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R E S E A R C H R E P O R T

STUDIES ON THE FUNCTION OF THE NERVOUS SYSTEM AND ON MECHANISM CONTROLLING BASIS FUNCTIONS OF THE ORGANISM

Department of Neurophysiology
Head: Prof. Witold Karczewski

FUNCTIONAL ORGANIZATION OF RESPIRATORY NEURONAL NETWORK - - MECHANISMS AND SOURCES OF THE RESPIRATORY DRIVE

The assumption that each half of the "split-respiratory centre" does independently respond to lateralized stimuli, has been fully confirmed in rabbits. On the other hand, in normocapnic, split-medulla cats respiratory activities were abolished both in the medullary neurones and in the phrenic nerves. Hypercapnia restored rhythmic firing in respiratory neurones and motoneurones, thus suggesting that a mid-line separation of both halves of the medulla affects the respiratory rhythmogenesis by increasing the threshold for rhythmic firing. A more rostral extention of the mid-line section irreversibly abolished all respiratory activities both in normo- and hypercapnic cats.

It is concluded that there are qualitative species differences between rabbits and monkeys on one hand, and cats on the other; in the former species two, relatively independent networks of respiratory neurones with predominantly ipsilateral connections with phrenic motoneurones were demonstrated, whereas in the latter the role played by transverse connections in the medulla in the genesis of respiratory rhythm was evident.

New data were obtained on the effects of hypoxia, hyperoxia and hypercapnia on laryngeal resistance before and after chemodeafferentation.

Mechanisms lowering the intracranial pressure during controlled hypotension in neurosurgical patients were studied. The results obtained strongly suggest a contribution of arteriovenous shunting as an important factor.

It has been shown that hypothermia increases the CO_2-response threshold in rabbits. It has been also demonstrated that there is a direct influence of temperature on the respiratory pattern generator.

See the list of publications:
4, 7, 8, 28, 34, 37, 49, 74, 75, 76, 77, 78, 79, 85, 88, 92

Department of Applied Physiology
Head: Prof. Stanisław Kozłowski

MECHANISMS CONTROLLING ENERGY METABOLISM AND HEMODYNAMIC ADAPTATION TO PHYSICAL WORK UNDER PHYSIOLOGICAL CONDITIONS AND IN SOME CIRCULATORY AND METABOLIC DISORDERS

In the studies concerning possible factors limiting working ability the effect of exercise-induced hyperthermia on endurance time was evaluated in dogs. It was found that preventing of hyperthermia by external cooling considerably prolonged time of exercise until exhaustion. This was accompanied by much lower increases in rectal and muscle temperatures and slightly lower enhancement of brain temperature in comparison with those in control dogs. It was also found that during the exercise with external cooling blood lactate concentration reached much lower values, and the muscle contents of high energy phosphates, glycogen and glycolitic intermediates as well as muscle lactate differed from those measured under control conditions.

Some of the above changes - especially the lower muscle lactate are relevent to the prolongation of exercise. It was concluded that exercise-induced hyperthermia profoundly affects muscle metabolism, thus contributing to fatigue.

In further studies on exercise hyperthermia it was demonstrated that the progressive enhancement of body temperature during prolonged intermittent exercise is, at least partly, related to the increasing activity of the sympathetic nervous system and calorigenic effect of catecholamines.

Continuing the investigations on neural and hormonal

responses to physical exercise changes in the plasma catecholamine and growth hormone concentrations were compared in human subjects exercising with different muscle groups at equivalent O_2 uptake. The results obtained indicate that the muscle metabolic receptors are involved both in activation of the sympathetic nervous system and in stimulation of growth hormone secretion.

Studies were performed on the usefulness of "the walking test" for an assessment of working acapacity in human subjects of different age groups, and working capacity as well as in patients with kidney indufficiency being chronically dialyzed.

Measurements of "anaerobic threshold" were used to evaluate effects of physical training, in different kinds of sports (endurance and high speed), on working capacity.

In the studies concerning effects of dietary modifications on exercise metabolism the fat-rich single meal was found to promote lipid utilization during subsequent exercise.

Continuing the investigations on the metabolic adaptation to fasting an effect of prolonged propranolol treatment as well as acute administration of this beta-blocking agent on lipid mobilization was evaluated during 3-day fasting in dogs. The data obtained indicate that catecholamines play a role in lipid mobilization during starvation, however, their action can be substituted by other hormones.

In further studies on exercise tolerance in coronary patients the effects of beta-blockers and beta-methyl digoxin (drugs commonly used in this disease) on hemodynamic as well as metabolic responses to exercise were investigated. Relationships between the pattern of cardio-vascular and ecg responses to graded physical exercise in coronary patients and daily doses, period of treatment as well as blood propranolol concentration were estimated.

MECHANISMS OF THERMOREGULATION UNDER DIFFERENT CONDITIONS OF EXTERNAL AND INTERNAL ENVIRONMENT

An influence of changes in water balance on thermoregulation during physical exercise was studied in healthy human subjects. An increased volume of body fluids (hyperhydration) reduced the exercise-induced increases in body temperatures. Hyperhydration increased water content in the skin, thus facilitating evaporative heat elimination by sweating. Similar cardiac output was attained at higher stroke volume and lower heart rate.

Studies on heat exchange during surgery were continued. Changes in deep body and skin temperatures as well as in heat production and elimination (by different means) were followed during long lasting operations on legs, performed under epidural analgaesia. The measurements were continued during the post-operative period. Several variables of thermal balance were also measured in the patients with thyroid goiter undergoing an operation with moderate haemodilution. Heat deficit deepened with duration of surgery, and fluid infusions significantly decreased deep body temperature of the patients.

CONTROL OF VOLUME AND COMPOSITION OF THE EXTRACELLULAR FLUID IN VARIABLE INTERNAL AND EXTERNAL ENVIRONMENT

A further progress was made in the development and evaluation of the new method for continuous measurements of the cortico-papillary tissue electrolyte gradient of the in situ kidney of experimental animals. In this original method total electrolyte concentration of the tissue is estimated from its electrical impedance measured by means of platinum-iridium electrodes reaching different zones of the kidney. It was established that sensitivity of the method can be greatly augmented by raising the measuring AC frequency used from 400 to 3500 Hz. A special technique was developed for tissue calibration of measuring electrodes, using tissue slices previosuly equilibrated with increasing concentrations of NaCl solution.

