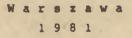
# POLISH ACADE.MY OF SCIENCES MEDICAL RESEARCH CENTRE

REPORT

ON SCIENTIFIC ACTIVITIES

. 1980



POLISH ACADEMY OF SCIENCES MEDICAL RESEARCE CENTRE 3, Dworkowa St., 00-784 Warszawa POLAND

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### RESEARCH REPORT

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### STUDIES ON THE FUNCTION OF THE NERVOUS SYSTEM

Basic chemoregulatory and neuroregulatory integration in the respiratory and cardiovascular systems

CORRELATION BETWEEN VAGAL AND CENTRAL MECHANISMS IN THE CONTROL OF BREATHING

Department of Neurophysiology Head: Prof. Witold Karczewski

Studies on correlated vagal and central mechanisms in the control of breathing have shown that not the ponto-medullary complex but the medulla itself stands up as the basic generator of the respiratory rhythm. The results confirmed the proposed hypothesis on the existence of a "critical" pool of neurones indispensable for regular generation of respiratory pattern. In these studies methods of macro- and microelectrode analysis were applied as well as focal pharmacological blockades and split-brain stem preparations.

Data were gained showing an activating influence of pontine structures in the generation of respiratory rhythm. The effect of endogeneous opiates on the pattern of breathing was confirmed.

New programmes of stochastic analysis of neural discharges were worked out, whereas mathematical description of intervals provided new data concerning characteristics of the activity of neurones allied to the control of breathing.

New results on the mechanism of "reversed" oxygen gradient in blood/cerebrospinal fluid relationship were re-established.

In studies on the neural control of tissue oxygen supply conditioned on the state of arterio-venous anastomoses, separate neural pathways to arterio-venous anastomoses and precapillary sphincters in the rabbit hind limb skin were demonstrated. Beneficial therapeutic effects of superficial electrical stimulation on "trophic" ulcers were established and data were obtained enabling to interpret the mechanism of this phenomenon.

See the list of publications: 7, 8, 20, 21, 22, 23, 44, 45, 46, 48, 49, 50, 51, 52, 61, 69, 70, 160, 161, 168, 180, 181.

THE ROLE OF BIOLOGICALLY ACTIVE SUBSTANCES IN THE REGULATION OF THE CIRCULATORY SYSTEM

Laboratory of Circulation Physiology Head: Assoc. prof. Krystyna Herbaczyńska-Cedro

Studies on metabolic and hormonal consequences of increased blood catecholamines have been completed and the methods of pharmacological and metabolic prevention of the myocardium in these conditions established /experiments on dogs/. Insulin with glucose, beta-adrenergic blockade, hydrocortisone with NaJ proved to be effective myocardium-protecting agents.

In collaboration with the Midhurst Medical Research Institute /UK/ it has been shown that in the intact dog deleterious effect of high blood catecholamines is related primarily to haemodynamic effects but not to alterations in myocardial metabolism.

Clinical study in collaboration with Queen Charlotte's Hospital /London/ points to the possibility of alterations in catecholamine metabolism in complicated myocardial infarction; there is high excretion rate of free catecholamines in these patients, whereas in uncomplicated disease excreted catecholamines are metabolized.

Increased circulating catecholamines stimulate prostacyclin /PGI<sub>2</sub>/ release into the blood, as shown in cats by bioassay. Contracting blood vessels are the source of PGI<sub>2</sub>. This might be protective mechanism against stress induced catecholamine excess. Study on the application of the antimony electrode for continuous pH measurements in working cat myocardium has been completed.

In continuation of the investigations on haemodynamic and metabolic effects of inosine, it has been shown that inotropic effect of this substance is due, in part, to stimulation of myocardial beta-adrenergic receptors.

Studies on the mechanisms of myocardial hypertrophy /collaboration with University of Chicago/ pointed to the role of phosphorylated form of myosine light chain 2 in the development of myocardial hypertrophy at an early stage.

It has been found that aspirin prolongs refractory period in the cat myocardium in situ. This effect might contribute to antiarrhythmic action of aspirin earlier observed by other investigators.

See the list of publications: 11, 57, 58, 87, 88, 123, 126, 129.

> Physiological basis of working ability and tolerance of environmental factors: Role of neurohormonal mechanisms

Department of Applied Physiology Head: Prof. Stanisław Kozłowski

NEUROHORMONAL RESPONSES TO PHYSICAL EXERCISE AND THE CONTROL OF ENERGY SUBSTRATE UTILIZATION UNDER DIFFERENT CONDITIONS OF WORK AND ENVIRONMENT

In seven review papers the following problems were presented: 1/ An impact of regular physical activity on the health status and risk factors of several so-called "civilization diseases" /e.g. coronary heart disease, hypertension, diabetes mellitus and obesity/, 2/ Recommendations of the desirable physical activity both for healthy people and patients, 3/ Suggestions concerning optimalization of occupational work loads and leisure-time activities.

The conclusions formulated in these publications were based mainly on the experimental data obtained in own research.

Physiological responses to static exercise, involving large muscle groups, were studied in subjects performing occupational work. The percentage of the maximum voluntary contraction force used when performing occupational tasks was determined. Energy expenditure, blood pressure and heart rate changes as well as urinary catecholamine excretion were measured during the work shift. On the basis of these data ergonomic improvements of the working places were postulated.

Investigations concerning the physiological mechanism of the observed improvement of exercise tolerance were carried out in patients during three years following mitral commisurotomy. In some cases a discrepancy was found between the increase in exercise tolerance and cardiac output changes. In such patients the improvement in exercise tolerance was due to the increase in peripheral /muscle/ oxygen extraction.

The sensitivity and specificity of the ergometric test was evaluated in patients with coronary heart disease. In many cases a discrepancy between subjective symptoms of myocardial ischaemia and ECG changes was found during graded exercise test.

The results of extensive studies on the neurohormonal control of body energy substrate utilization in diverse patterns of physical activity have been summarized in a monograph.

