This publication was prepared under contract by the UNITED STATES JOINT PUBLICATIONS RESEARCH SERVICE, a federal government organization established to service the translation and research needs of the various government departments.
12-14 on May 1959 in Liblice there was a symposium on the "Pharmacology of Nerve Stimulation" which was arranged by the pharmacological committee of the Physiological section of the Czechoslovak Medical Society named after J. E. Purkyně. Foremost workers in the field took part in this symposium. They were from the USSR (Anikov, Zakusov, Horzojan) and the peoples' democracies, East Germany (Jung, Hauschild, Scheer, Sieke, Wiegershausen), Poland (Kubikowski), Hungary (Borsi, Tarlós), and the Western European nations, England (Holton, Hunger), France (Cheymol), Austria (Kruke, Lembeck) and Belgium (Veymans, Feuse). In addition to this a fifteen-member tourist group of young scientific workers from the USSR took part in the meetings.

The symposium was opened by Prof. Paskova and the meeting was welcomed by Academicians Leufhager from the Czechoslovak Academy of Sciences. On the first day representatives of the Central Committee of the Czechoslovak Communist Party and representatives of MSVU also took place. The first day of the symposium was concerned with the pharmacology of the central nervous system.

The introductory lecture by S. V. Anikoiv (Pharmacological Division of the Institute for Experimental Medicine, Leningrad) was on "Pharmacology of the Central Cholinolytic Substances", and dealt widely with new concepts in the field of these substances. The author showed that trasentine, which had previously been considered as a substance which can replace atropine, has a substantially stronger effect on the cholinergic synapses of the central nervous system than atropine, while its peripheral effects are weaker. A whole series of esters and thiocesters related to trasentine act quite similarly. The central effects were studied chiefly on the conditioned reflexes of dogs, and also through their effect on the electroencephalograms in rabbits and studying the antagonism of these substances against nicotine and arecoline, whose action is destroyed by trasentine. There also exists an antagonism between the central cholinolytic substances and anticholinesterase substances (Michelson, Paskov). The following were chiefly used: physostigmine, prostigmin, phosphoacol and the alkaloid nivalin. It is interesting that beside
their depressing effect the central cholinolytic substances cause heightened activity of the center controlling the secretion of ACTH. Further the author summarized all evidence concerning the relationship between the structure and the central effect of the cholinolytic substances. For example transition to the aromatic esters of oxygenated acids increases the central effects of the esters, specifically the effect of these substances on conditioned reflexes (benzatine suppresses conditioned reflexes great deal more than the unconditioned, while the transentine ester of diphenylacetic acid acts equally on both sets of reflexes). Esters of the oxygenated acids have a primarily antagonistic effect against the central effect of arecoline, while the esters of oxygenated acids which had the hydroxyl removed have a similar effect on nicotine. The increase of the central effect has also been observed when oxygen is replaced with sulphur in the esteric bond. Their characteristics are sharply altered when the tertiary amines are transformed into quaternary. This lowers the effect on the brain and increases the effect on the bulbar centers. Pharmacological follow up of the effects of the central cholinolytic substances has made it possible to increase the area of their therapeutic use. (in stenocardia, spasms of the peripheral blood vessels, and bronchial asthma).

A. Zeleny and J. Kozak (Physiological Institute of the Medical Faculty of MU, Plzen) presented a report on "Relation of Acetylcholine to the Metabolism and Functional Estate of the Central Nervous System". They noticed an increase of the acetylcholine content in brains of rats after administering chlorprothamide; at the same time synthesis of acetylcholine was not affected. The hypothetical interference with metabolism, shown by lowered oxidation of glucose at several points in the "change sequence", was proven even when minimal doses were given (1 to 10 micrograms/ml) on an isolated heart of a rat after administration of chlorprothamide the inversion of the inotropic effect of acetylcholine was noted, in frogs the acetylcholine pull on the m. rectus abdominis is lowered, and the action of vagus nerve and acetylcholine on the heart is blocked. The influence of chlorprothamide on the effect of acetylcholine depends on the presence of calcium ions and the sulphhydril groups.

F. Svov and E. Hlavayova (Oncology, SAV, Bratislava) concerned themselves with the "The influence of Digitalis on the Synthesis of Acetylcholine in Vitro in a Brain Homogenate, and in an Artificial Enzyme System". By adding small concentrations of digitalized glycosides to a brain homogenate the normal aerobic synthesis of acetylcholine is increased, by adding higher concentrations it is suppressed. If acetylase obtained by drying brain cells with acetone is used digitalis has no effect; if to this cell-free enzyme system a cell suspension is added, it is possible in this case to cause an increase or suppression of the formation of acetylcholine. The authors explain this phenomenon either by an increased release of acetylcholine or even possibly an interference with its synthesis.
They state that the mechanism thus observed plays a part in influencing permeability of cellular structures and thus also cause the shift of ions, particularly potassium.

Z. Servit (Physiological Institute of the Czech Academy of Sciences, Prague) condensed the previous experiments of his laboratory in the report on "Comparative (Phylogenetic) Study of the Effect of Certain Anti-epileptic Substances". In comparing convulsive tendencies in frogs, mice, rats and rabbits, they discovered that convulsive reactivity to a pharmacological stimulus, rises with the phylogenetic evolution of the brain. Similarly the activity of the common anti-epileptic substances rises too. In experiments on frogs they compared the effect on convulsive reactivity and on the symptomatology of of the epileptic fit, brought out by a localized transcranial electric shock, with the effect of the same antiepileptic substances in mammals. The effect of Sondant and Dormea within this group increases, while Trimedal does not affect the electric shock convulsions either in amphibians or in vertebrates, while it does have an effect on the pentazol convulsions. These results are significant for the solving of theoretical problems concerning the pathophysiology of the central nervous system.

