# REPORT ON SCIENTIFIC ACTIVITIES 1987

# POLISH ACADEMY OF SCIENCES MEDICAL RESEARCH CENTRE

# REPORT ON SCIENTIFIC ACTIVITIES 1987

Warszawa 1988

# POLISH ACADEMY OF SCIENCES — MEDICAL RESEARCH CENTRE 3, Dworkowa Str., 00-784 Warszawa POLAND

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# PROFESSOR STANISŁAW KOZŁOWSKI, M.D. (1927-1985)

On October 29, 1985 died suddenly of heart attack Professor Stanisław Kozłowski, M.D. — Head of Department of Applied Physiology, MRC, a distinguished Polish Scientist of international reputation, an excellent, unforgettable teacher of many generations of medical doctors and physiologists — a man of admirable personality.

The late Professor Stanisław Kozłowski was born on March 12, 1927 in Białystok (Poland). He completed his medical studies at the Warsaw School of Medicine in 1952, received his M.D. degree in 1960, and finally his second scientific degree (Habilitation) in 1966 from that school. In 1974 he was nominated the Professor of Physiology.

Since 1950 he taught and conducted research first at the Warsaw School of Medicine and then (since 1969) also at the Medical Research Centre, Polish Academy of Sciences, being appointed Head of the Department of Work Physiology at the Warsaw School of Medicine in 1968 and Head of the Department of Applied Physiology, Medical Research Centre, Polish Academy of Sciences in 1969.

He served as President of the Polish Sports Association, President of the Sports Medicine and Physical Education Committees at the Scientific Council of the Polish Ministry of Health and Welfare, as well as the President of the Central Commission for Supervision of Research Involving Human Subjects at the above Ministry. He was also an active member of several Scientific Committees at the Polish Academy of Sciences, and Scientific Councils at Research Institutes, as well as a corresponding Editor of the International Journal of Sports Medicine, and a member of the Editorial Advisory Board of Annals of Sports Medicine.

Research interests of the late Professor Kozłowski concentrated on problems of human adaptation to physical work and environment concerning particularly: mechanisms controlling energy metabolism, water-electrolyte balance and body temperature under basal conditions, during exercise as well as during restriction of physical activity. He developed an original concept of the glucostatic control of exercise metabolism and its importance for exercise performance, and provided an evidence for the interaction between osmo-and -volume reception in the regulation of water-electrolyte metabolism. He is also widely known for his research concerning the influence of body dehydration and physical exersice on distribution of body fluids and electrolytes as well as by his recent studies on the importance of exercise hyperthermia as a factor limiting endurance performance. Although a part of the late Professor Kozłowski's research studies was conducted on laboratory animals they always aimed at extending our knowledge about functioning of human organism both in health and diseases. In his approach to human physiology he

attempted to recognize mechanisms determining function of the whole organism, considered as an integrated system undergoing changes with growth, development and aging, being under a constant influence of many environmental factors as well as of its own activity and pathological processes. Physiology of man performing physical exercise occupied a particularly important place in the late Professor Kozłowski's studies. He wrote a number of excellent review-papers, popular articles, chapters in text-books and monographies — among the latter: "Exercise Physiology" (2 eds), "Doping in Sports", "Introduction to Clinical Physiology", and "Limits of Human Adaptability".

The late Professor Stanisław Kozłowski had always emphasized necessity of physical activity as a part of a life-style of modern population. In recent years he devoted a large part of his work towards investigations on the role of physical activity in both prevention and therapy of the so called "civilization diseases" such as coronary heart disease, hypertension, diabetes and obesity and on the physiological basis of cardiac rehabilitation. His research on these problems was highly recognized internationally.

The late Professor Kozłowski was not onły an eminent, talented physiologist but also a man of outstanding knowledge of philosophy, biology and history — passionately interested in music and art. He was also known as the most reliable, decent, extremely honest person. Thanks to his true involvement in people problems he was immediately liked, and then implicitly respected and trusted by all who knew him. He made a lot of true friends both in Poland and throughout the world. One hundred forty scientists from 14 countries of the world paid a tribute to his memory attending the International Symposium on Exercise Physiology commemorating the late Professor Stanisław Kozłowski. The Symposium organized by the Medical Research Centre, the Polish Physiological Society and the Polish Society of Sports Medicine was held at Baranów Sandomierski on June 18-20, 1987.

Thinking about Stanisław, as he wished his friends to call him, we will always remember him as an esteemed master, a beloved friend and a great companion — full of vitality, anxious to work as much as possible, but ready to laugh, sing, make jokes — a man enjoying life...

Mirosław Mossakowski Hanna Kaciuba-Uściłko Krystyna Nazar

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## RESEARCH REPORT

# STUDIES ON THE FUNCTION OF THE NERVOUS SYSTEM AND ON MECHANISMS CONTROLLING BASIC FUNCTIONS OF THE ORGANISM

Department of Neurophysiology Head: Prof. Witold Karczewski

- I. INVESTIGATIONS OF PHYSIOLOGICAL-CLINICAL CORRELATIONS IN THE RESPIRATORY SYSTEM
- 1. Investigation of the role of respiratory chemoreceptors in apneustic respiration

It has been shown that apneustic respiration induced in cats by the anesthetic ketamine is normalized in consequence of increased peripheral and/or central chemoreceptors' input. Therefore, it seems that the afferentation from the chemoreceptors may directly stimulate the "off-switch" mechanism.

2. The effect of temperature on respiration

The results suggest that: a) changes in temperature result in changes of respiratory frequency, while the equivalent of tidal volume remains constant; b) during increased respiratory drive the necessity of maintaining the required minute ventilation seems to be preferentially subserved; c) in the above mentioned situation the proportion between the amplitude and frequency of respiration changes.

3. The mechanism of neurological deficit following subarachnoid hemorrhage (SAH)

The ultrastructural images of brain blood vessels' walls of rabbits, obtained following experimental SAH, suggest that the narrowing of the vessels may not be a consequence of vasospasm, but rather of changes in vessels' architecture. These changes may be stimulated by the noradrenergic system.

4. The role of opioids in the apneustic breathing

It was found that the induction of apneustic respiration by ketamine is not related to the opioid system.

5. The role of larynx as a source of afferent information influencing respiratory pattern

It has been shown that the larynx restricts tidal volume and minute ventilation due to mechanical resistance for air flow. Following the exclusion of supralaryngeal respiratory airways the larynx does not influence the time relations within the respiratory cycle.

6. Diagnosis and treatment of respiratory disturbances during sleep

A method of diagnosing respiratory disorders during sleep with the aid of "cephalometry" — the geometrical evaluation of cranial X-ray records has

been worked out. A method of surgical treatment of such disturbances (surgical restitution of the patency of the nose, "conchoplasty") has been developed. It was found that many of the heart and circulatory disturbances may be related to the upper airway compromise.

11.

- 1. The localization of respiratory-related units in the guinea pig have demonstrated their presence in nucleus parabrachialis (NPB), n. trig. mot. (NVmt) and n. ret. pontis caud. (RPC). The role of these neurones in the control of respiratory pattern was studied by means of a focal lignocaine microblockade. It was shown that such a blockade elicits an increase in the duration of both inspiratory and expiratory phase of the breathing cycle. Vagotomy combined with a unilateral blockade does not elicit apneustic breathing. It is suggested that the pontine structures in the guinea pig exert an excitatory influence on the respiratory pattern generator.
- 2. Studies on the motor nucleus of the Vth nerve (NVmt) and its role in the mechanisms of obstructive sleep have revealed that expiratory units of this nucleus may play a role in the control of the respiratory pattern; a short latency (2.5 msec) inhibiton of phrenic nerve motoneurones might even suggest a direct (or oligosynaptic) connection between NVmt and phrenic motoneurones.
- 3. Several papers have been recently devoted to respiratory neurones located in  $C_1$ - $C_3$  segments of the spinal cord in the cat. We have found them also in the rabbit, mainly in the  $C_2$  segment. They send their descending axons caudally to the phrenic nerve nucleus, possibly to thoracic interneurones. Their role is still obscure but one cannot exlude their contribution to the spinal coordination of breathing and locomotion.
- 4. Slowly adapting pulmonary stretch receptors (PSR) are known to play a role in controlling the breathing pattern. Lateralization of responses of phrenic, facial and hypoglossal nerves to PSR excitation was studied. It was shown that contralateral cranial nerves are inhibited by the input from PSR more strongly than ipsilateral and that this difference increases with the decrease in the chemical drive.
- 5. Clinical and experimental observations indicate that weak phrenic nerve activity persists after unilateral interruption of descending pathways at  $C_1$ - $C_3$  level. It was shown that fibres decussating at  $C_3$ - $C_6$  level are responsible for this phenomenon. They contribute to excitation of the contralateral phrenic motoneurones in about 23%.
- 6. Localization of phrenic motoneurones by means of early degeneration technique was studied in the rabbit. In all animal degenerating neurones were identified in anterior horns at the level of  $C_3$ - $C_5$  in the median part of the IXth Lamina of Rexed.

See the List of Publications: a) 4, 13, 34, 35, 36, 44, 46, 47, 58, 59, 60, 61, 62, 64, 87, 88, 95, 98, 103; b) 3, 17, 18, 19, 26, 32, 42, 43.

## Department of Applied Physiology Head: Prof. Hanna Kaciuba-Uściłko

## ADAPTATION TO PHYSICAL EXERCISES AND CHANGES IN ENVIRONMENT

#### 1. Metabolism and its control

The studies on the role of thyroid hormones in the control of skeletal muscle metabolism were continued. It was found that in rats thyroid hormone deficiency, caused by surgical thyroidectomy and propylthiouracil administration, results in a marked decrease of glucose tolerance accompanied by a dramatic inhibition of the soleus muscle reactivity to insulin, estimated in vitro on the basis of the hormone effect on lactate formation. Sensitivity of glycogen synthesis to insulin was not affected by the thyroid hormone deficit.

