POLISH ACADEMY OF SCIENCES
MEDICAL RESEARCH CENTRE

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POLISH ACADEMY OF SCIENCES
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RESEARCH REPORT

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

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Physiological and patophysiological aspects of cardiovascular and respiratory control (D.Nat.Sc. H. Gromysz)

Motoneurons of n. mylohyoideus and n. facialis have been located with the use of horseradish peroxidase technique. Motoneurones of n. mylohyoideus are concentrated in caudal (and some of them in mid-ventral) part of the motoric nucleus of the V-th cranial nerve. There are three parts of nucleus of the VII-th cranial nerve: a) paramedial, b) medial, c) lateral.
The paramedial part is composed of neurons which fire tonically and send axons to the upper branch and to the carotid artery branch of the nerve. The medial part includes neurons sending axons to the lower branch of the VII-th nerve. The lateral part of the nucleus consists of neurons, axons of which form the middle branch of the nerve. In the latter two branches of the upper parts have inspiratory, whereas the lower parts have expiratory activities.
The participation of cortex in the control of respiration was investigated with the transcranial magnetic stimulation (TMS) technique. It has been shown that a single magnetic stimulus causes a short-latency stimulation followed by an inhibition of phrenic motoneuron activities lasting for tens of miliseconds. TMS elicits similar response in both inspiratory and expiratory muscles of the chest. The magnitude of response to TMS depends on stimulus intensity, but its timing does not.
A short-acting anesthetic (althesine) increases the threshold of the response to TMS by 10-20 of the stimulator output, but timing of the response also does not change.
These results suggest that TMS stimulates both direct cortical- to - respiratory motoneurons and polisynaptic cortical- to - brain stem respiratory neurons pathways.
Barbiturate anesthesia has been employed as a model of peripheral sleep apnea. It has been documented that electrostimulation of n. hypoglossus decreases the upper airway resistance, so it may be useful in treatment of peripheral sleep apnea. It has also been found that respiratory activities in hypoglossal nerve are synchroneous with phrenic activities and they are important for proper positioning of tongue throughout the respiratory cycle, thus for the control of upper airway patency.

Physiological and clinical correlations in the respiratory system
(Assoc. prof. M. Pokorski)

The lack of ventilatory response to hypoxia in the guinea pig has been confirmed. These animals develop apnea during hypoxia. This anomalous reaction may be the result of genetic adaptation to high altitude (guinea pigs originally inhabitate mountain regions in Andes).
In experiments on cats of both sexes the time course of respiratory response to progesterone given intravenously, intramuscularly and locally to the brain stem, and also after pretreatment with a progesterone antagonist RU-486 (obtained by the courtesy of Roussel-Uclaf - France) has been evaluated. The fast (non-genomic) response to progesterone, reported previously by Millhorn et al., could not be reproduced in these experiments.
It has been found that during the initial deep breath followed by the respiratory stimulation, which occurs in response to peripheral chemoreceptor agonist almitrine, the inspiratory resistance of the larynx is significantly reduced.
The expiratory resistance of the larynx is significantly increased during the initial deep breath, but latter it tends to be lower than during the control period.
In experiments with human subjects with high spinal lesions (tetraplegics) a role played by the descending spinal pathways in chemoreceptive reflexes has been investigated. The results show that respiratory and cardiac responses to hypoxia and hypercapnia are generally well preserved in tetraplegics.
This finding indicates that spinal pathways are of no primary importance in these reflexes.
In the same group of patients the relationship between respiratory and cardiovascular responses to static muscular exercise was investigated. It has been found that respiratory stimulation does not depend on the concomittant cardiac output increase.
The frequency distribution of the Major Histocompatibility Complex (HLA) phenotypes in a group of victims of intracranial aneurysm rupture were compared with their distribution in the Polish population at large. The results suggest that some of the (potentially fatal) aneurysm ruptures are strongly correlated with bearing the DR 7 homozygote. Yet the frequency of the DR 7 homozygotes in the general population (0,45) is too low to make the HLA typing a feasible screening test for the presence of intracranial aneurysm.

See the list of Publications:
A) 32, 48, 78, 82, 83, 84, 85, 86, 110, 111.
B) 8, 34, 50, 60, 109, 142.

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Hormonal control of energy metabolism (Prof. K. Nazar)

1. An effect of 60h total fasting on metabolic and hormonal responses to endurance (45 min) exercise was studied in 7 middle aged healthy men. In comparison with 12h overnight fasting (PA) 60h food withdrawal (F) caused a significant increase in the plasma free fatty acid (FFA) and cortisol concentrations both at rest and during physical exercise. During exercise plasma catecholamine, growth hormone and glucagon levels rose considerably more in F than in PA state, while concentrations of insulin, triiodothyronine (T) and testosterone were lowered.
Blood glucose concentration was significantly diminished in F-experiments only during the post-exercise recovery period. Results of this study indicate that 2,5 day fasting leads to modifications of neuro-hormonal response to exercise which promote saving of carbohydrates as muscle energy substrate.
2. Continuing the study on muscle insulin sensitivity in the rat it was demonstrated that the exercise-induced increase in the sensitivity of glucose utilization by the soleus muscle in vitro can be abolished by 2-chloroadenosine (adenosine agonist) added to the incubation medium.
In another experimental series it was proved that the adenosine antagonist (8-phenyltheophyline) restores insulin sensitivity of the soleus muscle taken from thyreoidectomized rats. Results obtained in the above described investigations confirmed earlier suggestions about an inhibitory role of adenosine in determining skeletal muscle sensitivity to insulin under different physiological or pathological conditions (L. Budohoski, Ph.D., D.Sci).
3. Experiments were performed on hypothyroid and hyperthyroid rats with the aim to elucidate the effect of thyroid status on the plasma triacylglycerol (TG) metabolism. Simultaneous measurements of lipoprotein lipase activity (LPL) in skeletal muscle and myocardium, disapearance of labelled chylomicrons from blood, as well as plasma and skeletal muscle TG and FFA concentrations were made. It is of interest that both hypo- and hyperthyroidism enhanced the rate of plasma chylomicron disapearance, in spite of opposite changes of muscle LPL activity in these two states.
4. Changes in blood ammonia and lactate were followed after the maximal treadmill exercise test in circumpubertal (13 ± 0.5 years) boys and girls. It was found that in children the exercise-induced increases in the plasma ammonia are smaller to those in adults, both in absolute terms and in relation to blood lactate levels.

Consequences of hypokinesia

Continuing the study on the long-term restriction of physical activity in dogs the effects of 2- and 5-month cage confinement on ultrastructure of skeletal muscles at rest and after exhaustive exercise were investigated (in cooperation with Life Division, NASA Ames Research Center, Moffet Field, California, USA). The most important finding of this study is that physical exercise after 5 months of physical activity restriction leads to disruption of mitochondria, which does not occur either in dogs exercising under conditions of normal activity, or in those confined only for 2 months.

Dynamics of cardiovascular responses to physiological stimuli

(Prof. K. Nazar)

Cardiovascular response to glucose ingestion (75 g) was studied in healthy men and in patients with the border-line hypertension, obesity and insulin resistance. In healthy subjects glucose load caused a transient decrease in stroke volume (measured by impedance reography) and cardiac output . .(Q) followed by a significant increase in Q, persisting for 2 hours. Blood pressure (BP) showed a small increase in the 2nd hour of the test, while the total peripheral resistance (TPR) significantly decreased. In patients the changes in cardiac output were similar to healthy subjects, but the increase in BP occurred earlier and was more pronounced. Since TPR remained unchanged it was suggested that in patients with hypertension and obesity the vasodilatatory effect of insulin is inhibited because of resistance to this hormone.

