A MEDICAL STRATEGY FOR HEALTH AND WORK ENVIRONMENT PROBLEMS IN THE FERRO-ALLOY INDUSTRY

By R. Rylander, M.D.*
(presented by Professor Rylander)

SYNOPSIS

The basic principles for evaluating health risks of environmental agents are reviewed.

Appropriate measurements of the agent involved and evaluations of the toxicological and epidemiological implications of the exposure are required. The physiological and pathological mechanisms behind the development of airway disease and cancer are discussed and data from two epidemiological studies in a ferro-chromium industry are reported.

In one study the general mortality and tumor mortality was studied in a cohort of 1823 workers. No deviations in mortality patterns as compared to the general population could be detected.

A following study in the population around two ferro-chromium industries revealed an increase in lung cancer death rates over time but no relation between lung cancer and exposure to the environmental pollution from the industry. Recommendations as to further work to protect the health of workers in the ferro-alloy industry conclude the presentation.

Introduction

The title of this presentation is vast and the subject has been dealt with on a number of previous occasions, both by researchers outside the industry and by the industries' own specialist groups. The possible exposures and medical effects cover a wide range of potential problems, some of which are not unique to the industry but rather represent conditions of a general strain on the individual in an industrial environment. Major hazards encountered in the ferro-alloy industry are ergonomic problems, heat stress, hearing damage, skin disease and respiratory disorders such as chronic bronchitis and cancer. Particular problems are encountered in the various subgroups of the industry, neurological disorders in the ferro-manganese sector and silicosis in the ferro-silicium installations.

In this presentation I will concentrate on a few selected items of par-

* University of Gothenburg, Sweden

ticular importance for the planning of health services in the industry in the effort to establish a working environment which does not imply a risk of health for the employee. Although the examples are taken from the ferro-chromium industry, the general principles apply also to other subsections of the ferro-alloy industry.

I will initially discuss the principles for evaluating the effects of environmental agents on man, followed by specific comments on airway disease and cancer. A more detailed account will be given of two studies recently undertaken in Sweden on the health impact of the ferro-chromium industry. Some general conclusions and recommendations will terminate the presentation.

Setting the scene

One could easily get the impression from today's debate that the relation between the environment - particularly its chemical constituents - and health is a newly discovered problem. However, this concept has been discussed for several millenia. Hippocrates based his theories upon the influence of the environment on man upon knowledge inherited from Egyptian physicians, and the discipline of environmental medicine was allotted a special Goddess in Greek mythology - Hygiea.

Renewed interest in environmental exposures, particularly those of an industrial origin, was documented in Roman times and during the Middle Ages, when industrialization began to spread through Europe. Heated debates, punishments and stringent demands from various activity groups characterized the environmental activities also in those days.

To provide a rationale on how a particular industry, in this case the ferro-alloy industry, can influence human health, a few basic principles can be used :

The agent in the particular environment must be determined, chemically defined and measured. An assessment of conditions over the working day or longer time periods, such as several years, is required to appropriately assess the exposure level for the employees. The difference between peak and average values should be analyzed.

The effect on the exposed subject should be determined. Estimations of the risk involved when man is exposed to a particular substance, can be made using several different principles. A pharmacological assessment of the risk, for instance of cancer induction, can be made with the knowledge of the chemical structure of the substance and how it is metabolized in the body. Information on the effects taking place can be obtained from experimental studies, chiefly on animals but also sometimes on other organisms, such as microbes or cell cultures. The presence of a disease or changes presumably leading to the development of disease can be studied in epidemiological investigations on exposed populations.

In this connection, a distinction should be made between the biological property of the material and the effect actually occurring in the exposed person. Even if a substance has carcinogenic properties, it is not necessarily true that a risk for cancer will be present among those exposed. Factors such as exposure level, host defences and simultaneous exposure to other agents, e.g. cigarette smoke, will influence the final outcome of the exposure.

Information on effects at various dose-levels can be combined to form dose-response relationships. This constitutes the basis for the formulation of

standards or exposure limits. When standards are set, the biological consequences should be explained with reference to the specific effect criterion. A certain level of SO_2 may protect the employees from bronchial constriction, but may not necessarily protect against acute irritation in the upper airways. Likewise, the reduction of noise levels in an industry may reduce or eliminate the risk for occupational deafness but the speech interference or the fatigue producing effect may remain.

