### POLISH ACADEMY OF SCIENCES MEDICAL RESEARCH CENTRE

### REPORT OF SCIENTIFIC ACTIVITIES 1972-1973

# POLISH ACADEMY OF SCIENCES MEDICAL RESEARCH CENTRE 00-784 WARSAW 36, DWORKOWA Str. 3 POLAND

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#### CONTENTS

Introduction	
THIE OCCUPANT STATES OF THE PROPERTY OF THE PR	,
Obituary prof. J. Konorski	)
Scientific Council Medical Research Centre Polish	
Academy of Sciences 1	1
Staff	3
DETAILED OF SCIENTIFIC REPORTS	
2	6
A. Laboratory of Neurophysiology 2	.0
B. Laboratory of Neuropathology	5
C. Laboratory of Comparative Neurology 6	5
D. Laboratory of Neurochemistry 6	8
E. Department of Neurosurgery	76
F. Surgical Research and Transplantation Laboratory 9	92
G. Laboratory of Applied Physiology 1	22
H. Research Group of School Psychohygiene 1	38
I. Organization Team of the Department of	
Psychohygiene 1	44
J. Electron Microscopy Unit 1	49
K. MEDIPAN Scientific Instruments	154

Cooperation with Foreign Countries	156
Participation of the Scientific Staff of the Centre	
in Scientific Conferences, Congress, Seminars,	
Symposiums and Meetings	177
Varia	210
Name Index of Papers Published and Submitted	
for Publication	214

#### INTRODUCTION

Medical Research Centre of the Polish Academy of Sciences has been founded on July 1st, 1967 by an integration of medical institutions of the Polish Academy of Sciences existing in Warsaw.

The Centre is conducting basic and clinical research in the field of neurobiological sciences: neurochemistry, neurophysiology, neuropathology, neurosurgery, applied physiology and experimental surgery including transplantology.

The Report presents the results of scientific activities of the Centre for the period 1972 - 1973.



Jerzy Konorski 1903-1973

#### OBITUARY

Polish neurophysiology suffered the grevious loss of its distinguished pionier in the death, September 14, 1973, of Professor Jerzy Konorski, head of the Department of Neurophysiology of the Nencki Institute of Experimental Biology of the Polish Academy of Sciences, in the last years also director of that Institute and chairman of the Scientific Council of the Polish Academy of Sciences Medical Research Centre.

Prof. Jerzy Konorski was born December 1, 1903. His research work started in the twenties and involved studying motor conditioned reflexes in dogs. He spent two years /1931 - 1933/ in Pavlov's Laboratory in Leningrad. After his return he organized the Laboratory of Conditioned Reflexes at the Nencki Institute of Experimental Biology in Warsaw. Its work, interrupted by the World War II, was resumed in 1945. The Nencki Institute was reestablished initially in Lódź and later moved to Warsaw.

Under guidance of Prof. Konorski the Department of Neurophysiology developed to a leading research centre in physiology of
animal behaviour, classical and instrumental conditioning, physiology
of perception, physiological mechanisms of memory, control of
drives by the limbic system - the main problems on which Prof.
Konorski was working with his staff.

Prof. Konorski was author or coauthor of numerous papers published in Polish and international journals. His principal ideas were exposed in two books: Conditioned Reflexes and Neuron Organization /Cambridge 1949/ and Integrative Activity of the Brain /Chicago 1967/.

Prof. Jerzy Konorski, was the member of the Polish Academy of Sciences, and member of their Department of Medical Sciences, Doctor Honoris Causa of the Pemsilvania University, the member of the Roumanian Academy of Sciences, and member honoris causa of the American Academy of Sciences and Arts, and member honoris causa and ordinary of many Scientific Institutes in Poland and abroad, distinguished with many prices, honours and medals.

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I, GROMYSZ, D.Sc.

Mamber 01 Polish Paymological Society

K. HIRSHACZYNSKA-CERRO, M. D.

ber of: Poliss Physiological Society

society of Polick leteralst

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M TOKON KI, M. D.

of Sciences

Scientific Director W. KARCZEWSKI, M.D., D.Sc., Prof.

Administration S. SLEDZINSKI, B.L.

Chairman of the J. KONORSKI, M.D., D.Sc. + 14 Sept 1973

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British Physiological Society

American Association for the Advancement of Sciences Societas Europea Physiol. Respiratoriae International

Biological Research Organization

N. DZIADOSZ, M.Sc.

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P. GRIEB, M.Sc. and to would delive

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Member of: Polish Physiological Society

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Society of Polish Intermists
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International Society of Neuropathology

International Brain Research Organisation

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  Polish Biochemical Society
  International Society of Neuropathology

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International Society of Neuropathology
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Polish Society of Neuropathologists

International Society of Neuropathology

Managing Editor of "Neuropathologia Polska"

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International Society of Neuropathology
World Federation of Neurology
Deutsche Vereinigung der Neuropathologen und
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International Society of Neuropathology

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Polish Biochemical Society

International Society of Neuropathology

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Head of the Committee of the Neurological Sciences of Polish Academy of Sciences

18

Corresponding member of the American Association of Neurological
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Member h.c. of British Society of Neurological Surgeons,
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Member of: Polish Neurological Society

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Transplantation Society

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W. ROWINSKI, M.D.

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Polish Supplied Society

Polish Surgical Society

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J. SZMIDT, M.D.

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Research Council, Institute of Protection of Labour
Physiological Committee, Polish Academy of Sciences
Polish Physiological Society
International Working Group on Biological and Cosmic
Medicine "Interkosmos"
Polish National Committee of the International
Biological Programm / Subcommittee of Human
Adaptability/

American Association for the Advancement of Sciences
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Member of: Polish Physiological Society
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Member of: Polish Physiological Society

European Society for Clinical Physiology of

Respiration

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Member of: Polish Society of Mental Hygiene
The Orton Society Towson-Maryland, USA
Z. GAJEWSKA, M.D.

Member of: Polish Society of Mental Hygiene
Polish Society of Psychiatry
The Orton Society Towson-Maryland, USA
J. SIWKIEWICZ, M.A.

Member of: Polish Society of Mental Hygiene
Polish Psychological Society
The Orton Society Towson-Maryland, USA
S. SZMUKLER, M.A.

Member of: Polish Society of Mental Hygiene
The Orton Society Towson-Maryland, USA
B. ZAKRZEWSKA, M.A.

Member of: Polish Society of Mental Hygiene
Polish Psychological Society
The Orton Society Towson-Maryland, USA

#### I. ORGANISATION TEAM OF THE DEPARTMENT OF PSYCHOHYGIENE

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DETAILED OF SCIENTIFIC REPORTS

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Head: W.A. Karczewski, M.D., D.Sc., Professor.

Neural Control of Basic Vital Functions of the Organism.

Studies on the neural control of breathing have shown that increased activity of the central nervous system stimulates breathing and changes qualitatively its response to basic stimuli, such as e.g. carbon dioxide and hypoxia.

According to these data, a new hypothesis of the respiratory control system has been put forward; the role of feed-back mechanisms in breathing during artificial ventilation was demonstrated.

Respiratory reflexes in pathological conditions / pulmonary oedema, airway construction, asphyxia, laryngeal irritation/ were studied and important clinical observations were made.

Neuropharmacological studies revealed the presence of a complex system of excitations and inhibitions within the central nervous system.

#### Neural Control of Breathing

- The role of brain stem in the central and reflex control of breathing.
- Modelling of respiratory centres.

The increase of the central respiratory drive by elevating the body temperature was found to make the central mechanism to a great extent independent of the peripheral factors /vagus nerves/. In the rabbit the reaction to chemical stimulus /CO<sub>2</sub>/ is almost identical in normo-and hyperthermia and does not depend on the integrity of vagus nerves.

The phenomenon of thermal panting was observed to be strictly dependent on the decrease of carbon dioxide tension in the arterial blood and not to appear in normocapnic animals even at the body temperature exceeding 42°C. In the rabbits in which thermal panting has either developed spontaneously, or was evoked by hyperventilation, carbon dioxide exhibits the paradoxical /depressant/ effect previously described in cats and dogs.

#### Conclusions:

The so-called "thermal" panting is not a phenomenon specific of hyperthermia, but represents a secondary effect of the increased central respiratory drive leading to hyperventilation and hypocapnia.

The thermal panting might be directly caused by biochemical changes in the brain /hypoxia and hyperlactatemia related to the decreased cerebral blood flow/.

The studies were performed in cooperation with the Department of Neurosurgery. An original method of reversible blockade of nervous structures /lignocaine microinjections/ has been worked out. Its applications to the pontine- and bulbar structures enabled to obtain the pathological breathing patterns /apneustic and gasping/. The microelectrode technique of unit activity recording also has been worked out for the guinea pig.

Pathophysiology of Artificial Ventilation.

In the studies with the application of a biologically - controlled respirator, data were obtained describing quantitatively the role of integrity of feed back loops respiratory homeostasis in the processes of regulation of breathing rhythm and amplitude.

Analy is of the Reactions of Respiratory "Centres" - to the information from peripheral receptors in various pathological states of the respiratory system.

It was shown that in paralysed and artificially ventilated animals, the effect of peripheral afferentation from pulmonary receptors and intercostal muscle spindles determine the activity pattern of the brain stem respiratory neurons. This relationship undergoes changes with respect to the parameters of artificial ventilation /frequency and stroke volume of the respirator/ and becomes well manifested in the animals under light anesthesia.

Thus, the evaluation of the artificial ventilation level basing on the bioelectrical activity of the phrenic nerve, often proposed in the literature, appears inadequate in light anesthesia, when the peripheral reflex influences may strongly modify the activity of the respiratory "centres".

The studies on the experimental pulmonary edema aimed to evaluate quantitatively the role of the vagus nerves and the phenomenon of tachypnoe accompanying edema.

It was shown, that pulmonary stretch receptors are the main source of pathological stimuli; the role of the subepithelial - and J-type receptors has not been confirmed. The significance of hypoxia as a factor initiating tachypnoe in experimental pulmonary edema has been excluded.

The studies on the airway constriction it have shown, that phenyl-diguanide /an agent stimulating the "J"-receptors/, evokes the adduction of vocal cords infinity and the increase into in expiration of laryngeal resistance to air flow. This symptom was abolished by bilateral vagotomy performed below the origin of the recurrent laryngeal nerves.

Administration of histamine, -stimulating subepithelial recepto s -causes the increase of laryngeal resistance, particularly in expiration. Vagotomy strongly reduces this effect. Isoprenaline, dilating the airways, decreases the laryngeal resistance.

The above described phenomena are accompanied by respective changes in the activity of laryngeal motoneurons.

It was shown also that factors like: stimulation of carotid body chemoreceptors /KCN/, chemoreflexes /veratrine/, irritation of upper airways /ammonia vapours/, pneumothorax and breathing against resistances change reflexely the laryngeal resistance to air flow.

A mathematical method has been worked out for the analysis of changes in the activity of single stretchreceptors according to the magnitude and gradient of stimulus. Preliminary results indicate, that pulmonary stretchreceptors respond linearly to changes of the respiratory volume.

It was shown that during the first stage of asphysia, the impulsation of phrenic motoneurons increases-whereafter-their gradual decrease is taking place, sometimes preceded by continuous discharges. Chemoreceptive deafferentation prolongs the period of maintainance of neuronal functions, as well as the time of restitution of their activity. In the restitution period, impulsation of the phrenic nerve may decrease.

Neural Control of Respiration and Effect of Anesthetic Drugs on Central Neurons.

Studies on the Hering-Breuer inflation and deflation reflex: - In cooperation with dr Guz's group from Charing Cross Hospital.

Medical School in London, using the cardiopulmonary bypass technique it was found that vagus nerves, beside the effects of

Hering-Breuer's type, also transmit tonic activities, the level of which is determined by the duration of the expiratory phase and thus by the frequency and amplitude of breathing.

These results open quite new perspectives for evaluation of the role of vagus nerves in the regulation of breathing, particularly in view of the results obtained by means of the biologically controlled respirator.

Effect of Widely Used Anesthetic Agents on the Reaction of Respiratory Neurons of Brain Stem.

The effect of chloralose, urethan, pentone and epontol on the bioelectric activity of pontine neurons was examined. An enhancement of inhibitory processes was observed, the intensity of inhibition depending on the depth of anesthesia.

In a similar experimental set up the effect of hypercapnia was followed. These studies confirmed the earlier observations, that the sensitivity of the respiratory system to CO<sub>2</sub> decreases under the influence of anesthetic drugs. This is particularly strongly pronounced for frequency responses.

Neural Control of Circulation.

Mechanism of Regulation of Cardiac Function in Physilogicial and Pathological Conditions.

These studies dealt with the cardio-vascular reactions evoked by increased intracranial pressure. A significant increase of the release of important active substances /catecholamines/ and secondary changes of the arterial pressure were noted. The recently undertaken studies on prostaglandines revealed their crucial role in the auto-regulation of renal circulation.

Studies were initiated aiming to establish the factors responsible for the stimulation of sensory endings in the heart and for reflex activation of the adrenergic reaction in the early stage of heart infarct. Preliminary experiments being performed at present concern the effect of various concentrations of lactic acid applied epicardially or into the heart muscle, on the heart function, cardio-vascular reflexes and secretion of catecholamines. The results obtained hitherto are inconclusive.

In the experiments performed on cats under nembutal anesthesia, the effect of chronic intracranial hypertension on the secretion of endogenic catecholamines was studied. Two groups of experiments were performed. In the first group, the increased intracranial pressure was produced by supradural baloon implantation in the fronto-parieto-temporal region /model of supradural hematoma/. In the second group, 5 ml of the animals own blood were injected into the subarachnoidat space on the base of the skull /model of subarachnoideal hematoma/. Secretion of endogenic catecholamines was assayed continuously in the circulating blood, by means of a biological method.

The results revealed the appearance of adrenergic reaction in both models of experimental intracranial hypertension. Significant differences were observed, however, concerning both the course and character of changes according to the mode of producing the hypertension. In the first group /baloon implantation/ the adrenergic reaction appeared rapidly already in the first primates of hypertension and was manifested by the secretion and was manifested by the secretion of large amounts of adrenaline into the blood. This was accompanied by a marked, but short-lasting increase of arterial pressure. Thereafter the adrenaline secretion decreased, but still remained elevated. Partial decompression by reducing the volume of the baloon, -as a rule-caused inhibition of the adrenaline

secretion, refilling of the baloon, however led again to the increased secretion and to transient pressive effects. Bilateral adrenalectomy abolished the effects indicating, that in this model of intracranial hypertension, the selective stimulation of the secretory function of adrenal medulla took place.

In the second group, no such rapid increases of arterial pressure were observed and the adrenergic reaction was manifested by a slow increase of the noradrenaline level in the blood. Noradrenaline was being released from the extraganglial sympathetic endings, since adrenalectomy did not abolish this secretory effect. Only not earlier that after 3-4 hrs of hypertension, the enhanced secretion of noradrenaline was observed to be accompanied by the increased adrenaline secretion from adrenal medulla. The above results indicate, that depending on the cause, rate of development and duration of the intracranial hypertension functional stimulation of the adrenergic system may find expression either in the increased adrenaline secretion from adrenal glands, or by the enhanced noradrenaline secretion from sympathetic endings, or by the secretion of both amines simultaneously.

The second part of the work dealt with the structural and histoenzymatic changes appearing in the central nervous system in the conditions of intracranial hypertension and their possible relation to the concomitant adrenergic reaction. The results of these studies are in elaboration.

Moreover, a new series of studies was undertaken dealing with the role of prostaglandins in regulation of circulation /in collaboration with the Department of Pharmacology, Royal College of Surgeons of England, London/.

.The production and release of prostaglandins in kidney were shown to be one of the factors responsible for the increased flow in the

renal artery in reactive hyperemia. Endogenic prostaglandins were also shown to regulate the renal blood flow according to fluctuations, of the arterial pressure. Preliminary results were obtained suggesting that prostaglandines participate in dilatation of coronary arteries. Studies were undertaken aiming to find out whether or not acute heart muscle ischemia is a factor facilitating local generation of prostaglandins.

The problems studied in the Department in 1973: Neural Control of Basic Vital Functions of Organism. Concise presentation of the results:

The studies on the neural control of breathing revealed a significant reduction of the cerebral blood flow to be at the base of the respiratory disturbances in hyperthermia. The pathways and mechanism of regulation of the airway lumen were examined and the brain stem respiratory regions were localized. The studies may find clinical application /especially in anesthesiology and reanimation, in pulmonology, in neurosurgery/.

In the studies on the neural control of circulation the participation of endogenous prostaglandins in hyperemia in skeletal muscles as well as the influence of the former on the function of other vasoactive substances were stated.

Neural Control of Respiration. The role of brain stem in the central and reflex regulation of breathing.

In the studies on the polypnoeic states it was found, that hyperventilation leads to a marked increase of the lactate level in the cerebrospinal fluid- by 1,02 mg%/min in normothermia, by 2 - 1 mg%/min in hyperthermia with hyperphoea and by 4,7 mg%/min in hyperthermia with polypnoe/thermal panting/. Hyperventilation decreases the cerebral blood flow /in particular the cortical one/by nearly 50% as compared to normocapnia. Long-term hyperventi-

lation shifts the pH of blood towards the alkaline values and that of the cerebrospinal fluid - towards the acid values. It is postulated that the cerebral blood flow disturbances produced by hyperventilation lead to cellular hypoxia, of which the effects are aggravated by hyperthermia. Halotane anesthesia does not affect the dynamics of the reaction /respiratory rate of about 700/min was obtained/, whereas NLA blocks the ventilatory reaction to hyperthermia.

The respiratory effects of electric stimulation of area preoptica and nucleus reticularis tegmenti were shown to decrease with the increase of body temperature and p CO<sub>2</sub>. It was found that blocking of the dorsal group of brain stem neurons leads to the deceleration of the respiratory rhythm; blocking of the ventral group in the medulla inhibits the activity of the contralateral phrenic nerve; blocking of the central group in the pons produces apneustic breathing and clocking in the region of the bulbo-pontine junction leads to apnoea, which /with the increase of pCO<sub>2</sub> and drop of pO<sub>2</sub>/ develops to "gasping":

Preliminary studies of the changes of respiratory rhythm, amplitude of phrenic nerve discharges, minute ventilation and the inspiration exspiration ratio, depending on the adrenaline and angiotensin induced changes of the arterial pressure, were carried out. The respiratory effects of acute hypertension were found to depend on the way of its induction and on its absolute value. It was further stated, that the so-called: "postadrenaline apnoea" has a reflex character and may be related to the changes in pulmonary compliance.

A reversed proportional relationship was found between 'the duration of respiratory inhibition in the Hering-Breuer reflex and the  ${\rm CO}_2$  pressure in blood. The time of inhibition is postulated to be proportional to the tracheal pressure and to depend on  ${\rm pCO}_2$ .

It was shown, that the increase of laryngeal resistances for air flow in the anaphylactic shock does not depend on the contimuity of vagus increase; hypoxia and hypercapnia decrease the resistances, and hyperthermia abolishes them completely. The survival of rabbits in the conditions of chronic vagotomy was studied and the average time of survival was 4 weeks. Hyperthermia was found to modify and even to reverse the respiratory effects of excitation of vagus nerves; a phenomenon of particular interest was the paradoxal acceleration of the respiratory rhythm in response to inflation.

It was stated that the activity of pulmonary stretchreceptors is controlled by changes in the airway musculature tension. The relationships between the magnitude of stimulus and the receptor activity were described mathematically.

Neural Control of Circulation. Mechanism of Neural Control of Heart Function in Physiological and Pathological Conditions.

The participation of endogenous prostaglandins in reactive and functional hyperemia in the skeletal muscles as well as the modulating effect of prostaglandins on the reactivity of the vascular bed in the working skeletal muscles on the action of other vasoactive substances /noradrenaline, acetylcholine/ were stated.

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# B. LABORATORY OF NEUROPATHOLOGY Head: M.J. Mossakowski, M.D., D.Sc., Professor.

The problems studied in the Department, in 1972-1973, were a continuation of the investigations carried on 1971.

Effect of Oxygen Insufficiency on the Central Nervous System.

The studies dealt with changes in the central nervous system in carbon monoxide intoxication. The experiments performed both on rats and in tissue cultures revealed a selective vulnerability to CO of particular anatomical formations and cellular elements. Notwithstanding the generally accepted views, it was demonstrated that the demyelination following CO intoxication appears independently of brain edema and is causally related to selective degradation of oligodendroglia. Threshold values of CO intoxication, producing no histological changes in the nervous tissue, were shown to lead to metabolic disturbances becoming manifest with the increase of glycogen content and glycogen metabolizing enzymes activity, changes of adenine nucleotides content and short-term inhibition of protein biosynthesis in the polypeptide chain initation step. Repeated CO intoxication with a subhistological dose was found to lead to diminution, and later to disappearance of distrubances in protein synthesis asthe consequence of adaptation of the protein synthesizing system. These metabolic changes are accompanied by a transient decrease of

active amino acids transport to the brain. The histochemical studies confirmed the structural differentiation of the vulnerability to CO intoxication and disclosed a decrease of aerobic glycolysis, with a concomitant increase of anaerobic glycolysis and activation of glucose metabolism in the Leloir cycle.