The effect of 10-week endurance training on the cardiovascular response to posture changes and physical exercise was investigated in the previously sedentary, healthy young men. The data showed that the training programme does not modify the time course or magnitude of the transient changes in heart rate, stroke volume, and cardiac output in response to standing up, but it does enhance the increment in diastolic blood pressure during this maneouver. These findings suggest that even a moderate training may improve the orthostatic tolerance by the effect on the regulation of vascular tone.

It was also demonstrated that training slows down the kinetics of heart rate increase in the transition from moderate (100 watts) to heavier (150 watts) submaximal exercise.

Mechanisms of thermoregulation

Continuing the study on sweating kinetics in human subjects it was found that in female-athletes the thermoregulatory responses to exercise are different in follicular and lutheal phase of menstrual cycle. In the latter phase the sweating response was less pronounced than in the former. The differences were enlarged in women taking oral contraceptives. All the above findings point to the role of female sex hormones in the regulation of body temperature during physical effort (R. Grucza, Ph.D., D.Sc).
In cooperation with the Department of Physiology University of Kuopio (Finland) studies were carried out on thermoregulatory and metabolic responses to exercise of various intensities performed by healthy young men at low ambient temperature. It was demonstrated that the sweating threshold during exercise in cold environment is shifted towards lower body and skin temperatures. Besides, it was documented that subjects exposed to cold possess potentially higher work ability at moderate and high intensities than at 24°C, which is reflected by reduced increases in core body temperature, heart rate and blood lactate concentration (B. Kruk, Ph.D.).

Clinical evaluation of patients with coronary heart disease

(E. Wójcik-Ziółkowską, M.D.)

A complex analysis of the coronary heart disease (CHD) course was made in a group of 128 patients 15-18 years after their first myocardial infarction. In the group of patients participating in this longitudinal study 59 died. Among the remaining patients 10 had the coronary bypass because of increasing symptoms of coronary insufficiency and imminent infarction. Out of 69 patients, who were treated farmacologically, 32 had the second myocardial infarction, 60 cardiac insufficiency of various degree, and 45 ventricular arrhythmia. Angina was occurring only in 65 of the patients, whilst in 35 so called silent myocardial ischemia was observed.
A significant relationship was found between cardiac arrhythmias, registered by the Holter method, and impairment of systolic function of the left ventricle, evaluated by echo-cardiography.
The results obtained are in agreement with the literature data, although the longitudinal studies carried out by other authors covered shorter periods after the first infarction (up to 10-12 years).

Dynamic studies of medullary interstitial electrolytes
(Prof. J. Sadowski)

1. Mechanism of ANP action.

Own earlier studies of the mechanism of action of the atrial natriuretic peptide (ANP) in the rat have shown that atriuresis is not critically dependent on renal hymodynamic changes. However, a decrease in arterial pressure observed in those experiments complicated interpretation of ANP-dependent changes in renal blood flow and filtration rate and analysis of the possible relationship between hemodynamics and natriuresis. Therefore, in the present study a suprarenal aortic clamp was used to stabilize perfusion pressure of the rat kidney during ANP-dependent renal and systemic vasodilatation. The data obtained at constant perfusion pressure reinforce our previous conclusions and further dissociate ANP natriuresis from renal hemodynamic changes and from a possible wash-out of tissue electrolytes.

2. Ethacrynic acid dissipates renal electrolyte gradient.

Our previous work has shown that furosemide, a loop diuretic, dissipates the cortico-medullary tissue electrolyte gradient in the kidney whereas acetazolamide, a proximal transport inhibitor, does not. In order to find out whether the gradient dissipation is specific for furosemide or a simple consequence of any inhibition of loop transport in general, experiments were performed with ethacrynic acid (EA), a loop diuretic chemically unrelated to furosemide. Unlike in other species, EA is a relatively weak diuretic agent in the rat. In order to increase its potency, the drug was infused together, with cysteine, an expedient borrowed from in vitro studies reported in the literature.

Sodium excretion increased 1.7-fold with EA alone and 5-fold after EA + cysteine. The latter induced a profound reduction of the cortico-medullary electrolyte gradient, similar to that of furosemide.

The data indicate that sodium reabsorption by the ascending limb of Henle's loop is a critical determinant of electrolyte concentration in the renal medullary interstitim.

See the list of Publications:

A) 10, 11, 12, 13, 14, 15, 21, 37, 38, 47, 49, 59, 60, 62, 72, 96, 97, 109, 116, 119, 120, 121, 122, 123, 124, 125.

B) 5, 7, 9, 10, 11, 12, 13, 35, 36, 37, 38, 55, 56, 69, 70, 72, 73, 77, 78, 93, 94, 95, 96, 115, 132, 148, 161, 162, 163, 164, 165.

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Protective effect of magnesium upon catecholamine-induced myocardial damage

Over the last years, the recognition of the role of magnesium ion (Mg^{++}) in cardiac physiology has grown considerably. It has been well established that Mg supplementation suppresses arrhythmias and improves survival in patients with myocardial infarction (MI) whilst Mg deficiency was found to aggravate cardiotoxicity of catecholamines in animal studies. In the search for morphological basis of the beneficial effect of Mg in the myocardium exposed to catecholamine excess, we have investigated an influence of Mg (Magnesium sulfate, 50 mg/kg iv) upon ultrastructure and cytochemical calcium (Ca^{++}) localisation (oxalatepyroantimonate method) in hearts of rabbits inflused with adrenaline (1/ug/kg/min for 2 h) and in the controls. $MgSO_4$ infusion protected mitochondrial structure and diminished the catecholamine-induced endothelial and intracellular swelling. As shown ultracytochemically in adrenaline-treated hearts, the abundant Ca^{++} deposits located in mitochondria were unaffected by Mg suplementation. The results of the above studies provide morphological evidence for beneficial effect of Mg in the myocardium damaged by catecholamine excess, as shown by protection of cellular and intracellular membranes. Although Mg^{++} ion is considered as "physiological Ca^{++} antagonist" it does not prevent adrenaline-induced Ca^{++} overload, as shown cytochemically.

Inhibitor of NO synthase increases platelet deposition on damaged endothelium in vivo

In view of postulated role of Endothelium-derived relaxing factor, EDRF (NO) in the control of platelet-vessel wall interaction, we studied the effect of NO synthase inhibitor, N-monomethyl - L-arginine upon the platelet-endothelial cell interactions in the rabbit carotid artery *ex vivo*.
Scaning electron microscopy was used to visualize these interactions on an intact endothelium and on endothelium damaged by arterial constriction. It was shown that an inhibition of NO synthase does not affect platelet interaction with an intact endothelium, whereas it potentiates platelet aggregation and adhesion to damaged endothelial surface. These findings support the role of EDRF as a protective factor which promotes haemostasis and prevents thrombosis.

Calcium antagonist prevents stress induced stimulation of renin and aldosterone secretion in conscious pigs

In continuation of studies on hormonal and matabolic consequences of stress, an increased renin and aldosterone secretion was found in conscious pigs subjected to 24 h immobilization. This was prevented by pretreatment of the animals with the Ca^{++} antagonist - Nisoldipine. The inhibition of enhanced renin and aldosterone by Ca^{++} inhibitor may have clinical implications.

See the list of Publications:
A) 44, 45, 89, 90, 91, 92.
B) 48.