E. Scheerova and E. Siekeova (Institute of Corticovisceral Pathology, Berlin) carried out electroencephalographic studies of the effect of ethylarotylbarbiturate, a new hypnotic drug, compared to phenylethylbarbiturate. The first substance has a considerably shorter effect and the reaction of the animals to irritation with electric current is substantially different. The authors emphasize the significance of such complex study of the effect on the central nervous system, which enables one to fully explore the pharmacodynamic effect of a new drug.

M. Lukasiewicz (Pharmacological Institute of the Medical Faculty, Kosice) lectured on "Combined Relationships of Certain Drugs, both Centrally Stimulating and Depressing, to Reserpine". In experiments on mice and rats reserpine was given as premedication /predemiknac/ and then the effects of subsequently administered dihydroxycodeinone, amphetamine, nikethamide and bemegrade, were compared. In an experiment that was set up in the above manner- the dihydroxycodeinone lost some of its capacity as an analgesic and as respiratory depressant, but its sedative effect was enhanced; the stimulating effect of bemegrade on respiration and motion is increased slightly but so is lethality; the increase of lethality was likewise observed with amphetamine and nikethamide in the early stages, and then as the effect of reserpine was developed the lethality dropped. A hypothesis was expressed about blocking the "receptors" to achieve certain effects of these drugs.

J. Sterc (Physiological Institute Czech Academy of Sciences, Prague) in his work on "Reserpine and the Convulsive Reactivity" was trying to solve the problem of the pharmacological influences on the audiogenic
epilepsy of rats. He formed a hypothesis on the basis of reports in the
literature that reserpine has a depressing effect on the cortex of the
brain and a stimulating effect on the reticular formation which creates
a favorable environment for the irradiation of convulsive irritation.

This hypothesis was experimentally proved, with the interesting discovery
that this condition persists until one can assume that the organism no
longer contains even traces of the administered drug. In conditioned
reflexes disturbance in the internal depression mechanism was noted, as
evidenced by the negative differential stimuli coming out of the depressed
state.

The lecture of J. Bures and O. Buresova (Physiological Institute of
the Czech Academy of Sciences, Prague) was on the subject of "The Use
of Widening Depression as Environment for the Study of the Action of
Substances with an Affinity for CNS". This was a summary of previous
results of this working group dealing with widening cortical depression
after direct application of chemical stimuli to the surface of the brain
cortex. Thus this method is a sensitive indicator of the drugs' action
on the brain cortex, with particular emphasis on the processes maintaining
the integrity of the neuron cell membranes.

J. Vencek and H. Raskova (Chair of Pharmacology and Experimental
Pathology, Faculty Pediatric Division, Charles University, Prague) reported
on "Effect of Intracerebral Injection of Bacterial Toxins on Behavior of
cats". By using Feldberg's method of intracranial anmulae they deter-
mined the basis difference between the effect of Streptolysin O, after
which they observed almost immediate choreo-athetotic convulsions, and
the toxin of Shigella shigae, where the changes take place after a con-
siderable period of latency. The character of these changes then is
reminiscent of the effect caused by intracerebrally administered serotonin.
Varying mutual relationship of the toxicity of these two toxins, when
compared with intravenous and intracranial administration on mice, seems
to testify to neurotoxicity of Streptolysin O and simultaneously deny the
primary neurotoxic effect of the Shigella shigae toxin.

V. Vitek, K. Rysanek and M. Vojtechovsky (Institute for Further Edu-
cation of Doctors, Prague) noted in people "Certain Metabolic Manifesta-
tions of Experimental Psychosis after Use of Benactizine". The picture
resembles atropine delirium. They noted a considerable drop in the con-
tent of 5-hydroxyindoleacetic acid in urine in hourly relation to changes
in the higher nervous activity, and with a simultaneous drop in the activ-
ity of monoamineoxidase and increased elimination of the 17-hydroxyesters.
The authors expressed an opinion that the psychogenic effect of Benacti-
zine is related not only to the metabolism of acetylcholine, but also to
that of serotonin.

F. Von Brucke (Pharmacological Institute of the Medical Institute,
Vienna) dealt with "The Face-maker Zone in the Septum Pellucidum of Rabbits." His coworkers succeeded in isolating topically in the foremost part of the hippocampus a series of regular waves, observable in the EESG of the occipital cortex, on the thalamus, the septum and the dorsal and precommissural fornix during the course of the arousal reaction. Hardly noticeable lesions of the septum prevent their spreading. The arousal reaction brought forth by physostigmine can be blocked by the same action on the septum as the local application of procaine. The reactions brought about by local electrical stimulation were also noteworthy.

A. V. Valdman (Pharmacological Institute of the Medical Institute of I. F. Pavlov, Leningrad) dealt with "Pharmacology of the Reticular Formation". Important were certain variations determined in the sensitivity of the neurons of the reticular formation toward certain drugs. Using as models six kinds of experimental convulsions with the same external manifestations but with a different mechanism of origin he proved the hypothesis of the possibility of choosing drugs with a directed specific effect on the neurons of the reticular formation.

P. Kubikowski (Pharmacological Institute of the Medical Faculty, Warsaw) reported on the results of the experiments of Docent Venulet: "The Effects of Chlorpromazine and Acetopromazine on Conditioned Reflexes and their Changes after Application of Iproniazid". Both phenothiazines have a depressing effect on the defensive conditioned reflexes of rats, which had been strongly antagonized by iproniazid. At the same time the anti-serotonin effect of the phenothiazines was noted.

The second day the symposium continued to deal with the theme of pharmacology of the disturbance in the peripheral nervous system.