Studies on tissue culture confirmed the selective sensibility of oligodendroglia to the action of CO and showed that the degree of impairment of the particular cell elements is a function of the applied dose, of the time of exposure to CO, of the degree of maturity of the cellular elements and their different susceptibility. The morphological changes in the particular cell types are of the same kind as in the case of anoxic hypoxia, including intra-astrocytic accumulation of glycogen. The appearance of polysaccharide in extracorporeal culture is indicative of disturbances of intracellular glucose metabolism but not of its transport.

Electron- microscopic examination of glial culture subjected to short-term anoxia revealed a marked differences in the ultrastructural picture, depending on the degree of maturity of the cells.

The observed accumulation of glycogen, increase of the number of free mitochondria and free ribosomes and of gliotubules and gliofibules should be considered as compensatory phenomena. In conditions of transplacental hypoxia and ischaemia of foetuses, a decrease of oxygen metabolism of the nerve tissue was observed, persisting after birth. This indicates that impairment occurring during fetal life increases the vulnerability of nervous system to the physiological stress pertinent to birth. These disturbances are accompanied by a delay of maturation of the particular brain structures and the appearance of slight structural damages, the distribution of which points to a topographic differentiation of vulnerability to hypoxia, just as in the mature brain.

In 1973 the basic part of studies concerned the consequences of experimental ischaemia connected with a decrease of blood pressure. The experimental model applied was found to produce disturbances of cerebral circulation, with a decrease of blood flow in the oligenic period its transient increase after return of the blood pressure to the normal value, and again a decrease below normal persisting for several hours. Examination of the cerebral microcirculation revealed that the blood flow changes are accompanied by acute cerebral ischaemia with consecutive reactive hyperaemia and finnaly passive hyperaemia, preceding the normalization period. These disturbances reflect disorders of anatomic regulation of cerebral blood flow and might be responsible for the structural damage to the tissue.

The post-ischaemic blood - brain barrier disturbances were of focal character, without leading to generalized brain oedema. This found expression in histochemical abnormalities with in the vessel tissue junctions. Both during ischaemia and in the postischaemic period, disturbances of nervous tissue metabolism were shown to appear in regions exhibiting no changes. These metabolic disturbances were manifested by a decrease of the oxido-reducing enzymes activity and by on increased content of glycogen and of the glycogen metabolizing enzymes. The character of these changes was identical to those observed in other types of hypoxia, but the dynamics was quite different. Ischaemia of the tissue led to a transient decrease of protein synthesis at the polypeptide chain initiation level.

Studies of the cell-enriched fractions revealed that ischaemic hypoxia, simple hypoxia and carbon monoxide intoxication cause a reduction of protein biosynthesis in neurons and at the same time a hypercompensation of this process in the glial cells. An early decrease of glial protein synthesis was observed only in carbon monoxide intoxication, this being probably due to the cytotoxic activity of CO.

Measurements of oxygen consumption by single nerve cells in acute carbon monoxide intoxication "in vivo" revealed a decrease of oxygen metabolism in the neurons. This might be the cause of the metabolic and structural disturbances in the tissue.

The "in vitro" studies on the effect of short-term anoxia on the neurons tissue demonstrated that the most severe lesions involve the Schwam cells. This may be the cause of both the impairment of myelination.

Structural studies of the brain stem in newborn, who in the foetal life survived an anoxic incident, showed changes in the reticular formation. These changes might contribute to the deteriorated ability of these newborn to adapt themselves to altered enviromental conditions.

### Exogenic Toxic Encephalopathies,

The studies on our paint enecephalopathy, performed with application of low doses of glycoside not producing generalized convulsive seizures, evoked characteristic changes in the astroglia, consisting in the accumulation of glycogen deposits, disturbances of the activity of glycogen metabolizing, and Krebs-cycle enzymes and some hydrolytic enzymes. Selective localization of these disturbances in the grey structures in areas distant from the site of glycoside administration and showing no structural changes is indicative of rapid diffusion of our paint in the nerve tissue and of its selective action on the astrocytes of the grey matter, leading to of cytotoxic brain oedema.

The studies on transplacental alcohol encephalopathy in dogs revealed, that administration of alcohol to pregnant animals in the period after organogenesis in foetal brain had been completed, produces only insignificant structural damage in the brains of the newborn. These changes involve to an equal degree neurons and

glia and mostly consist in mitochondrial damage. A slower increase of the cholesterol esters, found in biochemical studies, may be indicative of retardation of the myelination process, which is not detectable by histological methods.

The studies on vasogenic oedema, performed on the compressive model, showed the dependence of the changes on local and general haemodynamic disturbances, a transient increase of the permeability of the vascular walls to protein tracers and consecutive disturbances of the histochemical pattern of the nerve tissue.

Postirradiative oedema was found to be characterized by a statistically significant decrease of the transport of low-molecular weight components, and in the electron microscopic picture, by the dilatation of the intracellular spaces and by the increase of the pinocytic function of the endothelium. Comparison of both types of vasogenic oedema revealed a different character of their pathogenetic mechanisms despite one common feature which was the impairment of vascular permeability.

Studies performed on a number of models of acute brain oedema revealed different pathomechanisms involved in this process. In the model of compressive brain oedema, simulating supradural haematoma in human pathology, generalized disturbances of the blood-brain barrier permeability were demonstrated to follow haemodynamic disorders and venous stasis. The picture of changes is suggestive of the coexistence of two types of tissue impairment - of that pertinent to hypoxic-ischaemic distrubances and another, characteristic of blood-brain barrier disruption with the consequent tissue reaction to oedema.

In acute postirradiative oedema the morphological manifestations of blood-brain barrier disruption included: opening of "tight-junctions", endothelial swelling, increased micropinocytosis and swelling,

increased micropinocytosis and swelling of perivascular astrocytic processes.

Cytotoxic oedema, as studied in the ouabaine encephalopathy model, was characterized by an increase of the brain water content without impairment of the blood-brain barrier.

The glycoside-induced disturbances of permeability of the cell membranes lead to irregularities of glucose metabolism persisting longer than oedema and structural changes.

Studies of transplacental viral and bacterial inflammations revealed that the Sindbis virus, nonpathogenic to adult animals, may pass through the placenta, producing meningitis in foetuses, the character of damage depending upon the degree of maturity of the nerve tissue. A similar dependence was observed to exist in inflammatory processes produced by transplacental infection with Streptococcus aureus.

Biological Properties of Neuronal and Glial Cells in Normal and Pathologic Conditions.

Studies on primary hepatic gliopathy revealed on ultrastructural manifestation of increased blood-brain-barrier permeability. This confirms the hypothesis that impairment of the blood-brain barrier is a factor facilitating the passage to the CNS of compounds damaging the nervous tissue. For the first time in the neuropathological literature the ultrastructure of Alzheimer cells has been described and the stages of their formation from astroglia have been followed.

The studies in vitro revealed that called hepatic glia, obtained by using sera from patients with hepatic coma and by administration to the culture medium of copper and ammonia, shows identical ultrastructural features, expressing the accumulation in glial cells of a substance of mucopolysaccharide type.

The observation in the Opalski' cells cytoplasm of copper deposits supports the hypothesis of the pathogenetic role of copper in the development of hepatic encephalopathy.

The participation of copper in the development of tissue lesions in hepatic encephalopathy may also be suggested from the increased copper content in the brains of patients who died in hepatic coma in the course of acute liver lesions in which this increase precedes the formation of the typical morphological syndrome. The results of observations carried out on tissue cultures with a number of chemical inhibitors of the Krebs-cycle enzymes revealed that, irrespective of the character and type of the noxious factor, the disturbed detoxication of ammonia is the factor responsible for the development of hepatic gliopathy.

Secondary gliopathies: gamma-irradiation of a glial tissue culture was shown to lead to characteristic changes in the most radio-sensitive element of astroglia.

Studies on beta-glucuronidase activity in the nervous tissue and in glial tumours revealed an increase of the enzyme activity related to both anabolic /degradation, differentation/ and catabolic /cell degeneration/ cellular processes. Ultrastructural studies on chemically induced glial brain tumours revealed their essential similarity to the respective human tumours. Gliomas of astrocytic origin were characterized by the presence of intracellular virus-like structures.

Studies on protein synthesis in the brain in stages preceding the formation of chemically-induced tumours involved intracerebrally implanted methylocholantrene or ethylnitroso-urea acting transplacentally on the foetal brain as inducing agents. Methylocholantrene was shown to produce disturbances of both the amino acid transport into the brain and its utilization in protein synthesis. The disturbances of amino acid transport and protein synthesis following transplacental administration of ENU are characterized by a different dynamics and might be related to the appearance of microcephalia.

Studies on the cell and myelin-enriched fractions revealed their antigenic differentiation. The neuronal fraction was found to contain

brain-specific antigens and one antigen showing only a partial identity with the antigen common to other organs.

The glial and myelin fractions contain, beside organ-nonspecific antigens, one specific antigen present only in the myelin fraction and another organ-specific antigen common to glia and myelin.

The "in vitro" studies revealed, that glutamate and alfa-oxo-glutarate prevent the development of hepatic gliopathy. Demonstration of the role of disturbances of ammonia detoxication in the development of hepato-encephalic pathology may be of practical significance in medical treatment of acute livre impairments.

An increased non-specific t-RNA-methylase activity, considered to be characteristic of human gliomas, was found to appear in the brain tissue in the period preceding tumour formation as well as in chemically induced animal brain tumours, irrespective of their histogenetic origin. In addition, in the chemically induced neoplasmas of the nervous system, marked differences in the mucopolysaccharide content were noted, the content depending on the rumour type.

Examination of mucopolysaccharide allows to distinguish between reactive and neoplastic glia. This observation could serve as base for differential diagnostics in clinical neurooncology. Microcephalia, produced by transplacental action of ethylnitroso-urea, was in later periods characterized by the presence of disseminated demyelination foci. This process be used as a model for studying primary myelin degradation in the central nervous system.

Studies on the antigenic properties of the nervous tissue in ontogenesis revealed changes in the electrophoretic properties of organ-specific and organ-nonspecific antigens in the course of development and maturation of the tissue. Immunofluorescent studies on the localization of organ-specific antigens showed their relation

to the glial tissue, mostly to the astrocytes both in the grey and white formations of the brain.

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# C. LABORATORY OF COMPARATIVE NEUROLOGY Head; E. Osetowska, M.D., Professor,

Hereditary disease of the central nervous system: the genetic, clinical and morphological studies on the model of rabbits with hereditary paralytic tremor/genetic symbol = "pt" rabbit; sex-linked inheritance/.

Further investigations proved that with the experimental mating between carriers and affected males; affected females and males change the clinical features. In the whole affected litter the disease becomes unevenly expressed; some animals may have hardly noticeable tremor and a very mild spastic weekness in the extremities. In the same litter other rabbits develop the worsening of the tremor and complet spastic paralysis. Nevertheless the rabbits with the rudimentary clinical syndrome can transmit to their offsprings the full heavy clinical course. The stock of about 150 rabbits, descending from the first cached carrier chinchilla-rabbit and different health chinchilla-rabbit-fathers is kept under regular clinical observation. The recent observations concern the VIIIth and IXth generation. The correlative histopathological study shows the pathognomonic changes in some cases as early as in the second day of noticeable tremor. The full neuropathologic picture appears regulary in the quadriparalytic rabbits. In about 50% verifications the changes of the retinal

neurone, the optic nerves and optic pathways are observed. The calcified neurone is still the most characteristic feature of the cerebral lesions. These neurones with strong Kossa and alizarine red-reactions appear in basal ganglia, reticular formation of the mesencephalon and medulla, in motor-nuclei of the cranial nerves. No interstitial or perivascular calcifications were observed.

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Nosówka nerwowa i toksoplasmoza czyli o interferencji dwóch różnych procesów zapalnych w mózgu. /Distemper and Toxoplasmosis-the-Interference of two Different Inflammatory Cerebral Processes/.

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D. LABORATORY OF NEUROCHEMISTRY Head; A. Gromek, D.Sc.

Intracellular Mechanisms Regulating the Metabolism of Central Nervous System Cells in Normal and Pathological Conditions.

The chemistry of intermediary processes occuring in nervous tissue cells is one of the basic research directions in neurochemistry. Studies concerned with mechanisms underlying the regulation of carbohydrate - energy metabolism, including the specific for the central nervous system transmitter metabolism, provide a better understanding of the complexity of physiological reactions occuring in the mervous system in normal and pathological conditions.

The hypoxia of the nervous tissue leads, as in other organs and tissues, to many alterations in the general cell metabolism.

The mitochondrial oxidative phosphorylation is in brain, pratically, the main source of ATP.

Oxygen defficiency / postdecapitative ischemia and anomia/ produces, as compared to the control, a decrease of oxygen utilisation in state 3, with a simultaneous decrease of respiratory control and phosphorilation yield coefficients - RCI and ADP/O.

Analogical results were obtained on cats in conditions of increased intracranial pressure /brain edems/. Disturbances of oridative phosphorilation are accompanied by a distinct increase of the content of free fatty acids and a decrease of the level of phospholipids. A

damage of the biochemical function of mitochondria was observed also in experiments "in vitro" in the presence of exogenous fatty acids: palmitate and oleate.

Fatty acids play an important role in the energy metabolism of the cell. They may be utilized as respiratory substrates, but are at the same time responsible for the uncoupling of oxidative phosphorilation, inhibit the translocation of adenine nucleotides and the gly-colysis, and in high concentrations disrupt the structure of mitochondrial membranes.

The alterations of the structure of mitochondrial membranes are expressed by the exhibition of activity and the releasing of mitochondrial enzymes.

It was demonstrated that in conditions of hypoxia, occurs an exposition of the rise of glutamate dehydrogenase activity and a partial release of alanine aminotransferase and NADP-dependent isocitrate dehydrogenase as well as of mitochondrial hexokinase to the cell's cytoplasm.

The accumulation of free fatty acids during hypoxia and the resulting damage of the structure of mitochondrial membranes may be responsible for the occurring changes in enzyme localization. This is supported by experiments "in vitro".

The NADP-dependent isocitrate dehydrogenase, localized mainly in the cytoplasm, participates in the newly described cytoplasmic process of citrate oxidation.

aconitase
citrate ------ isocitrate

NADP dehydrogenase

oxoglutarate ------ oxaloacetate

aspartate glutamate

The increase of NADP-dependent isocitrate dehydrogenase activity, observed in conditions of hypoxia, may be resulting from the release of mitochondrial enzymic protein to the cytoplasm, or from the activating effect of adenine and pyridine nucleotides. It was demonstrated on a 15-fold purified enzyme preparatio-, that these compounds exerce a regulative effect on the enzyme activity depending upon their concentration.

The change of the content of adenine nucleotides /AMP, ADP and ATP/ during hypoxia influences significantly the utilisation of glucose and the production of lactic acid. Increasing ATP concentrations /1-10 mM/ causes an intensification of glucose utilisation and of lactate production in guinea-pig brain homogenates. The effect of action of adenine nucleotides is localized mainly at hexokinase and phosphofructokinase steps and undergoes significant modifications in the presence of citrate.

Herokinase is localized mainly in the cytoplasmic, synaptosomal and the mitochondrial fraction of central nervous system cells. It was demonstrated that the activity of mitochondrial hexokinase, associated mainly with external mitochondrial membranes, may be released to the cytoplasm in the presence of increased concentrations of glucose-6-phosphate and fructose-6-phosphate, what happens during hypoxia.

The observed effect of glycolysis stimulation by mitochondria may be associated in part with the activity of hexokinase. The effect of releasing the enzyme from mitochondria to the cytoplasm may also depend on the acidification occurring during hypoxia, as well as on the action of free fatty acids upon the structure of mitochondrial membranes, however the inhibition of the enzyme by these compounds must be considered.

The demonstrated increase of glucose-6-phosphate dehydrogenase activity during hypoxia is associated in a large extent with a fall in

the amount of SH-groups and the rise of S-S-groups, which are responsible for the activation of glucose-6-phosphate dehydrogenase and the increase of glucose utilisation in the pentose phosphate shunt.

The disturbances of oxidative phosphorilation processes and of the activity and localization of enzymes which occur in conditions of oxygen defficiency are in a large degree abolished if animals are submitted to nembutal action before hypoxia. Anesthesia is a highenergy state of the cell, characterised by a decreased ATP utilisation.

It may be assumed that, taking the well known effect of anesthetics on the activity of phospholipases, the increased ATP level may facilitate the resynthesis process of mitochondrial membrane phospholipids.

On the other hand, in conditions of nembutal anesthesia, a distinct increase of free acetylcholine level was observed. Experiments "in vitro" show that acetylcholine diminishes the effect exerced on mitochondria by exogenous free fatty acids.

In the process of ageing of mitochondria, in the presence of acetylcholine, a small amount of released free fatty acids and a decreased swelling of mitochondria was observed.

It may be assumed that the mechanism of acetylcholine action is associated with the activation of the resynthesis process of phospholipids. This compound activates the incorporation of <sup>32</sup>P-phosphate into the phospholipid fraction.

In the collaboration with the Clinic Biochemical Department of the Pathology Institut of the Medical Academy in Gdańsk /Head: S. Angielski, M.D., prof./ in 1972-1973, the following problems were searched:

The demonstrated inhibitory effects of glutamate on ATP-dependent citrate liase, point to a close relation of the cell's glycolytic activity

to the amino acid metabolism, oxidative phosphorilation processes, lipid and fatty acid metabolism as well as to that of acetylcholine.

The studies included the subject: "Regulation of pyruvate- and oxoglutarate in mitochondria of the central nervous system" were concentrated on the problems of specific inhibition of ATP-dependent citrate liase in rat brain by 1-glutamate and on determining the kinetic properties of rat brain aminotransferases.

A method of isolation of citrate liase from rat brain has been worked out and, for the first time in the literature, this enzyme was shown to undergo specific inhibition by 1-glutamate, but no by other natural amino acids.

A complex of l-glutamate with magnesium was demonstrated to be the active form of the inhibitor and to act competitively relatively to ATP.

The inhibitory action of l-glutamate may represent a physiological mechanism of suppression of fatty acids synthesis in the brains of adult animals.

The studies on the kinetics of aminotransferase revealed the stimulatory effect of bicarbonate buffer on alanine aminotransferase activity and the inhibitory effect with respect to aspartate aminotransferase. The results indicate that the physiological buffer does neither produce changes in the kinetics of the reaction nor in the mechanism of function of alanine aminotransferase in brain; it might, however, play a significant role in regulating the enzyme activity in physiological conditions, as well as in alkalosis and acidosis.

In addition, a method of simultaneous determination of coenzyme A and citrate in the biological material has been worked out.

The following was shown;

1. In all the models of hypoxia, structural and functional disturbances of mitochondira were observed. They appeared to be related

- to the desintegration of phospholipids and accumulation of free fatty acids.
- Reversible impairment of the structure of mitochondrial membranes results in the decompartmentation of mitochondrial enzymes /IDH-NADP, alanine aminotransferase and hexokinase/, which markedly alters the endogenous regulatory mechanism of glucose metabolism.
- 3. Nembutal anesthesia prevents these disturbances, whereas acetylcholine might be one of the factors responsible for the protective effect of anesthesia by stimulating the resynthesis of mitochondrial membrane phospholipids.
- 4. The results, in several points original /evidence of the presence of cytoplasmic citrate oxidation, translocation of mitochondrial enzymes/, contribute to the understanding of pathogenesis of physiological disturbances of the CNS cells in pypoxia.
- More general consideration of the results in correlation with morphological and histochemical observations may lead to their practical application in clinical prophylactics.

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75 Se-selenomethionine incorporation into the CNS Proteins of Rabbit with regard to its Subcellular Localization.

Neuropat Pol 11, 1973, 373-387

#### E. DEPARTMENT OF NEUROSURGERY

Head: A. Kunicki, M.D., D.Sc., Member of Polish Academy of Sciences, Prof.

Pathogenesis, Treatment and Prevention of Brain Oedema

- a. Intracranial hypertension continues to be a very dangerous complication of various brain diseases. This is why continuos long-term measurement of ICP level and its proper evaluation are of great clinical importance. For that purpose a new system for the automatic long-term recording of ICP and others physiological parameters has been designed in our laboratory. The dynamics and physiological levels of lumbar pressure were observed, recorded and evaluated in 30 patients. The pressure in patients remaining in horizontal position ranged within the limit 2-20 mm Hg. Most of the measurements were in the range 5-12 mm Hg. The pressure was found to undergo periodic fluctuations, usually within 10% of the mean pressure amplitude.
- b. The effect of prolonged administration of Mannitol on intracranial pressure was evaluated. The studies were performed on thirty patients after neurosurgery with symptoms of increased intracranial pressure.

Immediately after the operation each patients was monitored for about 3 days. The ICP was sampled every 100 sec by the automatic

recording system. The data were processed off-line by a minicomputer.

According to the results obtained to-date, sets of statistical parameters such as histograms, mean values, or standard deviation as measured for consecutive 30-second sampling periods seens to be highly useful in patients state evaluation.

