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Research results of Soviet scientists in some problems of occupational medicine

Review of the years 1981–1984

by Hubert Kahn, MD¹

KAHN H. Research results of Soviet scientists in some problems of occupational medicine: Review of the years 1981–1984. *Scand J Work Environ Health* 11 (1985) 241–248. The paper reviews the extensive and manifold research of Soviet scientists in occupational medicine. Monographs published in 1981–1984 have been referred to. The data on the maximum allowable concentrations of 23 substances are presented. It should especially be emphasized that, at present, great attention is being paid in the Soviet Union to the mutagenic, gonadotoxic and embryotoxic, as well as other biological, effects of the substances under study. A short review has been presented of the research dealing with the setting of standards for substances coming in contact with the skin of the hands. Occupational hygiene aspects of problems related to the introduction of new substances and technological processes have been considered, and research on the effects of harmful factors (toxic substances, vibration, etc) on health and the early diagnosis of occupational pathology has also been reviewed.

Key terms: animal experiment, early diagnosis, entrance of chemical substances through the skin, low exposure, maximal allowable concentration, new products, occupational hygiene, occupational physiology, occupational toxicology.

The aim of the present review is to make some of the more recent research results of Soviet specialists in occupational medicine available to Western readers. In the Soviet Union the number of specialized institutes of occupational hygiene and occupational diseases amounts to 20. Moreover a considerable number of research institutes and higher educational institutions participate in the work on the all-Union problem "The Scientific Basis of Occupational Hygiene and Occupational Pathology" (chairman Professor NF Izmerov). It is therefore understandable that, due to the vast amount of work in progress, the present review cannot be exhaustive, either in depth or in breadth. Monographs, collections of research papers, proceedings of conferences and symposia, and papers from scientific journals [especially from *Gigiena Truda i Professionalnie Zabolevaniya* (Occupational Hygiene and Occupational Diseases)] have served as the main sources of information.

Before starting the review proper, I would like to draw attention to a few major areas of current research in the Soviet Union. For example, during the last few years, Soviet hygienists, occupational physiologists, and occupational pathologists have undertaken extensive research in the region of the Baikal-Amur railroad, its length exceeding 3 000 km, and in the petroleum production regions of western Siberia.

These regions are known to have severe climatic conditions, and traditional occupational hazards are accompanied by high psychoemotional stress. Work conditions in the ever-deepening mines and on deep-drilling sites have been investigated.

In addition ever-increasing attention is being paid to various aspects of occupational hygiene in agriculture, a fact which is illustrated by the manual *Occupational Hygiene in Agricultural Production* (38), published in 1981, with academicians LI Medved and YJ Kundiev as editors. Attention should be drawn to the fact that the research on the application of toxic chemical agents in agriculture has grown wider and more complex. This research is of great practical value to the setting of appropriate hygienic norms (45).

One topical problem is how to increase labor productivity by means of scientifically well-proved occupational regimens and better work conditions. The scientific-practical symposium held in 1982 in Tallinn on "The Role of Occupational Health and its Perspectives in Increasing Labour Productivity and Occupational Culture in National Economy" was a great success, and the proceedings of the symposium (editor H Kahn) (23) were in great demand, and they created a heightened interest both among physicians and among top managers of production.

Toxicologic qualities of new chemical compounds and materials are being studied intensively. The Soviet Toxicology Centre of the International Registry of Potentially Toxic Chemical Substances of the Ministry of Health of the USSR has issued the following two books in English: *Toxicometric Param-*

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eters in *Industrial Toxic Chemicals under Single Exposure* by Izmerov et al (21) and *Hygienic and Toxicological Criteria of Harmfulness in Evaluating Hazards of Chemical Compounds* by Sanotsky & Ulanova (44). In 1983 the manual *Medical Toxicology* (26) was published in Tallinn. It was to fill the gap in the Soviet literature on toxicology, for which, up to that time, no books existed dealing with toxicologic problems from the point of view of information sciences and a bibliography. The manual became quite a success throughout the Soviet Union.

As a generalization of the research of scientists of the COMECON (Council for Mutual Economic Aid) countries, in 1982, a collection of unified research methods in occupational hygiene and occupational diseases was published. It was of considerable practical value, being compiled by the Corresponding Member of the Academy of Medical Sciences of the USSR, Professor NF Izmerov.