The preliminary results obtained with the method showed that: /1/ an i.v. injection of furosemide, a potent blocker of NaCl reabsorption from the ascending limb of Henle's loop produced a significant increase in tissue impedance of the renal medulla, probably depending on reduced delivery of salt from the tubular lumen to the medullary interstitium; /2/ hypertonic mannitol raised medullary tissue impedance, presumably by both reducing tubular NaCl reabsorption and augmenting its wash-out from the interstitium by increased medullary blood flow; /3/ the increase in tissue impedance (a decrease in the cortico-papillary electrolyte gradient) dependent on the action of furosemide or mannitol could be corrected by an infusion of hypertonic saline, apparently due to an increase in NaCl delivery to and reabsorption from the tubules.

See the list of publications:
5, 6, 25, 26, 27, 29, 30, 38, 40, 50, 52, 64, 89, 98, 99, 101, 105, 111, 112, 113

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Head: Assoc. prof. Krystyna Herbaczyńska-Cedro

MECHANISM REGULATING FUNCTION OF CARDIOVASCULAR SYSTEM UNDER SOME PATHOLOGICAL CONDITIONS

Study on the role of adrenergic nervous system in the development of myocardial hypertrophy in the rats subjected to aortic constriction revealed that adrenaline and noradrenaline contents in the hypertrophic myocardium (4th day of stenosis) decreased significantly (198 $\pm$ 39 vs 934 $\pm$ 92 ng/g wet tissue, n = 9, p 0.001), whereas dopamine undetectable in controls, increased in hypertrophic hearts by 55 $\pm$ 17 ng/g wet tissue. Urinary excretion of dopamine was increasing progressively throughout 1-4 days of stenosis. These findings suggest a role of dopamine in the development of myocardial hypertrophy in this animal model.

Effect of i.v. inosine infusion on the left ventricular performance (LV) and myocardial O_2 uptake (MVO_2) was studied in dogs under beta blockade. Dp/dt_{max} increased markedly cardiac output rose by 11.7 ± 8.0%) while aortic pressure was not affected and LV end-diastolic pressure decreased. Coronary blood flow increased considerably whilst MVO_2 significantly decreased. The ratio of MVO_2 to mean LV pressure was significantly reduced indicating more efficient conversion of chemical to mechanical energy. The results demonstrated that inosine exerts positive inotropic effect while MVO_2 is decreased.

See the list of publications:
9, 10, 11, 16

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

CLINICAL AND EXPERIMENTAL STUDIES ON NEUROREGULATION OF PERIPHERAL CIRCULATION

Investigations carried out on the animal model during the past few years have shown that both direct sympathetic nerve stimulation and transcutaneous stimulation cause a realase of prostacycline - like substances into the blood stream. The data obtained in animals were the starting point of the investigations on the physiological mechanism of the clinically beneficial effects of electric transcutaneous stimulation currently used in the patients with peripheral circulation disorders.

The physiological effects of transcutaneous stimulation in the patients were assessed on the basis of:

1) platelet aggregation changes in the case of Raynaud and Bürger diseases,
2) thermal changes in the limbs in the above mentioned diseases, determined on the basis of thermo-graphical estimation.

Ad. 1 Platelet aggregation was measured with the Born method, using ADP as the aggregating agent. In blood samples taken before stimulation the platelets from the affected limb were

found to be more sensitive to the aggregating substance than those from the unaffected limb. This observation sugests an existence of local disturbances in the mechanisms regulating platelet aggregation in the affected limbs. In 60% of the patients examined electrical transcutaneous stimulation resulted in a two to threefold decrease in the sensitivity of the platelets to the aggregating substance.

Ad. 2 Thermografical investigations were carried out using an "Aga" unit with the possibility of detecting thermal changes to a depth of 5 cm from the skin surface. The measurements demonstrated a marked increase in the temperature of the stimulated limbs. In Raynauds disease the greatest increase in the limb temperature after 20-30 min of transcutaneous stimulation was on the average $3^{\circ}C$, whereas in the case of Bürger disease the increase after 30-40 min of stimulation was on the average $2^{\circ}C$.

In the patients with Raynauds disease the effect of elevated temperature continued for 24-48 hours after the stimulation, whereas in the case of Bürger disease the period was shortened to 4-8 hours.

The results of the aggregation tests and termography indicate a definitely greater effectiveness of electrical transcutaneous stimulation in the patients with Raynauds than with Bürger disease.

The applied methods were found to be useful in evaluation of the effects of electrical transcutaneous stimulation in the treatment of circulation disorders. They allowed to assess: 1) peripheral blood circulation (thermographical method), 2) effectiveness of the electrostimulation, and 3) to select individually the best stimulation parameters with regards to the frequency and duration of the stimulation (thermography and platelet aggregation methods).

On the basis of the obtained results the transcutaneous electro-stimulation was confirmed to be helpful in the treatment of diseases connected with peripheral circulation disorders and worth of further investigations on further mechanisms of its effects.

STUDIES ON THE STRUCTURE AND BIOLOGICAL PROPERTIES OF THE NERVOUS TISSUE

Department of Neuropathology
Head: Prof. M.J. Mossakowski

PATHOGENETIC MECHANISM OF DISTURBANCES OF THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM AND MUSCLE EFFECTOR INDUCED BY ENDO- AND EXOGENEOUS PATHOGENIC FACTORS

Investigations on the p a t h o m e c h a n i s m o f h e p a t o g e n i c e n c e p h a l o p a t h y included the morphological evaluation of the CNS in acute viral hepatitis patients who died in hepatic coma. The studies revealed presence of morphological manifestations of hepatogenic encephalopathy in conjunction with the features of acute toxic encephalopathy. The glial changes, typical of hepatogenic encephalopathy, showed a positive correlation with blood ammonia level.