Administration of Mannitol at a dose of 0,6 g/kg/h for a period of three hours causes an average decrease in ICF of 20%. By means of statistical analysis it was possible to eliminate some of those ICF changes which were not directly related to the effect of Mannitol. c. The aim of another study was to find some indices that would facilitate intracranial pressure evaluation. The relationship between the mean value of ICP, as calculated for consecutive 30 second intervals, and the corresponding standard deviations was investigated. It was found to be a good index of intracranial pressure decompen-

Just by looking at the plot the above mentioned relationship can be divided into two zones with significantly different slopes. One of these zones is considered to be a danger zone. The on-line system now being developed will make possible the continuous updating of this relationship. This would make it possible to act quickly if the patient's ICP level moves into the danger zone.

sation.

d. Experimental studies on intracranial pressure assymmetry as measured bilaterally in the epidural space were performed in 40 cats.

The intracranial pressure was increased by means of unilateral expansion of an epidural balloon. For measurement of epidural pressure a special pressure relay was prepared and applied. This relay consists of a metal ring tightly screwed into the cranium and containing a multi-hole plug enabling an efficient and occlusionless

connection of the pressure transducer with the epidural space. The above epidural device is the first of a series of similar devices which are being developed for application as pressure relays in neurosurgical intensive-care units.

The studies revealed a marked variability in the epidural balloon pressure at a constant balloon volume and the appearance in some animals of significant differences in the epidural pressure between the right and left side.

e. Effect of cranio-cerebral traumas in boxers on the nervous system function.

Comparative psychological and electroencephalographic examinations were carried out on 20 persons practicing boxing. After one year, control examinations were performed. In view of the limited number of comparative examinations no definite conclusions can be drawn as regards changes in cognitive and emotial processes. Preliminary observations allow to assume that traumas decrease the memory's efficiency and raise the level of neuroticity. This problem along with a review of the literature was presented at a scientific session of the Department of Neurosurgery and a paper was prepared for publication.

Control EEG examinations performed after one year of practicing boxing showed a great variability of EEG records. Therefore additional control examinations are necessary to evaluate the possible relationship between cranial traumas and EEG patterns.

Studies of the Effect of Brain Lesions produced by Stereotactic Procedure on the Emotional States, Memory and Bioelectric Activity of the Brain.

a. Studies of emotionality changes in patients subjected to stereotactic operations because of temporal epilepsy.

Comparative studies were performed during both the pre- and postoperative period in 40 patiens not responding to drug therapy, in
whom freezing of the dorso-medial part of amygdala was carried
out. The postoperative period of observation ranged from 1 to 5
years in 25 patients, the average value being 3 years.

In all the patients states of fear and attacks of fury and aggression
receded completely. The patients could control their behaviour
better, and the frequency of attacks showed a decreasing tendency.
Five patients had no attacks and there was no need for them to take
any drugs.

In the remaining patients the frequency of epileptic seizures decreased, which made possible a gradual reduction of the applied doses of anticonvulsive drugs. The patients in whom intelligence quotient examinations had not indicated significant mental deterioration in the preoperative period /60% of cases/, underwent resocialization readily more and could resume their interrupted studies or work. b. Memory examinations in patients after streotactic impairment of amygdalic bodies, hippocampus, thalamic nuclei and gyrus cinguli.

Comparative examinations during the pre- and post-operative period were made in 9 amygdalotomized patients and in 8 patients subjected to thalamotomy. The limited number of examinations performed was due to a small number of patients who underwent stereotactic treatment this year. The patients in whom the stereotactic impairments involved the ventrolateral nucleus showed no memory disturbances.

Analysis of the results of examination of 40 patients operated previously /1-5 years/ revealed that the most significant improvement as regards direct repetition occured in patients with a non-lowered intelligence quotient. No improvement of direct repetition was obser-

ved in the group of mentally deteriorated patients who had been subjected to temporal lobe resection.

Amygdalatomy does not decrease the ability to learn verbal material by heard, it also leads to improvement of this function after previous deterioration by active epileptic process. The improvement involved 82,5% of the patients.

c. Studies of the functions of amygdaloid nucleus neurons.

This subject has been studied experimentally for one year in cooperation with the Department of Neurophysiology, Nencki Institute, Polish Academy of Sciences /prof. Tarnecki M.D., prof. Fonberg M.D./. The problem of the present investigations is: "Studies of the bioelectric activity of neurons in cellular populations of amygdaloid nuclei in cat brain". The studies were carried out on 27 curarized cats under Nembutal anesthesia and controlled respiration using a microelectrophysiological method. The activity of 117 neurons was recorded.

As to the characteristics of spontaneous activity, two populations of neurons could be distinguished, characterized by a different frequency of spontaneous discharges and different localization. Electric stimulation of various hypothalamic nuclei produced four discharge patterns in the amygdaloid nuclei. They are either of stimulatory or inhibitory type, and differ in latency and duration. The results of the investigations are planned to be published in more detail next year.

d. Changes of the bioelectric activity of the brain following cryosmygdalotomy in epileptic patients.

Comparative examinations were carried out in 20 patients operated in the last 5 years. In most of the patients positive changes in the EEG record were noted. The abnormality of the EEG was found to decrease in respect of both frequency of discharges, and degree of

generalization. The regularity and quantitative participation of alpha rhythms were increasing. These data, plus data to be obtained from another, next year will be published in more detail. In two cases of epilepsy with severe disturbances of behaviour and emotionality complete resocialisation was achieved. The EEG and clinical symptoms were discussed at a joint meeting of the Polish Society of Neurosurgeons and the Polish Neurogical Society.

Gnostic disturbances produced by lesion of cerebral hemispheres.

It is a continuation of our studies of higher nervous activity, which for many years have been conducted in collaboration with the Nencki Institute of Experimental Biology.

a. Studies of visual and auditory perception in normal and pathological conditions in cooperation with Asst.prof. Budohoska, M.D., Department of Perception, Nencki Institute of Experimental Biology/.

These studies deal with Perception and recognition of simple visual and audiatory elements. The studies aim at detecting errors in the recognition of simple auditory stimuli. At present the method is being tested on healthy people and on patients, i.e. with disturbed auditory perception.

In this way it will be possible to develop methods of evaluating auditory recognition and kinestetic engrams.

b. Studies on child aphasia in children with deteriorated hearing /in cooperation with the Department of Diagnostic Rehabilitation, Institute of Mother and Child/.

These studies were carried out in children with a high degree of hearing deficit. In these children the speak faculty could not be developed by any of the previously known methods.

Therefore, a new procedure has been worked out for diagnostic purposes and subsequent speak development. In this procedure

kinestetic stimuli are used for improving auditory gnostic functions. Both in the Institute of Mother and Child, and in other Institutes, this method has become the basis of teaching the children to speak. A description of the method and its neurophysiological basis are included in the chapter entitled: "Neurophysiological aspects of aphasia in children" - of the book: "Studies on children with deteriorated hearing" /in press/.

Another item concerning the same subject was a film entitled: "Psychoneurological examinations of children with deteriorated hearing", in Polish and English versions. This film illustrates the neurophysiological and audiological principles and practical application of methods of teaching children with underdevelopment of speech. It was made in 1973, by PZWL /Polish Medical Publishers/ and a copy is kept at the Institute of Mother and Child, /Scientific consultation of the film: prof. Ciechocka and Asst.prof. Szumska/.

The results of studies on aphasia in children are presented at the conference on Examination and Rehabilitation Methods of Children with Deteriorated Hearing, in Rostock, DDR, 5 October 1973, in the form of a Communication entitled: "Audiological, logopedic and psychoneurological aspects of cerebral microlesions in children with deteriorated hearing". This paper has been accepted for publication in the proceedings of the Conference /co-Authors Borkowska M.D., Sawa M.D., prof. Wierzchowska M.D./.

The last item in this field was the work: "Audiological and neurophysiological aspects of aphasia in children", presented at the 3-day audiophonological conference in Milan, Italy, December 1973.

c. Studies of gnostic functions disturbed by neoplastic traumatic and stereotactic lesions of the brain. This subject is studied at the Department of Neurosurgery in the section:

Examinations of gnostic disturbances after localised brain lesions. Following a series of examinations of patients with neoplastic lesions of various parts of the dominant hemisphere, a simplified method of examining speech disturbances and classification of aphasia's was worked out for application in neurological and neurosurgical practice. The work was presented in December 1973, at a meeting of neurologists and neurosurgeons; it has been submitted for publication in "Neurologia i Neurochirurgia Polska".

Also a method of examining visuo - and audio-gnostic functions after lesions of the amygdaloid nucleus and gyrus cinguli was developed. The method consists in testing perceptive functions within the particular modality and aims to compare the results obtained with those of the examination of the "superficial" structures, i.e. cere-

When testing the method on 5 patients with various stereotactic brain lesions, it turned out to be necessary to add to the method extraverbal tests based on experimental work. This work is in the initial phase.

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Odległe następstwa zamkniętych urazów czaszkowo-mózgowych w świetle badań neurologicznych. /Late Consequences of closed cranio-cerebrai Traumas in Light of neurological Studies/. Neurol i Neurochir Pol - in press

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Afazja akustyczno-mnestyczna, objawy oraz metody i wyniki rehabilitacji. /Acustico-mnestic Aphasia, Symptoms, Methods of Rehabilitation and their Results/.

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Odległe następstwa wstrząśnienia mózgu w świetle badań elektroencefalograficznych. /Late Effects of Brain Concussion in Light of electroencephalographic Studies/.

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Odległe następstwa krwiaków i wodniaków półkul mózgowych w świetle badań neurologicznych, psychologicznych i EEG./Late Consequences of cerebral Hemispheres Hematomas and Hydroceles in Light of neurological, psychological and electroencephalographic Studies/.

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Korelacje kliniczno-patofizjologiczne w afatycznych zaburzeniach nazywania i wskazywania. /Clinico-pathological Correlations in Aphasic Disorders of Naming and Indicating/.

Zagadnienia patofizjologii wyższych czynności nerwowych po uszkodzeniach mózgu PZWL t.2, 1973, 48-63 F. SURGICAL RESEARCH AND TRANSPLANTATION LABORATORY Head; J. Nielubowicz, M.D., D.Sc., Prof.

Pathophysiology of Circulation.

a. Studies on the pathophysiology of lymphatic circulation.

In 1972 - 1973 succesive examinations of patients after lymphovenous shunt operations were performed.

A radiological method of evaluating lymph stasis by means of the so-called "100 steps" method was elaborated. This method allows to determine the degree of lymph stasis by aplying identical quantities of contrast medium and time of exposure to X-rays, and maintaining a standard number of lower limb movements.

A method of study of the intracellular fluid pressure with the so-called "tissue wick" was worked out. Using this method, the existance of negative / subatmospheric/ pressures in the interstinal space was confirmed.

Morphological studies of lymph capillaries in 6-years persisting experimental lymph stasis were performed by means of light and electron microscopy.

An experimental method of lymph vessels' permeability determination by means of a water contrast medium was worked out. Studies of lymph— and intracellular fluid pressure in various types of tissue edema were carried out. The rate of absorption of labelled albumine

from Guyton's capsules, representing a model of intercellular space, was studied, and studies of normal biochemical and immunological parameters of the lower limb lymph were undertaken.

In 1973, yearly succesive examinations of patients with lymph-edema after lympho-venous shunt operations were continued. In the
7 years follow-up the following results were obtained:

- In the group of primary lymphedema an improvement for a period of one year in 25% of cases;
- In the group of hyperplastic primary edema improvement in 60% of cases:
- In the group of secondary edema improvement after one year in 85% of cases.

Electron-microscopic pictures of the skin lymphedematous in patients were evaluated in collaboration with drs Papp and Viragh, -from the Hungarian Academy of Sciences in Budapest. In patients with:

- primary lymphedema, no lymph cappillaries were found in the skin
- in secondary lymphedema, basement membrane was found to develop both in lymph and blood capillaries of the skin,
- in four cases of patients with lymphedema, drainage of peripheral lymph vessels was performed. The biochemical, immunological and cellular assays of the lymph were made. Lymph was found to lack the complement activity and was characterized by very low complement protein content. This phenomenon requires futher investigations.

Similar studies were done on 5 dogs with 7-year persisting lymphedema. The results resembled those obtained in humans. The transosseous lymphography technique was elaborated. After introduction of the oily contrast medium into the tibial marrow cavity, pictures of lymph vessels draining the proximal epiphysis of the bone were visualized.

b. Studies on pathogenesis of arterio-venous communications.

Experimental studies on the pathogenesis of Bürger's disease included a preliminary series of experiments aiming to elucidate the role of peripheral nerves on the development of changes in arterioles. As a model served rabbits with unilaterally transsected sciatic nerve. In accordance with generally known observations ulcerations and trophic changes have appeared in the animals at various times after transsection, resembling some of those encountered in Bürger's disease.

A series of angiographic studies performed on rabbits clearly demonstrated that sciatic nerve transsection is accompanied by opening of arterio-venous communications in the skin and muscles. These communication change later on into permanent arterio-venous fistulae. In the regions with a-v communications regressive changes and ulcerations are formed due to compression.

In 1973, six dogs were subjected to transsection of the right sciatic nerve. This was followed by paresis of the feet and shank. No regressive changes in the limb skin were observed during 30 days. The arteriograms showed no features of open arterio-venous communications. In 20 dogs transsection of the right sciatic nerve was made together with right side lumbar symphathectomy. In 15 dogs in this group trophic ulceration of the limb was observed to appear between the 2nd - 30th day after operating. The ulceration did not heel. Arteriographies revealed in all cases features of open arterio-venous communications. In the remaining dogs, in which arteriographic examinations was performed before ulceration had appeared, features of open arterio-venous communications were noted prior to the appearance of regressive changes in the limb skin. Six dogs were subjected to right side lumbar sympathectomy, of L-2,3 and 4. In these animals paw ulcerations have never appeared. Arteriography showed features of open arterio-venous communications only during the 1st day after operation. Beginning with 2nd day the arteriographic pictures were normal.

In 14 dogs transsection of the brachial plexus was made. In 5 dogs of this group both trophic ulcerations of paw and the arteriographic features of open arterio-venous communications were observed. In 4 dogs the arteriographic picture corresponded to open arterio-venous communications, but ulcerations of paw not noted. In the remaining 5 dogs no ulceration had appeared and the arteriographic pictures were normal. Four dogs were subjected to transsection of the brachial plexus and at the same time to carotid sympathectomy removing the upper and lower carotid ganglia and the first thoracic ganglion. In all dogs, between the 4th and 14th day, trophic ulceration was formed on the front paw. All arteriographic studies in this group, both before and after formation of the ulceration, showed features typical of open arterio-venous communications.

In the next group, comprising 12 dogs, carotid sympathectomy was performed together with the transsection of one of the four main nerve trunks of the front limb, namely: in 2 dogs - radial nerve, in 3 dogs - dermato-muscular nerve, in 4 dogs - ulnar nerve, in 4 dogs - median nerve. Ulcerations of denervated paws of traphic type developed only after transsection of ulnar and media nerves with simultaneous sympathectomy. Only in these cases, arteriographic examination showed typical features of open arterio-venous communications. Transsection of the two other front limb nerves with simultaneous sympathectomy did not result in regressive changes in skin of the denervated paw. In those case the arteriographic picture of the paw was normal.

Tissue and organ transplantation.

a. Studies on organ transplantation.Studies on rejection of xenogeneic organ transplants.Model: porcine or rabbit liver to dog.

Studies on intravascular coagulation in a xenogeneic grafts and on the role of blood platelets.

In 1972, studies were continued on the effect of anticoagulative agents on the inhibition of intravascular coagulation in xenografts and thus on the prolongation of their survival. None of the applied agents /heparin in 1-10 mg/kg body weight doses, arvin, toluidine blue/ was able to prolong the graft's survival. It was noted that after the initial total blood flow arrest, heparin causes a recovery of traces of flow, lasting for 20 - 30 min. At present attempts are in progress to apply other agents, such as reptilase and Stypven.

Studies were undertaken on the role of blood platelets in the hyperacute rejection and intravascular coagulation processes. The technique of labelling the dog and rabbit platelets with <sup>53</sup>Cr was elaborated. Thereafter the uptake of labelled platelets by liver, lungs, spleen and lymph nodes, was studied in three separate control groups in the following sets of experiments:

- the platelets of a dog were administered after labelling into the circulation of the same dog,
- the platelets of a dog administered after labelling into another dog,
- platelets of a rabbit administered after labelling into a dog.

The aim of these preliminary studies was to establish whether or not allogenic and xenogeneic platelets are taken up more intensively by liver than autogenic platelets. The results suggest that there are significant differences in this respect between the xeno, -allo, and -autogenic platelets. Thus, it may be assumed that the parti-

cipation of blood platelets in hyperacute rejection process is passive and that their antigenicity plays no significant role in this process. These studies are still in the preliminary phase.

b. Studies on the mechanism of vascular wall damage in hyperacute xenograft rejection process.

The aim of these studies was in the first step to determine in the electron microscope the ultrastructural changes in liver sinusoids, endothelium and hepatocytes in the hyperacute rejection process. These studies, performed in collaboration with the Laboratory of Electron Microscopy, revealed the most intensive changes in endothelium and almost no changes in hepatocytes. This might be suggestive of a primarily intravascular process. Endothelium undergoes desquamation, a part of it desintegrates and thus the vascular wall permeability increases. Chinese ink administered into circulation passes into the Disse's space. Another part of these studies aimed to reproduce the hyperacute rejection process in vitro. The most difficult step in these type of experiments is to isolate living endothelial cells. The research group has got experience in isolating endothelial cells from large vessels; the percentage of dead cells, however, is as yet too high. In further studies, an effort will be made to isolate about 90% of living endothelial cells.

c. Immunofluorescent and isotopic studies of cells and immunoglobulins participating in xenograft rejection.

In cooperation with the Polish State Institute of Hygiene, anti-dog, anti-rabbit, and anti-porcine sera for immunofluorescent studies were prepared.

97

d. In addition /in 1972/ studies were carried out on the prolongation of xenograft survival following administration to the recipient of red cells, leukocytes, plasma and platelet rich plasma of the liver donor. Before and after infusion of donors cells, as well as five minutes after liver transplantation, the hemagglutinin, hemolysin, leucoagglutinin and lymphocytotoxin titres in recipient's serum against the antigens of donors blood cells were assayed. It turned out that administration to the recipient of red cells stroma causes a decrease to zero the hemagglutinin titre and the graft survives 60 - 120 min /in the control group 5 - 7 min/. Administration to the recipient of other cellular elements of the donor and of plasma did not affect the survival time of xenograft. These studies will be continued including greater numbers of animals, in order to obtain relevant statistical data.

Further studies on the applicability of the agents counteracting aggregation of blood platelets in xenograft revealed their inefficiency in prolonging xenograft's survival. Studies on the ability of endothelial cells to aggregate dog blood platelets and leukocytes gave negative results.

Immunofluorescent examinations of xenografts revealed IgG and complement deposition on the surface of endothelial cells. The effluent serum from kidney and liver xenografts was shown to possess the ability to inhibit migration of leukocytes of donor's peripheral blood.

In studies on liver allo-transplantation it was shown that the doses of immunosuppressive agents ought to be higher than in the case kidney transplantation.

Studies on intestine transplantation revealed that a majority of lymphocytes in the graft lymph and mucosa originate from recipient.

In 1973, studies on the recognition of the process of rejection of dog kidney allografts were continued. For this purpose the following parameters were tested:

- the reactivity of donor's lymphocytes in the consecutive days after transplantation,
- the titer of cytotoxic anti-donor lymphocyte antibodies in the recipient serum,
- the leukocyte migration inhibition test.

Attempts were continued to develop an external lymphovenous fistula. Due to technical problems these studies were not completed.

e. Studies on the rejection of organ xenografts.

Liver transplantation. Model: donor-rabbit, recipient-dog.

- Studies on intravascular coagulation in xenograft; attempts to counteracts with pharmacological agents. Further studies were performed on the effect of agents preventing aggregation of blood platelets on the prolongation of blood circulation tissue in liver and kidney xenografts. Periactin in high doses did not bring about prolongation of xenograft's survival, but only the increase in the recipients blood of the amount of circulating, non-aggregating blood platelets by 40 - 50%.

It was found, that the effluent serum from liver xenografts does not aggregate the recipients blood platelets, while in xenografts capillaries very intensive aggregation is taking place.

Further studies were performed on the uptake by liver of auto--allo-and xenogeneic platelets. Due to the insufficient number of experiments and technical difficulties, the results cannot be considered as conclusive.

Studies were undertaken on the determination of heparin utilized in xenograft /H.Łukasiewicz, M.D. in the Thrombosis Research Centre, Temple University, Philadelphia, USA/.

- Studies on the mechanism of cell well impairment in hyperacute rejection of xenograft.

It was attempted to determine in the "in vitro" conditions the role of vascular endothelia in the xenograft rejection.

These studies were carried out parallely in Warsaw and in the Institute of Experimental Surgery in Münich, BRD. The methodics of the studies consisted in testing whether or not the endothelial cells, isolated from hepatic sinusoids or aorta of rabbit:

- may cause the adherence of recipient's leukocytes,
- may cause the aggregation of recipient's platelets suspended in its own serum,
- are able to absorb the dog serum heterohemoagglutinines against rabbit erythrocytes antigens,
- may be applied to the cytotoxic test in a system; rabbit endothelial cells-dog serum.