In hypothyroid rats an enhanced activity of extracellular lipoprotein lipase (LPL) was demonstrated in skeletal muscles. Physical exercise performed by these rats further increased the enzyme activity. On the contrary, the thyroid hormone excess, induced by s.c. administration of triiodothyronine (T<sub>3</sub>) in a dose of 75  $\mu$ g/100 g for 3 days, caused a decrease in both extra and intracellular forms of LPL in the soleus m. and in myocardium. The above changes in the muscle tissue LPL activity may reflect either a direct action of thyroid hormones on this enzyme, or the indirect effect mediated by alterations of the metabolic state of cells e.g. availability of free fatty acids.

The role of thyroid hormones in the control of exercise metabolism was investigated in thyroidectomized dogs. The study demonstrated that thyroid hormone deficiency has relatively small effect on energy substrate utilization at low to moderate exercise intensity. At high work intensity, however, the energy metabolism becomes impaired which has been manifested by a reduced rate of glycolysis with the ensuing inadequate resynthesis of high energy phosphates. The above changes blunted the normal relationships between exercise intensity and the rate of lactate production as well as the depletion of glycogen, ATP and phosphocreatine.

— Investigations were continued on the effect of fasting on working ability and exercise metabolism in dogs. It was shown that food withdrawal for 7 days does not impair the animal's ability to perform even heavy (max. duration 15 min.) aerobic effort, in spite of marked reduction of body carbohydrate stores. Attenuated muscle glycogen breakdown and enhanced FFA supply to working muscles are the main alterations in exercise metabolism in the fasting state.

In normally fed dogs an excessive FFA availability-induced by fat meal ingestion followed by i.v. heparin administration, was found to favour carbohydrate sparing during exercise but it did not improve working ability. On the contrary, in 50% of animals examined duration of exercise until exhaustion was reduced. In the dogs with elevated FFA concentration oxygen uptake was greater and the exercise-induced body temperature increases, as well

as the depletion of high energy phosphates from skeletal muscles were more rapid than those occurring under normal conditions.

Changes in the skeletal muscle sensitivity to insulin were followed during 72 h of fasting in rats. A significant increase in the soleus muscle insulin sensitivity — measured in vitro — was found 48 h after food deprivation. Glycogen depletion from skeletal muscles induced by exercise preceding food withdrawal enhanced this effect.

- Continuing the studies on the influence of increased physical activity on skeletal muscle sensitivity to insulin in rats the effects of exercise of various characteristics on the soleus and epitrochlearis muscles were compared. Sensitivity of lactate production to insulin in the epitrochlearis muscle, composed mainly of fast-twitch (FT) fibers, was enhanced both after heavy ("sprint") and moderate (endurance) exercise, while that in the soleus (containing mainly slow-twitch fibers) was increased only after the endurance effort. The sensitivity of glycogen synthesis to insulin was elevated only in the epitrochlearis m. following heavy "sprint" exercise. The rate of glycogen synthesis unstimulated by insulin was markedly accelerated in both muscles and after the two types of exercise.
- The results of the oral glucose tolerance test (OGTT) in nondiabetic patients with coronary heart disease (CHD) were analysed and compared to those in men of similar age without CHD. It was found that the glycemic curves obtained in coronary patients and healthy men do not differ significantly. In both groups the curves were shifted to higher values in the overweight subjects. This study did not confirm the assumption that impaired glucose tolerance is an independent risk factor of CHD.
- In cooperation with the University of Oulu (Finland) the effect of physical training at low ambient temperature on metabolic adaptation to cold was investigated in guinea pigs. This study showed that training enhances the metabolic response to noradrenaline, which is accompanied by an increase of brown adipose tissue, with a concomittant elevation of its total protein content, mitochondrial density and activity of oxidative enzymes. The results indicate an increased contribution of nonshivering thermogenesis to the total heat production at low temperature under an influence of physical training in cold environment.
- In cooperation with the University of Kuopio (Finland) an evidence was provided that the "warming-up" causes an elevation of the anaerobic threshold in athletes. It was also demonstrated that this procedure modifies the intergrated electromiographic activity in working and nonworking muscles of men performing physical exercise of moderate intensity at low ambient temperature.
- Continuing common studies with the Institute of Experimental Endocrinology, Slovak Academy of Sciences in Bratislava (Czechoslovakia) an attempt was made to distinguish hormonal changes induced by physical exercise (acute and repeated) from those occurring in resting rats subjected to some emo-

tional stimuli associated with exercise experiments — such as handling, noise etc. It was found that the decreases in circulating insulin and thyroid hormones at rest as well as an attenuation of the plasma ACTH response to exercise can be considered as specific effects of increased physical activity.

In the investigations with human subjects hormonal responses to static exercise (hand-grip) were followed. The most important finding of this study is that this type of the effort is accompanied by a sharp increase in the level of plasma arginine vasopressin.

# 2. Dynamics of changes in the cardiovascular system in response to physiological stimuli

To study the effect of physical training on the mechanisms controlling the function of cardiovascular system 7 young, previously sedentary, men were subjected to 10-week endurance training. The training did not impair the circulatory adjustment to orthostatic changes — the dynamics and magnitude of the changes in stroke volume (measured by an impedance reography), heart rate and cardiac output were not altered, while an increase in the diastolic blood pressure in response to standing up was greater after than before training. Using the computer analysis of the heart rate variability a tendency towards an increase in the amplitude of the high frequency fluctuations, corresponding to the respiratory frequency was found in the subjects in supine position following 10 weeks of training. The results indicate an early development of resting vagotomy during endurance training. A decrease in heart rate response to the submaximal exercise was noted already after 2 weeks of training, while the time constant of the response became longer in comparison with the initial values after 4-5 weeks of the increased physical activity.

- In cooperation with the University of Yamagata (Japan) the studies were carried out with healthy untrained men on the relationship between aerobic capacity and the rate of hemodynamic and respiratory changes at the beginning of submaximal exercise and after its termination. A positive correlation was ascertained between the maximal oxygen uptake and the rate of both acceleration and slowing down of heart rate, stroke volume and pulmonary ventilation responses.
- Continuing the investigations on hemodynamic responses to static effort changes in heart rate (HR), blood pressure (BP), stroke volume (SV), cardiac output (Q) and plasma catecholamine concentrations were compared in healthy subjects exercising with one or two hands (hand-grip) at the some percentage of the maximal voluntary contraction. The important finding of this study is that handgrip performed in sitting position produces a marked decrease in SV even in healthy subjects. It was also demonstrated that the cardiovascular and sympatho-adrenal responses to this type of exercise do not depend on the muscle mass involved in the effort.

#### 3. Exercise tolerance in cardiac patients

Cardiovascular responses to a mixed (dynamic + static) exercise were followed in coronary patients and in asymptomatic subjects with risk factors of coronary heart disease (CHD). This study proved that including the static component into the standard exercise test improves markedly its diagnostic value. In coronary patients the ischemic changes in exercise ECG were considerably more pronounced, and arrhythmias appeared much more frequently than during the standard test. Moreover, application of the mixed test permitted to detect ischemic changes in some subjects being previously considered asymptomatic. An adverse effect of the mixed exercise in coronary patients was also proved in the field study during which the patients were examined when walking with or without an additional static component (carrying 2-4 kg weight).

- The effect of Molsidomine (Cervaton) on the circulatory response to static handgrip was investigated in patients with coronary heart disease and in healthy subjects. The study demonstrated a reduction in blood pressure response to exercise and an attenuation of ischemic changes after administration of this drug.
- Within the 12-year follow-up studies with coronary patients after myocardial infarction the effects of an increased physical activity for 3 years were evaluated. It appeared that in the patients taking part in this programme physical capacity was increased and the ischemic symptoms were reduced. However, these effects were only transient, so no differences between the physically active and sedentary patients were noted in the further stage of CHD.
- Usefulness of 24-h ECG recordings by the Holter method for an estimation of daily energy expenditure and of physical activity was evaluated in cardiac patients. It was proved that in spite of some limitations the method has unquestionable practical implications.

# 4. Dynamic studies of medullary interstitial electrolytes

Within the project aimed at elucidation of mechanisms determining tissue electrolyte concentration in the renal medulla, effects of blocking reabsorption of sodium chloride at two different sites along the nephron were examined in anesthetized rats.

Electrolyte concentration in the interstitium of the inner and outer medullary zones was estimated from tissue electrical admittance (reciprocal impedance) measured continuously by means of needle electrodes placed in an in situ kidney and connected with a laboratory conductometer. Renal blood flow (continuous venous outflow recording), glomerular filtration rate ( $C_m$ ) and excretion rates for water, sodium and total solutes were measured simultaneously.

The rats received either furosemide, 0.3 mg/kg i.v., followed by infusion at 0.3 mg/min · kg, or acetazolamide, as a single injection of 10 mg/kg. With si-

milar increases in renal excretion, the two diuretics affected medullary tissue admittance (electrolyte concentration) quite differently. After furosemide (a loop diuretic) admittance fell sharply within the first 10 min, then partly recovered and reached a plateau 35 min after injection. These changes were more pronounced for the inner than for the outher medulla. Acetazolamine (inhibitor of proximal reabsorption) caused no changes in admittance compared to the pattern observed in untreated control animals.

The data show that dissipation of tissue electrolytes from the renal medulla is not simply a consequence of diuresis and natriuresis but depends critically on the site of salt transport inhibition in the renal tubules.