The final phase of the basic concepts is the control. Exposure levels should be monitored and all incidences with values in excess of the standard should be investigated. Measurement programs should include area or site measurements, as well as personal dose estimations.

Against the above background, two different effects - airway disease and cancer - will be reviewed chiefly with reference to the mechanisms whereby they are induced.

Experimental airway disease

During a heavy work load, about 1.2 m3 of air is inhaled per hour by an average sized worker. Pollutants present in that air may penetrate down into the airways, depending upon the water solubility and particle size characteristics. Figure 1 demonstrates the importance of the particle size for penetration into and deposition in the lung. It can be seen that deposition in the upper respiratory airways is predominant for particles with a size larger than about 3 µm. A significant deposition in the lower respiratory tree only occurs for small particles. The total dose retained never exceeds 50 %, except for particles of an extremely small size, approaching that of individual molecules. Particles which deposit in the upper respiratory tract are normally carried upwards by the ciliary activity creating a continuously upward moving stream of mucus. The contact time with a specific part of tissue will therefore usually be short.

It has been demonstrated in recent years that a considerable amount of fluid transfer takes place through the upper respiratory epithelium and that particles may also penetrate into this tissue, particularly when the mucus flow does not function properly. Conditions which influence the efficiency of the mucus clearance are tobacco smoking, infections and an inadequate level of vitamin A - all factors which lead to morphological changes of the respiratory epithelium.

Particles depositing in the deeper parts of the lung are usually taken up by the scavenger cells - alveolar macrophages. These cells have as one major role to render inhaled particles of all kinds, including microbes, innocuous to the body. This can be achieved by engulfment, dissolution, secretion of enzymes or by the initiation of an immune response. For normally occurring air pollutants, this mechanism is highly efficient. Toxic particles may trigger the defense mechanism of the macrophages, however, in a direction which will in itself give rise to disease. An example of this is the induction of enzyme secretion caused by inhaled silica particles.

Using the knowledge on basic physiological functions of the lung, experimental investigations can be undertaken to evaluate the health hazards of various airborne substances. By depositing the particles at various levels in the lung and by following the changes induced, preferably at the cellular level, information on the mechanisms whereby different substances in inhaled air may induce disease, can be obtained.

To assess the risk for silicosis, several experimental models have been

developed. Animals may be given an intratracheal injection of a standardized dose of dust and the development of silicosis followed on sections of the lung. In models applied in our own laboratories, animals are exposed to the dust by inhalation for periods of several weeks, resulting in pulmonary dose levels more closely related to those present in industry. Instead of studying established silicosis, early indicators of the disease such as induced alterations of macrophage enzyme secretion are used.

Experimental carcinogenesis

An insight into the risk for the development of cancer requires knowledge of biochemical processes on the cellular level. In order to induce cancer, substances must be able to affect the cell systems in a way that interferes with its normal metabolism and division. According to modern concepts, the initiation of carcinogenesis is through the induction of mutations. Compounds may be able to initiate cancerous changes directly or after metabolic alterations in the cell, conceivably through the formation of such reactive intermediary metabolites as epoxides. The induction of tumors is probably a two or multiple phase process, where a previous exposure to non-carcinogenic substances - initiators - will lay the ground for the subsequent exposure to the active substance - the promotor. Several initiators may work systemically, i.e., they induce several cell systems in the body to become sensitive to a later local application of the carcinogen. Moreover, the risk is not directly associated with dose levels.

Exposure to a carcinogen causes the development of cancer at a specific site or of a specific type - benzene causes cancer in the lymphoid tissue, asbestos causes mesotheliomas. In a particular industry or in the general environment, the effect seen is thus not a general increase in all kinds of cancers, but an increase at specific sites determined by exposure routes, uptake and metabolism.

When assessing the risk for cancer in animal experiments, the absence of a dose-response relationship has practical consequences. The traditional toxicological concept to increase the dose to obtain an effect which is normally rare in a studied animal population can thus not be used in a larger number of animals. Metabolic differences between different species and between animals and man further add to the difficulty in interpreting data from animal studies, particularly when unknown risks are to be evaluated.