The first lecture by V. V. Zakusov (Institute for Pharmacology and Chemotherapy AMN USSR, Moscow): "The Influence of Pharmacological Substances on Reflexes of the Heart" described the importance of reflexogenic zones in the heart, whose irritation could be in close correlation with the pathological processes in various heart diseases. His coworker M. J. Ledinskaia dealt with the meaning of the pain syndrome for the changes in blood circulation and breathing in the presence of insufficiency of coronary circulation. She determined the influence of analgesic substances on these changes in reflexes in acute as well as chronic experiments. By using a very ingenious method on dogs, by stretching the ligature, which had been introduced under the coronary artery and then brought out to the surface of the body by a plexiglass cannula, she could cause an acute ischemia in the corresponding region of the myocardium. Ischemia brought about in this fashion could be influenced by analgesics (morphine, thecodine, promedole, phenadone) which lowered considerably and even suppressed circulatory reflexes of the respiratory changes, this was
particularly true of phenadone.

In acute situations in decerebrated cats she determined that the weakening of the heart reflexes by the analgesics does not depend on their effect on higher part of CNS, but is related to their effect on segmented divisions of the central nervous system. Likewise normalization of the EKG depends on the inhibition of the reflex element of the reaction, because it was determined that the speed of the total volume of the coronary circulation is not increased by any of the substances except morphine (N. V. Kaverine) Phenothiazines, meperidine, and aminazine acted in a similar fashion, and even though they were weaker they lasted longer. It was found that the most effective was a mixture of meperidine with phenadone, since it had a stronger effect, and lasted over 48 hours. Of the other substances procaine was also found to be effective.

This reaction was further tested on the changes in chemoreceptors in the coronary circulation. Coworker I. N. Plidvyd reported on influencing of changes caused by serotonin, blood serum and veratrine. The general effect was similar to ischemia, only it lasted less time and when medium doses of analgesics were administered it was only temporary. These observations could have considerable practical significance due to the fact that for example serotonin and ATP are active in the heart afflicted by an infarct of the myocardium and this fact undoubtedly plays a role in the development of pathological changes in the function of an organism. Similar results about influencing reflex changes in the pulmonary circulation were reported by Z. N. Ivanova.

N. V. Kaverina (Institute of Pharmacology and Chemotherapy, All USSR, Moscow) in her report "Influence of Pharmacological Substances on Reflex Reactions of the Coronary Vessels" was concerned with the mechanism of the effect of nitroglycerine and the analgesics on the blood supply of the heart muscle. The author was concerned with the controversy regarding the effect of nitroglycerine on the blood supply of the heart. Only those authors (Essex, Herrick, Baldes, Mann) who carried out their experiments by recording the blood circulation by a thermoelectric method noted considerable increase in the speed of the coronary circulation under the influence of the nitroglycerine involving the whole organism.

According to the results of investigators who had been using more thorough methods (Boyer, Green, Eckenhoff, Hafkenschiel, Kisin) nitroglycerine did not bring about any noticeable changes in the condition of the coronary vessels. The author herself used the method of measuring the resistance (change of pressure was recorded at the point where the outflow of the infusing pump enters the mouth of the left coronary artery). The reflex of narrowing of the coronary vessels was brought about by irritating the carotid sinus and electric irritation of afferent nerves. Nitroglycerine completely repressed the reflex changes of the coronary flow,
while reflex changes of the blood pressure reached as much as 50%. The hypothesis states that the removal of the pain syndrome in stenocardia by means of nitroglycerin is actually connected with improving of the blood supply of the myocardium, which, however, is achieved chiefly by suppressing the reflex spasms of the coronary vessels. It was determined that substances acting as analgesics have a similar capacity to suppress the reflex reactions of the coronary vessels however this effect is not as selective as with nitroglycerin (reaction to TK is correspondingly lowered) and it is impossible to suppress the reflexes completely with them. When higher doses are used the effect is actually reversed. The selectivity of the nitroglycerin effect give us hope that other substances might be discovered with a selective effect on the reflex regulation of circulation in other organs and organ systems as well.

The lecture of J. J. Peuse (Pharmacodynamic and Therapeutic Laboratory Med. Fac., Brussels) "The Effect of Reserpine of the Cardiovascular Reactions Caused by Symptometinics" dealt with the effect of reserpine on a heart-lung preparation in a dog. He noted that if the material came from an animal which had 24 hours previously received intraperitoneal reserpine in the dose 0.1-0.2 mg/kg the reaction to ephedrine and to reserpine itself disappeared. Rabbits that had not been narcotized showed after larger doses of reserpine an increased reaction to adrenaline and noradrenalin, which were followed in their blood pressure and in the disappearance of their reaction to 1-1-dimethyl-4-phenylpiperazine. In rabbits and guinea pigs previously influenced with reserpine, whose isolated atria were influenced by sympathomectinics, no particular changes were seen as compared to controls. When electric shock was used on the non-narcotized rabbits hypertension and tachycardia were brought about. This reaction changes strongly after administration of reserpine, in fact brachycardia and hypotension is caused.

The lecture of J. I. Vichlavjev (Institute of Pharmacology ANN USSR, Moscow) "Influence of Neuropilc Substances on Chemoreception" was concerned with influencing of the chemoreceptive zones and vessels of the rear extremity in cats. The experiments were carried out by using a donor or infusion pump on an isolated extremity with a preserved nerve connection through n. ischiadicus. The reflex changes were evoked by acetylcholine and 10% solution of NaCl. Chlorpromazine, mepromazine, propazine and etaperazine (Trylafon) were used. When irritating substances were introduced into the arterial system of an isolated extremity they were followed by a reflex rise in pressure in the recipient and lowering of pressure in the donor (this did not occur when NaCl was given). Introducing normal doses of neuropilc substances into the circulation of the donor did not cause reflex rise of pressure in the recipient. However it was possible to remove these reflexes by introducing the substances directly into the arterial system of the isolated limb or into the circulation of the recipient. Thus neuropilc substances do not show a notable effect on the sensitivity of chemoreceptors, in the doses that completely suppress
pressor reaction of blood pressure of a reflexive origin. A considerable suppression of the chemoreceptors is only possible when the preparations are highly concentrated in individual regions of the bloodstream, and this effect cannot be produced with the commonly used doses. This observation agrees with the work of Charikjeva and Decourt who showed that chlorpromazine when given in the usual dosage and method of administering does not block the ganglia. The author reasons that suppression of the chemoreceptors and the so-called endovascular anesthesia does play an important role in the mechanism of the suppressive effect of chlorpromazine and related substances on reflexes of the vessels.

