Polish Journal of Occupational Medicine Vol. 3, No. 3, 273–284, 1990

ORIGINAL PAPERS

THE STRATEGY OF TARGETTED HEALTH SURVEILLANCE *

I. EVALUATION OF THE HEALTH EFFECTS OF EXPOSURE TO CARCINOGENS. MALFORMATIONS AND NEOPLASMS IN CHILDREN. REPRODUCTION DISORDERS

JANUSZ INDULSKI AND ZBIGNIEW KOWALSKI

The Nofer Institute of Occupational Medicine, Lodz, Poland

Key words: Health effects, Carcinogens, Malformation, Neoplasms, Reproduction Disorders

Abstract. In highly developed countries, prophylactic medical examinations to evaluate the general health condition of workers and health effects of exposure to toxins have, in the past, been administered early in their work history. Presently, there is a trend towards developing new methods of early detection of occupational and work-related diseases. Thus, individuals oversensitive to agents in their working environment could be prevented from exposure. However, the gap between the capabilities offered theoretically by new methods and their practical application in prophylactic examinations remains quite large. Part I of the presented study is focused on three essential issues of public concern specified in the given subtitles.

INTRODUCTION

Considering the whole spectrum of issues on the targetted health surveillance, its significance for occupational health, its role in the protection of workers' health as well as its present development, a number of issues arise which are not always favourable to those who create scientific standards; doctors, executives or bodies responsible for health policy at all levels of state, public and economic administration. These issues arise mainly from the observed distance between scientific progress and practice; also from the evident lack of concentrated studies, and the search for entirely genuine discoveries. Direct cooperation between research clinics and working health institutions is almost non-existent; therefore, proposals concerning the preven-

* This is a more thorough version of the leading paper presented at the 17th International Congress on Occupational Health in the Chemical Industry, MEDICHEM '89, Cracow, Poland, 26–29 September, 1989.

Address reprint requests to J. Indulski, The Nofer Institute of Occupational Medicine, P.O.Box 199, 90-950 Lodz, Poland.

tive application of the research results contain too many "grey areas". Consequently, conclusions drawn from research are far from being procedures ready for implementation. All this delays the practical application of research output to health surveillance care.

There is also an ethical issue in targetted health surveillance connected to health economics, so much in fashion nowadays. We do not wish, by any means, to underplay the significance of cost-benefit analysis in the field of prevention or formulation of priorities, but there are certain limits within which the profitability of preventive measures could be considered. This refers specially to concrete cases, wherein obvious changes in workers' health due to harmful work conditions can be observed.

The general philosophy of health surveillance among workers in various branches of the national economy, exposed to hazards at work-places, is well known. But two points should be stressed here:

1. evaluation of the health effects of exposure; and
2. evaluation of the general health condition of workers during their employment.

The main aim of these studies is to define the working abilities needed for a given working post and to enumerate preventive measures to be taken in view of the observed changes in a worker's health condition which may influence his working ability by its limitation or loss, shorten life-span, or handicap family and inter-personal relations. It is also necessary to detect symptoms whose consequences may produce reproductive disorders and negative changes in health condition of future generations. This, however, requires elaboration of appropriate methods, and some attempts in this regard have already been made. Periodical check ups according to needs and facilities supplemented by epidemiological surveys may appear useful in verifying previously taken preventive measures: legislative (MAC), technical, technological and methodological. It should also be remembered that the results of periodical examinations should be used for identifying trends in the health condition of workers, selecting persons hypersensitive to factors existing in their working environment and setting up treatment needs.

Primary preventive examinations have quite a long tradition. At first they were aimed at protecting persons with given health disorders from employment at work places whose exposure could intensify those disorders and consequently cause a loss of working ability. They also served as a basis for eliminating employment candidates whose physical fitness was inadequate for a given job (i.e. dynamic and static load), especially in the case of sustained work. In time and with the growing progress of social policy, the goals and scope of these examinations have expanded. It was postulated that their results could become a starting point for evaluation of the impact of working conditions on the state of health, at least with regard to expected health damage resulting from the effect of given factors present in a working environment and connected with the work process. Then it was demanded that primary preventive examinations permit the optimal selection of workers for individual work posts, taking into account not only their health condition but

also their psycho-physical features, including resistance to stressogenic factors. Finally, in accordance with the philosophy of "wellbeing at the work-place", the primary and periodical examinations should secure such selection for individual work posts, or modification of the post in order to permit further favourable psycho-physical development of a worker.