The endothelial cells were obtained either by perfusion of the organ with a trypsin solution, or by mechanical scratching of the intimal of aorta. Unfortunately no proper method of evaluation of vitality of isolated cells had been found as yet. Preliminary experiments do not suggest that the rabbit endothelial suspended in the dog serum were causing aggregation of dog platelets and leukocytes. This possibility will be tested in additional control experiments of dogs immunized with rabbit endothelial cells.

 Immunofluorescent and isotopic studies of cells participating in xenograft rejection.

The immunofluorescent studies concerned rabbit livers transplanted to dogs. It was found that after 5 min from revascularization, the dog IgG deposits accumulated on the surface of the rabbit liver capillaries. After 20 min, fluorescence was visible in the Disse's space

100

and between hepatocytes. The same holds for the dog complement. Dog fibrinogen accumulated almost exclusively on the intima of the large vessels in the portal spaces. Immunofluorescent studies also involved the rabbit aorta perfused with the dog blood. In this case just as in the liver grafts, accumulation IgG and complement deposits was accompanied by a very poor accumulation of IgM.

The isotopic studies will be undertaken in 1974,

- Attempts to inhibit the hyperacute rejection reaction by means of depletion and absorption of antibodies in vivo.

Further studies on prolongation of xenografts survival were carried out, decreasing the hemagglutinin titers against donor's erythrocytes in the recipients blood by intravenous injection of donor's erythrocytes. It was not succeeded to prolong the xenograft's survival above 120 min.

Chronic immunization of recipient dogs with increasing doses of rabbit erythrocytes was initiated in order to evoke the active enhancement phenomenon. One group of dogs in given erythocytes alone, another one receives in addition chronic immuran doses. Preliminary experiments aiming to reduce in vivo the number of evaluating blood platelets and leukocytes were performed passing the blood of a living animal through an activated charcoal column.

- Studies on the inhibition of leukocytes migration by xenograft's effluent serum.

In the course of rejection, a xenograft retains a significant number of leukocytes. It was tested whether or not the recipients serum flowing out from a xenograft possesses the ability to inhibit the migration of own leukocytes. It turned out that such an ability already appears after 5 minutes of dog blood circulation through rabbit liver.

101

The same was observed after xenogeneic transplantation of kidney. The strong inhibitory activity is also pertinent to the graft lymph. The in vitro studies with erythrocytes, leukocytes, lymphocytes, and serum protein of the rabbit, revealed that none of these elements inhibits the migration of dog leukocytes. Likewise the lyophilisates of rabbit hepatocytes are free of this inhibitory activity. At a present, a method of quantitative determination of inhibition of migration is being elaborated, in order to evaluate the intensity of the rejection process.

- Transplantation of kidneys.
- Previous studies on the intrarenal blood flow disturbances with the use of \$^{133}\$Xe revealed that already on the 3rd day after allogeneic kidney transplantation in dogs without immunosuppressive treatment, disturbances of the intrarenal blood flow distribution appear, consisting in the decrease of the cortical flow and increase of the flow trough the juxtameduliary cortex and medulla. Analogical studies, performed in animals receiving immunosuppressive drugs, revealed a later apearance of blood flow disturbances.

A series of immunohistochemical studies following allogeneic kidney transplantation were carried out in dogs without immunosuppressive treatment and in those treated with antilymphocyte globulin preparations.

Kidney slices isolated by means of surgical biopsy in consecutive days after operation were tested for the presence of IgG, IgM, fibrin and complement deposits. In untreated dogs in the rejection period IgG, complement, and fibrin deposits were noted in glomerular capillaries, peritubular capillaries and in small vessel wall. In animals treated with antilymphocyte globuline the changes have appeared later and were less pronounced. No deposits of IgG of the animals

the serum of which served to prepare antilymphocyte globulin were found.

- Studies were undertaken on the elaboration of model of hyperacute rejection of kidney allograft. The dogs were immunized with a suspension of donor's leukocytes and platelets during 5 7 weeks and thereupon the kideny was transplanted. After 10 days rejected graft was removed and 7 days later the second kidney of the same donor was implanted. This kidney underwent rejection within 2 3 hours. A drop in level of leukocytes and platelets in the blood flowing out from renal vein and a gradual decrease of the intrarenal blood flow were observed. However, this model is not fully reproducible, which is related to the varying degree immunization of individual recipients. Further studies are in progress.
- Studies on interrupted drainage of thoracic duct in the initial stage due to technical difficulties in maintaining the patency of the lympho-venous shunt. Studies will be continued in the coming year.

In 1973, studies were performed on the methods of recognition of dog kidney allograft rejection. For that purpose, beside urea and creatinine assays, the of leukocytes migration of inhibition test was carried out, the recipient's serum was tested for the appearance of cytotoxic anti-donor lymphocyte antibodies and mixed cultures of donors and recipients lymphocytes were performed.

The studies were performed in two groups - in untreated dogs, and in those treated with antilymphocyte globulin.

The leukocytes migration was shown to be inhibited in the rejection period; however, the moment at which this inhibition had appeared was different in particular animals. No cytoxic antibodies were found to appear in recipient's serum after kidney transplantation. Evaluation of the results on mixed lymphocyte cultures in not yet completed.

The work on interrupted thoracic duct drainage was confronted with a number of technical problems. Recently it was succeeded to work out the method of performing shunt between the thoracic duct in its carotid segment, and superior vena cava. In order to sustain the patency of the shunt, the animal should be given antithrombotic drugs.

Evaluation of various immunosuppression schemes for prolongation of dog kidney allograft's survival. The animals were treated with antilymphocyte globulin administered by different routes. The results are presented in the consecutive part.

## - Liver Transplantation.

This was the continuation of studies aiming to work out the proper conditions for clinical transplantation of liver,

Studies on the early recognition of liver rejection and on the correlation of liver enzymes concentrations in serum and biopsy pictures in a light microscope. In this study the AspAT, ALAT and ADH activity and the bilirubine content in serum were measured in various periods of hyperacute rejection. Parallel samples of liver were taken for examination. The histological pictures of cholestasis in bile canaliculi and of pigment accumulation in hepatocytes correlated with the serum bilirubine level. The hepatocytic enzymes activity did not increase parallely with the enhancement of histological signs of rejection.

Attempts of prolongation of graft's survival by means of chemical immunosuppression and antilymphocyte serum.

The results, obtained so-far, indicate, that the serum doses prolonging the survival of allogeneic kidneys do not prolong the survival of transplanted allogeneic liver. Studies on the applicability of the leukocytes migration test in recognition of liver rejection. The observations made hitherto indicate that in the course of the rejection process, migration of peripheral blood leukocytes of allograft's recipient is inhibited, whereas at the moment of rejection it is normal or increased. Preliminary studies revealed that the effluent serum of liver allograft possesses the ability to inhibit migration of recipient's leukocytes. The most significant observation concerned the differences in the survival time between the kidney and liver allografts under the same immunosuppressive protocole applying anti-dog horse ALG.

This preparation did not affect the survival of liver, but markedly prolonged that transplanted kidneys. Preliminary bacteriological studies of peripheral blood and liver in dogs were performed. The idea of initiating those studies arose from the observation, that following liver transplantation and immunosuppression, the animals are mostly dying of infectious complications within the graft.

### - Small bowel transplantation.

Attempts of prolongation of graft's survival by means of chemical agents and antilymphocyte serum.

The aim of the studies was to examine the effects of immunosuppressive agents on the humoral and cellural processes in rejected small bowel. The experimental model consisted in transplantation of a small bowel fragment into neck of another dog with external lymphatic shunt. The graft lymph was collected continuously and tested for:

- a. The lymphocytotoxines and lymphagglutinins titers, both against donor's and recipient's lymphocytes,
- b. The number of blast forms.

The titer of antibodies against both donor's and recipient's lymphocytes was found to increase from the 1st day on. This may be clearly suggestive of the presence in the transplanted bowel fragment of a reaction against the host. This titer dropped to very low values with the complete rejection of the bowel.

In the group of animals which immunosuppression with immuran and steroid in standard doses was applied, the above procedure inhibited the GVH reaction. Parallel with this inhibition, the time of survival of the graft increased from 5-7 days to 12-14 days.

Further studies on the transplantation of small bowel fragments to the neck of another dog included:

- simultaneous administration of standard doses of immuran and steroids,
- application of antilymphocyte serum alone,
- administration of all the components together.

It turned out that a two times prolongation of allograft's survival can only be actived by combined application of chemical agents and ALG. Despite the application of high doses of immunosuppressive agents, it was not succeeded to prolong the time of survival for more than twice the control values.

Histological studies of the grafts were performed in the consecutive postoperative days. The microscopic picture turned out to correlate with the clinical symptoms of rejection, which accompanied even minimal small-cellular infiltrates in the graft. Pharmacological immunosuppression totally inhibited the GVH reaction in the graft lymph. Despite the lack of a marked graft-anti-host reaction, the rejection took place as rapidly as in the control group.

Studies on the transplantation of small bowel from female to male dogs with the application of cresylviolett staining of female sex heterochromatine in lymphocytes and using the immunofluorescence method, revealed that the lymph of a graft, on the 4th day after separation, contains only 5% of donor's lamphocytes and the mucosa - 41%. In the later periods these numbers decreased to minimal values. This renders the possibility to work out a quantitative test of the intensity of the rejection process in the bioptic material.

- Studies on the maintainance of the organ's function during storage for transplantation.

In 1973, the problems of vulnerability of vascular endothelia of liver to ischemia and hypothermic perfusion were investigated. The walls of the hepatic capillaries were found to undergo marked ultrastructural changes, consisting in desquamation of endothelia and intracapillary of blood platelets, whereas hepatocytes were characterized by relatively insignificant damages. A device for measuring the intracellular potentials in the hepatocytes was constructed for evaluating their vital activity.

Studies were continued on kidney preservation under hypothermia using a modified Collin's solution. It was shown that despite a 30 minute warm ischemia of the organ before the storage period, the kidneys were able to undertake their function and a part of the animals survived the observation periods of 3 - 6 monts. Functional studies will be performed after longer observation periods.

In collaboration with the Laboratory of Electron Microscopy, the effect of ischemia and of protective action of a number of perfusate on the kidney ultrastructure were investigated. The slightest morphological changes were found to appear following preservation in Collin's solution.

Quite recently studies were undertaken on kidney preservation means of periodic perfusion.

Examinations of oxygen consumption by heathly and postischemic renal cortex slices in Warburg apparatus were initiated. Due to severe technical problems with obtaining slices of an appropriate thickness, the studies are still in a preliminary step and will be continued in 1974.

- Preservation of the liver.

Biochemical studies of effluent blood of the liver after its preservation in hypothermia and perfusion in the autograft model were carried out. The aim of the studies was a biochemical evaluation of hepatocytes impairment during ischemia and in various types of preservation. Biochemical tests involved the activities of mitochondrial and cytoplasmic hepatocyte enzymes, potassium concentration and the products of anaerobic carbohydrate metabolism in effluent blood of the liver after ischemia and preservation. The studies were carried out in the following groups:

- a. Two-hour warm ischemia
- b. Instant hypothermia and continuous hypothermic perfusion for 2 hours.

It was found that the effluent blood of a liver, that was previously subjected to ischemia or stored in hypothermia, shows high AspAT, ALAT and LDH activities, high K<sup>†</sup> concentration /reaching 9-10 mEq/1/ and high concentrations of lactic acid and glucose. The obtained values will serve as a base for investigations in which under identical conditions the correlation of biochemical changes and changes in the intracellular electric potential in hepatocytes will be followed. This will be of practiced significance for objective evaluation of the preservation.

- Studies on the damages of capillaries in the liver preservation process.

Electron-microscopic studies were carried out on a dog liver after warm ischemia, cold ischemia, and cooling to  $4^{\circ}$ C, by a

108

number of solutions. It turned out that the first to be impaired are the endothelial cells of hepatic sinuses. The change included an increase of wall permeability /as studied by the use of Pelikan-Günther carbon/ and after revascularization-obstruction of sinuses lumen by aggregates of blood platelets. Intrahepatocytic structures undergo changes in later periods. The prototype of an instrument for intracellular potential measurements in the hepatocytes was constructed.

In 1973, studies were started on liver preservation by the so-called interrupted perfusion method including the removal of effluent perfusate. In view of its simplicity, the method may find clinical application.

#### - Preservation of the kidneys.

In 1972, studies were continued on the effectiveness of the previously described method of preservation of dog kidneys for 24 hours in hypothermia with the use of a modified Collin'solution. The composition of the solution had to be modified since the addition of magnesium sulphate caused precipitation of crystals. Chemical analysis revealed that these were magnesium phosphate crystals. In consecutive trials the amount of magnesium sulphate which could be added to Collin's solution without producing precipitation was established. The fluid was applied to perfusion and subsequent storage of kidneys before transplantation.

In the previous years a series of experiments was performed on 24 hours preservation of kidneys from donor's in which hemorrhagic hypotension was produced. After the preservation period the kidneys were transplanted in the allogeneic system. Since the dogs were not given immunosuppressive drug, the evaluation of the function of preserved and transplanted kidney was difficult. In 1972, a new series of experiments started in which the kidneys were subjected to warm

ischemia and thereafter transplanted to the same dog a 24 hour preservation,

Preliminary results, obtained in 4 experiments, point at the effectiveness of this preservation method. The effect of a number of perfusate on the renal cortex enzymes activity was tested directly after perfusion, after the preservations periods and after transplantations. At the same time kidney samples were taken for electromicroscopic studies. The studies failed to demonstrate any differences in relation to the applied fluids. Further studies on the evaluation of the kidney tissue vitality after preservation /oxygen and PAH consumption/, using a Warburg apparatus, are in the initial phase.

- Evaluation of the functional efficiency of an autogeneic kidney transplants preserved for 24 hours.

Five dogs survived 2 years following transplantation of kidney, preserved for 24 hours in hypothermia, periodically were tested the serum levels of the urea-creatine, -and electrolytes, and the morphological composition of blood remained within the limits of norm. At present clearance studies are carried on, the results of which will be presented in separate publications.

- Studies on the evaluation of tissue vitality before transplantation.

In collaboration with the Laboratory of Electron Microscopy, studies were carried out on ultrastructural changes in the kidney after perfusion with Collins'and Ringer's solutions and preservation in hypothermia. Perfusion with Ringer's solution, and preservation in Ringers'solution and plasma - produced significant damages of endothelial cells of peritubular cappillaries and destruction of tubule cells. Perfusion with Collin's solutions produced the slightest impairment of capillary endothelium and the structure of tubule cells was maintained even after 24 hor preservation.

In 1973, studies were initiated on oxygen consumption by slices of healthy and postischemic kidney with the use of the Warburg technique. Preliminary studies revealed that the healthy kidney utilizes 0,9 = 1,2 al 0 /mg of initial weight and the ischemic kidney- 0,5 - 0,7 al/mg = of initial weight. The wide range of values was related to the difficulties in preparing slices of equal thickness /0,3 mm/. For that purpose two tissue slicers were constructed.

Studies were performed aiming to evaluate the degree of postischemic impairment of the kidney by determining the LDH activity in effluent blood of the renal vein. Preliminary results point at a marked /5 = 6 fold/ increase of LDH activity in the renal serum following ischemia of the kidney.

- Studies on the practical use of immunosuppressive agents:
- Immunosuppression in transplantation of organs.

Investigations were carried out on the optimal scheme of immunization of horse for isolating ALS proper to apply both in dogs and in the clinic. However, studies were undertaken on the antibody specificity in various types of ALS obtained in different ways. The immunosuppressive activity of ALS and its fractions was evaluated in vitro /cytotoxic test, rosette test, effect on OND synthesis/ and in vivo, in order to establish the optimal mode of administration in the dog kidney allotransplantation model. Comparative studies were performed on the effect of ALS on the survival of kidney and liver allografts in the dog.

- Antilymphocyte serum /globulin/ production for application in humans.

Basing on the results of studies on the isolation of antylymphocyte sera for application to dogs, immunization of the next horse was

started using lymphocytes isolated from a long-term drainage of the thoracic duct of patients awaiting kidney transplantation. The immunization was started with living lymphocytes and was continued by using lyophilized antigen material. The immunization scheme was the same as that applied for the isolation of the dog anti-horse anti-lymphocyte serum. The first antigen dose was injected together with Freud's adjuvant subcutaneously and the next intravenously. Application of the plasmophoretic technique allowed to obtain in each immunization cycle 25 - 20 liters of serum. IgG was prepared by the rivanol method. In the course of immunization neither the horse serum, nor globulin, have contained antibodies against organs, as demonstrated by the double diffusion test and immunofluorescence test.

Immunosuppressive activity test in vitro revealed the following titres: lymphocytotoxic - 1: 256, lymphoagglutinating - 1: 256, opsonin - from 10<sup>-3</sup> to 10<sup>-1</sup>, depending on the type of sample, inhibition of rosette formation - from 1: 4000 to 1: 8000. All those titres, however were lower than in a horse immunized by the same method with dog lymphocytes /the only difference was the application of living lymphocytes exclusively/. This preparation has not yet been applied in patients after transplantation of the kidney.

- Preparation of antylymphocyte serum /globulin/ against the dog.

In the previous Report, 1969-1971, a method of short term immunization of horse with dog lymphocytes was described. This method, considered to correspond to the "two-pulse" method, generally used in immunization of rabbits, and consists in the injection of the first lymphocyte dose /of the order of 10 10 together with Freud's adjuvant subcutaneously, followed by repeared reimmunization by means of two identical lymphocyte doses injected intra-

venously. After bleeding /plasmophoresis/, and a two-weeks interruption, the second immunization cycle was started, consisting of 3-4 intravenous injections of lymphocytes at 4 days intervals. In that way the second pool of serum was obtained. The whole immunization period does not exceed 3 months. From both serum portions /so-called "early" and "late"/, IgG fractions were prepared by the rivanol method. Immunosuppression activity test in vitro /lymphocytotoxine, opsonines, Martin's test, rosette formation inhibition test/ were carried out. The results of all the tests were quite similar /lymphocytotoxic 1: 64 - 1: 256, opsonine 10<sup>-3</sup> - 10<sup>-4</sup>/. An exception was the rosette formation inhibition test, in which the "early" serum titre appeared markedly lower than the "late" serum titre.

Both preparations were applied in dogs after allogeneic kidney transplantation. The treatment protocols /dose, time of administration/ were the same as in the previous studies /described in the Report 1969-1971/, IgG prepared from the "late" serum markedly prolonged the time of survival of the dogs after allogeneic kidney transplantation /up to 50 days/. IgG derived from the early serum, characterized by the lower rosette formation inhibition titre, demonstrated a much weaker immunosuppressive activity, prolonging the survival only to 15 days. However a two-times augmentation of the dose of "early" preparation allowed to achieve the same immunosuppressive effect as obtained with the IgG preparation of "late" serum /prolongation to 50 days/. In 1972, studies were initiated aiming to evaluate the effectiveness of intravenous administration of antilymphocyte globulin preparation. The daily dose of heterologous protein was established to be the same as in the previously applied intramuscular administration scheme, Globulin preparations derived fron: "late" serum with confirmed immunosuppressive activity are being used.

Following horse was immunized by the same method. The obtained serum is now in the preparation stage and will be tested on animals after kidney, liver and bowel transplantation, in order to compare the effect of the same immunosuppression dose on the survival of different organs.

In 1972, likewise attempts were initiated to work out a method of immunization of pigs to obtain porcine antilymphocyte serum against dog/and in the future - against man/. For this purpose, a short term immunization protocol was applied. The first antigen dose /2 x 10 lymphocytes/kg body weight/was given intramuscularly, subcutaneously and intraperitoneally together with Freund's adjuvant.

The next antigen dose was administered by the same route after 14 days. Seven days after the second immunization the pigs were bled to death. As the serum contained no antibodies against dog plasma proteins, the IgG was prepared by the rivanol method without previous absorption of the serum. The hemagglutinine titre was in the final preparation somewhat lower than in the native serum; however, the absorption with dog erythrocytes was carried out. This modification of serum prevented a more significant reduction of antilymphocyte antibodies.

In this series of studies, the "in vitro" tests of immunosuppressive properties and examinations of immunosuppressive efficiency after kidney transplantation in dogs were started.

In 1973, the studies the isolation and immunosuppressive activity of the porcine antilymphocyte serum against dog were continued. The isolated antilymphocyte globulin preparation possess the immunosuppressive properties prolonging the survival of kidney allografts by more than 100% in relation to the control group. Further studies were performed on the effectivness of the horse antilymphocyte globulin against dog with respect to the administration route.

No differences in the time of animals survival were found irrespective of whether the administration was intramuscular or intravenous. The effectivness of the same dose of antilymphocyte globulin on the survival of kidney and liver allotransplant in dog was evaluated and in the case of liver transplantation, the requirement for a different immunosuppression protocol was demonstrated. Evaluation of a number of antilymphocyte globulin preparations by means of in vitro tests has been continued.

