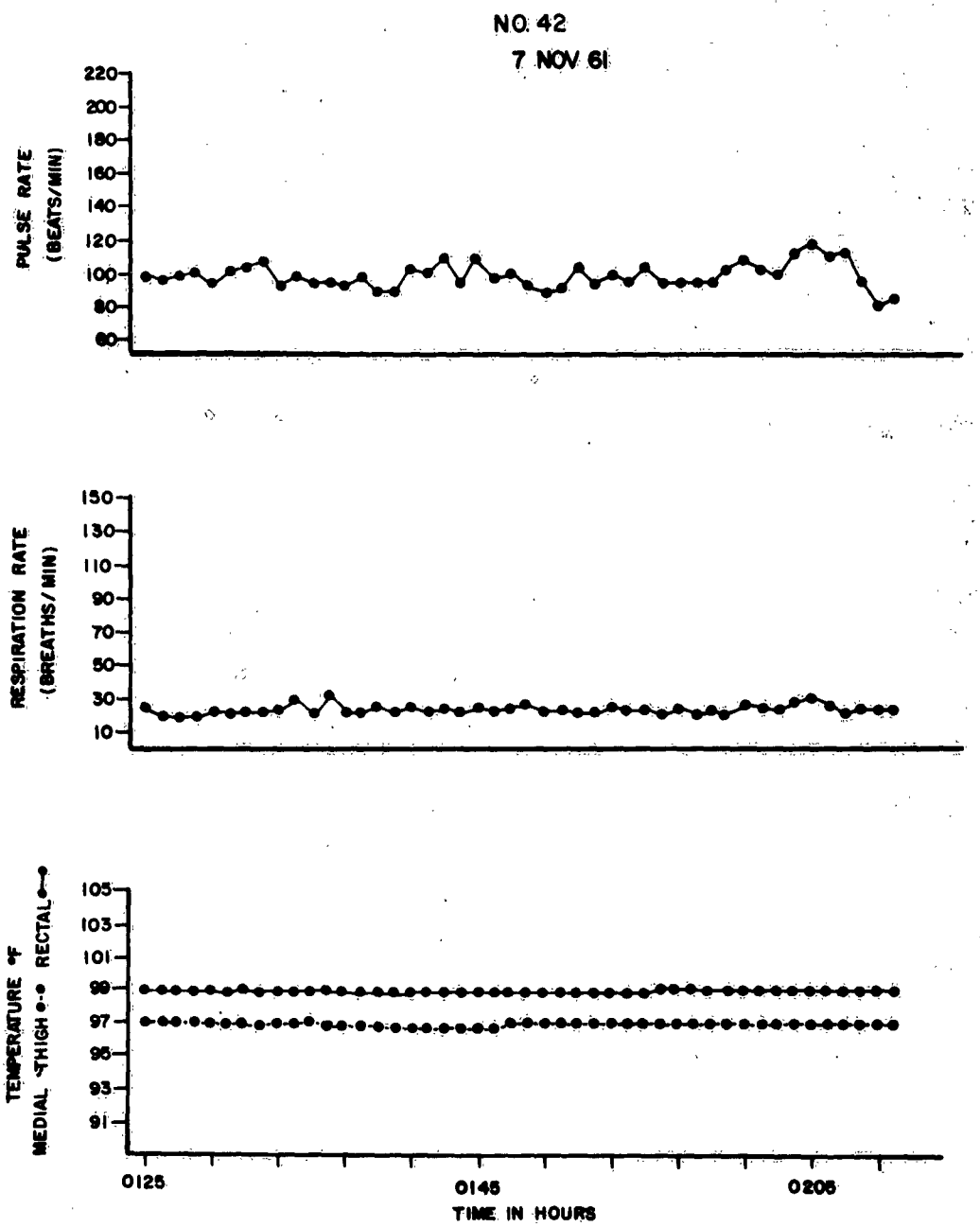
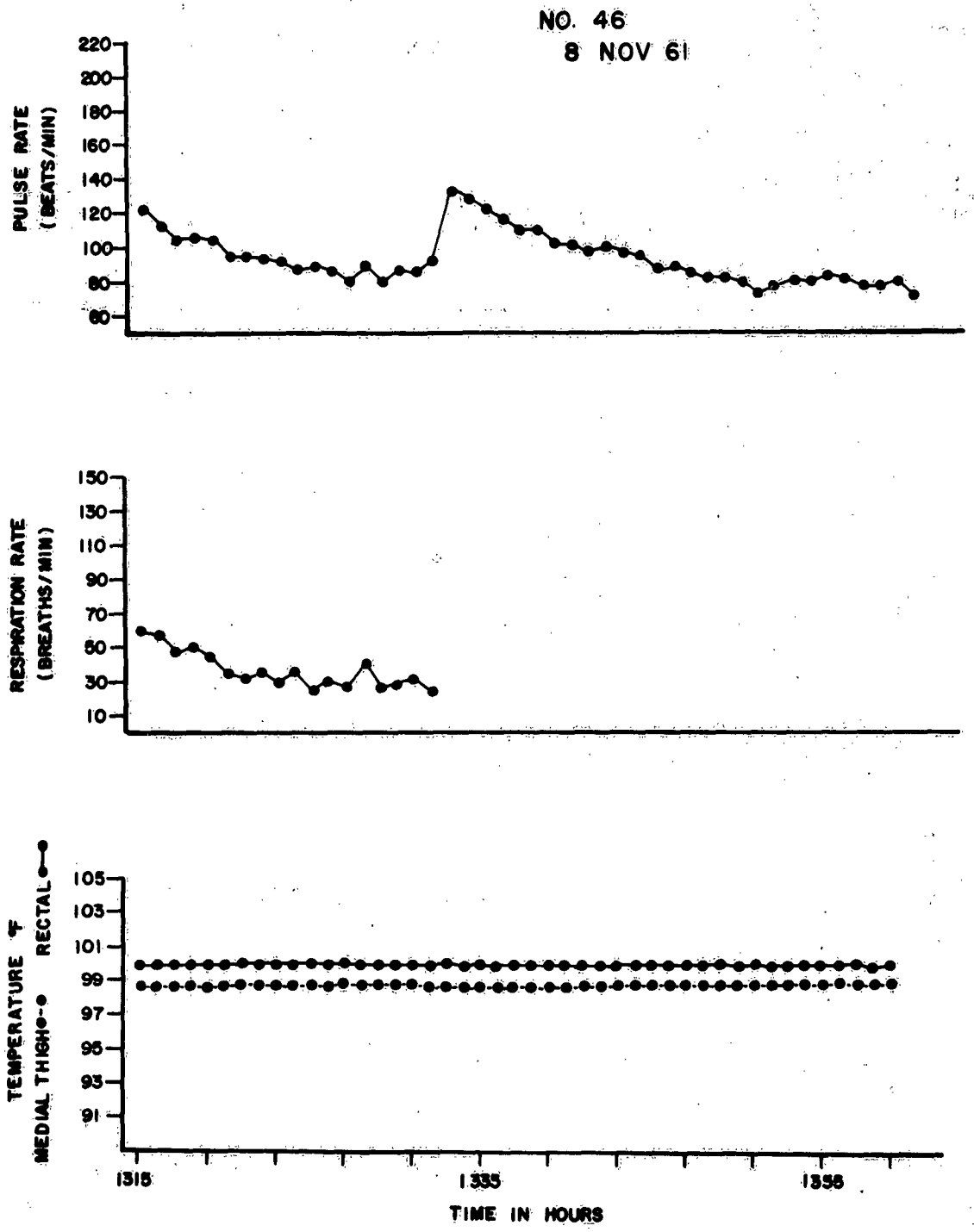
