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SOME PHYSIOLOGICAL LABORATORIES IN POLAND AND CZECHOSLOVAKIA

By R.R. Sonnenschein

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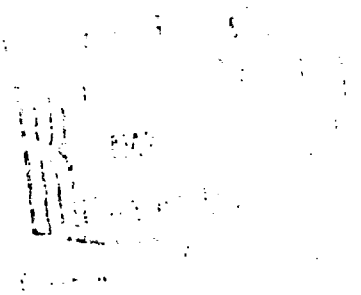

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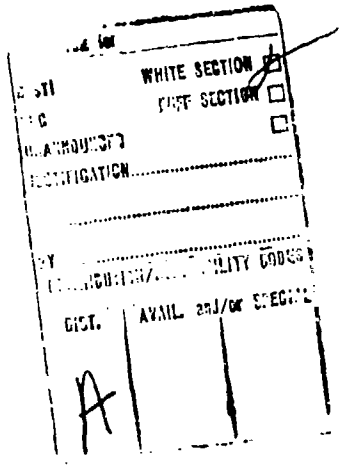

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A summary is presented os some of the current physiological research in Poland (Warsaw and Cracow) and Czechoslovakia (Prague, Brno and Bratislava).

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14 KEY WORDS	LINK A		LINK B		LINK C	
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SOME PHYSIOLOGICAL LABORATORIES IN POLAND AND CZECHOSLOVAKIA

This report summarizes a trip of about ten days in November 1971 to two Polish cities, Warsaw and Cracow, and three cities in Czechoslovakia, Prague, Brno and Bratislava. Of course, in such a brief trip it would be difficult, if at all possible, to survey all that is going on in physiology in these locations, but I was able to see and hear enough to form some definite impressions of the nature and quality of current work.

Fortunately, I had professional acquaintances at each of the centers I visited so that arrangements for the visits, as well as accommodations, travel, etc., were greatly facilitated. Both in Czechoslovakia, which I had visited in 1965 and 1969, and in Poland, the warmth of hospitality was striking. At each stop I was met by colleagues at train or plane, escorted to hotel and laboratory, shown about the town, invited to dinner, and finally taken to my plane or train on departure. Part of this may just be due to the relative dearth of visitors to the laboratories in Eastern Europe and the scientists' pleasure in having the occasional visitor for scientific discussions; I suspect, however, that the hospitality is to a large extent traditional in these countries.

Dr. John Foss of ONR London recently recounted in European Scientific Notes (ESN-25-11, p. 367) his difficulty and ultimate failure in obtaining a visa to Poland. At best, it is a terrible nuisance to arrange visas to any of the Eastern European countries when one is traveling on official business with an Official Passport. One needs some sort of "official" invitation, and these I had from the Professor of Physiology in Warsaw, who invited me also in his capacity as an officer of the Polish Physiological Society; and from the Director of the Slovak Academy of Sciences. In the end, I got visas to the two countries with no difficulty, although, as Foss pointed out, the decision to grant the visa could not be obtained from the Polish Embassy in London until the day before my planned departure. Once armed with the visas, however, I met no difficulties of any sort throughout the travels.

Currency transactions are strictly regulated in Poland and Czechoslovakia (and Hungary, as well). Foreign travelers legally get a favored rate of exchange for hard currency (e.g., dollars or pounds sterling), but such exchange is supposed to take place only at officially approved locations

(state tourist bureau, hotels, etc.). One is commonly approached on the street with offers to exchange the local currency for dollars at upwards of twice the official rate, but to do this is to court real trouble. The desire of the governments to get as much hard money as possible is shown by the existence of stores which sell items only for this currency. Interestingly, despite the lack of value of the local money outside each country, one is not allowed to take any out. If you happen to have some remaining which you have not been able to exchange back to dollars before you leave, you may be able to make the exchange outside the country, but at a considerable loss.