- Elaboration of an optimal protocol for immunization of pigs, /The scheme of the immunization see: "Report 1969-1971"/

In 1973, an IgG preparation was isolated by means of the rivanol method. This preparation was characterized by the following properties "in vitro" lymphagglutination titre - 1: 128 - 1: 256, lymphocytotoxic titre - 1: 256, opsonine titre - 10<sup>-3</sup>. It contained neither anti-plasma proteins antibodies nor antibodies against the basal membrane. The dogs with allogeneic kidney transplant were treated according to the previously accepted protocol; they were given 15 mg/kg body weight during the 2 days before transplantation, 25 mg/kg body weight during the first 3 days after operation and thereafter 15 mg/kg body weight until the 13rd day after operation. The control group consisted of animals treated with the IgG preparation isolated in the same way from heathly pigs. The mean time of survival of treated animals was 21 days, and of untreated animals 9,9 days.

- Isolation of horse antilymphocyte serum against dog.

The following horse was immunized using lymphocytes from the thoracic duct by the "six-pulse" method, /described in the previous Report, 1969-1971/. The IgG preparation was characterized by the lymphocytotoxic titre 1: 128, lymphoagglutination titre 1: 128 and

opsonine titre 10<sup>-3</sup>. This preparation is applied in animals after bowel transplantation.

Previously the ALIGG preparation had been administered into muscles. In 1973, the same preparation was given intravenously in two experimental groups. In group 1 - the animals were receiving every day the same globulin dose as previously in intravenous drip. In group 2 - the same total antilymphocyte globulin dose 260 mg/kg body weight was administered in three portions; on the 1st, 3rd and 7th day - after kidney transplantation. The mean time of survival in group 1 was 25 days in group 2 - 20 days. It is worth mentioning that in 2 out of 10 animals which received high dose of serum, thrombi were observed in vascular shunts. Further studies are needed to elucidate the causes of the complication /technical error, serum effect?/.

- Comparative evaluation of the effects of worse antilymphocyte globulin against dog on the survival of dog kidney and liver allografts.

Two consecutive preparations of antilymphocyte globulin were administrated in the same doses into dogs after kidney and liver transplantation. A marked prolongation of the animals survival was achieved after kidney transplantation  $/17^{2}$  and  $31^{2}$  12/ but no effect after liver transplantation  $/6.3^{2}$  2.8 and  $7.2^{2}$  3.4/ was observed.

Attempts to evaluate the effectivness of immunosuppressive treatment by means of the rosette formation test and mixed lymphocytes cultures.

A number of experiment on dogs have demonstrated, that rossettes are only formed by the lymphocytes from the thoracic duct, whereas the peripheral blood lymphocytes are forming them extremely rarely. This made it impossible to perform serial studies in the animals after kidney transplantation.

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# G. LABORATORY OF APPLIED PHYSIOLOGY Head: S. Kozłowski, M.D., D.Sc., Associate Professor.

One part of research was concerned with the contribution of the adrenergic component of the autonomous nervous system to the adaptation of the organism to physical work and thermal environment. It was found that activation of the adrenergic system in man during work depends on the intensity of work and physical working capacity.

An elevation of ambient temperature was found to influence the activity of the adrenergic nervous system at rest and during exercise both these changes and alterations of thyroid function participated in the chemical thermoregulation of the human organism in heat.

The orthostatic responses in human subjects were shown to depend on the experimentally body temperature; a field study which followed described the factors determining work load in foundry workers.

A powerful activation of the adrenergic system was demonstrated during static physical exercise. It was proposed that the adrenergic response is initiated in the "metabolic receptors" of the muscle, and the importance of this effect in medical prophylaxis was presented.

A pattern of changes in the adrenergic activity during prolonged physical exercise was described and shown to include two functional

phases. The increased release of norepinephrine late during exercise /second phase/ is related causally to the depletion of body carbohydrate stores. The role of catecholamines in mobilizing extramuscular energy substrates during work was explained and the importance of this mechanism in determining of the physical working capacity was demonstrated. A theory was developed on the role of the glucostatic mechanism which would be critical for the ability to perform prolonged muscular work; this was in part a continuation of the earlier research concerning adrenocortical activation during work.

An elevation of blood thyroxine level during exercise and the effect of thyroid hormones on lipolytic action of norepinephrine was the subject of another part of research.

Some mechanisms whereby emotion ca affect working capacity were described.

Earlier studies concerning neurohormonal mechanisms of adaptation of the organism to physical work were further developed. The subject was the relation of certain metabolic changes in working diabetic patients to the magnitude of the so-called relative work load; the practical conclusions were ensued concerning the physiological criteria for determination of acceptable work loads to be used in patients with diabetes.

In the study on physiological consequences of reduced physical activity the alterations of calcium metabolism, the adrenergic nervous system and the thyroid function, as well as in chemical thermoregulation were described.

The studies of central mechanism of thermoregulation furnished the data on the effect of hypothalamic temperature on the activity of nonspecific systems of rabbit brain and possible consequences for behavioral thermoregulation. The changes were described in pulmonary mechanics associated with respiratory thermoregulatory

responses in the rabbit; the contribution of peripheral and central thermal stimuli to the development of these responses was evaluated.

New data were presented on the effect of hyperthermia on the function of certain mechanisms of physical and chemical thermoregulation in the rabbit. It was shown that body dehydration modifies the respiratory response to an elevated hypothalamic temperature.

The experiments with dogs showed the effect of increasing osmolality of body fluids on deep body temperature during work. Another factor influencing temperature patterns in working animals was the Na<sup>+</sup>: Ca<sup>++</sup> ratio of peripheral blood plasma. Body temperature in dogs was observed to increase during positive emotional stimulation produced by stimulation of the hypothalamus. It was suggested that the function of the thermoregulatory center is modulated by the limbic system.

According to the classical concept the so-called cold diuresis is explained by an inhibition of ADH /antidiuretic hormone/ release in cold environment. This view was put to doubt by the new data and an original explanation was proposed. Principal parameters of renal function as well as plasma levels of ADH, cortisol and cate-cholamines were examined in dogs exposed to low ambient temperature; this enabled a complex evaluation of hormonal and renal function changes in cold.

An extrathyroidal metabolic action of TSH /thyroid stimulating hormone/ one the muscle tissue was described, and the new data on the ontogenesis of thermoregulation were presented.

The studies on the regulation of body water metabolism concerned the effect of angiotensin and aldosterone on the osmotic reactivity of thirst in the dog and the reflex effect of the liver portal blood osmolality changes on the thirst mechanism. A hypothesis was proposed on the role of this mechanism in the control of water intake.

The effect of ADH on the osmotic reactivity of the thirst mechanism, and a transient increase in blood ADH activity following an infusion of angiotensin II into the brain ventricle were described. The ADH secretion and osmotic reactivity of the thirst mechanism in dogs were found to vary with changes in hypothalamic temperature. In this connection suggestions were made concerning the relation of these phenomena to the mechanism of the so-called voluntary dehydration in man.

An original experimental model of an in situ nonfiltering nontransporting kidney was developed and applied for physiological studies of basal renal oxygen consumption, and for the studies on the mechanism of remain release.

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H. RESEARCH GROUP OF SCHOOL PSYCHOHYGIENE Head: H. Osiński, M.D., Ph.B.

The basic research problem is:

Adaptation of children and young people to school environment.

Within this problem the following subjects were investigated in the period 1971 - 1974:

1. Didactic and educational difficulties in children-example of one school.

This study was performed in 1971 and presented in the previous report. The control group in these examinations consisted of children that were excellent in behaviour and were having no difficulties with their studies.

The examinations performed in 1972 included 52 children from the same school and analogical classes and were performed by the methods applied in the basic group, modified adequately. After collecting the material analyses of family and school environment, psychological and medical examinations were carried out. The results were in part elaborated.

In 1973 the results of examinations of basic and control group served to work out in detail the model of a complex therapy of educational and didactic difficulties. 2. The problem of adaptation to school conditions in first class children.

Organization studies were prepared in two classes of the school chosen. The examinations were being performed during the initial periods of child's education.

The following examinations were performed: psychological tests and medical examination - internistic, neurological and psychiatric - as well as interviews with teachers, educators and parents concerning the children under examination, and also interviews with school direction about the teachers and educators.

In 1973 the studies on the adaptation of first class children to school environment were continued. The following results were obtained:

A majority of the children were from positive environments, 26 children /52%/ showed symptoms of bad adaptation. Only in 2 out of 50 children, the intelectual development was found to be below the norm.

However, the appearance of a number of irregularieties of various ranges and intensity in the psychomotoric development in children were noted. Fragmentaric deficiencies of the phsychomotoric development of a child most frequently concerned the audial and visual perception, and to a lesser degree the decreased motor and graphic efficiency, as well as incorrect lateralization.

Almost a half of the children showed minor deviations in physical development which were easy to correct.

In a significant number of children, disturbances of the dynamics of nervous processes were observed, mostly finding expression in psychomotoric and emotional hypersensibility. All those deviations from the norm impede and retard the correct adaptation to school conditions. In order to eliminate these difficulties in adaptation, already in the first class, appropriate correcting and therapeutic

action, adjusted to individual need of the child, should be undertaken and proper attitude school and home to the child should be ensured, regarding the individual abilities of a given child. Realization of these aims is only possible if based on an early biopsychosocial diagnosis of children initiating their learning at school, as well as on a good knowledge for their environment at home. Both the above conditions were fulfilled for the first time in Poland owing to the results obtained by Research Group. The contemporary school acquires only a part of such a knowledge about children and their family environment, and not earlier that after the children had spent a number of years at school. This is too late, since during these years, irreversible school conflicts are already developed and consolidated.

In the future, the schools will start their didactic, educational and correcting work with such examinations.

The results of studies on the first class children will serve to introduce into praxis the previously elaborated so-called model of prophylactic, therapeutic and correcting action of children with difficulties in adaptation to school.

3. The problem of adaptation of the school conditions of children of high intelligence.

The studies comprised 75 children of 1st - VIIIth class, selected by Primary Schools on the grounds of a specially prepared instructions. All the children had the opinion of very capables pupils. As follows from the examinations the children were from various social and familiar environments. A significant part of the children showed deviations in the physical development. It is note worthy that more than 33% of the children brought about significant educational and even didactic difficulties, despite the high intelligence quotient. A majority of the children showed enhanced emotional and psychomotoric

excitability and some of them even neurotic reactions. The causes of disadaptation are quite complex and differentiated. They depend on both the home- and school environment and may also be caused by selective retardations of various psychic functions - such as retarded development of audial and visual perception and decreased manual capability.

As may be concluded from the results of the studies, which are now being elaborated in detail, - these children deserve a special pedagogical, psychological and medical care and an appropriate therapeutic and correcting action in order to enable good adaptation to school. Leaving the without special help might in many cases be dangerous to their outstanding capabilities. Elaboration of these results tends also to establish appropriate indications for treating difficult and at the same time capable children.

#### PAPERS PUBLISHED AND SUBMITTED FOR PUBLICATION 1972 - 1973

1. OSINSKI H., PAWLIKOWSKA E.

Potrzeba poradni psychoprofilaktyki przestępczości przy Izbach Dziecka MO. /Requirement for a Dispensary of Psychoprophylactic of Deliquency in Child Chambres of MO/.

Zdrow Psych 11, 1972, 65-72

#### 2. ZAKRZEWSKA B.

Wybrane zagadnienia psychologiczne dzieci ze wsi woj.białostockiego. /Selected Psychological Problems of Children in the Country Region of Białystok woyvodship.

Rocz Socjol Wsi 11, 1972, 67-80

3. ZAKRZEWSKA B., MARKIEWICZ J.

O znaczeniu interkalacji w metodzie reedukacji dysleksji. /On the

Significance of Intercalation in Dislection Reeducation/. Zagadnienia Wychow 19, 1972, 40-52

4. GAJEWSKA Z., OSINSKI H.

Wyniki wielostromych badań medycznych u dzieci z trudnościami czytania i pisania. /Results of Multidirectional Medical Examinations in Children with Reading and Writing Difficulties/.

Zdrow Psych 12, 1973, 52-61

5. GAJEWSKA Z., PODGÓRSKI J.

Zastosowanie buerlecytyny u dzieci. /Application of Buerlecitine in Children/.

Probl Lek 13, 1973, 191-194

6. MARKIEWICZ J., ZAKRZEWSKA B.

Dwutorowa reedukacja dzieci dyslektycznych w Polsce. /Dual Remedial Training of Dyslexic Children in Poland/. Bull Orton Soc 23, 1973, 39-51

7. OSINSKI H., GAJEWSKA Z., SIWKIEWICZ J., ZAKRZEWSKA B., SZMUKLER Sz.

Dzieci z trudnościami dydaktycznymi i wychowawczymi jednej szkoły podstawowej w badaniach Zespołu Higneny Psychicznej. /Children with Didactic and Educational Difficulties in one Primary School in Studies Performed by the Psochohygiene Department/. Zdrow Psych 12, 1973, 40-47

8. OSIŃSKI H., GAJEWSKA Z., SIWKIEWICZ J., ZAKRZEWSKA B., SZMUKLER S2.

Srodowisko rodzinne dzieci z trudnościami wychowawczymi i dydaktycznymi. /Family Environment of Children with Educational and Didactic Difficulties/.

Zagadnienia Wychow Zdrow Psych 5, 1973, 162-168

## 9. SIWKIEWICZ J., ZAKRZE WSKA B.

Analiza wymików badania trudności czytamia i pisania 200 dzieci miejskich i wiejskich. /Analysis of Results of Examinations of Reading and Writing Difficulties in 200 Town and Country Children/. Zagadnienia Wychow Zdrow Psych 5, 1973, 169-173

## 10. SIWKIEWICZ J., ZAKRZE WSKA B.

Znaczenie percepcji słuchowej i wzrokowej w procesie nauki czytania i pisania. /The Significance of Audial and Visual Perception in the Process of Learning of Reading and Writing/.
Zagadnienia Wychow Zdrow Psych - in press

## 11. ZAKRZEWSKA B., MARKIEWICZ J.

Próba reedukacji dzieci z trudnościami czytania - założenia i opis przypadku. /An Attempt of Reeducation of Children with Reading Difficulties - Assumption and Case Description/.

Zagadnienia Wych - in press

# I. ORGANIZATION TEAM OF THE DEPARTMENT OF PSYCHO-HYGIENE

Head: Z. Poset, M.D.

Organization Team of the Department of Psychohygiene in Łódź was brought into being the decision of the Director of the Medical Research Centre at 13 Februar 1973. Its task is:

- 1. to undertake studies on the problems of psychic hygiene of children and youth,
- 2. to elaborate the program and organizational structure of the future Department of Psychohygiene.

Toxicomania in Youth: Causes, Consequences, Prevention.

1. Effect of tourism /realization camps/ on the attitude of alcoholizing young people.

A questionnaire for studying the attitudes was prepared. Twoweek wandering camps for these young people were organized, in order to subject them to detailed pedagogic influence. Thirty five participants were examined by means of the questionnaires. The results are now being subjected to final elaboration.

2. Familiar environment of juvenile alcoholics.

Basic literature this problem was collected and the documentate ion of chosen cases from the antialcoholic Dispensary for Juvenile Alcoholics in Łódź was studied. Basing on this, a comprehensive questionnaire for environmental inquiry was prepared.

 Comparison of social environments of juvenile alcoholics and drug addicts.

Disposals for directed environmental inquiry was prepared. The inquiry - officers were instructed and studies on drug and alcohol addicts were undertaken.

4. Consumption of middles producing dependence among young people in Łódź.

Disposals for directed environmental inquiry comprising school, family and working place, were worked out. Questionnaires for cathegorized psychiatric examination were prepared. Preliminary consultations concerning the methods of psychological examination were carried out. Studies twenty persons drug- and alcohol addicts were initiated.

5. Fate and delinquency of juvenile alcoholics.

Literature concerning the problem was gathered; 30 environmental inquires were carried out; 50 case histories from Antialcoholic Clinics and Disaccustoming Department as well as 75 dossiers were analyzed. Elaboration of the results is in progress.

Factors conditioning social Adaptation and Disadaptation / Come-back to society of people released under amnesty in 1969/.

Three hundred court's records, 20 prosecutor's records, and 180 records of Penal-Administrative Councils were analyzed. Coding for computer calculations of the material dealing with 326 people released under amnesty was initiated.

#### PAPERS PUBLISHED AND SUBMITTED FOR PUBLICATION 1973

1. PEŁKA-SŁUGOCKA M., SŁUGOCKI L.

Leczenie odwykowe alkoholików w zakładach karnych.

/Disaccustoming Treatment of Alcoholics in Penitentiaries/.

Prawo i Życie no 21, 1973

- 2. PEŁKA-SŁUGOCKA M., SŁUGOCKI L.
- 0 błędach w zapytaniach o karalności. /Errors in questions about penality/.

Probl Wymiaru Sprawiedl - in press

3. PEŁKA-SŁUGOCKA M., SŁUGOCKI L.

Potrzeba leczenia a faktyczne leczenie skazanych na przykładzie badań. /The Need of Treatment and actual Treatment of Men under Sentence as revealed by examinations/.

Alkohologia Łódzka - in press

4. PEŁKA-SŁUGOCKA M., SŁUGOCKI L.

Skazani leczeni na oddziałe odwykowym zakładów karnych w czasie odbywania kary pozbawienia wolności./Men serving Imprisonment cured in Disaccustoming Departments of Penitentiaries/.

Gazeta Sadowa no 22, 1973

5. PEŁKA-SŁUGOCKA M., SŁUGOCKI L.

Wywiad milicyjny jako dowód w procesie karnym. / Milice Interview as Evidence in Penal Process/.

Palestra, no 6, 1973

6. POSEŁ Z., TOMCZAK J.W.

Problemy psychiatrii społecznej w Związku Radzieckim, /Problems of social Psychiatry in Soviet Union/.

Ann Acad Med Lodzensis • in press

### 1. ZAKRZEWSKI P.

Alkoholizm a proces rozwarstwienia ludności ze względu na warunki bytowe. /Alcoholism and the Process of Stratification of Population due to Living Conditions/.

Problemy Alkoholizmu no 4, 1973

# 8. ZAKRZEWSKI P.

Alkoholizm na wsi. /Alcoholism in the Country/. Wieś Współcz no 6, 1973

### 9. ZAKRZEWSKI P.

Nie ma resocjalizacji bez wyleczenia. /No Resocialization without Cure/.

Gazeta Sadowa no 15, 1973

### 10. ZAKRZEWSKI P.

Przestępczość znęcania się pod wpływem alkoholu nad członkiem rodziny /analiza kryminologiczna/. /Delinquency of Persecution of Family Members under the Influence of Alcohol /Criminological Analysis/.

Państwo i Prawo no 6, 1973

Alkohologia Łódzka - in press

#### 11. ZAKRZEWSKI P.

Szansa realizacji artykułu 102 nowego Kodeksu Karnego a celowość leczenia odwykowego w zakładach karnych. /The Chance of Realization of Art. 102 of the new Penal Code and usefuliness of Disaccustoming Treatment in Penitentiaries/.

# 12. ZAKRZEWSKI P.

Wzrost spożycia alkoholu a zmiany w nasileniu i strukturze przestępczości./Increase of Alcohol Consumption and Changes in the Intensity and Structure of Delinquency/. Problemy Alkoholizmu no 8-9, 1973 J. ELECTRON MICROSCOPY UNIT
Head: J.Borowicz, M.D., Associate Professor

Neuroregulation of basis biological processes of the organism.

In 1972, the following subjects were investigated:

- 1. Ultrastructural changes in neurosecretive nuclei of hypothalamus under the influence of anesthetic and psychotropic drugs. Control experiments were performed, which established the dose of 300mg/kg body weight to be sufficient to produce acute morphine intoxication. Studies were initiated to define smaller morphine doses sufficient to produce chronic intoxication.
- 2. Effect of pharmacological dehydration on neurosecretive nuclei in healthy rats and in rats with experimental brain edema. Studies were performed on the ultrastructure of supraoptic nucleus in healthy rats after administration of mannitol. Extensive body dehydration was observed, giving changes in the hematocrit. In brain, within the first hours after administration, "swelling" of astrocytic processes in the vicinity of vessels was noticed, resembling that appearing in brain edema. The changes receded within 24 hrs.

  3. Ultrastructural studies of Opalski's glial cells in tissue cultures in vitro.

The cytoplasm of Opalski cells was found to be characterized by a great number of lysosome - like structures, a marked decrease of

content of mitochondria and accumulation of structures which might correspond to mucopolysaccharides observed in the light microscope. Moreover, histochemical reactions revealed the presence of copper in the cytoplasm of Opalski cells originating from the cultures grown on the sera of patients with liver cirrhosis and Wilson's disease.

4. Ultrastructural changes in cat brain in experimental brain

The studies were performed on the brains of cats, with the edema produced by compression with a baloon filled with 1 ml of physiological salt solution. In the first alternating experiment the compression lasted for 2 and 24 hrs. Already after a 2 hour compression a complete set of morphological changes typical of brain edema were observed to appear both in the cortex and in the white matter. After a 24-hour compression the changes grew markedly more intense and in some areas the astrocytic processes appeared bursted in the perivascular region.