The studies on the glucostatic mechanism were further extended and provided new data indicating that the modification of exercise-induced changes in the adrenergic system activity by repletion of body carbohydrate stores is not mediated by insulin.

An experimental model was developed for simulation of insulin-glucose relationship in the organism. Basing on the computer simulation studies the slopes of blood insulin increase with different infusion parameters were determined. These data were utilized in an algorhythm of insulin dosage.

Investigations on the dynamics and mechanism of triglyceride /TG/ metabolism during muscle contractions were performed in cooperation with the Department of Physiology, Upstate Medical

Center, N.Y. University, Syracuse N.Y., USA. It was found that the chylomicron TG uptake by skeletal muscles is considerably elevated by muscle stimulation. Although the TG uptake could account for only a small fraction of the total energy needs of the working muscle, it could contribute to the turnover of endogenous TG, especially in the high oxidative slow-twitch red muscle fibers.

In contrast to the prevailing view on the subject, it was established experimentally that the decrease in maximal oxygen consumption in response to hypokinesia in man is unrelated to the initial magnitude of this functional parameter /in cooperation with the Division of Human Environmental Physiology, NASA, Moffet Field, USA/.

See the list of publications: 5, 6, 9, 62, 67, 74, 75, 109, 127, 128, 130, 205, 206, 207, 208.

### NEUROHORMONAL REGULATION OF BODY TEMPERATURE AND WATER-ELECTRO-LYTE BALANCE /INCLUDING KIDNEY FUNCTION/ IN DIFFERENT CONDITIONS OF WORK AND ENVIRONMENT

The role of renal nerves in renal function changes occurring during physical exercise was investigated in the dog. The data contradict the prevailing opinion that increased impulse traffic in efferent sympathetic renal nerve fibers determines the depression of renal hemodynamics and excretion during exercise. It seems that circulating catecholamine levels are more important: quite remarkably the denervated kidney, which is hypersensitive to catecholamines, responded to exercise with more pronounced functional changes than did the innervated organ. There was also no evidence for significant neural mediation of renal function changes observed during exposure of dogs to low ambient temperature.

A method was developed for in situ measurement of electrical conductivity of the renal tissue, and applied for studies of urine concentration and dilution by the kidney. Preliminary experiments with anesthetized rabbits and dogs demonstrated the value of this technique in physiological research.

It was established, in studies with human subjects, that prehydration improves the efficiency of thermoregulation during physical exercise and modifies the pattern of hemodynamic adaptation by increasing the stroke volume. The activation of sweat glands becomes more uniform and heat elimination by conduction as well as by convection is augmented. These results may be utilized in ergonomics for improving heat tolerance during occupational work.

In exercising human subjects a relation was described between electrical resistance of the skin on one side and skin and body temperature on the other side. The data showed that skin resistance changes may be used as an index of thermal sweating in man subjected to endogenous or exogenous heat load.

Changes in body temperature, heat production and heat elimination were determined in patients during surgical operation under general anesthesia as well as in the post-operative period. A role of diverse factors determining heat exchange between the organism and environment was assessed. The data are of potential practical importance in clinical anesthesiology.

It was found in an experimental animal study that Nembutal anesthesia disturbs thermoregulation, primarily by decreasing the metabolic rate. This lowers the tolerance of low and increases the tolerance of high ambient temperature.

Complex studies on the mechanism of malignant hyperthermia, performed on pigs, showed that the development of this syndrome can be predicted prior to induction of anesthesia on the basis of skin and muscle temperatures as well as on the plasma noradrenaline level. The pattern of core and skin temperature changes as well as alterations of some neurohormonal and biochemical parameters in the course of malignant hyperthermia were described. The role of augmented heat production in the muscles and of adrenergic system activation was confirmed. It was found that breathing gas mixture with increased CO<sub>2</sub> content lowers hypothalamic temperature threshold for the vascular component of the thermoregulatory reaction, and inhibits thermal panting.

See the list of publications: 53, 86, 89, 106, 107, 108, 169, 170, 193.

Intracellular mechanisms regulating the metabolism of nerve cells

CORRELATION BETWEEN INTRACELLULAR MECHANISMS REGULATING CARBOHYDRATE-ENERGY METABOLISM AND STRUCTURAL AND FUNCTIONAL STATE OF SUBCELLULAR ELEMENTS WITH REFERENCE TO NEURO-TRANSMITTERS

Department of Neurochemistry Head: Assoc. prof. Jerzy Łazarewicz

In the studies of the effect of hypoxic-ischemic pathology on the properties of brain membranes new data were obtained, concerning the alterations of the composition and metabolism of the lipid and glycoprotein components of the membranes. It was demonstrated, that hypoxia inhibited the incorporation of intracerebrally injected radioactive arachidonic acid into acyl COA and glycerolipids, especially inositol ones. Ischemia and hypoxia led to a decrease in the content of unsaturated fatty acids in glycerophospholipids of the synaptosomal membranes. It was shown, that intracerebral administration of CDPcholine and CDP-ethanolamine prevents alterations in the composition and metabolism of brain lipids induced by ischemia. It was demonstrated that hypoxia results in a decrease in superficial sialic acids and in the lowering of fucose content in the glycoproteins of the synaptosomal membranes, as well as in a decrease of concanavalin A binding by fucose. Simultaneously, an increase in the content of galactose residues and the activation of galactose transferase were observed in these membranes.

It was shown that mild hypoxia is without any effect on the brain content of cerebrosides /level of which is decreased in ischemia/ in parallel to the energy disturbances. The content of NANA in gangliosides was decreased in hypoxia, but remained unchanged in ischemia.

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Studies on the regulation of brain energy metabolism were continued. Significant differences were revealed in the kinetic properties and temperature dependence of cytoplasmic and mitochondrial brain hexokinase activity. It was shown that the activation of adrenergic and cholinergic receptors on the cultured glioma cells leads to the mobilization of intracellular calcium. This suggests that calcium may play the role of intracellular regulator, adjusting the metabolism of astroglia to the activity of adjacent synaptic endings.