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Head: Assoc. prof. Maciej Borkowski

Peripheral circulation in patients with vascular diseases

Own experience was gained on making the arterio-venous fistulae for dialysis by subcutaneous transposition of cephalic vein in the arm. Duration of the fistula potency was from 1 to 20 months. Up to now 9 out of 13 fistulas are under observation. In our opinion this is a very useful, generally uncomplicated method to get an access to the vessels for extracorporeal dialysis. The aim of some other studies was to estimate quantitatively and qualitatively blood flow in the hand of patients with Raynaud's syndrome treated with transcutaneous electrical stimulation (TES). Such treatment proved to have considerable therapeutic value in certain peripheral vascular diseases.
Medical doctors applying TES are looking for an optimal method of the evaluation of its effectiveness in patients with Raynaud's syndrome.
It was concluded that: 1. Transcutaneous electrical stimulation significantly increases blood flow in the stimulated area of the hand in the patients with Raynaud's syndrome. 2. Electro-impedance rheography is a good method of quantitative-comparative estimation of electrotherapy in the patients.
In other studies an effect of PGE_1 on filterability of whole blood was investigated in 10 patients with ischaemic vascular disorders of lower extremities. Intraarterial infusion of the synthetic PGE_1 resulted in temporary deterioration of blood rheologic properties.
However, after cessation of the infusion an improvement of rheologic indices occurred due to beneficial PGE_1 action on erytrocyte deformation.

See the list of the Publications:
A) 8, 35, 58.

RESEARCH REPORT

STUDIES ON THE STUCTURE AND BIOLOGICAL PROPERTIES OF THE NERVOUS TISSUE

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Metabolic and immunomorphologic basis of progressing postresuscitation encephalopathy: the "maturation phenomenon" in selected central nervous system structures.

The studies were conducted with the use of 2 experimental models: global CNS ischemia (in the course of cardiac arrest) in the rat and a short-term forebrain ischemia in Mongolian gerbil and they were supplemented with an analysis of clinical material.

Studies on the cardiac arrest model have focused on the blood and brain cGMP and atrial natriuretic factor (ANP) levels in the period of ischemia and early postischemia. An increase in the cerebral ANP level was noted in the early postischemic period, which was followed by a rise of cerebral cGMP accompanying compensative hyperemia. These two events are likely to be interrelated.

A systematic analysis of the dynamics of structural changes in global cerebral ischemia revealed that general neuronal loss, becoming apparent after 9-12 months following the ischemia, have an autoimmunologic basis, thus showing analogy to neuronal loss accompainying physiological brain aging. The ·maturation phenomenon· in this model became manifested by the steady progression of abnormalities in the distribution of a number of neuropeptides (calcitonin-dependent peptide, neuropeptide Y and enkephalins), as demonstrated by immunohistochemical methods.

Studies on the short-term forebrain ischemia in the Mongolian gerbil considered mainly the immunoreactivity of astrocytes (GFAP immunoreactivity) in the selectively vulnerable CA1 region of the hippocampus. The glial reactionvity to was present both within and outside the regions of neuronal damage. This observation indicates that the astrocytic reaction may represent a primary response to ischemia and not merely a reaction secondary to neuronal damage.

The same model of ischemia was used to establish a protocol of a calcium channel blocker - nimodipine administration that would most effectively prevent delayed neuronal death. Effective cell protection was obtained after late administration of the drug - even in a single dose - confirming the role of calcium influx in the pathogenesis of the delayed postischemic neuronal death.

An analysis of the autopsy material of cardiac arrest cases revealed a biphasic character of neuropathological changes, similar to that observed in the experimental studies. The early phase may be considered as an

immediate consequence of acute ischemic episode, whereas the late phase characterized by widespread changes most pronounced in the region of vascularization of large cerebral vessels, seems to be related to secondary disturbances of microcirculation and cerebral edema. The autopsy material of stroke cases was used to analyze a relationship between the blood-brain barrier damage and the cellular hamatogenic reaction, assessed by immunomorphological methods. The immunomorphological analysis of the sera taken from of patients with ischemic cerebral stroke revealed in a half of them the presence of antibodies against CNS components (neurons, myelin and glia). This observation confirmed the earlier experimental data.

Transport and metabolism of amino acid neurotransmitters and their precursors in metabolic compartments of the CNS: effects of hepatic encephalopathy and metabolic disorders

The process of glutamine-tryptophan exchange across the blood-brain barrier was examined in vitro using a preparation of cerebral blood capillaries. Tryptophan stimulated glutamine efflux via the sodium-independent L-transport system for neutral amino acids, without participation of γ-glutamyl transpeptidase.

Tryptophan-dependent glutamine release showed an increased activity in the presence of ammonia, as well as in capillaries isolated from the rats with hepatic encephalopathy. These findings point to the contribution of enhanced glutamine-tryptophan exchange to amino acid in the brain typical of various forms of hyperammonemia.

The effect of ammonia or agents simulating its action on the release of amino acid neurotransmitters and neuromodulators from astrocytes was examined in vitro in primary astrocytic cultures. Ammonia was found to stimulate release of taurine an inhibitory neuromodulator and glutamine - a mojor precursor of amino acid neurotransmitters, but did not affect the release of other neurotransmitters e.g. GABA and D-aspartate. The massive release of glutamine from astrocytes was also induced by L-methinine-DL-sulfoximine (MSO), which is both a potent convulsant and a specific inhibitor of glutamine synthetase in astrocytes. The latter observation seems of particular importance, since it is the first demonstration showing that gliotoxicity of an agent may be directly coupled with its potency to affect neural transmission.

Studies on the alpha-ketoglutarate dehydrogenase activity revealed marked differences between the sensitivities of this enzyme to ammonia and hepatic encephalopathy in synaptic and nonsynaptic mitochondria. These differences may be of importance for neural transmission, since alpha-ketoglutarate is a precursor of the neurotransmitter pool of glutamate.

Immunohistochemical studies on glial markers in vitro

These studies have dealt with the expression of glutamine synthetase (GS) in astrocytes and oligodendrocytes cultured in vitro. In both types of cells, GS was activated by db cAMP and a number of hormones. The oligodendroglial enzyme appeared refractory to growth factors (EGF, FGF or PDGF). In view of these results, GS cannot anymore be considered as an astroglia-specific protein.

Effects of selected neurotoxins on CNS neurotransmitter systems, including neuropeptides

Studies on the late effects of quinolinic acid (QUIN) following its administration in vivo revealed delayed neurodegenerative changes in regions of the selective neuronal loss. They differed from the early necrotic changes and corresponded to neuronal degeneration of the dark type and apoptosis of these neurons. The authors have speculated that the changes may be related to the increased QUIN synthesis in hypertrophied astrocytes. Subtoxic doses of QUIN added to dissociated hippocampal cultures produced typical postsynaptic changes. These alterations were ameliorated by the calcium channel blocker - nimodipine, and NMDA receptor antagonist - magnesium ions.
Administration of kainic acid (KA) to the rat striatum induced changes in the striatal capillaries indicating an increased intracellular transport rather than impairment of tight junctions.
Studies on the neurotoxic action of cobalt acetate in the rats subjected to CNS ischemia revealed a decrease in DA and HVA contents and specific MAO activity, but also a fall in the substance P level in the nigrostriatal tract, presumably related to its decreased synthesis. An injection of cobalt acetate to the common carotid artery, (cca) when accompanied by an occlusion of both cca, produced inflammatory changes in the eye ball, involving all the anatomic structures. No such changes were observed following occlusion of one cca only, which points to the role of ischemia in the development of inflammatory changes.

See the List of Publication:
A) 1, 2, 3, 30, 31, 46, 52, 53, 54, 56, 57, 65, 67, 70, 71, 73, 79, 87, 93, 113, 114.

B) 1, 2, 30, 31, 49, 59, 61, 63, 64, 65, 66, 67, 68, 89, 90, 91, 107, 110, 143, 144, 145, 156, 157, 158, 160.

