

REVIEW

ON THE OCCASION OF THE 50TH ANNIVERSARY OF THE INSTITUTE

HEALTH EFFECTS STUDIES RELATED TO OCCUPATIONAL AND ENVIRONMENTAL EXPOSURE

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This paper describes adverse health effect studies conducted at the Institute for Medical Research and Occupational Health since its foundation fifty years ago to the present day. The presentation of the studied problems is based mainly on the type of exposure – occupational or environmental – and partly on disease entities. The review is organised around the following topics: metals, organic solvents, and other organic chemicals, pneumoconioses and occupational pneumopathies, bronchial asthma and nonallergic bronchoconstrictive impairments, chronic nonspecific lung disease, studies of respiratory effects of exposure to air pollutants in schoolchildren, other problems concerned with pathology of work and workers' health protection, epidemiology of chronic noncommunicable diseases in general population groups, criteria for the assessment of disability and ability to work. The review concludes with a short description of achievements at the national and international level, and gives an anticipation of future research needs. Literature references provide a selection of publications on research activities presented herein.

Key words:
chronic noncommunicable diseases, metals, organic solvents, respiratory impairments, work ability, work disability

The earliest concern of the research work in the field of occupational diseases was intoxication with heavy metals. The reason was the substantial growth of metal industry and the increasing occupational pathology. The investigations later included many other problems arising from industrial development and agricultural modernisation. Some problems were anticipated, but, as a rule, most arose from practice.

In addition to occupational diseases, studies focused on the workers' general morbidity, absenteeism, and disability. The primary concern was to improve methods for the study of workers' morbidity, particularly the one caused by the chronic degenerative diseases, to facilitate their early diagnosis, and to determine risk factors for

their development and occurrence (1). Later the concern extended to the assessment of disability. A number of studies included inhabitants of areas contaminated with plant emissions.

As far as methodology is concerned, it included clinical studies and observation of exposed workers, epidemiological methods, and, in some cases, experimental studies. When necessary, interdisciplinary approach was included in a study design and cooperation was established with practising medical professionals and professionals from other related fields.

This paper has eight sections which follow the types of exposure – occupational or environmental – and their health effects, including specific disease entities and other problems related to pathology of work and worker's health protection.

POLLUTANTS AND DISEASE ENTITIES

Metals

Ever since the beginning of the Institute, one of great concerns has been to study noxious effects of lead, mercury, and manganese on human health. The development of methods for determination of lead and mercury, both in the atmosphere and in biological material, deserved special attention, as it was one of fundamental prerequisites for further investigation in the field. In addition, extensive studies focused on the effects of metals on blood pigments and their derivatives (2–4). All these investigations had the purpose to develop sensitive tests for an early diagnosis of occupational poisoning. Important research concerned the effects of metals on synaptic transmission, skeleton muscles, and peripheral nerves. Their aim was to explain the mechanisms of individual reactions, which were considered to be of utmost importance for therapy (5). Additional studies on animal models investigating factors which affect the toxicokinetics of lead will be presented in one of the following reviews of the Institute's work on mineral metabolism.

Some other specific and less investigated effects had also been studied, such as the effect of lead exposure and lead intoxication on the kidney (6). Later studies renewed the issue, corroborated the earlier findings, and showed that lead poisoning impaired the glomerular filtration rate in the kidney later in life (7).

The effects of lead on the central nervous system were also investigated and critically reviewed (8). At the early stage, the Institute conducted several clinical studies of frequent and severe cases of lead intoxication and chelating therapy. The source of exposure to lead was the use of lead-glazed pots produced with primitive technology (9, 10). A number of field and clinical observations included mercury miners of Idria (Slovenia), workers in a felt hat factory in Škofja Loka (Slovenia) (11, 12), and lead miners and lead smeltery workers in Mežice (Slovenia). The neurological effects of occupational exposure to manganese were the subject of a clinical investigation of intoxicated workers from a ferromanganese plant in Šibenik, Croatia and a manganese mine in Čevljanovići, Bosnia and Herzegovina (13). Some studies were related to haematological changes and exposure to manganese (14). Further studies of neurological impairment in workers from the ferromanganese plant in Šibenik included the

relationship between the degree of exposure and health effects. The studies showed that some of the subjective symptoms in the manganese alloy workers occurred more often in smokers, particularly in heavy smokers (15). Another finding was that the airborne manganese in the working environment reduced the systolic blood pressure values (16).