The tenth number of the collection of research papers on occupational hygiene and occupational pathology (2) contains the results of numerous studies of the scientists of the Institute of Experimental and Clinical Medicine in Tallinn. In this volume the research results in occupational hygiene in the oil-shale industry are generalized. The edition was dedicated to the long-standing director of the Institute, Professor P Bogovski, a Corresponding Member of the Academy of Medical Sciences of the USSR, on his 60th birthday. In 1984 the Institute also had the pleasure of participating in the publication of the proceedings of the third joint symposium of the Institute of Experimental and Clinical Medicine in Tallinn and the Institute of Occupational Health in Helsinki (editors H Kahn and S Hernberg) (24).

Due to the manifoldness of occupational medicine, the materials which I have chosen to review are presented in three parts, divided somewhat conventionally as follows: (i) occupational hygiene and experimental toxicology, (ii) occupational physiology and occupational psychology, and (iii) effects of hazardous factors on the human organism (including occupational diseases) or, in other words, problems of occupational pathology.

Occupational hygiene and experimental toxicology

The task of first and foremost importance would be to study new industrial toxic substances in order to justify their maximum allowable concentrations (MAC) in the air of the work zone. A part of the results of this research is presented in table 1. This is a field in which the research seems to intensify from year to year. As a result we have set MAC values for more than 800 chemical substances. At the same time, it should be noted that it is primarily during the last few years that this research has become more complicated because the traditional toxicologic experiments must now be supplemented by studies of various other biological effects, such as the sensitization of the organism and mutagenic, teratogenic, carcinogenic, and other effects. For example, studies of some diphenyl derivatives have shown that, while trichlorodiphenyl exerts embryotoxic, mutagenic, and, especially, gonadotoxic effects, dichlorodiphenylsulphone does not, even at the MAC levels (6).

Table 1. Maximum allowable concentrations (MAC) scientifically documented for some chemical substances during the last few years.

Chemical substance	MAC (mg/m ³)	Reference
Dibutylphenyl phosphate	0.1	Bezsmertniy et al (3)
Cadmium telluride	0.5	Vorobieva & Bubnov (56)
Magnesium-manganese-ferrite, Manganese-zinc-ferrite	1	Prilipko (40)
Nickel-zinc-ferrite, Nickel-copper-ferrite	2	Prilipko (40)
Ethylene glycol	5	Filatova et al (10)
Nitrochlorine	0.5	Ryazanova & Abramov (42)
Iron pentacarbonyl	0.1	Quev & Baranov (60)
Isobutyl alcohol	10	Kushneva et al (33)
Silver	1	Smirnov (47)
Silver nitrate (AgNO ₃), Silver carbonate (Ag ₂ CO ₃), silver chloride (AgCl), silver oxide (Ag ₂ O)	0.5	Smirnov (47)
Benzoate monoethanolamine	3	Korolenko (31)
Dicyclobutylidene	10	Ivanov et al (19)
Dimethylcyclohexylamine	3	Smirnov (48)
α,α,α -Trifluor-4-chlorotoluene	20	Khalenko et al (28)
Anisole, methoxybenzene	5	Uzhdavini et al (54)
Methylal	10	Tomilina et al (52)
Sodium perborate	1	Silayev (46)
Chlorobenzene	10	Filatova et al (11)

Fomenko et al (13) experimentally studied the mutagenic and gonadotropic effects of a low concentration of vinyl chloride (4.8 mg/m³, at the MAC of 30 mg/m³). It was ascertained that at such concentrations vinyl chloride exerted no mutagenic effect on genital cells, but it did on the medullar cells. Moreover, gonadotropic effects could also be observed. The authors concluded that it is namely these factors that must be considered the critical ones when the MAC value is established for vinyl chloride.