During recent years a number of methods have been developed and modified which allow the identification of persons with an increased, genetically-conditioned susceptibility to certain factors present in their working environments, mainly chemicals. While these methods should still be verified, the possibility exists to include them in preventive procedures. Since all stipulations about the goals and scope of health surveillance refer to every kind of employment in the national economy, they include workers in the chemical industry.

Attention should also be given to the fact that people often change their jobs and sometimes even their acquired profession. This especially refers to migrating workers, emigrants and persons with little concern for stability. They may already have existing health problems when applying for a job, which are not always detected during the primary examination. Thus, a complete evaluation of the so called "starting health condition" as a basis for qualification for a given working post may be a difficult task for the doctor conducting the health investigation. It can be assumed that a considerable part of the 15 recommendations included in J. S. Felton's publication of 1989, Occupational and Environmental Medicine Report (7), will apply to many encountered cases; in principle, however, the recommendations refer to emigrants. It seems that we may disregard the discussion taking place for some time in the USA on an expanded programme testing for drug and alcohol consumption in workers applying for jobs in aviation, transportation, industrial pipelines, and driving heavy vehicles (6). Bearing in mind the liability for damages and accidents caused by employees, the postulates of mandatory examination of blood and urine samples during pre-employment screening for this kind of job, seem to be fully justified. It is quite obvious that regardless of the kind of health surveillance undertaken, its strategy depends, to a great extent, on analysis of work conditions, identification of biological factors, the intensity of hazards occurring in the working and life environment and their potential, observed or anticipated adverse effect on health. Results of such an analysis should serve as a basis for decisions regarding the frequency of periodical health check ups, selection of detection methods, monitoring of exposures and their biological effects, selection of clinical examinations, and justification of appropriate epidemiologcal surveys.

It should be admitted that because of various obvious reasons, the development of preventive philosophy, whose progressive humanisation and advances in research provide answers about prevention, outpaces the feasibility of practical application of newly created ideas, rules and the methodology of preventive measures, at least with respect to the working population as a whole and the complete panorama of working conditions in all branches of the national economy. That the gap is considerable it is proven by the fact that

despite the attained progress, there are social and economical losses caused by unfavourable working conditions. This is reflected by accidents at work, occupational diseases of well known etiology, and work-related diseases. These losses are great and they continue to evoke general concern.

The most common occupational diseases, accidents at work and work--related diseases are the causes of untimely work disability and shortening of life-span. These issues have recently become the main agenda of national health care programmes in many countries. This also influences the allocation of funds for preventive measures and research. Such allocation of funds for the health protection of working people can be accepted under the principle of cost-effectiveness, but it must not be forgotten that research in the field of occupational medicine should still be continued. Available relevant preventive measures should be taken when justified by the health and hygienic situation; by technical and economical facilities; and availability of qualified personnel responsible for application of those measures.

These brief comments indicate that the detailed strategy of preventive activities and related strategy of health surveillance must be diversified in content and format even within one country; depending on targets, real needs arising from economical structure; health and hygienic condition of workers and the competence of preventive services. Despite existing and expected differences especially in regard to preventive strategy, health surveillance must become its cornerstone if basic goals are to be achieved.

The two following preliminary remarks should be mentioned here:

1. The question of targets and the kind and scope of health surveillance is not new. Literature on this subject is quite rich, including WHO publications produced by groups of specially assigned experts (10, 15, 21, 22, 25, 29);

2. For reasons of space, the scope of the problem, which encompasses proposals, results or a critical review of methods applied in targetted health surveillance and epidemiological surveys, cannot be presented in detail in an editorial.

Therefore, it seems advisable to limit the range of the problem to these questions which are current now because of their significance and concern of the whole society, and are related to occupational exposure especially in the chemical industry. An attempt may also be made to present some new ideas which have aroused interest due to the emerging possibilities of their application in prevention, and which are the subject of interesting publications in world literature.