5. Ultrastructural studies on liver transplantation.

The studies were performed on livers that were prepared for transplantation, i.e. cooled and rinsed of the blood content by perfusion with Ringer's solution, polyelectrolyte Collins'solution and plasma. In all the perfused livers, more or less intense damages of endothelial cells and Browicz cells covering the sinusoides could be observed, which is probably related to the perfusion technique. The hepatocytes showed diminution or disappearance of glycogen granules and structural changes in mitochondria. The changes in hepatocytes were the slightest after perfusion with plasma and the most severe after perfusion with Ringer's solution.

In 1973, the following subjects were investigated:

- 1. Studies on brain edema:
- a/ The first step of studies on the ultrastructural changes in brain edema in cats was terminated.

edema.

b/ Morphological and biochemical studies on the brains of healthy rats after intraperitoneal administration of acute doses of mannitol were carried out.

- 2. Ultrastructural changes in neurosecretive nuclei of hypothalamus under the influence of anesthetic and psychotropic drugs. The experimental part on the acute and chronic morphine intoxication model in rats were completed. Further investigations in progress.
- 3. Ultrastructure of glial cell in gliopathies induced in vitro in tissue culture. This work has been performed in cooperation with the Laboratory of Neuropathology. The studies on Opalski's cells in tissue culture in vitro produced by addition to the medium of either the serum of patients with liver cirrhosis or ammonia or copper were terminated.
- 4. Transplantology.

In 1973, the following subjects have been elaborated:

- 1. In cooperation with the Surgical Research and Transplantation Laboratory - the ultrastructure of liver and kidney prepared for transplantation and of terminal lymphatic vessels in chronic lymphatic edema.
- 2. The electron microscopic appearance of blood vessels /mostly cappillaries/ in allogenous kidney transplants in dogs.

PAPERS PUBLISHED AND SUBMITTED FOR PUBLICATION 1972 - 1973

BESKID M., BOROWICZ J., NIELUBOWICZ J.
 Histochemical, Microscopic and Electron Microscopic Examinations of Adrenal Cell Cortex in two Cases of Thrombangitis Obliterans.
 Acta Histochem 44, 1972, 264-277

# 2. BOROWICZ J., GAJKOWSKA B.

Zmiany w ultrastrukturze neuronów jądra nadwzrokowego szczura w wyniku odwodnienia organizmu. /Ultrastructural Changes in Neurons of Supraoptic Nucleus of Rat Following Dehydration of the Organism/.

Patol Pol 23, 1972, 247-259

3. BOROWICZ J., DANIELEWICZ-KOTOWICZ A., OLSŻEWSKA K. Badania w mikroskopie elektronowym wątroby świni po perfuzji klinicznej. /Electron microscopic Studies on the Pig Liver after Clinical Perfusion/.

Acta Med Pol 14, 1973, 99-106

- 4. BOROWICZ J., DANIELEWICZ-KOTOWICZ A., OLSZEWSKA K.
  Ultrastruktura watroby świni w perfuzji doświadczalnej./Ultrastructure of Pig Liver in Experimental Perfusion/.
  Acta Med Pol 14, 1973, 91-96
- 5. BOROWICZ J., GAJKOWSKA B.

  The Golgi Apparatus and GERL System in Secretory Neurons of the Supraoptic Nucleus in Rats During Dehydration.

  Ann Med Sec Pol Acad Sci 18, 1973, 7-9
- 6. BOROWICZ J., JURKIEWICZ J., CZERNICKI Z.
  Badania mikroskopowo-elektronowe mózgu kota we wczesnym obrzęku doświadczalnym./Electron microscopic Studies of Cat Brain in early Experimental Edema/.

Neuropat Pol - in press

# 7. DANIELEWICZ-KOTOWICZ A.

Ultrastructural changes in the Rat Neurohypophysis in Hyper- and Hypofunction of Adrenal Glands.

Folia Histoch Cytochem 11, 1973, 309-310

## 8. GAJKOWSKA B.

Ultrastructural Changes in Nucleus Supraopticus and Paraventricularis of Rat Hypothalamus in Hyper - and Hypofunction of the Adrenals.

Folia Histochem Cytochem 11, 1973, 311-312

# 9. JURKIEWICZ J., BOROWICZ J.

Electron Microscopic Studies of Experimental Brain Edema. Folia Histochem Cytochem 11, 1973, 327-328

10. ŁAWKOWICZ W., KRZEMIŃSKA-ŁAWKOWICZOWA I., BOROWICZ J., KNAP J., KRÓLIKOWSKA I.

A Case Familial Thrombocytopenia /Thrombocytopathia Associated with Haemolitic Anaemia of unknown Heredity Pattern, An Interdisciplinary Approach.

Folia Haemat 99, 1973, 191-201

11. RUDOWSKI W., SCHIER J., BOROWICZ J., KLAWE Z., SIELCZAK M., KNAP J.

Two Cases of Chemodectoma of the Carotid Body.

Neuropat Pol - in press

# K. "MEDIPAN" SCIENTIFIC INSTRUMENTS Head; S. Karałow, M.Sc.

In January, 1973, the hitherto existing Electronic and Mechanics Medical Laboratory of the Research Centre was reorganized to the "MEDIPAN - Scientific Instruments".

The decision was stimulated by the growing needs of modernization of the technical equipment in all the Laboratories and Departments of the Research Centre.

"MEDIPAN" specializes in projectings and constructing prototypic research instruments for all the Departments of the Medical Research Centre as well as in adapting for other purposes the instruments which are in operation at present.

In 1973, the Laboratory patented two new constructions of scientific apparatuses:

1. Photo-box for oscilloscope camera,

Short description: The oscilloscope camera is composed of an optic system, with 8 gear transport-box/with speeds from 0,6 to 27 cm/sec/ and a photo-box- the construction of which was the subject of patenting. Photo-box is working as a consigning box, collecting-box and a special mechanism for moving the light-sensible non-perforated paper /70 mm width/. The box holds the exposition field in which the photos are recorded, when the photo-box is connected to the camera.

2. Pipette Puller, typ GMP-1, for pulling glass microelectrodes. Short description: two micro-electrodes are obtained from one glass canule. The canule is fixed in self containing seize, heated to glass fusibility temperature and then bursted by spring straining. The time and temperature of heating, and the straining force, - are regulated so, as to obtain the required form of the electrodes. Fixation of glass canules, the shape of heating elements and the characteristics of the straining force, allow to obtain concentric symmetric electrodes with parameters manifold repeated.

Puller type GMP-1 provides the possibility to prepare the micro-electrodes both in horizontal and vertical positions.

"MEDIPAN" patented the above mentioned constructions in July, 1973 in Patent Centre PAN, Warsaw, 21, Świętokrzyska Str.

### COOPERATION WITH FOREIGN COUNTRIES 1972 - 1973

# A. LABORATORY OF NEUROPHYSIOLOGY

In 1972 - 1973, the Laboratory of Neurophysiology has continued cooperation with the following foreign Institutes:

- Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, England, London/A.Guz, M.D., Prof./
- Clinical Research Laboratories, St.Georges Hospital Medical School, England, London /J.G.Widdicombe, M.D., Ph.D., Prof./
- Nobel Institute for Neurophysiology, Karolinska Institutet, Sweden, Stockholm /C. von Euler, M.D., Prof./
- Department of Physiology, Comenian University, Czechoslovakia, Martin /Z. Tomori, M.D./
- Department of Pathophysiology, Charles University, Czechoslovakia, Prague/F.Palećek, M.D./
- Department of Physiology, University of Milano, Italy /G.Sant'Ambrogio, M.D./
- Wellcome Research Laboratories, England, Beckenham /J.R.Vane, M.D., Prof./
- 8. Institut für Physiologie, BDR, Bochum /H.Loeschcke, Prof./

The cooperation consisted in joint studies, conferences and discussions on the results, exchange of publications and scientific worker.

In the 1972 - 1973 following scientific workers of the Laboratory stayed abroad for scientific training or to perform joint research program:

M. GŁOGOWSKA, M.D.-3 July - 30 August, 1972, Oxford University Laboratory of Physiology, England.

Completion of the experiments and elaboration of the results of studies on the peripheral regulation of breathing in pulmonary edema, extended by studies on the "rapid shallow breathing" mechanism.

K. HERBACZYŃSKA-CEDRO, M.D. - 1 September 1971 - 30 September 1972, Royal College of Surgeons, London, England.

The aim of the stay was to perform studies on the effect of anesthetic drugs on neural control of breathing and circulation within the joint research program of the Department of Neurophysiology of the Warsaw Centre and the Royal College of Surgeons. Extension of the studies on the role of the autonomic system in neural control of breathing and circulation in various types of general anesthesia.

J. STASZEWSKA-BARCZAK, M.D. - 15 - 23 March, 1972, University of Amiens, Faculty of Medicine and Pharmacology, France.

The aim of the stay was a continuation of studies on the neurophysiology of breathing and circulatory system and elaboration of the results for publication.

M. SZEREDA-PRZESTASZEWSKA, M.D. - 8 October 1971-8 October 1972, Oxford University, Laboratory of Physiology, England.

The aim of the stay were the studies on respiratory reflexes in bronchoconstriction produced by physical, chemical and immunological factors. The studies are included in the program of cooperation of the Department of Neurophysiology with the Laboratory of Physiology in Oxford.

A. HUSZCZUK, M.D. - 1 September 1973 - 1 March 1974 - Department of Medicine, Charing Cross Hospital Medical School, London, England.

The aim of the stay are the studies on the participation of the mechanisms of Hering-Breuer inflation and deflation reflexes in the reflex and chemical control of breathing.

M. POKORSKI, M.D. - 6 August 1973 - 30 September 1974, Ruhr-Universität-Bochum, Institut für Physiologie, BRD.

Studies on the correlation between vagal afferentiantion—and the function of chemosensitive regions. The studies comprise in particular the behaviour of basic respiratory reflexes in the conditions of stimulation and destruction of these regions.

T. TRIPPENBACH, M.D. - 1 October 1973 - 1 October 1974, Karolinska Institutet, Stockholm, Sweden.

Studies on the problems concerning regulation of rate and depth of breathing.

In 1972 - 1973, the Department of Neurophysiology received the following foreign guests:

A. GUZ, M.D., Prof. - 8 - 15 October 1972, Department of Medicine, Charing Cross Hospital Medical School, London, England.

The aim of the stay was to carry out discussions on the physiological role of vagal reflexes.

- F. PALACEK, M.D. 8 15 October 1972, Department of Pathophysiology, Charles University, Prague, Czechoslovakia. Discussions of results.
- S. SANT'AMBROGIO, M.D. 8 15 October, 1972, University of Milano, Laboratory of Physiology, Italy.

The aim of the stay was the presentation of the results of studies on the role of respiratory muscles and establishment of the program of further cooperation of the Department of Neurophysiology of the Centre and the Laboratory of Physiology, University of Milano.

Z. TOMORI, M.D. - 8 - 15 October 1972, Comenian University Department of Physiology, Martin, Czechoslovakia.

The aim of the visit was the elaboration of the technique for studying the role of reflexes from the upper airways.

J.G. WIDDICOMBE, M.D., Ph.D., Prof. - 8 - 15 October, 1972 Oxford University, Laboratory of Physiology, England.

During the visit, the joint studies on the role of vagal reflexes were discussed in view of preparing the results for a paper.

C.von EULER, M.D., Prof. - 2 - 5 May 1973, Karolinska Institutet, Nobel Institute for Neurophysiology, Stockholm, Sweden.

Lectures and discussions in the Laboratory.

J.G. WIDDICOMBE, M.D., Ph.D., Prof. - 3 - 12 Februar 1973, Oxford University, Laboratory of Neurophysiology, England.

Was giving presentation of the results of joint investigations on the role of vagal reflexes with the discussions and preparations of the scientific materials for joint publications.

#### B. LABORATORY OF NEUROPATHOLOGY

In 1972 and 1973, the Department continued cooperation based on the previous appointments with the following Institutes:

1. Institute of Physiology, Georgian Academy of Sciences, Tbilisi /G.Mchedlishvili, M.D., Prof./. The cooperation concerned problems of the morphological, metabolic and pathophysiological consequences of hypoxia of the central nervous system.

The pathophysiological part of the studies was performed in the Institute of Physiology of the Georgian Academy of Sciences, the morphological part in the Department of Neuropathology of the Centre and the biochemical part in the Departments of Neuropathology and Neurochemistry of the Centre and in the Institute of Physiology of the Georgian Academy of Sciences.

Institute of Experimental Medicine, Academy of Medical Sciences, Leningrad, USSR /J.Zabotyński, M.D., Prof./.

The cooperation concerned problems of myelination, demyelination and remyelination in conditions of tissue culture. The Soviet group performed studies on myelin impairment basing on immunological reactions; the Polish group - in hypoxic conditions.

3. National Institute of Nervous Diseases NIH, Bethesda, USA /I.Klatzo, M.D./ the cooperation concerned the biology and pathology of glia and pathogenesis of brain edema.

In the framework of this cooperation, dr Z.Rap, senior assistant of the Department, has been working for 1,5 year in the NIH on the effect of hypertonic solutions on the permeability of cerebral vessels.

In September 1973 M.Spatz, M.D., from NIH, visited the Department with the aim of discussing the results of joint studies and their further directions.

- 4. Institute of Pathology, University of Halle, DDR, /H.Jānisch, M.D., Prof./ in the field of chemically-induced brain tumours. In this connection dr G.Musil stayed in the Department of Neuro-pathology and received training in histochemistry of experimental brain tumours.
- 5. Institute of Pathology, Albert Einstein College of Medicine, New York, USA/E.Terry, M.D., Prof./ - in the field of the ultrastructure of carbon monoxide encephalopathy. In the framework of this cooperation, dr J.Korthals assistant of the Department, is staying since September 1972 in New York.
- 6. Centre of Nuclear Medicine, University of Alabama, Birmingham, USA /W.N.Tauxe, D.M., Prof./ in the field of cerebral ischemia. Dr A.Kapuściński, senior assistant of the Department of Neuro-pathology stayed in this Institute for 1,5 year.

Moreover, the information and documentation exchange with the Institute of Neurology, University of Vienna, Institute of Neurobiology in Göteborg, and Department of Neuropathology of the University in Paris were continued.

The Laboratory, in cooperation with the Committee of Neurological Sciences Polish Academy of Sciences organized the International Symposium of Neurology, Child Neurology and Neuropathology.

The chief problems of the Symposium included:

- 1. Conscience and its disturbances, clinical, experimental, morphological and metabolic aspects.
- 2. Development of motor functions and their disturbances.

In this Symposium 100 persons participated, among them 37 from the scientific centres in Czechoslovakia, Hungary, Austria, DDR, BRD, Italy, Holland and Yugoslavia.

The following persons have payed short-term scientific visits abroad:

M. SMIALEK, M.D. - in the Institute of Pathophysiology, Ljubljana University, Yugoslavia - with the aim to practice the Carthesian microdiver technique.

M.J. MOSSAKOWSKI, M.D., Prof. - with the aim to obtain information on the activity and lines of work of the Neuropathological and Neurochemical Centres in BRD.

A. KAPUŚCIŃSKI, M.D. - stayed in the period 26 May 1971 - 27

November 1972 at the University of Alabama, Birmingham, USA with the aim to obtain some additional training in the isotopic
technique with emphasis its application in studies on the effect of
oxygen insufficiency on the central nervous system and pathomechanism of cerebral oedema.

Z. RAP, M.D. - in National Institute of Health, Bethesda, USA,
15 October 1971 - 28 August 1972. The aim of the visit were studies on the pathology of the hypothalamic-hypophyseal system.

I. ZELMAN, M.D. - in Max Planck's Institut, Munich, BRD, 16 November 1971 - 16 Februar 1972. The aim of the visit were studies of exogenic encephalopathies and toxic brain oedema, accompanying most of exo-and endogenic intoxications.

In 1973, the following persons visited foreign Institutes for scientific training:

M. DAMBSKA, M.D., Associate prof. - in the Laboratory of Prenatal Physiology, Bethesda, USA, 20 October 1973 - 1 March 1974. The aim of the visit was to compare the results of neuropathological examinations of lesions of the immature central nervous system in humans with the results of experimental studies carried out on monkeys in Bethesda.

- J. KORTHALS, M.D. in the Albert Einstein College of Medicine, Yeshiva University, Bronx N.Y., USA, 1 September 1972 31

  August 1974. The aim of the visit was to acquire more experience in the electron microscopy technique, to become acquainted with a special method of fixing and staining of the nerve tissue, to learn to apply histochemical methods in ultrastructural studies and to carry out electron microscopic studies of experimental carbon monoxide encephalopathy.
- K. RENKAWEK, M.D. in the Institute of Neurology, London, England, 16 January 1973 16 March 1973. The aim of the visit were electron-microscopic studies of the ultrastructural features of nerve tissue in normal and pathologic conditions. Evaluation of the differentiation of glial cells and of the pathological changes occurring in encephalo-hepatic syndromes.
- K. RENKAWEK, M.D. in the Laboratory of Neuropathology and Neuroanatomical Sciences, Bethesda, USA, 1 July 1973 30 June 1974. Studies on the role of microelements in the biology and pathology of nerves and glial and on the solubility of cell membranes in conditions of hypoxia of neurons and glia.

The following foreign guests visited the Department:

- I. KLATZO, M.D. Head of the Department of Neuropathology National Institute of Health, Bethesda, USA, 6 - 12 April 1973, for discussion of the program of further cooperation, consultations and scientific conferences were hold on 6 - 11 September 1973 for establishment of further cooperation within the Polish-American scientific agreement.
- W. KRÜCKE, M.D., Prof. Director of the Department of Neuropathology, Max-Planck Institute, Frankfurt/Main, BRD, 19 - 25 September 1973. Consultations and scientific discussions in the

Departments of Neuropathology, Neurophysiology and Neurochemistry.

- I. VIKTOROV, M.D., N. VIKTOROVA, M.D. Brain Institute and Institute of Neurology, Academy of Medical Sciences, USSR, 17 27 December 1973, for familiarization with the problematics of the Laboratory and lectures concerning the subjects of their studies.
- J. ZABOTYŃSKI, M.D., Prof. Head of the Department of Neuropathology, Institute of Experimental Medicine, Academy of Medical Sciences, Leningrad, USSR, 2 9 June 1973. The aim of the visit was to discuss the results of joint studies on myelination, demyelination and remyelination in the conditions in vitro. The studies are included in the agreement between the VIth Department of the PAN and the Academy of Medical Sciences in Leningrad. The guest discussed the plans of further cooperation and delivered a lecture.

# C. LABORATORY OF COMPARATIVE NEUROLOGY

E. Osetowska, M.D., Prof. - Grant of Max-Planck-Institute for Hirnforschung, Frankfurt a.M., October-December 1972. Co-working with W. Krücke, M.D., prof. on the calcified neurones in "pt" rabbit /see IVth Danube Symposium of Neuropathology, Vienna 1973/.

1973. In problem "Experimental studies on the hereditary disease of CNS with model of the "pt" rabbit" / "pt" genetic symbol for "hereditary paralytic tremor"/: co-working since 1 February with National Health Institute, Bethesda, USA /PL-480, agreement 05-035-1 for three years/.

# 1973 the Laboratory was visited by:

- J. ZABOTINSKI, M.D., Prof., Head, Laboratory of Pathology of the Nervous System, Institute for Experimental Medicine, Acad. Med.Sci, USSR, Leningrad.
- W. KRÜCKE, M.D., Prof., Director, Division of Neuropathology, Max-Planck-Institut for Hirnforschung, Frankfurt a.M.

### D. LABORATORY OF NEUROCHEMISTRY

In 1972 - 1973 the Department cooperated with the following foreign scientific Institutions:

1. Department of Biochemistry and Department of Pathophysiology of the Georgian Academy of Sciences - in solving the problems of the intracellular mechanism regulating the metabolism of CNS cells in normal conditions and in pathology /hypoxia, anesthesia, pharmacological agents/.

Subjects: a/ carbohydrate and energy metabolism; b/ biochemical properties of mitochondria; c/ metabolism of mediators; d/ the role of cyclic 3' = 5' AMP in the regulation of the metabolism of biogenic amines and mediators and of the carbohydrate and energy metabolism.

Assistant Prof. Czikwaidze, M.D., from the Department of Biochemistry Georgian Academy of Sciences, was staying for 3 months in the Department of Neurochemistry. During his visit the results of investigations were discussed, the problems of further cooperation were established and the papers for the working symposium to be hald in may 1973 were selected. The methods of fatty acid determination and of isolation of mitochondrial fractions for studies on oxidative phosphorilation were presented to him and a number of experiments have been carried out together on the

effect of 3' - 5' cyclic AMP on the ACh metabolism and on the releasing of fatty acids.

Results: A close correlation was shown to exist between the hypoxia - induced disturbances of the metabolism of biogenic amines, lipids and carbohydrates and the system directing the synthesis of the cyclic form of AMP.

2. Department of Biochemistry, Karl-Marx's University, Leipzig, DDR.

Subjects: a/ protein and amino acid metabolism in the CNS in normal and pathological conditions; b/ metabolism of neurotransmitters.