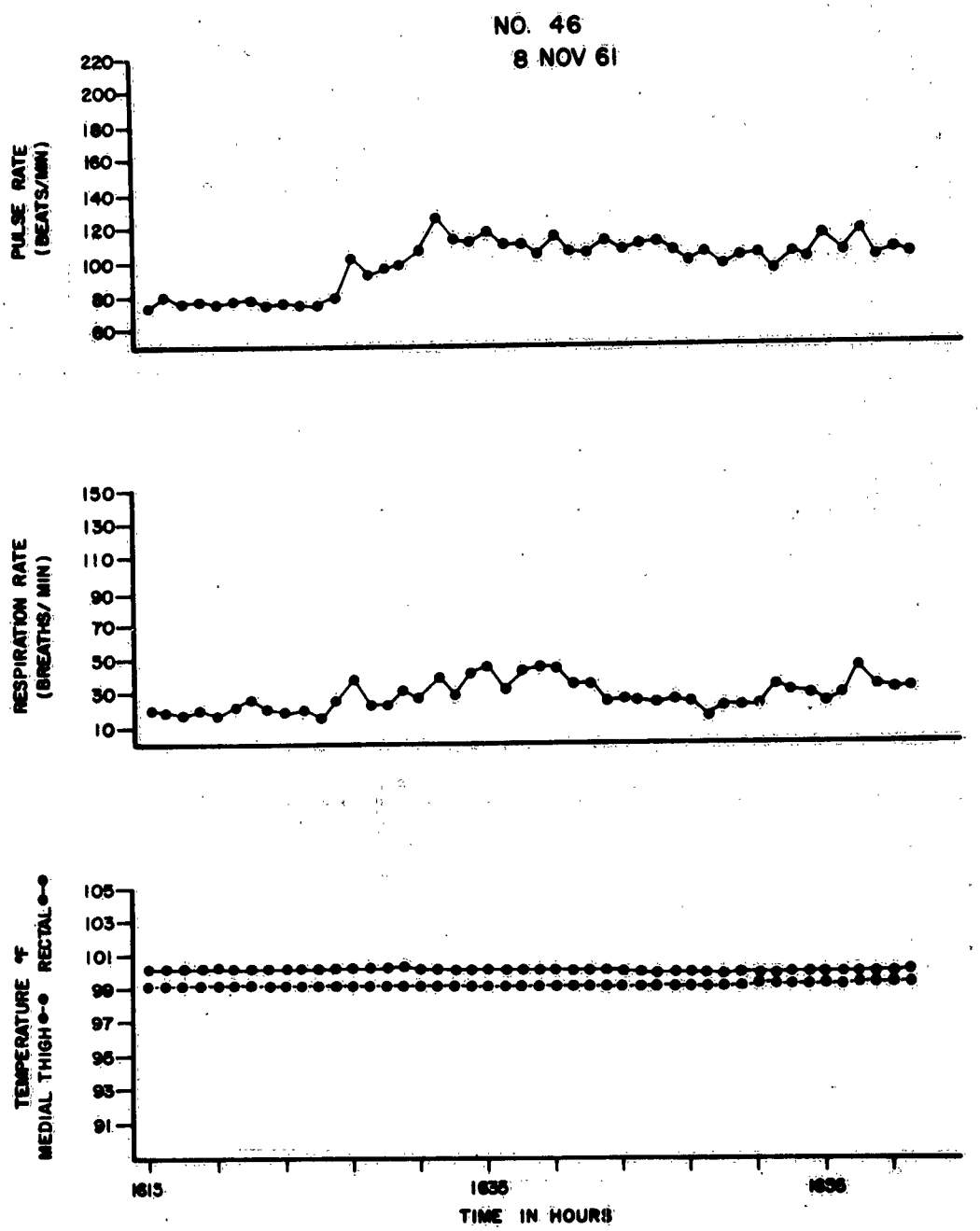