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Disorders of neurotransmission in the pathogenesis of ischemic brain injury

1. The results of previous studies indicated the role of excessive stimulation of glutamate receptors, decompartmentation of calcium ions to neurons and arachidonate release in the ischemic brain injury. A variety of in vivo and in vitro techniques have been employed to evaluate interrelations of these putative pathogenic factors. Continuous dialysis of rabbit hippocampus in vivo with 10 μM nimodipine, in spite of its negligible protective effect on calcium homeostasis and amino acid release, exerted local protection of hippocampal neurons against their early injury and accelerated postischemic reappearance of EEG activity, which suggests the existence of intraneuronal sites of nimodipine action.
Locally applied ethanol in pharmacologically relevant concentrations was shown to inhibit in a dose-dependent manner the NMDA-evoked decrease of extracellular calcium concentration in the hippocampus, which confirms biological importance of previously observed in vitro ethanol-evoked inhibition of NMDA-sensitive glutamate receptors in neurons. It was demonstrated that pretreatment of gerbils with MK-801, a noncompetitive antagonist of NMDA-sensitive glutamate receptors, significantly inhibits accumulation of thromboxane B_2, and to a lesser extent of prostaglandin D_2 and 6-keto-PGF_{1a}, in the brain 5 min. after 5-min bilateral common carotid artery occlusion. These results suggest involvement of NMDA receptors in the mechanism of ischemia-evoked arachidonate release in the brain.

2. The studies concerned also taurine and GABA fluxes, since both these neuroactive inhibitory substances may play a compensatory role in pathogenic neurotransmitter imbalance in the ischemic brain. To evaluate potential involvement of astroglia in ischemia- and excitotoxin-evoked taurine release to extracellular compartment of the hippocampus, an effect of various receptor agonists on taurine efflux was studied in vitro on isolated astroglia-enriched fraction.
It was shown that noradrenaline, glutamate and kainate, but not NMDA stimulate taurine release, which indicates the absence of NMDA receptors on isolated astroglia and is contradictory to the role of astroglia in the release of taurine in brain ischemia. In accordance with the suggested role of taurine in osmoregulatory mechanisms, in cooperation with the Institute of Neurobiology, University of Goeteborg, Sweden, relationships between the blood osmolality, the brain cortical specific gravity, Na^+, K^+, and amino acid contents were analyzed in mice, rats and guinea-pigs in normal

and hiposmolal conditions. Correlations between the blood osmolality, cortical specific gravity and taurine content were demonstrated in normal, but not hiposmolal animals. These results indicate a close relationship between taurine and water contents in the brain, but did not bring evidences for involvement of taurine in rapid osmoregulatory mechanisms. Preliminary data were obtained demonstrating interference of histamine with GABA transport in the rat brain synaptosomes, which may suggest colocalization of both neurotransmitters in brain synaptic endings.

Interreceptor relationship and the role of some agonists in second messengers release in normoxic ischemic and aged brain
(Assoc. prof. Joanna Strosznajder)

In 1990 our studies concerned the inter-receptor interactions and biochemical processes involved in signal transduction in normoxic, ischemic and aged brain. It was found that 15 minutes of induced brain ischemia in rats produced an agonist - mediated modification of adenylate cyclase activity. The results suggest that the post receptor activation of protein kinase C (PKC) is involved in this process (Domańska-Janik and Pylova). Brain ischemia, probably by an increase of Ca^{2+} ion in cells, produces suppression of the catalytic acitivity of PKC which is similar to the effect of phorbol esters (in vitro). These findings suggest that after an initial activation of PKC a subsequent inhibition occurs (Domańska-Janik and Zalewska).
Our previous studies demonstrated that brain ischemia induces dramatic changes in the liberation of lipid-derived second messengers. Present investigations have shown that brain ischemia suppresses the activity of phosphatidylinositol (PI) kinase and phosphophosphatidylinositol (PIP) kinase - enzymes involved in the synthesis of PIP_2. Phospholipase C degrades PIP_2 into the two second messengers DAG and IP_3. It was found that gammabutyrolactone (GBL) injected intraperitoneally 10 min before ischemia in a dose of 300 mg/kg b.w. has a protective effect on both phosphoinositide kinases as well as against degradation of membrane lipids. It is suggested that an appropriate level of PIP_2 plays an important role in maintaining the integrity of cytoskeleton dynamics via PIP interaction with actin binding protein (Strosznajder and Wikieł).
It is known that the inositol phospholipids from synaptic membranes are enriched with arachidonic acid which is an important lipid-derived second messenger and concomitantly the substrate for the synthesis of several eicosanoids. Thus, the mechanism of arachidonic acid release was investigated and the Ca^{2+}-independent, Ca^{2+}-dependent, as well as the receptor mediated processes of AA liberation were studied.
It was found that Ca^{2+}-independent arachidonic acid release occurs by the action of both phospholipases PLA_2 and PLC on phosphatidic acid and poly-phosphoinositides (PIP and PIP_2). Ca^{++}-dependent and carbachol mediated arachidonic release is regulated by PLA_2 acting on PI. Brain aging

affects AA release, particularly the Ca^{2+} -dependent action of PLA_2 and also suppresses significantly the muscarinic receptor mediated AA liberation. On the other hand aging has no effect on PLC mediated phosphoinositides degradation (Strosznajder and Samochocki).

In 1990 some studies on dolichol metabolism and distribution in the brain were carried out to evaluate its role in the modification of membrane function in aged brain (Strosznajder and Jankowski).

See the List of Publications:
A) 1, 2, 20, 34, 65, 88, 95, 103, 104, 108, 117.
B) 21, 22, 23, 80, 81, 82, 110, 114, 122, 123, 124, 125, 135, 136, 154, 159.

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Brain bioelectrical activity as a concequence of lesion in neurosurgical patients

(Prof. Eugeniusz Mempel)

Analysis of brain mapping by the BEAM method (brain electrical activity mapping) in the patients with Parkinson's disease who underwent cryothalamotomy revealed the characteristic asymmetry of normal alpha rhythms in the patients, with a distinct prevalence on the operated side. The results of BEAM examination were correlated with the postoperative clinical improvement.

Comparative analysis of the somatosensory evoked potentials (SSEP) in Parkinson's disease treated by cryothalamotomy and pharmacologically demonstrated the synchronizing influence of surgical intervention on the function of the operated hemisphere. The postoperative SSEP were closer to those in healthy subjects as compared with patients treated pharmacologically.

Brain mapping in atonic epileptic seizures with loss of consiousness in school children allowed to establish the cortical origin of epileptic discharges (in the frontal region), in contrast to the so far prevailing views regarding their centroencephalic provenience.

The influence of L-deprenyl on SSEP's in Parkinson's disease was tested. The results, supported by electromyographic examination, demonstrated a marked inhibitory effect of L-deprenyl on parkinsonian tremor at rest.

SSEP analysis in patients with lumbar discopathy indicated the usefulness of this noninvasive method in neurological diagnosing of the lesion level as well as in prognosing the results of surgical treatment of patients with discopathy.

Analysis of special computer software for brain mapping in epilepsy and Parkinson's disease (elaborated together with the team of prof.Tarnecki from the Institute of Experimental Biology, Polish Academy of Sciences) and verified on an extensive clinical material, proved fully useful both for theoretical research and clinical practice.

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

The investigation concentrating on the evaluation of intracranial volume reserve by the CT images numerical analysis (CTINA) were continued. The CTINA was applied in experimental vasogenic brain edema and it was found very useful in evaluation of brain edema spreading. The first significant changes in CTINA index were determined after 4 hours of edema development.
The effect of superior saggital sinus (SSS) occlusion on intracranial volume pressure relations (IVPR) were studied in acute experiments in the cat and under chronic conditions in patients. The experimental studies showed marked changes in intracranial volume pressure relations. On the other hand, clinical studies revelaed no effect of the SSS occlusion caused by saggital meningiom on brain edema and intracranial volume pressure relations in pre-and postoperative periods. Studies carried out on hydrocephalic patients indicated the usefulness of somatosensoric evoked potentials in hydrocephalus diagnosis. The part of studies concerning the Cushing response was completed. The role of brain ischemia in Cushing phenomenon was confirmed, however the cerebral perfusion pressure value was found to be unsuitable for the phenomenon prediction. The subject of investigations presented in the habilitation thesis of Dr J. Jurkiewicz was the complex evaluation of IVPR in the stage of compensation. The usefulnes of visual evoked potentials studies in determination of the intracranial volume reserve was fully proved.
The current results were presented and discussed at the 2nd International Symposium on Intracranial Hypertension and Cerebral Ischemia organized by the clinic.