Z. I. Vedenejeva (Pharmacological Division of the Institute for Experimental Medicine, Leningrad) presented a report on "The Effect of Neural and Humoral Factors on Appearance of Experimental Myocarditis". The author caused experimental myocarditis by high doses of adrenaline or noradrenaline and by mechanical damage of the stellate ganglia. The changes were followed by EKG and histological analyses. In the attempt to prevent damage to myocardium by using drugs she used sympatholytin, chlorpromazine, chloralhydrin, hexethonium, luminal, amytal, and procaine. The only substances that were effective were sympatholytin and chlorpromazine. Considering the fact that chloralhydrin, which has a similar structure to chlorpromazine and similar action, (however, not the same sympatholytic effect) was not effective one can assume that sympatholytic effectiveness is very important for prevention of experimental myocarditis.

The lecture of A.A. Mirzoyan (Chair of Pharmacology, Med. Fac., Jerevan) "The Influence of Ganglione on the Transfer of Irritability and on the Content of SH-groups in Tissues", was concerned with the mechanism of the effect of the chloride of the alpha-beta-dimethyl-gamma-diethylaminopropionic ester of isobutoxybenzoic acid on the central and vegetative system. This substance blocks the transfer in the ganglia. This blocking action can be destroyed by cysteine, which was demonstrated in experiments using a perfused ganglion of Cervicalis super.

D. A. Charikjeva (Institute for Pharmacology and Chemotherapy, AMN USSR, Moscow) in his very interesting report on "Influence of Ganglione-blocking Substances on the Subsequent Suppression in the Ganglia" noted the difference in the action of hexethonium, pendiomide, mesamylamine on the one hand and TEAB on the other. He tried out the effect of these substances on the stellate ganglia, where the first group of substances caused the disappearance of the posttatic facility, while TEAB caused its increase. The author thinks that this phenomenon depends not only on the change in sensitivity of nerve cells in the ganglia, but also on the reactivity of the presynaptic endings.

J. Vik (Physiological Institute, Med. Fac., Ru, Plzen) in his contribution "Remarks on the Method of Determining Content of Acetylcholine in the Heart and Its Significance in the Action of the Heart", was concerned
with the meaning of acetylcholine for automatic heart activity. The author followed the factors which influence the amount of bound acetylcholine (probably to proteins) in the heart.

To measure the content of acetylcholine he used the improved method of Rotheschuh by testing on a isolated straight abdominal muscle of a frog, which was sensitized by addition of adenosine triphosphoric acid to the bath. This addition not only increases the contractions after acetylcholine, but also prolongs the longevity of the preparation without influencing the contraction of the muscle. The author determined that in several kinds of animals (rat, dog, guinea pig) there is parallel between the content of acetylcholine in different parts of the heart and the so-called autonomic gradient (Gaskell) that is places with the highest autonomic contain the highest amount of acetylcholine. Further he observed an increase in the content of acetylcholine in the heart in the first months after the birth of the dogs. Again the highest increment was in those regions of the heart which had the highest autonomic.

N. V. Visockaga (Institute of Pharmacology and Chemotherapy AN USSR, Moscow) in her report "The Influence of the Ganglic-blocking Substances on the Metabolic Processes in the Vegetative Ganglia" concerned herself with the metabolism of phosphorus in the ganglion cervicale super, where the blockade by nicotine, pendomide and pachycarpine was combined with lowering of ATP and creatine phosphate in the ganglion. Hexamethonium did not have this effect. Further studies showed that both the activity of ATP is heightened and the content of glycolase is increased. Thus it seems that the effect of hexamethonium in contrast with the other tested substances does not depend on the changes in the phosphorus metabolism.

O. Guda (Chair and Pharmacology, Fao of Pediatric Medicine, Charles U, Prague) described in his lecture "Changes in the Reactivity of the Organism to TEAB after a Laparotomy" his observations on anaesthetized cats where he determined that a laparotomy substantially changes the response of the organism to administration of TEAB. The main change was in the reaction of the nictitating membrane following a preganglionic irritation of the sympathetic nervous system of the neck, and in the changes of the reaction of blood pressure particularly of the quantitative type. Phaco reactions were also noted.

V. Tróka (VUFB, Prague) described the characteristics of three new types of ganglioplegic substances, as follows: 2-dimethylaminoisocamphene (dimokamine), trimethyl/ethyloxyhexyl(dimethylamine (ponhexamine) and 2-dimethyl-amino-2,3,3-trimethylbutane (penbutamine) synthetized at the VUFB with low toxicity and administered orally. He showed that the cyclical nucleus is not a necessary condition for activity of the tertiary amines. These substances are at the present time being clinically tested.

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The afternoon session was opened with a lecture by C. Höymans winner of the Nobel prize for his work on the physiology of the carotid sinus (Pharmacological Institute of the Medical Faculty, Ghent). The subject of his lecture was "The Cardiovascular and Pulmonary Reflexogenic Areas". The baroreceptors of the nerve endings, which are concerned with maintaining blood pressure, are in the arc of the aorta and the region of the carotid sinus. These receptors are sensitive to the pressure of the arterial wall, within which they are contained. The presence of baroreceptors was demonstrated in other areas as well, which have a primary significance in reflex adaptations of local character. It seems that the most common effects on the cardiovascular system are produced on the receptors in the atrium of the heart, in the vena cavae, and in the pulmonary circulation. These receptors influence the adaptation of the venous return of the blood volume and also the heart beat. Chemoreceptors sensitive to the physiological composition of blood and to pharmacological stimuli are located in the aorta and the carotids. Irritation of these receptors evokes specific and non-specific circulatory and respiratory reflex reactions. Current experimental material is not too convincing about the existence of chemoreceptors in other areas. Perhaps in the future specific chemical stimulants will be discovered for them.

