# INFORMATION REPORT INFORMATION REPORT

CENTRAL INTELLIGENCE AGENCY



C-O-N-F-I-D-E-N-T-I-A-L

COUNTRY Yugoslavia

REPORT [redacted] 25X1

SUBJECT 1959 Annual Report of the Institute for Medical Research (Incorporating the Institute of Industrial Hygiene), Zagreb

DATE DISTR. 21 Jul 60

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The Yugoslav Academy of Sciences and Arts
INSTITUTE FOR MEDICAL RESEARCH
(INCORPORATING THE INSTITUTE OF INDUSTRIAL HYGIENE)
Z A G R E B

# ANNUAL REPORT

# 1959

## ORGANIZATION

The Institute is one of the research institutions of the Yugoslav Academy of Sciences and Arts. It was founded by the Academy in 1948 as the Institute of Industrial Hygiene. In 1953 other medical research units were included into the Institute and its name was changed into the Institute for Medical Research, incorporating the Institute of Industrial Hygiene.

In 1959 the reorganization of the Institute based on a new law concerning the organization of scientific work (1957) was completed. The new director of the Institute, Professor V.B.Vouk, and Assistant Director Dr.M.Šarić, took over their duties in January 1959. A new By-laws of the Institute was worked out, determining the organization and the tasks of the Institute. According to it, the Institute is an independent scientific institution within the framework of the Yugoslav Academy. Its basic policy is submitted for approval to the Presidium of the Academy. This policy is decided by the Council of the Institute consisting of 20 members: a) 5 members representing the Institute, chosen by the Institute's scientific staff among themselves; b) 7 members appointed by the Presidium of the Academy either among its members or other scientific and public workers; c) 3 members representing the University and Governmental bodies dealing with medical research; d) 2 members representing industry, and e) Director of the Institute as a member of the Council ex officio. The Council of the Institute is appointed for a period of 2 years. The present chairman of the Council is Dr.Todo Ćuruvija, President of the Council of Public Health of P.R.Croatia. The whole work of the Institute is directed by a Director appointed by the Yugoslav Academy for a period of 5 years. The Director is advised by the Managing Committee of the Institute consisting of the Director, the Assistant Director, the elected representatives of each department, and the representatives of junior research staff, laboratory technicians, and administrative and technical auxiliary staff. The Managing Committee is formed every two years.

According to the By-laws, the tasks of the Institute are as follows: a) to organize and carry out research work in the field of medicine and related disciplines, b) to examine and study the physical and biotic conditions of work and the problems of occupational health, c) to develop and improve methods of research work, d) to promote the economic and public health conditions of the country by tackling current research problems and collaborating with all interested institutions, e) to take part in undergraduate

and postgraduate university teaching, f) to spread knowledge and information relating to industrial health, h) to collaborate with scientific institutions in this country and abroad, and i) to carry out other work that it may be entrusted with by law or the founder's orders.

According to the By-laws, the Institute has 5 departments: Environmental Hygiene and Engineering, Occupational Diseases, Toxicology, Psychology and Physiology of Work, and Biophysics. (The Department of Biophysics has not as yet been formed, and its work has been carried out in other departments.) The Department for the History of Medicine was at the end of 1959 handed over to the Academy as a part of its new Institute for the History of Natural, Mathematical and Medical Sciences.

In 1959 the Centre for Radiological Protection, formed on the basis of an agreement between the Institute and the Federal Nuclear Energy Commission in 1957, has been working as a separate unit within the framework of the Institute, but preparatory work has already been done to incorporate the activities of the Centre into the Institute's scientific programme, in accordance with the Institute's perspective research plan.

The Institute has continued to collaborate with various institutions both in Croatia and other federal republics. There was a close contact with the Research Council of P.R.Croatia, Federal Nuclear Energy Commission, Commission for Medical Research Work, the Bureaus of Social Insurance, the University of Zagreb, and the School of Public Health "Andrija Štampar" of the Medical Faculty in particular, the Council of Public Health of P.R.Croatia, Central Institute of Hygiene, Institute of Hygiene of the City of Zagreb, the Nuclear Institute "Ruđjer Bošković", Federal Commission for Standardization, and a number of industrial enterprises on the basis of special agreements.

There is no formal connection between the Government health agencies and the Institute. The Institute has no authority to act as an agency of the Health Service or Labour Inspection. The representatives of the Health Service are in the Council of the Institute and may in this way influence its research policy. Other administrative channels of contact are different advisory committees set up by the Government, and several members of the staff of the Institute are members of such bodies.

## PERSONNEL

At the end of 1959 the Institute had a total staff of 79 full-time workers (35 with academic degrees in medicine, chemistry, psychology, engineering, biology, and physics, 20 technical staff, 9 administrative staff and 15 technical auxiliary staff) and 5 part-time scientific workers.

The list of the Institute's scientific staff is given as follows:

Professor V.B.Vouk, Ph.D.

Assistant Director

M.Šarić, Dr.Med.,Dr.Sc.

Department of Environmental Hygiene and Engineering

N.Toskorodžić, Dipl.Ing.
(Head of the Department)
Prof.B.Kosić, Dr.Med., Dr.Sc.
M.Fugaš, Dipl.Ing.
Z.Topolnik, Dipl.Ing.
M.Hrmat, Dipl.Physicist
D.Mujoon, Dipl.Ing.
R.Paukoviđ, Dipl.Ing.
Z.Vuić-Drolc, Dipl.Physicist

Department of Occupational Diseases

T.Beritić, Dr.Med.
(Head of the Department)
A.Markičević, Dr.Med.
B.Prpić, Dr.Med.
D.Majić, Dipl.Ing.

Department of Psychology and Physiology of Work

Prof.Z.Bujas, Dr.Phil.,
(Head of the Department)
B.Petz, Dr.Phil.
V.Horvat, Dr.Med.
B.Srbinec, Dipl.Phil.
S.Vidaček, Dipl.Phil.
Gj.Vukadinović, Dr.Med., Dr.Sc.