Speech disorders and other gnostic functions in focal brain lesions
(Assoc. prof. Jadwiga Szumska)

In investigations concerning visual perception it was established that recognition of emotional stimuli is connected with the right nondominant brain hemisphere.
Neuropsychological examination of children with subacute sclerotising encephalitis (SSPE) demonstrated usefulness of such studies for evaluation of the degree of improvement after combined treatment with isoprinazin and bacterium.
In patients with lesions of the right and left prefrontal region a slowing down of motor reaction was noted when sensibilisation trials were applied, although there was no paresis.

In children with spinal muscle atrophy it was found that motor paralysis of the lower extremities and inability to walk do not affect the development of orientation in space.

See the List of Publications:
A) 16, 17, 61, 68, 69, 79, 112.
B) 14, 54, 86, 87, 88, 105, 106, 111, 133, 134, 141, 146, 147, 149, 150, 151, 152, 153.

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

Morphometric investigations of neuronal population in the hipocampal cortex and Purkinje cell layer of cerebellar cortex were carried out in newborns at 32-40 weeks of conceptional age who died without brain lesions. The loss of neurons due to prenatal and perinatal hypoxia was analysed in both structures in age mached cases. Some differences in the degree of neuronal damage, related to pathomechanism of lesions, were demonstrated. The pathomechanism of four-layered and unlayered polymicrogyria was studied in five cases and the role of disturbances of blood perfusion was discussed. Some aspects of lectin histochemistry in peripheral nervous system were found useful for early diagnosis of Batten disease.
A comparative study concerning an influence of vincristine and cyclophosphamide on maturing nervous system of rabbits was performed. Both drugs administered intraperitoneally or orally were found to penetrate to the CNS and provoke perivascular edema. Besides, vincristine induced also chronic changes in the cytoskeleton of nerve cells. It seems worth mentioning that the rat showed greater resistance than the rabbit to vincristine administration.

See the List of Publications:
A) 18, 19, 55, 63, 64, 115.
B) 16, 17, 76, 79, 85.

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Alterations in the neurosecretory system after cerebral ischemia

Ultrastructural changes in the neurosecretory nuclei and in neurohypophysis were examined in the rats subjected to 5 and 10 min. cerebral ischemia in the course of clinical death. The animals were kept alive for 16 weeks or 10 months after the experiment was initiated. The following ultracytochemical methods were applied: alcian blue and tannic acid staining of glycoproteins, Ca^{2+} ions staining by the pyroantimonate method. Results of these studies revealed the nerve cell apoptosis in different stages and presence of the cells with macrophage properties in the perivascular spaces. In vicinity of the apoptotic cells the phagocytic microglia was found.

In the rats surviving 10 months following the epizode of clinical death lesions of some neurons in the supraoptic and paraventricular nuclei and glial elements in the hypothalamus as well as in the neurohypophysis were demonstrated. The role of microglia in the control of neurosecretory system was discussed.

The cytochemical method detecting Ca^{2+} ions was used for identification of post-ischemic changes in the neurosecretory system of the rats after 5 min. ischemia. An increased accumulation of intra- and extracellular calcium was found in ischemic animals. These changes were recorded on the first and the 3^{rd} day, as well as on the 10^{th} month after blood recirculation. The link between calcium accumulation and ischemic injury of the nervous tissue has been discussed.

Moreover, the presence of substance P in neurohypophysis was compared in control and ischemic rats using the immunogold method.
An increased gold labelling on the surface of the neurosecretory granules in the ischemic animals suggests a role of this substance as a local modulator of neurosecretion.

See the List of Publications:
A) 27, 28, 118.

RESEARCH REPORT

STUDIES ON TRANSPLANTATION AND EXPERIMENTAL SURGERY

MECHANISMS LEADING TO HEREDITARY AND ACQUIRED NEUROMUSCULAR DISEASES

Department for Surgical Research and Transplantation
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Telephone: 21 49 23

Head: Prof. Waldemar Olszewski

Allogeneic skin transplantation for clinical purposes

Characterization of dendritic cells from the dog afferent lymph and skin was carried out. It was found that dendritic cells, migrating from skin to lymphatics, strongly stimulate allogeneic lymphocytes. After separation of the light density cellular fraction into adherent (macrophages) and nonadherent (dendritic) subsets, an inhibitory activity of lymph macrophages in the mixed lymphocyte reaction (MLR) was observed. Supplementing the mixed culture with polyvalent anti-dendritic cells serum resulted in an inhibition of MLR. In another part of the study, mouse anti-human monoclanal antibodies, cross-reacting with the dog cells, showed that blocking of Ia antigens, but not T6, may be responsible for the inhibition of MLR. The anti-dendritic cell serum inhibited also the accessory function of dendritic cells during the response of lymphocytes to PHA. Local injection of the serum caused a transient disappearance of dendritic cells from lymph draining skin.

The mechanism of spontaneous formation of aggregates between lymph dendritic cells and autologous lymphocytes was examined. In canine lymph an average of $3.3 \pm 2.8\%$ aggregate/dendritic cells were observed. Incubation of cells in lymph for 1 h at 37°C caused a slight increase of the aggregate number to $9.5 \pm 6.1\%$, while treatment with proteolytic enzymes did not influence the number. The process of aggregate formation was found to be independent of the presence of Ca^{++} (EDTA) while xylocaine possessed an inhibitory activity. Incubation of lymph cells in the presence of neuraminidase caused a significant increase in the number of cell aggregates. The effect was abolished by treatment with EDTA or xylocaine. Formation of aggregates was temperature-dependent, the highest number was formed at room temperature. Monosaccharides and heparin did not affect aggregate formation, whereas vitamin A decreased their number. Aggregates formed in the presence of neuraminidase remained active in mitogenesis induction of lymphocytes by PHA, however they did not influence the responsiveness in auto-MLR.

The process of migration and redistribution of the rat liver sinusoidal marginating cells was examined. Mononuclear liver washout cells migrated preferentially to the liver. The number of these cells migrating to lymph nodes was 2-times lower than that of peripheral blood cells. The fraction

enriched in LGL (65% LGL) showed even more pronounced migration to the liver sinusoids than the nonfractionated population.
An effect of hyperthermia on the activity of NK cells from the rat liver was studied. After 3 h of incubation at 41°C NK cells showed a decrease of cytotoxic activity while the number of LGL remained unchanged. The NK cell activity measured at the single cell level showed that hyperthermia decreases a number of complexes formed between NK and tumor (K 562 and YAC 1) cells. These results suggest that hyperthermia acts at the stage of target cell recognition.
The functional evaluation of human peritoneal cells revealed that human peritoneal lavage fluid contains 45% monocytes/macrophages, 7,5% NK cells, 42% $CD2^+$ cells whereas only 2% $CD22^+$ B lymphocytes. The $CD4^+/CD8^+$ cell ratio was 0,4. The results point to a preferential accumulation of cells with cytotoxic/suppressor phenotype in the peripheral cavity. The responsiveness of mononuclear peritoneal cells to PHA, ConA and PWM was lower than of blood cells, while autotransformation level was similar. It can be inferred that peritoneal fluid does not contain activated lymphocytes.