In connection with the setting of norms for toxic substances, those compounds which can be absorbed through the skin must receive attention. For some substances tentative MAC values have been established in the Soviet Union (eg, 0.05 mg/cm² for benzene, 2.4 mg/cm² for nitrobenzene). Here the findings of Gostinsky are of importance. In his research, where the dose-effect relationship has been dealt with (14), he presents a number of regularities which determine the absorption of toxic substances into the organism through intact skin both in man and in experimental animals. He noted that the absorption of substances like aniline, trichloroethylene, ammonium chloride, ethylene chlorohydrin, and lithium chloride through the abdominal skin of mice is from 9 to 40 times greater than through human skin, and through that of rats it is from 3 to 10 times greater than through human skin. For most of the substances, the velocity of absorption was of much more importance from the point of view of the toxic effect than the amount that permeated the skin. On the basis of a number of calculations, the author concluded that the results on the experimental animals may, in principle, be extrapolated to man, and hence it will be possible to work out well founded norms for skin contact. Still, in his next paper (15), the same author called attention to the fact that under industrial conditions the real pollution of skin is practically impossible to evaluate. Removal of a chemical substance from skin by washing and its determination thereafter cannot be considered informative enough. The author comes to the conclusion that the determination of chemical substances from skin surfaces may serve as an exposure test, but that it does not make it possible to determine the amount of a chemical substance which has entered the organism through the skin.

Proceeding from practical necessities, the interest in studying the combined effects of various hazardous factors has constantly been increasing. For example it has been shown that the carboxyhemoglobin content in blood increases more rapidly when exposure to carbon monoxide is accompanied by vibration (34). According to Sterenhart (50) the combined effect of carbon monoxide, nitric oxide, formaldehyde, sulfur anhydride, benzene, and tetrachloromethane with whole-body vibration (at the frequency of 4–32 Hz) at the MAC level and the accompanying noise increases the toxicity of the afore-

mentioned substances by 2.5 to 3 times (Lim_{ac} decreased 2.8 times, Lim_{ch} decreased 3 times).² Noise and physical and mental load all affect man in one direction and augment the extent of the damage (61). Noise, accompanied by mental and physical load, affects acoustic analyzers when the intensity of noise exceeds 80 dB(A). Changes in higher nervous activity and the cardiovascular system are observed already at noise levels of 70 dB(A).

Attention should be paid to the research (5) ascertaining that the toxic effect of sulfur anhydride on sick animals develops nearly 2.5 times quicker than that on healthy ones. For a weakened animal one-fourth of the concentration of a given substance will suffice to cause an equally serious intoxication. As a result the authors concluded that for sickly workers the MAC should be applied with a certain supplementary coefficient.

New products have been a matter of permanent concern for hygienists. For example Fedyakina (9) has studied the dust of carbon fibrous materials. Due to their strength and heat-resistance, these fibers are used widely in industry. Fedyakina found that the dust of these fibrous materials is both irritating and fibrogenic. The latter characteristic was proved by an increase in the oxyproline concentration in pulmonary tissue. The MAC for this dust should, advisably, be 4 mg/m³.

Work conditions in enterprises where a new pyrometallurgical method of processing oxidized ore into ferronickel has been introduced have been thoroughly studied. In this processing, there is no need to use sulfur, but a considerable health hazard is air pollution from carbon monoxide and silica, nickel, cobalt, manganese, and chromium dust (43).

Interesting data have been presented in a paper on the effect of pesticides on explanted cells (55). The effect of a number of pesticides, such as 2,4-dinitro-6-methylphenol, sevin, betanal, carbathion, cineb, tetramethyl thiuram disulfide, trichlorofon, metaphos, and copper sulfate on cell cultures of human embryo fibroblasts have been studied morphologically, cytochemically, and electron microscopically. At the same time the effect of the same toxic substances on experimental animals has been studied. Unlike earlier researchers who are of the opinion that the toxicity of pesticides in vitro and in vivo are in direct correlation, the author concluded that no such direct correlation exists and that experiments with cell cultures do not suffice for determining the toxicity of pesticides. The author also points out that their application in a modeled experiment may render useful information on the pathogenesis of intoxication.

² Lim_{ac} (acute limit): the threshold of the acute effect, ie, the lowest concentration (dose) of a given substance which causes a change in a particular biochemical index in a whole organism and which is beyond the organism's capacity for physical adaptation; Lim_{ch} (chronic limit): the value of the chronic effect threshold.

