REPORT
ON SCIENTIFIC ACTIVITIES
1983

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POLISH ACADEMY OF SCIENCES
MEDICAL RESEARCH CENTRE

REPORT
ON SCIENTIFIC ACTIVITIES
1983

Warszawa
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POLISH ACADEMY OF SCIENCES
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STUDIES ON THE FUNCTION OF THE NERVOUS SYSTEM AND ON MECHANISMS CONTROLLING BASIC FUNCTIONS OF THE ORGANISM

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FUNCTIONAL ORGANISATION OF RESPIRATORY NEURONAL NETWORK–SOURCES AND MECHANISMS OF RESPIRATORY DRIVE

The hypothesis of „critical mass" of respiratory neurones has been confirmed in split-brainstem rabbits (split-respiratory centre preparation). It has been shown that both halves of the respiratory „centre" are capable of responding to hypoxia and hypercapnia provided that their connections with the rostral structures of the brainstem are preserved.

The localisation of vagal, recurrent laryngeal and phrenic motoneurones was described in the guinea-pig by means of HRP technique.

Reflex and central factors influencing laryngeal contribution to the respiratory pattern were studied in rabbits with chronically denervated lungs.

CHANGES IN THE ACID-BASE BALANCE AND THE REGULATION OF BREATHING

It has been shown that hypothermia reduced minute ventilation both by lowering $PaCO_2$ and by a direct effect of brainstem temperature on the generation of impulses in the respiratory neuronal network. Inhalation of CO_2 mixtures elicits in hypothermic animals a decrease in blood flow in the common carotid arteries.

Experiments with perfusion of ventriculo-cisternal system in the rabbit have shown a quick exchange between cerebrospinal fluid and cerebral tissues. A similar perfusion in which CSF taken from patients with cerebral vasoconstriction was used (instead of mock CSF with variable Cl^- contents) elicited brain oedema in experimental animals.

In another series of experiments it was shown that morphine selectively increases the strength of Breuer-Hering inflation reflex, whereas non-opiate substances elicit a respiratory depression with no effect on this reflex.

See the list of publications:
1, 7, 8, 9, 15, 19, 32, 33, 34, 37, 38, 46, 67, 112, 127

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ADAPTATION TO PHYSICAL EXERCISE AND CHANGES IN ENVIRONMENT

a) Studies on exercise metabolism and its control

A relationship between tissue (skeletal muscle and adipo-

se tissue) lipoprotein lipase activity (LPLA) — estimated in vitro — and uptake of chylomicron-triglycerides (TG) — determined in vivo — was studied on dogs in different metabolic states (rest, exercice, fasting, glucose loading). It was found that both LPLA and ^{14}C-triglyceride uptake depend on physical activity and nutritional status. An inverse correlation was ascertained between the tissue TG uptake capacity (as judged by LPLA) and in vivo uptake of TG. The latter was found to depend, to a considerable degree, on TG inflow to the tissues.

Continuing the studies on the influence of nutritional factors on exercise metabolism the effects of fat-rich diet, on exercise performance, as well as on metabolic and hormonal adjustments to prolonged treadmill exercise were investigated in dogs. After 2 weeks on the fat-rich diet duration of exercise until exhaustion was significantly reduced, which can be attributed to the markedly diminished muscle glycogen content. On the other hand, contribution of free fatty acids (FFA) to exercise metabolism was increased and hormonal responses to exercise were modified.

In other series of experiments the effect of the elevated plasma FFA concentration, due to intravascular lipolysis, on metabolism of exercising muscles was studied in dogs. An excessive supply of FFA to working muscles reduced work performance. It was accompanied by a slower rate of glycolysis in contracting muscles and diminished utilization of muscle glycogen and glucose.