Later studies of biological effects of manganese investigated possible respiratory impairments and extended to environmental exposure to this metal. The obtained results confirmed the risk of pneumonia observed earlier, as well as the risk of acute bronchitis and of chronic respiratory impairment in the manganese alloy workers who smoked. The results suggested that the frequency of these diseases and subsequent impairments depended on the ability of manganese to inhibit the function of the alveolar macrophages, making thus the organism more susceptible to respiratory infections (17, 18). This effect of manganese was confirmed *in vitro* and in animal experiments (19, 20). The idea of macrophage inhibition was supported by the fact that the incidence of acute respiratory infections was higher than expected in rather low manganese exposure (only 10–50 times higher than the normal urban concentrations of 0.01–0.03 $\mu\text{g}/\text{m}^3$), as shown by a four-year epidemiological study in an area with a ferromanganese plant (21).

The interest in lead exposure was soon extended to possible health effects on people living in the vicinity of lead emissions sources. The incidence of ischaemic heart disease, hypertensive disease, cerebrovascular disease, and kidney impairment were studied in inhabitants of the Meža Valley (Slovenia) (22). The rate of spontaneous abortions was studied separately, relying additionally on the rate of twin births which is known to be inversely proportional to the rate of spontaneous abortions (23). This method was also applied in studies of reproductive effects of environmental exposure to manganese.

Some studies concerned the physiological and psychological effects of lead exposure in children with blood lead levels within permissible values. No consistent differences were found in the scores of general cognitive development, visual motor integration, and attention, although these could have been expected having in mind the differences in lead absorption (urban conditions) (24). A number of studies dealt with the effects of lead and some other metals on the male reproductive function. The results suggested that long-term moderate occupational exposure to lead can considerably reduce the semen quality. Cigarette smoking, cadmium and alcohol consumption, zinc and copper (although the blood levels of those two metals were in the range for normal values) were also found to influence the male reproductive capacity (25, 26).

Organic solvents and other organic chemicals

The first investigations focused on biological significance of exposure to carbon tetrachloride and other chlorinated hydrocarbons. Because of their toxicity and/or frequent application, special attention was given to benzene, trichloroethylene, and tetrachloroethylene. The studies later included exposure to toluene and xylene. The aim of methodological studies was to devise sensitive, accurate, and reproducible methods to determine benzene in blood, its metabolite phenol in the urine, trichloroethylene and tetrachloroethylene in blood, and their metabolites trichloroethanol and trichloroacetic acid in blood and urine. Particular attention was paid to the choice of the

most appropriate biological indicator of exposure and of the optimal timing for collection of biological material: blood, urine and exhaled air for analysis (27, 28).

Measurements of blood benzene concentrations and urine phenol concentrations in shoe factories workers before and after the work shift confirmed occupational exposure to benzene although the declarations on operating materials such as glues, lacquers, and cleaning solvents failed to mention benzene. Benzene appeared as an impurity in toluene (29). Investigations of workers exposed to trichloroethylene in dry-cleaning establishments showed that trichloroethylene concentration in blood or in the expired air immediately after exposure was an indicator of concentration at the end of work. Trichloroethanol concentrations in blood and urine reflect exposure of the day before and trichloroacetic acid in blood and urine reflects exposure of several previous days (30).

Concerning a possible health risk of occupational exposure to trichloroethylene, the impurities carbon tetrachloride and chloroform were early incriminated as responsible for its hepatotoxicity (31). Possible effects of occupational exposure to trichloroethylene on the liver cytochrome P-450 monooxygenase were studied through the metabolic activity of salivary antipyrine. The results showed that trichloroethylene as such did not induce monooxygenase, but that the responsibility for induction was likely to lie with the impurities (32). The potential genetic damage associated with occupational exposure to low benzene concentration was evaluated through structural chromosome aberrations and sister chromatid exchanges. The obtained deviation could serve as a warning against potential genotoxic risk to workers occupationally exposed even to low benzene concentrations (33).