Department of Toxicology

K.Weber, Dr.Phil.
(Acting Head of the Dpt.)
K.Kostial, Dr.Med., Dr.Sc.
K.Schulz, Dipl.Ing., Dr.Sc.
M.Vandekar, Dr.Med., Dr.Sc.
O.A.Weber, Dipl.Ing., Dr.Sc.
D.Floš, Dipl.Ing., Dr.Sc.
Y.Škreb, Dr.of Sc.
V.Turner, Dr.Vet.Sc.
D.Basler, Dipl.Ing.
A.Baumann, Dipl.Ing.
Lj.Bovillacqua, Dipl.Biol.
A.Karšano, Dipl.Biol.
H.Lorković, Dipl.Biol.
A.Lutkić, Dipl.Ing.
T.Maljković, Dipl.Biol.
E.Reinor, Dipl.Chem.
M.Škrinjarić, Dipl.Ing.
B.Šlat, Dipl.Biol.
P.Cugić, Dipl.Ing.

Department of the History of Medicine

M.D.Grmek, Dr.Med., Dr.Sc.

Attached Workers

Z.Skurić, Dipl.Ing. (Institute of Hygiene of the City of Zagreb)
A.Erković, Dipl.Phil. (Faculty of Philosophy)
R.Bujanović, student (Faculty of Philosophy)
M.Vagdić, student (Faculty of Philosophy)
M.Krizmanić-Vodanović, student (Faculty of Philosophy)
M.Branica, Dipl.Chem. (Institute "Rudjer Bošković")
J.Matković, Mr.Pharm. (Institute "Rudjer Bošković")
V.Popović, Dipl.Ing. (Institute "Rudjer Bošković"
D.Rajić, Dr.Med. (Army Hospital)
B.Svetličić, Dr.Vet.Sc., (Veterinary Faculty, University of Zagreb)

## ACCOMMODATION AND FACILITIES

The premises of the Institute are located in Zagreb, Moše Pijade 158, having a surface area of about 2,000 $m^2$. They consist of three buildings: a small ground-floor laboratory and two buildings of one and two storeys respectively. These buildings house the main part of the Institute, i.e. the Administration, the Department of Environmental Hygiene and Engineering, the Toxicology Department, the Department of Psychology and Physiology of Work, the Biophysics Department, the Lecture Theatre, the workshops, and the animal house. The Internal Clinic of the Medical Faculty of the University of Zagreb has provided space for the Department of Occupational Diseases with its clinical ward.

An investment programme is accepted for the extension of the Institute's useful surface area for about 1,000 $m^2$ to house new laboratories for radiological protection work. The building of the first part of the project is in progress.

The facilities of the Institute include a laboratory for air analysis with an experimental gas chamber, an analytical chemistry laboratory equipped for the analysis of traces of metals in biological material (spectrophotometry, polarography, flame-photometry), a biochemistry laboratory for studies on the metabolism of toxic substances, a physiological laboratory for large animals, a laboratory for determination of toxicity, electrophysiological laboratories, and a laboratory for functional testing of cardiovascular and respiratory system (human physiology laboratory). There is also a histology and a hematology laboratory, as well as a clinical chemistry laboratory. The Department of Occupational Diseases has hospital facilities (12 beds).

## FINANCE

The financial sources of the Institute derive from the annual budget allotted to the Institute by the Yugoslav Academy of Sciences and Arts (which is financed by the State), and from research contracts with various governmental institutions and industrial enterprises. In 1959 the budget allotted by the Yugoslav Academy amounted to Din 44.469,000, and the financial means obtained on the basis of various contracts to Din 46.128,000.- Out of the latter sum Din 11.950,000.- were given to the Institute by the Research Council of P.R.Croatia for the building of the Institute's new laboratories for work on the problems of radiological protection.

In 1958 the Rockefeller Foundation gave a grant to the Yugoslav Academy amounting to 33,000 dollars for further expansion of its research programme in experimental medicine.

In this section we are giving a brief review of the Institute's research activities in 1959. These activities have not been divided according to the departments of the Institute, but in 5 broad groups according to the problems treated. This is in agreement with the Institute's research policy which favours team work carried out by various kinds of research workers belonging to various departments of the Institute, while departments themselves are considered administrative units rather than units with strictly defined fields of work.

## Occupational and Public Health

### (1) Environmental studies

a) Air pollution analysis

Work was continued on the development of methods for the preparation of calibration mixtures of gases and vapours.

Work was also continued on the determination of formaldehyde in the air. The method with the Schiff reagent is abandoned, since it gave no reproducible results. A British method with phenylhydrazine is being developed.

In connection with work on chlorinated hydrocarbons the absorption efficiency of atmospheric trichlorethylene in amyl acetate at different temperatures and with different sample sizes was investigated.

b) Working environment analysis

The assessment of thermal environment in the enamel ware manufacture "Gorica" Zagreb was performed. The results have shown that heat load at enamel stoves, by the index of Bolding & Hatch, was near the upper permissible limit.

Microscopic analysis was carried out of dust samples collected by means of a thermoprecipitator in the factory of cement-asbestos sheets and tubes "Antiša Vučičić" Solin.

In collaboration with the Central Institute of Hygiene, the Institute of Hygiene of the City of Zagreb and the Sanitary Inspection, analysis of raw material, unfinished and finished products, and equipment was carried out in the factories of an industrial district of Zagreb in order to evaluate the degree of outward air pollution produced by these factories. Methods are suggested for the prevention, or at least diminution, of air pollution in the vicinity of these works.