Studies on the metabolic properties of brain synaptosomes were also continued. It was shown that only in starved rats hypoxia led to a slight decrease in the synaptosomal respiration in the presence of various respiratory substrates and to the 10% decrease of cytochrome C reduction. It was demonstrated that hydrolysis of the synaptosomal membrane phospholipids by exogenous phospholipase  $A_2$  leads to an inhibition of depolarization-dependent calcium accumulation in brain synaptosomes in.vitro.

Studies were developed on the new methods of efficient and specific isolation and quantitative determination of endorphins as well as on the assay of the enkephalinase activity with the application of Sephadex LH-20 chromatography and HPLC.

1000

### See the list of publications:

12, 19, 24, 25, 26, 27, 71, 72, 101, 102, 139, 140, 146, 147, 148, 163, 164, 165, 172, 173, 174, 175, 176, 177, 178, 179, 196, 197, 201, 202, 203. STUDIES ON THE STRUCTURE AND BIOLOGICAL PROPERTIES OF THE NERVOUS TISSUE

Nerve tissue reaction to endogenous and exogenous damaging factors

Department of Neuropathology Head: Prof. Mirosław J. Mossakowski

ENDOGENOUS ENCEPHALOPATHIES CONNECTED WITH IMPAIRMENT OF HEPATIC AND RENAL FUNCTION

In investigations on the pathomechanism of central nervous system damage in hepatic diseases it was shown that hepatic encephalopathy, induced by both chronic intoxication with carbon tetrachloride and portosystemic venous shunting, is accompanied by a selective increase of RNA synthesis in nuclear fractions enriched in astrocytic nuclei. This observation is consistent with morphological findings concerning predominant reaction of astroglia. Comparative analysis of the pathomorphology of various types of hepatic encephalopathy revealed that pathology of astrocytes is the common element. Some other features known from human hepatic encephalopathy occur in the experimental models with low frequency and they are related to additional factors accompanying hepatic failure. The most severe brain tissue damage has been observed to develop in cases of massive accumulation of copper in the brain, which usually coincides with hyperammonemia.

Hepatic encephalopathy in the two above mentioned models is characterized by excessive accumulation of ammonia in brain occurring in the period of the most severe tissue damage development. At the same time glutamine synthetase activity increases in both models, and glutaminase activity only in the chemical model. The above observations confirm the earlier hypothesis on the pathogenetic role of disturbances in ammonia detoxication in the development of hepatic encephalopathy. In investigations on the pathomechanism of nervous system damage in renal failure it was established that uremia, developing in the course of chronic serum sickness, leads to peripheral nerves impairment manifested by the presence of inflammatory infiltration, damaged vascular walls, demyelination of nerve fibres and desintegration of axons. The apparent deposition of immunoglobulins, C<sub>3</sub> adjuvant component and immunological complexes in the vascular walls and their vicinity indicate participation of the immunopathological process in the pathogenesis of peripheral nerve damage in renal failure of this type. -

The morphological picture of uremic encephalopathy in humans is characterized by coexistence of toxic encephalopathy features and the inflammatory process. The latter is accompanied by deposition in and around vessels of immunoglobulins, fibrin, i C, adjuvant component and immunopathological complexes. The immunopathological process, underlying renal impairment, modifies the pattern of uremic encephalopathy by introducing elements of the inflammatory process, whereas impairment of vascular permeability potentiates the features of brain edema.

Investigations on antigenic properties of the nerve tissue revealed a selective damaging effect of antiglial sera on the oligodendroglia, with almost no effect on the astrocytes. The oligodendroglial damage is accompanied by structural changes in the myelin sheaths, indicating disturbanced myelination. The stronger effect of antiglial sera on oligodendroglia may indicate a relatively lower content of antibodies against astrocytes.

See the list of publications: 1, 2, 3, 34, 59, 60, 76, 77, 78, 79, 117, 124, 125, 155, 194, 195

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STRUCTURAL AND METABOLIC CONSEQUENCES OF CENTRAL NERVOUS SYSTEM ISCHEMIA

Investigations on two models of complete brain ischemia, being due to acute intracranial hypertension and ligation of all arterial trunks supplying the brain, revealed characteristic changes in the pattern of systemic blood pressure. These changes consist in acute arterial hypertension in the early stage of cerebral ischemia followed by hypotension both in the late stage and in the postischemic period. They are accompanied by fluctuations in blood catecholamine levels - their increase in the hypertonic and a decrease in the hypotonic phase. At the end of the hypotonic phase blood catecholamine level becomes elevated again; this coincides, however, with morphological manifestations of adrenal and cardiac impairment. A hypothesis has been put forward that ischemia of the cerebral stem centres leads to enhanced release of adrenal catecholamines, followed by exhaustion of adrenals, a decrease of catecholamine levels and arterial hypotonia, hampering the recovery of normal cerebral circulation.

Complete cerebral ischemia, following ligation of the arteries branching from aortal arch, leads to severe disturbance in blood gas content and acid-base balance. The latter are considered to be a marker of brain damage and they may be of prognostic value as to the possibility of the central nervous system recovery after ischemia.

Enzyme studies on the vascular - tissue junction in brain revealed that ischemia is accompanied by changes in enzymatic reactions of capillaries in the barrier - but not barrier free areas. Both during and after ischemia, ultrastructural changes become apparent in the capillaries and their immediate surroundings. These abnormalities are indicative of disturbances in the polarity of enzyme systems related to transport and may be a marker of impaired barrier function of the junction.

Studies on the same enzymatic systems in organotypic nervous tissue culture have demonstrated their membrane location in

neurons and glial cells, but not in vascular wall structures; their occasional presence in the membrane of the capillaries was an exception. Anoxia exerted no influence on the enzyme topography. The results point at a number of different properties of vascular-tissue junction elements in tissue cultures in vitro.