The complexity of the central nervous system function and exposure to solvents, particularly with regard to the assessment of solvent-related systemic dysfunction, instigated the studies of visual evoked potentials provoked by means of structured chessboard, cognitive evoked potentials provoked by visual stimulation, and brain stem evoked potentials in workers with long-term exposure to low levels of toluene (34, 35). Psychological test methods in the assessment of neurotoxic effects induced by organic solvents were also evaluated (36).

The studies included colour vision loss as an indicator of solvent-related neurotoxic alterations. The results revealed a prevalence of quantitative colour vision loss, more frequent blue-yellow loss, and more frequent blue-yellow and red-green loss in subjects exposed to organic solvents than in controls (37, 38).

Granulocyte response to glucocorticoid stimulation was studied as a test used in the assessment of bone marrow functional capacity in chronic benzene poisoning. In benzene-treated rats the white cell count displayed a dose-related depression, primarily on circulating lymphocytes (39). The harmful effects of low benzene exposure (<52.2 mg/m³) and early detection of the haematotoxic effects of benzene were also studied (40).

Environmental exposure to trichloroethylene and tetrachloroethylene of the general population in Zagreb was assessed by biological monitoring. A wide range of biological indicators proved environmental contamination (air, food, and drinking water) with those solvents (41).

The studies also included impairment of blood flow through the liver in the exposure to vinyl chloride monomer, as well as mutagenic changes (42–44). Acroostheolysis was detected in workers engaged in polymerisation in the PVC production. In 1975, the first cases of the angiosarcoma of the liver caused by exposure to VCM

in a Croatian plant were discovered and described (45). A year later, followed an epidemiological study of malignant tumours of the liver and lungs in the same PVC producing area. The results did not indicate that the occurrence of malignant tumours, other than the already detected angiosarcoma, could be associated with exposure to VCM (46).

Pneumoconioses and occupational pneumopathies

Pneumoconiosis in coal workers opened investigation of the etiopathogenesis of progressive massive fibrosis (PMF). The analysis of data obtained from a number of studies performed on coal miners throughout the country suggested that the development of PMF depended on the presence and quantity of SiO_2 in the dust to which the miners were exposed. The exposure duration was also found to be very important (47). These indications encouraged a similar study in Istrian bituminous coal mines which were known for a very low free silica content in the dust. The latter study corroborated the expectations from earlier studies by failing to produce positive evidence of PMF in the Istrian miners.

Asbestosis was another issue to receive scientific attention. An early study dealt with asbestosis in an asbestos-cement plant, showing that asbestosis could also occur in factories manufacturing asbestos products (48). Until then, reports of asbestosis were limited to the extracting industry in former Yugoslavia. Early diagnosis of asbestosis with particular emphasis on functional parameters and the relationship between functional and X-ray findings were studied (49). Studies on mid-expiratory flow rate and diffusion capacity indicated a biphasic change with initially increased values during the first years of exposure followed by a decreased tendency later on (50, 51). Pathophysiological interpretation stressed the possibility to use these findings, particularly the increase in $\text{FEF}_{25-75\%}$, as an early functional sign of the development of parenchymal asbestosis.

Malignant tumours were studied in areas with an asbestos processing plant and an asbestos-cement plant. The incidence rates of respiratory and gastrointestinal tract tumours were studied retrospectively. The investigations put into focus the role of environmental exposure to asbestos in the occurrence of some of studied tumours, particularly lung cancer, pharyngeal and laryngeal cancer, and peritoneal mesothelioma. The occurrence of the pleural mesothelioma was particularly associated with occupational exposure to asbestos (52–54).

Some of the clinical studies in the field of occupational pneumopathies investigated hard metal disease in workers manufacturing hard metal in a process of powder metallurgy involving tungsten and carbon with cobalt as a binder (55). Some clinical and laboratory studies included allergic alveolitis (56). The pathogenesis of metal fume fever had also been studied. Immunoelectrophoretic investigation of the serum of subjects exposed to zinc vapours indicated that the hypothesis about the formation of foreign albumins during zinc vapour inhalation might be correct (57).

Bronchial asthma and bronchoconstrictive impairment

Bronchial asthma has been one of the most thoroughly studied problems of occupational exposure, particularly in chemical and pharmaceutical industries, in the electrolytic extraction of aluminium, and other industries, as well as in general population.