The induction of mutagens can be studied using bacterial cell culture systems - the Ames' test. This test system implies the mixing of the substance to be tested with metabolic enzymes to simulate activation in the body and bacteria with particular requirements for growth. The substance, the enzymes and the bacteria are incubated, and if the bacteria afterwards show changes in their growth requirements, a mutation has been induced. This type of test represents a great improvement in the evaluation of known and unknown carcinogens. The test also has limitations, however, and at present no completely satisfactory experimental model to evaluate the risk for cancer can be said to exist.

Epidemiological approach

The two sections experimental lung disease and carcinogenesis have demonstrated some of the difficulties associated with the interpretation of such studies. Epidemiological studies must also be undertaken to complete the evaluation of environmental hazards. I will now illustrate the epidemi-

ological approach with the aid of two studies done by our department in Gothenburg.

In the first study, an investigation was carried out of the cause of death and the tumor incidence among workers in a ferro-chromium industry in Sweden. The main exposure agents in the plant environment were metallic and trivalent chromium (Cr^{3+}); hexavalent chromium (Cr^{6+}) was also present at certain working operations.

The subjects in the study were defined as all males employed for at least one year during the period January 1, 1930 to December 31, 1975. The plant had retained all employment cards on individual workers since 1913. The workers were traced in parish registers and elsewhere - all except one of those defined in the original cohort were finally located.

The different working sites within the industry were classified into four groups with regard to exposure to Cr^{3+} and Cr^{6+}. Approximate calculations of the exposure levels were made based upon recent measurements and discussions were held with retired workers and foremen employed in the 1930s. Estimated exposures to Cr^{3+} were highest for workers at arc furnaces, including maintenance personnel, and for those working with metal grinding and sample preparation. The highest exposure to Cr^{6+} was found in arc furnace operations. Asbestos containing materials such as textiles, plates and tubes had been used at some working sites in the plant. The data on causes of death for the cohort during 1951-1975 were obtained from the Swedish National Central Bureau of Statistics. Data from the employees were compared with causes of death in the male population in the county in which the industry was situated, using age stratified cohorts in five year age intervals.

For the study of the cancer incidence, a manual search was made at the Cancer Register at the National Board of Health and Welfare. All employed who were alive on January 1, 1958 were checked against the register for the period 1958-1975.

Among the 1,876 persons who were alive on January 1951, the number of deaths to the end of 1975 was 380. Table 1 reports the causes of death with relation to the working site. It is seen that the total death rate was equal to the expected value. The number of deaths from tumors in this material was slightly lower than the expected value. The number of tumors in the respiratory organs was less than the expected value, independent of the duration of employment. Even among the highly exposed workers at arc furnaces, the observed number of deaths was not higher than expected, neither totally nor for any length of employment.

With relation to cancer incidence, no significant differences were found between the observed and expected number of cases in the cohort. A significantly higher incidence of respiratory tumors was found among maintenance workers but no relation between exposure to the ferro-alloy products and the individual cases could be found.

The study could thus not demonstrate an increased mortality or cancer incidence among workers at the ferro-chromium plant. It was concluded that the risk for the development of respiratory tumors after inhalation of trivalent chromium compounds was considerably less than the risk for developing such tumors after exposure to chromates.

In a similar study in Norway, Langård and co-workers (1980) studied a cohort

of workers in a ferro-chromium plant comprising 976 persons. Contrary to the findings in the Swedish study, 7 cases of lung tumor were found in this population against the expected rate of 3.1. The authors suggested that these tumors were caused by exposure to Cr^{6+} at the plant.

A retrospective observation in the Swedish study concerning clinical observations of the workers, revealed that perforations of the nasal septa had been observed in three persons specifically engaged in chromate handling. None were observed among workers in the ferro-alloy processing.