I. POLAND

A. Warsaw

Alfredo Baños, in a recent ONRL report (R-37-71), vividly described Warsaw as it has been reconstructed since the war, and also discussed the general history and status of the Polish universities. My own reaction to Warsaw was like his -- astonishment at the remarkable reconstruction of the city, with all the effort and dedication that this must have entailed, particularly in the face of the economic devastation experienced by Poland during the war. Today, the entire center of the city is rebuilt as it had been, save for a few modern buildings and the almost totally destroyed Royal Palace whose reconstruction has now begun.

Shops generally seem well stocked; clothing, whether seen on the street or in store windows, is quite fashionable, although I was told that quality may not be up to Western standards. To the casual visitor, the living standard seems relatively good. Hotel prices are surprisingly low: $4.00 for a small single room with bath in one of the better Warsaw hotels, $8.00 for a very large room in an elegant Cracow hotel. Souvenirs and handcraft, of very good quality, are quite inexpensive.

1. The Department of Human Physiology, School of Medicine

Interestingly, some years ago the schools of medicine in Poland were divorced from the universities administratively, and are now independent institutions. I was unable to learn what the implications of this arrangement are.

The Department of Physiology is headed by a relatively young, energetic man, Professor Andrzey Trzebski, who spent a year at the University of Pennsylvania in the early 60's and has traveled widely in the US and Western Europe. Equipment in this laboratory, as at the Nencki Institute (see below), is first-rate. Much of it is American-made (e.g., Tektronex), some is Polish, such as a neat instrument for determining and plotting interval histograms of action potentials (ANOPS, made by the Warsaw Polytechnic Institute).

Trzebski's main interest is in cardiovascular control mechanisms. He and his coworkers have been investigating four main topics:

a) Role of the chemosensitive areas on the ventral surface of the medulla, and feedback between the medullary centers and the carotid body. Perfusion of solutions of low pH over the ventral medullary surface produces increased discharge in cervical sympathetic fibers supplying the carotid body. There is also an output to the carotid body from non-sympathetic glossopharyngeal fibers, as shown by Biscoe. Trzebski is concerned with the possibility of a resetting of the carotid chemoreceptors via the sympathetic innervation (a local vascular effect?) and/or via the efferent glossopharyngeal innervation.

b) Central nervous control of cardiac vagal tone. In experiments on dogs, Trzebski finds that the heart slows or that spontaneous discharge in single vagal motor fibers increases after diencephalic decerebration, whether performed in the otherwise intact, anesthetized animal or in the encéphale isolée preparation. Stimulation in the hypothalamic "defense area" inhibits vagal tone in the encéphale isolée preparation. Pulmonary distension inhibits vagal activity -- the so-called "pulmonary-cardiac reflex"; this reflex is abolished by midcollicular decerebration, which indicates a link for the reflex high in the brainstem.

c) Vascular responsiveness in skeletal muscle. Dr. H. Janczewska had earlier studied the reduction in sympathetic vasoconstriction which takes place in a working muscle, as well as in areas distant from the muscle (Bull. Acad. Polon. Sci., Ser. sci. biol. 12, 103 (1965) and 15, 697 (1967)). Present experiments concern the prolonged enhancement of the dilator effect of acetylcholine, and of some other vasoactive substances, following a period of muscle work.

d) Role of catecholamines in reducing the resistance of the myocardium to anoxia. Trzebski's group have shown that the resistance to anoxia of the heart, either isolated, in the Starling heart-lung preparation, or in situ, (as judged by dP/dt or work output) is enhanced by prior depletion of norepinephrine by reserpine. This is a large effect: the reserpinized heart can perform three times as much work during anoxia as can the untreated heart. Administration of norepinephrine restores the sensitivity to anoxia. Anoxia also increases coronary blood flow, and Trzebski has found that reserpine treatment delays the onset of this increase. Thus, it appears that endogenous catecholamines, which are released from the heart during anoxia, are somehow involved in the coronary flow response, as well as in the resistance of the heart to anoxia.

Among Trzebski's future research plans is analysis of the central organization of vagal output, chiefly in the nucleus ambiguus, attacked through recording of single unit activity in the nucleus.

2. The Department of Neurophysiology, Nencki Institute of Experimental Biology of the Polish Academy of Sciences

The Institute, founded in the early 1900's, has three departments: Biochemistry, Experimental Biology (chiefly protozoology) and Neurophysiology. It is situated a little from the center of Warsaw.

