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MEDICAL RESEARCH CENTRE

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

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PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS OF RESPIRATORY AND CARDIOVASCULAR CONTROL

I. Functional organization of the respiratory neural network

1. Electrical stimulation of n. hypoglossus as well as of some accessory respiratory muscles decreases respiratory resistance during both inspiration and expiration. These findings may be useful in treatment of obstructive sleep apnea syndrome in humans.

2. Transcranial magnetic stimulation of cortical input to the brainstem respiratory complex in conscious monkeys showed that a single magnetic stimulus results in a short-latency extitation and inhibition of diaphragm, and a change of amplitude and timing of the respiratory cycle — which is suggestive of a brainstem processing of cortical activity.

3. Expiratory activities were found in neurons of the motor nucleus of trigeminal nerve. Also, pharmacological blockade of this nucleus results in apneustic breathing and the reversal of inflation and deflation of Hering-Breuer reflexes. Intravenous ketamine depresses expiratory activities there, which is accompanied by prolongation of expiration with unchanged amplitude of phrenic activity. It is concluded that expiratory activities of the motor nucleus of trigeminal nerve are crucial for respiratory phase switching, Hering-Breuer reflexes, and apneustic respiration — being an anatomical substrate of the pneumotaxic center.

4. Reflex response of upper airway muscles and diaphragm to negative pressure in the larynx has been investigated. An increase in activity of XII and VII cranial nerves and

a small desrease in phrenic activity has been found. The response was dependent on the integrity of the superior laryngeal nerve, which confirms the basic role of this reflex in maintaining potency of the upper airways.

II. The study of physiological and clinical correlations in the respiratory system

1. Following experimental subarachnoid haemmorrhage (SAH) immunostimulants enhance, while immunodepressants prevent the development of cerebral vascular angiopathy. These observations rationalize the use of SEVAC skin immunotest for prognosis of clinical outcome of SAH. They also may explain an improvement of SAH outcome resulting from the use of Sandimmun (cyclosporine A) in patients with ruptured intracranial aneurysm.

2. Endogenous opiates modulate the perception of pain associated with exhaustive exercise, but this mechanism does not limit the exercise performance.

3. Oxygen and carbon dioxide chemoreflexes are intact in tetraplegic humans, which indicates that the pathways descending to spinal intercostal respiratory motoneurons are not involved in the chemoreflex mechanisms.

4. The stimulatory responses of respiratory and cardiovascular system to static hand-grip exercise in humans are independent (not coupled to each other).

5. The carotid chemoreception plays an increasing role during the consecutive phases of dynamic exercise in human subjects.

6. Almitrine, a stimulant of peripheral chemoreceptors dilates the larynx during both inspiration and expiration; this observation rationalizes use of the drug in cases of obstructive sleep apnea.

7. Unlike rats, guinea pigs do not increase ventilation in response to hypoxia. Therefore the guinea pig is the animal which lacks one of the basic peripheral chemoreflexes.

8. Sex steroid receptors were found in brain stem areas, but not in carotid bodies. Respiratory effects of steroids may be mediated by these receptors.

See the list of Publications: a) 6, 15, 16, 45, 54, 67, 69, 93, 97, 98, 105, 108, 109, 120, 121; b) 22, 23, 28, 45, 47, 48, 52, 66.

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ADAPTATION TO PHYSICAL EXERCISE AND CHANGES IN ENVIRONMENT

1. Consequences of restriction of physical activity

In cooperation with whe N.A.S.A. Moffett Field Research Center, C.A. (U.S.A.) it was proved that in dogs 8-week restriction of physical activity (in specially made cages) impairs work tolerance with accompanying development of hyperthermia during moderate intensity running on the electric treadmill. Restriction of physical activity caused also a decrease in the muscle glycogen content measured at rest, a tendency towards the

diminished plasma free fatty acid (FFA) concentration, and a significant reduction of FFA increases both in response to exercise and intravenous infusion of noradrenaline. Eight-week physical conditioning of the previously immobilized dogs led to the reversal of all the above changes. Neither immobilization nor physical training influenced tolerance of glucose administered intravenously to dogs.

Dynamics of changes in carbohydrate tolerance and muscle sensitivity to insulin were studied in rats immobilized for up to 14 days in hipokinetic cages. There was a tendency towards decreased glucose tolerance after 7 days and its significant impairment after 14 days of hipokinesia. Sensitivity of glucogen synthesis to insulin determined in vitro, in the soleus muscle was significantly diminished already after 3 days of immobilization. The sensitivity of glycolysis in the same muscle was unimpaired until 7 days and thereafter declined significantly. It has been concluded that physical activity plays a role in determining sensitivity of glucose utilization by skeletal muscle to insulin.

2. Effect of fat-rich diet on lipid and carbohydrate metabolism

In growing rats maintained for 4 weeks after weanling on diets containing 30% of fat in the form of sun-flower oil, butter plus lard, or cod-liver oil a significant increase was found in circulating triacylоglicerols (TG) accompanied by an elevation of TG in myocardium, and reduced activity of the extracellular lipoprotein lipase activity (LPLA) in the heart. In animals fed butter plus lard, and cod-liver oil activity of the heparin unreleasable (most probably intracellular) LPLA in myocardium was also diminished. These findings suggest a feed-back mechanism between intracellular lipid content and LPLA synthesis and/or the enzyme transport from myocytes to the extracellular space, where it is acting.

In cooperation with the Department of Biochemistry, University of Oxford (U.K.) and the National Institute of Food and Nutrition in Warsaw an effect of fat-rich diet on the soleus muscle sensitivity to insulin was studied in young rats maintained for 4 weeks after weanling on the diet containing 60% of plant or animal fat. Both the polyunsaturated and saturated fat-diets caused a significant decrease in the sensitivity of glycolysis to insulin. Feeding the rats the animal fat-rich diet resulted in the increased glycogen synthesis rate in the soleus with a concomitant reduction of responsiveness and sensitivity of this process to insulin. The investigations demonstrated that a very high content of fat in a diet impairs muscle insulin sensitivity irrespectively of the fat origin.

The results obtained in this study differ from those previously reported in which a diet containing only 30% of polyunsaturated fat improved insulin sensitivity of skeletal muscle to insulin.

Continuing the study on the effect of diet on exercise metabolism, experiments on dogs fed for 10 days a diet containing 70% of soya-bean oil were completed. The results showed a marked reduction of prolonged exercise tolerance, accompanied by increased energy expenditure, heart rate and body temperature during a moderate effort.

3. Factors determinign carbohydrate tolerance and thermogenic action of glucose ingestion in human subjects.

In cooperation with the Institute of Gerontology, N.I.H. in Baltimore (U.S.A.), relationships between glucose tolerance and age, body mass, aerobic capacity and body fat distribution were calculated in 742 human subjects aged from 17 to 92 years. The

analysis revealed that aging is an independent factor responsible for impairment of glucose tolerance.

In the study performed in 35 women aged 19-55 years with normal glucose tolerance it was found that thermogenic effect of glucose ingestion (100 g) occurred only in 65% of them. Among the nonresponders there were both obese and lean subjects. In spite of that a significant correlation was ascertained between body mass index (B.M.I.) and the magnitude of thermal effect of glucose (T.E.G.). The latter correlated positively with noradrenaline level, measured after glucose ingestion, and negatively with both fasting and post-glucose insulin concentration. A close correlation was also found between T.E.G. and the post-glucose ratio of blood glucose to insulin concentration. These findings emphasize an importance of both the insulin sensitivity and the post-glucose sympathetic activation in determining calorigenic effect of carbohydrate ingestion.

4. Body temperature, metabolism and skeletal muscle function during physical work in men

In cooperation with the Department of Physiology, University of Kuopio (Finland) the effects of low ambient temperature and active warming up on body temperature, and electromyographic activity (E.M.G.) of various muscles were studied in athletes exercising at 5C with moderate intensity. It was found that pre-cooling of subjects at 5C decreasing their body temperature, results in significant enhancement of E.M.G. activity of both working (rectus femoris) and nonworking (trapezius) muscles and in an increased energy cost of work.