These studies demonstrate the need for a continuous monitoring of work related exposure and the keeping of records on workers for long time periods. The Swedish study was initiated against the background of suspicions concerning a cancer producing activity of Cr^{3+}, which precipitated a request for tight dust standards by central authorities. Had the employee registers not been present, it would not have been possible to demonstrate that the risk due to Cr^{3+} exposure was apparently low. A need for control of the present high dust levels still exists but must be based upon other criteria than respiratory tumors. The dusts emitted from ferro-chromium industries contain chromium and manganese. Estimations of the pollution levels in the environment of 2 Swedish industries were made between 1976 and 1979 in an air pollution control program. The average monthly values of chromium dust in the air were determined at five measuring stations and were found to vary between 100 and 400 $\mu g/m^3$ at the most polluted site. This level is 50 - 100 times higher than the concentration in a rural area without industrial emissions.

Although the previous study could not demonstrate that exposure to trivalent chromium in the industry increased the lung cancer risk among employees, a different exposure situation could be present with relation to the environment. A synergistic effect of other air pollutants cannot be excluded and the difference in population characteristics, particularly with reference to age distribution and health status, could be other factors which would result in an increased risk for malignant tumors, particularly lung cancer.

In order to evaluate this risk, a register study was undertaken in the county where the ferro-chromium industries are located. The mortality from lung cancer was analysed for the years 1961-1975, using data from the National Central Bureau of Statistics. The data were collected for three time periods and the age specific mortality was calculated for five year classes and for both sexes. The mortality rate was age adjusted and related to a standard population of the whole county.

The mortality rates in different parts of the county were calculated. The material was further divided into three groups according to the population size of the parishes in 1961 - three parishes had 20.000 or more inhabitants, 7 had 5.000 - 19.999 and 205 parishes had less than 5.000 inhabitants. The two communities with ferro-chromium industries are Trollhättan and Vänersborg. The mortality rates in these two communities were compared to the remaining parishes in the county of the same population size.

The results demonstrated that the mortality rate for lung cancer in the county was significantly lower than the rate for Sweden as a whole. The rate for one of the communities with a ferro-chromium industry - Trollhättan - was slightly higher than for the county but still lower than the rate for Sweden. The mortality in the other community - Vänersborg - was low.

Over the time period studied, the mortality rate in the county increased

from 136 per million during 1961 to 1964 to 243 during 1970 - 1975. This increase in the county is statistically significant but still significantly less than the increase for Sweden as a whole during the same time period (243 - 400). For females there was a slight increase in the mortality rate in the county over the time period but this increase was again lower than that for the whole Sweden. Interesting findings were made with relation to the population size of the parishes. Figure 2 shows the age adjusted lung cancer mortality rates in the parishes according to population size. The lung cancer mortality was related to the population size, both for males and - although less pronounced - for females. This finding shows that a correct evaluation of the lung cancer mortality in the two communities with ferro-chromium industry must be made through a comparison with other parishes with the same population size. Table 2 shows the lung cancer mortality rates in the two communities compared to other parishes with the same size in the county. For one of the communities - Trollhättan - the mortality rate was very close to the other parishes whereas for the other - Vänersborg - the mortality rate was slightly lower although the difference was not statistically significant.

The increase in the mortality rate from respiratory tumors among males during the time period studied has earlier been reported for Sweden as a whole and for other countries. This increase over time is generally interpreted as being due to increased tobacco smoking but air pollution and industrial exposure could also play a role.

The relationship between the population size of the parishes and the lung cancer death rate which was demonstrated in this study has previously been found in investigations in the United States. Again a possible cause for this relationship is differences in tobacco smoking habits although, as is the case with the increase over time, general air pollution and industrial exposure could also play a role.

Finally the study clearly demonstrated that no increase in the lung cancer mortality could be demonstrated in the two communities with ferro-chromium industries.

Health strategy

For the future work on the control of the environment in the ferro-alloy industry, I think it will be useful to formulate certain guidelines which emerge from the experience reviewed in this presentation.

1. Exposure conditions. Measurements should routinely be undertaken to estimate the exposure level present at various working sites. It is important that such measurements are biologically relevant. The total dust dose overestimates the exposure which should instead be evaluated using the respirable fraction. Among the workers, the individual dose varies greatly, depending upon working tasks, etc. which causes deviations in the personal dose from the area exposure level.