Physiological Data Oxygen Tolerance Test 07, Fifth "Work Session"



Physiological Data Oxygen Tolerance Test 08, First "Work Session"



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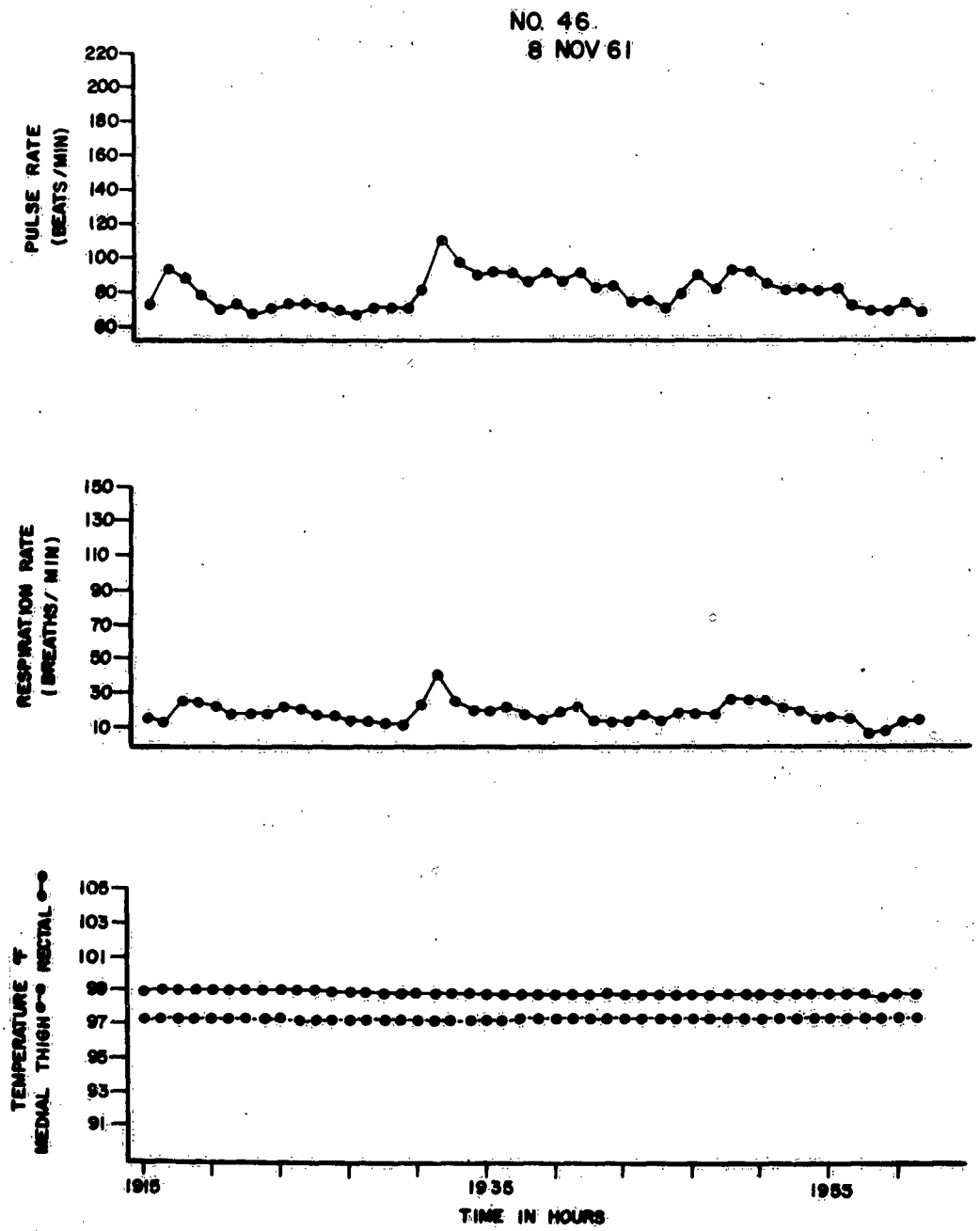