Studies on ammonia metabolism in brain under conditions of thioacetamide-induced hepatogenic encephalopathy have demonstrated that the ammonia detoxification system operates at full capacity. The pathomorphological changes have been tentatively ascribed to the action of α-ketoglutarmate - a neurotoxic metabolite of glutamine. The studies further revealed minor disturbances in the metabolism of γ-aminobutyric acid (GABA) - an inhibitory neurotransmitter synthetized from glutamate and thus a "byproduct" of ammonia detoxification. Studies on organotypic cultures of astrocytes in vitro provided evidence that the development of hepatic gliopathy, following intoxication with thioacetamide, is due rather to compounds released to serum in relation to liver lession than to thioacetamide itself.

Studies on c h r o n i c s e r u m d i s e a s e, which was considered as a model of kidney damage resulting in uremic syndrome, disclosed immunological complexes to be the factor impairing the cerebral blood vessels and leading in

consequence to brain edema. These changes appeared unrelated to the occurrence of uremia.

Investigations on the p a t h o g e n e s i s o f i s c h e m i c b r a i n damage revealed that an efficient arterial system of the base of cerebrum in the rat prevents cerebral ischemia following uni- or bilateral occlusion of carotid arteries, provided the above-threshold arterial blood pressure is maintained. Features of ischemia become apparent following complete occlusion of the spinobasal and arteriocervical systems. The maintainence of normal arterial blood pressure ensuring adequate blood supply to the spinal cord centres enables the animals to survive even under these conditions. Treatment with indomethacine - the cyclooxygenase and thus the prostaglandine synthesis inhibitor, prevents the microcirculatory disturbances of the brain in the postischemic period and the development of vasogenic brain edema, as well as the damage of nerve cells in the cortex and subcortical grey formations. The same treatment, however, remains without any effect on ischemia in the border zones of vascularization by internal carotid artery and the border area of the spinobasal and arteriocervical systems. Differences have been demonstrated in the vulnerability of the motor and sensory cortex of the rabbit brain to 30-minute complete ischemia. Transient oxygen insufficiency (anemic hypoxia) was shown to lead to changes in the intensity and localization of the adenylate cyclase in the elements of cerebrovascular junction, indicating the participation of the enzyme in the blood-brain barrier transport mechanism. Investigations of the pial vascular network in tissue culture in vitro revealed the occurrence of blood vessels fulfilling the morphological criteria of authentic brain capillaries.

Studies on the morphological maturation of pituicytes in the posterior lobe of hypophysis in vitro revealed that the cells belong to the class of fibrous astrocytes.

Investigations on m o d e l l i n g o f t h e p a t h o m o r p h o l o g y o f c h r o n i c c h o r e a with the use of kainic acid demonstrated that the neurotoxin affects selectively the postsynaptic part of the striatal

glutaminergic system, only under conditions of preserved synapse integrity. Fibrous glial reaction that was found to involve protoplasmic and fibrous astrocytes both in vivo and in vitro, is a primary process independent of the extent of neuronal damage.

Studies on the m a n g a n e s e e n c e p h a l o p a t h y demonstrated that the early stage of intoxication is accompanied by generalized vasogenic brain edema with damage of axons located in the white matter. In the later stage of intoxication features of cytotoxic edema predominated being manifested by spongy degeneration of the white matter with fibrous reaction of glia and selective impairment of substantia nigra. Ultrastructurally, the spongy degeneration of white matter was related to swelling and severe damage of axonal mitochondria. Manganese intoxication was also demonstrated to result in the increased GABA level in all cerebral structures, with no discernable changes in the dopaminergic system. The increased GABA content has been postulated to be confined to the glial compartment, which may be related to the enhanced glial reaction demonstrated with morphological methods. Studies in vitro have shown that $MnCl_2$ produces lesions in the glial population, axons, myelin and - selectively - small neurons of striatum. The involvement of myelin sheaths and oligodendroglia distinguishes the in vitro changes from those observed in vivo.

Investigations on the antigenic properties of the nervous tissue in pathological conditions have focused on the pathogenic effect of ethylnitrosourea on the glial tissue culture in vitro. The studies revealed morphological abnormalities of astrocytes and ependymal cells indicative of blastomatic changes, which proceed with the increased accumulation of the previously described glial antigen. Sera analysis in the patients with neurological syndroms demonstrated accumulation of antibodies against the nervous tissue. The affinity of the antibodies to the particular tissue elements of the central nervous system was different in various pathological processes.

See the list of publications:
41, 42, 43, 44, 58, 59, 60, 61, 81, 83, 84, 97, 114

Department of Neurochemistry
Head: Assoc. prof. Jerzy Łazarewicz

CHANGES IN THE CELL MEMBRANE INTEGRITY AND IN CHEMICAL NEUROTRANSMISSION AS PATHOGENIC FACTORS IN C.N.S.

Studies concerned mainly a relationship between physicochemical properties of synaptosomal membrane and metabolic as well as transport processes in isolated brain nerve endings under pathological conditions.

It was observed by Dr. Pylova, the visiting scientist from Moscow collaborating with Dr. Rafałowska and Dr. Łazarewicz, that ischemia influences the distribution of protein in brain subcellular fractions in a reversible manner, leading to the alteration of electrophoretic picture of soluble and membrane-bound proteins.

The studies by Dr. Zalewska and Dr. Łazarewicz on the rat cell-free system exhibited an inhibitory effect of calcium on protein biosynthesis as a consequence of calcium-magnesium competition. The collaboration studies of Dr. Łazarewicz, Dr. Kanje and Dr. Edström from Sweden performed on the frog sciatic nerve demonstrated the proteolytic activity of calcium dependent neutral protease towards high molecular weight proteins transported by rapid axonal transport.

Dr. Strosznajder collaborating with Dr. Sun and Dr. Horrocks (USA) observed that acute hypoxia and ischemia induced pronounce changes in the fatty acid metabolism of membrane phospholipids particularly arachidonic acid, precursor of prostaglandin biosynthesis.