The investigations combined the epidemiological, clinical, and laboratory approach. The mechanism of bronchoconstrictive reaction to occupational sensitising agents and extracts of green coffee and tea was examined using a specific bronchoprovocative test in healthy volunteers and in exposed workers (58, 59). The specificity of the skin test was examined with extracts of inhaled occupational agents in industrial manufacture of hemp, cotton, jute, sisal, soy bean, and animal food in groups of exposed and non-exposed workers, and, experimentally in isolated guinea pig trachea. Immunologically and nonimmunologically mediated reactions of the respiratory system were determined (60, 61). Studies related to exposure to organic agents made part of investigations run by E. Žuškin of the School of Public Health »Andrija Štampar«, Faculty of Medicine, Zagreb. Sensitization to storage mites in the urban working environment has been one of the most recent subjects of scientific investigation (62).

Some studies included respiratory impairment following exposure to gaseous irritants of the upper respiratory tract. The results of the studies performed in the electrolytic extraction of aluminium indicated that acute respiratory disorders (of the asthmatic type) due to exposure to hydrogen fluoride (and particulate fluorides) as well as to SO₂, released during the technological process could be explained by the induced bronchial hyperreactivity (63). An investigation of a possible role of allergy failed to yield results confirming such mechanism (64). Once induced, bronchial hyperreactivity has a tendency to persist in spite of the cessation of exposure (65).

The impact of simultaneous exposure to gaseous irritants of the upper respiratory tract and to aerosols of solid particles of small aerodynamic diameter attracted the research interest. It was assumed that gaseous compounds adsorbed on particles and were transported into deep parts of the lung, which they normally do not reach due to high solubility in water. As adsorption is reversible, it is possible that some of the gaseous irritants are released deep in the lung causing a local irritative effect (66). This interpretation has partly been proven on model systems (67).

Nonspecific nasal reactivity was investigated in groups of healthy subjects, subjects occupationally exposed to respiratory irritants, and in those with allergic disease of the respiratory system (68, 69). Concerning the mechanism of changes, the results showed that nonspecific bronchial reactivity is mediated via a reflex starting with afferent nerve fibres from the nasal mucosa and resulting in stimulation of prejunctional beta-2 parasympathetic receptors in paratracheal or parabranchial parasympathetic ganglia or in neuromuscular junction on bronchial smooth muscle.

Based on the observations that allergic diseases have a tendency to grow, a recent study dealt with the prevalence of markers of atopy in the adult population of the Zagreb region, Croatia (70). The study consisted of an intradermal test with 13 inhalatory allergens, total serum IgE determination, and nonspecific bronchial reactivity measurements by histamine test on a sample of 583 subjects. It also included history on respiratory symptoms. A larger number of allergens better discriminated skin reactivity between symptomatic and asymptomatic women than between symptomatic and asymptomatic men. The level of IgE discriminated significantly the prevalence of persons with mean urtica diameter in the group of symptomatic women. Bronchial hyperreactivity only partially coincided with mean urtica diameter and raised IgE in symptomatic subjects, and only in men among the asymptomatic subjects.

Chronic nonspecific lung disease (CNLD)

Early studies indicated that exposure to mineral and organic dusts could play an important role in the development of chronic nonspecific lung disease. Epidemiological investigations corroborated the assumption that long-term occupational exposure to different dusts increased the risk of CNLD. The investigation included dusts with possible fibrogenic effects as well as inert dusts, for instance, dusts in the manufacture of sanitary ceramics, cement, barite mills, brown coal, and lignite mines (71–74).

The results obtained were based on both cross-sectional and follow-up epidemiological studies. A number of studies dealt with exposure to organic dusts. The highest prevalence of CNLD was found in exposure to flax and hemp dusts (75, 76).

Chronic nonspecific lung disease is usually age-related and is found mainly in senior workers. It is common to associate the rate of the disease with the length of exposure, but age and, often, long history of smoking have been found to interfere. Furthermore, some socioeconomic factors such as the standard of living, nutrition, and alcohol consumption may also play a role in the development of chronic nonspecific lung disease (77).

Recent studies dealt with problems of chronic nonspecific lung disease and ambient air pollution (78) and the relationship between the suspended particulate matter and excess mortality in general population (79).

Studies of respiratory effects of exposure to air pollutants in schoolchildren

The aim of a number of studies of schoolchildren was to understand the significance of exposure to atmospheric pollution in childhood for the development of chronic nonspecific lung disease.