### (2) Occupational Diseases and Industrial Medicine

a) Occupational mercury poisoning

Observations of occupational mercury poisoning at the factory "Radonja" Sisak have continued. Only a limited number of

dermatitis due to mercury compounds was evidenced. No systemic injuries due to mercury were observed.

b) Asbestosis

3 cases of asbestosis are evidenced by health examinations and radiography of 60 workers exposed to asbestos in the cement-asbestos sheet plant at Vranjic. They are the first verified cases of asbestosis among workers engaged in production and handling of asbestos in Yugoslav industry.

c) Occupational Heat Exposure

A study is undertaken on the effect of heat in the enamel ware production "Gorica" Zagreb. It has been demonstrated that there is no significant difference in the type and frequency of diseases or absenteeism between the workers of this factory and the control group. Investigations are continued in some other factories in order to obtain more reliable data.

d) Systematic Examinations in Industry

On the basis of the results obtained in 1958 methods are developed for systematic examination procedures in industry.

e) The Effect of Nutrition on Workers' Health

An experiment was undertaken to study the effect of nutrition (an additional breakfast at the beginning of work) on the nutritional status, hemoglobin level, morbidity, absenteeism, accidents, and working effect of workers in the factory "Moša" Zagreb. The experimental group consisted of 300 workers who in the course of 5 months were given an additional meal of about 600 calories. The control group was a group of 200 workers of the same factory. The evaluation of the results has not as yet been completed.

f) Routine Work

In 1959, 1348 patients were examined in the Outpatient Department of the Department of Occupational Diseases. In the Clinical Ward 46 occupational and 98 non-occupational poisonings were treated, as well as 177 cases of internal diseases. Chemical Laboratory of the Department carried out over 600 analyses, and the Hematological Laboratory over 5,000 analyses, either in connection with the working programme of the Department itself or at the request of other health institutions.

Further work on occupational diseases is described in the section on Clinical Toxicology.

(3) Occupational Health Engineering

a) Protective devices

At the request of the firm "Rudar" and the Labour Inspection canisters with regenerating material for oxygen breathing apparatuses of Hungarian make were tested on the basis of Yugoslav and German standards. It has again been proved that in quality Hungarian canisters can match the canisters of the German firm Dräger.

The testing of fine dust filters for respirators made by the firm "Ris" Zagreb, and of sandblast filters made by the Boiler Plant in Zagreb was carried out. Miners' helmets produced by the firm "Galdovo"

Sisak were also tested.

b) Ventilation Projects

A ventilation project was designed for the Virus Research Laboratory of the Central Institute of Hygiene in Zagreb. For ventilation projects designed for various radioisotope laboratories see p.8.

c) Work on Industrial Hygiene Standards and Regulations

In collaboration with the Central Institute of Hygiene, regulations have been drawn out for safety measures in the Steel Works Zenica. The Institute took part in the work of the Subcommittee for Standardisation of the Federal Commission for Safety Standards.

## (4) Industrial Psychology

a) A working programme was drawn out for the study of absenteeism and motivation in Yugoslav industry. Preliminary work has been done for the organisation of technical training of textile workers.

b) The analysis of working places in the factory "Rade Končar" is completed. Work on rational distribution of workers in the same factory is in progress.

## (5) Public Health

On the basis of a contract with the Social Insurance Bureau and in collaboration with the School of Public Health "Andrija Štampar" the study on the role of a rural health station has continued. The experiments have been carried out in a small village Rude near Zagreb. The Health Station Rude is organised on the basis of minimum personnel and specific rural conditions in this country. The problems to be solved are as follows: a) what minimum personnel is required under given conditions, b) how much work does it mean for the Station if it offers free of charge health service also to non-insured inhabitants, and c) what improvement in hygiene and public health is observed if the principle of integrated medicine is systematically obeyed. The study is meant to continue for about 3 years.

## R[illegible]iation Hygiene and Radiobiology

### (1) Dosimetry

Since February 1959 personal monitoring using film badges has been applied to the personnel handling radiation sources. Checking intervals was 4 weeks. Up to the end of the year 12 institutions and industrial enterprises with a total of 141 persons were under control.

Comparisons were made between Adox-Radius and Adox-Dosis films simultaneously exposed to X-rays of 50 and 250 kV both in film holders after Dressel and in a sort of film badges after Stakolenburg. It has been shown that the Dressel method, although much more complicated, is not more accurate. Experiments are continued with mixed radiation, where the Stakolenburg method is expected to be given [illegible]/somewhat.

The effect of the length of interval between the exposition and development of a film on the fading of the latent image was also investigated.

The systematic monitoring of radiation sources has continued. In 1959, 32 isotope sources in 16 places in industry, medicine, and other institutions were under control, as well as 271 X-ray apparatuses (20 in industry, 251 in medical institutions). Special attention was paid to radiotherapeutic units using radium. It has been proved that safety measures in those departments are not satisfactory.

## (2) Air Cleaning and Ventilation

A few absolute filters used for purifying the atmosphere from radioactive substances were tested. Preparatory work is done for designing an installation for filter efficacy testing by means of methylene blue.

Ventilation projects were designed for the Radioisotope Laboratory of the Veterinary Faculty in Belgrade and the Institute's own new Radioisotope Laboratory. The Institute took part in the ventilation design for the cyclotron wing of the Institute "Rudjer Bošković" and the extended ventilation system for the reactor and a hot laboratory at the Institute "Boris Kidrič" Vinča.

## (3) Radiobiology

a) The Effect of Ionising Radiation on Blood

Hematological analyses were carried out in a large number of persons working with radiation sources or exposed to radiation for therapeutical purposes in order to elaborate methods for the early detection of blood cell changes.

b) Oxygen Consumption in the Fragments of Radiated Amebas

This is the continuation of research work started a few years ago. Its purpose was to add a quantitative evaluation of the radiation effect to the knowledge of qualitative changes produced by radiation studied in previous years. The results have shown that the respiration of the fragments of amebas with the nucleus is normal after radiation. In parts of amebas without the nucleus respiration was inhibited by 50%. Hypotheses concerning a protective effect of the nucleus are put forward.

c) The Determination of Ribonucleic Acid

The content of ribonucleic acid in the amebas exposed to ultraviolet radiation of various intensity was determined. The experimental groups radiated at 1200, 2400, and 3600 ergs/mm$^2$, were compared with the control group. The extraction of ribonucleic acid was carried out at various intervals after radiation. The determination of ribonucleic acid was performed by the spectrophotometric method. The results have shown that the content of ribonucleic acid does not decrease immediately after radiation, but only on the third day after exposure. These preliminary results suggest that radiation acts as enucleation, i.e. it increases the effect of enucleation if enucleation has already taken place.

d) Environmental Radioactivity

Preliminary work has been done for systematic analysis of environmental radioactivity in air, water, soil and milk, which is to start

For preliminary work on toxicity of radioactive substances see the section on Toxicology of Metals.