These disturbances included:

1) a reduction of fatty acid acylation activity,
2) an inhibition of fatty acid incorporation into phospholipids,
3) specifically lower incorporation of arachidonic acid into phosphatidylinositol and its concomitantly higher incorporation into diglycerides,
4) an activation of acyl-CoA incorporation into phospholipid,
5) an inhibition of acyl-CoA hydrolase activity,

6) a stimulation of calcium-independent phosphatidyl-ethanolamine phospholipase A_2 activity.

Acyl-CoA hydrolase activity was inhibited by calcium ions, as a consequence of complex formation among acyl-CoA, Ca^{2+} and membrane phospholipids.

It was observed by Dr. Łazarewicz in cooperation with Dr. Sun (USA) that depolarization and calcium-dependent release of neurotransmitters is accompanied by the liberation of arachidonic acid from prelabeled synaptosomal phospholipids.

The common studies of Dr. Dąbrowiecki and Dr. Strosznajder with Dr. Porcellati (Italy) and Dr. Horrocks (USA) indicated that in the liberation of fatty acid in ischemic brain the reversibility of ethanolamine and choline phosphotranspherase may play an important role. The stimulation of phosphotransferases by intracerebral injection of CDP-choline has a preventive effects on membrane lipid disturbances induced by ischemia.
The study on ischemic gerbil brain synaptosomes indicated disturbances in energy and lipid metabolism and the inhibition of neurotransmitters uptake without changes in respiration and Ca^{2+} uptake (Dr. Dr. Domańska-Janik, Khachatrian, Łazarewicz, Noremberg, Strosznajder, Zalewska).
It was observed that hypoxia produced decrease in ganglioside content in brain synaptosomes and changes in their composition (Dr. Domańska-Janik).

Dr. Pastuszko in cooperation with Dr. Erecińska and Dr. Wilson (USA) carried out the study on neurotransmitter metabolism in brain synaptosomes.
In vitro studies have demonstrated that high affinity ^3H-GABA uptake into synaptosomes in 90% consisted of the net uptake and that both - the membrane potential and gradient of sodium ions serve as the energy source for this transport.
Anaerobic preincubation of synaptosomes causes an irreversible decrease in the rates of neurotransmitter accumulation. The inhibitory effect of anaerobiosis is enhanced by increased concentration of H^+.
The uptake of dopamine appeared to be the most susceptible to hypoxic conditions.

In vivo brain ischemia decreased the level of neurotransmitters, particularly the content of dopamine in the cortex, striatum and hypocampus and also the amount of dopaminergic receptors in striatum.
Lipid peroxidation has a stimulatory effect on the uptake of dopamine into striatum synaptosomes (Dr. Dr. Pastuszko, Gordon-Majszak, Dąbrowiecki).

See the list of publications:
2, 15, 20, 33, 62, 63, 71, 72, 73, 80, 110

Department of Neurosurgery
Head: Prof. Eugeniusz Mempel

BIOELECTRICAL ACTIVITY OF THE BRAIN AND THE MEMORY PROCESSES AFTER STEREOTACTIC LESIONS AND ELECTRICAL STIMULATION OF SELECTED SUBCORTICAL STRUCTURES

The following electrophysiological studies were performed:

1) the influence of cryosurgical thalamic lesions on somatosensory evoked potentials (SEP).

SEP were registrated in two groups of patients with extrapyramidal diseases: a. parkinsonian syndromes with VOp lesions and b. torticollis spasmodicus with VOa (VOi) lesions. Short latency components of SEP's were analysed. It was concluded that stereotactic VOa and VOp lesions reduced but not abolished the specific SEP. In the presence of oscillatory potentials before the surgery their disappearance was found to be correlated with clinical improvement.

2) Somatosensory thalamic evoked potentials (STEP's) after peripheral stimulation and SEP's after electrical stimulation of the thalamic nuclei VOa and VOp.

STEP's and SEP's were performed during thalamotomy in 10 patients with extrapiramidal disorders. On the thalamic level the short latency positive - negative potential had its maximal amplitude on one of the levels of the multilead electrode,

indicating an existance of exact somatotopy. SEP's registrated from the scalp during the stimulation of the thalamic nuclei had often a biphasic character and the stimulation of VOa and VOp resulted in potentials of similar configuration of the phase. The observed close somatotopy in the thalamic nuclei can be of a great value for the exact localization of stereotactic targets in humans.

ICONIC MEMORY OF EPILEPTIC PATIENTS AFTER PARTIAL AMYGDALOTOMY AND HIPOCAMPOTOMY

The visual memory of letter material was investigated using Sperling method (extended with stimulus applications to the left and right visual field) in experimental laboratory conditions. The investigations were performed in a group of 8 patients with deep damages of temporal structures. The control group consisted of 10 healthy subjects. In the patients disturbances of both the short-term memory stage and the sensory stage (an earlier stage of information processing) were proved. Sensory stage disturbances resulted in a reduction of the Sperling effect (decay superiority of a partial-report in comparison with the whole-report of the material) and the postcuing delay influence on the stability of the memory trace.
The lower level of performance was found in the patients when the material was exposed to the left visual field (being addressed mainly to the right hemisphere of the brain).

CLINICAL METHODS FOR THE EARLY DETECTION OF MALFUNCTIONS IN THE INTRACRANIAL PRESSURE - VOLUME RELATIONSHIPS IN PATIENTS WITH INTRACRANIAL PATHOLOGY

Following clinical verification a working version of the computerised infusion test (CIT) was implemented. Preliminary data were obtained by performing the CIT in patients with disturbances in the absorption of the cerebro-spinal fluid, with different types of pathology (hydrocephalus of various origin, severe head trauma, brain tumors and others). It was found,

that the informations obtained from the CIT are a great value in the diagnosis of hydrocephalus and determination of the type of ventricular shunt to be used. Significant disturbances in the absorption mechanism were also observed in the early period of head trauma with subarachnoid haemorrhages.