In athletes trained in endurance and speed an interrelationship was established between E.M.G. activity of various muscles and the anaerobic threshold during the incremental exercise test. It was found that E.M.G. activity shows a nonlinear increase at the exercise load corresponding to the individual anaerobic threshold, determined on the basis of blood lactate concentration.

In cooperation with the Department of Human Performance, Ball State University in Muncie I.N. (U.S.A.) it was demonstrated that active warming up attenuates the acid-base disturbances accompanying the supramaximal efforts.

5. Factors modifying the hemodynamic responses to physiological stimuli

In the investigations on strength and endurance athletes as well as on untrained subjects significant correlations were found between the anaerobic capacity (evaluated on the basis of 30s Wingate test) and the arterial blood pressure response to submaximal dynamic or static exercise. These findings suggest a coincidence of the motor system characteristics and predisposition to hypertension. It was also demonstrated that in the strength-trained athletes an exaggerated pressor response to exercise occurs more often than in the endurance trained or untrained men. Such response depends predominantly on an excessive increment of cardiac output and is not accompanied by higher increases in the plasma catecholamine, and vasopressin concentrations or the plasma renin activity.

Continuing the study concerning the effect of endurance training on cardiovascular responses to static effort changes in blood pressure, heart rate, stroke volume (determined by the impedance reography) during a sustained hand-grip were compared in healthy untrained women and field-hockey female competitors. No significant differences between these two groups were ascertained.

A spectral analysis of the heart rate (HR) variability was made in healthy men during breathing at 6 and 15 breaths x min ^{1} in supine and standing position. The data showed that a decrease in the amplitude of HR fluctuations after standing up is less pronounced at the lower breathing rate. This suggests that the HR variability during deep breathing is determined by both the sympathetic and parasympathetic nervous systems.

6. Clinical evaluation of patients with coronary heart disease

Continuing the longitudinal studies on patients with coronary heart disease (CHD) the incidence of the late microvolt potentials in ECG was investigated in 58 patients being 15—18 years after the first myocardial infarction. In 69% of these patients the late microvolt potentials were found, and their appearance correlated well with the incidence of ventricular arrhythmias observed using 24 h—Holter ECG recording. The data emphasize the diagnostic value of the late microvolt potentials for prediction of severe cardiac arrhythmias.

The effects of 12h bed-rest daily for 2 weeks on the clinical state of CHD patients, with cardiac insufficiency were investigated. Restriction of physical activity improved the clinical state of these patients (a decrease in frequency of angina or rhythm disturbances and reduction of requirement for diuretics). The „low activity" treatment did not impair the patients glucose tolerance or their response to the orthostatic test. The study concerning the value of mixed (static-dynamic) exercise test for CHD diagnosis was completed. It was proved that this type of test is more sensitive than the standard exercise-test for detection of coronary insufficiency, particularly in asymptomatic patients with CHD risk factors.

7. Studies of the atrial natriuretic peptide (Prof. Janusz Sadowski)

The main objective of the work was to delineate the role of changes in renal hemodynamics in the mechanism of natriuresis developing in response to exogenous atrial natriuretic peptide (ANP).

In anesthetized rats the total renal blood flow (RBF) of the experimental kidney was precisely determined by continuous renal vein outflow recording and the glomerular filtration rate (GFR) by two methods: as a clearance of inulin (C_{in}) and as rénal plasma flow times renal extraction ratio of inulin ($RPF \cdot E_{in}$). Simultaneously, in order to assess a possible contribution of a wash-out of medullary solutes to ANP natriuresis, electrolyte concentration in medullary tissue was continously recorded in vivo as tissue electrical admittance (reciprocal impedance).

At the lowest ANP dosage (0.35μg/kg·min i.v.) sodium excretion and diuresis increased without any change in RBF, C_{in} or $RPF \cdot E_{in}$ or in tissue admittance. In higher dosage groups (2 and 6 μg/kg·min) an acute increase in C_{in} but not in $RPF \cdot E_{in}$ was observed. The discrepancy was obviously related to a spurious increase in GFR measured as C_{in}, an unrealiable index of filtration during a sharp increase in urine flow.

The decreases in admittance (electrolyte concentration in medullary tissue) were minor and transient, a small fraction of those previously observed after blockade of the ascending limb of Henle's loop.

It was concluded that (1) Significant natriuresis after ANP can occur without a genuine change in GFR, (2) C_{in} is not a reliable index of filtration rate during major ANP diuresis, (3) Absence of major changes in tissue electrolyte concentration speaks against

a role of solute wash-out in ANP natriuresis, and (4) The ascending limb of Henle's loop is unlikely to be the site of tubular action of ANP in the nephron.

The interpretation of the above data is complicated by decreasing arterial blood pressure after ANP; hence a need for supplementing the present studies by experiments in which renal perfusion pressure would be controlled and maintained constant.

See the list of Publications: 1) 3, 7, 8, 9, 10, 18, 36, 37, 38, 47, 48, 49, 58, 60, 61, 79, 81, 82, 83, 94, 115, 122, 125, 128, 132, 135, 136, 137, 138; b) 5, 16, 21, 24, 51, 69.

Cardiovascular Laboratory
Head: Prof. Krystyna Cedro-Ceremużyńska

1. Activity of human blood leukocytes in acute myocardial infarction

There were two reasons for undertaking the present investigation: 1) both the animal and human studies have shown that the invading leukocytes are involved in the pathogenesis of infarction, 2) functional state of blood leukocytes in patients with acute myocardial infarction (AMI) has not been defined.

We have examined activity of the polymorphonuclear leukocytes (PMNL) in patients with AMI (1—3 days) by monitoring the ex vivo aggregation of these cells. It was found that AMI leads to increased sensitivity of blood PMNL to ex vivo aggregation iduced by N-formyl-metionyl-leucyl-phenylalanine (0.03—10 μM) or arachidonic acid (0.1 — 100 μM). The increased sensitivity was prevented by pretreatment of leukocytes with BW 755 but not with aspirin, suggesting that the activation of PMNL in AMI is due to stimulation of cellular lipoxygenase.

2. Protein metabolism in myocardial hypertrophy

Studies on the mechanism involved in protein synthesis in myocardial hypertrophy (aortic construction in rats) were continued. It was demonstrated that activity of protein C kinase increases in hypertrophic hearts. Phorbol ester, a specific activator of this enzyme, increases myosin light chain phosphorylation in both normal and hypertrophic myocardium suggesting involvement of protein C kinase in this process.

See the List of Publications: a) 14, 42, 68, 100, 101.

Laboratory of Experimental Surgery
Head: Assoc. Prof. Maciej Borkowski

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

1. To evaluate an effect of prostaglandins on filterability of whole blood in patients with

ischaemic vascular disorders of lower extremities intraarterial infusion of synthetic PGE_1 was applied. Changes in fibrogen concentration, hematocrit, red blood cell (RBC), withe blood cell (WBC) and platelet counts were examined in 10 patients. It was found that during PGE_1 infusion there is a temporary deterioration of blood rheologic properties, whereas after cessation of the infusion an improvement occurs, due to a decrease in erytrocyte deformity.

2. Studies on application of Nd Yag laser in venous surgery were continued. Venotomies repaired by lasing were patent in 100%, and a video film illustrating a technique of this operation was made. On the other hand, an attempt to perform the veno-venous anastomoses was unsuccesful because of insufficient resistance of the lased junction, uneven thicknese of cut vessel walls, and problems with accurate adjustment of cut vessel walls necessary for a tight anastomosis.

3. Retrosternal esophageo-gastrotomy was performed in 9 patients with advanced esophageal cancer. In 6 out of them a complete relief of dysphogia occurred which makes the treatment encouraging.

See the List of Publications: a) 30, 57.