A remarkable achievement in the field of hygiene is, without a doubt, the book *Occupational Hygiene in the Conditions of Electromagnetic Fields*, published in 1983 (32). In this book the research on magnetic fields, electrostatic fields, and other nonionizing electromagnetic irradiation has been reviewed.

Occupational physiology and psychology

In spite of the fact that numerous studies in occupational physiology have been published during the last few years, their value is still specific and their interest regional. Perhaps the results of an investigation by Bobrisheva-Pushkina (4) might deserve special emphasis however. The author has studied how successful future operators in the chemical industry will be in their speciality, depending on their personality characteristics and on the level of their psychophysiological capabilities. The author concluded that, for such work, sedate, balanced persons with a well-developed visual and operative memory, quick reactions, attentiveness, and the ability to concentrate (quickly switching from one thing to another) and think deductively will be best suited. These are the qualities that the author considers important, and they should be taken into account when persons are chosen for this occupation.

The study of the changes in the physiological functions and metabolic processes of conveyor workers is also important. Numerous physiological and biochemical studies have shown that, in spite of physically light work, rather considerable changes have taken place in many functions by the end of the shift (eg, a statistically significant increase in the levels of lactic acid, lipids, and nonesterified fatty acids in blood). As regards the cardiovascular system, an increase in diastolic pressure, a lengthening of the P-Q interval, and a decrease in the amplitudes of the QRS complex and T wave were observed at the end of the shift. All the aforementioned changes were more evident in overweight women with a weaker general physical condition. The authors came to the conclusion that the changes which they had observed were due to hypodynamia and high stress on the nervous system during work (39).

In another interesting paper (57) the preventive role of background music on students in stress situations during examinations has been studied. Electroencephalography was applied, and the main findings were at the level of the general activation of the brain and the coefficients of the fronto-occipital and bilateral imbalance. The author succeeded in arguing that background music decreases cortical activation and the aforementioned coefficients and the decreases are objective proof that in such stress situations music acts favorably on brain activities.

Ljakh (35) has studied adaptation mechanisms of the cardiovascular system at high temperatures

among copper smelters of one Kazakhstan integrated metallurgy plant. The average air temperature in the work zone was 37.8 (SD 0.34) °C in the summer. Under such conditions there was profuse perspiration accompanied by a sharp decrease in pulse pressure and the pulse wave, as well as an increase in diastolic pressure, peripheral vascular resistance, and pulse rate. The author showed that in the case of a sharp increase in venous pressure in the portal vein, the surplus blood amount is retrogradely directed from it into the vena cava superior system via the gastric and esophageal veins. Detailed study of the mechanisms of blood circulation made it possible to conclude that blood vessels of the portal system are of exceptional importance to the cardiovascular adaptation and thermoregulation of the organism under conditions of high temperature. It has also been shown that administering sodium carbonate with mineral water promotes the normalization of the parameters of the cardiovascular system.

Yakovlev (58) applied a complex of psychophysiological examinations for the early diagnosis of the effects of chromium compounds. He found that the earliest symptom is a weakening of short-term memory and attention. Disturbances in abstract-logical thinking are observed later, when the clinical picture of chromium intoxication has fully developed. An analogous regularity was shown by Ilvest & Mürsepp (18) for vibration disease. Rheoencephalographic examinations gave evidence of disturbances in the cerebral blood circulation both in the arterial and venous systems. The authors were of the opinion that the disturbances in cerebral hemocirculation are the reasons for the development of certain psychic changes.

The research by Tuulik (53) is also important. She demonstrated a number of regularities by neurophysiological and psychological methods when examining workers exposed to styrene and lead. She described, separately for styrene and lead, the comparatively specific syndromes of the functional disturbances of the nervous system, already evident at the subclinical stage. In addition, the results allowed the author to state that exposure to styrene causes damage mainly in the functions of the right cerebral hemisphere.

In general it must be noted that research on occupational psychology is still rather scarce from the medical viewpoint.

Occupational pathology

The papers dealing with either the effects of hazardous factors on the human organism or the pathogenesis and diagnosis of occupational diseases are interesting thanks either to their scientific novelty or practical value. First, during the last few years, more attention has been paid to the degree to which different factors in industry are harmful to the cardio-

vascular system and blood circulation. This is a most welcome trend as these very diseases are the greatest cause of worry in contemporary medicine.