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In studies on the vegetative innervation of pial vessels, supplying cerebral cortex, the uni- and bilateral extraction of superior cervical ganglia was shown to alter the innervation pattern of both vegetative system components. Unilateral sympathectomy caused more pronounced changes on the ipsilateral side and, in general, noradrenergic innervation was more severely affected. In sympathectomized animals ischemia has produced changes in the pattern of pial vascular reaction in a different way than in intact controls. The histochemical reactions of the vessels underwent considerable changes; however, the differentiated character of vascular muscle fibres remained preserved.

In investigations on the pathomechanism of cerebral edema accompanying ischemia and venous stasis it was shown that, immediately before appearance of edematous changes, the mechanical properties of the brain tissues - in particular their plasticity and elasticity - undergo pronounced changes. These changes seem to determine the rate of development and the severity of edema. The above observations point at the role of the mechanical properties of the brain in pathogenesis of brain edema. In addition it was observed that, in some cases of the preedematous state, the increase in brain volume is proportionally much lower than the increase of blood volume in the vascular bed. This phenomenon appears to manifest the process of water translocation from the tissue to the vascular bed as one of the compensatory mechanism counteracting the development of brain edema.

See the list of publications: 68, 118, 119, 141, 142, 156, 157, 184, 185, 186, 189, 190, 191. NERVOUS SYSTEM DAMAGE RELATED TO HYPOXIA AND THE ACTION OF EXOGENOUS CHEMICALS

Studies on the effect of kainic acid on the nervous tissue culture grown in vitro revealed that this toxic analogue of glutamic acid selectively affects the astroglia. The astroglial changes depend on the maturity of the cells and time of exposure. The most characteristic feature is the enhanced production of glial filaments. The results suggest that fibrous gliosis represents the primary effect of kainic acid, independent of nerve cell damage.

In search for a model of Parkinson disease it was shown that i.v. administration of manganese chloride leads to spongy changes in the cerebral white matter suggesting development of cytotoxic edema, and to symmetric damage of substantia nigra. The results appear to justify the selection of the model for studying the pathomechanism of the Parkinsonian syndrome.

In studies on the disturbances of neuromediatory functions in experimental coma it was shown that hypoglycemic coma leads to regionally differentiated changes in the **~**-aminobutyric /GABA/ content. The period of the most severe hypoglycemia after insulin administration is characterized by a decrease of GABA level in striatum, cerebral hemispheres and cerebellum. The changes in GABA content are not related to the activity of the GABA synthesizing enzyme /glutamate decarboxylase/ which remains unchanged throughout.

In investigations on the effects of a neurocarcinogen ethylnitrosourea /ENU/ on organotypic nervous tissue culture, it was shown that this compound produces reversible cytotoxic changes in all nervous tissue elements. The most intensive and durable damages occur in oligodendrocytes being accompanied by features of impaired myelination of the nerve fibres. Another type of tissue reaction to ENU is a progressive, enhanced proliferation of astrocytes and ependymal cells, with features of blastomatic transformation. This reaction continues after cessation of carcinogen administration.

In connection with the observation of myelinoklastic activity of ENU, related to primary damage of oligodendroglia, an analysis of the myelin sheaths was performed in experimental brain tumours of oligodendroglial origin. The analysis revealed myelin damage ranging in its appearance from changes in the staining pattern to complete desintegration. The damage may depend on such factors as mechanical effects of the growing tumour, edema and impairment of the myelinogenic function of neoplastically transforming oligodendrocytes.

In investigations on the role of the hypothalamo-hypophyseal system in the pathogenesis of brain edema, the antiduretic hormone was shown to participate in controlling the extracellular fluid balance during the brain edema development. The influence of increased ADH levels in blood and cerebrospinal fluid on such processes as: cerebral vasomotoric reactions, cerebral blood flow and formation and/or resorption of cerebrospinal fluid, appears to be the major link in this mechanism. • A hypothesis has been put forward that the beneficial effect of hyperosmotic agents on cerebral edema may be exerted via the neurosecretory hypothalamo-hypophyseal system.

See the list of publications: 80, 81, 82, 83, 84, 149, 150, 151, 152, 153, 154, 158, 159, 199.

TOXIC AND ANOXIC DAMAGE TO THE DEVELOPING NERVOUS SYSTEM

Laboratory of Developmental Neuropathology Head: Prof. Maria Dambska

1. Autopsy material of the newborn brains collected during the last 10 years was evaluated from the point of view of the character of injuries to the brain stem structures, depending on the period, when the injurious factor had acted. Chronic asphyxia during pregnancy, caused by changes in the placenta, was accepted as the clinical model of the discussed syndrome. The investigations were conducted on the selected group of 25

newborns prematures and full-term who died not later than 7 days after delivery. The character and degree of the placental injury was always determined and only such cases were qualified for the study in which the intensity of placental injury enabled to diagnose chronic asphyxia of the fetus. It was confirmed by the type of lesions in the central nervous system. In most of the cases the brain stem injuries were greater than the hemisphere injuries and their topography within the structures of the brain stem depended on the developmental age of fetuses. In the younger group, up to the 30th week of fetal . life, mainly neurons of the cranial nerve nuclei /maturing in this period/ were damaged. In full-term newborns, chronic asphyxia exerted its influence during the last weeks of pregnancy. The most extensive injury was found in the reticular formation. Evaluation of the pathways of myelination of this complex formation suggests that in the perinatal period there are very intensive processes of maturation. The observed changes enabled to conclude that sensitivity to asphyxia is very clearly connected with the developmental phase of particular elements of the central nervous system structure.

In the investigations based on the autopsy material of two full-term newborns microcephaly was found with congenital malformations, very rarely encountered delayed maturation and injuries of the encephalopathy type.

Despite the lack of clinical data concerning the course of pregnancy it is possible to estimate the time of the injurious factor action and the course of farther, pathological maturation of the brain basing on the neuropathological examination.