2. Health controls on workers should have a specific aim and be directed towards early detection of the suspected disease. So-called general health check-ups which are in great demand, are almost useless with relation to preventing disease. Instead, specific programs where early indicators of effects and physical measurements are combined should be performed.

3. Records should be kept of the workers, with a description of exposure conditions and health record data which have prevailed during his / her

stay in the industry. As previously mentioned, the possibility to deduct the presence of health risks from animal experiments is limited. Epidemiological studies will always have to be performed, and adequate exposure records will greatly increase the precision of such studies. Records should be kept permanently in order to allow comparisons between different time periods, as illustrated in our own study on workers in the ferro-chromium industry.

4. To maintain a meaningful development of the preventive measures program, special health and safety groups should be formed. It is essential that within these groups, the collaboration is established with research centers or other specialists in the field. This can be made in forms of small symposia or workshops from which the written proceedings will be distributed to the different members in the industry.

5. Cooperation. A successful prevention program requires cooperation between workers, medical specialists and management. Management has to realize that medical problems may be present in their workforce. Management and unions must jointly realize that there are ways to avoid excessive exposures at the workplace.

   With regard to the ferro-alloy industry, an important step forward in terms of meeting the above guidelines has been made by the formation of the occupational health study group (OHSG).

REFERENCES

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TABLE 1

Death and working site

	arc furnace		grinder sampler		maintenance		office storage	
	O	E	O	E	O	E	O	E
Total	139	145,3	138	127,3	56	67,3	47	42,4
Tumors	23	28,1	19	25,8	18	13,6	9	9,2
Circ. disease	75	65,9	65	59,9	22	30,8	20	17,8
Resp. disease	5	8,4	9	7,1	1	3,7	1	2,0
Urogenital disease	3	4,6	5	3,9	1	2,1	2	1,1

O = observed
E = expected

TABLE 2

Lung cancer death rate with ferro-alloy industry (deaths per million)

Population		Trollhättan	Vänersborg	Other
5.000	M	141	96	144
	F	34	76	69
5.000 - 19.999	M	-	227	247
	F	-	80	95
20.000	M	288	-	278
	F	82	-	93