In further studies on temperature regulation during exercise an influence of altered supply of energy substrates to working muscles on the exercise-induced changes in body temperature was evaluated in dogs. Glucose infusion, given during exercise, attenuated significantly the increases in body core (T_{re}) and muscle (T_m) temperatures, whereas an elevated plasma FFA concentration (due to heparin- induced intravascular lipolysis in fat- fed dogs) enhanced the temperature changes during prolonged physical effort.

b) Studies on exercise tolerance in cardiac patients

Longitudinal studies on the course of coronary heart disease (CHD) were completed in 145 patients surveyed 10 years follo-

wing the first myocardial infarction. The control group consisted of 97 age-matched healthy subjects with CHD risk factors. The studies include complex clinical and physiological examination of patients with a particular regard to the exercise tests. The studies provided several substantial data on the dynamics of changes in the clinical state of the patients and their coronary circulation. An importance of exercise tests for optimalization of therapy as well as for assignation of recommendations concerning everyday life and professional activities of the patients was proved. It was found, however, that none of the indirect indices of hemodynamics or coronary blood flow insufficiency determined in the early post-infarction period, has a substantial prognostic value.

In further studies performed with coronary patients it was demonstrated that a moderate exercise, well tolerated by the patients, is effective in lowering of their enhanced blood glucose and TG concentrations.

Besides, the physiological responses to various kinds of typical activities in everyday life were investigated in the coronary patients. Appearance of ischemic changes in the heart was related to energy cost of the tasks and compared with those evoked by ergometric exercise.

Physiological criteria of tolerance of various everyday activities were established.

Changes in physical working capacity were examined in patients 10 years following mitral commissurotomy.

c) Physiological basis of physical training

A relationship between exercise load, onset of blood lactate accumulation (OBLA) and the hyperventilation treshold was studied in young boys (15 years old). The hyperventilation threshold was found to occur at lower exercise loads and lower heart rates than OBLA.

Continuing the studies on the minimal effective training an influence of typical recreation activities on some indices of working capacity were analyzed in adult human subjects. Jogging was found to be the most effective, swimming-moderately, while gimnastics even when practised for 7 months did not influence working capacity.

d) Studies on thermoregulation

A relationship between the rate of sweating and increases in body core temperature in response to heat load was studied in healthy untrained men and women. The results indicate that the speed of sweat gland activation on heat exposure determines, to a marked degree, an increase in body temperature. A delay of sweating response to heat load was greater in women than in mean.

Studies on thermal balance in patients during different kinds of anesthesia and surgery were continued.

Thermoregulatory responses to heat exposure were compared in normally hydrated and dehydrated rabbits examined in Summer and in Winter. In Winter an increased respiratory rate and cutaneous vasodilation were the main thermoregulatory mechanisms against hyporthermia, while in the animals examined in Summer a decrease in the metabolic rate was the prevailing response to heat exposure. Dehydration markedly reduced the respiratory response to heat, and the inhibition was particularly well expressed in the Summer experiments.

e) Control of volume and composition of the extracellular fluid in variable internal and external environment

The original method for continuous measurement of interstitial electrolyte concentration of the in situ kidney on basis of electrical admittance (1) was applied for extensive studies on the renal tubular transport of sodium chloride as affected by furosemide, a potent transport inhibitor (2).

In anesthetized rabbits with electrodes recording admittance of the papillary region, inner medulla, outer medulla and cortex of the left kidney was injected i.v. in the dose of 1.5 or 3.0 mg per kg body weight. In another group 15% mannitol solution was infused i.v.; the rate of infusion was adjusted in a way to induce urine flow comparable to that after the small dose of furosemide. The renal blood flow, glomerular filtration rate and sodium excretion were measured throughout experiments. At the end of studies to-

tal osmole and Na^+ concentration of kidney tissue slices were determined.

The admittance changes measured reflected changing interstitial electrolyte concentration and, indirectly, in tubular reabsorption of NaCl. The large dose of furosemide and mannitol infusion decreased admittance (i.e. decreased NaCl concentration) in all four renal zones, whereas the small dose of furosemide which induced but a small increase in sodium excretion, affected only the inner medulla and papilla. Sodium concentration in medullary tissue slices positively correlated with their admittance. The absence of admittance response to a small dose of furosemide observed for the outer medulla does not support the common view that the drug's main site of action is the thick segment of the ascending limb of Henle's loop. Hypertonic mannitol decreased admittance of all renal tissue zones, in accordance with its osmotic action along the whole length of the renal tubule.