A case-report was made about the brain of a child with the toxoplasmosis most probably congenital, and leucaemia treated with irradiation and cytostatic drugs. The structure and topography of injuries as well as connected with age sensitivity of the periventricular region of the brain enabled to explain scintigraphically detected presence of the nervous system noted so far only in few cases, mainly in newborns.

2/ On the basis of the results obtained in the studies carried out during the last 5 years, a comparison was made between the effects of halothams and ethrane on the immature rabbit brain. Both drugs examined cause disorders in the circulation haemodynamics and transient, moderate cerebral hypoxia. There are however some differences in the action of these anesthetic drugs. During a second exposure halothane causes a delayed brain development, and used repeatedly or for a long time may induce irreversible changes in the nerve cells. On the contrary, ethrane does not induce any irreversible changes in the nervous tissue.

3/ A detailed biochemical and histochemical analyses were made on the effect of dichlorvos on acetylcholinesterase activity. Kinetics of these changes in acute and chronic intoxication and histochemical observations of the site of renewal of acetylcholinesterase activity, together with the results of serotonin level in the cerebral structures /published last year/ were used for analysis of the pathomechanism of behavioral alterations induced by phosphoorganic pesticides both in men and animals. The effect of dichlorvos on the level of catecholamines in various regions of the brain was also examined. The obtained results indicate that pesticide alters mainly dopamine content in the rabbit brain during its development. Basing on these data it is possible to investigate the mechanism of the disease symptoms occurring in the course of pesticide intoxication, as well as to follow up the biochemical changes occurring during development of the cerebral structure and function. Additionally, a comparison was made between the effects of dichlorvos on the rabbit brain in various periods of maturation both during fetal development and after birth. It was pointed out that DDVP, a widely used phosphoorganic pesticide, inhibiting acetylcholinesterase activity exerts a harmful effect on the maturing elements of the nervous tissue. It delays the nervous tissue development, and during more severe intoxication leads to irreversible injuries which undoubtedly affect its function.

A comparative study concerned maturation of synapses in various philogenetic regions of the cortex. The aim of these investigations was to obtain data about normal development of the rabbit brain needed for comparison with experimental injuries. Two other studies concerned the senile changes occurring both in human and animal brains.

See the list of publications: 13, 14, 15, 16, 17, 18, 28, 29, 31, 32, 33, 90, 91, 92, 100, 110, 111, 112, 113, 114, 115, 116, 171.

#### Nervous system ultrastructure

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

STUDY ON THE ULTRASTRUCTURE OF THF NERVOUS SYSTEM TUMOURS IN CHILDREN

Electron-microscopic examinations of neuroblastoma after treatment /X-ray and chemiotherapy/ revealed degenerative changes both in anaplastic, and in more differentiated cells. In the mechanism of tumour involution processes of connective tissue proliferation dominated in the host, whereas the mononuclear-phagocytic system was not mobilized. The recessive changes in the neoplastic cells involved to a higher degree the cytoplasm than the cell nucleus.

# CHANGES IN THE HYPOTHALAMO-HYPOPHYSEO-ADRENAL SYSTEM UNDER UNFAVOURABLE ENVIRONMENTAL CONDITIONS

An influence of exogenous vasopressin on the hypothalamohypophyseal nervous lobe system was investigated in rats. For morphological examinations sections were taken of the supraoptic and paraventricular nuclei of the hypothalamus, and the nervous lobe of the hypophysis. The results demonstrated that

a single administration of Pitressin in a dose of 50 µU, in spite of increasing considerably the vasopressin level in the blood, fails to inhibit the synthesis of neurosecretory granules in the hypothalamic supraoptic and paraventricular nuclei neurons. A large number of neurosecretory granules was also observed within the parikaryon, as well as in the neuronal fibres of the hypothalamo-hypophyseal system and their terminal axons within the nervous lobe of hypophysis - without any morphological signs of secretion. This indicates that the increased blood vasopressin level, being due to Pitressin administration, does not exert any inhibitory influence on the synthesis of neurosecretory granules in the hypothalamic nuclei. It causes, however, an inhibition of neurosecretion in the hypophyseal nervous lobe.

See the list of publications: 30, 35, 36, 37, 38, 39, 40, 41, 42, 43, 93, 94, 95, 96, 97, 98, 99, 120, 162.

EVALUATION OF INTRACRANIAL PRESSURE FOR NEUROSURGERY DIAGNOSIS

Department of Neurosurgery Prof. Adam Kunicki

One of the methods used for evaluation of the intracranial volume compensating mechanism is the subarachnoid infusion test. The EEG frequency characteristics were studied before and after subarachnoid infusion test. The mean frequency of EEG activity before infusion test was compared with that 10 minutes after performing the test, as well as 1 h and 24 hours later. The EEG frequency data collected after the test as compared to the EEG control, were statistically insignificant. There was no statistical significance between the EEG frequency and the indexes of intracranial volume compensating mechanisms efficacy - namely elastivity and resorption resistance, or between the EEG frequency and the amount of the infused saline.

It was proved that the standart infusion test, as applied in the clinic, is uninvasive, as far as EEG activity is concerned.

An influence of short term increases in intracranial pressure during the infusion test on the serum levels of cortisol, somatotrophin and prolactin was studied. The results obtained in the patients examined with and without IT suggest some influence of intracranial pressure disturbances on the levels of the above hormones.

These studies were performed in the patients with the suspected insufficiency of the CSF resorptive capacity. The efficiency of the CSF resorption capacity was evaluated by using computerisedpressure-elastance-resistance test.

See the list of publications: 66, 132, 182, 183.