Cellular mechanisms of allograft rejection and acceptance

The process of repopulation of bone marrow in irradiated recipients from the hind limb transplant of syngeneic female WIS-WAG rats was studied. In the group I recipients underwent total body irradiation, in the group II donors of grafts were irradiated while in the group III rats remained untreated. In the group one 5 out of 6 animals, receiving syngeneic limb graft, survived 4 weeks after transplantation, whereas in the control group without grafting all were dead 7 days after irradiation. Bone marrow of recipients displayed karyotype of donor origin (XX). In group II bone marrow of transplanted limb was repopulated with recipient cells after 4 weeks (karyotype XY). In the group III chimeras formation with 65-95 of recipient cells was observed. Ten days after irradiation and transplantation the number of bone marrow cells in irradiated limb did not differ from control values and histology of the thymus, spleen and lymph nodes revealed only slight depopulation.
In the group of irradiated rats without transplantation 25 survived 10 days, while only few cells were present in bone marrow. Their lymphatic organs were depopulated.
The rejection pictures were evaluated in the rat skin, muscles, nerves, vessels, bone and bone marrow of the hind limb allograft. BN (RT1S) rats served as donors and Lew (RT1S) rats as recipients. On the day 1 skin in allografts

remained unchanged although thickening of walls of small vessels, partial disappearance of sarcolemmal nuclei and overpopulation of bone marrow with multiple megakaryocytes were observed. On the day 3rd oedema of skin, degeneration of epidermis, separation of sarcoplasm from sarcolemma and multiple magakaryocytes in bone marrow were noted. On the day 5 cellular infiltrates in the skin and muscles and, around nerves as well as disappearance of osteocytes were seen. No further changes in bone marrow were recorded. On the day 8 necrotic changes in the skin and muscles, partly in the central parts of compact bone layers, thrombosis of vessels and profuse infiltrates around nerves were observed. On the day 14th most parts of the skin, muscles and bone were necrotic. Rarefaction of bone marrow with partial replacement with fat cells was also seen. The above results suggest that skin and muscles are the most sensitive to rejection in limb transplants whereas the bone marrow remains relatively resistant.

The effect of immunological enhancement, cyclosporin A (CyA) and donor blood transfusion (DST) on prolongation of survival time of i.v. infused allogeneic lymphocytes and heart grafts was examined in rats. The following protocol of enhancement was applied: 1.5 x 10 AUG splenocytes i.v. on the day -1 and 1 ml antiserum WIS anti-AUG splenocytes i.v. on the day -10 were injected to donor (AUG) rats.

In CyA group AUG rats were treated daily with 5 mg/kg CyA whereas in DST group animals received 1 ml of blood on the day -7. Survival time of heart allografts was 40 days in comparison with 7 days in control untreated group, while transplanted splenocytes were eliminated immediately. These findings suggest that immunological enhancement, DST or CyA treatment, protects organ allograft while it does not evoke tolerance to donor transplantation antigens. Distribution of allogeneic graft was studied. Male AUG or WAG rats were injected with ^{51}Cr-labelled AUG splenocytes and ^{125}I-labelled globulin fraction of WAG anti-AUG lymphocyte or normal WAG serum. Antibodies against splenocytes were only a small part of injected globullins. Despite this, binding of antibodies to splenocytes enhanced their destruction. This effect was most pronounced when splenocytes were preincubated with antibodies before injection.

Mechanisms of capillary transport of immune proteins to tissues and lymph

An influence of intraarterial infusion of adrenaline (A), noradrenaline (NA) and histamine (H) on transcapillary transport was examined in dogs. No changes in total protein, IgG and IgM transport were observed after A and NA treatment. Histamine caused an increase of protein transport by approx.

2.5 times of IgG-11 times and IgM-9 times. Leucocyte transport was only slightly decreased after A and NA treatment, while H caused a drop of output by 16-times. Extravasation of erytrocytes was not changed in A and NA groups whereas it was increased by 5.6-times after H infusion. In A-treated dogs a correlation between lymph flow and leucocyte and erytrocyte output was ascertained, while in NA group lymph flow correlated only with the erytrocyte output. In H-treated dogs a correlation between lymph flow and protein, erytrocyte and leucocyte transport was noted. These observations indicate that A and NA do not influence transport of leucocytes from capillaries to the interstitium and lymph, although receptors for these compounds are present on both endothelial cells and leucocytes.

Peripheral neuroregulation of the circulating lymphocytes distribution was investigated. It is known that thermal shock causes changes in the whole body distribution of recirculating lymphocytes. This phenomenon is an integral part of the immune response to trauma. An increased body temperature (41°C) during 8 hours of the whole body hyperthermia correlated with hypercorticosteronemia and hypoadrenalinemia, causing an inrease of lymphocyte homing to bone marrow and a decrease of homing to lymph nodes and spleen. Adrenalectomy abolished this effect. Dexametasone treatment enhanced homing to bone marrow, despite of endogenous corticosterone release blocking. Chemical sympatectomy with 6-hydroxydopamine and labetalol (α- and β-blocker) did not influence the lymphocyte homing. These results indicate that a decrease of homing receptor expression due to steroids, but not blocking of receptors or sympatectomy of lymphatic organs, are responsible for the changes of lymphocyte redistribution during thermal shock.

The cytokine activity of lymph was examined in human subjects. The IL1 activity as well as IL1 inhibitors were detected in human peripheral lymph. The molecular weight of active fractions was:

a) for IL1 >70kD, 13-16kD and 5-5,5kD, and

b) for IL1 inhibitors >70kD, 22-30kD and 5.5-8kD.

Both forms of IL1 (α and β) were present in the lymph.

Lymph and the fraction containing highest IL1 concentration, inhibited proliferation of the mouse tumor fibroblast cell line L929. The data suggest that lymph IL1 may play a role in controlling the tumors growth.

Presence of interleukin 6 in the human lymph was found, using the biological test with hybridoma B6 cells. Its activity was observed in fractions with molecular weight 49, 24 and 22 kD. both interleukins were produced locally, since their concentrations in lymph were much higher than in blood.

See the List of Publications:

A) 29, 36, 66, 74, 75, 76, 77, 80, 102, 106.

B) 15, 32, 33, 71, 74, 75, 83, 84, 92, 99, 100, 101, 102, 103, 104, 108, 120, 121, 130, 131, 155.

Neuromuscular Unit
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Head: Prof. Irena Hausmanowa-Petrusewicz

Duchenne dystrophy

1) Investigations of DNA samples were carried out using the deletion and restriction fragment length polymorphions (RFLP). Out of 60 DNA samples taken from Duchenne or Becker patients in 24 deletions were found. The samples from the mothers of affected boys were also checked with intragenic probs in order to find out heterozygotes. Thirty eight of them were proved to be heterozygous for one, two or more probes using DNA and/or polymorphic probes. Forty eight families were identified in which prenatal diagnosis could be performed if required.

2) Fluorescent probe analysis of muscle plasme membranes and erythrocyte ghosts was done in 10 patients with Duchenne dystrophy, 10 healthy controls and 5 cases of other neuromuscular diseases. Results of these studies indicate that in Duchenne's dystrophy there are changes in the apolar-polar interface of the membranes present.

Spinal muscular atrophy (SMA)

1) The rational for classification of proximal childhood SMA has been discussed on the basis of 568 patients observed during almost 30 years.

2) The complex potentials were analyzed in 115 Emg records from the patients with acute (18 cases) and chronic (29 cases) forms of motor neuron disease. This kind of potentials are a sign of compensatory phenomenon mostly expressed in chronic SMA type II and III. The repetitive firing may occur both in chronic and acute forms being a sign of reintegration or desintegration of motor unit.