FIGURE 1 - DEPOSITION OF PARTICLES IN RESPIRATORY TRACT ACCORDING TO PARTICLE SIZE

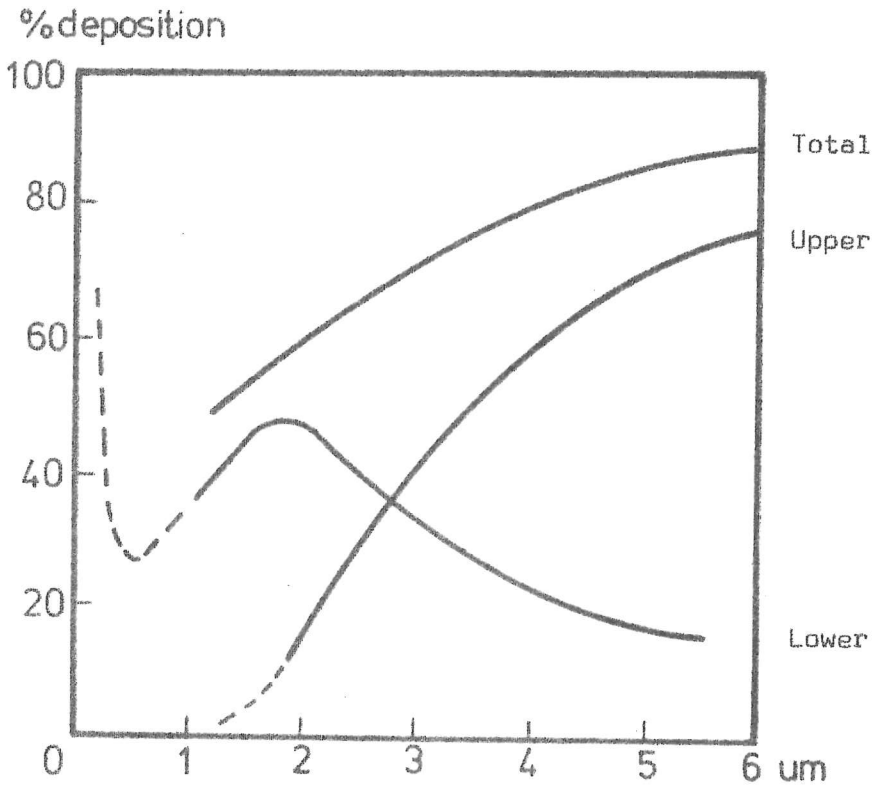
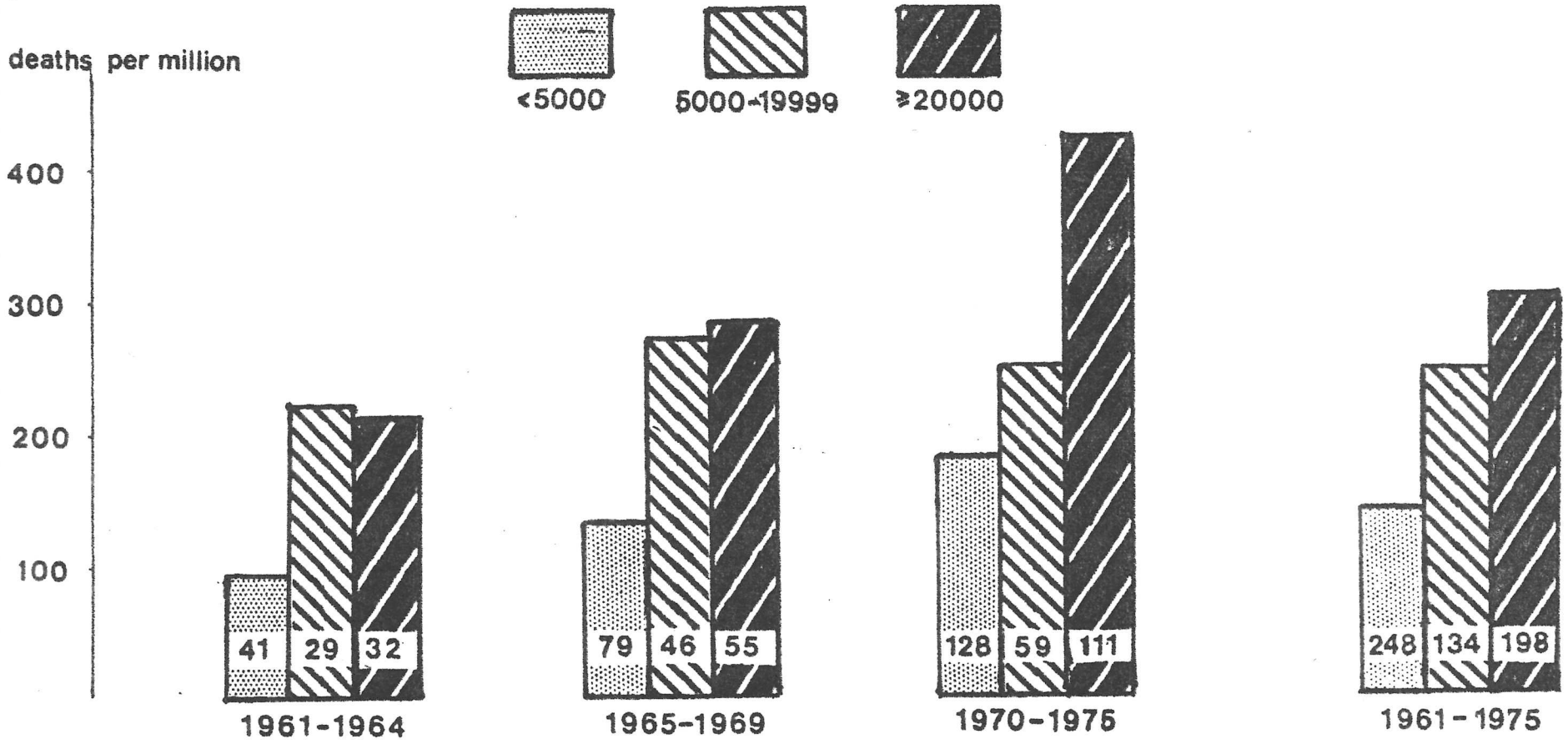


FIGURE 2 - LUNG CANCER DEATH RATE IN PARISHES
ACCORDING TO POPULATION SIZE



DISCUSSION

Mr. E. Madero B.*

I think your paper is an excellent research work and I would like to know if you have made any determination of the maximum concentration of manganese dust microgrammes per cubic meter of air that a worker can safely be subject to?