In addition to the studies already mentioned in connection with environmental exposure to manganese, investigations were carried out in schoolchildren living in the vicinity of cement plants (80), in an urban area with higher concentrations of SO₂ and suspended particulates (81), and in an area with an establishment producing fertilisers (82). The exposed children showed a tendency of increase for acute respiratory infections with respect to controls, as well as less pronounced changes in forced expiratory volumes measured throughout the course of investigation (six months or longer). It is possible that bronchial damage occurs during childhood infections and steadily progresses for many years, involving more and more bronchioles, but causing no symptoms until it manifests itself with obstructive changes in the middle or older age.

The above studies of schoolchildren were also undertaken to see whether the actual exposure levels of incriminated air pollutants might have detectable adverse health effects at the moment of measurement.

Other studies concerned with pathology of work and workers' health protection

Beside topics already described above, there were other specific workers' health problems which attracted our research interest.

A number of studies was related to health control of workers occupationally exposed to ionising radiation. The activities in this particular field started very early (83, 84) and have continued until the present time. In the meantime, biomedical

effects of non-ionising radiation have also been included in the research programmes. Beside haematological and biochemical aspects in the estimation of the health condition and assessment of working capacity, studies of persons exposed to ionising radiation included somatic cell mutations (85–89). The aim of the investigation of non-ionising radiation was to contribute to the knowledge of the actual risk of such exposure, with special reference to possible chronic damages. The investigation involved epidemiological studies (90, 91) and biological experiments *in vitro* (92, 93). Health effects of exposure to microwaves and radio frequencies were studied in selected groups of subjects (radar technicians). Epidemiological studies aimed at determining ergonomic aspects of work with video display units (94). Mutagenic effects of non-ionising radiation were investigated using cytogenetic methods (chromosome aberration assay, micronucleus assay, mitotic activity) and capilaroscopic analysis of the peripheral blood flow.

A follow-up of genotoxic effects of antineoplastic drugs and ionising radiation in the working environment showed increased structural chromosome aberrations and sister chromatid exchange frequencies in nurses and medical technicians (95, 96).

Some studies focused on occupational skin diseases (97, 98). Clinical studies had a particular interest in the vibration disease (99).

Studies of socioeconomic aspects of workers' life and habits included inadequate distribution of the workers' daily meals. The investigation showed that because of the early start of the morning shift a substantial number of workers did not take breakfast before work. The evaluation of implied consequences of such behaviour on health and on fitness to work relied on the results of the experiment with the organised early morning meal in the plant (100).

An interesting study on immediate and late psychological reactions to a major external stress was carried out after the flood in Zagreb in 1964 which affected a factory with over 7,000 employees (101). The absolute and the relative number of neurotic reactions significantly increased immediately after the disaster. Absenteeism caused by neurosis and by peptic ulcer increased immediately and remained high for several months. A year later, residual changes were still present. This study is worth mentioning because it anticipated the issue of psychological stress at work which now shows an increasing trend. Psychological stress caused by running against the clock and by hectic work has become ever more prevalent since the past decade. Other work factors which may have adverse psychological effects include high responsibility for human or economic resources, monotonous work or work which requires constant concentration, and shift work. Severe psychological conditions (psychotraumas) may be seen among workers (and others) involved in serious disasters or major accidents in which human lives are endangered or lost. Some of the later studies concerned released prisoners from Serbian camps during the war that Croatia recently experienced (102–104).

Chronic noncommunicable diseases

In addition to the previously described studies of chronic nonspecific lung disease, descriptive epidemiological studies focused on chronic noncommunicable diseases in general population and selected groups of workers.

An investigation of the prevalence of chronic noncommunicable diseases was performed in 1,600 male and 1,700 female subjects aged between 38 and 57 years

as a population sample of six communities in Croatia chosen on the basis of two distinctions: urban-rural and continental-coastal. Several years later an additional population sample of 614 male and 633 female subjects aged between 22 and 45 years was examined, again with emphasis on chronic diseases. The results of these investigations performed by *Mimica and co-workers* were presented in 24 publications (105). Their analysis included the prevalence of chronic diseases by occupation.