3) The most prominent features of motor control in patients suffering from proximal childhood SMA is coactivation of both ipsilateral and contralateral muscles during the motor performance which does not require participation of these muscles in control subjects. This phenomenon was examined in 39 childhood SMA cases and in 17 age-matched controls using polymyographic recording from 12 muscles. An interpretation of this phenomenon takes into account the possible compensatory meaning, there is however, an evidence indicating that the activity performed in this way is not efficient.

4) In experimental work on rats the transplantation of embrionic motoneurons into anterior horn of adult animals was performed. The transplantated motoneurons were found to be able to reinervate the denervated skeletal muscle and to induce a differentation of muscle fibers into different types.

Polyneuropathy

1) The case of pure motor neuropathy with multifocal block of conduction and immunological abnormalities was described. The immunosupressive treatment was succesful. The possible immunological differences between myelin of motor and sensory fibers have been discussed.

2) Statisticall significant differences in analysed EMG-parametres between HMSN II versus HMSN I and the control group were found. In HMSN I, EMG-changes are rare and not marked. Probably they are connected with secondary axonal lesions.

3) The occurrence of Guillain-Barre syndrome with axonal nerve abnormalities was demonstrated.

Other activities of the Unit involved

1) Reaching an experiance in steroid treatment of 260 myasthenic patients.

2) An observation that in case of severe neonatal nemaline myopathy the signs of immaturation of motoneurons occur.

3) Finding that in rats the apoptosis results in a characteristic death of immature muscle fiber.

4) Showing that within spinal cord there are tracts undergoing myelination of astroglial cell immunoreactivity to S-100 and SFAP. Immunoreactivity to S-100 was found to be more distinct in astrocytic perikarya; whilst astrocytic processes were clearly visible in SFAP reaction.

See the List of Publications:
A) 4, 5, 6, 7, 9, 22, 23, 24, 25, 26, 33, 39, 40, 41, 42, 43, 50, 51, 94, 98, 99, 101, 105, 107.
B) 3, 4, 6, 18, 19, 20, 24, 25, 26, 27, 28, 29, 39, 40, 41, 42, 43, 44, 45, 46, 47, 57, 58, 97, 98, 112, 113, 116, 117, 126, 127, 128, 129, 137, 138, 139.

RESEARCH REPORT

OTHER RESEARCH WORKS

Mental Health Department
12 Żeromskiego Str. 90-711 Łódź
Telephone: 33 64 57

Head: Assoc. prof. Zygfryd Juczyński

The evaluation of some causes of children and adolescents social maladjustment

Two main sources of maladjustment syndrome were accepted hypothetically. They are connected with individual predispositions and social influences.
The examined children and adolescents (aged 6-12) represented several forms and levels of maladjustment. The maladjustment of the examined children and adolescents were found to be mainly related to the lowered efficiency of adjustment, in approx. 40% of cases, resulted from several abnormalities in the perinatal period and brain disfunction in the early childhood. Environmental factors, unproper parents' attitudes and disturbed intra-family relations intensify and consolidate the process of social maladjustment. A connection between unfavourable biological inheritance factors in the infantile development with pathogenic effects of family environment leads directly to a child's social maladjustment.

An influence of motivation function of personality and its psychological conditioning in the course of cancer treatment

Patients (180) with: breast cancer, colorectal cancer and cervical cancer were examined. The course of treatment was found to be essentially connected with the attitude to the value system, especially to the self-concept. The attitude towards one's own illness is related to the need of social approval: the higher the social approval - the lower level of anxiety. The achieved results make it possible to organize the specific therapeutical actions, positively influencing the treatment outcomes.

The problem of life stabilization of drug addicts

Among the group of 107 drug addicts 97 cases were analyzed after 12 years; 70 were still addicted to drugs and 16 died. Only 14 refrained from taking drugs for two years or more.
Four primary and four secondary factors differentiate the abstinent group

from the group still taking drugs. Abstinence retainment has been found to be supported by: the limited time of systematic drug taking; engagement in housework and family duties; full-time job; achievement of higher level of education.
In the process of giving up this habit, social factors play the essential role; in the case of continuation of drug use - personal factors are the most important.

See the List of Publications:
A) 100.
B) 51, 52, 53, 62, 118, 119, 140.

The Library
75 Rolna Str. 02-813 Warsaw
Telephone: 43 34 94
Head: Krystyna Marczakowska

The library 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) - 17411
periodicals, newspapers (number of titles) - 465
unpublished documents (dissertations, research reports - SYNABA, in hard copies) - 241
microfiches - 5631

Reference aids:
catalogues - alphabetical: books, periodicals and microfiches,
- subject: books
main card-files - bibliographical list of papers published by scientists of the Medical Research Centre Polish Academy of Sciences from 1967.

Number of inquiries and services per year:
circulation of documents (original or copies):
reading room and library loan - 11.389
interlibrary loan - 1.801
direct reference services (in person, by telephone) - 520
circulated news current books and periodicals for the Departments users - 4.238
reprographic services: xerocopies - 4.250
systems of the user-oriented information services:
current and retrospective dissemination information - 23
MEDLINE - 17
SYNABA - 58
scientists citation reports - 1.650 (1984-88)

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
7/11 Wiktorska Str. 02-287 Warsaw
Telephone: 48 22 62

Head: Andrzej Lasek

MEDIPAN Pilot Plant is a producer of a special equipment for the Institute of Experimental and Clinical Medicine (MRC) of the Polish Academy of Sciences as well as the medical equipment for other medical Service units.
Infusion pumps represent the basic assortment of the Plant produced for Medical Service needs.
Additionally the Plant manufactures cytologic centrifuges and a device for exercise testing consisting of a physiotest, bicycle ergometer as well as a printer for results recording.
MEDIPAN infusion pumps can be classified into two basic functional groups.
A Syringe Pumps Models 610 AS and 610 BS as well as microprocessor-controlled Model 611 Syringe Pump belong to the first category of instruments.
The models mentioned above are designed for a long lasting intravenous injections of small quantities but highly concentrated drugs.
Microprocessor-controlled Model 611 Pump, worked out in the year 1989 and put into a serial production in 1990, is the newest one among infusion syringe pumps manufactured by MEDIPAN.
It collaborates with a 50 ml syringe, ensures a microprocessor-controlled inspection of performing elements, has a numerical indication of a current working parameters such as a dosed volume, the flow rate and a dosing time.
The pump represents a modern construction competitive with similar ones produced in highly developed western countries.
The second category of pumps consists of peristaltic pumps designed for intravenous drips. Manufactured in 4 models:
601 SP, 602 SP, 605 SP and 6050 representatives of this group are characterized by modern construction, functionality and ergonomy of manipulating elements.
Each model of a pump differs from the others in a range of functions that can be performed. Model 601 SP enables setting up a flow rate, dosing volume, indication of a currently dosed volume as well as legible signalization of alarm states. The model 602 SP represents a simplest pump, which enables setting only a flow rate valume.
In 1990 some modernization of the pumps was introduced and a numerical indicator of a dosed volume was additionally built in.The most functionally developed Model 605 SP gives the possibility of programming a flow rate in a few time periods, has a microprocessor built in to indicate and inspect all

parameters on the 32-position alphanumerical display.
The model 6050, construction and prototypes of which were worked out in 1990, represents the newest microprocessor-controlled infusion drip pump. The pump is a combination of two independently working systems, which enable simultaneous injection of two different medicines.
Infusion pumps described above have got several awards both in Poland and abroad during International Fairs. Some of them are the Gold Medals of Leipzig and Plovdiv Fairs.
Recently they received the Gold Esculape at the International Medical Fair SALMED-90.