See the List of Publications:

a) 6, 7, 9, 19, 25, 26, 27, 37, 43, 48, 54, 75, 76, 108, 115, 120, 121, 122, 123; b) 2, 4, 5, 6, 7, 8, 9, 12, 13, 14, 20, 21, 22, 23, 24, 25, 30, 31, 41, 44, 45, 46, 47, 48, 49, 51, 55, 56, 57, 58, 65, 68, 69, 70, 81, 86, 87, 91, 92, 93, 94, 95.

Cardiovascular Laboratory
Head: Assoc. prof. Krystyna Cedro-Ceremużyńska

## I. Myocardial lipid peroxidation in stress, ischemia and hypoxia

In conscious intact pigs, stress of immobilization led to enhanced myocardial lipid peroxidation, a decrease in mitochondrial adenine nucleotides and distinct ultrastructural alternations showing that the free radical-mediated membrane damage contributes to the stress-induced heart injury. In anaesthetized pigs subjected to acute coronary occlusion, lipid peroxidation of myocardial membranes was intensified not only in ischemic region, but also within the nonischemic area. This suggests that the free radical—mediated lipid peroxidation is involved in the development of myocardial alterations in the nonischemic portion of locally ischemic heart. In the isolated working heart of rat's subjected to ischemia reperfusion, calmodulin antagonist, trifluoperazine (5  $\times$  10 $^7$  M) attenuated release of malondialdehyde and LDH and improved postischemic recovery of hemodynamic function. These results indicate involvement of calmodulin-dependent mechanisms in peroxidative injury of cellular membranes.

# II. Effects of sympatholytics and sympathomimetics on the protein phosphorylation in hypertrophic myocardium

In the rat heart mitochondria, two types (I and II) of  $Ca^{++}$  — activated neutral protease were found. In hypertrophic hearts, activity of the type I of

mitochondrial protease predominates. Propranolol exerts differential effects on each type of protease: inhibitory on the type I, and stimulatory on the type II. These findings suggest different function of each type of enzyms.

In the isolated rat heart myocytes, isoproterenol ( $2 \times 10^{-6}$ ) was found to stimulate protein phosphorylation, whereas propranolol ( $2 \times 10^{-5}$  M) inhibited this process. The latter mechanism might contribute to the therapeutic effectiveness of propranolol in myocardial hypertrophy.

See the List of Publications: a) 31, 38, 65, 117.

Laboratory of Experimental Surgery Head: Assoc. prof. Jerzy Borkowski

# EVALUATION OF THE STATE OF PERIPHERAL CIRCULATION IN PATIENTS WITH VASCULAR DISEASES

1. It was proved that the beneficial effect of transcutaneous electric stimulation — a supporting method in the treatment of peripheral circulation disorders — is connected with the release into the circulation of endogenous prostanoids with the platelet disaggregating properties. The biological activity of these substances can inhibit formation of the new and "dissolved" thrombi formed earlier.

In the effect of transcutaneous electric stimulation blood flow in the limbs was found to increase in patients with Raynaud's disease or symptoms. Impedance reography applied in the patients enabled to evaluate these changes quantitatively.

- The sympathetic inhibition induced by i.v. infusion of a sympatholytic drug
   — reserpine to artificially ischemic limbs showed its limited usefulness (a short
   therapeutic effect) in the treatment of Raynaud's disease or symptoms.
- 3. Prostaglandin E<sub>1</sub> was found useful in the treatment of peripheral artery disorders. The results of clinical tests performed will serve for determining the best administration mode, optimal dosage, and the methods of objective evaluation of the therapeutic effects.
- 4. Concurrently with the investigations described above an experimental work has started on the evaluation of the usefulness of  $Nd:Y_{ag}$  laser in surgery. The preliminary results on the application of the laser for arresting bleeding from the gastric ulcers, and for joing blood vessels will make it possible to proceed with a detailed elaboration of the new research project.

See the List of Publications: a) 144.

# STUDIES ON THE STRUCTURE AND BIOLOGICAL PROPERTIES OF THE NERVOUS TISSUE

Department of Neuropathology Head: Assoc. prof. Irmina B. Zeiman

## 1. Pathomechanism and prevention of postischemic encephalopathy

The studies have dealt with the description of the dynamics of ischemic encephalopathy following clinical death and included attempts to assess the condition of the blood-brain barrier and the responses of the immunological system as well as certain aspects of maturation of the pathological process. An acute ischemic episode following 15-minute clinical death in rats characterized by nonspecific degenerative changes and moderate cell loss was observed to develop into an encephalopatic process progressing up to 6 months after the episode. The process showed features of systemic lesions and involved both nerve cells and glia. Ultrastructural changes showed the pattern and dynamics depending upon the duration of both the ischemic episode and postischemic period. They involved the cerebral cortex, the selectively vulnerable segment of hippocampal gyrus, and distinctly affected the synaptic junctions. Examination of the blood-brain barrier with radiolabelled tracers revealed no damage to the barrier mechanisms. However, the use of more sensitive immunocytochemical methods allowed to detect in the early postischemic periods, extravasation of serum proteins into the brain tissues and their quite intensive inhibition in the periventricular region indicating transient alterations to the barrier. Postischemic changes in the permeability of the cerebral vessels became manifested by disturbances in the activity of two vascular transport markers - alkaline phosphatase and adenylate cyclase. Immunocytochemical studies revealed under the same conditions, a transiently decreased immunoreactivity of the CNS cell antigens (\$100 protein - the neuron-specific enolase) and reaction with monoclonal antibodies Leu-7/HNK-1disclosing epitopes, common to the hematopoetic and nervous system. The development of postresuscitation encephalopathy was accompanied by appearance in the blood serum of antibodies againts nerve cells of cerebral and cerebellar cortex, basal ganglia, hippocampal formation and some of the brainstem structures. The immunoreactivity was organ- but not species-specific.

A detailed ultrastructural characterization of synaptic junctions located in different fragments of perikarya and dendritic processes of pyramidal cells of the Ammon's horn (individual cortical layers) was carried out as an introduction to studies on the mechanism of their selective vulnerability to ischemia.

Studies on the reaction to hypoxia of neurons of the substantia nigra in organotypic culture revealed a selective vulnerability of the so-called light cells. Their damage was accompanied by a glial reaction and an absence of changes within synaptic junctions. Other studies, with the organotypic nerve tissue culture subjected to hypoxia, revealed a cytoprotective effect of the calcium channel blocker — nimodipine, directed towards both neurons and glial cells.

# 2. The role of glia in the physiological and pathological processes of the central nervous system

The studies have focused on the transport and metabolism of amino acid neurotransmitters in astrocytes and nerve endings (bulk isolated fractions) in experimental hepatic encephalopathy (HE) in the thioacetamide model. Advanced stages of HE were found to be accompanied by severe disturbances in the astrocytic transport of glutamic acid (decreased uptake) and GABA (increased spontaneous release, indicating "leakage"). In completion of the studies on the early "metabolic" stage of HE the previously observed increased GABA transport in either direction (uptake/release) has turned out to be GABA specific: no such effect was observed with glutamic acid, histamine. or histidine. Astroglial metabolism in the advanced, but not in the early stage of HE, was characterized by an increased vulnerability to an excessed ammonia load, as manifested by a markedly decreased utilization of glutamic acid as energy substrate. This observation is consistent with the decreased utilization of deoxyglucose in discrete brain regions, as revealed by quantitative autoradiography. Advanced HE in the same model stimulated the activity of gamma-glutamyl-transpeptidase — an enzyme involved in glutamine transport across the blood-brain barrier, in astrocytes as well as in cerebral capillaries and nerve endings. This effect is understood to aggravate amino acid imbalance in the brain. The nerve endings were found to react to HE with an increased potential to utilize arginine in glutamic acid and GABA synthesis which provided the first evidence for metabolic (adaptive?) stimulation of the synapses by HE. The observation of a decreased Ca2+ transport into astrocytes offered an additional indication of a decreased neuroregulatory potential of these cells during HE.

Another line of investigations has dealt with the immunomorphological characterization of astroglia. Studies on astrocytes contacting (or lining) cerebral tumors revealed the role of alpha-1-chemotrypsin as a marker of cell activation towards neutralization of proteases originating from peritumoral edematous fluid. Astrocytes in organotypic culture of the rat cerebellum were shown to be rich in a number of macrophagic and astrocytic markers.

# 3. Action of specific neurotoxins as a pathological basis of degenerative processes in the central nervous system

The studies have dealt with two neurotoxins: the parkinsonism-inducing drug MPTP and the excitotoxic glutamate analogue quinolinic acid (QUIN). In vivo administration of MPTP into mice C57 was found to produce different effects on the mouse striatal GABA-ergic and dopaminergic system (DA): a pronounced decrease of DA and increase of GABA content. Coadministration of the reduced glutathione decreased the deleterious effects of MPTP on both the neurotransmitter systems, possibly by inhibiting the formation of the active MPTP metabolite — MPP\*.

QUIN, as analysed both in dissociated and organotypic cultures of hippocampus, was found to selectively affect dendritic processes and pyramidal neurons, while sparing granular cells, axonal processes and glial cells. The effect of QUIN was only observed in cultures with mature synaptic junctions. When administered in situ into the rat brain hippocampus, QUIN reduced the GABA content, in the degree depending, in a predictable way, upon the site of injection and the vulnerability of particular structures.

In extension of the studies on the other excitotoxin glutamate analogue — kainic acid (KA) it was found that Tiapride, a drug counteracting involuntary movements in Huntington's chorea is ineffective towards KA-induced changes in the organotypic striatal cultures.