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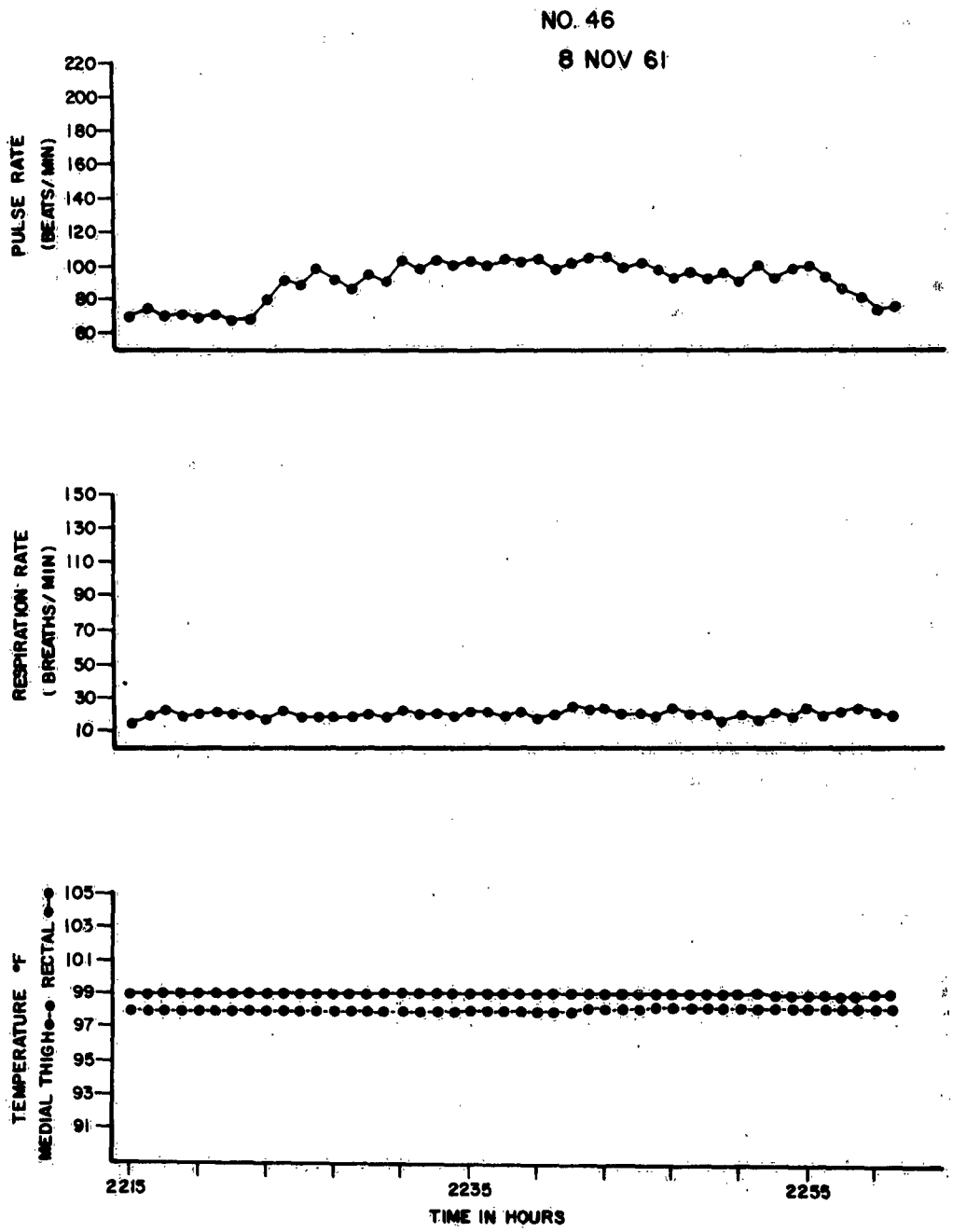
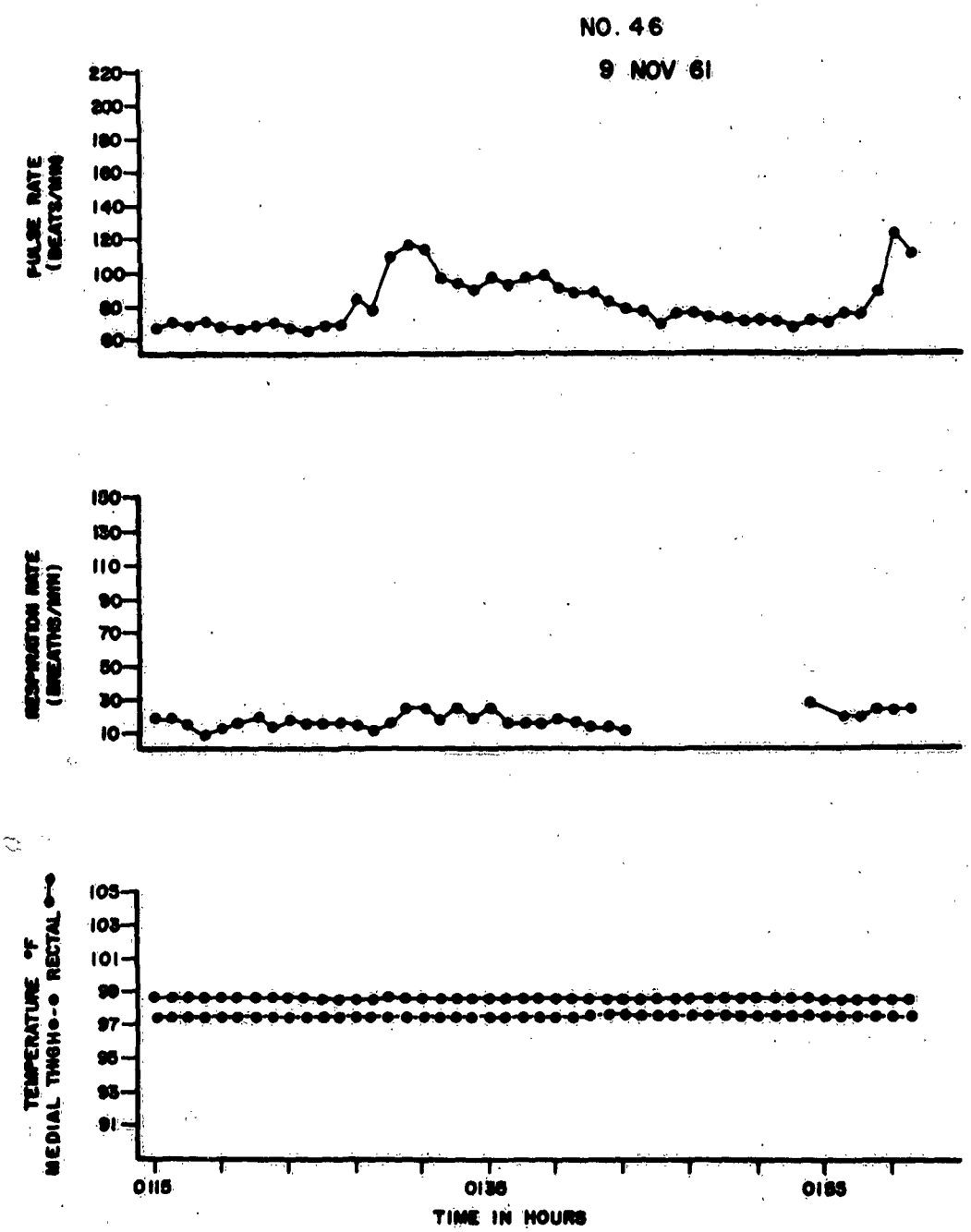