INTERNATIONAL COOPERATION

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van Heerden P.D.R	Medical Research Council, Tygerberg, Republic of South Africa

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	University of Munich, Germany
	Thanjavur Medical College, Thanjavur, India
Płachta J.	IInd Department of Dermatology, University of Vienna, Austria

PARTICIPATIONS IN INTERNATIONAL MEETINGS

April

4. Rostocker Symposium "Aktuelle Psychiatrie und Neurologie des Kindes- und Jugendalters", Rostock, Germany, April 9-12
Z. Rydzyński

35. Jahrestagung der Deutschen Gesellschaft für Neuropathologie und Neuroanatomie e V., Munich, Germany, April 25-28
S. Krajewski

May

25th Congress of the European Society for Surgical Research, Berlin, Germany, May 6-9
H. Gałkowska, W. Olszewski, J. Płachta, D. Sadowska-Szablisty

Tagung zum Thema "Lebensqualität in der Onkologie" der Chirurgische Klinik Psychosoziale Nachsorgeeinrichtungen, Heidelberg, Germany, May 10-12
R. Rożeńska

Third International Symposium „Functional Neurosurgery", Tbilisi, USSR, May 21-25
E. Mempel

1st International Congress of Neuroimmunomodulation, Florence, Italy, May 23-26
M. Krynicki

Danube Symposia of Neurological Sciences - Curatorium Meeting'90, Budapest, Hungary, May 25-27
M.J. Mossakowski

May/June

7th International Conference on Prostaglandins and Related Compounds, Florence, Italy, May 28-June 1
R. Pluta

June

Meeting on "New Frontiers of Exercise: From Scientific Research To Application", Padua, Italy, June 27-30
K. Nazar

11th European Section Meeting International Society for Heart Research, Glasgow, U.K., June 27-30
K. Cedro-Ceremużyńska

Drug Treatment of Stroke and Ischemia Brain - Satellite Symposium of the 11th International Congress of Pharmacology, Scheveningen, Netherlands, June 28-30
J. Łazarewicz, M.J. Mossakowski

July

European Conference on Parkinson's Disease and Extrapyramidal Disorders, Rome, Italy, July 10-14
I. Hausmanowa-Petrusewicz

Second World Week of Professional Updating in Surgery and in Surgical and Oncological Disciplines of the University of Milano, Milan, Italy, July 15-21
W. Olszewski

8th Symposium of the European Society of Neurochemistry, Leipzig, Germany, July 23-28
J. Albrecht, K. Domańska-Janik, W. Hilgier, J. Łazarewicz, M. Puka, E. Salińska, M. Samochocki, M. Śmiałek, J. Waśkiewicz,

August

13th International Congress of the Transplantation Society, San Francisco, USA, August 19-24
B. Łukomska, W. Olszewski

20th Meeting of the Federation of European Biochemical Societies, Budapest, Hungary, August 19-25
M. Samochocki

September

11th International Congress of Neuropathology, Kyoto, Japan, September 2-8
M. Dąmbska, M.J. Mossakowski

13th Annual Meeting of the Europaean Neuroscience Association, Stockholm, Sweden, September 8-12
W. Janczewski

Joint Meeting SEP-SEPCR, London, U.K., September 9-14
M. Szereda-Przestaszewska

5th European Congress of Clinical Neurophysiology, Paris, France, September 9-18
E. Mempel

Meeting of the European Federation of Immunological Societies, Edinburg, U.K., September 10-12
H. Gałkowska, U. Kubicka, D. Sadowska-Szablisty

Satellite International Symposium on Development and Involution of Neurones, Tokyo, Japan, September 11-12
M.J. Mossakowski

12th Congress of the European Society of Cardiology, Stockholm, Sweden, September 16-20
K. Cedro-Ceremużyńska

7th International Congress on Neuromuscular Diseases, Munich, Germany, September 16-22
B. Emeryk-Szajewska

International Congress of Neurotoxicology and Occupational Neurology, Prague, Czechoslovakia, September 24-29
U. Rafałowska, M. Śmiałek

September/October

Sales/Marketing Meeting of Dakopatts, Copenhagen, Denmark, September 30 - October 4
A. Ziółkowska

October

23rd Danube Symposium En Erwin-Riesch Symposium for Neurological Sciences, Berlin, Germany, October 10-13
M. Dąmbska, B. Gajkowska, H. Kroh, I. Kuchna, M. Laure-Kamionowska, D. Maślińska, G. Szumańska, A. Taraszewska, H. Weinrauder

Intrakranieller Druck, Hirnödem und Hirndurchblutung der Deutschen Gesellschaft für Neurochirurgie, Bonn, Germany, October 25-27
Z. Czernicki

November

5th European-American Symposium on Venous Diseases, Vienna, Austria, November 7-10
B. Łukomska

2nd Interdisciplinary Symposium Peritoneum Peritoneal Access, Vienna, Austria, November 13-16
U. Kubicka

December

International Symposium of Sport Medicine, Berlin, Germany, December 5-7
K. Nazar

Conference of French Society of Neuropathology, Paris, France, December 7-8
M. Dąmbska

SCIENTIFIC DEGREES

DOCTOR'S DEGREES

Gerard Cybulski

Analysis of hemodynamic response to active orthostatic load in humans using impedance cardiography: influence of age and physical training

(Department of Applied Physiology)

Liu Ningfei

The influence of local hyperthermia on the lymphedematous skin of lower limbs

(Department for Surgical Research and Transplantation)

Katarzyna Sieradzan

Transplantation of embrionic motoneurons into spinal cord of adult rat

(Neuromuscular Unit)

Jolanta Waśkiewicz

Metabolism and function of neuronal histamine under normal, hypoxic and hyperoxic conditions

(Department of Neurochemistry)

HABILITATIONS

Leszek Budohoski

Physioiogical and pharmacological factors modifying sensitivity of skeletal muscles to insulin

(Department of Applied Physiology)

Jerzy Jurkiewicz

Usefulness of estimation of volumes-pressures responses and visuals evoked potentials for calculation of intracranial volumes reserve in the period of compensation

(Department of Neurosurgery)

Barbara Łukomska

Studies on function and origin of hepatic sinusoidal cytotoxic cells

(Department for Surgical Research and Transplantation)

Marek Radomski

Endothelium - derived relaxing factor in the control of platelet activation. Interaction with prostacyclin

(Cardiovascular Laboratory)

SCIENTIFIC MEETINGS ORGANIZED BY THE MEDICAL RESEARCH CENTRE

Course of techniques of monoclonal antibody staining, Warsaw, Poland, February 1-2

18th course of the basic microsurgical techniques, Warsaw, Poland, February 5-7

Practical course of immunoenzymatic techniques of antigen staining, Warsaw, Poland, June 5-6

19th course of the basic microsurgical techniques, Warsaw, Poland, July 18-20

1st Symposium on Contemporary Surgery of Japan - Polish Society for Exchange in Surgery, Warsaw, Poland, July 22-23

2nd International Symposium on Intracranial Hypertension and Cerebral Ischemia in Clinical Practice, Warsaw, Poland, October 11-12

Polish-Finnish Symposium "Electromyographic (EMG) activity and thermoregulation during physical exercise", Jelenia Góra, Poland, October 12-13

20th course of the basic microsurgical techniques, Warsaw, Poland December 19-20

LIST OF PUBLICATIONS

A) Original works

1. Albrecht J., Hilgier W., Rafałowska U.: Activation of arginine metabolism to glutamate in rat brain synaptosomes in thioacetamide-induced hepatic encephalopathy: An adaptive response? *J. Neurosci. Res.* 1990, 25, 125-130.

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14. Chwalbińska-Moneta J.: Lactate accumulation threshold in skeletal muscles and blood during incremental exercise. *Sport Wyczynowy*, 1990, 5-6, 51-60 (in Polish).

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