Visits: A one-week stay of the Head of the Department of Biochemistry, Leipzig University, in the Laboratory of Neurochemistry in Warsaw and a two-week stay of A.GROMEK, D.Sc., the Head of this Laboratory, in the Department of Biochemistry in Leipzig.

The hitherto obtained results were discussed, the program of further cooperation was established and a paper entitled: "The properties of mitochondrial hexokinase" was submitted for publication in "Neuropatologia Polska". The other scientific contacts were connected with the Department of Neurochemistry of the Psychological Institute in Jena, with the Institute of Pharmacology in Magdeburg and with the Institute of Molecular Biology in Berlin.

Institute of Physiological Chemistry University of Köln, BRD.
 Problem: Lipid metabolism in the brain.

'The Head of the Laboratory of Neurochemistry, A. GROMEK, D.Sci., delivered a lecture on the problems studied in the Laboratory and discussed the problems concerning the scientific cooperation and exchange of coworkers. Scientific contacts have been esta-

blished with the Max-Planck Institute for Experimental Medicine in Göttingen and with the Institute of Neurobiology in Frankfurt/Main.

Senior assistant of the Laboratory of Neurochemistry, J. STRO-SZNAJDER, M.D., stayed in the Department of Physiological Chemistry of the above mentioned Institute /Head H. Debuch, M.D., Prof. / in the period from 1 March 1972 - 15 Februar 1973, as a stipendiary of the Alexander von Humboldt grant. During her stay J. STROSZNAJDER, M.D., has been working on the biosynthesis of plasmalogen, one of the phospolipid from the phosphotidyl-ethanolamine fraction in the rat brain during myelination. A series of experimental investigations on this problem have been performed. Two communications concerning this work were presented at biochemical meeting in Stockholm and Nottingham. The results in the final form will be published. In cooperation with the above Institute, the studies on the synthesis of nerve tissue specific phospholipids were continued. In the cadre of this cooperation Prof. H. Debuch has visited our Centre in the period from 1 June - 15 June 1973. The established program of furtner cooperation is being continued.

4. Institute of Neurobiology, University of Göteborg, Sweden /A. Hamburger, M.D., Prof./

A scientific cooperation on the problem concerning the biochemical properties of neuronal and glial cells was established.

As a result of this cooperation, a communication of J.W. LAZARE-WICZ, A. HAMBURGER, H. HALJAMÄE entitled: "Studies on calcium uptake by brain subcellular fractions" was presented at the International Congress of Biochemistry in Stockholm /1 - 7 July, 1973/. The material of this communication was included in the paper already accepted for publication in Journal of Neurochemistry. In addition, further joint studies on the characteristic of calcium tran-

sport in brain mitochondria were carried out. The results were published in 1974.

5. Department of Physiology, Medical School University of North Carolina, Chapel Hill, USA - in cooperation of the Laboratory of Neurochemistry September 1972 - September 1973; -

Senior assistant of the Department of Neurochemistry,

B. BRONISZEWSKA-ARDELT, M.D., has undertaken studies on
the hexokinase activity in the brain. The studies concerned both
the adult and immature animals. In the brains of adult animals hypoxia was shown to shift the hexokinase activity from mitochondria
to cytoplasm.

These changes were not observed in the brains of 5-day rats. The results of these studies were included in the publication entitled: "Hypoxic changes in brain hexokinase distribution: phylogenetic and developmental considerations", which will appear in "Comparative Physiological Biochemistry" /USA/.

6. Institute for Brain Research, Amsterdam, Holland.

Studies were continued on the effects of hypoxia on the glucose metabolism and high-energy compounds level in the brain, taking into account the influence of adenine nucleotides on the glycolytic activity of cytoplasm.

7. K. DOMAŃSKA-JANIK, M.D. - participated in the EMBO course on "Micro-methods in Molecular Biology" - Gottingen, BRD,

Max-Planck Institute of Experimental Medicine, 17 - 30 September 1973. During this course new biochemical methods adapted to studies using small quantities of biological material were presented.

#### E. DEPARTMENT OF NEUROSURGERY

The Department cooperates with the Centre of Classification and Nomenclature of Nervous System Tumors of the World Health Organization /Köln, BRD/.

In 9 - 15 December 1973, the staff of the Department participated in meeting whose aim was to establish scientific cooperation between the Department of Neurosurgery of the Medical Research Centre and the Burdenko's Institute of Neurosurgery in Moscow. The subject of the joint investigations will be the pathogenesis and methods of prevention and treatment of brain edema.

The clinical part of these studies will be carried out in the Burdenko's Institute of Neurosurgery, while the experimental part will be done in the Department of Neurosurgery in Warsaw.

The problem will include:

- 1. Effect of intracranial pressure on the blood flow in venous sinuses of the brain.
- 2. Reactivity of blood vessels in brain edema.
- Mechanism of therapeutic function of osmotically active drugs and indications for osmotherapy.
- 4. Methods of studying the blood-brain barrier in brain edema.

It is planned to publish the results in Polish scientific journals and to discuss them at joint meetings, twice a year, in June in Moscow and in November in Warsaw.

The first meeting is going to be held on Summer 1974.

Scientific training abroad 1972 - 1973:

- E. MEMPEL, M.D. Functional Neurosurgery Centre, Paris, France, 2 Januar - 28 March 1973, aiming:
- 1. Familiarization with the most recent research methods in neuroanatomy and with complex clinical studies of various specialties of

the surgical treatment of epilepsy. During this stay he visited also, in February 1973, the Neurosurgical Clinic Fock's Surgical Centre, Paris, France; the aim: Familiarization with the most recent achievements in the field of brain stereotaxia in man; and in March 1973 the Neurosurgical Clinic Canton Hospital, Zurich, Switzerland; the aim: Familiarization with new methods of antipain operations and diskineses treatment in man by means of stereotactic operations on cerebellar nuclei, as well as of vascular brain diseases.

# F. SURGICAL RESEARCH AND TRANSPLANTATION LABORATORY

According to the cooperation agreement between the Polish Academy of Sciences and the Czechoslovak Academy of Sciences, H. ŁUKASIEWICZ, M.D. spent two weeks at the Institute of Experimental Medicine in Prague.

The purpose of the visit was to study the immunological tests /cytotoxic, opsonine, inhibition of leukocytes/ for the diagnosis of rejection kidney and liver grafts and the coagulation process in the rejection process.

In 1972, the Department was visited by the following foreign guests:

- S. BENMARK, M.D., Prof. University of Lund, 17 26 March 1972.
- R. SELLWOOD, M.D., Prof. Department of Surgery, University of Manchester, 21 28 May 1972.
- P. KLOPPER, M.D., Prof. Department of Surgery, University of Amsterdam, 23 30 September 1972.
- M. LUNING, M.D. Head of Lymphographic Laboratory, Humboldt University, Berlin, 9 14 September, 1972.

The purpose of their visits was to become acquainted with the research programme of the Department on liver and kidney transplantation and the pathophysiology of lymphatic system. Each of the invited guests delivered a lecture concerning the experimental problems.

- S. BENMARK, M.D., Prof. "Problems of transplantation of auxilliary liver"
- R. SELWOOD, M.D., Prof. "Problems of breast cancer"
- P. KLOPPER, M.D., Prof. "Problems of liver transplantation, pathophysiology of gastric secretion"
- M. LUNING, M.D. "Problems of pathophysiology of lymphedema".

  Scientific visits and training abroad in 1973:
- H. ŁUKASIEWICZ, M.D. Center for Thrombosis Research, Temple University School of Medicine, Philadelphia, USA, 1 September 1973 1 Februar 1974.

Studies on coagulation disorders following immunological reactions, immunology of blood platelets and participation of the coagulation process in rejection of organ transplants.

W. OLSZEWSKI, M.D., Associate Prof. - Institut für Chirurgische Forschung, Munich, BRD, 23 October 1972 - 23 Januar 1973. Studies on the cellular and humoral phenomena in the process of hyperacute rejection of xenogeneic grafts. Studies on preservation of organs. Studies on selection of donors and recipients of organs grafts.

J. POLAŃSKI, M.D. - Institute of Clinical Studies, Belfast, Ireland, 1 September 1972 - 1 September 1973.

Studies on basic problems of liver physiology and liver preservation for transplantation.

In 1973, the Department was visited by the following foreign guests:

W. HARTIG, M.D. - Karl-Marx University, Leipzig, DDR, 9 - 14 April, 1973.

Delivered a lecture on the modern methods of parenteral alimentation.

P. STRASSBURGER, M.D. - Karl-Marx University, Leipzig, DDR, 17 June - 7 July 1973.

A training visit for study of technical problems in transplantation,

S. VIRAGH, M.D. and M. PAPP, M.D. - Hungarian Academy of Sciences, 5 - 17 November, 1973.

Delivered lectures entitled: "Ultrastructure of Lymphatics", and:
"Lymph flow and pressures in experimental pancreatitis".

K. MESSMER, M.D. - Institute of Experimental Surgery, Munich, BRD, 21 - 25 November 1973.

The purpose of the visit was to become acquainted research with the programme on the pathophysiology of the liver and to deliver a lecture on the experimental and clinical aspects of hemodilution. A cooperation apreement was signed with the Laboratory of Organ and Tissue Transplantation of the Academy of Medical Sciences, USSR.

It was decided to carry out joint studies on the problem of:

- 1. hyperacute rejection of organ transplants,
- 2. preservation of organs and changes in their blood capillaries,
- 3. changes in the lymphatic system of the intestine in ischemia.

#### G. LABORATORY OF APPLIED PHYSIOLOGY

In the cadre of permanent cooperation with the Cosmic Biology and Medicine Section, appointed through the mediation of the Committee of Studies of Peaceful Utilization of Cosmic Space- of Polish Academy of Sciences, studies were carried out on the effect of limited motor activity on the organism and on the body temperature regulation in diverse environmental conditions.

The following scientific works were performed:

- 1. Calorigenic activity of catecholamines in the conditions of limited motor activity of the organism;
- 2. Changes in the daily excretion of catecholamines in rats in the conditions of hypokinesia;
- 3. Effect of heating of rabbit nostrils on the course of thermogenesis.

A temporary discussion on the course of cooperation took place during the meeting of the Permanent Working Group on Cosmic Biology and Medicine of the Socialist Countries, in Berlin, May, 1973.

A scientific contact with the Institute of Biophysics of the Czechoslovak Academy of Sciences in Brno was initiated with the aim to perform joint studies on some aspects of thermoregulation within the limits of the Interocosmos program.

In 1972 - 1973, the following scientific workers of the Department stayed abroad for scientific training:

J. ŁYSZCZARZ, M.D., Associate Prof. - visited the Physiological Institutes, BRD, 16 November 1971 - 16 February 1972.

The aim of the visit was familiarization with the research methods applied in the study of the mechanism of adaptation of breathing to temperature changes and the establishment of scientific contacts which would allow to enlarge the spectrum of studies on thermo-

regulation performed in the Laboratory of Applied Physiology.

K. NAZAR, M.D. - in Institute of Gymnastics and Sports, Stockhom, Sweden, 1 October - 31 December 1972.

The aim of this visit included studies on the adaptation of human organisms to long-term effort and familiarization with some methods of studies of the central and peripheral circulation and the muscle metabolism in man.

S. KOZŁOWSKI, M.D., Associate Prof. - in Department of Physiology, Cambridge University, England, 1 November 1973 - 31 Januar 1974.

The aim of the visit was the continuation of the joint studies of the Laboratory of Applied Physiology and Department of Physiology on the central regulation of water metabolism of the organism.

J. SOŁTYSIAK, M.D. - stayed in the Institute of Applied Physiology, Stockholm, Sweden, 28 December - 27 April 1973.

The aim of the visit was:

- 1. Familiarization with new research methods: measurement of minute volume of the heart application of breathing mixtures in studies of the mechanisms responsible for high physical efficiency of man muscle biopsy technique PO<sub>2</sub>, PCO<sub>2</sub>, and blood pH-measurements after Astrup.
- 2. Studies on the effect of physical training on the mechanism of neuroregulation of heart frequency during submaximal and maximal efforts in men, -application of pharmacological blockade of the sympathetic system /atropine, propranolol/.
- 3. Participation in the meeting of the Scandinavian Physiological Society, concerning the structure and metabolism of slow and fast muscle fibres.

E. TURLEJSKA-STELMASIAK, M.D. - was staying in the University of Lille, Faculté de Médicine et de Pharmacie, Laboratoire de Physiologie, Lille, France, 1 December, 1973 - 22 April, 1974. The aim of the visit was familiarization with microelectrode methods for study of the morphology and function of hypothalamic structures controlling the thermoregulatory mechanisms in experimental animals. Participation in experiments aiming to elucidate the function of these structures in man, significant for organisms protection against thermal stress.

#### Beside that:

- 1. Participation in the Congress of the French Physiological Society, Bordeaux, France, 24 25 May, 1973. Communication: "Responses thermoregulatrices á la stimulation thermique de l'hypothalamus chez le lapin déshydraté". /Thermoregulatory responses to the thermal stimulation of the hypothalamus in dehydrated rabbits/.
- Participation in the International Colloquium in Strasbourg
   13 July, 1973 entitled: "Quantitative prediction of physiological effects of thermal environment in Man".
- 3. Work entitled: "The influence of dehydration on heat dissipation mechanism in the rabbit", accepted for publication /9 October 1973/in the J de Physiol.

The following foreign scientists visited the Department on invitation:

P.O. ASTRAND, M.D., Prof. - Head of the Department of Applied Physiology, Stockholm, Sweden, 10 - 18 March, 1973.

The aim of the visit were scientific consultations and participation in the experiments performed in the Laboratory of Applied Physiology.

J.T. FITZSIMONS - Head of the Department of Physiology, University of Cambridge, England, 28 August - 7 September, 1972.

The aim of the visit was consultation of studies on the central regulation of heat in relation to electrolyte level, participation in the experiments and presentation of the results of own studies.

In 1973, the Laboratory of Applied Physiology was visited by 11 foreign guests. These were mostly short-term visits, not exceeding 10 days, of which the aim was familiarization with the scientific problems of the Laboratory as well as discussions and mutual exchange of scientific experience.

In the cadre of the exchange program between the American and Polish Academy of Sciences, in our Laboratory stayed for three months J.E.Greenleaf, M.D., from the Laboratory of Environmental Physiology of Man for Ames Center, California. A number of experiments were performed together on the regulation of inner temperature during physical exercise. The cooperation with Greenleaf's Laboratory is being continued according to the previously outlined program. The results of the experiments are discussed by correspondence and printed, or prepared for publication in the nearest future.

In 1973, in addition, a close scientific cooperation with the Department of Physiology of the Medical Academy in Pecs, Hungary - was established, the Department being run by a world famous specialist in thermoregulation, Prof. Donhoffer, M.D.

The scope of cooperation and the possibilities of performing common studies on various aspects of thermoregulation were discussed.

PARTICIPATION OF THE SCIENTIFIC STAFF OF THE CENTRE IN SCIENTIFIC CONFERENCES, CONGRESS, SEMINARS, SYMPOSIUMS AND MEETINGS, 1972 - 1973

# A. LABORATORY OF NEUROPHYSIOLOGY

XIIth Congress of the Polish Physiological Society, Poland, Olsztyn, 13-17 September, 1972.

KARCZEWSKI W.A., KARCZEWSKA E., RYCEMBEL Z. BAIMBETOWA-DZIADOSZ N.

Badania nad reakcjami oddechowymi u normo- i hipertermicznych królików./Respiratory Control in Normo- and Hyperthermic Rabbits/.

#### PRZYBYLSKI A.

Impulsacja pressorecepcyjna, niektóre spostrzeżenia.

/Pressoreceptor Impulsation - some Observations/.

### STASZEWSKA-BARCZAK J.

0 mechanizmie aktywizacji reakcji adrenergicznej w ostrej fazie doświadczalnego zawału serca. /On the Mechanism of Adrenergic Response in the Acute Stage of experimental Myocardial Infarction/.

Vide A45

# TRIPPENBACH T.

Wpływ obwodowej informacji nerwowej na aktywność motoneuronów przeponowych w warunkach sztucznej wentylacji. /The Influence of some Peripheral Factors on the Phrenic Motoneurones in artificial Ventilation/.

Vth International Congress of Pharmacology, USA, San Francisco, 23-28 July, 1972.

GRYGLEWSKI R., FLOWER R., HERBACZYŃSKA-CEDRO K., VANE J.R.

Inhibition of Prostaglandin Synthesis by Antiinflammatory Drugs. Abstracts of Volunteer Fapers  $N^{\circ}539$ .

HERBACZYŃSKA-CEDRO K., VENE J.R.

An Intrarenal Role for Prostaglandin Production. Abstracts of Volunteer Papers N<sup>0</sup>595.

VIth World Congress of Cybernetic Medicine, Italy, Napoli, 5 - 9 April, 1972.

PRZYBYLSKI A.

A Theoretical Approach to the Theory of Biological Stimulus.

International Conference on Prostaglandins, Austria, Vienna, 25 - 28 September, 1972.

HERBACZYŃSKA-CEDRO K., VANE J.R.

Local Prostaglandin Production Contributes to Blood Flow Autoregulation in the Dog Kidney.

IIIrd Martin Meeting of Respirology, Czechoslovakia, Martin, 12 - 17 September, 1972.

GŁOGOWSKA M.

Some Aspects of the Reflex Control of Breathing during Lung Edema.

GROTEK A., HUSZCZUK A.

Studies on the Input-output Relationship in Artificially Ventilated Rabbits.

KARCZEWSKA E., KARCZEWSKI W.A., RYCEMBEL Z.

The Role of the Vagus Nerves in the Ventilatory Response to
Carbon Dioxide during Hyperthermia.

STRÂNSKY A., SZEREDA-PRZESTASZEWSKA M., WIDDICOMBE J.G.

Activity of N. Recurrens Motoneurons during some Respiratory Reflexes.

SZEREDA-PRZESTASZEWSKA M., STRÁNSKY A.
Reflex Effects of Bronchoconstruction on Laryngeal Calibre.

Symposium of the European Society of Clinical Respiratory Physiology and Turkish Society of Studies on Breathing, Turkey, Stambul, 3-8 September, 1972.

KARCZEWSKI W.A.

Some Effects of Anesthetics on the Functional Organisation of the Bulbo-pontine Respiratory Complex. Vide A36

II Krajowe Sympozjum Biocybernetyki, Biomatematyki i Biotechniki, Polska, Warszawa, 6 - 8 kwiecień, 1972. /IInd Symposium of Biocybernetic, Biomathematics and Biotechnics, Poland, Warsaw, 6 - 8 April, 1972/.

PRZYBYLSKI A.

 Ekstremalna charakterystyka bodźca i minimalizacja energetyczna reakcji układu żywego. /Extremal Characteristic of Stimulus and Energetic Minimalization of Reaction of a Living System/.

# PRZYBYLSKI A.

Niektóre dane i uwagi o impulsacji neuronalnej. /Some Data and Remarks about Neuronal Impulsation/.

PRZYBYLSKI A.

Ogólne założenia koncepcji bodźca biologicznego. / General Assumptions of the Concept of Stimulus/.

PRZYBYLSKI A.

Spontaniczna impulsacja neuronalna. /Spontaneous Neuronal Impulsation/.

2nd Congress of Electroencephalography, DDR, Weimar, 21 - 24 May, 1973.

PRZYBYLSKI A.

Die Korrelation zwischen EEG-Synchronisation und Atmung und Zirkulationssystem bei Anoxie. /The Correlation between EEG Synchronization and Respiratory and Circulatory System in Anoxia/.

IV Kongres Polskiego Towarzystwa Farmakologicznego, Polska, Łódz, 28 - 30 Sierpień, 1973. /IVth Congress of the Polish Pharmacological Society, Poland, Łódz, 28 - 30 August, 1973/.

HERBACZYŃSKA-CEDRO K., STASZEWSKA-BARCZAK J., JANCZEWSKA H.

The Release of Prostaglandin - like Substance Accompanying Muscular Exercise in the Hind-Limb of the Dog.

Congress of the European Society of Clinical Respiratory Physiology, England, Oxford, 4 - 8 September, 1973.

Symposium on Lung Reflexes

Chairman - KARCZEWSKI W.A.

SZEREDA-PRZESTASZEWSKA B.

The Reflex Effect of Pneumathorax on Laryngeal Lumen.

Colloquium Euromech N<sup>o</sup>32: Cardiovascular and Respiratory Mechanics, England, London, 17 - 20 September, 1973.

SZEREDA-PRZESTASZEWSKA B.

Pressure-Flow Relationships of the Cat Larynx and their Reflex Control.

IVth International Symposium of Cybernetics organized by Physiologisches Institut-Leipzig, 19 - 22 September, 1973.

PRZYBYLSKI A.

Some Implications of the Extremal Relationship between Energy and Information of Biological Stimulus.

Vide A44

IVth International Congress of Biomathematics, France, Paris,6-7 September, 1973.

PRZYBYLSKI A.

Functional and Structural Information in Biological Organization.

Vide A43

Symposium on Pharmacodynamics of Circulation, Czechoslovakia, Smolenice, 11 - 13 November, 1973.

STASZEWSKA-BARCZAK J.