See the list of publications: 4, 11, 36, 39, 40, 41, 52, 55, 56, 57, 58, 59, 60, 61, 62, 65, 68, 76, 94, 107, 117, 118, 126, 131

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CONTROL MECHANISMS OF CARDIOVASCULAR SYSTEM IN DEFINED PATHOLOGICAL CONDITIONS

1) Investigations on the role of adrenergic nervous system in the development od cardiac hypertrophy concentrated upon the effect of propranolol on the development of hypertrophy induced by aortic stenosis in rats. In view of individual variations in the intensity of myocardial growth, there was no clear-cut response to propranolol treatment in vivo. However, there was a marked (30%) inhibitory effect of propranolol (10^{-6}M) upon protein biosynthesis in vitro, as shown by a decrease in the incorporation of labelled ami-

noacids into postmitochondrial fraction from hypertrophic hearts. Investigations on the content of biogenic amines in hypertrophic myocardium have shown depletion of catecholamines and significant increase in dopamine content. The above changes were accompanied by increased excretion of dopamine in urine.

2) Studies on the mechanism of inotropic action of inosine in canine myocardium were completed and clinical investigations with administration of inosine in cardiac low-output states were undertaken.

3) Studies on the effect of prostacyclin upon anoxia-induced morphological and enzymatic properties of CNS cultures (joint project with Dpt of Neuropathology) demonstrated the cytoprotective effect of this drug on neurons and glia reflected by preservation of cellular structure, diminished tissue acidosis and activation of glial cells.

4) Experiments carried out conscious pigs on the effect of stress upon humoral and metabolic indices showed that oxygen free radicals mediating peroxidation of membrane lipids and affecting mitochondrial energy metabolism of the myocardium, are important components of the stress induced myocardial injury. (Joint project with the Centre of Medical Education and Institutes of Animal Physiology and Experimental Biology Polish Academy of Sciences.

See the list of publications:
10, 13, 14, 66, 136

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

CLINICAL AND EXPERIMENTAL STUDIES ON NEUROREGULATION OF PERIPHERAL CIRCULATION

Experimental and clinical investigations are focused on treatment of vascular diseases (Buerger disease, Raynaud disease, diabetic foot) by TNS (Transcutaneous Nerve Stimulation). Our research work was centred on both: 1) physiological explanation of beneficial clinical effects obtained by TND, 2) estimation of proper parameters of electro-stimulation (frequency, voltage, resistance) for a given patient. It was proved that high frequency TNS causes a release of the platelet disaggregating substance which is responsible for beneficial clinical effects of the treatment (e.g. temperature rise, healing of ischaemic wounds). This substance, as it was showed applying a bioassay technique, is reluctant to inactivation in lungs and its half life is longer than that of synthetic PGL_2.

To estimate efficiency of TNS thermographic and isotope techniques as well as the human skin resistance measurements were used. It was demonstrated that TNS is not only the highly effective method of treatment of vascular diseases but it is also very efficient in preventing development of Raynaud phenomenon.

ring the observation period an insignificant increase of natural suppressor activity as well as an increase of the titer of cytotoxic antibodies were observed.

Pretreatment of recipient with kidney donor blood in the volume of 3 ml/kg b.w. on day −1, +1, +5, associated with administration of immuran in a dose 1 mg/kg brought a mean survival time of 11 days despite of the increase in the specific suppressor cell activity.

Blood pretreatment in the volume of 3 ml/kg b.w. on days −22, −21, −16, −15, −11 and −10, associated with immuran on days −21, −15 and −10, and after transplantation — immuran 2 mg/kg b.w. + prednisone 1 mg/kg b.w. brought a survival time similar to that in the control group.