Other studies were specifically oriented to certain disease entities such as ischaemic heart disease, arterial hypertension, and diseases of the locomotor system (106–113). Some of those studies facilitated better evaluation of the potential of occupation as a risk factor in the occurrence and development of the above diseases. The follow-up included the natural course of some of the diseases, as well as the lifestyle and habits as risk factors (114). Special attention was paid to osteoporosis. Bone status and fracture rates were evaluated in two population groups from contrasted Croatian regions. The results showed that a relatively low calcium intake in Istria (400 mg/day) was associated with lower metacarpal bone mass and a higher incidence of spontaneous fractures of the proximal end of the femur, whereas the high calcium intake in Podravina (1,000 mg/day) was associated with increased bone mass and fewer fractures (115, 116). More details on calcium metabolism and osteoporosis will be presented in one of the following reviews of the Institute's research on mineral metabolism.

Criteria for the assessment of disability and ability to work

A number of studies aimed at determining the criteria for the evaluation of working capacity and disability in alcoholics (117, 118), subjects with chronic bronchitis and lung function impairment (119), and subjects with arthrotic changes in lower extremities (120). Studies dealing with work ability were connected mainly with the evaluation of predicted (normal) functional capacities in the Croatian working population and with formulation and evaluation of reliable methods for the occupational health practice, including the validation of the prognostic value of the fitness, health, and work capacity tests used in vocational guidance medicine (121–124).

CONTRIBUTION AT THE NATIONAL AND INTERNATIONAL LEVEL

National

Beside research, the Institute was providing occupational medical services and set up a clinical ward and the related outpatient clinic. At the beginning, the clinical ward functioned within the Clinic of Internal Medicine of the Faculty of Medicine, University of Zagreb. It was later accommodated within the Institute's own premises. The clinical ward, the outpatient clinic, and specific laboratory facilities enabled the Institute to offer specialised services and expert opinion on practical issues related to occupational medicine.

In order to meet the requirements of medical professionals and general population, the Institute set up a Poison Control Centre which started to operate in 1975.

Professional work was later extended to the assessment of workers' disability based on an agreement with the Pension and Disability Insurance Organisation for Croatia.

Between 1950 and 1994, about 18,000 persons were hospitalised in the Institute's clinical ward and about 105,000 were treated in the outpatient clinic and underwent diagnostic procedures (and treatment) connected either with suspected occupational diseases and impairment or with the assessment of disability to work.

In the recent years those activities decreased or completely stopped due to the decision of the Croatian health insurance organisation not to finance these services of the Institute. The Croatian Pension and Disability Insurance Fund also discontinued the agreement with the Institute to provide expert disability assessment services.

From the very beginning, the Institute has been training physicians within programmes of specialisation in occupational health and postgraduate courses. The teaching activities resulted in a number of textbooks written by the Institute's scientists.* The production worth mentioning includes many chapters published in other books concerned with occupational health, as well as a great number of professional papers.

In 1996, the Institute prepared an overview entitled *Environmental Exposure Assessment and Health Effect Studies in the Republic of Croatia (1980–1995)* published by the Croatian Academy of Sciences and Arts.

Until quite recent legislative changes, the Institute had the authority given by the University of Zagreb to conduct examinations of candidates for M.Sc. and Ph.D. degrees in medical sciences. To date 48 masters' theses, and 40 doctoral theses related to occupational and environmental health have been prepared at the Institute.

The Institute was directly involved in the founding of the Section of Occupational Health of Croatia (now Croatian Medical Association – Croatian Society on Occupational Health) as well as in a specific form of cooperation with occupational health institutions and units in the organisation and preparation of relevant bills and proposals related to occupational health issues. The Institute was also involved in the founding of the Croatian Toxicology Society.

The Institute organised the First, the Second, and the Third Conference of Industrial Hygiene (medicine) in Zagreb in 1950, 1953, and 1958, respectively. The Conferences paved the way for the organisation of the First Yugoslav Congress on Occupational Health (Belgrade, 1963). The Institute was directly involved in the organisation of the Second Yugoslav Congress on Occupational Health in Split in 1967, and of the First Croatian Congress on Occupational Health (after Croatia became independent and sovereign) in Opatija in 1995, as well as of a number of scientific meetings dealing with specific problems in occupational and environmental health (Symposium on Lead Poisoning, Trepča-Zvečan, Kosovo, 1968; Workshops (four) on Diagnostic Criteria and Disability Assessment in Asbestos Induced Occupational Disease, Dubrovnik, Zagreb, Nova Gorica in the period 1985–1990; National meetings: Occupational Health in the Reconstruction of the Country, Zagreb, 1992, and Toxi-

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ological Services in the Defence of the Country, Zagreb, 1993; Conference on Ergonomics and Occupational Health, Zagreb, 1994).