A clinical method of anaesthesia in neurosurgical patients presenting a high operative risk was elaborated and used. During surgery of 32 patients, apart from conventional NLA, Menbutal was given in continuous infusion until the appearence of isoelectric line in the eeg. As a result a considerable drop in the intracranial pressure (ICP) was obtained, bleeding was reduced and the surgical conditions were improved. There were no cases of postoperative brain oedema.

Similar results were obtained when the barbiturate was replaced by Etomidate infused during NLA anaesthesia. In 37 patients operated under NLA and Etomidate a significant reduction of ICP and operative bleeding was observed. A comparison of the two methods used showed that NLA + Etomidate had less depressive effect on the respiratory and circulatory systems.

Studies on the effect of increased ICP on the circulatory and respiratory systems showed that the increased ICP causes several cardiac disturbances, including ventricular fibrillation, and temporary ischaemia of the cardiac muscle similar to the symptoms of the coronary infarct.

SPEECH DISORDERS AND DISTURBANCES OF OTHER GNOSTIC FUNCTIONS IN FOCAL LESIONS OF THE BRAIN

Examinations of memory and intelect were performed in children with speech disorders.

The control group consisted of normal children, 5 children with motor aphasia and 5 children with problems of auditory system. Two kinds of tests: verbal and non-verbal were applied for memory examination. Intelect was examined using the Binet-Terman test. The results of both tests in the control group of children were within norms. The non-verbal tests were easier for children with aphasia than the verbal ones. The verbal tests were easier

for children with troubles in the auditory system than non-verbal tests.

See the list of publications:
95, 96

Laboratory of Developmental Neuropathology
Head: Prof. Maria Dąmbska

DEVELOPMENT OF THE NERVOUS SYSTEM UNDER CONDITIONS OF NORMAL AND DISTURBED STRUCTURAL MATURATION

The investigation on chronic intoxication of young animals with organophosphorus inhibitor of acetylcholinesterase-dichlorvis (DDVP) revealed that it induces a decrease of serotonin level in some brain structures. Serotonin is substantial for brain maturation since it takes part in the protein synthesis, neurogenesis and release of growth hormone. Therefore, serotonin metabolism following dichlorvos treatment became the main subject of this studies. In order to classify the effect of this compound on serotonin metabolism in brain the following determinations were carried out:

1) blood concentration of amino acid and nonestrified fatty acids,
2) level of total and free fraction of blood tryptophane,
3) tryptophane content in the brain,
4) activity of brain mitochondrial enzymes participating in serotonin metabolism,
5) turnover rate of serotonin in different brain regions.

It was previously stated that dichlorvis does not influence the blood brain barrier permeability for serotonin. It was found that this pesticide increases significantly the level of non-estrified fatty acids in plasma and leads to an increase in plasma free tryptophane. Concentration of the neutral amino acids, which competited with tryptophane (precursor of serotonin) for the brain barrier protein carrier was not changed by

DDVP intoxication. Significant increases of tryptophane level in all brain regions was found. The decreased activities of brain mitochondrial enzymes (monoamine oxidase A and tryptophane hydrolase) after dichlorvis exposure well explain the low level of serotonin in midbrain and pons. These results confirmed and explained the low turnover rate of serotonin in the examined brain regions. The disturbances in brain proteins and phospholipids found after dichlorvis treatment let us to suggest the following pathomechanism of the changes in serotonin metabolism. The inhibition of acetylcholinesterase by dichlorvos led to the increase in acetylcholine concentration. The high level of acetylcholine stimulated the synthesis of some phospholipids in brain and caused the imbalance in the protein phospholipids relation. Such changes in biological membranes may influence activity of mitochondrial enzymes. The low activity of tryptophane hydroxylase explained the low concentration of serotonin following dichlorvos intoxication and the low activity of monoamine oxidase A - the low turnover rate of serotonin in midbrain and pons - brain stem.

See the list of publications:
12, 13, 14, 35, 54, 55, 56, 57, 103, 104

Department of Comparative Neurology
Head: Assoc. prof. Irmina Zelman

EFFECT OF "pt" MUTATION ON VARIOUS LINKS OF CLOSED NEURONAL CIRCUITS

In further investigations on pt rabbits carried out for explaining the nature of myelin abnormality data were obtained that point out on defective myelination in this mutant.

Histological evaluation of myelin in symptomatic pt rabbits of the age ranging from 10 days to 6 months revealed the delayed, prolonged and incomplete myelination of all central white structures, whereas peripheral myelin seem to be structurally

unaffected. The varying intensity of the disturbances in myelin development corresponded to the severity of clinical symptoms, being the most pronounced in animals with the severe progressive course of the disease.

On the electron microscopic level the decreased number of myelinated axons was accompanied by structural abnormalities of myelin sheaths: decreased number of myelin lamellae and alterations in lamellar arrangement, which was due to the partly underdeveloped intraperiod lines, derrangement of dense lines and to the presence of fragments of oligodendroglial cells cytoplasm within myelin sheaths.

The defective myelination was associated with the increased and prolonged myelination gliosis. Oligodendrocytes did not appear strikingly abnormal, however, they showed ultrastructural features of immaturity.

The remarkable pathological finding, considered as a primary phenomenon, was the temporary accumulation of lipid droplets in the cytoplasm of hypertrophic fibrous astrocytes, selectively abundant in cerebellar white matter of severely affected pt rabbits.

The yield of myelin isolated from brains of 6-week old pt rabbits with progressive clinical course was only 10-15% of that from littermate controls. SDS-polyacrylamide gel electrophoresis demonstrated reduction of proteolipid protein, whereas intermediate protein and Wolfgram protein were present in a higher proportion.

The adult pt-rabbits with almost complete recovery after the acute clinical stage did not show any histologically distinct myelin abnormalities exhibiting only slight myelin pallor and less compacted fibre arrangement.