STUDIES ON THE STRUCTURE AND BIOLOGICAL PROPERTIES OF THE NERVOUS TISSUE

Department of Neuropathology
Head: Assoc. Professor Irmina B. Zelman

PATHOGENETIC MECHANISMS AND PREVENTION OF ISCHEMIC ENCEPHALOPATHY

The studies were conducted with the use of three experimental models: a) the „clinical death" model (compression ischemia after Korpachev) in rat, b) global cerebral ischemia in rabbit and c) short-term forebrain ischemia in Mongolian gerbil.

Studies on the clinical „death model" revealed a certain degree of correlation between the changes in blood and brain catecholamines and brain cAMP levels at various stages of the ischemic incident. In particular, a decrease in brain catecholamines in the ischemic period coincided with a decrease in cAMP, whereas the above control increase of blood catecholamines at 15 min of resuscitation was accompanied by a transient return to the control level of cAMP. Both parameters showed a decrease at later postresuscitation periods. The results suggest that a decrease of brain catecholamines may markedly contribute to the fluctuations in cAMP levels and in this way induce a chain of metabolic disturbances complicating the recovery of brain function.

An analysis of morphological changes in the postresuscitation period after 10 or 15 min of clinical death revealed that degenerative changes, which predominate in the early period, later give way to neuronal losses in regions vulnerable to ischemia. However, at

very distant periods of resuscitation, degenerative changes begin to appear in previously unchanged regions, indicating the involvement of secondary autoimmunological reactions.

A search for immunomorphological markers of ischemic cell damage has been continued using the above model. A feature common to a variety of brain regions was postischemic weakining of immunoreactivity against neuron-specific enolase (NSE) and the Leu-7/HNK-1 epitope, which often preceded morphological manifestation of tissue damage. Histochemical analysis of brain glycoconjugates with the lectin technique revealed postischemic changes in the localization of glycoproteins both in the vascular network and in various cellular elements, confirming the utility of this procedure as a sensitive marker of ischemic tissue damage.

The ability of prostacyclin PGI_2 to prevent or counteract ischemic brain tissue damage was tested in a model of acute cerebral ischemia in the rabbit. PGI_2 administered in the course of ischemia was found to reduce the time period needed to attain recovery of bioelectric activity of the brain, to attenuate the blood-brain barier impairment and structural damage of different cellular elements, as well as to improve many biochemical and rheological parameters of blood.

Short-term forebrain ischemia in Mongolian gerbil is known to affect selectively, irreversibly and with a considerable delay, the pyramidal neurons of Amon's horn CA_1 sector, the phenomenon being defined as „delayed neuronal death". Ultrastructural analysis of the affected region revealed changes in the synaptic junctions involving both presynaptic and postsynaptic elements. In particular, profound changes of synaptic vesicles seem to indicate that disturbances in neural transmission contribute to the neuronal damage. The damage may be compounded by hemodynamic disturbances, easily predictable in this region because of its unusual angioarchitectonics.

THE ROLE OF GLIA AND CEREBRAL CAPILLARIES IN THE PHYSIOLOGICAL AND PATHOLOGICAL PROCESSES IN THE CENTRAL NERVOUS SYSTEM

Studies have been continued on the cerebral transport of glutamine — an amino acid that is synthetized in astrocytes and is the final product of ammonia neutralization. The controversial hypothesis that γ-glutamyl-transpeptidase (GGT) is involved in the L transport system for large neutral amino acids in the brain capillaries has been tested. The release of radiolabelled glutamine from rat cerebral capillaries in vitro was measured in the presence of GGT inhibitor — serine borate (SB). It was found that tryptophan and its nerutoxic catabolite — quinolinic acid, stimulated glutamine release only in the absence of SB. The results support the notion that, in cerebral capillaries, GGT catalyzes the exchange between glutamine leaving the brain and tryptophan entering it. This reaction may be of significance under hyperammonemic conditions, when the brain is excessively loaded with glutamine.

The effects of hepatic encephalopathy in the thioacetamide model and in vitro treatment with ammonia, on the kinetics of α-ketoglutarate dehydrogenase in highly purified nonsynaptic cerebral mitochondria were measured. Both pathogenic conditions

inhibited the enzyme activity when the α-ketoglutarate concentration in the incubation mixture was kept at, but not below, the physiological level. A detailed analysis of the enzyme kinetics performed in a wide concentration range revealed at least two distinct components of the enzyme complex. The same mitochondrial preparation was tested for its ability to oxidize glutamic acid to CO_2. No effect of either hepatic encephalopathy or ammonia added in vitro was observed, indicating that transamination rather than dehydrogenation, is mainly responsible for glutamate consumption in the brain.

The effect of thioacetamide-induced hepatic encephalopathy on the release of the inhibiotory neuromodulator-taurine in vitro from various brain regions was measured using the slice superfusion technique. A stimulation of the depolarization-induced, but not the basal release was observed in stratial slices. Thus, stratial taurine may participate in the neuroinhibitory phenomena accompanying this disease.

The localization of glutamine synthetase (GS) — an enzym so far believed to be strictly confined to astrocytes, was evaluated immunochistochemically in primary mixed, but also in pure oligodendrocytic cultures derived from neonatal rat cerebral hemispheres. In mixed cultures, positive GS reaction was observed not only in astrocytes, but also in single oligodendrocytes. Moreover, a very strong GS immunoreactivity was noted in oligodendrocytes grown in defined medium. The above findings prompt to reconsider the utility of GS as an astrocytic marker.

The remnants of axons including sheaths and myelin bodies have been found on the semithin and thin sections during the studies on demyelination process induced by ethylnitrosourea. Damage to the vascular endothelia, including necrotic changes observed in the early stage of action of carcinogenous substance, favour the idea of the transportation of axonal fragments by the cellular elements. The damage of the vascular walls can facilitate myelin removal.

PATHOGENETIC MECHANISMS OF EXO- AND ENDOGENEOUS DEGENERATIVE PROCESSES IN THE CNS: THE ROLE OF SPECIFIC NEUROTOXINS

Ultrastructural analysis of the effects of two neurotoxic glutamate receptor agonists: NMDA and quinolinic acid (Quin), on the dissociated hippocampal culture derived from C57 mice, revealed that the former is a more potent toxin than the latter. In particular, NMDA but not Quin, induced severe damage in perikarya of pyramidal cells. Studies on the organotypic rat hippocampal culture showed that 100 μm Mg^{2+} ameliorates Quin neurotoxicity with regard to postsynaptic dendrites and abolishes the effect on axons. The results confirmed the affinity of Quin to NMDA receptors.

Earlier investigations demonstrated protective effects of Zn^{2+} against Quin toxicity in cultured hippocampus. In contrast, the present studies have shown that Zn^{2+} administered to rats in vivo potentiates the neurophysiological, morphological and biochemical effects of Quin. Seizures induced by the combination of Quin and Zn^{2+} correlated well with, and could be causally related to, the decreased hippocampal content of the inhibitory neurotransmitter GABA.

Quin administered in vivo was found to increase the arginine leu-enkephalin content in

mesencephalon, but not in frontal cortex, hippocampus or striatum. This finding may be explained by assuming that Quin accelerates the neuropeptide synthesis in prodynorphic striatal neurons. Subsequently, increased amounts of the enkephalin could be axonally transported to substantia nigra of mesencephalon. In turn, the Quin-induced decrease of the GABAergic activity would counteract the release of the dynorphin from mesencephalic synapses.

See the List of Publication: a) 1, 21, 23, 43, 44, 50, 51, 52, 53; 55, 56, 70, 74, 76, 80, 95, 102, 103, 104, 123, 124, 127; b) 29.