International

The Institute carried out several projects in the field of occupational and environmental health in collaboration with and support of the National Institute of Occupational Safety and Health (NIOSH), United States Environmental Protection Agency (US EPA), and International Lead and Zinc Research Organization (ILZRO): Study of the effects of non-siliceous dusts on chronic respiratory diseases (1967–1972); Study into biological effects of manganese (1971–1975); Study of the role of exposure in cement production in the occurrence and development of chronic nonspecific lung disease (1972–1977); Study of regional prevalence and incidence of chronic bronchitis and asthma in adults (1972–1975); Lead and peripheral neuropathy (1972–1975); Health study of a lead exposed population (1974–1977); Health effects studies in people working in a coal gasification plant (1984–1988); Delayed effect of lead on kidney function and structure (1984–1988); The effect of lead on the reproductive system of males (1987–1991); and The relationship between characteristic indicators of lead absorption and psychological functions in school children (1990–1994).

The Institute's activities described in this paper included participation in the following WHO programmes worth the mention: Assessment of human exposure to pollutants (lead and cadmium) through biological monitoring (1981–1982); Human Exposure Assessment Location (HEAL) (1990–1991).

The Institute's scientists gave their worthy contribution in the preparation of a number of WHO criteria and other documents such as: Recommended Health-Based Limits in Occupational Exposure to Heavy Metals, Geneva, 1980; Guidelines on Studies in Environmental Epidemiology, Geneva, 1983; Air Quality Guidelines for Non-carcinogenic Metals, WHO Regional Office for Europe, Copenhagen, 1984; Early Detection of Occupational Diseases, Geneva, 1986; Setting Environmental Standards. Guidelines for Decision Making, Geneva, 1987.

The Institute's scientists participated in the preparation of a Health Assessment Document for Manganese, Cincinnati: US EPA, 1984.

Worth mentioning are the contributions (chapters) by the Institute's staff in international monographs and textbooks such as *Encyclopaedia of Occupational Health and Safety* Geneva: ILO, 1972, 1980, 1983, and 1993; Manganese (M. Šarić) in the *Handbook on the Toxicology of Metals*, Amsterdam, 1986; Air Pollution Epidemiology (M. Šarić and E. Žuškin) in *Environmental Respiratory Diseases* (Cordasco E, Demeter SL, Zenz C, eds.) New York, 1995.

The Institute had the honour to organise the 19th International Congress on Occupational Health in Dubrovnik in 1978.

CURRENT AND FUTURE RESEARCH

Assuming that – despite the present difficulties – the development of Croatia will also include current trends in technological progress characteristic of industrialised coun-

tries, our occupational health service will have to face specific tasks. On one hand, it will have to solve classical occupational health problems still present and more widely spread than in the industrialised countries. On the other hand it will be increasingly engaged in problems characteristic for the developed world.

Even the industrialised countries have to deal with traditional occupational diseases caused by physical, chemical, and biological factors, heavy physical work, ergonomic problems, and the prevention of occupational injuries. These problems apply to smaller high-risk groups, yet 20–30% of the workforce in industrialised countries are still exposed to noise, vibration, ionising and non-ionising radiation, and microclimatic conditions which are known to affect health. In the industrialised world, the problems of the modern work environment such as psychological stress, new models of work organisation, computerisation of tasks, and indoor air quality including office buildings are the priority issues for most workers.

The implementation of new technologies, new demands for productivity and quality, and the need to support innovation and work motivation will require new types of work organisation, new forms of employment, new arrangements for work hours, and new management systems. Due adjustment of occupational health and safety to new development is expected.

The priorities in many industrialised countries are to maintain and promote working capacity of elderly persons. This problem is becoming increasingly important for us too.

Actual and particularly predicted occupational health problems connected with anticipated new technological development require adequate organisational approaches and adjustment of our occupational health service. At the same time, the expected trends, which include persisting problems in practice, constitute the framework for the selection and formulation of research programmes and priorities.