A beneficial effect of cellular antigen pretreatment (lymphocytes, erythrocytes and platelets) combined with allosera (recipient antiserum against transplantation antigens of a donor) on the survival time of heart allografts in rats was examined. It was found that alloserum caused an increased accumulation of alloantigen in the liver. These findings and the prolongation of survival time of heart allografts suggest that the regulation of the „enhancement" process may take place in the liver.

In the preliminary studies on the autologous mixed lymphocyte reaction (AMLR), which seems to represent the reaction providing normal homeostasis of immunological system, the AMLR assay in healthy donors was established. The stimulator and responder cell populations as well as the time of culture maintenance sufficient for maximal proliferative response in AMLR were determined.

See the list of publications:
2, 3, 42, 43, 44, 47,72, 73, 74, 75, 96, 97, 98, 99, 100, 101, 102, 103, 113, 114, 115, 116, 133.

OTHER RESEARCH WORKS

Mental Health Department
Head: Z. Juczyński, Ph. dr

PSYCHOPHYSIOLOGICAL AND SOCIAL DETERMINANTS OF ACTIVITY IN PATIENTS AFTER MYOCARDIAL INFARCTION

The studies were performed in 54 patients one year following myocardial infarct. In the previous year the same patients were examined just after recovery from the infarct.

The purpose of the analysis was the evaluate an impact of psychophysiological factors and social conditions on physical and mental load tolerance.

Sixty percent of the patients returned to work within the year after heart infarct, the remaining were on sickleaves. It was found, that medical aspects of the disease do not exclusively determine the process of recovery, including the level of load tolerance. Social status described by the level of education, kind of profession and the managerial post — constitutes the most useful predictor of return to work and tolerance to loads within 1 year after heart infarct.

Studies were carried out in 110 subjects with alcohol-dependence syndrome or alcohol abuse. Employed men (204 subjects) served as a control group. Within the alcoholic group the lower level of education, higher criminality and frequent job changes were found. Psychological examination of this group revealed lower intelligence index, lack of adequate self-evaluation, self-acceptance and sufficient internalization of values.

See the list of publications:
48, 105, 106, 108

Research Group of School Psychohygiene
Head: Dr Henryk Osiński

THE DYNAMIC PATTERN OF APTITUDE AND INTEREST DEVELOPMENT IN YOUNG INDIVIDUALS IN RESPECT TO THEIR MENTAL HEALTH

The longitudinal investigations were continued in 1983, on a group of 183 students of the last classes of high school who had been examined for the first time when they had entered the school. The special aptitudes, interests in various types of activity, interest in the taught subjects, neuroticism and extraversion, hidden anxiety, personality traits and scholastic achievements were estimated. A total number of 78 indices was obtained characterising the above mentioned variables, and they were compared with appropriate values obtained at the beginning of high school studies.

Interests in main activities decreased with the exception of those in creative work which remained unchanged.

A dynamic increase was observed in all aptitudes with an exception of perceptive ability which showed a high degree of stability. The highest dynamics of special aptitude development was observed in verbal aptitides, aptitudes related to mathematical operations and spatial imagination.

An increase was observed in mental efficiency, initiative, inquistiveness, ambition, tolerance and success through independence.

During the period high school study there was an increase in the negative effect of neuroticism on intellectual efficiency and of hidden anxiety on both the spatial imagination and artistic interests.

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109. RAFAŁOWSKA U., ERECIŃSKA M., WILSON D.: Effects of free fatty acids on synaptosomal neurotransmitter transport systems in rat brain. Postępy Biologii Komórki (in press, in Polish).

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113. RUKA M., PRZEOR A., OLSZEWSKI W.L.: Permeability of lymph vessels and nodes. Hungarian Experim. Surgical Congress, Debrecen (Hungary), 24—26 Aug. 1983, Abstr. 33.

114. RUKA M.. OLSZEWSKI W.L.: Effect of infusion of hyperosmolar and hyperoncotic solutions on the distribution of water in inflamed tissues. LI Symp. of Polish Soc., Łódź, 19—21 Sept. 1985, Abstr. 336 (in Polish).