I had a very brief visit with Prof. J. Konorski, for many years head of the Department of Neurophysiology, and, for a period recently, director of the Institute. Konorski is internationally known among neurophysiologists and physiological psychologists for the work he and his collaborators have done over the years on the physiological mechanisms of instrumental conditioning and the functional organization of the brain, especially in the frontal and prefrontal cortex and in the limbic system. Dr. B. Zernicki is in charge of much of the neurophysiological work. An example of the type of work going on in the laboratory is an experiment I saw on the response of midbrain neurons to patterns presented to the eyes in a trigeminal-decerebrate cat.

My time at the Institute was too short to learn much about details of recent experimental work. Those interested will find a list of all papers from the Department which have been published in Acta Neurobiologiae Experimentalis,

Supplementum 1, 1971. That journal has served as an organ for the Institute, but does take papers from other laboratories.

Konorski told me that a large proportion of his department's budget is supported by PL-480 (counterpart) funds, in conjunction with the National Institute of Mental Health (Bethesda); at one time these funds constituted over 50% of their budget.

B. Cracow

My visit here was confined to the Department of Physiology of the School of Medicine, headed by Professor Stanislaw Konturek, a man in his 40's who spent a year in Dr. M.I. Grossman's laboratory in Los Angeles, in the early 60's, working in gastrointestinal physiology. This continues to be Konturek's main area of interest, especially on mechanisms of hormonal regulation of secretion.

In one project Konturek has demonstrated that surgical vagotomy reduces the pancreatic secretory response to the presence of amino acids in the duodenum; as a rule he uses a combination of leucine and tryptophane. On the other hand, vagotomy has little effect on the response of the pancreas to intravenously administered cholecystokinin (CCK), the duodenal hormone which is involved in regulation of pancreatic enzyme secretion, or caerulein, a polypeptide which closely mimics the action of CCK. This implies that vagal activity is somehow necessary for the normal release of CCK from the duodenum by the presence of amino acids.

Konturek has also investigated the concentration gradients of the gastrointestinal hormones along the gut in the dog. Such a gradient of CCK exists down to the distal jejunum, about 100 cm distal to the pylorus; secretin can be detected only for about 75 cm.

It has been possible to produce peptic ulcers in cats by continuous intravenous infusion of pentagastrin or histamine for 36 hours. The ulceration is prevented by concomitant administration of secretin, or reduced by administration of caerulein. With either of the latter agents, no change in gastric HCl production occurs, and Konturek thus infers that the increased production of pancreatic HCO_3^- induced by these agents causes sufficient neutralization of gastric acid to prevent the ulceration.

One of Konturek's assistants, Dr. Pawlik Wiestow, is studying some cardiovascular actions of the hormones CCK and secretin. So far, he has looked only at effects on arterial and venous pressures of single intravenous injections of rather large doses of the agents. Hence, little is known yet of the hemodynamic events which are involved, no of the physiological significance of any such actions.

I also had very pleasant discussions with the retired Professor of Physiology, Jerzy Kaulbersz, who has an apartment in the Department, maintains an active interest in physiology, and continues as a world traveler. Kaulbersz had his eightieth birthday in 1971 and is remarkably active.

II. CZECHOSLOVAKIA

The economic, political and scientific picture in Czechoslovakia is at the moment rather bleak. Since the Russian invasion and occupation in 1968, many basic goods, including some foods, have been in short supply, although the situation in this regard seems to have improved since I visited there in 1969. Politically, the situation has hardened considerably. Dissent against the regime, and especially against the occupation and reversal of the reforms of early 1968, has been rather stringently repressed. As a result, a good number of first-rate scientific workers left the country, usually escaping with few of their belongings, especially in the first year of occupation. Some who remained and were known to be or suspected of being opposed to the turn of events were deposed from their positions as directors of departments or laboratories. In the best of such cases, the individuals have been allowed to continue with their own work; in the worst, they are without salary and forced to seek any sort of job to make a living. Travel outside the country is virtually impossible now for the scientists.