## Experimental and Clinical Toxicology

### (1) Toxicology of Metals - Clinical

1. Effect of Lead on the Kidney

The follow-up of lead poisoned patients has shown that only functional kidney injuries are produced by lead, and that only in the cases of prolonged, intense exposure, or repeated poisoning these functional lesions may become irreversible organic lesions.

Studying the etiology of chronic nephritis in some parts of Yugoslavia the kidney functions and lead content in blood were examined on 500 inhabitants of Bodenoe, a village engaged in pottery production and using lead-glazed earthware for household purposes. It was evidenced that there was no significant difference in the occurrence of kidney injuries in this village and the control group consisting of the persons who had not been exposed to lead. This speaks against the assumption that lead is the main etiological factor in the occurrence of chronic nephropathy in some parts of Croatia, Bosnia, and Serbia.

2. Siderocyte and Sideroblast Incidence in Heavy Metal Poisoning

Preliminary results are confirmed concerning the high incidence of sideroblasts in the bone-marrow of lead poisoned patients.

3. The Effect of Chelating Agent Ca Na-Ethylene Diamine Tetraacetic Acid - Mesatil Bayer

Systematic observations have started on the effect of Mesatil on the elimination of lead from the human body. The effects of intravenous and peroral application are compared. Special attention is paid to the kidney function in the persons observed.

4. Liver Injuries in Workers Exposed to Chlorinated Hydrocarbons

After obtaining evidence on the frequency of liver lesions in workers continually exposed to carbon tetrachloride, trichlorethylene, hexachlorethane, and hexachlorcyclohexane, investigations have started on the frequency of liver lesions in workers non-exposed to hydrocarbons. Preliminary results have shown that the effects of toxic liver injuries and infective liver injuries cannot be distinguished by simple laboratory analyses. The statistical evaluation of the results obtained on 200 workers gave no satisfactory results either. A method is being elaborated for the determination of transaminase in the serum. It is meant to be of use in the detection of early cellular changes due to chlorinated hydrocarbons.

### (2) Toxicology of Metals - Experimental

1. Determination of Stable Strontium in Biological Material

Two methods are chosen: flame-photometry and spectrography. The calibration curve was made by flame-photometry in the strontium

concentration range of 50-500 µg/ml. In the same concentration range a calibration curve was prepared by the spectrographic method. Preparation of biological material for analysis is in progress.

2. Determination of Uranium in Biological Material

In continuation of work from the previous year a detailed study has been carried out on the effect of inorganic salts on the extraction of uranium by tetrahydropyrane.

3. Synthesis of Chelating Agents and Physico-Chemical Properties of Chelates

A series of derivatives of ethylene-diamine-tetraacetic acid were synthesized. The properties of DIMEDTA have been investigated in detail. The work is being continued.

4. Acute Toxicity of Uranil-Nitrate and Uranil-Acetate

The experiments are carried out on albino rats. The acute toxicity of uranil-nitrate was determined on males and females after intravenous, intraperitoneal, and peroral application, and of uranil-acetate on females after intravenous and intraperitoneal application. The work is meant to serve as a starting-point for a study of the therapeutic effect of antidotes, which is also in progress.

5. The Effect of CaEDTA on Lead Content in Blood and the Kidney after a Single Exposition

The purpose of this work was to gain experience in the determination of the distribution of metals in blood and other organs in certain intervals after exposition, as well as to study the effect of chelating agents on the distribution and elimination of metals. Lead was used as a model system, since the Institute's collaborators have considerable experience in this field. The experiment was carried out in two parts. In the first part female rats were used; one group was given an intraperitoneal injection of lead ions, and another group only CaEDTA; the third group was given CaEDTA 30 minutes after exposure to lead, and the fourth was the control group. 84 animals in all were used in the experiment. In certain intervals lead content in the kidney and blood was analysed. In the second part of the experiment a total of 126 female rats were used. They were divided into 5 groups. Each animal was given two intraperitoneal injections in the interval of 30 minutes, while the addition of $Na_2EDTA$ and newly synthesized chelating agent of DIMEDTA respectively, varied from group to group.

6. Toxicity of Chelating Substances

Work was started on the determination of LD50 for CaEDTA, $Na_2EDTA$ and DIMEDTA in order to obtain data on the toxicity of chelating substances. Female rats have been used in these experiments.

7. Kinetic Studies on the Elimination of Metals from the Organism.

Preliminary work has been done on the selection of convenient metabolic cages for the study of the metabolism of radioactive isotopes.

8. Respiration of Tissue Slices and Mitochondria

Respiration of mitochondria was studied in normal and deionized water [illegible] and without addition of EDTA as controls. The respiration of kidney slices of the rats poisoned by uranil-nitrate was analysed. Respiration coefficients in poisoned rats were reduced to 2o - 3o%. Experiments on liver mitochondria are in progress, but the method used has not as yet proved satisfactory.

9. The Effect of Uranium, Lead, Strontium, and Mercury on the Osmotic Resistance of Erythrocytes

The experiments have shown that the presence of small amounts of strontium, mercury, and uranil ions in blood does not change the osmotic resistance of erythrocytes to hypotonic solutions. On the contrary, lead ions produce a statistically significant increase of hypotonic resistance of erythrocytes.

lo. The Sensitivity of Ganglionic Cells to Acetylcholine and Potassium in the Presence of Strontium. The Effect of Strontium on the Release of Acetylcholine

Strontium, even in high concentrations, does not influence the sensitivity of ganglionic cells to acetylcholine. However, in comparatively low concentrations it decreases their sensitivity to potassium. The effect is reversible. Strontium does not influence the release of acetylcholine from preganglionic nerve endings.

ll. The Effect of Cobalt on the Ganglionic Transmission

The presence of cobalt in the perfusion solution decreases the contraction of the nictitating membrane to the preganglionic nerve stimulation. The effect is reversible. The ions of cobalt increase the sensitivity of ganglionic cells to acetylcholine and potassium up to a concentration of 5o µg/ml, whereas in higher concentrations their sensitivity is decreased.