As far as the environmental health studies are concerned, a more comprehensive approach needs to be carried out under better defined conditions with the goal to gain more information on the dose-response relationship. Particular attention should be paid to selected population groups with atopy or those with bronchial hyperreactivity besides atopy, elderly persons, and persons with chronic diseases. In investigations of possible biological effects of industrial emissions prospective follow-ups should be applied more frequently. Such studies are particularly interesting when changes in pollution sources (or levels) have occurred.

The new approach merges sophisticated and highly sensitive laboratory methods (biological markers) with the analytical epidemiological studies, including the study of environmental exposure and cancer.

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*Sažetak***ISTRAŽIVANJA ZDRAVSTVENIH UČINAKA PROFESIONALNIH I
AMBIJENTALNIH IZLOŽENOSTI**

Prikazana su istraživanja zdravstvenih učinaka različitih profesionalnih izloženosti kao i onih vezanih za okoliš u kojem ljudi borave i žive u razdoblju od osnivanja Instituta za medicinska istraživanja i medicinu rada, tj. za 50 proteklih godina. U uvodnom je dijelu istaknuto da se pregled odnosi na provedena klinička istraživanja i opažanja te epidemiološka ispitivanja. Jednim su dijelom, kad je to bilo potrebno, provedena i eksperimentalna istraživanja, odnosno u oblikovanju istraživačkog programa primjenjivao se interdisciplinarni pristup. Osim suradnje koja je ostvarivana u okviru Instituta, odnosno s istraživačima i jedinicama iz drugih njegovih dijelova, u istraživanja su se uključivali i stručnjaci koji su djelovali u praksi medicine rada i zdravstvene ekologije. Pregled se pretežno temelji na vrstama izloženosti odnosno njihovim mogućim učincima na zdravlje. Dijelom su istraživanja prikazana po entitetima bolesti ili prema definiranom problemu koji je bio predmet istraživanja. Tekst je složen pod ovim naslovima: metali, organska otapala i drugi organski kemijski spojevi, pneumokonioze i profesionalne pneumopatije, bronhijalna astma i bronhokonstriksijska oštećenja nealergijske prirode, kronična nespecifična bolest pluća, istraživanja zdravstvenih učinaka onečišćenja zraka u školske djece, druga istraživanja specifičnih problema patologije rada i zdravstvene zaštite radnika, kronične nezarazne bolesti u skupinama općeg stanovništva – epidemiološka ispitivanja te kriteriji u ocjeni nesposobnosti za rad, odnosno radne sposobnosti. Završni dio pregleda odnosi se na sažeti prikaz profesionalnih i nastavnih djelatnosti koje su ostvarivane u Institutu odnosno koje su se provodile na području njegova djelovanja povezano s prikazanim istraživačkim aktivnostima. Ukratko je prikazana i ostvarena međunarodna suradnja u koncipiranju i provedbi odgovarajućih istraživačkih programa i projekata te doprinos koji su suradnici Instituta – uključeni u ovaj dio njegovih aktivnosti – dali u pripremi različitih međunarodnih dokumenata (poglavito u okviru Svjetske zdravstvene organizacije) s područja medicine rada i zdravstvene ekologije. Na kraju su izložena pitanja koja bi mogla biti predmet istraživačkog interesa u razdoblju koje je pred nama, anticipirajući pritom razvojne potrebe i trendove u skladu s aktualnim kretanjima u razvijenom svijetu i suvremenim tehnološkim napretkom. Radovi suradnika Instituta sadržani u popisu literature, samo su selekcionirani dio objavljenih radova koji se odnose na područje djelovanja koje je predmet ovog pregleda. Izbor radova bio je uvjetovan time da se na zadovoljavajući način dokumentiraju opisana istraživanja i postignuti rezultati, s time da se nabranjem radova ne ide previše u širinu. Znači da je bilo i drugih jednako vrijednih radova koji su se mogli naći u popisu, ali su izostavljeni kako bi se izbjegla preopširnost, održala potrebna ravnoteža i dokumentirali pojedini dijelovi teksta koje pregled sadržava.

Ključne riječi:

epidemiologija, invalidnost, kronične nezarazne bolesti, metali, organska otapala, radna sposobnost, respiratorna oštećenja

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