115. RUKA M., PRZEOR A., OLSZEWSKI W.L.: Permeability of

lymph vessels to proteins. 9th Intern. Congress of Lymphalogy, Tel-Aviv, 2—7 Oct. 1983, Abstr. 86.

116. RYFFA T.: Experimental microsurgical organ transplantation. I Intern. Symp. of Microsurgery in Reconsturctive and Plastic Surgery, Jena, 2—4 Sept. 1983.

117. SADOWSKI J., PORTLASKA E. (with the techn. assist. Zwolińska J.): Dynamic evaluation of renal electrolyte gradient by in situ tissue impendance studies. Kidney Internat., 1983, 24, 800.

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119. STROSZNAJDER J.: Arachidonic acid uptake by hypoglicemic brain membranes. ISN Satellite Merting on „Physiological role of phospholipids in the nervous system", Harrison Hot Springs, B.C., Canada, 17—20 July, 1983.

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122. STROSZNAJDER J.: The influence of hypoglycemia on the incorporation of myoinositol into phospholipids of brain cortex synaptosomes. J. Neurochem. 1983, 41, Suppl. p. S22 B.

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between lipid disturbances and uptake of GABA and calcium in ischemia brain cortex synaptosomes. J. Neurosci. Res. (in press).

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126. SZCZEPAŃSKA-SADOWSKA E., NIEWIADOMSKI W., SOBOCIŃSKA J., KOZŁOWSKI S.: Thirst and solute excretion: their effectiveness in osmostatic control of body fluid. Am. J. Physiol., 1983, 244, R-23.

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131. TERJUNG R.L., MACKIE B.C., DUDLEY G.A., KACIUBA-UŚCIŁKO H.: Influence of exercise on chylomicron triacylglycerol metabolism: plasma turnover and muscle uptake. Med. Sci. Sport Ex., 1983, 15, 340.

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Neuropat. Pol., 1983, 21, 241—255 (in Polish).

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VISITING SCIENTISTS

Department of Neurophysiology

Kirkwood P.A.	Inst. of Neurology, Univ. of London, London, U.K.

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Jokl E.	Dept. of Physiol., Univ. Kentucky, USA
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VISITS ABROAD

Department of Neurophysiology

Budzińska K.	The Nobel Inst. for Neurophysiol. Sztokholm, Sweden
Głogowska M.	Dept. of Physiol. Univ. of Goteborg Sweden (long term visit)
Grieb P.	Dept. of Physiol. Univ. of Pennsylvania, USA
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Kozłowski S.	Dept. of Thermoregul. Physiol. Univ. of Lille, France

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	Dept. of Clinical Path., St. Mary's Hosp. Univ. of London, U.K.
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	Dept. of Clinical Path., St. Mary's Hosp. Univ. of London, U.K.
	August Krogh Inst. Univ. of Copenhagen, Denmark
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Department of Neuropathology

Hilgier W.	Inst. of Occupational Health, Helsinki, Finland
Kapuściński A.	Indiana Univ., School of Medicine, USA (long term visit)
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Dąmbska M.	Centre d'Etudes de Recherches d'Anthropologie Fondamentale CERAF, Paris, France
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Department of comparative Neurology

Zelman I.	Inst. of Neurology, Univ. of Wien, Austria

Department of Neurochemistry

Czechmańska T.	Dept. Zoophysiol. Univ. of Lund, Sweden
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Noremberg K.	Inst. of Biochem., Univ. of Perugia, Italy
Pastuszko A.	Dept. of Biochem., Biophys. Univ. of Pennsylvania, Philadelphia, USA (long term visit)
Rafałowska U.	Dept. of Biochem., Biophys. Univ. of Pennsylvania, Philadelphia, USA
Strosznajder A.	Dept. of Physiol. Chem., State Univ., Columbus/Ohio, USA
Zalewska T.	Max-Planck Inst. für Neurol. Forschung, Köln, DFG
	Inst. Zoophysiol. Univ. of Lund, Sweden