Department of Neurochemistry
Head: Prof. Jerzy Łazarewicz

REGULATION OF BRAIN METABOLISM AND NEUROTRANSMISSION IN NORMAL AND PATHOLOGICAL CONDITIONS

1. Involvement of glutamatergic and histaminergic neurotransmission in the pathogenesis of brain injury

Studies concerning the hypoxic/ischemic impairment of neuronal structure and function, were directed upon these putative mechanisms of the lesion, which may be casually related to calcium redistribution and free radical oxidation, and become targets for therapeutic interventions. It was demonstrated in the studies performed in collaboration with the Department of Neuropathology, Medical Research Centre (Dr. R. Pluta), that both systematically applied prostacyclin and nimodipine, locally infused to the hippocampus, advance a recovery of the brain bioelectric activity after ischemia. Morphological studies confirmed the protective effect of prostacyclin on hippocampal neurons, as well as on pyramidal neurons situated in the vicinity to the nimodipine-distributing dialysis probe. Prostacyclin slightly reduced the ischemia-evoked drop of extracellular calcium concentration and an increase in the blood-brain barrier permeability to fluorescein in the hippocampus. Nimodipine, given locally, had even less pronounced effect on extracellular calcium and did not influence the permeability of blood-brain barrier. These results revealed diversity of the potential protective mechanisms of nimodipine and prostacyclin, comprising their vasotropic, vasodilatory activity along with a direct cytoprotection of the brain neurons. This effect of nimodipine on the hippocampus may be unrelated to the inhibition of calcium influx to neurons.

As it was shown in a collaborative study with the Pavlov's Institute of Physiology, USSR Academy of Sciences, Leningrad (Prof. M.O. Samoilov, Dr. D.G. Semenov), polyphosphoinositide hydrolysis and the release of calcium bound to intracellular membranes (measured with chlortetracyclin, a fluorescent calcium chelate probe), are among the earliest metabolic disturbances in the hypoxic brain, noticeable already after 30 s of anoxia. These changes are accompanied by phasic alterations of neuronal activity. Similar simultaneity of changes in the content of polyphosphoinositides and memb

rane-bound calcium in the brain cortex with changes of neronal activity was observed during reoxigenation after anoxia. These data, which demonstrate an importance of phosphoinositides in intracellular calcium binding, point to the regulatory role of calcium and polyphosphoinositide-related signal transduction mechanisms in the modulation of neuronal activity during and after hypoxia.

It was shown, that in vitro peroxidation of the rat brain synaptosomal fraction results in the inhibition of histamine metabolism, a decrease in histamine contents and in the reduction of the uptake of histamine precursor — histidine in isolated synaptic endings. The above effects were not prevented by an acute pretreatment of rats with dexamethasone. These data reflect the high susceptibility of brain synaptic endings to the peroxidation-induced pathology.

2. Role of bioactive lipid and protein in signal transduction (Assoc. Prof. Joanna Strosznajder)

In the year 1989 the studies concerned an importance of signal transduction process in the brain during normoxia, ischemia and aging. The disturbances and other changes of metabolic processes during ischemia may specify directions and suggestions for effective therapeutic interventions. The modification of receptor(s) responses connected with phosphoinositides metabolism, lipid dependent second messengers formation, enzymic processes involved in signal transduction in normoxia, ischemia and aging of c.n.s. were under investigations. The activity of phospholipase C, A_2 and neutral Ca^{2+} dependent proteinases and protein kinase C were examined. It was found that prolonged 10 min brain ischemia stimulates phospholipase C, and hydrolyses phosphatidylinositol (PI) in subsynaptosomal fraction except the enzyme of synaptic cytosol. Concomitantly the activity of phospholipase C degraded 4,5 bisphosphophosphatidylinositol was decreased in all subsynaptosomal fractions, probably as a result of enzyme phosphorylation by DG-activated protein kinase C. These findings indicate that phospholipase C, acting on PI, is mainly responsible for the increase level of diacylglycerol during ischemia.

The studies have shown the high susceptibility of synaptic vesicle-bound phospholipases C and A_2 acting on PI to brain ischemia. The results suggest a stable activation of the enzymes by ischemia which are not further susceptible for Ca^{2+} stimulation. Stimulation of $PhLA_2$ and C by ischemia produced formation and accumulation of many fusogenic substances leading to vesicle-membrane fusion and neurotransmitter release.

The studies on the regulation of arachidonic acid (AA) release indicated that a significant amount of AA is released by the action of Ca^{2+} independent enzymes that means by phospholipase A_2 and by sequential action of phospholipase C and digliceride lipase. Release of arachidonic acid by Ca^{2+} independent enzymes occurs by hydrolysis of phosphatidic acid, polyphosphoinositides phosphatidylserine. Endogenous Ca^{2+} level increases AA liberation significantly and higher 2 mM $CaCl_2$ has only a small effect. These results indicate that physiological increments of Ca^{2+} may have serious implication. Carbachol-nonhydrosylable analog of acetylcholine, stimulates exclusively Ca^{2+}-dependent AA release specifically from phosphatidylinositol. In the following studies it was observed that higher level of AA and degradation of PI affected high affinity ^3H muscimol binding into $GABA_A$ receptor. It is suggested, that both these processes are responsible for higher agonist binding into $GABA_A$ receptor induced by ischemia.

In the signal transduction processes Ca^{2+} dependent neutral proteases play also an important role. These enzymes are involved in regulation of the agonist binding into $GABA^A$ receptor. Moreover, they exert a modulary effect on protein kinase C and may be responsible for changes in these processes during brain ischemia. The Ca^{2+} dependent neutral proteases exert a specific action against myelin proteins, particularly the basic protein during development of c.n.s. which suggests that these enzymes are involved in maturation of myelin structure.

Studies on the regulation of GABA and cholinergic receptors and the metabolic process connected with these receptors during aging were initiated in cooperation with the Department of Biochemistry, University of Perugia, Italy.

Summarizing. It seems that phospholipase C reaction is an important step for the therapeutic interventions. The higher Ca^{2+} binding into the membrane during prolonged ischemia and aging, probably responsible for the stable activation of some phospholipases and calpains, ought to be taken into consideration in therapy with Ca^{2+} channel blockers.

See the List of Publications: a) 17, 39, 70, 102, 103, 112, 116, 117, 118, 119, 133; b) 27, 36, 47, 48, 52, 53, 58, 59, 61, 62, 63.

Department of Neurosurgery
Head: Prof. Eugeniusz Mempel

1. Changes concerning volume-pressure relations and electrophysiological parameters caused by the additional intracranial volume (assoc. prof. Zbigniew Czernicki)

Changes in the cerebrospinal fluid (CSF) outflow resistance depending on ICP were studied. It was found, that the CSF outflow resistance is first rising together with the ICP (till the ICP value of 25 mmHg) and then falling down. These results have to be taken into account in further studies on the CSF outflow resistance in neurosurgical patients.

Investigations on the intracranial volume reserve (IVR) changes following the increasing intracranial additional volume were performed using the epidural balloon compression model. The earliest informations about the IVR changes were obtained using the CSF outflow resistance and volume pressure response determinations. The CT images numerical analysis is of a comparable value. The visual-evoked potential changes were observed later.

The ICP changes were found much less informative, since they provided the significant information very late. Additional investigations udertaken in 1989 concerned: the changes following the sagittal sinus occlusion, the role of ischemia in Cushing reflex and the physiological volume-pressure loadings of the cranio-spinal system.

2. Bioelectric activity of the brain and disturbances of processes of transmission on this activity in neursurgical patients
(Prof. Eugeniusz Mempel)

For analysis of disturbances of bioelectric activity transmission in epilepsy, brain

electric activity mapping (BEAM) was made with the use of three computer measuring systems (Neuroscan, Neuroscience and Dantec) in primarily generalised epileptic seizures (PM and GM). In some of the examined 20 cases cortical trigger zones were detected releasing PM seizures from the frontal and temporal region of the brain. Moreover, the mapping analysis allowed, to trace the directions of spread of the frontal wave epileptic discharges in the brain.

It should be mentioned that in cases with clinical symptoms of temporal epilepsy the brain electric activity mapping (BEAM) was performed using the new Polish software in the computer measuring system „Neurotrack". In 56 per cent of cases the investigations revealed more pronounced focality of the changes and improved possibility of detecting a direction of the discharge propagation as compared with the results of conventional eeg examination.

It was demonstrated that BEAM is a valuable uninvansive method supplementing classical electroencephalography and useful instrument for pathophysiological investigations in epileptology.