## (5) Toxicology of Organo-Phosphorus Compounds

1. Therapeutical Effect of Pyridine-2-Aldoxime (P2AM) and Atropine in Parathion Poisoning

In continuation of work on the therapy of organophosphorus poisoning the combined effect of P2AM and atropine in horses poisoned by parathion was studied. Intravenous application of parathion in horses produced a kind of poisoning typical of cholinesterase poisons. At high parathion doses the cholinesterase of erythrocytes and the plasma was reduced to lo - 2o% of the normal values. The injection of P2AM can in a large measure reduce the symptoms of poisoning by first removing the central effect, then the muscarine effect, and finally the nicotine effect. As to the speed of its action, atropine surpasses the effect of P2AM, but the symptoms reappear one hour after application. The simultaneous application of P2AM and atropine removes the symptoms of poisoning very quickly and efficaciously. For a lasting recovery of animals poisoned by parathion, large, repeated doses of P2AM should be administered, by which atropine considerably increases the therapeutic effect of oximes.

2. Toxicology of p-Nitrophenyl Ethyl-Phosphonate

Some physico-chemical characteristics of p-nitrophenyl ethylphosphonate, which are important for biochemical and toxicological investigations, have been analysed. These characteristics should be taken into account in the study of acute and chronic toxicity. Acute intravenous toxicity, acute intraperitoneal, subcutaneous, percutaneous, and perceral toxicity of p-nitrophenyl ethylphosphonate are determined. Toxicity produced by slow intravenous infusion is determined as well. Experiments are in progress concerning the inhibition of cholinesterase in vitro, and enzymatic cholinesterase in the plasma, liver, and kidney extracts.

3. The Effect of Diacethyl Monoxim (DAM) on the Metabolism of Parathion

Continuing the study of synergistic effect of DAM and parathion, the effect of DAM on A-esterase activity was investigated. On the basis of the results obtained synergistic effect of DAM and parathion could be explained either by accelerated conversion of parathion into paraoxon or retarded enzymatic hydrolysis of paraoxon. A combination of these two mechanisms may also be the clue to this problem.

4. The Effect of pH on the Inhibition of Cholinesterase by R6Zoo and R88o2 and Reactivation of Cholinesterase Inhibited by these Compounds

In continuation of work on biochemical properties of R6Zoo and R88o2, the effect of pH on the inhibition of non-specific cholinesterase of the horse serum was analysed. Both inhibitors have a pH value at which maximum inhibition is observed. In connection with this work the effect of two nucleophilic reactivators, belonging to the group of oximes, on cholinesterase inhibited by R6Zoo and R88o2 was investigated. C-3-dioxim has proved to be a better reactivator than C-5-monoxime.

5. Synthesis of Nucleophilic Substances belonging to the Oxime Group

The following oximes are synthesised: bis (pyridinium-4-aldoxime)-trimethyl dibromide (C-3-dioxim) and 2,7-octane dioxime. While C-3-dioxime has already been described in literature, 2,7-octane dioxime and a series of 3-acethylphenotiazine derivatives have not as yet been recorded.

6. Detection and Determination of Organo-Phosphorus Compounds

Work is continued on the construction of a very sensitive apparatus for the intensity measurement of the fluorescence of oxidating indol (indoxyl) products and the luminescence of luminol. The effect of various substances on the chemiluminescence of luminol and the fluorescence of indoxyl is studied. Hydrolysis of organo-phosphorus compounds by the methods of fluorescence and chemiluminescence under different experimental conditions is investigated. The results were evaluated from the kinetic point of view. The whole study aims at determining optimum conditions for detection of organo-phosphorus compounds.

(4) Toxicology of other substances

1) Carcinogenic Properties of Soot

Carcinogenic substances contained in the soot of some Yugoslav factories were extracted. The fluorescence of these extracts was analysed, and their cancerigenic properties were studied on a number of experimental animals. Further studies are in progress.

2) Toxicity of Soparan

At the request of the chemical plant "Motan" Rutina, subacute and acute toxicity of Soparan was determined on rats. The results have shown that after purification no Soparan added to soja bean oil in the course of production is left in the oil, or if there are any signs of it, this is too little to produce any toxic effect.

(?) C[illegible] Field Work

As a measure of health protection of workers exposed to organophosphorus compounds the cholinesterase activity in the blood, both in erythrocytes and the plasma, was determined in 22 persons employed at the Institute for Plant Protection and the firm "Cijanisacija".

## Physiology

1. Restitution Rate in Electrically Provoked Muscular Work

The purpose of this experiment was to enlarge the knowledge of the nature of fatigue provoked by this kind of work. The evaluation of results is in progress.

2. The Effect of Prostigmine and Atropine on the Work Output and Restitution in Electroergography

According to literature data, prostigmine facilitates muscular contraction in the patients suffering from Myasthenia gravis. Experiments were carried out to observe the effect of prostigmine on healthy subjects. The experiments are in progress. Prostigmine seems to increase the working effect in healthy persons.

3. The Phenomenon of the Stimulus Intensity Optimum in Electroergography

In the course of work mentioned under 1) it was observed that the working effect of the subject increased with the increase of the stimulus intensity, but only to a certain level, and after reaching this level it went down. Experiments are in progress to study this phenomenon.

4. The Effect of Phenamine on the Endurance in Repetitive Dynamic Work

On the treadmill adjusted to a certain gradient and speed the subjects perform repetitive work (running) with certain pauses up to exhaustion. Their endurance and pulse changes are compared in the experiments with phenamine and without it. The experiment is [illegible] to check the "long-term" efficacy of [illegible] substances which are considerably assumed to have an unfavourable effect on the

5. The Effect of Phenamine on the Endurance of Albino Rats in Repetitive Dynamic Work

The experiment is undertaken for the same purpose as under 4. The dynamic work of rats consisted in loaded swimming. The experiment is also in its final stage.