Mr. and Mrs. Gerový (Institute for Experimental Medicine SAV, Bratislava) gave a very interesting lecture on the meaning of frequency and amplitude of pulsation in relation to irritation of receptors in the carotid sinus. They concentrated on the question of the mechanism of the irritation of baroreceptors and the related question of the elasticity of the blood-vessel wall. Very ingenious experimental work of both the authors brought proof of the significance of pulse frequency and threw new light on the importance of this parameter for evoking a reflex response. Further the authors followed, in varying hemodynamic situations, the mutual relation of the pressure and volume oscillations, as an indication of the elasticity of blood-vessel wall in sinoarterial area in situ and in vitro. They interpret the differences that they determined in the stretching of the blood-vessel wall (on the one hand in the "stimulus" phase, on the other in the "regulation" phase during a cardiovascular reaction) from the standpoint of the influence on the liquidation of given hemodynamic situations.

S. S. Krylov (Institute of Experimental Medicine, Pharmacological Div., Leningrad) lectured on "Pharmacological Analysis of the Sensitivity of Receptors in the Sinus Caroticus". He determined that the sensitivity of the sinus, influenced by acetylcholine, remained unchanged after treatment with nicotine and sodium cyanide, while after treatment with nicotine the response of the chemoreceptors to acetylcholine is missing, parallel to unchanged response to sodium cyanide. After treatment with sodium cyanide the area is no longer sensitive to any other stimuli. Likewise the electrical activity of the appropriate nerve is completely
suppressed. The author reasons that the acetylcholine stimulus and the 
stimulus after treatment with sodium cyanide evokes different reactions 
in the CNS. For example he noted that after acetylcholine stimulus there 
is reflex contraction of the intestines, while after sodium cyanide there 
is a relaxation.

The extensive lecture of J. Cheymol (Pharmacological Institute of the 
Med. Fac., Paris) was on the subject of "The Excitability of the Motor 
Barrier". It dealt with structures and physiological mechanism of the 
neuromuscular synapse. First he presented the review of recent work on 
the motor barrier by means of an electron microscope. The following 
factors chiefly affect the main anatomical structures: the nerve, the 
motor barrier and the muscle and these are acetylcholine, potassium ions, 
and electric stimuli. Further the author explained various ways of action 
by curare-like substances. Then he related the activity of these sub-
stances to their chemical structure.

V. M. Karasik (Institute of Experimental Medicine, Leningrad) 
reported on "Differentiation of the Structure of Skeletal Muscles, Re-
acting to Potassium Ions and to Acetylcholine" and showed that different 
groups of drugs (substances which block the sulphydryl groups, substances 
which influence phosphorylation, and narcotics) can affect in different 
ways the reaction of the musculus rectus of a frog to potassium ions and 
to acetylcholine. The author hypothesizes that different structures 
which participate in transfer of the nerve stimulus react either to the 
potassium ions or to the acetylcholine.

V. Grossmann (Pharmacological Institute Med. Fac., Ch. Univ., Hradec 
Kralove) presented "Contribution to the Clarification of the Relation-
between the Central and Peripheral Effects of Certain Myorelaxing Sub-
stances". His report dealt with the capacity of the central tubarine and 
decamethonium. By analysing the relation of both substances to strychnine 
in mice it was determined that an antagonism exists between strychnine 
and tubarine, while between strychnine and decamethonium there is synergy. 
Experiments were carried out in which the effect on the latent period --
according to Zakusov's method -- was tried using both substances in rabbits 
both normal and myelotomized. Since decamethonium, which increases the 
effect both with a weakened and heightened influx of stimulation, loses 
its effectiveness considerably after a myelotomy, the author thinks that 
what occurs is a change in the sensitivity of the neuromuscular connection.
When tubarine is used the weakened effect in the first phase can be brought 
about by removal of the active depressant, evoked by irritation of the 
central nervous system. In higher doses it overcomes the depressant and 
thus the increase of its effect by influencing the blockade of the spinal-
cord synapses.

E. V. Moreva (Institute for Experimental Medicine, Pharmacological}
Division, Leningrad) reported on the pharmacological influence on the changing sensitivity of the muscle to potassium ions. She showed that anaesthetics can completely suppress the effect of potassium ions on muscles. And, dinitrophenol, e.g., sensitizes the muscle to these effects. It is interesting that reactivity to acetylcholine is not influenced by anaesthetics. This suppression of the synaptic component of the potassium effect by narcotic substances may play an important role in the mechanism of the effect of the narcotic substances.

Z. Finek and M. Saída (Military Research Medical Institute, Hradec Králové) lectured on "The Mechanism of the Antiacetylcholine Effect of Certain Substances" and reported on experiments on the ileum of a guinea pig, and on the attempts to synthesize acetylcholine in the organism following administration of a series of substances with an antiacetylcholine effect. They selected for testing certain tertiary and quaternary basic nitrogenous esters of substituted acetic acids and also the preparation Arten. They determined that some of these substances affect the action of free acetylcholine, while others do not have this effect but do strongly inhibit the synthesis of acetylcholine (pyridine-2-aldoxime methiodide).

F. V. Selecky, L. L. Vrbovský and L. Róssival (Pharmacological Laboratory of the Chemical Institute SAV, Bratislava) reported on the non-specific effects of certain organic phosphates. Lipertex, phosphothione, melithione, eoctina, dimethylchlorovinylphosphate and Timet were followed in chronic experiments lasting 10 weeks, and also in acute ones. Toxicity in different kinds of animals and percutaneous activity were determined.