Many papers in this field can be found in a special collection of research papers published in 1982 by the Moscow FF Erisman Research Institute of Hygiene. This collection contains research results of many different centers. In over 1 000 workers, working under noisy conditions [95—105 dB(A)], the cardiovascular and blood circulation systems have been examined. Disturbances in cardiac rhythm, tachycardia or bradycardia, hypotension or hypertension, hypercholesteremia, low index of lecithin cholesterol, and an increase in the velocity of the pulse wave were observed in these persons two or three times more frequently than in the referents (59).

The scientists of the Gorki Institute of Occupational Hygiene and Occupational Diseases (27) studied 4 000 case records and outpatient cards and came to the conclusion that an increase in arterial blood pressure can be due to vibration and that already at the initial stage of vibration disease hypertension may be observed in about 20 % of the workers exposed. Chekunova & Suvorov (7) from the Leningrad Institute of Occupational Hygiene and Occupational Diseases proved that catecholamines participate in the pathogenesis of the damage caused by heavy metals in the heart. They demonstrated that lead, cadmium, mercury, chromium, manganese, cobalt, and nickel cause a decrease in the norepinephrine contents of the cardiac muscle; these metals increase the adrenaline and norepinephrine concentrations in the blood and also their secretion in urine. Good results in eliminating such changes have been obtained with beta-adreno-blocking agents and monoaminoxidase inhibitors.

Timofejeva (51) used rheoencephalography to study cerebral hemodynamics in workers systematically exposed to mercury, lead, or carbon disulfide. In approximately two-thirds of the persons examined, dystonia of the cerebral blood vessels was observed — in some the tension was increased and in others it was decreased. These changes, as the author emphasized, are of importance for the detection of the early effects of the aforementioned substances.

Ignatyeva (17) studied the diseases of the nervous system in miners of the far north. As could be supposed, nervous diseases played a great role in the general structure of morbidity — they accounted for altogether 40.5 % of all the cases of morbidity. The most important group is osteochondrosis (56.5 %), followed by neurotic disturbances (21 %) and diseases of the cerebral blood vessels (19.9 %). The author considered it necessary to apply complex measures in the prevention of nervous diseases in this region, which is characterized by severe natural conditions.

Numerous studies on the phosphorite industry have been carried out by the scientists of Alma-Ata. Chernikovskaya (8) has studied the function of the

thyroid gland in workers occupationally exposed to yellow phosphorus. It was found that, as the length of service increased, the concentration of total and free thyroxin in the blood decreased. In persons with more than 10 years of service the levels of the thyrotropic hormone had increased also. Animal experiments proved the clearly expressed effects of yellow phosphorus, both on the thyroid and on the pituitary gland. The author concluded that monitoring the function of the thyroid gland in the workers of this branch of industry is extremely important for the early diagnosis of the hazardous effect of phosphorus.

The reasons for the adipogenic effect of methyl methacrylate and vinyl chloride have been studied in one investigation (37), with the examination of more than 100 workers as to their hormonal status. In a comparison with referents, these workers had statistically significant increases in their insulin and prolactin secretions and a decrease in the synthesis of the somatotrophic hormone. These changes, which the authors attributed to vinyl chloride, are considered to play the decisive role in obesity.

Of the biochemical research in which some particular problems have been studied in depth, the all-round research of the effects of lead and benzene on porphyrin metabolism both experimentally and clinically should be mentioned (25). It is intriguing that according to the results of this research, a rather close connection between porphyrin metabolism and nervous system functions is obvious. The essence of this connection is considered to be the participation of porphyrins in myelin synthesis and the inhibitory effect of the aforementioned toxic substances on some key enzymes of porphyrin synthesis and the resultant demyelination.