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

THE RESPONSE OF NERVOUS TISSUE TO HIGH AMBIENT TEMPERATURE

The studies were carried out to elaborate an experimental model and to perform morphological analysis of dynamics of changes in the central nervous system of the rabbit after three hours of heat exposure at ambient temperature of 38 - 39° C and a relative humidity of 50%. It was shown that overheating was accompanied by structural changes in the brain expressed by the features of progressive edema, generalized non-specific neuron degeneration, particularly noticeable in the formatio reticularis of the brain stem. These changes occured together with histochemical changes indicating activation of mitochondrial and lysosomal enzymes and Leloire's cycle. Electron microscopic studies revealed transitory damage of cerebral cortex cellular elements affecting both cytoplasmic and nuclear structures. Some changes indicating activation of the hypothalamo-neurohypophyseal neurosecretory system were also noted.

See the list of publications:
17, 18, 19, 22, 23, 24, 51, 102

STUDIES ON TRANSPLANTATION AND EXPERIMENTAL SURGERY

Department of Experimental Surgery
and Transplantation
Head: prof. Waldemar Olszewski

IMMUNOLOGICAL DIFFERENTIATION OF LIVING ORGANISMS

1. Lymphocyte recirculation in recipients of allogenic heart transplant under various immunosuppressive protocols

Recirculating long-lived lymphocytes play a dominant role in the process of rejection of allograft. While circulating in the blood compartment or migrating spontaneously through the lymphoid and non-lymphoid tissues they receive the primary information about the presence of foreign antigens. This information is then transferred to the nearest lymphoid tissue accumulation where a cooperation between various subsets of lymphoid and macrophage-like cells takes place and as a result specifically instructed cells are released to the circulation and recruited at the site of allograft. The kinetics of the circulating lymphocyte distribution should be different in allograft recipients as compared with normal subjects. It reflects the specific assignments of primed lymphocytes, as well as the intensity of immune reaction in lymphoid organs. The aim of the study was to investigate the distribution of recirculating lymphocytes in recipients of allogeneic heart allograft without immunosuppression, in immunologically enhanced animals and in animals treated with Cyclosporin A. In control animals with acutely rejecting allografts lymphocytes accumulated in the lymphoid tissues at a higher rate than in recipients of isografts. This process was most evident in the spleen. In rats with immunological enhancement in the course of treatment with Cyclosporin A lymphocytes had a tendency to accumulate in lymph nodes and Peyer's patches. In these groups the blood level of labelled lymphocytes remained high for a longer time than in the control animals.

Immediately after i.v. administration of antigen (day - 11) and alloserum (day - 10) accumulation of lymphocytes in lymphoid tissues became evidently higher than in normal rats or isograft recipients. The data indicate that the allogenic grafts affect the kinetics of lymphocyte recirculation. The altered lymphocyte distribution may be due to the increased activity of lymphoid tissues receptors, responsible for recruitment of lymphocytes and structural alterations of lymphocyte membranes causing changes in recognition of cells migrating through the spleen and lymph nodes. A different ratio of lymphocyte accumulation in the spleen and lymph nodes depending on the type of immunosuppression, supports this supposition.

2. Prolongation of heart allograft survival after pretreatment with splenocytes or lymph node lymphocytes and alloserum

Various populations of lymphocytes induce immunological enhancement in heart allograft recipients to different extents. In this study the blood platelets, erythrocytes, lymph node lymphocytes, thymocytes and splenocytes were tested for their enhancing properties in Wistar rats receiving heart transplants from August rats. The mean survival time in the rats pretreated with platelets and alloserum was 7.4 days, in the rats receiving erythrocytes - 9.8 days, those receiving thymocytes - 9.7 days. Pretreatment of the graft recipients with lymph node lymphocytes and alloserum prolonged graft survival to a mean of 34.8 days and pretreatment with splenocytes to a mean of 75.4 days. The immunological enhancement was antigen-specific. It seems that cells with a high density of Ia-surface antigen (monocytes, B-cells, dendritic cells) are more potent in inducing the immunological enhancement than cells which are Ia-negative (erythrocytes, platelets).

3. Cellular immune response in peripheral blood after surgical trauma

The influence of operative trauma on subpopulations of peripheral blood mononuclear cells (PBM), the responsiveness of PBM to PHA and ConA and the level of ConA - induced suppressor cell (ConA-SC) activity towards autologous responder cells (RC) were examined in patients with stage 0 uterine cancer after hysterectomy in the early postoperative period (0 - 7 days).

Changes in mononuclear cell populations were examined using monoclonal antibodies. There was an increase in the percentage of $OKM1^+$ cells (monocytes) by 12.4% and of large $OKIa^+$ cells (bearing Ia antigen on the surface) by 189.9% on the first postoperative day. At the same time the percentage of $OKT3^+$ cells (T-lymphocytes) was decreased by 17.4%, $OKT4^+$ cells (helper/inducer) by 27.9%, $OKT8^+$ cells (cytotoxic/suppressor) by 24.6% and small $OKIa1^+$ cells by 49.4%. The percentage of monocytes increased until day 3 (by 24.8%) and returned to normal by day 7, while the percentage of $OKIa1^+$ cells had already recovered by day 3. The percentage of T cells remained below the preoperative level throughout the observation period. However, the number of helper cells had increased significantly on day 5 while suppressor cells remained below the preoperative level during the entire observation period. The rising ratio of $OKT4^+/OKT8^+$ cells reflected the kinetics of recovery of helper over suppressor cell population.

The operation brought about a decrease (on the second postoperative day) in the responsiveness of PBM to various concentrations of PHA (4.5 - 90 µg/ml) by 19.2 - 28.8% and to ConA (1 - 5 µg/ml) by 31.2 - 41.8% with a concomitant decline in ConA-SC activity from 43.7% to 22.0% (PHA - 4.5 µg/ml) and from 19.8% to 5% (PHA - 18 µg/ml).
When the ConA-SC were tested against RC obtained from blood samples drawn prior to surgery and stored at - 196°C, an

increase in the postoperative SC activity from 41.6% to 52.2% was observed which might indicate a postoperative stimulation of CS. On the other hand, when ConA-SC, were isolated from PBM drawn before surgery and tested against RC obtained postoperatively, they displayed a decreasing suppressive activity from 27.2% to 2.7%. This might be due to the pre- and postoperative stimulation of RC.