Physiological Data Oxygen Tolerance Test 08, Fourth "Work Session"

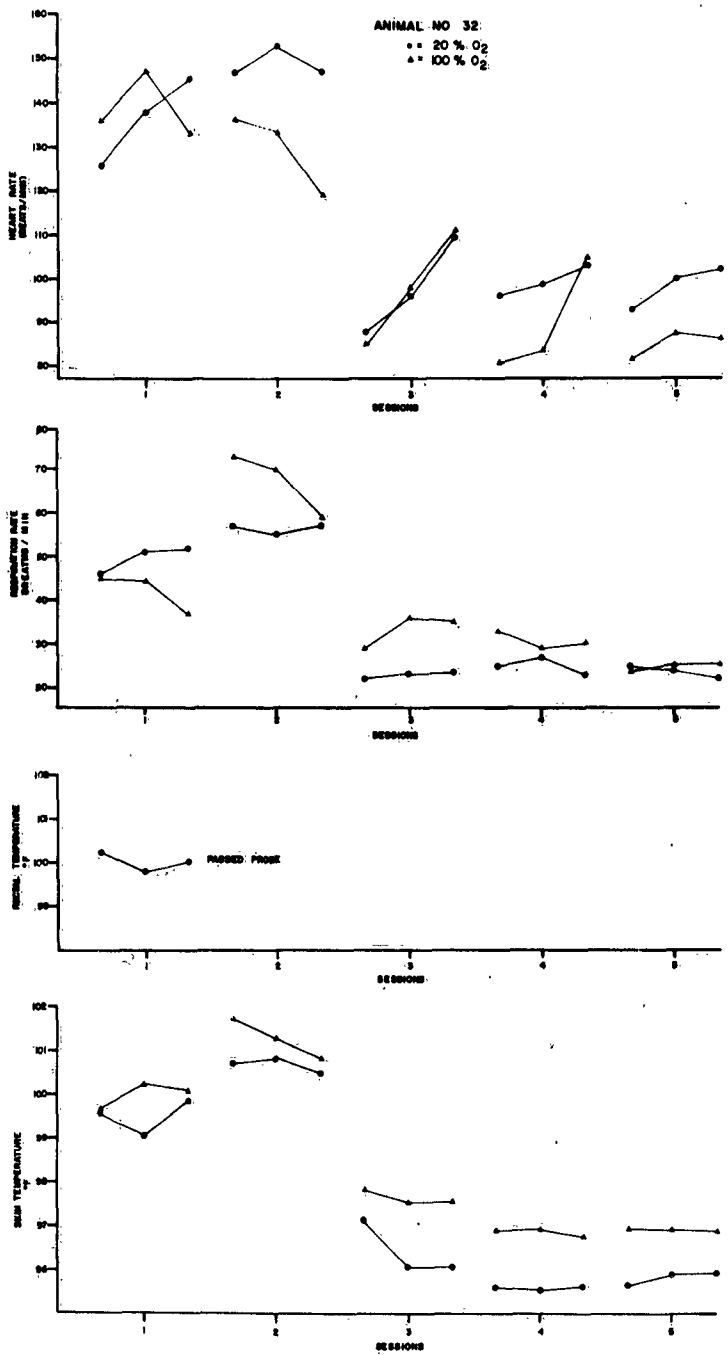


Physiological Data Oxygen Tolerance Test 08, Fifth "Work Session"