The atmosphere one senses is that of hopelessness for improvement, at least in the foreseeable future. Scientific work that continues is still of the high quality we have come to expect from Czechoslovakia. But the loss of good people and the inevitable effects of the political happenings have certainly injured scientific productivity. It is depressing to witness this, and one can only hope for improvement soon in the entire picture.

A. Prague

1. The Institute for Cardiovascular Research

This group is housed in the Thomaier Hospital, a large hospital in the Krč district of Prague. It formerly consisted of eight or nine active workers headed by Dr. Jan Brod who left in 1968 and is now in Hannover, West Germany. The group now has three senior workers, Drs. I. Přerovský, J. Linhart and A. Hlavová, and continues its combined clinical and research activities.

Hlavová's main current interest is in the effects of exercise on blood flow in skeletal muscle in normal subjects and patients with intermittent claudication. She finds that the normal untrained subject shows a rather marked reduction in blood flow in the gastrocnemius during daily treadmill exercise, as early as on the second or third day of the regime. The extent to which psychological factors play a role in this rapid adaptation is unknown. Patients with intermittent claudication have been given daily, graded exercise and have manifested marked clinical improvement as well as improvement of blood flow, as indicated by ^{133}Xe clearance. The patients also show a progressive decrease in post-exercise hyperemia on successive days of therapy.

During rhythmic exercise of the leg, skin blood flow, monitored by ^{131}I clearance, rises. This is associated with a fall in venous pressure presumably as a result of action of the muscle pump, and Hlavová believes that the increase in flow is secondary to increase in the A-V pressure gradient.

Přerovský has recently studied the well-known phenomenon that blood flow in the skin, as determined by isotope clearance, decreases when the subject assumes an upright position. Interestingly, the same degree of vasoconstriction occurs in the skin of the leg of patients who have undergone unilateral sympathectomy. The decrease also occurs in the arm, where no change in venous pressure had occurred. Thus, a sympathetic reflex is apparently not essential. The response in the arm suggests some systemic factor, while that in the leg apparently results from some local change. Přerovský suggests that the latter may be the Bayliss response: both arterial and venous pressures rise with assumption of the upright posture, thus increasing the distending pressure on arterioles which may lead secondarily

to vasoconstriction. The systemic factor might be the reflex release of catecholamines from the adrenal, but no evidence is at hand on this. Additionally, no change in venous capacity in the legs occurs with tilting.

Another project which Přerovský is directing, actually being carried out by a young assistant, Dr. L. Razgova, is the determination of capillary filtration coefficient (CFC) in man. The problem here, as contrasted with experiments in the usual way on animals, is that following application of the occlusion there is a very slow increase in venous pressure. Therefore, the vascular components of the increased volume have been mathematically analyzed; this has allowed some calculations of CFC in man.

Linhart has been concerned with the therapy and pathogenesis of arterial occlusive disease. He has found that the usual pharmacological agents are generally ineffective in increasing flow below the level of occlusion, i.e., in opening up of collateral vessels. Reflex heating is effective, however, both in increasing flow and improving the clinical condition. Whether heating may potentiate the action of vasodilator drugs and unmask some favorable action of these remains a possibility.

Linhart has also been measuring pulse wave velocity, as a measure of elasticity of arteries and finds that with incipient atherosclerosis it increases from the normal of 13-14 up to 18-20 m/sec, along with changes in shape of the pulse wave. A clinical trial over a year and a half with chlorfibrate indicated that while this drug reduced blood lipids, it did not effect pulse wave velocity or cause resorption of atheromata, although it may have slowed development of the process.

2. The Czechoslovak Academy of Sciences

The Academy, also located in the Krč region of Prague, has four departments within its Institute of Physiology: metabolism, developmental (headed by Dr. Jelinek), neurophysiological (Drs. Weiss and Bureš) and neuromuscular (headed by Dr. P. Hnik); the overall director is Dr. Vyklicky. My host, Prof. E. Gutmann is a very kindly man with an international reputation for his work on problems of innervation and so-called trophic effects on skeletal muscle. He now heads one of four teams in the neuromuscular department, where previously he was director.