The closing lecture was by M. Banner (Pharmacological Institute of the Med. Fac. Bratislava) "Muscular Activity of Certain Derivatives of Basic Isopropanols". He evaluated new synthetic substances, from the viewpoint of myorelaxing effect on an isolated diaphragm and on a preparation of ischiadic-gastrocnemius in cats. He determined that these substances cause paralysis of the extremities much sooner than paralysis of respiration. This paralysis is freed by synthostigmin and TEA. These substances are effective in doses from 10-20 mg./kg.

The third day of the symposium, concerned with the pharmacology of nerve mediators, focused its attention on reports dealing with several newly discovered substances, whose function in the nervous system is not entirely clear. Thus in the opening lecture by F. Lambeck (Pharmacological Institute of the University, Graz) was on "Localization of the P-Substance in the Central Nervous System" and presented a summary of great many experimental results, both his own and foreign. Detailed analysis of the cholinergic transfer of stimulation showed that alongside of cholinergic neurons there are also "non-cholinergic" neurons, to which belongs, for example, the first sensitive neuron, the pyramidal path, and
the nervus opticus. Stemming from a whole series of observations on the
P substance some tend to believe that this substance could be this very
humoral transferrant, while others are opposed to this theory. Both in
the cerebrum and in the cerebellum there is a small quantity of the P
substance; mesencephalon, extended spinal cord, fasciculi and nuclei
gracilis a cuneati, grey matter of the spinal cord, the retina and parti-
cularly the area postrema all contain high amounts of the P substance.
Contrasted with this there are small amounts in the pyramidal path, in
the bulbus olfactorius and nervus opticus. In the peripheral nerves
the dorsal roots of the spinal cord contain 5-10 times more P substance
than the ventral. Also a greater amount is contained in the truncus
sympateticus, medium amount in the mm. ischiadiceps and saphenus, little
in acusticus, phrenicus and splanchnicus. Comparison of the contents
of this substance in other animals showed that phylogenetically older
parts of the CNS contain more P substance than the phylogenetically
younger ones. Tumors from tissue with gliosis or immature cellular ele-
ments did not contain a significant amount of P substance. By fraction-
ation of the cellular elements in an ultracentrifuge it was shown that
the highest amount of P substance (combined with nitrogen) is contained
in the granular fraction. Thus it appears that similarly to serotonin,
adrenalin and noradrenalin it is bound to definite cellular structures.
The amount of P substance in the brain can be influenced by various drugs.
Drugs with irritating effect increase its content, narcotics lower it
(Zetler, Ohnesorge). Retina of the eyes that were closed 2 hours before
the animals were killed, contained more P substance, however in animals
that were kept in the dark the content was less (Kocic-Mitrovic). Upon
denervation the amount of P substance in the nerve was less. (Holton)
By following the effect of the P substance on the action of different
drugs it was determined that it suppresses the irritating effect of
harmine, strychnine, picrotoxin, and pervitin, similarly it suppresses
convulsions after tetanotoxin, it does not influence electric shock, or
the effect of cardiazol and nicotine (Stern, Zetler). In addition it has
certain antagonistic effect toward morphine (Zetler). Stern noticed
considerable similarity between the effect of P substance and mephinesine
and designated P substance as a "physiological tranquilizer". Intravenous
injection of this substance in people did not evoke any central effects.
(Liljedahl, Wattson and Pernow) On spinal cats there was no proved effect
on the spinal cord reflexes (Kissel, Domino), however some authors see
a depressing effect of the P substance on the polysynaptic reflexes
(Stern). After injection into the a. carotis one can note "arousal
reaction" on the EEG (Lechner, Lembeck) Injection into the side chamber
of the brain led to noticeable motor calming down of the cats (Fuler,
Pernow). On the peripheral endings of the afferent nerves in a perfused
rabbit ear the P substance caused reflex hypertention and a drop in
pressure (Lembeck). The author emphasized that in spite of a large num-
ber of experimental results only future experiments will enable us to
form a clear idea of the physiological significance of the P substance.
The second report by P. Holton (Physiological Institute of the Med.
Fac., St. Mary's Hospital, London) "The Probable Role of the P Substance
and ATP in the Chemical Transfer from Nerve Endings" is thematically
closely related to the first one. By comparing P substance and ATP with
acetylcholine, one can conclude, that P substance can be the transferring
agent just like acetylcholine while ATP cannot even though it is released
when the nerve is irritated. In experiments with a perfused rabbit ear
the author showed that ATP was present in the perfusate, if sensitive
nerves were irritated. This depended on the capacity of the nerve to
take the disturbance and on whether the release did not take place after
the degeneration of the nerve. ATP is released at the nerve endings not
on the axons themselves, because during the irritation of a part of a
perforated ischiadicus, which did not contain any nerve endings, it was
impossible to demonstrate any ATP. ATP is likewise released from the
sympathetic ganglia during irritation of the preganglionic nerve. These
results show that release of the ATP is not a specific characteristic
of the sensitive neurones, but of the others as well. Most likely it is
at least in part the cause of antidromal vasodilation. The substance was
determined in normal and degenerating nerves. Its concentration dropped
degenerating sensitive nerves as compared to a contralateral control.
The same results were achieved for the axons of the primary afferent
fibers of the posterior parts of the spinal cord. These results testify
to the fact that P substance (or its precursor) is formed within the
nerve cell and moves in the direction of the nerve endings. This was
proved by determining the presence of this substance in the proximal
stumps of the severed nerves, in which an increase in the amount of P
substance was noted in the first few days after they were severed. This
behavior, which is similar to the behavior of cholinesterase, choline-
esterase, and acetylcholine (McIntosh, Hebb and Waites, Sawyer, Cavanagh,
Nachmenschn et al.), supports the theory that P substance is an analogue
of acetylcholine. Preliminary observations showed that this substance
is bound in the nerve cells in particles of the magnitude of mitochondria.
Thus even in this way it resembles acetylcholine and noradrenaline. In
conclusion the author expressed an interesting opinion that the carriers
of all types are bound in the nerve cells in particles together with ATP
and if during transfer of a stimulus the carrier is released then ATP is
released as well. Even though one cannot consider this view as a proven
theory, it might be useful as a working hypothesis for further experiments.