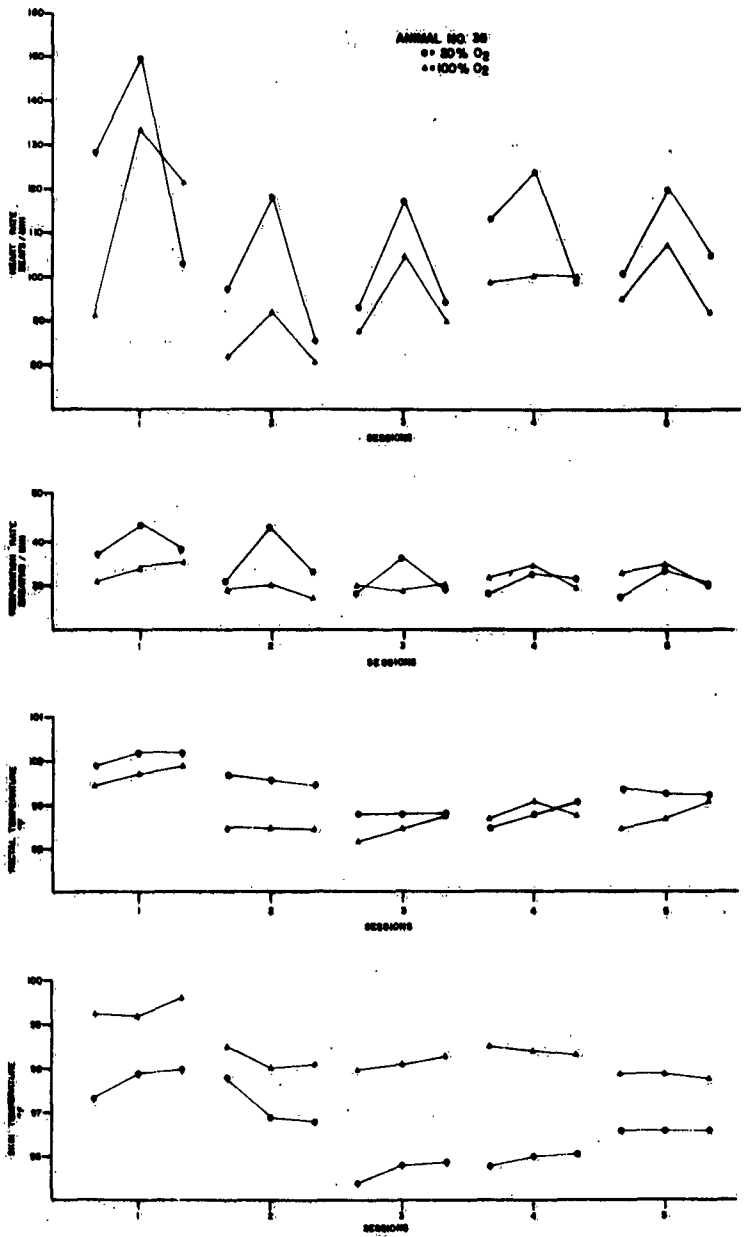
APPENDIX V

Comparison of Oxygen Tolerance Tests 1 and 5; 2 and 6;
7 and 3; and 8 and 4

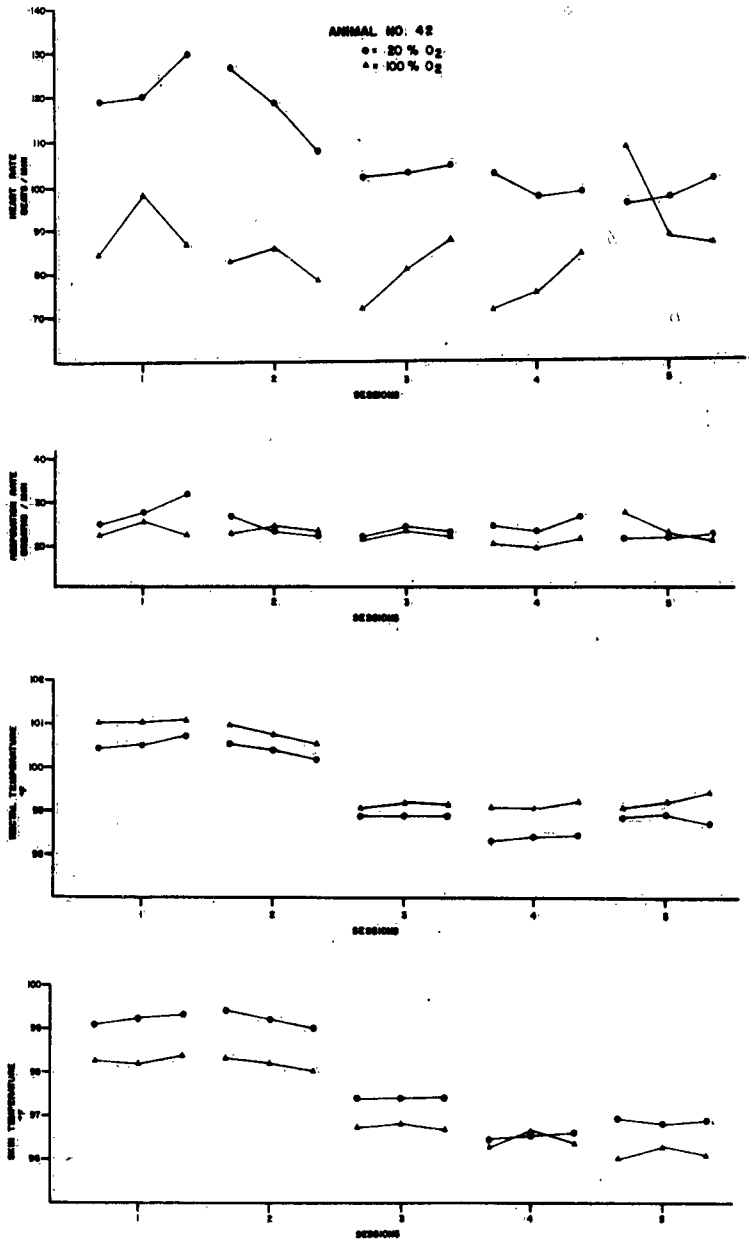
(Means of the Physiological Data for Five "Work Sessions")