# 4. The pathomechanism of deficient myelination in the pt rabbit

An analysis of ultrastructure of axons revealed the axonal changes to codevelop with the formation of myelin and to be the most intensive in nonmyelinated or ill-myelinated fibres. This indicates that axonal abnormalities may contribute to the disturbed axonnal-glial interrelation in this mutant.

See the List of Publications:

a) 1, 2, 3, 8, 18, 21, 45, 49, 50, 51, 52, 53, 72, 73, 74, 81, 82, 85, 86, 89, 90, 91, 92, 93, 94, 98, 101, 104, 105, 106, 107, 111; b) 1, 15, 16, 33, 34, 35, 36, 38, 39, 40, 50, 52, 53, 54, 60, 61, 75, 76, 77, 78, 83, 84, 85, 88, 90.

Department of Neurochemistry
Head: Assoc. prof. Jerzy Łazarewicz

## PRESYNAPTIC PROCESSES IN BRAIN DURING NORMOXIA AND ISCHEMIA

The studies carried out in 1987 were performed to understand better the pathomechanism of brain disfunction during ischemia. The effect of brain ischemia on glutamatergic and histaminergic neurotransmission and calcium

ion homeostasis was investigated. The agents protecting the brain against ischemic damage was included in the studies. It was shown in "in vivo" and "in vitro" studies that anoxia is manifested in a decrease of a portion of Ca<sup>2+</sup> bound with membrane hydrophobic domains monitored by chlortetracycline fluorescent chelate probe.

The anoxia-evoked displacement of a membrane bound Ca<sup>2+</sup> to the free ionic form may trigger a complex intracellular reactions (cooperation with Pavlov Institute of Physiology, Leningrad).

The effect of nimodipine (a voltage dependent calcium channel blocker) applied either systemically or locally to hippocampus of the rabbit submitted to 15 min cerebral ischemia was studied. It was found that nimodipine significantly accelerated the disappearance of bioelectric activity in hippocampus during ischemia as well as the time of EEG recovery and improved the pattern of EEG recordings. Nimodipine significantly reduced the drop of extracellular calcium and ischemic release of glutamate to extracellular space of hippocampus and the leakage of methionine during recirculation.

Systemic application of nimodipine completely inhibited the brain-blood barrier damage (cooperation with the Department of Neurology).

Nimodipine remained without any effect on the elevation of intracellular calcium produced by kainic acid. The results suggest that voltage-dependent calcium channels are involved in ischemic pathology. During brain ischemia there is liberation of purines (adenosine, hipoxanthine and inosine) into the extracellular compartment. During postischemic period normalisation of these changes occurs with an elevation of xanthine.

It seems likely that adenosine exerts some protective effect but the elevation of xanthine may be connected with an activation of the xanthine oxidase, involved in the liberation of free radicals (cooperation with the Institute of Neurology, University of Goeteborg).

Studies concerning metabolism of histamine were performed in synaptosomes and astroglia cells. Histamine (HA) was found to be actively taken up by astrocytes while histidine uptake by synaptosomes was more active than by astrocytes.

Kinetic analysis of the astrocytic HA uptake revealed a high-affinity-low capacity system similar to the astroglial transport system for the other neuro-transmitters.

Histamine methyltransferase (HMT) was 70% more active in astrocytes than in synaptosomes, whereas histidine decarboxylase (HD) was not different in these two preparations.

The results indicate that astrocytes could be the major site of histamine inactivation (cooperation with the Department of Neuropathology).

Ischemia induced an increase in both enzyme activities involved in histamine metabolism and caused a derease in the level of HA and uptake of histidine. The effect of ischemia appeared to be reversible within one hour of resuscitation.

Hypoxia produced only some insignificant changes in all the parameters studied (cooperation with the Institute of Reanimatology, Moscow).

ROLE OF MODULATION MOLECULES AND BIOACTIVE LIPIDS AND PROTEINS IN SIGNAL TRANSDUCTION FROM RECEPTOR(S) INTO THE CELLS

The studies in 1987 concerned the enzymes and intermediate molecules involved in the modulation of signal transduction from receptor(s) into the cells.

The receptor mediated hydrolysis of inositol phospholipids through the action of phospholipase C provides two second messenger molecules, namely 1,2-diacylglycerol (DAG) and inositol 1,4,5 trisphosphate (IP<sub>3</sub>). The activity and regulation of phospholipase C degraded phosphoinositides was investigated in the brain plasma membrane microsomes and cytosol. It was found that phospholipase C in the brain plasma membrane degrades diphosphophosphatidylinositol (PIP<sub>2</sub>) independently of Ca<sup>2+</sup>. Phospholipase C acting against PIP<sub>2</sub> and phosphophosphatidylinositol (PIP) are stimulated by Ca<sup>2+</sup> and regulated by guanine nucleotides independently of Ca<sup>2+</sup> in the plasma membrane of brain.

GTP remained without any effect on the enzyme located in cytosol and microsomes (Strosznajder).

For better understanding of the role of phosphoinositides and modulating factors (such as: diglycerides, Ca<sup>2+</sup> and guanine nucleotide) in signal transduction, further studies were carried out using the cell culture of Ehrlich Ascites tumor cells.

When growth of these cells was stimulated by 1-oleoyl-2-acety-sn-gly-cerol (OAG), the membrane permeable analog of DAG, the labelling of phosphoinositides with [3H] inositol and the level of radioactivity in the inositol phosphates including IP<sub>3</sub> revealed lower levels versus the non stimulated cells (cultivated in presence of 2% serum).

The activity of phospholipase C from OAG-activated cells (membrane bound and cytosolic enzyme) was suppresed and it was activated by GTP. The other pathway of phosphoinositide metabolism — phosphatidylinositol kinase was stimulated.

These results provide a strong support of the hypothesis according to which the endogenous diglycerides play a critical role in the control of cell proliferation through the regulation of phosphoinositide metabolism (Strosznajder and Haeffner — German Cancer Research Centre, Heidelberg).

In the OAG-stimulated cells, the intracellular Ca2\*-concentration increased by about 41% despite the lower level of IP3. Protein kinase C and phosphorylation were activated. It seems possible that activation of the protein kinase C by diglycerides with the subsequent stimulation of protein phosphorylation

(including phospholipase C) may be responsible for the feedback regulation of phosphoinositide metabolism (Strosznajder, Seibicke, Haeffner — German Cancer Research Centre, Heidelberg).

The calcium-dependent neutral proteases may be involved in the activation of phospholipase C and protein kinase C.

Studies on the intracellular localisation of calcium-activated neutral proteases in the brain showed that 80% of the total enzyme(s) activity (stimulated by mM Ca2 $^{+}$  and  $\mu$ M Ca2 $^{+}$ ) is localised in cytosol and 20% in membrane fraction.

The enzyme activity-dependent on mmol Ca<sup>2+</sup> concentration-had higher activity in all the membrane fraction except mitochondria (Zalewska and Kawashima — Tokyo Metropolitan Institute of Gerontology, Tokyo).

The other important enzyme system involved in the signal transduction is adenylate cyclase. This enzyme is activated in the brain by ischemia. Moreover, ischemia stimulates the responsiveness of adenylate cyclase system to noradrenaline and histamine, indicating participation of adenosine and the receptor  $A_2$  in brain ischemia.

In postischemic period the responsiveness of adenylate cyclase is depressed, probably by activation of lipid peroxidation processes (Domańska-Janik, Pylova — Institute of Reanimatology, Moscow). The activation of lipid peroxidation in myelin membrane significantly decreased the Na<sup>†</sup>K<sup>†</sup> ATPase, affected 5' nucleotidase and remained without any effect on the CNP-ase activity.

The activation of free radical lipid peroxidation may influence signal transduction in the central nervous system (Domanska-Janik, Bourre — INSERM, Paris).

See the List of Publications:

a) 17, 23, 30, 66, 68, 69, 89, 100, 112, 113; b) 11, 37, 59, 66, 67, 71, 72, 73, 74, 82.

Department of Neurosurgery Head: Prof. Eugeniusz Mempel

I. BIOELECTRICAL ACTIVITY OF THE BRAIN AFTER STEREOTAXIC LESIONS IN NEUROSURGICAL PATIENTS

Electrophysiological investigations concerning the influence of L-dopa derivatives on somatosensory evoked potentials (SEP) were performed in patients with extrapyramidal diseases. An influence of Nakom and Madopar on neurotransmission in different cases of Parkinson disease and various forms of muscular dystonia was investigated.

The distinct influence of the above drugs on normalization of SEP curves and simultaneosuly a positive influence on neurotransmission in the pa-

tients with Parkinson disease was observed. However, in severe cases of Parkinson disease, treated for several years with L-dopa derivatives and showing signs of the drugs' intolerance, the effect of L-dopa derivatives on neurotransmission was distinctly negative ("depressive curve" of SEP's with lowered amplitudes and delate latencies). The above symptoms indicate a diminished or retained responsiveness to the L-dopa treatment.

Stereotaxic thalamotomy in these cases reduced the symptoms of L-dopa intolerance and improved the clinical state of the patients.

The electrophysiological data are of practical importance since they make it possible to predict results of the treatment of parkinsonian patients with L-dopa derivatives. In cases of muscular dystonia the L-dopa derivatives did not shown any positive influence on neurotransmission.

### II. VOLUME-PRESSURE RELATIONS IN DIFFERENT INTRACRANIAL PATHOLOGY

The computer controlled infuser has been developed using the previously built digital infusion pump. The new infuser enables different infusion and withdrow rates, depending on the chosen parameters measured by the computer. The preliminary infusion tests were performed and further minimalization of the test invasity was achieved.