6. The Effect of Phenomotrazine and Meprobamate on Endurance in Repetitive Static Work on the Henry Dynamometer

The experiment had the similar purpose as those under 4. and 5. It gave information about the effect of phenomotrazine and meprobamate on static endurance.

7. Metric Characteristics of Tests for the Determination of the Functional Capacity of the Cardiovascular System

According to the results obtained, the maximum oxygen consumption can be used as the individual criterion of cardiovascular capacity, while the step test may serve for group testing. The experiments were carried out on the treadmill under a comparatively high loading.

8. Restitution Rate after Static Effort of Maximum and Submaximum Intensity

In the experiment the subjects hung on their arms by maintaining their own weight. The main problem was to find out the mechanism by which restitution is obtained after an effort of submaximum intensity.

9. Subjective Fatigue Testing Scales

By comparing endurance and electromyogram with the subjective evaluation of fatigue it was aimed at throwing more light on the possibility of subjective fatigue evaluation in general. The experiments are in their first phase.

10. Hypothermia and Effect of Low Temperature

a) The Effect of Low Temperature on the K Contracture of M.Rectus and Sartorius

Experiments on M.Sartorius started in 1958 are supplemented by some quantitative data. Attempts are made to explain the prolonged contracture at low concentrations of KCl by using the auxotonic lever and determining "the active state" of slow and twitch rectus fibres. It has been demonstrated that these fibres react by a prolonged contracture if the concentration of KCl is low, and by a weaker contracture, if the concentration of KCl is over 14 mM. Successive contractures at low temperature without intermittent rewarming gradually lessen. The cooled muscle is poorly expansible. M.Sartorius at low temperature is not sensitive to pH changes.

b) Blood Clotting Changes in Hypothermia and during Reanimation

Continuing the earlier investigations, the effect of cooling rate on changes in blood clotting activity in hypothermia was studied. The results have shown that quicker cooling produces more pronounced changes in blood clotting activity.

c) Thrombocyte Preservation in the Stored Blood

It has been shown that the addition of Heparin to the donour increases the number of preserved thrombocytes in the stored blood. Experiments were performed on dogs. The evaluation of the results is in progress.

11. The Effect of the Stabilizer on the K Contracture of the Frog Rectus

The effect of procaine, antistine, pyribenzamine, quinidine and strophantin was studied, and the results of preliminary work, started in 1958, are confirmed. It has also been demonstrated that quinidine does not produce "Lundsgard's effect" but a spontaneous contracture, while strophantin at lower concentrations produces an increase in the mechanical reaction of the rectus to kalium.

12. Relaxation of Slow Fibres of the Rectus in the K Contracture in a Solution without Ca-Ions

So far only preliminary results are obtained. The reappearance of the excitability by K-ions of M.Sartorius, which has for a certain time been kept in a solution without Ca-ions, has again been proved by thiocyanate.

## History of Medicine

1. Study of the Slav medical history.

2. Systematic study of the mediaeval manuscripts of the Serbian, Russian, and Bulgarian redaction, with particular reference to their content relating to natural sciences.

3. The continuation of the transcription of a mediaeval codex from Milander. The study of this codex has offered new concepts of latin influence on the Serbian mediaeval medicine.

4. Work is continued on the collection, arrangement, and catalogue of the material for the second volume of the Croatian Medical Bibliography.

5. Medical connections between Dalmatia and the Italian Adriatic Coast have been studied.

6. A study on health conditions in Dalmatia under French rule is continued, with particular reference to the first organized forms of social care and the care for the poor and mentally ill.

7. Byzantine medical literature and its influence on Slavic and [illegible] medicine in the late Middle Ages have been investigated.

## TRAINING ACTIVITIES

The collaborators of the Department of Environmental Hygiene and Engineering and the Department of Occupational Diseases were lecturers in the postgraduate courses for industrial physicians. These courses have been organized by the School of Public Health "Andrija Štampar". Dr.M.Vandekar from the Toxicology Department was also lecturing in these courses, as well as Dr.B.Pots from the Department of Psychology and Physiology of Work, who is also lecturer at the Faculty of Philosophy. Mr.N.Teskeredžić prepared cyclostyled lectures on industrial ventilation for postgraduate courses in industrial health. The staff of the Department of Occupational Diseases carried out practical work with medical students. Professor V.B.Vouk was lecturing at the Medical Faculty, the Faculty of Natural Sciences, and the Technological Faculty. Dr.M.D.Grmek was lecturer at the Medical Faculty.

Within the framework of the Centre for Radiological Protection Mr.P.Gugić, incollaboration with Mrs.M.Fugaš, Mrs.Z.Vuić, Dr.K.Kostial, and Dr.B.Prpić, organized a six-day course in radiological protection for the personnel of the firm "Naftaplin". There was also a course in safety measures for X-ray apparatus operators organised for the personnel of the firm "Rentgenmehanika" Zagreb.

Mrs.M.Fugaš held a short course on the determination of dust concentration in the working atmosphere by thermo- and electro-precipitators to the collaborators of the Centre for Radiological Protection, Medical Faculty, Beograd.

The collaborators of the Toxicology Department organised lectures on selected chapters of physiology and biochemistry for the Institute's scientific staff.

In the course of the year about 28 research or field workers from different parts of the country spent a certain time at the Institute to obtain individual training in some specialised field of work. Two of them prepared their doctor thesis at the Institute. 47 graduates in medicine carried out part of their practical work at the Department of Occupational Diseases.

Several collaborators of the Toxicology Department attended a course in radiobiology held by Professor Errera from Bruxelles at the Institute "Rudjer Bošković".

In July, as a guest of the Institute, Dr.N.W.Aldridge from the Toxicology Research Unit, Carshalton, England, gave 3 lectures on the toxicology of organophosphorus compounds.