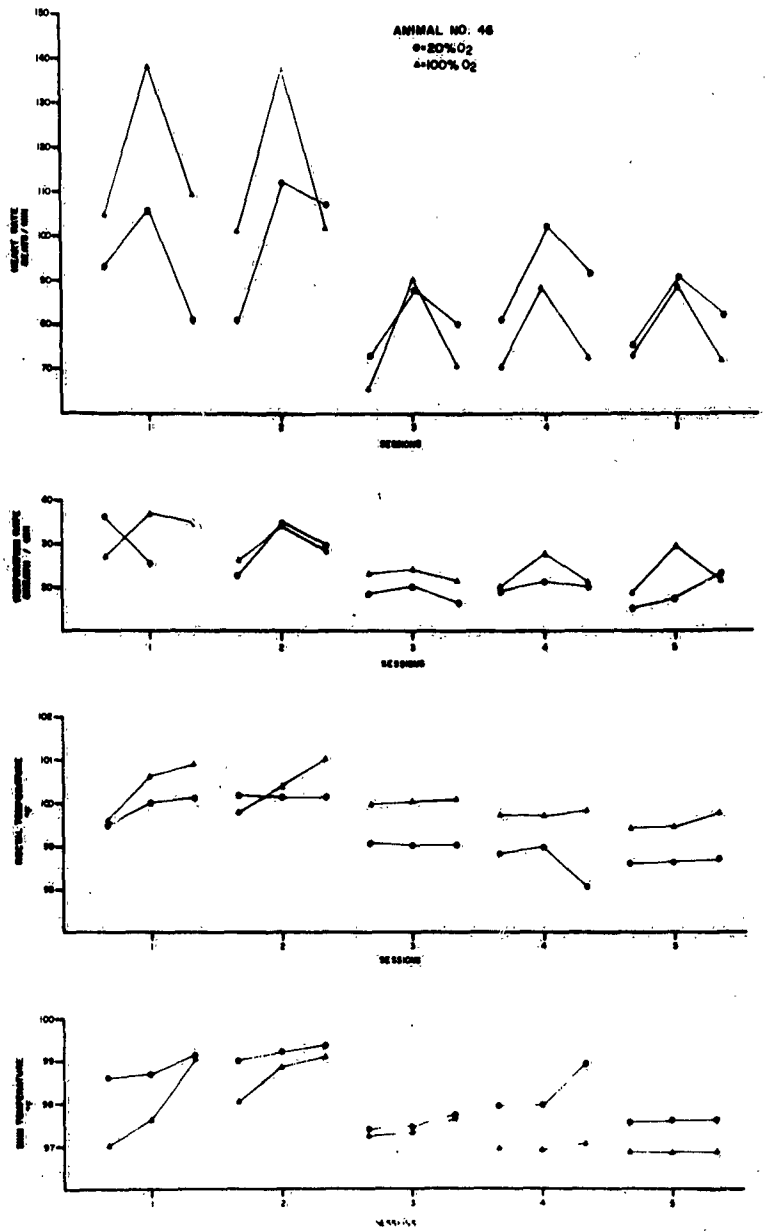
Oxygen Tolerance Tests 1 and 5, Means of Physiological Data for Five "Work Sessions"



Oxygen Tolerance Tests 2 and 6, Means of Physiological Data for Five "Work Sessions"