EFFECT OF STEREOTAXIC SURGERY OF THE LIMBIC SYSTEM ON MEMORY, EMOTIONAL STATE AND BIOELECTRICAL ACTIVITY OF THE BRAIN

Department of Neurosurgery Head: Assoc. prof. Eugeniusz Mempel

1/ Research on memory long after stereotactic procedure in epileptic patients

Memory processes concerning direct memory, actions based on direct traces in memory in different types of distraction and processes of learning in epileptic patients treated by selective amygdalotomy and hippocampotomy were examined and characterized. The results were compared with control group of nonepileptic subjects. Both qualitative and quantitative analysis of these results indicates that patients who were examined long after the operations /2-12 years/ and who showed great clinical improvement, are quite successful in learning lexical material /close to the control group/ and their ability to actualize words is much higher than before the operation.

Patients who do not show any marked clinical improvement are much worse in recalling memory material after distraction as compared to the pre-surgical test-results. The patients examined were particularly sensitive to interference in auditory material, mostly in verbal exercises. Results in visual material were close to the control group.

The data obtained confirm the participation of deep structures in temporal lobes in memory processes. This is particularly true when one considers the increased sensibility of the memory trace to the interfering factors in case of lesions of these structures.

2/ Brietal and gamma-OH effects on bioelectrical activities
of the brain during stereoelectroencephalographic /SEEG/
investigations

During SEEG investigations patients with temporal epilepsy were treated with brietal and gamma-OH which werevorally and intravenously separately. Intensified excitement elements of both quantitative and qualitative character were found mostly in the cortex and less in deep temporal structures. Epileptic activity was also found, which had not been observed before. No clinical effects were observed during the investigations.

Both the above mentioned agents were proved to be quite safe, and they can play an important role in epileptic diagnostics.

See the list of publications: 103, 121, 122, 131.

DISORDERS OF SPEACH AND OTHER GNOSTIC FUNCTIONS IN THE LOCAL LESIONS OF THE BRAIN

Department of Neurosurgery Assoc. prof. Jadwiga Szumska

Complex studies concerning speech disorders in children have been started with the aim of developing clinically useful methods of both examination and rehabilitation of children

with aphasia. This project is a continuation of previous . studies of adult pathology, but it has been adapted to suit the special characteristics of speech disorders in adolescence. The investigations have been conducted in a comprehensive way including studies on the adolescent aphasia, intelligence quotient, as well as visual and auditory perception. A review paper entitled "Neurophysiological fundamentals of speech disorders in children" was submitted for publication as the introductory chapter of a text-book dealing with speech disorders in children.

See the list of publications: 187, 188.

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

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

In microscopic investigations on the brain alterations in pt-mutant it was disclosed that the primary pathological process involves both grey and white matter and leads to progressive degeneration of nerve cells and their processes. The tissue abnormalities predominate in structures maturating earlyer in ontogenic development.

The most obvious microscopic feature of white matter alteration consists of diffuse pallor in myelin stain, which in the early stage of the disease reflects delayed myelination, whereas in the later symptomatic and in the chronic periods it is attributed to incomplete myelination and secondary intercurrent myelin destruction. In 'the preferentially affected cerebellar white matter, the disturbed myelin formation is accompanied by the accumulation of large amounts of sudanophilic deposits in cytoplasm of astroglia.

The topography of lesions have no direct causal relation to the essential clinical symptom in pt-rabbits /tremor/. However, the extend and multisystemic brain involvement suggest the possible participation of several neuronal links /especially cerebellar and brain stem structures/ in the tremorogenic mechanism.

In investigations on the damage to the visual system in pt-rabbits permanent involvement of optic pathways in pathological process was stated. However, the abnormalities in the visual system were less pronounced than those in other brain structures. The morphological alterations are unevenly distributed in particular centres and segments of the optic system. They predominate in certain anatomical regions such as: retrobulbar part of optic nerves, lateral geniculate nuclei, superior colliculi.

The primary character of changes in the optic fibers and the preference for involving the distal parts of the optic axons were established.

Differences in the character and intensity of structural changes, depending on the stage of the disease, indicate coexistence of the primary lesions with secondary transneuronal degenerations.

See the list of publications: 137, 204.

Studies on transplantation and experimental surgery

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

RECIRCULATION OF LYMPHOCYTES AND TRANSPORT OF IMMUNE PROTEINS

1/ Immunological characterization of mononuclear cells in the portal blood revealed a low percentage of T cells and high of cells possessing Fc receptor. Also, a high concentration of cells with Fc receptor was found in the spleen and small bowel mucosa.

2/ The NK and K cell activity in the portal blood was found similar to that in the peripheral venous blood, however, it was significantly higher in the liver sinusoidal blood. This finding indicates that naturally cytotoxic cells play a role in elimination of foreign cells in the liver.

3/ Antigen specific cells migrate spontaneously to the site of allograft, depending on the population. Thoracic duct lymphocytes migrate to the lymph nodes draining the graft and in a limited manner to the graft itself. Splenocytes do not migrate spontaneously to the graft within the first twentyfour hours after its transfer.

4/ Macrophages infiltrating the sponge matrix allograft are more numerous on the day 3 than in the syngeneic grafts.

See the list of publications: 85, 104, 105, 134, 135, 136.

#### ANTIGEN - SPECIFIC PROLONGATION OF ALLOGRAFT SURVIVAL

1/ Significant prolongation of skin allografts across the major histocompatibility barrier was obtained in rats in a combined treatment protocol: donor antigen, allo-antiserum and antithymocyte serum. Concomitantly, a decrease in response of donor lymphocytes to non-specific mitogens was observed.

2/ A prolongation of dog kidney allograft was found after treatment with ALS for 3 days before and 7 days after transplantation and donor thrombocytes on day 11. The mean survival time was 50 days.

See the list of publications: 4, 54, 55, 56, 133, 166, 167.

NEUROREGULATION OF TISSUE OXYGEN SUPPLY IN RELATION TO THE ARTERIOVENOUS ANASTOMOSES IN MICROCIRCULATION

Laboratory of Experimental Surgery Head: Prof. Jan Nielubowicz

Basing on the results obtained previously a hypothesis was put forward according to which there are separate nerve fibers leading to the arteriovenous anastomoses and to the precapillary sphincters in the skin of the rabbit hind-limbs. The arteriovenous anastomoses are mainly innervated by the sympathetic fibers of the ischiatic nerve, whereas the fibers innervating the precapillary sphincters are not.