The report of R. Capek (Pharmacological Laboratory CSAV, Prague) dealt
with a comparison of the action of two biologically active peptides of
the P substance and bradykinine. The author followed the effect on the
irritability of an isolated nervus ischidicus in a frog, of rhythmical
irritation by right-angle pulse of varying frequency and duration. During
slow frequency both substances raise the threshold, not directly in ratio
to the length of duration of the stimulus. Dependence of the increase
of the substances on frequency was different for each of the substances.
While bradykinine raised the threshold equally at all frequencies, P

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substance definitely raised the threshold at high frequencies. Further
the influencing of the convulsive effect of pentazol by both the sub-
stances was studied. While previous application of bradykinine lowers
the ED$_{50}$ of pentazol, a previous application of the P substance in-
creases it. The author explained that the disagreement with previous
findings in the literature, that is that the P substance does not influ-
ence the convulsive effect of pentazol (Zetler and others) can be ex-
plained by a different method of application and by a different evaluation
of the effect. Further he pointed out how complex is the analysis of the
effect of substances such as these peptides, which has such many-faceted
central and peripheral activity.

O. Benesová (Pharmacological Institute Med. Fac. Hygiene KU, Prague)
presented a report on "Effect of ATP on the Central Effects of the Barbi-
turates" She followed the length of thippental anesthesia by checking the
straightening reflex in rats, and the depth of anesthesia in rabbits with
embedded epidural electrodes, by determining the motor threshold following
application of ATP. ATP shortens and lightens the anesthesia, if it is
administered 20-25 minutes before thiopental. These findings testify on
behalf of Quastel's hypothesis that the mechanism of the action of anes-
thetics depends on the inhibition of splitting of glucose at a certain
step. This causes a considerable lowering of the formation of macroergic
phosphate compounds and synthesis of the bound acetylcholine. Thus in-
creased presence of ATP lowers the effect of the anesthetics. The ob-
jection that here we are dealing with a increased detoxication of thiopental
in the liver (which requires macroergic compounds) can be countered by the
fact that simultaneous or subsequent application of ATP produces no effect,
while with the detoxicating mechanism it is still effective.

The lecture of J. L. Mongar (Pharmacological Institute of the Univer-
sity, London) dealt with "Mediators of the Allergic Reactions". In his
experiments the used isolated tissue, in order to eliminate the
participation of the nervous system in allergic reactions, since he thinks
that simple cellular mechanisms are the basis of allergic reactions in
the whole organism and are merely modified by the nervous system. He
visualizes the allergic reaction as a series of steps, according to the
following scheme:

1. antibodies $\rightarrow$ cells $\rightarrow$ sensitized cells
2. antigen $\rightarrow$ sensitized cells $\rightarrow$ activated enzyme system (tissue
   complement)
3. enzyme $\rightarrow$ bound histamine $\rightarrow$ free histamine
4. histamine $\rightarrow$ receptors $\rightarrow$ contraction of the smooth muscle, etc.

In 1. In order that sensitization take place the circulating antibodies
must be fixed on the cells. Particularly important is their fixation on
the fatty cells which contain the largest amount of tissue histamine.
The reaction of the antibodies with the cells is specifically inhibited
by "non-antibody gammaglobulin", which competes with the antibodies in its fixing on the cells. Warm temperature is likewise very important for the occurrence of this fixation.

In 2 and 3, when the antigen reacts with the fixed antibodies, an intracellular process takes place, which to some extent resembles the activation of complement in serum. An enzyme reaction starts, which requires the presence of Ca++. This reaction leads through hitherto unknown steps to the release of histamine which is bound to the intracellular granules of the fatty cells and other active substances. It was possible to show a significant lowering in the number of metachromatic granules in the fatty cells a few minutes after addition of antigen. Certain inhibitors, for example phenol, make desensitization possible without the release of histamine, probably by preventing the effect of the enzyme, but not its activation and subsequent inactivation. The effect of warmth and pH on this mechanism is similar to the effect on the enzyme system. After the muscle is warmed at 44°C for 15 minutes it is impossible to evoke an anaphylactic reaction, even though the muscle remains sensitive to histamine.

In 4, the allergic reaction is mainly caused by substances which are released from tissues. Histamin is released not only from sensitized guinea pig tissue, which was used for the experiments, but also from pieces of human asthmatic lung tissue, when placed in contact with a specific antigen. Thus, the author reasons that there is a great similarity between the reaction of human asthmatic bronchi and isolated sensitized smooth muscle of a guinea pig to an antigen. However, one cannot ascribe all effects to histamine, since beside it the "slow-reacting substance" is released as well, which also contributes to the bronchoconstriction.

The report of H. Rasekova and J. Vanecek (Chair of Pharmacology and Experimental Pathology Fac. Med. Charles U., Prague) dealt with "Release of Products in Intracerebral Administration of Bacterial Toxins" and was thematically closely related to the report of these authors on the first day of the symposium. Typical changes in behavior in non-narcotized cats after intracerebral administration were brought about as well by the streptococcal toxin Streptolysin O. It had been shown earlier that this toxin produces after a prolonged latent period a slow contraction of an isolated uterus of a rat. Since in both cases the cause could be the release of active substances from tissues, the relation of this toxin to brain tissue was studied. In cats a perfusion of the liquor cavities zones according to the method of Bhattachary and Feldberg was tried. The perfusate was tested on an isolated rat uterus in an atropine solution of de Jalon and then chromatographically measured. Samples taken immediately post-operatively caused a contraction, and after 40-50 minutes were inactive. After application of Streptolysin O myotropic activity appeared
anew. The contraction was not brought about either by histamine or by acetylcholine or serotonin, because it could not be blocked by specific antagonists of these substances. Myoactive samples likewise showed changes in the chromatograms, by appearance of a ninhydrin positive spot, which had not been present either in Streptolysin alone or in the liquor. The character of the contraction testified to the possibility that the "slow contracting substance" might be released. The fact that the release takes place even after postoperative trauma reminds the author of the work of Fine and others concerning the irreversible stage of hemorrhagic shock. Specifically these authors prove that irreversibility is caused by departure of the bacteria from the intestines. However, it is also possible that both the trauma and the bacterial toxins release active substances in the body which are responsible for the irreversibility of shock. Some recent experiments testify to this thought indirectly in trying to increase the resistance of mice to bacterial toxins by repeated administration of phenol or repetition of the Collip shock. The author noted that her results do not warrant more concrete conclusions.