The Mechanism and Significance of Adrenergic Reaction in the early Stages of Myocardial Infarction in the Dog.

Symposium on Respiratory Neurophysiology, England, Oxford,

3 - 4 September, 1973.

KARCZEWSKI W.A.

Polypnoea - a Component of the Neural Control of Breathing.

# SZEREDA-PRZESTASZEWSKA B.

Reflex Control of the Larynx and its Relation to Breathing.

Meeting of the British Physiological Society, England, Southampton, 13-14 April, 1973.

SZEREDA-PRZESTASZE WSKA B., WIDDICOMBE J.G. Reflex Changes in the Lumen of the Cat Larynx due to Chemical Irritation of the upper Airways.

Vide A49

Seminar in the Nobel Institute in Stockholm, Sweden, September, 1973.

KARCZEWSKI W.A.

On the Mechanisms of Polypnoea.

# B. LABORATORY OF NEUROPATHOLOGY

XIII Congress of Cell Biology, England, Brighton, 3 - 8 September, 1972.

MOSSAKOWSKI M.J., BOROWICZ J., KRAŚNICKA Z.
Ultrastructure of Experimental Hepatogenic Gliopathy in Tissue
Culture.

VIIIth Congress of Federation of European Biochemical Societies, Holland, Amsterdam, 20 - 25 August, 1972.

ALBRECHT J.

Rat Brain Polysomes in Carbon Monoxide Hypoxia. Vide B26 The IIIrd Danube Symposium on Neuropathology, Poland, Warsaw, 11 - 14 October, 1972.

DAMBSKA M., FERENS Z., TAYTSCH-KAPULKIN Z. The Infection by Coxsakie B<sub>3</sub> Virus in Mouse Pregnancy.

HOPPE B., KORTHALS J.

The Morphological, Histochemical and Ultrastructural Picture of Carbon Monoxide Gliopathy in Vitro.

MASLINSKA D.

Effect of Transplacental Asphyxia on Rat Brain.

NYKA W.

Damage of Nervous System following Perinatal Hypoxia.

OSTENDA M.

The Histological, Histochemical and Ultrastructural Picture of Glial Tissue in Vitro following gamma-Irradiation.

RENKAWEK K., KRASNICKA Z., MAJDECKI T., MOSSAKOWSKI M.J.

Experimental Gliopathy in Vitro Induced by the Inhibitor of Succinic Dehydrogenase.

RENKAWEK K., MAJDECKI T., KROH H.

Ultrastructural Study of Experimental Brain Sarcomas.

ŚMIAŁEK M., MOSSAKOWSKI M.J.

The Morphological Changes and quantitative Topography of Copper in Brain of Patients with Hepatic coma in the Cours of Viral Hepatitis. VI Dzień Neurochemii Klimicznej Polskiego Towarzystwa Biochemicznego i Komisji Neurochemii Polskiej Akademii Nauk, Polska, Zielona Góra, październik, 1972. /VIth Day of Clinical Neurochemistry organized by the Polish Biochemical Society and the Neurochemical Committee of the Polish Academy of Sciences, Poland, Zielona Góra, 28 October, 1972.

WEINRAUDER H., ŚMIAŁEK M., ALBRECHT J.

Lokalizacja komórkowa antygenów mózgu szczura; doniesienie wstępne. /Cellular Localization of Rat Brain Antigens; preliminary report/.

ALBRECHT J.

Protein Biosynthesis in Rat Brain in Carbon Monoxide Intoxication.

International Symposium on Brain Oedema, BRD, Mainz, 19 - 21 June, 1972.

KLATZO I., SPATZ H., RAP Z.

The Effect of Hypertonic Solution on Glucose Transport in the Brain.

Il Konferencja Neuropatologiczna Stowarzyszenia Neuropatologów Polskich, Polska, Warszawa, marzec, 1972./Ilnd Neuropathological Conference Society of Polish Neuropathologists, Poland, Warsaw, 23 - 25 March, 1972/.

DAMBSKA M., KORTHALS J., MOSSAKOWSKI M.J.

Wieloogniskowa leukoencefalopatia w przypadku zaawansowanych
uszkodzeń naczyń mózgu. / Multifocal Leucoencephalopathy in

Case Advanced Lesions of Brain Vessels/.

FERENS Z., KANSY J.

Naczyniakowatość opon w przypadkach siniczych wad serca.

/Meningo-vascular Malformation in Cases of Cyanotic Heart Failures/.

#### MAJDECKI T.

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189

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Vide C2

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Vide D4

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Vide G53

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Vide G48

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Vide G45

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#### Vide G66

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## ŁYSZCZARZ J.

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## H. RESEARCH GROUP OF SCHOOL PSYCHOHYGIENE

III Ogólnokrajowa Konferencja Naukowa Psychohigieny Rodziny, Polska, Warszawa, 1 - 2 grudzień, 1972. /IIIrd Scientific Conference of Family Psychohygiene, Poland, Warsaw, 1 - 2 December, 1972/.

OSIŃSKI H., GAJEWSKA Z., SIWKIEWICZ J., ZAKRZEWSKA B. SZMUKLER S.

Środowisko rodzinne dzieci z trudnościami dydaktycznymi i wychowawczymi. /Family Environment of Children with Didactic and Educational Difficulties/.

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#### J. ELECTRON MICROSCOPY UNIT

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VII Konferencja Naukowa Komisji Mikroskopii Elektronowej
Komitetu Badania Komórki, Polska, Uniejów, 26 - 28 październik,
1972. /VIIth Scientific Conference of the Electron Microscopy
Commission of the Committee of Cell Studies, Poland, Uniejów,
26 - 28 October, 1972.

DANIELEWICZ-KOTOWICZ A.

Zmiany mikroskopowo-elektronowe w płacie nerwowym przy-

sadki szczura w nadczynności i niedoczynności nadnerczy.
/Electron-microscopic Changes in the Neural Lobe of Rat
Hypophysis in Hyper- and Hypofunction of Adrenal Glands/.

JURKIEWICZ J., BOROWICZ J.

Obraz mikroskopowo-elektronowy doświadczalnego obrzęku mózgu. /Electron-microscopic Pictures of Experimental Brain Edema/.

IV Konferencja Naukowa Sekcji Mikroskopii Elektronowej Polskiego Towarzystwa Anatomopatologów, Polska, Poznań, 13 maja, 1972.

/IVth Scientific Conference of the Electron Microscopy Section of the Polish Anatomopathological Society, Poland, Poznań, 13 May, 1972/.

GAJKOWSKA B., BOROWICZ J., KRAŚNICKA Z.

Morfologiczne i histochemiczne badanie komórki glejowej z

hodowli in vitro./Morphological and Histochemical Study on
a glial Cell from a Culture in Vitro/.

VIII Ogólnopolska Konferencja Mikroskopii Elektronowej, Polska, Poznań, 8 listopad, 1973. /VIIIth National Conference of Electron Microscopy, Poland, Poznań, 8 November, 1973/.

BOROWICZ J., GAJKOWSKA B.

Badania mikroskopowo-elektronowe jądra nadwzrokowego i przykomorowego podwzgórza szczura w ostrym i przewlekłym zatruciu morfiną. /Electron Microscopic Studies of the Supraoptic-and Periventricular Hypothalamic Nuclei of Rat in Acute and Chronic Morphine Intoxication/.

BOROWICZ J., GAJKOWSKA B., JURKIEWICZ J., HEREĆ S. Badania mikroskopowo-elektronowe kory mózgu i podwzgórza szczurów zdrowych pod wpływem leków przeciwobrzękowych.

/Electron-microscopic Examination of Cerebral Cortex and Hypothalamus of Healthy Rats Subjected to Treatment with Antiedemal Drugs/.

BOROWICZ J., OLSZEWSKA K., JURKIEWICZ J.

Badania mikroskopowo-elektronowe kory mózgowej szczura
w ostrym i przewlekłym zatruciu morfiną. /Electron microscopic Studies of Rat Cerebral Cortex in Acute and Chronic
Morphine Intoxication/.

#### TRAN VAN LIEU

Badania mikroskopowo-elektronowe wątroby szczura w ostrym i przewlekłym zatruciu morfiną. /Electron microscopic Studies of Rat Liver in Acute and Chronic Morphine Intoxication/.

Vth International Congress of the Society of Child Oncology, Holland, Amsterdam, 4-8 October, 1973.

BOROWICZ J.

The Evaluation of Catecholamine Patterns in Electron Microscopic Pictures in the Cases of Neuroblastoma in Children.

#### VARIA

#### STATE DISTINCTIONS 1972 - 1973

Jan Kądziela - Golden Cross of Merit

Adam Kunicki - Polonia Restituta, Officer Cross

Eugeniusz Mempel - Golden Cross of Merit

Jan Nielubowicz - Polonia Restituta, Officer Cross

Teresa Zalewska - Bronse Cross of Merit

# SCIENTIFIC AWARD OF THE SCIENTIFIC SECRETARY OF POLISH ACADEMY OF SCIENCES 1972 - 1973

#### A. LABORATORY OF NEUROPHYSIOLOGY

- J. Staszewska-Barczak, L. Ceremużyński, K. Sroczyńska,
- K. Semerau-Siemianowska,

for the work;

"Effect of increased catecholamine excretion in the acute phase of heart muscle infarct on the apperance of heart rhythm disturbances".

#### D. LABORATORY OF NEUROCHEMISTRY

A. Gromek, U. Rafalowska, M. Skorupka, for the work:

"Citrate oxidation in the cytoplasmic fraction of rat brain".

210

#### F. SURGICAL RESEARCH and TRANSPLANTATION LABORATORY

- J. Nielubowicz, W. Olszewski and coworkers, for the work:
- "Methodical elaboration of experimental liver transplantation, its preservation, rejection tests and immunossupresion".

#### G. LABORATORY OF APPLIED PHYSIOLOGY

- S. Kozłowski, Z. Brzezińska, K. Nazar, J. Sołtysiak,
- W. Radziszewska, E. Ostrowska,

for the work:

"Studies on the role of adrenergic system in organisms adaptation to physical effort".

#### AWARD OF THE DEPARTMENT OF MEDICAL SCIENCES

#### F. SURGICAL RESEARCH AND TRANSPLANTATION LABORATORY

- W. Olszewski, W. Rowiński, H. Łukasiewicz, J. Polański,
- M. Rossowska,

for the work;

"Experimental studies on extracorporeal liver perfusion".

#### INDIVIDUAL AWARDS OF SCIENTIFIC SOCIETY

- Society of Polish Neuropathologists
- К. Domańska-Janik.

for the work:

"Oxidative glucose metabolism in the central nerwous system in the conditions of norm and hypoxia". G. Szumańska,

for the work:

- "Histochemical picture of rat brain in acute carbon monoxide intoxication".
- Polish Physiological Society
- J. Sadowski,

for the works:

- "Glomerular filtration changes during renal artery infusion of various hypertonic solutions in one dog".
- "Effects of renal artery infusion of various hypertonic solutions on the renal blood flow and renal handling of PAH in the dog".
- "A simple venous outflow recorder".
- M. Kaciuba-Uściłko,

for the works:

- "Hormonal regulation of thermogenesis in the newborn pig".
- "The effect of ambient temperature on urinary catecholamine excretion".
- B. Kruk,

for the work:

- "Effects of emotional factors on physical performance of dogs on the treadmill".
- International Lymphological Society, Towson, USA
- W. Olszewski,

for the work:

"On the pathomechanism of development of lymphedema".

#### DEGREES AWARDED 1972 - 1973:

Doctor of Medicine

Agnes Danielewicz-Kotowicz Lubomira Dydyk Danuta Maślińska Mieczysław Pokorski Jerzy Polański Teresa Trippenbach

Doctor of natural sciences

Barbara Gajkowska
Roman Gadomski
Henryk Gromysz
Andrzej Huszczuk
Alicja Pronaszko
Elżbieta Turlejska-Stelmasiak
Teresa Zalewska

Doctor of Philosophy

Katarzyna Tubylewicz-Olsnes

Training of foreign research workers in the Centre: -Tran van Lieu, M.D./Med.Ac. Hanoi - Viet-Nam/. A three-year scientific training in the Laboratory of Electron Microscopy.

Translator: J. Albrecht, D.Sc.

# NAME INDEX OF PAPERS PUBLISHED AND SUBMITTED FOR PUBLICATION

G54 Adolfson S. CI

Albert K.

B1, B2, B7, B25, B26, B60 Albrecht J.

Araszkiewicz Z. E8 . E17 . E30 Augustyniak B.

A15 Bartoli A.

B3, B40, J1 Beskid M. B56, B57 Bicz W.

D3 Biesold D. F4. F8 Borkowski M.

B9, B37, B45, B46, F18, F23, Borowicz J.

J1, J2, J3, J4, J5, J6, J9, J10,

G1, G25, G28, G67

J11

D1 Broniszewska - Ardelt B. F25 Brühl A.

G4, G5, G10, G17, G29, G30, Brzezińska Z.

G34, G36, G37, G45, G52

A1, A2, A15, A16 Bystrzycka E.

G31 Chwalbińska-Moneta J. D8 Czajkowska D.

D8, E5, J6 Czernicki Z.

Danielewicz-Kotowicz A. F23, J3, J4, J7

Dambska M. B4, B27, B28, B29, B30, B43

Debuch H. D'

Dembińska M. G32, G57

Dietrich-Rap Z. E1, E6, E10, E11, E13, E18, E19,

E20, E27, E28, E31

Dixon M. A17

Domaniecki E. G6

Dydyk L.

Gadomski R.

Domańska-Janik K. D2, D3

Drzewiecki K. G7, G11, G43

Duroš H. B28, B30

Dziduszko J. E1, E2, E3, E4, E6, E7, E8, E14,

B31, B32

E16, E17, E30

Dziewanowska-Kunert Z. A3, A18

Ekbloom B. G33

Ferens Z. B5, B27

Flower R. A4
Franczyk M. G5

Fürhiss H. D7

Gajewska Z. H4, H5, H7, H8

Gajkowska B. B9, B37, B38, B46, B52, J2, J5,

B62

18

Gayny-Brzozowska K. B5

Gęsik D. E12

Giacobini E. A5

Głogowska M. A19, A20, A21, A22, A23, A24, A25,

A53

Głuszcz A. B55

Goertz J. B29

Greenleaf J. G34

Grieb P. A26, A27

Grochowski W. E9, E10, E11, E13, E18

Gromek A. D1, D4, D5, D6, D8, D9, D11

Gromysz H. A1, A28, A29

Gryglewski R. A4

Guz A. A2, A15

Hartmann G. G20

Herbaczyńska-Cedro K. A4, A6, A7, A8, A9, A30, A31, A32,

A35

Herczyński R. A33

Honowska W. B44

Hoppe B. B6, B34
Huszczuk A. A1, A16, A34

Jain S. A2, A15

Janczewska H. A30, A31, A35

Januszewski S. B2, B7
Jurkiewicz J. D8, J6, J9

Kaciuba-Uściłko H. G18, G34, G35, G36, G37, G39, G45, G64

G35,

Kansy J. B27, B32

Kapuściński A. B2, B7

Karczewska E. A37, A38

Karczewski W. A26, A27, A29, A33, A36, A37, A38

Karliński A. G24

Karwacka H. B34

Kassur B. B47, F9

Kilbom A. G33

Kirschner H. G38

Jusiak R.

Klatzo I.	B14, B21
-----------	----------

	•	
Królikowska I.	J10	

Kruk	В.	GIZ,	013,	GIO
Kruś	S.	F5		

Księżak H.	D9
Kulegyeki I	B29

Lucer C. B5

Luszawski F. C3, C4, C5

Ławkowicz W. J10 Łazarewicz J. D5, D6

Łuczywek E. E10, E11, E12, E13, E18

Łukasiewicz H. F6, F7, F9, F15, F16, F17, F24,

F25

Lyszczarz J. G14, G15, G48, G49, G50 Machowski Z. F2, F3, F18, F21, F22, F26

Majdecki T. B3, B40, B41, B42, B43, B53, B54

Majzel F. G9

Marciniak M. B3, B28, B30, B40, B43

Markiewicz J. H3, H6, H11

Maálińska D. B44

Mempel E. E19, E26, E32

Michałowicz B. F19

Mossakowski M.J. B4, B7, B14, B15, B16, B18, B35,

B36, B45, B46, B47, B48, B49, B53,

**B57** 

Muszyński M. F11, F19, F22

Nazar K. G4, G5, G8, G16, G17, G23, G29,

G30, G34, G44, G51, G52, G53, G54

Nielubowicz J. F1, F2, F3, F7, F8, F9, F10, F11,

F17, F21, F25, F28, J1

Noble M.J.M. A2, A15 Olejnik Z. B6, B47

Olszewska K. F23, J3, J4

F2. F3. F5. F6, F7, F9, F10, F11, Olszewski W.

> F12, F13, F14, F15, F16, F17, F18, F19, F20, F21, F22, F23, F24, F25,

F26, F27, F28

B41, B43 Opałka S.

F9 Ortowski T.

C2, C3, C4, C5, C6 Osetowska E. H1, H4, H7, H8 Osiński H.

B17, B18, B48, B50, B51, B61 Ostenda M.

HI Pawlikowska E.

11, 12, 13, 14, 15 Pełka-Sługocka M.

**B16** Penar B. **G54** Piehl K. Pluciński S. F20 Poczopko P. G26 Podgórski J. H5

A39, A40, A41 Pokorski M.

F5, F7, F9, F21, F22, F24, F25 Polański J.

16 Posel Z.

B18, B35, B48, B49 Pronaszko A.

A5, A10, A42, A43, A44 Przybylski A.

**D4** Rafałowska U.

Rap Z. vide ... Dietrich-Rap Z.

B21, B22, B52 Rap Z.

B21 Rapoport S.I.

G18, G30 Reklewska B.

B8, B10, B15, B19, B20, B37, B38, Renkawek K.

B39, B53, B54

**B42** Reński A.

Rewerski W. G55 A21 Richardson P.S. D10, D11 Rossowska M. F9. F23, F25 Rowiński W. 311 Rudowski W. A37, A38, E1 Rycembel Z. G13, G19, G20, G24, G56, G57, Sadowski B. G58, G63 G21, G22, G23, G47, G50 Sadowski J. C1Sawicki J. F2, F3, F11, F19, F21, F22, Sawicki Z. F26, F27 **B55** Schenk V.W.D. J11 Schier J.

Schier J.

Schmidt-Sidor B.

Semerau-Siemianowska K.

Semerau-Siemianowski Z.

All

Sielczak J.

J11

 Sikorska M.
 B56, B57

 Siwkiewicz J.
 H7, H8, H9, H10

 Słowik T.
 E14, E15, E16, E20

 Sługocki L.
 I1, I2, I3, I4, I5

 Śmiałek M.
 B22, B36, B56, B57

Sobocińska J. G31, G62 Sokołowski J. F3

Soltysiak J. G9, G10, G33, G38, G45, G60

Spatz M. B21, B58
Sroczyńska K. A27

Stadnicki R. E7, E8, E10, E11, E13, E17, E18,

E19, E27, E28, E30, E31

A8, A9, A30, A31, A45 Staszewska-Barczak J. E20 Stępień L. A12, A13, A22, A46, A54 Stránsky A. D5, D6, D7 Strosznajder J. B51 Strugalska H. G1Styszewska H. G11, G23, G61, G62, G63 Szczepańska-Sadowska E. A12, A13, A17, A18, A46, A47, Szereda-Przestaszewska M. A48, A49, A50, A54, A55 B62 Szewczykowski J. F25 Szmidt J. H7. H8 Szmukler Sz. B12, B52, B58, B59, B63 Szumańska G. E19, E21, E22, E23, E24, E25, Szumska J. E26, E27, E28, E31, E33 B22 Szydłowska H. C4, C5, C6 Taraszewska A. G24, G55 Tarczyńska K. G53 Taton J. G1, G10, G18, G25, G26, G28, Tomaszewska L. G64, G67 16 Tomczak J.W. A2, A15 Trenchard D.W. A14, A51, A52 Trippenbach T. E7, E8, E15, E17, E19, E20, Tubylewicz K. E27, E28, E29, E30, E31

F25 Tupalska B. G27, G50, G65, G66 Turlejska-Stelmasiak E.

**G58** Vainstein J. Vane J.R.

A4, A32

Vermes J. G20
Viale G. B23

Weinrauder H. B60, B61

Widdicombe J.G. A12, A17, A22, A23, A24, A25,

A34, A46, A48, A49, A50, A53,

A54, A55

Wiśniewska A. G53
Wiśniewski H. B22

Witkiewicz B. E19, E27, E28, E31

Wrutniak A. B49
Wuttke B. C2

Zalewska T. B22, D12

Zakrzewska B. H2, H3, H6, H7, H8, H9, H10, H11

Zakrzewski P. 17, 18, 19, 110, 111, 112

Zawadzki Z. F22 Zbrodowski A. E4

Zelman I. B24, B55, B62, B63

Zerbino D. F3

Zieliński J. G28, G67
Zwierzchowski S. G46, G68

Zarski S. E1, E2, E3, E4, E16, E26, E32,

E33

Žurawski W. G7
Žurawski S. F27
Žytkowska L. F25

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