The posttraumatic brain volume enlargement was studied in patients and in cats. The dynamic computerized tomography (CT) was used to measure the tissue density changes and to evaluate the cerebral circulation. The vasodilatation was found to be responsible for the ICP increase directly after the trauma. In animal experiments the dynamic CT was very useful in evaluating the cerebral circulation, and a very close correlation was ascertained between the CT findings and the morphological picture of the blood-brain barrier disturbances.

#### III. PERCEPTION OF NONVERBAL STIMULI IN BRAIN DAMAGE

- 1. Ten healthy subjects and 10 patients with lesions of either the right or the left hemisphere of the brain were examined for recognition of visual nonverbal material developed in this Clinics (overlapping letters and graphic signs). It was found that in patients with the right hemisphere lesions (in the parietal-temporal-occipital region) impaired recognition of nonverbal graphic signs was associated with disorders of spatial construction and drawing. Results of this study, especially those concerning the spatial examination, may be useful for rehabilitation of alexia.
- 2. Eighteen healthy subjects and 10 patients with focal lesions of either the right or left hemisphere of the brain were examined in a soundproof camera.

They were asked to look at a central fixation spot and to recognize nonverbal stimuli (pictures of human faces) projected either to the right or left visual half-field. The right cerebral hemisphere was found to be responsible for the perception of faces, irrespectively of the locus of lesion. As regards the left hemisphere lesions, the obtained results were similar to those obtained in the subjects without any brain damage.

See the List of Publications: a) 10, 11, 12, 70.

Laboratory of the Developmental Neuropathology Head: Prof. Maria Dambska

A COMPARISON OF NORMAL BRAIN DEVELOPMENT WITH ITS DISTURBANCES PROVOKED BY SELECTED DAMAGING FACTORS AND PATHOLOGIC PROCESSES

Investigations carried out in 1987 concerned the relations between the period of brain development in the moment of being subdued to the brain damage and the final picture of consecutive encephalopathy. Human autopsy and experimental materials were examined.

The central nervous system changes in newborns and small infants deceased from acute respiratory distress syndrome were investigated. Lesions of the brain stem structures responsible for the regulation of respiration were found in majority of cases with deterioration of the clinical state.

The study of myelination of the brain stem in newborns and of the temporal lobe in small infants proved that severe and prolonged diseases may provoke retardation of this process.

The paraneoplastic cerebellopathy occurred very frequently and it was similar to that observed in adults with additional damage of the external granular layer in small infants.

Prolonged behavioral changes were observed after treatment with vincristine (a known antimitotic drug) early after birth.

See the List of Publications: a) 14, 15, 16, 32, 33, 63; b) 10. Laboratory of the Ultrastructure of the Nervous System Head: Prof. Jerzy Borowicz

ULTRASTRUCTURAL CHARACTERISTICS OF THE HYPOTHALAMO--NEUROHYPOPHYSEAL SECRETORY SYSTEM FOLLOWING COMPLETE TRANSIENT CEREBRAL ISCHEMIA

The electron microscopic studies were carried out to elucidate ischemic and postischemic changes in the hypothalamic neurosecretory nuclei: n. supraopticus and n. paraventricularis, as well as in the neurohypophysis of rats that underwent the incident of clinical death. The tissue samples were taken 3 hours and 7 days after complete cerebral ischemia of short-duration and in case of neurohypophysis also immediately after as well as 3 days after the experiment. Marked alterations concerned neurocytes of the hypothalamic secretory nuclei. They exhibited dilatations of the Golgi cisternae and some areas of granular endoplasmic reticulum, as well as occassional swelling of the presynaptic endings. These changes as well as moderate edema of the region examined were observed 3 hours after ischemia. Seven days after cessation of the experiment only minimal changes were perceptible in some areas of the hypothalamic nuclei. Majority of the secretory neurons did not reveal any ultrastructural alterations. Examination of the neurohypophysis provided an evidence for numerous alterations in pituicytes, indicating a high sensitivity of these cells to ischemic conditions. Four types of pituicytes were revealed basing on their ultrastructural characteristics, namely: swollen, dark, vacuolate, and "intermediate". Enclosure of neurosecretory axons by pituicytes was commonly observed. These results suggest involvement of pituicytes in the mechanism of control (inhibition) of neurohypophyseal hormone release. On the same experimental model the nucleus gigantocellularis of the medullary reticular formation was also examined. A transient, complete cerebral ischemia resulted in striking ultrastructural changes affecting large neurons. In these neurons swollen mitochondria, vacuoles, and electron-lucent areas in cytoplasm were observed. These ultrastructural changes persisted and became even more pronounced seven days after the experiment. They were accompanied by edematous changes in this brain area, particularly well pronounced in the perivascular tissue. Small neurons did not show any changes.

See the List of Publications: a) 20, 21, 67, 110, 118, 119.

### STUDIES ON TRANSPLANTATION AND EXPERIMENTAL SURGERY

Department for Surgical Research and Transplantation Head: Prof. Waldemar Olszewski

THE MECHANISM OF IMMUNE PROTEIN CAPILLARY TRANSPORT INTO TISSUE SPACE AND LYMPHATICS

The increased capillary filtration of proteins and cells in venous hypertension was studied. The biological and biochemical assessment of interleukin 1 and 2 in the tissue fluid and lymph of the man was made. We have found that increased hydrostatic pressure in the venous part of the capillary caused an increase in IgG output in lymph, whereas the IgM output was unchanged. Increased hydrostatic pressure caused also an increment in the transport of migrating cells and erythrocytes into the lymph. Increased filtration pressure, when combined with increased blood flow, provoked a rise in the IgG and IgM levels in lymph, whereas the albumin to globulin ratio was at the control level. No correlation between the output of total protein and migrating cells was found. The obtained results suggest that the kinetics of protein transport and migration of the cells from the blood to the lymph are regulated by different mechanisms. The activity of interleukin 1 and IL-1 inhibitor was measured in human lymph after separation the lymph into different fractions on chromatographic column. It was found that the molecular weight of active fractions was for IL1 fraction >70kD, 13-16kD and 5-5.5kD, while for the IL1 inhibitor fraction >70kD, 22-30kD and 5.5-8kD.

# THE INFLUENCE OF DONOR SPECIFIC TRANSFUSIONS ON THE ALOGENEIC GRAFT SURVIVAL

The effect of allogeneic donor specific blood transfusion (DST) on the heart graft survival in BN to LEW rat strain combinations was studied. We found that blood transfusion in this strain combination was as effective as in AUG to WIS strain combination. Both strain combinations differ in strong histocompatibility antigens. Blood transfusion did not influence the class II antigen expression on the cell surface in lymphoid organs (blood, spleen and lymph nodes) as compared to untreated controls. The expression of IL-2 receptor (ART18 monoclonal antibody) on the cells from lymphoid organs of the recipients after DST on freshly isolated cells and cells stimulated for 48 hr with PHA was also investigated. The IL-2 receptor was not found on cells freshly isolated from the blood and spleen. However, the higher number of ART18+ cells was found among PHA stimulated blast cells from DST recipients compared to control rats.

#### ALLOGENEIC SKIN TRANSPLANTATION FOR THE CLINICAL PURPOSE

Passenger-Langerhans cells migrating through the skin were characterized functionally. The rabbit anti-dog immune serum against Langerhans cells was prepared. Two methods of Langerhans cells isolation from the afferent lymph of dogs suffering from chronic lymph stasis were established: one, using Percoll gradient and the second, using metrizamide gradient. Isolated cells showed slight peroxidase (10%) and acid phosphatase (40%) activities. In about 60% of these cells a nonspecific esterase activity was demonstrated. All dendritic cells displaying positive staining for ATP-ase, were class II and S-100 protein positive. When 5% of these cells were added to the lymphocyte culture, the enhancement of mitogen stimulation was observed. They were also capable to stimulate MLC and auto-MLC. The rabbit immune serum, prepared by immunization with fraction enriched in lymph dendritic cells, was cytotoxic for those cells (aglutination titer 1:256, cytotoxic titer 1:8). In next experiments, anti-dendritic immune serum will be used to remove passenger cells from skin allografts in dogs in in vivo studies.

# CELLULAR MECHANISMS OF REJECTION AND ACCEPTANCE OF ALLOGRAFTS

The function of class I and II antigens in elimination of allogeneic lymphoid and nonlymphoid cells after grafting was studied. It has been shown, that allogeneic lymphocytes when transplanted intravenously in AUG to WIS rat strain combination were eliminated within 6 hr. In order to check whether this phenomenon is exclusively restricted to lymphoid cells, the non lymphoid cells (erythrocytes, chondrocytes, fibroblasts, intestinal and renal epithelial cells) were transplanted into allogeneic and syngeneic recipients. Moreover, the expression of class I and II MHC antigens by those cells was studied. We found that allogeneic erythrocytes (OX18+) were eliminated in the same rate as syngeneic ones. Allogeneic fibroblast (OX18+, OX6-) and intestinal epithelial cells (OX18+, OX6+) were eliminated slighty faster than syngeneic ones, whereas renal epithelial cells and chondrocytes (OX6-), both allogeneic and syngeneic, were eliminated in the same maner. Our results suggest, that lymphoid cells may possess some structure which allows their active elimination by recipient cytotoxic cells.