Gutmann told me how the creation of research institutes under the Academy of Sciences after the War (WWII) led to large advancements in physiological (and other scientific) research. At the same time, however, many of the best people were drawn from the universities to the Academy institutes to the detriment of research in the universities. The latter are poorly funded, and officially the job of university faculty is just to teach; nevertheless, they, like their counterparts in other countries, wish to do research and do it under very great limitations of time and money.

Among recent experiments, Gutmann has analyzed the mechanism of compensatory hypertrophy of muscle induced by functional elimination of synergistic muscles (Experimental Neurology 31:451-464 (1971)), and the differences in the reaction of muscle to compensatory hypertrophy and to increased phasic activity (Physiol. bohemoslov. 20:205-212 (1971)). He has recently worked on the mechanisms of hypertrophy of cardiac muscle, as induced by isoprenaline, and finds it similar to compensatory hypertrophy in the soleus muscle, in terms of contraction time and rate of tension development.

I saw briefly some experiments being done by Dr. P. Hnik on the concentration of K^+ in interstitial fluid of skeletal muscle during contraction. He uses an open-tip glass electrode, about 0.1 mm outside diameter, filled with an ion-specific liquid ion exchanger (Corning No. 47132; see Walker, J.L., Analyt. Chem. 43:89-92A (1971)). This has a specificity for K^+ over Na^+ of about 100:1. With the electrode placed in muscle, and with controls for tissue injury, he finds a rise in interstitial $[K^+]$ from about 5 to about 10 mM during telanic exercise. Hnik is concerned with the possible role of the increased $[K^+]$ in exciting receptors in muscle which may be involved in autonomic reflexes. Dr. Bureš is using a similar electrode to monitor changes in cortical interstitial K^+ during spreading depression.

B. Brno - The Department of Physiology, Faculty of Medicine, J.E. Purkyně University

The Department was formerly headed by Prof. V. Kruta, known for his work on the heart and also for his interest and activity in the history of physiology. Although not yet at retirement age, he no longer has his official university post, but continues actively with his historical interest. He,

Dr. Jan Peňáz and Dr. S. Doležel were my hosts in Brno. This was where Mendel made his classical observations on inheritance of characteristics in the pea. I had the opportunity of visiting the monastery where he worked; this is now maintained as a museum, and his experimental garden is kept much as it had been in his time.

Dr. Jan Peňáz is currently the senior man in the Department. His main interest is in cardiovascular control mechanisms, chiefly from the point of view of systems theory. Much of his own experimental and theoretical work is summarized in a recent review ("The Blood Pressure Control System: A Critical and Methodological Introduction" in Psychosomatics in Essential Hypertension, ed. M. Koster, M. Musaph and P. Visser, Bibl. psychiat. No. 144, pp. 125-150, Karger-Basel/München/New York, 1970). He has also designed some clever and very useful experimental devices. One is a pressure-regulating valve for physiological perfusions, consisting of a very simply constructed lucite chamber and diaphragm arrangement (Scripta medica 41:249-254 (1968)). Another, much more elaborate, is for indirect continuous recording of arterial pressure in man. In this system, the optical density of the finger under a pneumatic cuff is continuosuly measured by a photoelectric plethysmograph whose signal controls the cuff pressure to maintain vascular volume constant. It is described briefly in Physiol. bohemoslav. 19:341 (1970).

Work along the lines that Kruta had pursued for many years is being followed up by a young man, Dr. P.Braveny, who is studying some aspects of excitation-contraction coupling and frequency-force relations of the myocardium. He is especially concerned with the relation of CA ion to the action potential. He considers the following points to be of significance: the duration of the action potential (AP) governs the active state; the duration of the AP is proportional to Ca^{++} influx, with influence on the following beat; increase in contractile force leads to shortening of the individual AP, leading to a feedback regulation of force by this shortening of the AP; excitation-contraction coupling involves a two-step reaction: influx of Ca^{++} and release of Ca^{++} by the sarcoplasmic reticulum.