In 1959, 3 members of staff of the Institute, i.e. Dr.B.Kosić, Dr.Gj.Vukadinović, and Dr.M.Šarić, obtained their Doctor of Medical Science degree.

## PUBLISHING ACTIVITY

The Institute has continued to publish its quarterly review "Arhiv za higijenu rada i toksikologiju" (Archives of Industrial Hygiene and Toxicology). In exchange for this review, the Institute was receiving 39 foreign and 21 Yugoslav periodicals.

In the series of text-books and manuals, the book "Psychophysiology of Work" by Professor Z. Bujas was published by the Institute in 1959.

## SCIENTIFIC CONFERENCES, TRAVEL GRANTS AND FELLOWSHIPS

Dr. Y. Škrob attended the Meeting of Yugoslav Radiologists, Belgrade, June 30-July 2.

Dr. M. D. Grmek took active part and was also chairman at the Italian Congress of the History of Medicine held in Formo, April 22-27. He also gave a lecture on the "Social Status of Physicians in the Past" in Padua on April 30. At the invitation of the Paris University Dr. Grmek delivered a lecture on "Natural Sciences in old Slavic Manuscripts" at the Palais de la Decouverte in Paris on June 6. Dr. Grmek also attended the International Congress for the History of Pharmacy held in Dubrovnik, August 26-31, and gave a lecture on the "Significance of Dubrovnik in the History of Medicine and Pharmacy".

Dr. O. A. Weber has continued his study at the Inorganic Chemistry Laboratory, University of Oxford, as a research fellow of the Oxford University.

From May 1959 Dr. K. Schulz has been in the United States on a study at the Clarkson College of Technology, Potsdam.

In September Dr. V. Horvat started work at the Max-Planck Institute of Physiology of Work as a fellow of the European Productivity Association.

In October Dr. Gj. Vukadinović went to Glasgow to do research work at the Institute of Physiology, University of Glasgow, as a research fellow of this University.

In November Dr. T. Beritić started his 3-month study in France as a fellow of the International Atomic Energy Agency.

The International Atomic Energy Agency also gave a 6-month fellowship to Dr. B. Prpić. He started his study in France in December.

In December Mr. Z. Grgić started his 6-month work at the Max-Planck Institute for Physiology of Work. This work has been supported by the Max-Planck Institute.

Professor B. Kesić spent 3 months on a study travel in the United States as a Rockefeller Foundation fellow.

Professor V.B.Vouk spent 2 months on a travel study in France, England, Belgium, and Germany as a WHO fellow.

Dr.F.Valić has continued his work on the staff of the World Health Organization in Alexandria.

## OTHER ACTIVITIES

### Library

In the course of 1959, 56 new books (124 volumes) were received, out of which 47 (97 volumes) were purchased and 9 (27 volumes) were presented as gift or exchanged. At the end of 1959 the Library had a total of 4,608 books (6,224 volumes).

The number of foreign periodicals regularly received amounted to 184 (89 in exchange for the "Archives", 7 as gift, and 16 purchased). The Library had a total of 1,647 volumes of bound periodicals.

In 1959 the Library was given 85 photocopies. In total there are 1,055 photocopies and 102 microfilms available in the Library.

The exchange of periodicals has for years been established with various institutions in the country and abroad. The foreign countries participating in this exchange are as follows: Austria, Argentina, Belgium, Canada, Czechoslovakia, Chile, China, Denmark, England, Egypt, Finland, France, Germany, Holland, Italy, Japan, Mexico, Poland, Rumania, Spain, Switzerland, Sweden, Turkey, USA, USSR, Western Africa (French). There is a regular exchange of publications with the World Health Organisation, International Labour Office, and UNESCO.

The Library, being one of the best libraries in the field of occupational health in this country, has been used not only by members of the Institute, but also by a great number of research and field workers from all parts of Yugoslavia.

### Electronics Laboratory

In 1959, besides its regular work on the maintenance of the Institute's electrical and electronical equipment, the Laboratory was engaged in the supply of nucleonic instruments for the Institute's programme on radiological protection, and in the organisation of radioactivity testing service. It also designed an apparatus for low radioactivity testing. Mr.P.Gugić, Head of the Laboratory, participated in the installation and testing of all the electronic equipment of a new Radioisotope Laboratory of the Department of Medicine, Medical Faculty, University of Zagreb.

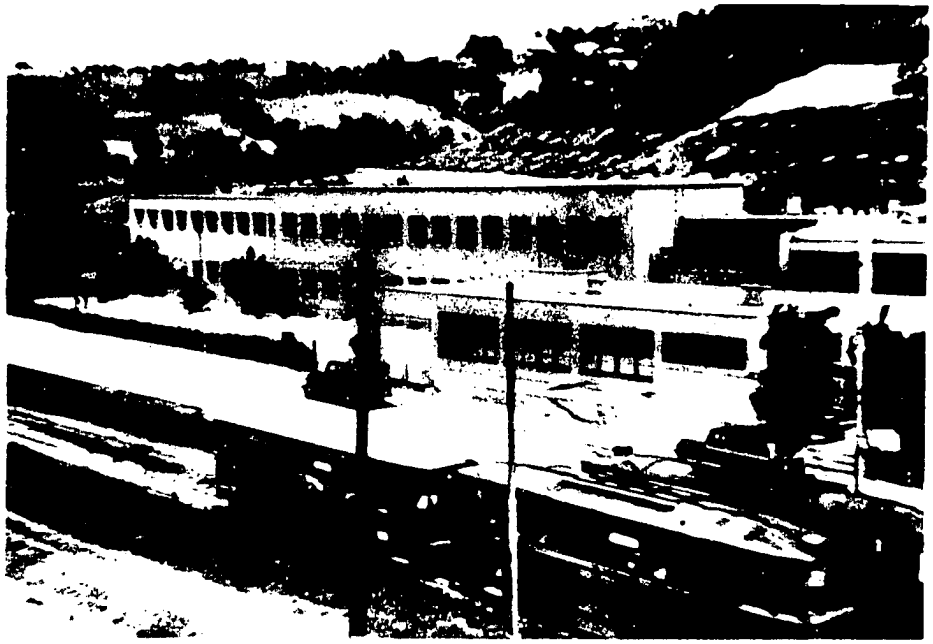
### Workshops

The Institute has a mechanical workshop, an electrical workshop, and a glassblower workshop. They all have been doing routine work on repair and the maintenance of the Institute's installations