#### IMMUNE STATUS OF THE IMMUNOSUPPRESSED HOST

The kinetics of interleukin 1 and 2 production and secretion by blood mononuclear cells from patients after operative trauma (cholecystectomy) was studied. IL-1 was measured in supernatants of mononuclear blood cells and monocytes stimulated with LPS, using thymocytes of C3H/HeJ mice. IL-1 acti-

vity in culture supernatants of mononuclear cells was significantly increased on days 1 and 3 after the operation, and returned to the preoperative values on days 5 and 7. Similar activities of IL-1 were found in culture supernatants of monocytes. IL2 activity was measured in culture supernatants of mononuclear blood cells stimulated with PHA, using IL-2 dependent cell line CTLL2. IL-2 activity in the culture supernatants decreased significantly on days 1, 3 and 5 after the operation and returned to the preoperative values on day 7. The increased number of cells expressing IL-2 receptor was found 1 day after the operation on cells cultured with PHA. It was again within the range of preoperative values on days 3, 5 and 7. It seems that one of the mechanisms responsible for a decreased immune response after the operative trauma is IL-2 insufficiency. Therefore, the clinical studies on the IL-2 therapy in patients suffering from postoperative infections, difficult to treat with antibiotics, would be of a great value.

See the List of Publications: a) 5, 22, 24, 28, 29, 55, 56, 57, 71, 77, 78, 79, 80, 96, 97, 109.

#### OTHER RESEARCH WORKS

Mental Health Department Head: dr Zygfryd Juczyński

1. EVALUATION OF SOME FACTORS OF SOMATIC HEALTH AND THE FREQUENCY OF PSYCHOPATHOLOGICAL SYMPTOMS IN SELECTED GROUPS OF CHILDREN

More than 2 000 children and adolescents from 6 to 20 years, with behaviour and school problems, mental and emotional disorders and without any evident mental pathology were included into the research program.

Percentages of "normal" children, selected to dispensary groups ranged from 33 to 68%. Among disorders of health conditions as the most frequent were found: the anomalies of physical development, ophtalmic diseases and retardation of mental and/or somatic development. According to the factor of biological risk 1/4 of children were qualified to the group of higher risk.

In the group of children with educational problems the disorders of somatic conditions were found in 6% of cases. Neurological examination and EEG recording revealed pathological changes — localized in 35% and generalized changes of a minor degree in 35% of cases. The psychopathological "picture" was very differentiated. In the group of "normal" children some psychopathological symptoms were found and their dynamics were connected more with age, than sex of a child. Among children with educational problems behaviour disorders and vegetative dysfunctions were frequent. In the group with the mental state pathology 49% of cases were diagnosed as the personality disorders.

#### 2. AN ANALYSIS OF LIFE-STABILIZATION IN DRUG DEPENDENT PEOPLE

The study was based on the catamnestic evaluation of drug addicts who were found drug dependent 10 years earlier. The biggest group (50% of cases) is represented by individuals, who periodically stopped or reduced drug use. This group presents several social as well as health problems connected with the earlier periods of intensive drug abuse. Next group is formed by the recovered patients with normal social life who stopped completely drug usage. To the last group persons deeply dependent may be included. The first, largest group, with reduced drug consumption, needs the most intensive medical and psychological care.

# 3. SOMATIC CONDITIONS AND LIFE-ACTIVITY OF PATIENTS WITH DIAGNOSIS OF CANCER

Among 104 subjects, aged 25-65, with the cancer of breast, cervix and large intestine 71% are still working. As the result of disease, evident changes in the self-concept, lowering of self-acceptance, and diminished self-esteem — mainly in the patients with the breast cancer — were revealed. Patients with the cervix cancer demonstrate more frequently the attitude of resignation and insecurity, which is connected with the decreased needs of achievement and endurance. In all groups the majority were the external-oriented persons. This fact can facilitate the therapeutic actions.

See the List of Publications:

a) 39, 40, 41, 42, 99, 102, 116; b) 27, 28, 29, 62, 63, 64, 79, 80, 89.

#### The library

Head: Krystyna Marczakowska

The Library has been organized on July 1st 1967 by an integration of many small medical libraries belonging to the Polish Academy of Sciences. Now, it constitutes one department of the Medical Research Centre and acts as an information source for scientists.

Library structure: main library with affiliated special library in Łódź. Scope and the subject profile: physiology, neurosciences, and experimental surgery including transplantology.

Present holdings:

books — monographic and serial volumes (Polish and foreign) — 17344, periodicals, newspapers (number of titles) — 465

unpublished documents (dissertations, research reports — SYNABA, in hard copies) — 170

microfiches - 3800

Reference alds:

catalogues - alphabetical: books, periodicals and microfiches,

- subject: books,

main card-files — bibliographical list of papers published by scientists of the Medical Research Centre from 1967.

Number of inquiries and services per year:

circulation of documents (original or copies):

reading room and library loan - 7500

interlibrary loan - 1335

direct reference services (in person, by telephone) — 566, circulated news, current books and periodicals for the Departments users — 3770

reprographic services: xerocopies — 1385 systems of the user-oriented information services:

SDI — manual 11 topics current and retrospective dissemination information — 37 MEDLINE — 6 SYNABA — 53 scientists citation reports — 950 (up to 1984)

Users:

scientific workers of the Medical Research Centre,

interlibrary loans available for all scientific Institutes in Poland and abroad. Bibliography of library: list of new books and current periodicals prepa-

red weekly.

# MEDIPAN — Scientific Instruments Department Head: Andrzej Lasek

"MEDIPAN" is a scientific enterprise which is a part of the Medical Research Centre Polish Academy of Sciences.

There are 50 employees in this enterprise, including 20 persons with technical and economical university education. In the Development Department there are 12 permanent employees including 9 persons with technical university education. Temporarly in order to solve a special problem, the Development Department employs specialists well familiar with a particular branch of science. "MEDIPAN" develops unique scientific research devices according to the needs of its own Institute or other scientific Institutes.

This enterprise specializes in producing various types of infusion pumps (601, 602, 604, 605, 610) used in the health service. They are also applied in the cardiological therapy departments. Technical parameters of these pumps are equal or even better than those of the pumps produced by some other leading producers all over the world e.g.: B. Braun Melsungen — GFR, Fresenius — GFR, IVAC — USA, VIAL — France.

"MEDIPAN" produces also the unique device called: "physiotest" and "chloridometer". The "physiotest" is used in various human exercise tests. It can be also applied in the tests serving for evaluation of the progress in rehabilitation of coronary patients after myocardial infarction. The "chloridometer" is used for measuring chloride content in human body fluids. It may be also applied for other fluids (e.g. cow milk, water etc.). All the above mentioned devices are made using Polish parts or the parts from other socialistic countries.

"MEDIPAN" is not subsidized by government so it must earn all the money needed to cover its activity.

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- Strosznajder J.: Molecular mechanism involve in modulation of GABA receptor binding in normoxic and ischemic brain. International Meeting of the International Society for Neurochemistry, La Guaira, Venezuela. J. Neurochem. 1987, 48, Suppl. S91-C.
- 72. Strosznajder J.B., Haeffner E.W.: 1-oleoyl-2-acetyl-glycerol (OAG) effect on phosphoinositides metabolism in growth-stimulated ascites tumor cells. Effect of GTP on phospholipase C activity. Herbstlagung der Gesellschaft für Biologische Chemie, Erlanger, September 27-30, 1987. Biological Chemistry Hoppe-Seyler 1987, 368, 1117.
- 73. Strosznajder J., Wikieł H.: Ischemia specifically enhances phospholipase C activity in brain synaptosomes. International Meeting of the International Society for Neurochemistry, La Guaira, Venezuela. J.Neurochem 1987, 48, Suppl. S122-A.
- Strosznajder J., Wikieł H.: Receptor linked polyphosphoinositides hydrolysis in gerbil brain during ischemia. 17th Congress of the Polish Physiological Society, September 15-18, 1987. Acta Physiol. Pol. 1987, 38, Suppl. 30(31), 180.
- 75. Szumańska G., Vorbrodt A.W., Mandybur T., Wiśniewski H.M.: Lectin histochemistry of Alzheimer disease. Abstr. of II World Congress of Neuroscience (IBRO), Budapest, August 16-21, 1987, 1319 P.
- 76. Śmiałek M.: Effect of MPTP on redox reactions in the mouse brain. Abstr. of II World Congress of Neuroscience (IBRO), Budapest, August 16-21, 1987, 178 P.
- 77. Śmiałek M.: Evaluation of the MPTP neurotic effect of oxidation-reduction processes in the mouse brain. Abstr. of VII Conference of the Association of Polish Neuropathologists and V Polish-Hungarian Neuropathological Symposium, Gdańsk, June 4-6, 1987, 65 (in Polish).
- 78. Taraszewska A.: Axonal changes in the course of deficient myelination in pt rabbit. Abstr. of VII Conference of the Association of Polish Neuro-