Of special importance is Kleiner's research on the informativeness of different symptoms from the point of view of the early diagnosis of dust bronchitis and the determination of the stage of the disease (30). Thirty-two clinical, functional, and laboratory parameters in a scored system (mostly 0—3) have been the basis for the examination. The patients were carefully examined in a hospital, and a card containing information on the parameters under study was compiled for every patient. Then the data were processed by a computer. The most characteristic manifestations of dust bronchitis were the characteristics of the cough, the volume of sputum, the degree of panting, the frequency of disease recurrence, the character of the pulmonary hawking, and pneumotachometric findings. Both in experimental and clinical research, as in this study, there is a trend towards an increasing application of different mathematical-statistical programs and computer data processing, which has considerably contributed to the detailed processing of huge amounts of initial data and which has increased the representativeness of the research results.

I consider those papers to be of special importance which deal with the mutagenicity of hazardous in-

dustrial agents or with the effect of these factors on reproductive functions. Fomenko et al (12) have studied the mutagenicity and the gonadotropic effects of lead on male workers and have also carried out corresponding animal experiments. The experiments with Wistar male rats [lead concentration 0.023 (SD 0.015) mg/m³] have shown that, due to lead, the number of chromosome aberrations of the medullar cells does not increase considerably, nor are more frequent dominant lethal mutations observed. Both the studies of the peripheral blood lymphocytes in the workers showed that, when the number of metaphases with aberrations was 1.25 (SD 0.38) in the reference group, the corresponding value for a group of workers exposed to the MAC level (0.01 mg/m³) was 2.31 (SD 0.51). The examination of the workers' ejaculate showed that, in comparison with the referents, there were statistically significantly more immobile and morphologically changed spermatozoa. These findings were more evident in workers exposed to higher concentrations of lead. The authors concluded that the mechanism by which lead inhibits spermatogenesis is not mediated through the hypothalamus or the endocrine system, but the action occurs directly on the gonads.

Rüütel & Kõrges (41) have examined the urine of workers in the oil-shale chemical industry by means of the Ames test (*Salmonella typhimurium* strains TA 1535 and TA 1538) indirectly. In 57.8 % of the persons examined, the urine contained mutagenic substances.

Aleksandrov & Zhurkov (1) have found that, in workers of the rubber industry, the number of aberrations in the lymphocytes of the peripheral blood was doubled in comparison with that of referents. This finding was attributed to the effect of chemical substances (thiuram, etc) used to speed up the vulcanization process.

Makarov (36) has studied the effect of methyl metacrylate (10 mg/m³) and vinyl chloride (30 mg/m³) on the sexuality of 198 male workers at concentrations exceeding the MAC level. The reference group consisted of 95 men not exposed to hazardous factors. Both the aforementioned substances were found to cause hypogonadism. The reasons for the sexual disturbances in the case of vinyl chloride were organic disturbances of the nervous system. Methyl metacrylate caused functional disturbances that could easily be treated by Sustanon-250. In the case of both of these chemicals the disturbances in sexuality could be observed one to two years before the development of chronic intoxication, a fact which shows that sexual disturbances may be of use in early diagnosis.

Of the studies carried out in experimental therapy, one which deserves mentioning deals with tetrachloromethane-intoxicated rats whose liver was irradiated by helium-neon laser (wavelength 632 nm, power output 25 mW) during 5 min for 20 d (29). The

authors found that low-intensity laser irradiation (permeating the skin) increases the functional activity of the intact hepatocytes of the liver, causes antitoxic effects, and stimulates the recovery of the damaged liver parenchyma.

In 1981 a book was published in Kiev for practitioners. It is entitled *Roentgen-Diagnosis of Occupational Diseases* (49). The authors, Sokolik et al, have given a thorough review of the roentgenological diagnosis of pneumoconiosis, dust bronchitis, occupational damage of joints and bones, and a number of other occupation-related disturbances.

In epidemiologic research, a translation from Polish of Jedrychowski's book *Methods for Epidemiological Studies on Occupational Medicine* (22) should be of great help, as well as the literature review *Epidemiological Studies in Occupational Hygiene*, compiled by Gurvich & Stonogina (16).

As a conclusion to the preceding discussion, I would like to emphasize that the rapid development of contemporary science and technology is accompanied by a broadening of the problems of occupational health both in width and in depth. Hence the information exchange between scientists of different countries in this field is extremely necessary and useful in the interest of the health and well-being of the working people throughout the world.

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