Oxygen Tolerance Tests 7 and 3, Means of Physiological Data for Five "Work Sessions"



Oxygen Tolerance Tests 8 and 4, Means of Physiological Data for Five "Work Sessions"

APPENDIX VI

Hematological and Serum Biochemical Values of
Chimpanzees No. 32, 35, 42 and 46

and

Directional Changes in
Hematological and Serum Biochemical Values during
Test Periods in 20% and 100% Oxygen

SERUM BIOCHEMICAL VALUES OF FOUR SUBJECTS OVER A PERIOD OF EIGHTEEN MONTHS

Subject No.	CO_2 Vol %	K mEq/L	Na mEq/L	Cl mEq/L	pH	Urea N mg %	Total Protein gm %	Creat-inine mg %	Ca mg %	P mg %
No. 32										
Range	51-74.8	3.0-4.7	139-148	95-108	7.34-7.48	7.5-17.1	6.5-7.6	1.0-1.2	9.6-10.6	2.6-3.3
N	5	4	5	5	3	4	4	3	3	2
Median	61.6	3.6	141	101	7.42	14.5	7.2	1.1	10.2	-
No. 35										
Range	64-67	3.9-4.4	133-144	97-102	7.42-7.55	8-16.2	6.4-8.5	1.02-1.45	9.3-10.9	-
N	5	5	5	5	3	4	5	3	4	1
Median	64	4.1	139	99	7.47	12	6.8	1.02	9.9	5
No. 42										
Range	38-66	2.9-5.0	136-146	94-106	7.29-7.49	10.6-13.6	6.1-7.5	0.72-1.6	9.7-11.8	3.6-4.1
N	8	8	10	9	6	5	6	5	9	4
Median	56	3.9	144.5	102.5	7.38	12.0	7.1	1.4	10.2	4.0
No. 46										
Range	39-63	4.0-5.0	135-147	96-100	7.37-7.65	6.3-13	6.8-7.6	0.54-1.5	9.7-11.4	-
N	5	7	7	7	5	4	5	4	7	1
Median	51	4.2	144	99	7.42	11.0	7.2	1.1	10.1	3.67

HEMATOLOGICAL VALUES OF FOUR SUBJECTS OVER A PERIOD OF EIGHTEEN MONTHS

Subject No.	RBC mil/mm^3	Hemoglobin gm %	Hcrt %	WBC /mm^3	Polys /mm^3	Immature Polys /mm^3	Mono-nuclears /mm^3	Eosin /mm^3	Sed Rate mm/hr
No. 32									
Range	4.09-7.05	10.4-14.8	35-46	7000-22000	1400-11000	0-450	5100-11000	117-354	2-52
N	10	14	14	12	12	-	12	5	10
Median	5.22	13.15	42.5	11350	3430	-	7250	160	11
No. 35									
Range	4.20-5.45	11.8-14.4	35-49	7600-23000	1800-16000	0-5%	4200-9800	70-744	20-42
N	10	12	12	12	12	-	12	10	10
Median	4.85	13.3	41	12650	7500	-	5500	165	34
No. 42									
Range	4.0-6.3	11.8-15.9	36-48	6400-21000	870-15000	0-1240	2900-11000	100-2000	3-34
N	17	17	18	18	18	-	18	6	18
Median	5.3	13.0	44.5	11100	3500	-	5800	200	11
No. 46									
Range	4.6-6.4	13.0-15.5	40.5-48	6900-19000	2800-9000	0-500	2500-11000	75-324	2-22
N	7	6	8	11	9	-	9	6	8
Median	5.4	13.6	44	10800	4800	-	5800	101	17

DIRECTION OF CHANGE IN HEMATOLOGICAL AND SERUM BIOCHEMICAL VALUES DURING TEST PERIODS IN 20% AND 100% OXYGEN*

	20% Oxygen				100% Oxygen			
	No. 32	No. 35	No. 42	No. 46	No. 32	No. 35	No. 42	No. 46
RBC	down	up	up	-	down	up	0***	down
Hgbin	-	-	-	-	up	-	0	down
Hcrit	-	down	-	-	up	-	0	down
WBC	-	-	down	-	up	down**	0	-
Polys	-	-	down	-	up	down**	0	-
Bands	-	-	-	-	up	-	0	-
Mononuclears	down**	down	down	-	up	down	0	up
Eosinophiles	-	down**	0	-	-	-	0	down**
Sed Rate	-	-	down**	-	down	-	0	-
CO_2	down	up**	up	-	up	up	up	up
K	up**	-	-	up**	-	0	-	up**
Na	up**	-	-	-	-	up**	up	up
Cl	-	-	-	-	-	-	-	-
pH	-	-	-	down**	down**	-	up	down**
Urea N	up	-	-	up	-	down	-	-
Tot Prot	up	-	-	-	down	up	-	-
Creatinine	-	-	-	-	-	down	-	up
Ca	-	up	-	-	-	-	-	down
P	-	-	up	-	-	-	-	-

* Blank spaces represent either no essential change in value or an "abnormal" pre-test value

** Very significant directional change in value since pre-test value fell within "normal" range and post-test value outside of "normal" range

*** 0 represents undetermined value

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