- pathologists and V Polish-Hungarian Neuropathological Symposium, Gdańsk, June 4-6, 1987, 68 (in Polish).
- 79. Tomalak E., Juczyński Z., Krawczyk L., Rendecka A., Starzyński P.: Somatic health and intensivity of psychopathology and social adaptation of school children in different developmental stages. Proc. of the IX Symp. of Child Psychiatrists, Łódź 1987, 91-103 (in Polish).
- 80. Tryzno W.W.: The informal youths group "Za Żelazną Bramą" as an example of the out institutional conective body performing ISM's the self treating of disordered social adaptation. Proc. of the IX Medical National Medicine and Child Psychiatrists, Łódź 1987, 155-157 (in Polish).
- 81. Turlejska W., Baker M.A.: Les facteurs responsables de la restitution rapide de la polypnée thermique chez la chien rèhydratè. Abstracts of Association des Physiologistes Conference on Physiologie Appliquee, Rouen, December 11-12, 1987, Abstr. 19 (in French).
- 82. Waśkiewicz J., Albrecht J., Rafałowska U.: Relationship between metabolism and transport of histamine in synaptosomes and astrocytes. XXIII Meeting of Polish Biochemical Society, Białystok, September 1987. Abstr. p. 356, comm. no I-130.
- Weinrauder H.: Immunocytochemical characterization of rat cerebellum in vitro by means of indirect immunofluorescence and avidin-biotin-complex method. 20 Donau Symposium for Neurological Sciences, Innsbruck, October 8-10, 1987, P24.
- 84. Weinrauder H., Zaręba-Kowalska A.: GFAP in neonatal astrocytes and pituicytes differentiating in vitro. Second World Congress of Neuroscience, Budapest, August 16-21, 1987, 1212 P.
- 85. Weinrauder H., Zaręba-Kowalska A.: Specific markers in nervous tissue culture. Abstr. of the VII Conference of the Association of Polish Neuropathologists and V Polish-Hungarian Neuropathological Symposium, Gdańsk, June 4-6, 1987, 71 (in Polish).
- 86. Wójcik-Ziółkowska E.: Application of the ergometric test with a static load component in the diagnosis and evaluation of coronary insufficiency. Abstracts of the International Symp. on Exercise Physiology dedicated to the memory of the late Prof. S. Kozłowski, Baranów Sandomierski, June 18-20, 1987, 94.
- 87. Wójcik-Ziółkowska E., Ziółkowski L., Szulczyk G.A., Płachcińska-Bijak M.: Changes in the exercise ECG and hemodynamic responses to physical exercise with various isometric components in patients with coronary heart disease. Abstracts of the 17th Congress of the Polish Physiol. Soc. Warsaw, September 15-18, 1987. Acta Physiol. Pol. 1987, 38, Suppl. 30(3), 210.
- 88. Wysmyk-Cybula U., Albrecht J.: Energy metabolism in neurons and astro-

- cytes of rats in thioacetamide induced hepatic encephalopathy. Abstr. of the VII Conference of the Association of Polish Neuropathologists and V Polish-Hungarian Neuropathological Symposium, Gdańsk, June 4-6, 1987, 73 (in Polish).
- 89. Zakrzewski P.: Syndrom of early social maladjustment and the beginning of alcohol-use or other drug abuse. Proc. of the IX Symp. of Child Psychiatrists, Łódź 1987, 63-70 (in Polish).
- Zelman I.B., Mossakowski M.J.: Remote pathomorphological changes in the central nervous system of rats following 15 min. clinical death. Abstr. of VII Conference of the Polish Neuropathologists and V Polish-Hungarian Neuropathological Symposium, Gdańsk, June 4-6, 1987, 74 (in Polish).
- 91. Ziemba A.W., Andres R., Fleg J., Blackmann M.: A relationship between physical fitness, body mass index and resting and post exercise serum testosterone level in healthy males of different age. Abstracts of the 17th Congress of the Polish Physiol. Soc. Warsaw, September 15-18, 1987. Acta Physiol. Pol. 1987, 38, Suppl. 30(3), 215.
- 92. Ziemba A.W., Fleg J., Andres R.: Interregulationships between age, obesity, pattern of fat distribution, physical fitness and metabolic risk factors of coronary heart disease. Abstracts of the International Symp. on Exercise Physiology dedicated to the memory of the late Prof. S. Kozłowski, Baranów Sandomierski, June 18-20, 1987, 96.
- 93. Ziemba A.W., Fleg J., Andres R.: Metabolic and circulatory responses to the prolonged physical exercise in elderly people. Proceedings of the 20th Congress of the Polish Soc. of Sports Medicine, Warsaw, October 15-17, 1987, 82-84 (in Polish)
- 94. Ziółkowski L.: Effect of an increased physical activity for 3-4 years after myocardial infarction on the course of coronary heart disease: 12 years follow up study. Abstracts of the International Symp. on Exercise Physiology dedicated to the memory of the late Prof. S. Kozłowski, Baranów Sandomierski, June 18-20, 1987, 98.
- 95. Ziółkowski L.: Hemodynamic response to exercise-tests in coronary patients in relation to the degree of myocardial ischemia. Abstracts of the 17th Congress of the Polish Physiol. Soc. Warsaw, September 15-18, 1987. Acta Physiol. Pol. 1987, 38, Suppl. 30(3), 216-217.

### SCIENTIFIC DEGREES AND HONORS OBTAINED

### D.Sc. degree thesis:

- Grieb Paweł: Probing tissue oxygen environment with the indicator dilution technique using stable oxygen isotope <sup>18</sup>O (Department of Neurophysiology).
- Maślińska Danuta: Some metabolic and structural effects in the developing central nervous system of intoxication with an phosphoorganic compound (Laboratory of the Developmental Neuropathology).
- 3. Romaniuk Jarosław R.: Control of the breathing pattern (Department of Neurophysiology).

#### M.D.

- 1. Grochowicz Paweł: Allogeneic peripheral nerves transplantation in rats under CyA immunosuppressive therapy (Department for Surgical Research and Transplantation).
- 2. Kida Elżbieta: Morphological changes in the central nervous system in patients with parkinsonism associated with arteriosclerosis (Department of Neuropathology).

#### Ph.D.

- 1. Gordon-Majszak Wanda: Metabolic changes in brain synaptic endings as a consequences of free readicals peroxidation in vivo and in vitro (Department of Neurochemistry).
- 2. Wojtal Ewa: The release of disaggregating prostanoids into circulation in the effect of limb transcutaneous electric stimulation in experimental and clinical investigations (Laboratory of Experimental Surgery).

# Honors and prizes

- Joint prize of the Polish Academy of Sciences and Soviet Academy of Sciences for a group of Polish and Georgian scientists most actively involved in realization of studies on "Chosen aspects of ischemic lesions of the central nervous system (Department of Neuropathology: M. Mossakowski, R. Gadamski, S. Januszewski, A. Kapuściński, G. Szumańska).
- Prize of the Scientific Secretary of the Polish Academy of Sciences for the study on physiological mechanisms determining carbohydrate tolerance (Department of Applied Physiology: K. Nazar, H. Kaciuba-Uściłko, L. Budohoski, Z. Brzezińska, A. Dubaniewicz, J. Langfort, B. Bicz, J. Chwalbińska-Moneta).

# SCIENTIFIC MEETINGS ORGANIZED BY THE MEDICAL RESEARCH CENTRE

- 1. Course of the techniques of organ transplantation, sponsored by ETHICON, February 23-28, 1987, Warsaw.
- Symposium on Parenteral Nutrition, sponsored by FRESENIUS, March 4th, 1987, Warsaw.
- Symposium on monoclonal antibodies and their applicability in the clinical work, sponsored by BIOTEST, April 27th, 1987, Warsaw.
- Course of the basic microsurgical techniques, sponsored by DAVIES & GECK, May 25-30, 1987, Warsaw.
- International Symposium on Exercise Physiology dedicated to the memory of the late Prof. S. Kozłowski, June 18-20, 1987, Baranów Sandomierski.
- Symposium: "Control of Breathing During Sleep and Anaesthesia", sponsored by Societas Europaea Physiologiae Clinicae Respiratoriae, September 10-12, 1987, Warsaw.
- 7. Symposium on operative trauma and immune response, sponsored by RHONE POULENCE, November 9th, 1987, Warsaw.

#### **VISITING SCIENTISTS**

### Department of Neurophysiology

Be W.K. Bellia V.

de Berry Borowiecki B.

Bonsignore G. Breslav I.S. Chernicka N.S.

Euler C.von

Glebowski W.D.

Guz A.

Kaziennikov O.W.

Lugaresi E.

Millhorn D.A.

Morin-Surun M.P. Pack A.J.

Saunders K.

Selionov W.A.

Siafakas N. Siesiö B.K.

Williams T.

Radbout Hospital, Nijmegen, Holland

Medical Institute, Palermo, Italy University of California, Irvine USA Univ. degli Studi di Palermo, Italy

Academy of Sciences, Leningrad, USSR School of Medicine, Cleveland, USA

Nobel Institute for Neurophysiology, Karolinska

Inst., Stockholm, Sweden

Medical Institute, Leningrad, USSR Charing Cross Hospital, London, U.K.

Inst. of Information Problems, Academy of Scien-

ces, USSR

Univ. of Bologna, Italy

University of North Carolina, USA

CNRS, Paris, France

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London, U.K.

Institute of Information Problems, Academy of

Sciences, USSR

Evangalcismos Hospital, Athens, Greece

Lund Hospital, Lund, Sweden

St. George's Hospital Medical School, London,

U.K.

# Department of Applied Physiology

Beck F. Inst. of Physiology, Univ. of München, GFR Dobrakova M. Inst. of Experimental Endocrinology, Centre

Inst. of Experimental Endocrinology, Centre of Physiology Sciences, Bratislava, Czechoslovakia

Gollnick P. Dept. VCAPP, Washington State Univ., Pullman,

USA

Huttunen P. University of Oulu, Finland

Jokl E. University of Kentucky, Medical Centre, Lexington,

USA

Monod H. Dept. of Work Physiology SNRS, Paris, France Terjung R.L. Dept. of Physiology, Health Sciences Centre, Sy-

racuse N.Y.. USA

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### Cardiovascular Laboratory

Comline R.S. Univ. of Cambrige, U.K.

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Linden R.J. Univ. of Leeds, U.K.