To check out this hypothesis both histological and histochemical examinations of the sympathetic nerve endings around the arteriovenous anastomoses and the precapillary sphincters were made using different models of the rabbit hind limb skin denervation.

Clinical observations of patients with the surface electrostimulation proved that this method is beneficial from the therapeutical point of view.

In cooperation with the Cardiovascular Laboratory /dr Cedro/ investigations have been started to elucidate additional aspects of electrostimulation, besides its effects on the functional state of arteriovenous anastomoses. In experiments, carried out on dogs and cats, the surface stimulation has been replaced by electrostimulation of the cut sympathetic trunk at the level of  $L_2-L_3$  and  $L_3-L_4$ . It was observed that during such stimulation venous blood leaving the dog's hind limb and washing coronary arteries of the bovine heart causes their dilatation.

Besides, in the experiments carried out on cats it was found that a factor, released during the sympathetic trunk stimulation causes deaggregation of blood pellets /aggregated before the stimulation/ on the rabbit tendon.

Administration of indometacin inhibited the above mentioned effects of electrostimulation. Further studies showed that  $PGE_1$ ,  $PGD_2$ ,  $PGI_2$  as well as one of the products of  $PGI_2$  degradation may play a role in the mechanism of the described phenomena.

#### OTHER RESEARCH WORKS

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BIOLOGICAL, PSYCHOLOGICAL AND SOCIAL CONDITIONS OF DEVELOPMENT OF ABILITIES IN CHILDREN AND ADOLESCENTS

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

The study conducted this year was a continuation of research work on the conditions determining the development of outstanding abilities. In the preceding year the level of intelligence was examined using Wechsler's scale, interests were studied using the Kuder Preference Record Vocational, and a special method evolved by this Laboratory and special abilities were tested with the Employee Aptitude Survey of Grimsley, Ruch, Warren and Ford.

In 1980 investigations were carried out with the same group of 178 school children for establishing the degree of neuroticism and extroversion by the Personality Inventory of Eysenck, latent anxiety by Cattell's test and Gough's California Psychological Inventory, and for evaluating scholastic progress reflected in marks received, and achievements not measured with school marks. The calculations of the correlations of 78 variables obtained in these investigations had the character of correlation matrix and multiple regression, are they were done by the Polish Academy of Sciences Computer Centre in Warsaw.

The degree of neuroticism found in the examined children is within normal limits, indicating a normal general adaptation level. The neuroticism is manifested in its various aspects tested in this study: in the neuroticism-equanimity balance, latent anxiety, and personality traits expressing emotional equilibrium.

It was shown that the intelligence-level of the children is the factor responsible, in the highest degree, for differences in their educational achievements. It was found that an important variable making possible an estimation of the general, verbal and non-verbal intelligence, is the mean value of marks received in all school subjects. In the case of general and verbal intelligence a role was played by numerical reasoning. An additional factor important in the case of general intelligence estimation was the knowledge of words, and in the cases of verbal intelligence it was the responsibility and social interests. In the case of nonverbal intelligence a factor enabling its estimation was the eyes and spatial imagination.

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It was found that abilities were more frequently associated with educational achievements than with individual interests.

The study described is a multifarious approach to the basic problem of the research, that is determinants of outstanding intellectual abilities. The obtained results are important from the theoretical as well as practical point of view. In the former aspect the study enriched the basic psychological data concerning the mutual determinations of the individual traits of human character.

The results of the present study, apart from their theoretical value, can be of use for psychologists and teachers working in occupational and educational counselling services for selection of proper school and educational profile in accordance with the abilities and interests of children.

See the list of publications: 138.

#### FACTORS DETERMINING MENTAL HEALTH OF ADOLESCENTS

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Comparative investigations were carried out with a group of 617 human subjects aged from 15 to 22 years. They involved 310 students of the secondary schools, 110 drug users, 94 subjects after suicidal attempts and 103 individuals avoiding

work or/and study. Each person was subjected to medical, psychological and sociological examinations.

Mental health disorders were found to be caused by biological, psychological and/or social abnormalities. Disfunctional behaviors such as personality disorders, neurotic reactions and diminished mental ability have been predominantly observed. as a secondary symptoms of mental disorders. Psychological mechanism causing difficulties in adaptation are connected with the diminished mental ability or with the structural and functional personality disorders. Disfavourable effects of family on the disfunctional behavior of adolescents are stronger than other environmental factors /e.g. school, peers/.

Various forms of deviancy behaviors are caused by particular factors. Adolescents with behavior disorders had, in great majority, difficulties with adaptation already in their childhood.

Additional studies were carried out with 316 teachers from various schools. It was shown that teachers, being greatly responsible for education of youngsters, are overworked discouraged and emotionally unbalanced.

Methods of the primary prevention gained from the above described investigations fall into two categories:

- a/ unspecific prevention directed on the whole young population. Special attention should be paid to the main environmental factors creating personality such as: family, school and peers.
- b/ specific prevention connected with particular forms of behavior disturbances such as drug using, suicide attempts and avoiding work or/and study.

Activity of the Psychoprophylactic Centre for Youth, created in 1977 by Mental Health Department in cooperation with Federation of Polish Youth Socialist Associations was directed to give help and advice concerning the preventive methods.

See the list of publications: 10, 47, 62, 64, 65, 73, 143, 144, 145, 192, 198, 200.

CONSTRUCTIONS OF BIOMEDICAL EQUIPMENT

MEDIPAN Laboratories Head: S. Karałow, Msc.eng.

In 1980 Medipan Laboratories were manufacturing the following types of equipment: 3-channel recorder /3 units/

Infusion pump type 680 /130 units/ Oscilloscope camera OK-3 /10 units/ Classic animal pump /10 units/ Other small equipment.