3. Speech disorders and other gnostic functions in focal lesions of the brain (Assoc. Prof. Jadwiga Szumska)

A hand-book for neurologists, logopeds and psychologists was prepared containing basic informations on development and pathology of speech in children as well as suggestions of various methods of speech therapy. Examinations of verbal memory in children with SSPE were made. In 10 cases with SSPE the disturbances of short and long-term memory were observed. Early symptoms of gnostic function disturbances were also studied in children with SSPE. In 13 cases the selected visual-spatial disturbances were observed.

In further investigations the effect of the left and right hemisphere lesions (12 cases) on the emotional and neutral faces was examined and compared with those in normal subjects (n = 20). In the patients after the right hemisphere surgery predominance of negative emotional stimuli was observed while in the patients after the left-hemisphere lesions a balance of emotional stimuli (negative and neutral) was observed.

Examination of the electrical activity of the brain during exposure to emotional stimuli was performed in patients with focal lesion of the brain. In patients with left hemisphere lesions the predominance of right hemisphere was found while in those with right hemisphere lesions the short-latency waves were symetric. The results obtained indicate predominance of the left hemisphere for emotional processes.

See the List of Publications: a) 40, 77, 78, 92,; b) 6, 12, 35, 65.

Laboratory of Developmental Neuropathology
Head: Prof. Maria Dąmbska

A comparison of normal brain development with its disturbances provoked by selected damaging factors and pathologic process

Early, but above all late changes after perinatal damage of the central nervous system

were analysed. The brains of children with mainly hemispheric white matter changes demonstrated a GFAP positive oboundant, early reaction, which was morphometrically veryfied. A dense fibrillary gliosis was found to increase with longer survival. After many years definite degeneration of neuroectodermal elements particularly in watershed areas of the brain hemisphere was seen.

The late changes occurring after intraperitoneal administration of vincristine — a known antimitotic drug — were investigated. Generalyzed, chronic alterations of cytoskeleton in axons (diminished number of neurotubules and increased number of neurofilaments) were morphometrically veryfied.

See the List of Publications: a) 13.

Laboratory of the Ultrastructure of the Nervous System
Head: Prof. Jerzy Borowicz

HISTOCHEMICAL AND IMMUNOCYTOCHEMICAL EVALUATION OF THE HYPOTHALAMO-HYPOPHYSEAL NEUROSECRETORY SYSTEM OF THE RAT FOLLOWING CEREBRAL ISCHEMIA

Studies of ultrastructural changes in secretory nuclei (nucleus supraopticus (SO) and nucleus paraventricularis (PV)) and hypophyseal neural lobe were performed after experimentally evoked brain ischemia (the method described by Korpaczev et al. 1982).

Under these conditions clinical death occurs several seconds after cardiac arrest and cessation of respiratory function, as revealed by disappearance of the bioelectrical potential of the brain. However, application of external heart massage and artificial ventilation with air at a frequency of 20 min after 5 min lasting ischemia allowed for return of the heart function, blood circulation and respiration. Three, 14 and 28 days after recovery of blood circulation animals were subjected to morphological, cytochemical and immunocytochemical studies.

The aim of this work was to elucidate post-ischemic changes appearing in the hypothalamo-hypophyseal system of the rats which underwent the incident of clinical death. SO and PV neurons showed an increased number of polymorphic lysosomed lipid droplets as well as an aludance of eytoskeleton elements, i.e. neurotubules and neurofilaments. Some astrocytic processes in neuropil were swollen. Synaptic endings of the SO and PV neurons had normal ultrastructure. An increased number of lysosomes and dense bodies was observed in some axons and pituicytes in the neurohypophysis.

Using the oxalate-pyroantimonate technique ultrastructural localization of Ca^{2+} was determined in SO and PV and neurohypophysis after complete cerebral ischemia. An increased calcium accumulation in mitochondria of some neurons was observed. Calcium precipitate was also found in vesicles, in cytoplasm of neurons and their swollen dendritic processes. Abundand Ca^{2+} precipitate occurred in synaptic vesicles and within synaptic eleft. It was present between disjuncted lamellae of the myelin sheath in profiles of myelinated axons, present in neuropil. Piffuse precipitate was visible in the cytoplasm of

pituicytes, as well as in microvesicles in the neurohypophysis. The enhancement of intracellular and extracellular calcium contents suggest that the lost of Ca^{2+} homeostasis during ischemia may eventually lead to some neurosecretory disturbance.

The immuncytochemical distribution of Len, and Met-enkephalin in the rat neurohypophysis was studied using the immunogold staining method. Immunolabelling was performed by applying of the 5 mm goldantibody complex for Len, and Met-enkephalin. The only organelles consistently labelled were neurosecretory granules in axonal terminals. An increased number of labelled neurosecretory granules was noticeable in the neurohypophysis after ischemia in comparison with the control group. This may suggest the participation of enkephalins in the regulation of neurohormone release.

The effect of ischemia on morphology and possible function of the Gigantocellular reticular region was evaluated.

See the List of Publications: a) 22, 23, 24, 25, 26, 80, 124, 126, 134.

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 asessment of capillary permeability revealed that local intraarterial administration of catecholamines (epinephrine and norepinephrine) elevates both venous and arterial pressures in the dog's limb vessels, without changing the skin lymph formation rate, lymph protein and cellular composition. Histamine augments the lymph flow in the skin by a factor of 4, whereas total protein IgG and IgM output are increased 3 times. These results indicate that catecholamines stabilize the capillary permeability for cells and proteins, while histamine causes relaxation of the capillary barrier.

It was found that human lymph, and its fractions containing the highest concentrations of IL-1, inhibit the growth of the neoplastic fibroblast line L 929. It points to the possible involvement of IL-1 in the defence processes against some types of neoplasms. Human lymph contains both (α and β) forms of IL-1.

The experiments on mitigation of rejection of the allogenic peripheral nerve grafts have shown, that treatment of the recipient with CyA prolongs the survival time and facilitates the vascularization and reinnervation of the graft. The data emphasize the important role of Schwann cells in the rejection process. These cells possess physiologically only MHC class I molecules, but reveal strong MHC class II antigen expression during rejection. The preliminary investigation on the immunogenicity of Schwann cells in vitro revealed that neither freshly isolated cells nor those cultured for 5 days in the presence of γ interferon expressed the class II antigens.

FUNCTIONS OF LYMPHOCYTES ISOLATED FROM DIFFERENT SOURCES

Dendritic cells of the prenodal skin-draining lymph were shown to be potent stimulators of allogeneic lymphocytes, in contrast to the stimulated lymph macrophages. Blocking of the Ia antigens by murine monoclonal antibodies or polyclonal anti-dendric cell serum inhibited the MLR. Administration of polyclonal serum in vivo transiently eliminated dendritic cells from lymph for a period of 2 hours. This indicates that anti-dendritic cell serum can affect in vivo local migration and functions of dendritic cells.

The experiments concerning the cells isolated from the liver sinuses revealed an inhibitory effect of in vitro (41C) hyperthermia on the natural killer (NK) cytotoxic activity, without alteration in the number of LGL. This finding suggests that hyperthermia affects the process of recognition and complex formation between NK and target cells.

In previous studies, the preferential accumulation of cells of cytotoxic/suppressor phenotype in the human peritoneal fluid was found. These cells revealed similar level of autotransformation as the peripheral blood cells, but responded less to PHA, thus suggesting that the peritoneal cells remain in a resting state.

TRANSPLANTATION OF ALLOGENEIC CELLS AND ORGANS

Bone marrow cells of irradiated recipients of syngeneic limb graft showed the karyotype of donor origin. The bone marrow of the tranplanted extremities from irradiated syngeneic donors was repopulated within 4 weeks by recipient cells. In the allogeneic graft group, the mononuclear cell infiltration was observed after 3, 5 and 8 days, mainly around the dermal vessels. After 14 days the vascular damage occurred in the muscles, with necrosis and infiltrations around the vessel wall, accompanied by the thrombotic changes. Bone marrow pictures included myelofibrosis and pancytopenia.