Changes in CS population elucidated using monoclonal antibodies correlated well with changes in SC activity obtained by functional assay. The decrease in the responsiveness of lymphocytes to mitogens was most likely caused by changes in proportions of T cells and monocytes in peripheral blood and not by changes in the number and activity of suppressor cells.

IMMUNE PROTEIN TRANSPORT BLOOD-LYMPH

1. Kinetics of water mobilization from the interstitial space after administration of diuretics

This study was devoted to the problem of pharmacological dehydration of tissues around the surgical wound by measuring lymph outflow and concentration of lymph components. A hypertonic solution of mannitol and furosemide decreased the volume of the intravascular compartment but that of the interstitial space remained unchanged at the expense of cellular dehydration. The bulk of mobilized water originated most likely from the splanchnic area. In the injured edematous skin and subcutaneous tissue mannitol brought about partial dehydration but water content did not return to physiological levels. The lymph outflow from the injured tissues and lymph composition did not change. After treatment with furosemide, in spite of a negative total water balance, the hydration of injured tissues remained unchanged. These observations indicate that: a) the capillary transport of water and proteins as well as lymph outflow in the injured tissues are probably limited by the

physicochemical changes of the ground substance, b) treatment with diuretics has a limited effect on dehydration in areas with restricted lymph outflow.

2. Active transport of lymph in human lymphatics

The study was continuated on the spontaneous rhythmic contractility of human lymphatics generating forces necessary for lymph flow. A low-flow flowmeter was constructed and used for continuous lymph flow measurements. It was found that lymph flow is dependent on the frequency of contractions of lymph vessels segments, whereas the stroke volume and systolic pressure are of less importance. Comparison of flow and pressure curves obtained during active movements of the extremity with those recorded during external massage of the foot revealed major similarities in shape.

These findings indicate that an increase in interstitial pressure by external pressure and not the contractions of the foot and calf muscles is responsible for creation of a hydrostatic gradient between the tissue space and initial lymphatics.

3. Penetration of antibiotics to the tissues

The kinetics of antibiotic distribution in the tissues of human extremities were investigated after oral or intravenous administration of erythromycin, ampicillin, amoxycillin and timocillin. The concentrations, time of peak concentration, half time of elimination, area under the concentration curves and protein binding capacity were measured simultaneously in serum and peripheral lymph. It was found that the time of equilibration between the intra- and extravascular compartment, the peak concentrations and the time of elimination from both compartments were dependent on the antibiotic - protein binding capacity. The lymph peak concentration of each drug was lower than the serum concentration. The half time of elimination from the extravascular compartment was longer than that from the

blood circulation, especially for drugs with lower protein-binding capacity.

The data obtained permit to establish mean concentrations of antibiotics in the lymph necessary for inhibition of bacterial growth.

THE INFLUENCE OF ACUTE AND PROLONGED HYPERTHERMIA ON HUMORAL AND CELLULAR IMMUNITY

1. The influence of hyperthermia on recirculation of lymphocytes in the lymphoid and nonlymphoid tissues

It was found that hyperthermia causes a decreased accumulation of intravenously injected 51-chromiun-labelled lymphocytes from mesenteric lymph nodes in the spleen, mesenteric and peripheral lymph nodes and an increased accumulation in the bone marrow. There was an uneven distribution of the labelled lymphocytes in the bone marrow. Most of the radioactivity was found in the hind-limbs and spine, with lower activities in the ribs and fore-limbs. Adrenalectomy performed 24 h before the experiment totally abrogated the influence of hyperthermia. Furthermore, a decrease in accumulation of labelled lymphocytes in the bone marrow was observed. The control studies on accumulation of non-migrating erythrocytes have shown that hyperthermia and adrenalectomy do not have any influence on the distribution of these cells in the lymphoid and nonlymphoid tissues, with the exception of the spleen. Changes in blood flow did not influence the total body distribution of lymphocytes under hyperthermic conditions. These studies indicate that hyperthermia induces major changes in the distribution of the recirculating pool of lymphocytes. This phenomenon is mediated by the cortical hormones.

2. The effect of local hyperthermia on lymph formation in human limbs

Physical hyperthermia brings about an increased formation of tissue fluid and lymph and their transport through

lymph vessels by means of an increased frequency of spontaneous contractions, without evident changes in the amplitude of lymphatic pulse and stroke volume. Local hyperthermia of a subcutaneous lymph vessel segment was found to have only a limited effect on the frequency of lymph vessel contractility.

See the list of publications:
1, 3, 21, 31, 32, 45, 46, 47, 48, 53, 65, 66, 67, 68, 69, 70, 86, 87, 93, 94

OTHER RESEARCH WORKS

Research Group of School Psychohygiene
Head: Dr Henryk Osiński, M.D.

THE DYNAMIC PATTERN OF APTITUDE AND INTEREST DEVELOPMENT OF SECONDARY SCHOOL PUPILS IN THE ASPECT OF MENTAL HEALTH

The aim of the longitudinal studies is to evaluate the secondary school pupils from a city population in the aspect of some fundamental features determining the psychic functions: intelligence, special aptitudes, interests as well as personality traits.

The study included 183 pupils (mean age 18 years) from six classes of the last secondary school year. Each of them was subjected to several psychological tests determining the basic psychic functions. Besides, their interest in school subject and the scholastic progress were evaluated. All the pupils had been previously examined by the same method in the first class of the same school.

The data (78 results from each subject) have been subjected to an extensive statistical computer analysis.

Mental Health Department
Head: assoc. prof. M. Pełka-Sługocka

BIOLOGICAL, PSYCHOLOGICAL AND SOCIAL CONDITIONS OF HUMAN ACTIVITY

The investigations included mental and somatic evaluation, psychological tests and sociological interviews with 200 clinically healthy men aged 30 years employed in a large industrial town.
Only 32% of the subjects could be classified as representing the full health. Their mental state could be considered as acceptable, but high incidence of somatic disturbances was noted. Social adjustment of the subjects did not show any special disturbances. The examined group served as a control for comparisons with other groups of patients presenting various forms of deviant behavior such as e.g. drug or alcohol dependence.