I. S. Zavodskaja (Pharmacological Institute of the Institute of Exp. Med., Leningrad) reported on "Role of Nerve and Humoral Factors in Producing Experimental Stomach Ulcers". It dealt with the author's own method of producing stomach ulcers in rats by a mechanical traumatization of the duodenum, which consisted of applying a 10-mm long 10 minutes. This procedure could, besides others traumas, also lead to increased secretion of ACTH and because of this to increased production of the corticosteroids, which could play an important part in causing the ulcers. Thus the author followed the Vitamin C level in the adrenals after her procedure, and showed that even in 2 hours it was lowered. This effect was not produced in hypophysectomized animals. However, since ulcers can be produced in both hypophysectomized and adrenalectomized animals, the hypophysoadrenal system does not play the decisive role in their formation. Even the role of histamine is not decisive, since production of ulcers can be prevented by ganglion-blocking substances and subdiaphragmatic vagotomy. These results testify that the chief cause for the production of ulcers is the reflex change in the trophic quality of the stomach wall, evoked by the traumatization of the duodenum.

Z. Votava (VUFB, Prague) reported on "Antiserotonin effect of the derivatives of the diethylamide of lysergic acid". He dealt with cyclopropyl, butyl, penty1, hexyl, and heptylamide of lysergic acid. Their antiserotonin effect was followed on an isolated rat uterus, on isolated strips of rat duodenum and on serotonin buds that were produced in rats. Even when certain difference in the antiserotonin effect were apparent depending on the method used, it is possible to say that the original derivatives of lysergic acid showed that the antiserotonin effect declined as the cyclical nucleus increased. However all these substances were considerably weaker than LSD. Antiserotonin effect is also possessed by ergometrine, and by chlorpromazine which has quite a high effect in doses
of 40X higher. Of the whole series of synthetically prepared derivatives of lysergic acid only LSD has psychogenic effect, while a whole series of other effects is common to all these substances. Thus it seems that LSD has in this direction a specific effect on the higher nervous activity of man.

The report of V. Troka (VUFH, Prague) "A Structural Analogue of Reserpin" was concerned with the Relation Between Chemical Structure and Pharmacodynamics Effect of Certain Structural Analogs of Reserpine". The many-faceted effects of reserpine force us to pose the question as to whether its effect is bound up with the whole molecule in its spatial arrangement, or just with a certain part of the molecule. From the many derivatives prepared by Protiva and Co., the author compared certain derivatives of 1,2,3,4-tetrahydrocormaraine in their centrally depressant effect, by using the test of a rotating stake(?) in mice and by measuring the hypotensive effect on cats. Tetrahydrocormaraine alone has a weak centrally depressing and hypotensive effect. Its 1-benzyl derivative has both these effects in a much greater measure, 1-methoxy derivative is on the contrary less effective and more toxic. 2-benzyl derivatives do not have a depressant effect, while effect on blood pressure remains unchanged. A clinical check on this showed that 1-benzyl derivative (phencormaraine) has a tranquilizing effect. However the effect on blood pressure in hypertensive patients was not sufficient. Another part of the reserpine molecule is represented by the trimethoxybenzoic ester of N-methyltryptamionoethanol and further alcohols. The first of the homologues has a depressant effect, while the blood pressure is noticeably elevated. With the lengthening of the alkyl chain the central depressant effect drops and the effect on blood pressure distinctly turns hypotensive.

The next report by A. Dlabač (VUFH, Prague) "Phencormaraine", completed the preceding with an attempt to analyse the effects of one of the derivatives of cormaraine. Since the effects of reserpine are closely related to those of serotonin, the author followed the elimination in the urine of dogs of the final metabolite of serotonin, 5-hydroxyindole acetic acid, after administration of phencormaraine and reserpine. Following both substances there is an increase in the elimination of 5-hydroxyindole acetic acid in the urine, however it is less pronounced with phencormaraine. Reserpin and phencormaraine cause general depression and ptosis of the eye-lid in mice. If imipramine (Marcilid) is given, the substance which blocks monooxoxygenase and thus prevents oxidation of serotonin, then the effect of phencormaraine disappears and the onset of the effect of reserpin is put off, occasionally, even excitation and exophthalmos is brought about. Qualitative differences between reserpin and phencormaraine are noticeable only in higher doses, when the reserpin effect is deepened while phencormaraine rather causes excitation similar to the effect following administration of 5-hydroxytryptophane. The experiments described above testify to similarity of the effect of these two substances and the similar mechanism of interference in relation to serotonin.
The participants in the symposium exchanged views in rich and lively discussions concerning the newest concepts in the field of neuropharmacology. The hospitable environment which enabled all participants to have uninterrupted personal contact helped in establishing personal contacts and exchanging experiences of the individual European work-centers. The guests particularly valued the organizational aspect, where the only drawback was an imperfect translating service.

Professor Heymans, the chairman of the international physiological and pharmacological society, in his closing speech recommended setting up similar symposia in other European states, which would be one of the main tasks of a new European Pharmacological Society, which he proposed. Tightening of the friendly and scientific contacts of the participating scientific work-centers is surely a significant stimulus to world cooperation.