Ziembowicz A.	Faculty of Medicine, Univ. of Göteborg, Sweden

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Loesch A.	Dept. of Anatomy, Univ. College, London, U.K. (long term visit)

Department of Neurosurgery

Jurkiewicz J.	Neurochir. Klin., Aarau, Switzerland
Mempel A.	Neurochir. Klin., Aarau, Switzerland
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Szumska J.	Neurochirurgische Klinik, Aarau, Switzerland

Department for Surgical Research and Transplantation

Jarosz G.	Inst. for Surgical Research, Univ. of Oslo, Norway (long term visit)
Grochowicz P.	Inst. für Chirurgische Forschung, München, DFG (long term visit)
Kubicka U.	Chirurgische Universitätsklinik und Poliklinik, Bonn, DFG (long term visit)

Kwaszczyńska H.	Inst. of Molecular Genetic, Prague, Czechoslovakia
Olszewski W.	Radiumhospital, Oslo, Norway Univ. Bonn and Monachium, DFG Univ. Groningen, Holland
Ruka M.	Surgery Clinic, Univ. of Groningen, Holland (long term visit)

PARTICIPATION IN INTERNATIONAL SCIENTIFIC MEETINGS IN 1983

Colloque Intern. „Physiologie Spatiale", Toulose, France
1—4 March
Kozłowski S.

Symposium über Experimentalle Urologie mit Internat. Beteiligung Rostock-Warnemünde, DDR, 7—9 April
Ruka M., Ryffa T.

Annual Meeting of the Europ. Soc. for Clinical Investigation, Travemunde, GDR, 21—23 April
Herbaczyńska-Cedro K.

IV Hungarian-Polish Neuropath. Symposium, 8—10 May
Dąmbska M., Iwanowski L., Maślińska D., Laure-Kamionowska M., Tomaszewska A., Renkawek K., Zaręba-Semkow H., Zelman I.

XVIIIth Congress of the Europ. Soc. for Surgical Res., Athens, Greece, 15—18 May
Grzelak I., Jarosz G., Łukomska B., Olszewski W.

Intern. Symp. „Termophysiol. in Medicine and Zootechnic, Brno, Czechosłowacja, 6—9 June
Kaciuba-Uściłko H., Łaszczyńska J.

Congress of the Societas Europaea Physiologiae Clinicae Respiratoriae (SEPCR), Bratislava, Czechoslovakia, 20—25 June
Budzińska K., Głowicki K., Gromysz H., Janczewski W., Karczewski W., Romaniuk J.R., Szereda-Prustaszewska B.

Symposium on Biology of Cardiacoverload, Paris, 7—9 July
Kwiatkowska-Patzer B.

IXth Meeting Intern. Soc. for Neurochemistry, Vancouver, British Columbia, Canada, 10—15 July
Strosznajder J.

XI Congress of Intern. Soc. For Heart Research, London, Great Britain, 11—14 July
Kwiatkowska-Patzer B.

Vth Intern. Catecholamine Symposium, Göteborg, Sweden, 12—16 July
Czarnecki W.

Congress of Experimental Surgery, Debrecen, Hungary, 24—26 August
Gałkowska H., Grzelak I., Łukomska B., Olszewski W., Ruka M.

Intern. Symposium of Microsurgery in Plastic and Reconstructive Surgery, Jena, GDR, 2—4 September
Olszewski W., Ryffa T.

XVIth Doan Symposium für Neurologische Wissenschaften, Innsbruck, Austria, 29 September — 1 October
Dąmbska M., Kroh H., Maślińska D., Renkawek K.

9th Intern. Congress of Intern. Soc. of Lymphology, Tel Aviv, Israel, 2—7 October
Olszewski W.

Symposium Elektroencefalografii, NRD, Czechosłowacja, Węgry, Polska, Lipsk, DDR, 25–29 October
Ligęzińska B.

First Congr. of the European Soc. for Organ Transplantation, Zürich, Switzerland, 23—25 November
Olszewski W.