Dr. R. Rylander:

We have done animal studies on manganese dioxide. The importance of that work was to demonstrate that the respiratory trouble that arises sometimes, particularly among workers in mines, is not a silicotic disease and it is not an infectious disease, but what we call a chemical pneumonia due to the manganese dioxide exposure. We have not been involved in any dose-response or criteria work on manganese dioxide, so for the question on safe levels I have to refer you to the criteria either from OHSA or from the World Health Organization.

Mr. E. Madero

I would like to take the opportunity to make available to you through the Manganese Center the research work that we have done in that respect since 1956: we have determined that the maximum concentration of dust to which a worker can safely be exposed should not be higher than 6 microgrammes per cubic meter of air during the 5-day weekly exposure.

Dr. A. Schmidt**

I want to refer to Prof. Mancuso's data which show Cr_{3+} has carcinogenic effects. Why are your results contradictory?

Dr. R. Rylander:

We can look upon this from the toxicological point of view and an epidemiological point of view. There is no firm toxicological evidence that Cr_{3+} as such should be carcinogenic. It does not react like carcinogenes in any of the test system used. I am not excluding the possibilities that it is transformed in the body to Cr_{6+} but again, as I know, there is very little information and some contradictory information on the subject. Now the epidemiological side: this goes back to work by Professor Mancuso in the US who, several years ago, suggested that Cr_{3+} was carcinogenic. He was working with data from a work place where Cr_{6+} was the major exposure agent but Cr_{3+} was also present. By grouping people in various work places together, keeping the Cr_{6+} constant, he suggested that the variations seen between those strata were due to Cr_{3+} exposure. No statistics were presented in this study and the trend that he described was not consistent throughout the set of data. Also, in the article itself, he is very cautious about the interpretation. I think that a lot of the trouble arises from the press releases from this article where the scientific nuances, which are appropriately expressed in the paper, are lost and suddenly Cr_{3+} is carcinogenic. Our study was done in an environment where the Cr_{3+} exposure through a long time period has been really excessive. If the data came out negative from such a study, that should carry more weight than the preliminary data reported by Prof. Mancuso.

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* Compania Minera Autlan S.A. de C.V., Mexico; ** Ferrolegeringar Trollhätteverken/Vargön Alloys, Sweden

Mr. F.V. McMillen*

I would like to ask a question if I may. Could you perhaps describe the level of co-operation that takes place either within the European Community, within Scandinavia or internationally regarding these kinds of problems?

Dr. R. Rylander:

There is co-operation on different levels. From the side that I represent, the scientific collaboration on international meetings and congresses is by far the most rewarding. One of the major events in this area is the Inhaled Dust Congress that the British Society for Occupational Medicine organizes every four years. Now, apart from this scientific collaboration, there is organizational collaboration through WHO, through OECD and through other international bodies. There is also international co-operation through interested scientists, under a very loose format.

I think that as far as your industry is concerned, you have a large potential in the Health Study Group that has been formed. To invite individual researchers in Europe and in the US to symposia or small informal workshops is the type of collaboration I would very strongly recommend. Let me also say that, particularly in the US, researchers are hesitant and this applies particularly to official government researchers, to collaborate with the industry. I think this is an erroneous point of view because we scientists are mostly doing work at the lab bench. We have to come out and have to look at the industry, to collaborate with industrial people in order to understand the processes involved, in order to understand the local problems. Without this collaboration, we will just be sitting behind our closed walls, suggesting standards and regulations which have no anchor in real life. In this respect, the situation in Sweden or in Scandinavia is better than in many countries. Before we go into an industry and make measurements we always have meetings with safety committees, labour unions and management together. I think this a formula that should be introduced also in other countries.

* Union Carbide Europe S.A., Switzerland