The influence of immunological enhancement, CyA and donor specyfic transfusions (DST) on the prolongation of survival of allogeneic lymphocytes and heart graft has been studied. Mean survival time of the heart grafts reached 40 days (compared to 7 days in the control group), while the splenocytes underwent instant elimination. Hence, the enhancement of CyA and DST seem to exert a protective effect on the organ graft, but does not induce tolerance for the donor antigen.

POST-TRAUMA IMMUNE RESPONSE

The influence of surgical trauma on the appearance of activated and proliferating lymphocytes and their precursors in the peripheral blood has been studied. The increased levels of OKT6+ cells (thymocytes) and OKT9+ cells (transferrin receptor) were observed on the day 7 after the operation. The number of OKT10+ cells (precursors) was significantly increased on days 5 and 7. These results show that the surgical trauma of moderate degree (cholecystectomy) leads to the clinically detectable activation of patient's immune system.

THE INFLUENCE OF DONOR-SPECIFIC TRANSFUSIONS ON THE ALLOGENEIC GRAFT SURVIVAL

The immunological reactivity of the rat peritoneal cavity cells after intraperitoneal syngeneic blood transfusions was investigated. Administration of whole blood, cells alone or serum bring about mobilization of peritoneal exudate cells, and increase the size of macrophage fraction in the cellular composition of the exudate. This effect was still observed after 96 hours, which was not the case when other stimulators had been used.

See the List of Publications: a: 4, 5, 11, 12, 27, 28, 29, 31, 33, 34, 35, 59, 62, 63, 65, 66, 71, 72, 73, 87, 88, 89, 90, 91, 96, 106, 107, 111, 114, 129, 130, 131; b) 1, 2, 3, 4, 7, 8, 9, 10 ,11, 13, 14, 15, 25, 26, 30, 31, 32, 33, 34, 37, 38, 39, 40, 41, 42, 43, 44, 46, 49, 50, 54, 57, 60.

Neuromuscular Unit
Head: Prof. Irena Hausmanowa-Petrusewicz

MECHANISMS LEADING TO HEREDITARY AND ACQUIRED NEUROMUSCULAR DISEASES

The main topics beeing currently under investigations are as follows: an attempt to transplant the embrionic motoneurons into anterior horn deprived from motoneurons. The

rationale is an assumption of disturbed immature muscle and nerve interaction as pathogenetic mechanism of the spinal muscular atrophy (SMA).

The other main line of the research is to study regeneration of the denervated immature muscle, which is also an experimental model for childhood spinal atrophy. In the genetical studies concerning childhood spinal muscular atrophy (SMA) — we have participated in the commom international project on DNA linkage in the childhood spinal atrophy. The multiplex Polish families with SMA show a great interfamilial variability which is of importance for genetic studies. The epidemiological investigations on SMA in Warsaw established the incidence and prevelance of childhood SMA and also gene and carriership frequency.

DNA linkage studies on the genetics of Duchenne dystophy are also of the greatest importance. They have been already introduced into the clinical practice and prenatal diagnosis. Experiments on dystrophin — i.e. a protein being a gene product — have been recently started with patients and on mice mxd. Other studies on Duchene dystrophy are concentrated on the role of Ca^{++} in the dystrophic process.
pa11k-hd2pol-acad-T-M

The lata post-polio syndrome observed recently in Poland (similarly as in some other countries) provides a model for following-up the desintegration and reintegration of motor unit, which is the subject of intensive studies.

See the List of Publications: a) 2, 19, 20, 41, 84, 85, 86, 110, 113; b) 17, 20, 55, 64, 70.

OTHER RESEARCH WORKS

Mental Health Department
Head: Assoc. Prof. Zygrfryd Jurczyński

1. Motivative function of personality and psychosocial condition in the course of cancer disease

Among 154 patients the highest social activity was found in the group of patients with breast cancer, lower in the group with large intestine cancer and the lowest in patients with cervix cancer. The last group showed, however, the highest work activity directly after the treatment.

It can be concluded that there exists a strict connection between a kind of cancer and psychosocial activity. This activity lowers, however, with duration of illness.

2. An evaluation of social maladjustment causes in selected groups of children and adolescents

Children and adolescents, aged 6 — 20, with maladjustment of different intensity and forms were included to this research study. From the psychological point of view the level of mental development is the most important indicator of adjustment. From the sociological point of view the impact of family is crucial.

Retardation of mental development is conncted with poor adjustment. Intra-family relations and uniformity of parents' attitudes are more important in the process of child adaptation than the family structure (full or borken). Parental attitudes towards socially

maladjusted children were characterized by feeling of helplessness. Better adjustment was found to be connected with elimination of intellectual deficit and with changes of family interactions.

3. An analysis of drug dependence process — a catamnestic study

The study was based on medical and sociological examinations of 81 drug-dependent persons (17 women and 64 men). Almost 50% of them were found to continue abstinence (at least 2 last years). Death of 9 drug addicts was indirectly connected with drug abuse.

See the List of Publications: a) 32, 46, b) 18, 19, 56, 67, 68.

The Library
Head: Krystyna Marczakowska

The Library has been organized on July Ist 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) — 17 276, periodicals, newspapers (number of titles) — 451

unpublished documents (dissertations, research reports — SYNABA, in hard microfiches) — 5202

Reference aids:

catalogues — alphabetical: books, periodicals and microfiches,
— subject: books,

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

Number of inquairies and services per year:

circulation of documents (original and copies):
reading room and library loan — 8662
interlibrary loan — 1186

direct reference services (in person, by telephone) — 644, circulated journals, current books and periodicals for the Departments users — 3934

reprographic services: xerocopies — 4000

systems of the user-oriented information services:
SDI — manual 15 topics
current and retrospective dissemination information — 27
MEDLINE — 8
SYNABA — 49

Users:
scientific workers of the Medical Research Centre, interlibrary loans available for all Scientific Institutes in Poland and abroad.

Bibliography of library: a list of new books and current periodicals prepared weekly.

Medipan — Scientific Instruments Department
Head: Andrzej Lasek

MEDIPAN a scientific enterprise, being a part of the Medical Research Centre, invents and produces special medical equipment such as: cytologic centrifuges, infusion pumps and a device used in various human exercise-tests called „Physiotest".

MEDIPAN infusion pumps can be classified into two basic functional groups. Syringe pumps Models 610 AS and 610 BS as well as the microprocessor-controlled Syringe Pump model 611 belong to the first category. They are designed to serve for prolonged intravenous infusions of several drugs. The model 611 is the newest one, elaborated in 1989. It works jointly with a 50 ml syringe, ensurs a microprocessor-controlled inspection of performing elements, indicates the current working parameters such as a dose volume, flow rate and time of infusion. Thus, the pump represents a modern construction comparable with similar devices produced in highly developed western countries.

Peristaltic pumps, designed for intravenous drips (Models 601 SP, 602 SP, 604 P and 605 SP), belong to the second category. They have modern construction, are easy to operate, their elements are effective and durable. Each model of the described above pumps difers from another in respect to the operation it can perform. The model 602 SP represents a simplest pump type, enabling only setting the flow rate. The model 601 SP enables a precise of a flow rate, dosing volume, indication of a currently dosed volume as well as a legible signalization of alarm states. The model 604 performs the same functions as 601 but using minimal power (i.e. 5 VA). Because of it this pump can operate for 8 hours with an internal battery power supply.

The model 605 SP is the best functionally developed pump which creates a possibility of programming a flow rate in a few time periods. It has a microprocessor built in to inspect, indicate and control all parameters on a 32-position alpha-numerical display.

The infusion pumps described above have been awarded several prizes both in Poland and abroad during International, Commercial Fairs. Some of them obtained the gold medals at Leipzig and Plovdiv Fairs and Gold Esculape at the International Medical Fair SALMED-90.