In spite of possible doubts regarding the selection of issues suggested for presentation, one should admit that two of them deserve special attention: namely; occupationally-related neoplasms linked mainly with exposures to chemical substances as well as other factors occurring in the working environment, and penetrating into the general living environment, including radioactive substances; and exposure of workers to factors causing malformations in their children, risk pregnancies, affecting reproduction and producing adverse health effects in future generations.

There are also other issues of less social concern, which are becoming

subjects of interest in various research centres dealing with occupational health, such as:

a. genetic over-susceptibility to certain chemical substances present in the working environment;

b. evaluation of exposure and adverse health effects caused by mixtures of chemical substances;

c. health condition and working abilities of persons at a more advanced age – a problem that exists regardless of exposures, but becomes especially severe when these persons fall into risk groups; and

d. effect of electromagnetic fields and their evaluation.

The latter four issues are related, to a certain extent, to occupationally-related neoplasms.

It may also be helpful to state an opinion on psychological methods currently recommended in health surveillance.

While the range of issues is very broad, space is limited, therefore details on methods and their interpretation will be omitted.

It should be admitted that the problem of neoplasms, including those of occupational origin and those resulting from environmental factors, (which effect reproduction and impede development in children) are the subject of great concern among international organizations involved in health care and bodies responsible for social policy in various countries and research centres. Their concern is justified by the range of those problems, as well as social worries and socio-economical consequences.

It is also observed that, despite of the progress of science, technology and civilisation, gaps in knowledge do exist, and prevent application of preventive methods which could detect such changes as might identify individual over-susceptibility to carcinogenic factors, long before the onset of cancer. Obviously, this is associated with economical constraints which limit the application of preventive measures of the highest standard.

As to occupationally-related neoplasms, discussion continues regarding their share in the total number of diagnosed cancer cases. Whether they account for 2 or 20 per cent of the total number, some opinions hold, nevertheless, that such neoplasms react much more effectively to preventive procedures in contrast to, for example, endogenic neoplasms.

A review of the literature permits one to draw the conclusion that at present a number of methods are at our disposal for evaluating the range of exposure to chemical carcinogens and/or exposure-related biological effects.

The following methods belong to the most promising ones and in certain cases they are already being applied practically:

1. measurement of the number of carcinogens or their metabolites in body fluids, including also thioether in urine;

2. determination of mutagenic activity in excrement;

3. cytogenetic methods facilitating detection of chromosome aberrations, sister chromatids or micronucleoli;

4. determination of carcinogenic adductors with proteins and nucleininc acid; and

5. determination of proliferation indicators or cellular transformation, i.e. neoplasm markers.

It can be generally stated that beside methods listed in item 1 (except determination of thioethers), the remaining four belong to the group of nonspecific methods in regard to exposure factors or, as in the case of neoplasm markers, the specificity is limited. That does not mean, of course, that they are useless in drawing general conclusions as to the potential risk of cancer, especially when the opportunity exists to compare results obtained in an exposed group of workers and in a properly matched control group. As it is well known, such a procedure is neither simple nor cheap and it is beset by many doubts. Many of these methods are still waiting for supplementary elaboration and validation of technical procedures. Almost six years ago, during the symposium on monitoring of exposures to carcinogenic and mutagenic factors organised by IPRCS, IARC, CEC and the Institute of Occupational Health in Helsinki (2), an attempt was made to evaluate 11 methods in view of two main aspects:

a. their application as exposure indicators; and

b. their application as indicators of the biological response of an organism.

Factors influencing the usefulness of individual methods both in biological monitoring and in epidemiological research were also considered. Comments on the five methods or a group of methods, considered to be promising ones, are presented in Table 1, these seem to speak for themselves.

Perhaps doubt could be cast on the method mentioned in item 1, namely whether it is appropriate for exposure evaluation and whether it could appear as an extraordinary precaution, since it could be considered that, in regard to carcinogens absorbed by an organism in various ways, this method proves to be better than measurement of their concentration in the working environment. An answer to this question (of whether determination of carcinogens or their metabolites in excrement is more appropriate for the evaluation of health effect) is not simple, and there exist no data on relationships between the range and time of exposure and its effect; vinyl chloride is one of very few exceptions. It can be assumed that fragmentary data on exposure effects of a certain order of magnitude, even at different periods of exposure for a given group, could undergo some kind of interpretation: however, many questions remain open.