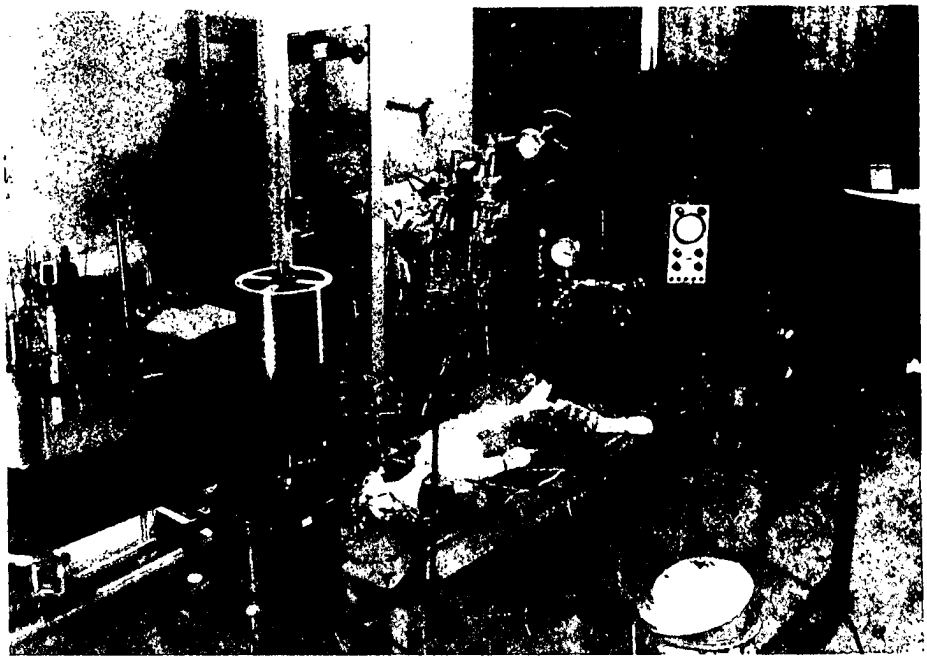
and laboratory glassware supply. Besides this work, the Electrical Workshop carried out the installation of a distiller and 3 waterheaters with continuous flow, as well as a considerable alteration of the Institute's lighting system. The Glassblower Workshop made a perfusion apparatus, 10 distilling installations, and an installation for the digestion of biological material.

## Animal House

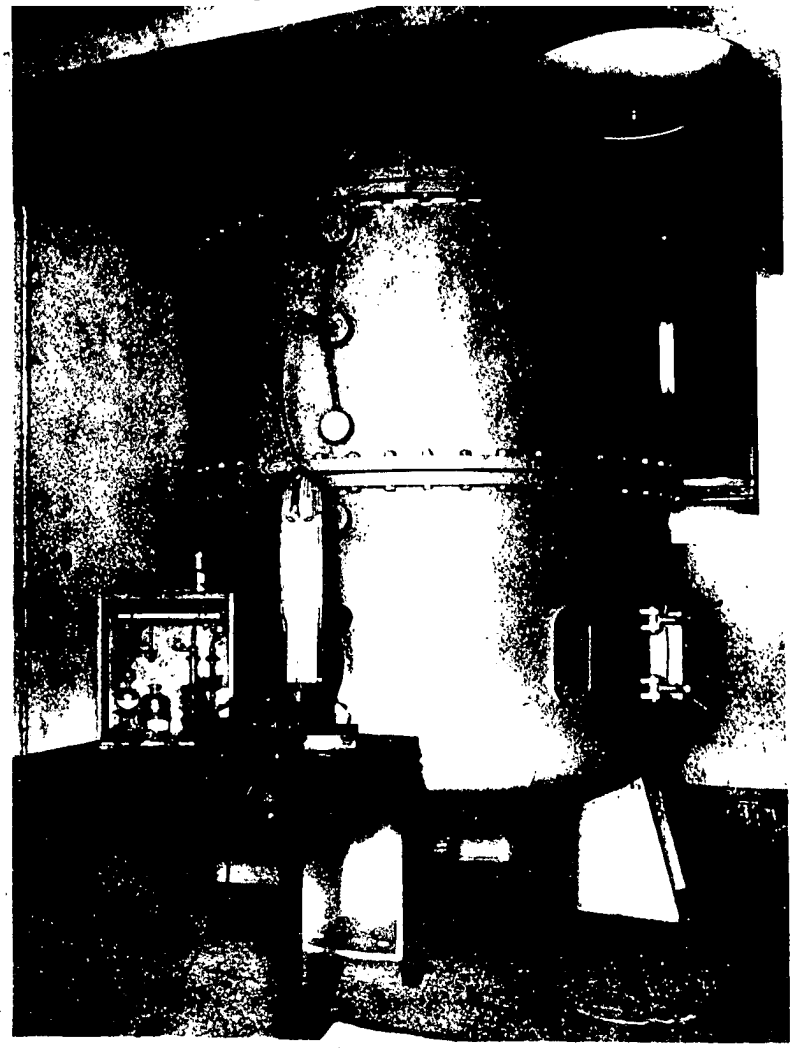
In the recently enlarged Animal House only rats (about 210 a month) were bred in 1959. Other animals were supplied from other institutions. The animals were on standard diet supplied from the firm "Veteserum". In the course of the year, 2091 rats, 60 mice, 134 cats, 186 frogs, 3 rabbits, and 7 dogs were used in experiments. A basin for frogs was put up, and 50 new cages were purchased in 1959.



Institute for Medical Research
(incorporating the Institute of Industrial Hygiene)



Physiological Laboratory



Gas Chamber

Library