Dr. Z. Franc is investigating differential effects of splanchnic afferent activity on heart rate and arterial pressure, but unfortunately was unavailable for discussion when I was at the laboratory.

Finally, I had a discussion with Dr. S. Doležel of the histological laboratory of the Slovak Academy of Sciences. While administratively part of the Academy, the laboratory is situated in the medical school in Brno, and Doležel has very close relations with the Department of Physiology. He has been concerned for many years with innervation of blood vessels which he has investigated with both classical, e.g., silver staining, and fluorescence techniques. He has found great differences in extent and pattern of adrenergic innervation of vessels among different organs of various species, and with stage of development. A few years ago in collaboration with Gero and Gerová (see below), he demonstrated with the fluorescence method the release into the vascular muscle of norepinephrine by vasomotor nerves.

C. Bratislava - Institute of Normal and Pathological Physiology, Slovak Academy of Sciences

This Institute, with about twenty-five professional workers, consists of five departments: general physiology (Head, Dr. Zachar), neurophysiology (Dr. Duda), clinical electrophysiology (Dr. Cernacik), human physiology (Dr. Ruttkay), and cardiovascular physiology. I spent all my time at the latter department whose director had been Dr. Ján Gero. He had returned to the laboratory just prior to my visit after a several months recuperation from a heart attack, during which time Dr. Josef Török was acting head of the department.

Gero and his wife, Dr. Maria Gerová, both in their late 40's or perhaps early 50's, along with their younger colleagues have been interested for many years in the functional properties of arteries and their innervation. In contrast to what was earlier generally believed, Gero and Gerová have firmly established that the large "conduit" arteries are under strong control by sympathetic vasomotor innervation. Generally they have directly measured vessel diameter with an inductive transformer device, and have worked out for various vessels, veins as well as arteries, the quantitative stimulus-response and temporal relations.

Sympathetically induced arterial constriction occurs even in the aorta -- up to 5% decrease in diameter just above the bifurcation in adult dogs; peripheral arteries of puppies may decrease by up to 32%, of adults up to 13%. Some of their recent work, as well as reviews of earlier work, is in the following: Experientia 26:1318 (1970); Proc. Symp. Physiol. Pharmacol. Vasc. Neuroeffector Systems, Interlaken 1969, pp. 86-94 (Karger, Basel, 1971); Circulat. Res. 24: 349-359 (1969).

Dr. V. Smiesko has recently completed a most interesting analysis of the active vasodilatation in the vascular bed of the gracilis muscle that occurs with a rapid increase or decrease (one-second square wave) in perfusion pressure. This dilatation is independent of polarity of the pressure change, is directly proportional to the magnitude of the change, and depends on the ascending component of the change. It is hence separate from the Bayliss response which depends primarily on the perfusion pressure level. (The work appears in Pflügers Arch. 327:324-336 (1971)). Smiesko feels that this rate-sensitive response may be involved in the initial vasodilation in skeletal muscle at the onset of exercise following transmural pressure changes that accompany muscle contraction.

Dr. Josef Török, who returned to Bratislava in 1970 after more than a year in the Department of Pharmacology at UCLA, has had little opportunity for research because of his administrative duties. He plans, however, to continue studies started at UCLA on penetration of norepinephrine into blood vessels, as well as experiments he was earlier involved in on the "veno-vasomotor" reaction in the intestine.

Just leaving Bratislava at the time I visited, after spending a month in Gero's laboratory, was a young, personable man, Dr. A.V. Samoilenko, from the Department of General Physiology in the Institute of Experimental Medicine of the Academy of Medical Sciences of the USSR, Leningrad. He has worked on reflex changes in vascular resistance and capacitance (Cor. Vasa 13:136-146 (1971)).

Although time did not allow a visit to her laboratory, I should mention the interesting work of Dr. Eva Kellerová of the Department of Human Physiology, whom I had met previously. She has been working chiefly on human vasomotor reactions in skin and muscle (see Zeit. f. Kreislaufforsch. 9:917-925 (1969); Clinical Sci. 40:271-282 (1971)), and has investigated both rhythmic changes and reflex responses to such stimuli as deep breathing and mental strain.