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b) Communications

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SCIENTIFIC DEGREES AND HONORS OBTAINED

Habilitation, 2nd scientific degree thesis:

1. Badurska B: Childhood myasthenia: clinics and therapy (Neuromuscular Unit).
2. Grucza Ryszard: Efficiency of human thermoregulatory system under endogenous and exogenous heat loads (Department of Applied Physiology).
3. Juczyński Zygfryd: Predictors of cardiological rehabilitation effectiveness after uncomplicated myocardial infarction: a psychological perspective (Mental Health Department).

M.D.

1. Górewicz R: The method of formation and evaluating the suitability of certain types of subcutaneous arteriovenous fistulas for extracorporeal dialysis (Laboratory of Experimental Surgery).
2. Orlewska Ewa: Evaluation of the mechanism of immunological enhancement: entrapment of allogeneic cells injected i.v. with alloantiserum in the liver of prospective allograft recipient (Department for Surgical Research and Transplantion).
3. Szczypaczewska Maria: Coincidence of predisposition to hypertension and high anaerobic capacity in athletes and untrained men (Department of Applied Physiology).
4. Wójcik-Ziółkowska Ewa: Electrocardiogram and hemodynamic responses to mixed (static-dynamic) exercise test in patients with coronary heart disease and asymptomatic men with coronary risk factors (Department of Applied Physiology).

D.Nat.Sc.

1. Atta Ali Mohamed Fathy: The influence of whole-body hyperthermia on cellular composition of lymphoid organs in rats (Department for Surgical Research and Transplantation).
2. Bądzyńska Bożena: Mechanism of action of atrial natriuretic peptide (ANP) on diuresis and natriuresis in rat kidney (Department of Applied Physiology).
3. Kubicka Urszula: Normal human immune peritoneal cells: phenotypic characteristics (Department for Surgical Research and Transplantation).
4. Langfort Józef: Physical activity as a factor modifying sensitivity of skeletal muscles to insulin (Department of Applied Physiology).

5. Pawłowski Grzegorz: Sinusoidal volume loads of the intracranial system as the diagnostic infusion tests (Department of Neurosurgery).
6. Wikieł Hanna: Mechanism of inositol lipid degradation in normoxic and ischemic gerbil brain (Department of Neurochemistry).

Honors and prizes

1. Prize of the Scientific Secretary of the Polish Academy of Sciences for the study on the cellular mechanisms of acceptation and rejection of the allogeneic graft (Department for Surgical Research and Transplantation: W. Olszewski, H. Gałkowska, E. Orlewska, J. Płachta, B. Łukomska, A. Ziółkowska, I. Grzelak, M. Dąbrowski).
2. Prize of the Scientific Secretary of Polish Academy of Sciences for the study on the role of metabolic changes and disturbances of neurotransmission in brain nerve endings in the pathogenesis of brain injury (Department of Neurochemistry: J.W. Łazarewicz, W. Gordon-Majszak, R. Pluta, M. Puka, U. Rafałowska, E. Salińska, J. Waśkiewicz.
3. Prize of the Scientific Secretary of Polish Academy of Sciences for the work: A research strategy for the resolution of childhood spinal muscular atrophy (Neuromuscular Unit).

SCIENTIFIC MEETINGS ORGANIZED BY THE MEDICAL RESEARCH CENTRE

1. Symposium „Isolation of cells with use of monoclonal antibodies" sponsored by Becton-Dickinson, Warsaw, January 10—11th.
2. Long-Term Monitoring During Sleep and Wakefulness in Epilepsy and other Episodic Disorders, Warsaw, April 19—22nd.
3. Symposium „Progress in vascular surgery" sponsored by Gore, Warsaw, April 28th.
4. Symposium on Malnutrition, Trauma and Immunity, sponsored by Frasenius, Warsaw, May 11th.
5. Course of the basic microsurgical techniques, sponsored by Cyanamid, Warsaw, February 20—29th and June 19—24 th.
6. Neurobiology of ischemia and hypoxia with special reference to the problem of maturation syndrom and late changes, Poznań, June 29th — July 1st.

VISITING SCIENTISTS

Department of Applied Physiology

Greenleaf J.E.	Laboratory of Human Environmental Physiology, Space Branch NASA Amies Research California, USA
Kapitaniak B.	Centre Nacionale Res. Science, Paris, France
Levis S.	Health Science Center, University of Texas, Dallas, USA
Porta S.	Institute of Functional Patophysiology, University of Graz, Austria

Cardiovascular Laboratory

Parrarata J.	Department of Physiology and Pharmacology, University of Strathclyde, Royal College, Glasgow, U.K.

Department of Neuropathology

Baramidze G.	Institute of Physiology, Academy of Sciences, Moscow USSR
Chaspiekowa L.	Institute of Brain Research, Academy of Medical Sciences, Moscow, USSR
Gurwicz W., Ganuszkina I.	Institute of Neurology, Moscow, USSR
Pyłova S.I., Wasilewa T.N.	Institute of Reanimatology, Academy of Medical Sciences, Moscow, USSR
Rechardt L.	University of Tampere, Helsinki, Finland
Samoilova M.O., Semionov G.	Pawlows Institute of Physiology, Academy of Sciences, Moscow, USSR

Department of Neurochemistry

Razumovski A., Szachnowicz A.	Burdenko Institute of Neurosurgery, Academy of Medical Sciences, Moscow, USSR

Department of Neurosurgery

Hartman A.	Neurosurgical Clinic, University of Bonn, GFR
Papo I.	Division of Neurosurgery, General Regional Hospital, Aneona, Italy
Winkelmüller W.	Neurosurgery Clinic, Osnabrück, GFR

Laboratory of the Developmental Neuropathology

Wiśniewska K.	Institute of Basic Research of Developmental Disabilities, New York, USA

Department for Surgical Research and Transplantation

Kiessling R.	Karolinska Institutet, Stockholm, Sweden
Lee Chong Ook	Seoul National University, South Korea

Participants of the Jubilee Meeting of the Polish Surgeons Society, Cracow, September 17—20th:

Lie T.S., Lie S., Preissinger Kreimeier	West Germany
Kwang Soo Lee, Kim Young-Kyoon	South Korea
Kajiwara T., Idezuki Y., Ogawa K., Ohigashi S., Hirai M.	Japan
Rostad H., Rostad E.	Norway
Galetti G.	Italy
Lozano R., Navarro M.	Spain
Lommen	Holland

Neuromuscular Unit

Angellini C.	Neurological Clinic, Padua, Italy
Askanas V., Engel K., Engel V.	University of Californa, Los Angeles USA
Hecht B.M., Strokow I., Szagal D.	Institute of Pathophysiology, Academy of Medical Sciences, Moscow, USSR
Korczyn A.	Sackler School of Medicin, Tel Aviv, Israel
Kraft G.	University of Washington, Seattle, USA
Scherwood A.	Baylor College, Houston, Texas, USA
Winiczai Z.	Neurological Clinic, Sopron, Hungary

VISITS ABROAD

Department of Neurophysiology

Głogowska M.	Department of Pathophysiology, Safarik University, Košice, Czechoslovakia
Jernajczyk U.	Laboratory of Anatomy and Neurobiology, University of California, USA
Karczewski W.	The Royal Society, London, U.K.