Observations and knowledge gained in the Nofer Institute of Occupational Medicine, and the Regional Sanitary and Epidemiological Station, Lodz, Poland, deserve mention here. This knowledge was gained from looking at a dye factory during the period of 1923–1981, during which time its workers underwent occupational exposure to benzidine. The time of observation refers only to the period during the years 1945–1985, but exworkers, who are still alive, continue to be observed.

The observations revealed that during the period of highest exposure to benzidine (until 1960), its concentration in urine during summertime reached values of 200 μg/l. When, in 1961, a rigid hygienic regime was introduced together with changes in technology, hermetization of production devices, and

TABLE 1. Assessment of methods proposed as indices of exposure to carcinogens and/or as indices of biological response

Name of the method	Comments on usefulness	Comments on validation criteria
1	2	3
1. Determination of carcinogens' quantity or their metabolites in organic fluids	sufficient technical advancement; in the case of low exposure more sophisticated methods are required; usually specific for individual compounds except determination of thioethers in urine;	adequate for: – assessment of exposition? – assessment of health effect?
2. Determination of mutagenic activities in excrement	non-specific for exposure factor; possible changes in mutagenic activity depending on preparation of samples; possibility of false positive results depending on techniques and quantity of aminoacids in the sample	repeatability and comparability of results
3. Cytogenetic methods facilitating detection of chromosomal aberration, sister chromatids and micronuclei	non-specific for exposure factor; labor-consuming and expensive; usually applied in research; can be used for detection of suspected exposures	– specifity, repeatability – detection limits – in the case of sister chromatids determination of individual internal variability required between non-exposed groups of population (race, sex, age, etc.)
4. Determination of carcinogenic adducts with protein and nucleic acids	can be sensitive and specific for determination of exposure; determination of mixtures with nucleic acids more useful in the risk assessment;	– lack of initial levels; – necessity of identification of causal factors and a quantitative evaluation of risk evoked by them
5. Determination of proliferation or cellular transformation i.e. neoplasm markers	application in treatment and neoplasm diagnostics in general, low specifity and sensitivity (except tumour of endocrine gland)	– at the present stage of development cannot be used in biological monitoring and requires further investigations

ventilation, concentrations dropped down to 6–9 μg/l (1, 2). Until 1975, cancer of the urinary bladder was diagnosed in 94 cases, equal to 9% of the total working population of this section employed in the previous 20 years (11).

From 1975 to 1984 further 32 cases of urinary bladder cancer were detected and the major part of these cases included workers who had been employed in the factory before the year 1961. The mean latency period was 20 years from the beginning of exposure.

Due to various reasons, including simultaneous exposure to other carcinogenic factors such as 2-naphtoloamine, it was not possible to identify a relationship between the level and period of exposure and its effect. Detection of urinary bladder cancer in persons working in the factory after 1961 proves undoubtedly that the decrease of exposure by 20 times was not sufficient to obtain a level of safety and the decision to close production in 1981 was correct. A pity that it was taken so late!

From 1956 to 1981 continuous biological monitoring was carried out consisting of a search for benzidine in urine, together with periodical endoscopy of the urinary bladder and removal of papillomas – a preliminary form of neoplasm. The given example indicates that making a proper conclusion is not dependent upon the availability of a complete set of data and prior validation of the screening method.

In the literature on this subject, it is difficult to accept the notion that decisive progress has been made in the advancement of promising methods, nor in those intentionally ignored, such as: detection of changes in sperm; determination of protein sub-species and mutation points in lymphocytes; detection of improvement processes in somatic cells; and determination of attachment of cytochrome P-450 to a given cytochrome family (27). This was all noticeable in findings presented during the latest International Congress on Occupational Medicine in Sydney, which specially referred to a case where an attempt was made to determine neoplasm markers in persons exposed to carcinogenic factors (17), and also in other publications (3, 16, 20).