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Bechterev Institute of Psychoneurology, Leningrad, USSR

## PARTICIPATION IN INTERNATIONAL SCIENTIFIC MEETINGS in 1980

Congress SEPCR, Sheffield, Great Britain, September 2-6: Głogowska M., Karczewski W., Romaniuk J., Szereda-Przestaszewska B.

XXVIII International Congress for Physiological Sciences IUPS, Budapest, Hungary July 13-19: Głogowska M., Gromysz H., Herbaczyńska-Cedro K., Przybylski A., Romaniuk J., Sadowski J., Szereda-Przestaszewska B., Turlejska E.

3rd International Symposium on Prostaglandins and Thromboxanes in Cardiovascular System, Halle, GDR, May 5-7 Herbaczyńska-Cedro K.

Meeting of the European Society for Clinical Investigations, Sallzburg, Austria, April 22-27 Herbaczyńska-Cedro K.

X Congress of International Society for Heart Research, Moscow, USSR, September 23-28 Patzer B., Ziółkowski L.

VIII European Congress for Cardiology, Paris, France, June 22-26 Czarnecki W., Herbaczyńska-Cedro K.

Symposium on Microcirculation of the Heart , Heidelberg, GFR, February 10-14 Herbaczyńska-Cedro K.

Satellite Symposium on Thermoregulation in Physiology, Pecs, Hungary, July 7-12 Turlejska E.

FIMS Meeting and Symposium on Sports Cardiology, Rome, Italy, September 17-23 Kozłowski S.

Seventh International Conference on the Physiology of Food and Fluid Antake "IUPS", Warsaw, Poland, July 7-10 /co-organized by the Medical Research Centre/ Grucza R., Kaciuba-Uściłko H., Kapitaniak B., Kozłowski S., Ziemba A.W. Meeting of the Executive Board of International Neuropatholo- . gical Society, Vienna, Austria, May 4-5 Mossakowski M. /Vice President/ Days of Polish Culture, University of Dusseldorf, GFR, April 28-May 1 Mossakowski M. International Erwin Riesch Symposium on Cerebral Microcirculation and Metabolism, West Berlin, July 9-12 Kapuściński A., Kroh H., Mossakowski M., Rap Z. First European Neuropathology Meeting, Vienna, Austria, May 6-8 Kroh H., Maslińska D., Mossakowski M., Ostenda M., Rap Z., Weinrauder H. 2nd Common Symposium of the Society of Neuropathology of the GDR and the Association of Polish Neuropathologists, Erfurt, GDR June 9-11 Albrech J., Dambska M., Hilgier W., Krajewski S., Kroh H., Maślińska D., Mossakowski M., Renkawek K., Szumańska G., Zelman I. 2nd Symposium on Patophysiology and Pharmacotherapy of Cerebrovascular Disorders, Tübingen, GFR, July 21-27 Rap Z. Congress of the Hungarian Society for Neurology and Psychiatry, Budapest, Hungary, January 9-17 Renkawek K., Szumańska G. General Assembly of the World Federation of Nuclear Medicine and Biology, Manila, Philiphines, October 29-November 10 Kapuściński A. Symposium on Biological Reactive Intermediators, Gillford, Great Britain, July 14-17 Albrecht J. Symposium on Central Organization of the Autonomic Nervous System, Heidelberg, GFR, July 6-9 Przybylski A. Donal Symposium of Neurological Sciences, Erfurt, GDR, September 26-29 Ostenda M., Śmiałek M. Polish-German /GFR/ Symposium on Spongious Degeneration of the Nervous System and Neuroanatomy and Neuropathology of the Development and Aging, Cracow, Poland, September 17-20 Kapuściński A., Krajewski S., Iwanowski L., Mossakowski M., Ostenda M., Pluta R., Rap Z., Strosznajder J., Szumańska G., Śmiałek M., Zalewska T.

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Symposium of the German Neuropathology and Neuroanatomy Societas, Essen, GFR, October 14-16 Dambska M. Meeting of the International Society for Developmental Neurosciences, Strassburg, France, June 30-July 4 Dambska M. FEBS Course on Modern Micromethods for Proteins Determination. Praque, Czechoslovakia Bicz B. XXVIII International Conference on the Biochemistry of Lipids, Milan, Italy, May 25-June 1 Strosznajder J. Third Meeting of the European Society for Neurochemistry, Bled, Yugoslavia, August 31-September 5 Wideman J. ECBO Conference on Structure Function Relationship in Eukaryotic Cells, Onzain de Seillac, France, May 11-14 Gajkowska B. 31 Meeting of German Neurosurgeons, Erlangen, GFR, April 29-May 7 Czernicki Z. Conference of the European Physics Society, Karlove Vary, Czechoslovakia, September 13-21 Klonowski W. Neurosurgical Intensive Care Symposium, University of Wisconsin, USA, June 12-15 Szewczykowski J. 1st Czechoslovakian Congress for Electroencephalography and Clinical Neurophysiology, Bratislava, Czechoslovakia, May 28-30 Nowak J., Pawłowski G. VII International Congress of the Transplantology Society, Boston, USA, June 28-July 10 Łukomska B., Olszewski W. 2nd Symposium on Experimental Surgery, Meissen, GDR, September 25-26 Olszewski W. Meeting on "Lymphographysche Arbeit Stagung I", West Berlin, December 8-10 Olszewski W.

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Conference of the International Society for Lymphology, Freiburg, GFR, October 11-19 Olszewski W.

Meeting of the Society for Surgical Research, Dresden, GDR, January 25 Olszewski W.

XV Congress of the European Society for Surgical Research, Brussels, Belgium, April 29-May 4 Gałkowska H., Lukomska B., Murawska M., Olszewski W.

IVth Congress of Neurology, Psychiatry and Neurosurgery, Sophia, Bulgaria, October 5-10 Posel Z., Tomczak J.

XXII International Congress of Psychology, Lipsk, GDR, July 6-12 Juczyński Z., Poseł Z., Tomczak J.

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