Fifty male patients aged 31-55 years were examined after their first myocardial infarction, during 6-week staying in the Cardiac Rehabilitation Centre, to evaluate their tolerance of both mental and physical loads. During a routine program of physical exercise heart rate and blood pressure were measured. Basing on the mean values the patients were divided into 2 groups: A - "controlling" and B - "not controlling" physiological responses to exercise. No significant differences between the groups were found in the symptoms of depression, attitudes towards illness, treatment or rehabilitation. However, the factor "job-involvement" markedly differentiated both groups. Patients belonging to the group B had a high pressure job challenging them.

See the list of publications:
36, 39, 82, 90, 91, 100, 106, 107, 108, 109

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Kozłowski P.	Institute for Basic Research in Mental Retardation, New York, USA (long term visit)

Department of Neurochemistry

Broniszewska-Ardelt B.	Department of Neurochemistry, Purdue University, West Lafayette, Indiana, USA (long term visit)
Kasprzak M.	Institute of Biological Chemistry, University of Perugia, Perugia, Italy
Khachatrian L.	Laboratory of Preclinical Pharmacology Saint Elizabeths Hospital National Institute of Mental Health, Washington, USA (long term visit)
Łazarewicz J.	Department of Zoophysiology University of Lund, Sweden, (long term visit)
Noremberg K.	Institute of Biolog. Chem. University of Perugia, Perugia, Italy (long term visit)
Rafałowska U.	Biochemistry and Biophysic Department, University of Pennsylvania, Philadelphia, USA (long term visit)
Strosznajder J.	Institute of Neurochemistry, Paris, France
	Institute of Physiological Chemistry, University of Missouri, Columbia, USA (long term visit)
Wildeman J.	Roche Institute of Molecular Biology Nutley, New Jersey, USA (long term visit)
Wróblewski J.	National Institute of Mental Health, Laboratory of Prediclinical Pharmacology, Washington, USA (long term visit)

Zaleska M.	Department of Pharmacology and Therapeutics State University of New York at Buffalo, USA (long term visit)

Department of Neurosurgery.

Czarnicki Z.	Neurochirurgische Universitätsklinik, Bonn, FRG (long term visit)
Jurkiewicz J.	Neurochirurgische Klinik Kantonsspital Aarau, Switzerland (long term visit)
Szewczykowski J.	Memorial Sloan - Kattering Cancer Center, New York, USA (long term visit)

Department of Surgical Research and Transplantation

Gałkowska H.	Transplantation Division, Surgical Department University of Bonn, FRG
Grzelak-Puczyńska I.	Norwegian Radium Institute, Oslo, Norway
Kupiec-Węgliński J.	Surgical Research Laboratory, Harvard Medical School, Boston, Mass., USA (long term visit)
Łukomska B.	Norwegian Radium Institute, Oslo, Norway
Murawska M.	Department of Durgery State University Groningen, Netherlands (long term visit)
Olszewski W.	Norwegian Radium Institute, Oslo, Norway
	Surgical Clinic, University of Lund, Mälmö, Sweden
	Harvard Medical School, Department of Surgery, Boston, USA
Orłowska E.	Harvard Medical School, Beth Israel Hospital, Boston, USA (long term visit
Płachta J.	Institute for Surgical Research University of Oslo, Norway, Long term visit)
Ryffa T.	Friedrich-Schiller-Universität, Klinik für Chirurgie, Jena, DDR
Ziółkowska A.	Norwegian Radium Institute, Oslo, Norway (long term visit)

Laboratory of Ultrastructure of the Nervous System

Gajkowska B. — University P.M. Curie, Laboratory of Cytology, Paris, France

Mental Health Department

Zakrzewski P. — International Council on Alcohol and Addictions, Lausanne, Switzerland

PARTICIPATION IN INTERNATIONAL SCIENTIFIC MEETINGS IN 1982

The First World Congress of IBRO "The brain in health and disease", Lausanne, Switzerland, March 31 - April 6
Romaniuk J.

XVIth Annual Meeting of the European Society for Clinical Investigation, Luxemburg, April 15-17
Czarnecki W.

XVIIth Annual Meeting of the European Society for Experimental Surgery, Stressa, Italy, May 1-6
Olszewski W., Orłowska E.

IVth European Colloquy for Kidney Physiology, Prague, Czechoslovakia, June 13-17
Portalska-Suryn E., Sadowski J.

Third World Congress of World Federation of Nuclear Medicine and Biology, Paris, France, August 29 - September 2
Kapuściński A.

International Symposium of Neurology and Neuropathology, Bucharest, Romania, September 28 - October 2
Renkawek K.

IXth International Congress of Neuropathology, Vienna, Austria, September 5-10
Dąmbska M., Iwanowski L., Loesch A., Kroh H., Maślińska D., Renkawek K.

A Meeting of the European Society of Clinical Respiratory Physiology, (S.E.P.C.R.), Symposium "Hypoxia", Palermon, Italy, October 4-8
Karczewski W., Szereda-Przestaszewska B.

Vth Symposium of Experimental Surgery, Oberwiesenthal, DDR, October 26-29
Łukomska B., Olszewski W., Romaniuk A., Ryffa T.

Deutscher Sportärzte Kongress, Köln, FRG, September 9-12
Kozłowski S.

IXth International Congress of the Transplantation Society, Brighton, Great Britain, August 23-27
Łukomska B., Olszewski W.

VIIth Congrés International de Microchirurgie, Lyon, France, August 30 - September 2
Olszewski W.

XVIth International Congress of Internal Medicine, Prague, Czechoslovakia, August 23-27
Czarnecki W., Kwiatkowska-Patzer B.

IVth Meeting of the European Society for Neurochemistry - Catania and Special Joint ESN-WFN Meeting, Roma, Italy, September 20-21
Domańska-Janik K., Pastuszko A., Rafałowska U., Strosznajder J.

Symposium for Clinical and Experimental Investigations Coloidyne Essen, FRG, December 2-4
Herbaczyńska-Cedro K.

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