## Department of Neuropathology

Diemer H. Inst. of Neuropathology, Univ. of Copenhagen,

Denmark

Ganuszkina I.W. Inst. of Neurology, Moscow, USSR Mai J.K. Inst. of Anatomy, Düsseldorf, GFR

Mchedliszwili G.J. Inst. of Physiology, Academy of Sciences, Geor-

gian SSR

Sicharulidze N.W. Inst. of Physiology, Bierutaszwili, Georgian SSR

Stastny F. Inst. of Physiology, Czechoslovakia
Viktorov J.W. Academy of Medical Sciences, USSR
Zirnova A. Inst. of Neurology, Moscow, USSR

### **Department of Neurochemistry**

Martiniak J. Inst. of Neurobiology, Slovak Academy of Scien-

ces, Kosice, Czechoslovakia

Nakagawa Y. Tokyo Segamiko University, Japan

Samojlov M.O. Inst. of Physiology, Academy of Sciences, USSR Suzuki K. The Tokyo Metropolitan Institut of Medical Scien-

ces, Japan

# Department of Neurosurgery

Wassmann H. Surgical Clinic, University of Bonn, GFR

Weidner A. Paracelsus Clinic, Osnabrück, GFR

# Laboratory of the Developmental Neuropathology

Larroche J.C. Neonatal Biol. Centre, Port-Royal Hospital, Paris,

France

Wisniewski H.M. Inst. for Basic Research in Development Disabili-

ties, New York, USA

# Department of Surgical Research and Transplantation

Bartos V. Internal Medicine in Medical Research Center,

Prague, Czechoslovakia

Gruvez J. Surgical Clinic, University of Leuven, Belgium

Hansson M. Dept. of Immunology, Karolinska Institute, Stock-

holm, Sweden

Hoover B. Research Unit, University of Pennsylvania, USA Hoover J. Research Unit, University of Pennsylvania, USA

Johannenssen J.V. Radium Institute, Oslo, Norway

Norgre L. Surgical Institute, Lund University, Lund, Sweden

Sandra J. University of Madras, India

Wildevuur C. Department of Cardiopulmonary Surgery, Univer-

sity Hospital, Groningen, The Netherlands

#### **VISITS ABROAD**

## Department of Neurophysiology

Budzińska K. Case Western University, Cleveland, USA (long

term visit)

Czerwosz L. St. George's Hospital, Medical School, London,

U.K.

Karczewski W. Charing Cross Hospital, Medical School London,

U.K.

St. George's Hospital, Medical School, London,

U.K.

University of Oxford, U.K.

Inst. of Physiology, University of Zurich, Switzer-

land

Centro Nacional de Investigaciones Cientificas,

Havana, Cuba

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den

Romaniuk J.R. Inst. of Information Problems, Academy of Scien-

ces, USSR

# Cardiovascular Laboratory

Cedro-Ceremuzyńska K. Welcome Research Laboratory, Beckenham, U.K.

Division of Pharmacol. Research, Bayer A.G.,

Wuppertal, GFR

# Department of Applied Physiology

Budohoski L. Dept. of Endocrinology, Royal Prince Alfred Ho-

spital, University of Sydney, Australia

Dept. of Biochemistry, University of Oxford, U.K.

Inst. of Physiopathology, University of Graz, Austria

Chwalbińska-Moneta J. Ball State University, Muncie, Indiana, USA (Iong term visit)

Flisowska-Badzyńska B. Inst. of Medical Physiology, University of Copenhagen, Denmark

Kaciuba-Uściłko H. Inst. of Physiology, University Justus-Liebig, Giessen, GFR

Kruk B Dept. of Physiology, University of Kuopio, Finland

Krzemiński K. Rehabilitation Research Center of Social Insuran-

ce Institution, Turku, Finland

Inst. of Experimental Endocrinology, Slovak Acad-Nazar K demy of Sciences, Bratislava, Czechoslovakia

Inst. of Functional Pathology, University of Graz,

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## Department of Neuropathology

Albrecht J Brain Research Group, The Open University Mil-

ton Keynes, U.K.

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Inst. of Physiology, Georgian Academy of Scien-

ces, Tbilisi, Georgian SSR

Inst. of Brain, Moscow, USSR

Inst. of General Reanimation, Caliningrad, USSR Kapuściński A. Krajewski S.

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of Düsseldorf, GFR

Inst. of Reanimation, Academy of Sciences, Mos-

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Berlin

Inst. of Neuropathology, University of Steglitz.

West Berlin

Dept. of Neurophysiopathology, Universita Degli Majkowska-Wierzbicka J.

Studi di Genova, Italy

Pluta R National Inst. of Health, Bethesda, Maryland, USA

(long term visit)

Renkawek K Inst. of Neurology, Nijmegen, Holland (long term

Szumańska G University of Tampere, Finland Weinrauder H. Inst. of Neurology, Academy of Sciences, Moscow,

USSR

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## Laboratory of the Developmental Neuropathology

Dambska M. Centre de Recherche de Biologique Neonatales,

Paris, France

Neuroscience Society in Göteborg, Sweden

## **Department of Neurochemistry**

Domanska-Janik K. National Inst. of Health and Medical Research,

Paris, France

Gordon-Majszak W. Inst. of Reanimatology, Moscow, USSR

Łazarewicz J. Fidia Georgtown Inst. of the Neurosciences, Wa-

shington, USA (long term visit)

Nowińska H. Lab. of General Reanimation, Academy of Scien-

ces, Moscow, USSR

Puka M. Pavlov Inst. of Physiology, Moscow, USSR

Rafałowska U. Medical Research Fundation, Oklahoma City, USA

(long term visit)

Strosznajder J. Cancer Research Center, Heidelberg, GFR

# Laboratory of the Ultrastructure of the Nervous System

Borowicz J. Jeol LTD, Akishima, Tokyo, Japan

Gajkowska B. Inst. of Cancer Research, Villejuif, France

Loesch A. Dept. of Anatomy and Embriology, University of

London, London, U.K.

Jeol LTD, Akishima, Tokyo, Japan

# **Department of Neurosurgery**

Czernicki Z. Divisione de Neurochirurgia Ospedale Generale

Regionale, Ancona, Italy

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Moscow, USSR

Jurkiewicz J. Budenko Inst. of Neurosurgery, Samarkanda,

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Dept. of Surgery Kantonsspital Aarau, Switzerland

Mempel W. St. Anne Hospital Centre, Paris, France

Budenko Inst. of Neurosurgery, Samarkanda,

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Śliwka S Budenko Inst. of Neurosurgery, Samarkanda,

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## Department for Surgical Research and Transplantation

Gałkowska H. Dermatological Clinic, Univeristy of Wien, Austria

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Dept. of Immunology, Karolinska Institute, Stock-

holm. Sweden

Inst. of Immunology, Basel, Switzerland

Radium Institute, Oslo, Norway Olszewski W

Surgical Clinic, University of Bonn, GFR

Limphological Clinic, Freiburg, GFR University of Hangzhou, China

The Egiptian Society of Haematology, Kairo, Egypt Romaniuk A

#### PARTICIPATIONS IN INTERNATIONAL MEETINGS IN 1987

21st Congress Collegium Francais Pathologie Vasculaire, Paris, France, March 18th-20th

Olszewski W.

International Symposium on the Immunology of the Gastrointestinal Tract and Liver, Jerusalem, Israel, March 22th-27th

Łukomska B., Olszewski W.

Annual Conference of European Termoregulation Group, 9-12 April, Pecs, Hungary

Kaciuba-Uściłko H.

22nd Congress of European Society for Surgical Research, Aarhus, Denmark, May 10-13

Grzelak I., Wąsowska B., Kubicka U.

Satellite Symposium International Society of Neurochemistry and the American Society for Neurochemistry "Biochemical Pathology of Astrocytes", 26-29 May, Florida, USA

Albrecht J.

Satellite Symposium of the ISN-ASN Joint Meeting "Phospholipids in the Nervous System: Biochemical and Molecular Pathology", 6-9 June, Venezuela Strosznajder J.

3rd Congress of European Society for Organ Transplantation, Goteborg, Sweden, June 11-13

Romaniuk A., Grochowicz P., Olszewski W.

VI International Catecholamine Symposium, 14-19 June, Jerusalem, Israel Cedro-Ceremużyńska K.

Annual Meeting Austrian Society of Neuropathology, Symposium "Medical Brain Research: State and Perspectives", 18-21 June, Wien, Austria Kroh H., Kaczmarczyk E.

International Conference on Peritoneum and Peritoneal Access, Lund, Sweden, June 22-26

Kubicka U.

S.E.P.C.R. Congress "Mechanisms and Management of Respiratory Symptoms", June 22-26, Antwerp, Belgium

Karczewski W., Romaniuk J., Kubin L., Janczewski W.

International Symposium on Bone Marrow Transplantation, Leipzig, GDR, June 29-30

Ratajczak M.

4th International Symposium on Peritoneal Dialysis, Venice, Italy, June 29th-July 2nd Kubicka U.

4th World Congress for Microcirculation, Tokyo, Japan, July 26th-August 2nd Olszewski W.

II World Congress of Neurosciences, August 16-21, Budapest, Hungary Śmiałek M., Weinrauder H., Zaręba-Kowalska A.

European Congress of Nuclear Medicine, August 24-28, Budapest, Hungary Kapuściński A.

8th European Immunology Meeting, August 30th-September 5th, Zagreb, Yugoslavia

Łukomska B., Orlewska E., Wąsowska B.

8th European Congress of Neurosurgery, September 6-11, Barcelona, Spain Mempel E.

VIII Congress of International Society for Heart Research, September 13-16, Budapest, Hungary

Kwiatkowska-Patzer B., Zalewska T.

11th International Congress of Lymphology, September 24-27, Vienna, Austria Gałkowska H., Ryffa T., Olszewski W.

International Brain Edema Symposium, October 7-10, Baltimore, USA Czernicki Z.

Congress of International Union of Phlebology, October 7-11, Essen, GFR Olszewski W.

XX Donau-Symposium of Neurological Sciences, October 8-10, Innsbruck, Austria

Dambska M., Weinrauder H., Kida E.

Quadrilateral Congress of Surgical Research, November 1-3, Szeged, Hungary Ryffa T., Orlewska E.