A high percentage of infertility, (comprising in industrialised countries 10–15 per cent of all couples of reproductive age), frequent pregnancy disorders, and a high rate of congenital defects, raise the question as to what extent noxious factors in the working environment may contribute to these phenomena.

The available data do not permit to estimate the frequency of reproductive disorders of occupational origin, as they do in the case of carcinogenic factors, but one may presume that it is not very high.

A few chemical compounds have been thus far responsible, according to the existing data, for reproductive disorders caused by occupational exposure. But in many cases, there were several discrepancies in results of epidemiological surveys.

An international or national list of reproductive toxicants including their effect, mechanism and singularity could be of great use; as far as we know only some attempts have been made to prepare such a list.

Neoplasm in children is also attributable to the consequences of occupational exposure, now emerging in new generations.

An increasing number of neoplasm cases in children shows that there is a need to evaluate the correlation between factors present in working conditions and the incidence of cancer diseases in off-spring up to 15 years of age.

Among the wide spectrum of questions on fertility and occupational exposure, including reproductive disorders and sexual behaviour through congenitive malformations, only those causing great social concern should be discussed.

In contrast to previous decades, special attention in recent years has been turned to spermato- and spermogenetic disorders induced by chemical factors. In the latter case the examination of sperm should be included in health surveillance if the analysis of working conditions indicates factors which may produce certain abnormalities.

The collected data prove that occupational exposure to non-organic lead (12, 14), alkyl mercurium (9), 1,2-dibromo-3-chloropropan (24), some carbamates (28), chloropran, antimonit (18), anestetic gases (19) and synthetic estrogens and progesterones (4, 13) affect the reproductive function in males by decreasing the number of sperm cells and mobile sperm cells; increasing the percentage of sperm cells of abnormal structure; and increasing excretion of estragens, feminine symptoms and/or increase of spontaneous abortions in females whose sexual partners are exposed.

Damage to spermatogenesis and the quality of sperm cells depends on the level of exposure and it seems to be reversible after cessation of exposure. The available data is insufficient to allow evaluation of the real impact of occupational exposure to the majority of investigated chemicals and physical factors on male fertility and genetics of sperm cells. The disclosure of other kinds of reproductive functions evoked by occupational factors seems to be impossible within routine health surveillance, since it requires epidemiological methods which simultaneously facilitate elimination of the influence of non-occupational factors.

Analyses of past epidemiological surveys indicate frequent mistakes; there is a need for enhanced methodology and standardization of certain epidemiological methods employed in the assessment of relationships between environmental factors and reproductive disorders.

Congenital malformations are, at present, the dominant cause of juvenile death in developed countries (5). The etiology of congenital malformations is known in 60–70 per cent of cases and the etiological role is attributed to environmental factors (26).

Studies performed on animals show that many chemical factors, present in the working environment, should be included in the group of known and suspected teratogenes. However, it should be admitted that data on this subject are extremely limited.

According to Hemminki et al. (8) certain epidemiological proofs exist that the increase of risk of congenital malformations may be related to the occupational and environmental exposure of pregnant women to: methyl mercurium, polychlorinated biphenyls, 2,4,5-T (pesticide containing TCDD), vinyl chloride, anestetic gases, work in copper-works, and in laboratories. These data, however, require further confirmation to be generally approved.

Quite recently, data as well as methods of evaluation of impact of occupational factors on reproductive functions have been assessed by a group of experts assigned by the World Health Organization (1987). The recommended methods, evaluation and risk management of reproductive disorders, together with a description of the role of preliminary and periodical examinations, were presented in a document published by WHO (23).

It should be stressed that preventive measures of legislative and organizational nature are available only for about 60 chemical substances which have been identified in experiments on animals as factors causing neoplasm in children as a consequence of parents' exposure (especially transplacental exposure, i.e. pregnant women).

The introduction of, and strict compliance with regulations forbidding exposure to carcinogenic substances should be of the highest priority.

Bearing in mind the significance of exposure of pregnant women and those of reproductive age to the development of neoplasm in children, consideration should be given to employing methods facilitating the evaluation of working environment in view of its genotoxic and potentially carcinogenic factors, as a means of establishing employment contraindications.

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Received for publication: 30th October, 1990.
Accepted for publication: 20th, November, 1990.