Department of Applied Physiology

Budohoski L.	Department of Anatomy, University of Toronto, Canada Department of Biochemistry, University of Oxford, U.K.
Brzezińska Z.	Institute of Rehabilitational Medicine, University of Gothenburg, Sweden (long term visit)
Grucza R.	Department of Physiology, University of Kuopio, Finland
Langfort J.	Institute of Functional Pathology, Graz, Austria
Kaciuba-Uściłko H.	Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Czechoslovakia Medical Research Center, Syracuse, USA Institute of Functional Pathology, Graz, Austria
Nazar K.	Department of Physiology, University of Kuopio, Finland Institute of Functional Pathology, Graz, Austria Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Czechoslovakia
Wójcik-Ziółkowska E.	Cardiological Clinic, University of Lille, France

Cardiovascular Laboratory

Cedro-Ceremużyńska K.	Bayer Research Centre, Wuppertal, GFR
Kwiatkowska-Patzer B.	University of Minnesota, Duluth, USA (long term visit)
Radomski M.	The Welcome Research Laboratories, Beckenham, U.K. (long term visit)

Department of Neuropathology

Albrecht J.	Medical Center, Miami, USA (long term visit)

Gadamski R.	Department of Cytology and Embriology, Academy of Medical Sciences, Wladywostok, USSR
Hilgier W.	Institute of Physiology, Czechoslovakian Academy of Sciences, Prague
Kida E.	Institute for Basic Research in Development Disabilities, Staten Island, USA (long term visit)
Krajewski S.	Neurological Clinic, Munich, GFR Institute of Neuropathology, Düsseldorf, GFR
Kroh H.	Institute of Neuropathology, University of Berlin,
Mossakowski M.	Institute of Basic Research, New York, USA Medical Research Council, London, U.K. National Institute of Neurology, London, U.K. Institute of Brain Research, Academy of Medical Sciences, Moscow, USRR
Szmielow A.	Institute of Brain Research, Academy of Medical Sciences, Moscow, USSR
Taraszewska A.	Institute of Neurology, University of Wien, Austria

Department of Neurochemistry

Gordon-Majszak W.	Institute for Basic Research and Developmental Disabilities, New York, USA (long term visit)
Łazarewicz J.	Georgetown University, Washington, USA Pavlov Institute of Physiology, Leningrad, USSR
Majszak W., Nowińska H.	Institute of Experimental Reanimathology, Academy of Medical Sciences, Moscow, USSR
Puka M.	Fonyo Department of Physiology, Semmelweis University, Budapest, Hungary
Strosznajder H.	Cancer Research Center, Heidelberg, Wiesbaden, GFR Institute of Physiological Chemistry, University of Perugia, Italy

Department of Neurosurgery

Czernicki Z.	Neurosurgery Clinic, Kantonspital, Aarau, Switzerland Council of Scientific and Industrial Research, New Delhi, Madras, India Institute of Physiology, Georgian Academy of Sciences, Tbilisi, USSR
Grochowski W.	Burdenko Institute of Neurosurgery, Moscow, USSR
Jurkiewicz J.	Neurosurgery Clinic, Aarau, Switzerland
Łuczywek E.	Israel Institute of Technology, Faculty of Medicine, Haifa, Israel
Mempel E.	Neurosurgery Clinic, Aarau, Switzerland
Miłach-Uchman G.	Burdenko Institute of Neurosurgery, Moscow, USSR
Pawłowski G.	Institute of Neurosurgery, Academy of Medical Sciences, Moscow, USSR
Tychmanowicz K.	Centre Hospitalier Regional et Universitaire de Neurochirurgie, Cean, France

Laboratory of the Ultrastructure of the Nerwous System

Gajkowska B.	Cancer Research Center, CNRS, Villejuif, France
Loesch A.	Department of Anatomy and Developmental Biology, University College, London, U.K.

Department for Surgical Research and Transplantation

Łukomska B.	Immunology Department of Karolinska Institut, Stockholm, Sweden Cellular Interactions Laboratory, University Bordeaux II, Bordeaux, France
Olszewski W.	Rene Huquenin Centre, Saint-Claud, France
Płachta J.	Immunological Laboratory of Puerto de Hierro Clinic, Madrid, Spain
Romaniuk A.	Thoraxcentrum, Cardiopulmonary Surgery, University of Groningen Hospital, Groningen, Netherlands
Wąsowska B.	Duke University, Medical Centre, Department of Pathology and Immunopathology, Durham, USA (long term visit)

Mental Health Department

Szamburska J.	Neurosurgery Clinic, Haidelberg, GFR

PARTICIPATIONS IN INTERNATIONAL MEETINGS

International Conference in Brain Research Institute, Moscow, USSR, January 23-28th
Zelman I., Kida E., Śmiałek M., Taraszewska A., Kosicka B., Szmielew A.

15th Annual Meeting of EBMT, Bagdastein, Austria, February 26th — March 2nd
Ratajczak M.

International Symposium „Central Nervous System and Postreanimation Pathology", Moscow, USRR, March 13-17th
Łazarewicz J.

Austrian Neuroscience Winter Meeting, Kitzbuhel, Austria, March 14-18th
Kroh H.

INTERVISC Meeting on the „Regulation of endocrine function in stress"Budapest, Hungary, April 5-6th
Kaciuba-Uściłko H., Nazar K.

Meeting of Royal Physiological Society, London, U.K., April 6-7th
Sieradzan K.

Annual Meeting of British Cardiological Society, Oxford, U.K., April 6-7th
Cedro-Ceremużyńska K.

23rd Annual Meeting of European Society for Clinical Investigation, Athens, Greece, April 19-22nd
Kamińska A.

12th International Meeting of Neurochemical Society, Algarge, Portugal, April 23-28th
Strosznajder J.

2nd International Symposium „Transplantation and regeneration in central nervous system", Štrbské Pleso, Czechoslovakia, May 17-20th
Łazarewicz J., Rafałowska U., Zalewska T.

12th Congress for Experimental Surgery of Hungarian Surgical Society, Budapest, Hungary, May 18-20th
Dąbrowski M., Grzelak I., Sadowska-Szablisty D.

24th Congress of the European Society for Surgical Research, Brussels, Belgium, May 28-31st
Grzelak I., Kubicka U., Łukomska B., Olszewski W.

14th International Symposium on Cerebral Blood Flow and Metabolism, Bologna, Italy, May 28th — June Ist
Pluta R., Puka M.

11th International Lectin Conference, Tallinn, Estonia, USSR, June 4-9 th
Szumańska G.

24th Annual Congress of the SEPCR, Lozanna, Switzerland, June 26th — July Ist
Karczewski W.

31st International Congress of Physiological Society, Helsinki, Finland, July 9-14th
Borkowski M., Janczewski W., Kruk M., Kubin L., Wojtal E.

Symposium on Physical Follow-up Methods of Sports Training, Tampere, Finland, July 9-15th
Chwalbińska-Moneta J.

Thermal Physiology — IUPS Satellite Symposium, Tromso, Norway, July 16-21st
Grucza R., Kaciuba-Uściłko H., Kruk B., Turlejska E.

7th International Congress of Immunology, West Berlin, July 29th — August 5th
Gałkowska H., Grzelak I., Krynicki M., Łukomska B., Olszewski W., Sadowska-Szablisty D., Sitnicka E.

12th International Congress of Lymphology, Tokyo, Japan, August 27th — September 2nd
Gałkowska H., Łukomska B., Olszewski W.

EAMD Conference on Spinal Muscular Atrophy (SMA), Paris, France, AugustSeptember
Strugalska H.

10th Eurpean Section Meeting of the International Society for Heart Research, Rotterdam, The Netherlands, September 7-9th
Cedro-Ceremużyńska K., Kwiatkowska-Patzer B.

International Workshop on Childhood SMA, Lembiez, France, September 18-20th
Kamińska A.

25th Conference of the European Federation for the Study of Diabetes, Lisbon, Portugal, September 19-23th
Budohoski L.

French-German Joint Meeting for Neuropathology, Frankfurt, GFR, October 19-23rd
Dąmbska M., Krajewski S.

World Congress of Neurology, New Delhi, India, October 22-27th
Hausmanowa-Petrusewicz I., Kamińska A., Strugalska H.

4th Congress of the European Society for Organ Transplantation, Barcelona, Spain, November 1-4th
Olszewski W.

Symposium „Das Spectrum der Neurochirurgie", Bonn, GFR, November 3-4th
Czernicki Z.

22nd Denube Symposium for Neurological Sciences, Innsbruck, Austria, November 9-11th
Mossakowski M.

5th Symposium of International Neumologia, Sevilla, Spain, November 15-18th
Pokorski M.

International MDA Conference on Motor Neuron Diseases, Tucson, Arizona, December 2-7th
Hausmanowa-Petrusewicz I.

Symposium on Theoretical Basis and New Methods of Functional Diagnosis of the Neuromuscular and Peripherial Nerves Disorders, Barjomi, Georgia, USSR, December 4-8th
Rowińska K.