

It has frequently been stated in the United States that the experience of insulators exposed prior to the introduction of amphibole asbestos in their products was the same as the experience of insulators exposed after the introduction of the amphiboles. However, Dr. Nolan and I found no evidence to support that assertion. On the contrary, for the Insulator Union (The International Association of Heat and Frost Insulators and Asbestos Workers), the mortality due to asbestos diseases, i. e., the worst of the experience, occurred after the introduction of amosite in their products. That is, from about 1930 through 1934, amosite became widely used in thermal insulation products. As consumers, we are now 67 years into that exposure experience. Evaluation of the mortality and morbidity experience of insulators, clearly demonstrate a dramatic increase in mesothelioma post 1940; virtually all began exposure during and after the war years (World War II). Again, as one of the speakers indicated this morning what we see today in terms of asbestos disease is the legacy of the past, the result of past exposures.

Careful analysis of insulator cohort data over time shows a greater incidence of mesothelioma mortality following employment in shipyards and among all insulators post World War II. The incorporation of amphibole asbestos (especially amosite) into ship insulation products, higher exposures due to poorly ventilated work environments, were important factors in the appearance of excess mortality.

Dr. Graham Gibbs reviewed the data produced by the McGill group's study of chrysotile miners and millers from the Asbestos-Thetford areas of the Eastern Townships. The majority of persons in this cohort have been traced, followed, and for those who died their causes of death ascertained. No increase in excess lung cancer was detected in workers who were subjected to exposures of 900 f/ml-years or less (e.g., 20 f/ml for 45 years), except in those workers who smoked cigarettes. Pleural plaques occurred far more frequently among workers from the Thetford area as compared to those in the Asbestos area; twenty-five of 33 mesotheliomas (61%) known to have occurred following exposure to chrysotile, also occurred in the Thetford population. The importance of tremolite contamination of Thetford ores was put forward. Could tremolite account for the 0.4 percent proportional mortality due to mesothelioma?

There was a discussion concerning the relative hazards of amphibole asbestos minerals as compared to chrysotile asbestos. The worst experience of the US insulators occurred following an average exposure of 500 fiber/ml years (20 f/ml x25 years). The insulator data indicate that about 9.3 percent currently die of mesothelioma as compared to 0.4 percent workers in the chrysotile-exposed population, and a 16 percent mortality due to excess lung cancers as compared to no excess lung cancers. These figures taken in context of exposure differences indicates the biological potency among the fiber types is very different.

Dr. Silvestry presented data on Balangero. He indicated that no dust control was in place until about 1975. Dr. Magnani indicated that there were excess cancer of the larynx in the workforce; the issue of alcohol (ethanol) consumption was raised.

The general conclusion was that malignant diseases following exposure to chrysotile in the workplace was very much lower than found for workers exposed to amphibole asbestos in similar circumstances.

Environmental Mesothelioma

Dr. Browne discussed exposure to asbestos from such sources as soils, living in the vicinity of manufacturing sites and in the general ambient air of communities. He described mesothelioma occurrence around the crocidolite mines and mills of South Africa, within 10 km of the crocidolite mines and mills of Wittenoom Gorge in Australia; mesothelioma following exposure to mineral fiber in soil materials (the use of soil material for whitewash) on the Island of Corsica, in the Metsovo area of northwestern Greece, and in western Turkey. There are new descriptions of mesothelioma around the nickel mines and mills on the Island New Caledonia; there was follow-up of mesotheliomas around shipyards in Europe. The agent implicated in the appearance of all these clusters is tremolite and the commercial amphibole asbestos minerals amosite and crocidolite. When these experiences are compared with those around mines and mills of chrysotile producers, and chrysotile-using industries, they are very different, virtually no mesotheliomas have been identified around chrysotile sites.

Dr. Wagner stated that only one environmental mesothelioma has been associated with chrysotile mining and milling in South Africa; Dr. Nolan, with Drs. Shcherbakov, and Kashansky, reported no environmental mesotheliomas in Asbest City, in the Russian Federation, around the mine, mills, and numerous chrysotile production facilities. Drs. Domnin, Plotko and Shtol presented some data which suggest that pulmonary problems in children in Asbest City may be related to total dust content of the air; asbestos fiber component was a different issue; Dr. Gibbs reported no environmental mesotheliomas linked to chrysotile in the Eastern Townships of Canada. Drs. Camus and Siemiatycki reported no excess mortality due to lung cancer among women in households of chrysotile workers, from the Townships although calculated cumulative exposures were about 25 f/ml-years. Some cancer of the pleura were detected and these are currently under investigation.

The Italian experience reported on by Drs. Magnani, Silvestri and Calisti, is one which contains interesting anomalies. In Casale Monferrato, around an asbestos cement plant, about one third of the mesothelioma cases are associated with some occupational history of exposure. Of those with no apparent occupational history, seven cases were determined to be a different tumor type, 14 cases may or may not have been mesothelioma, and 11 cases could not be reviewed due to loss of histologic material. Some of the mesotheliomas were linked to a small crocidolite plant in the area, chrysotile exposure alone occurred in but a few cases. Ascertainment and incomplete occupational histories have severely limited data interpretation. As for the occupational setting, amphibole asbestos has produced the bulk of environmental mesotheliomas.

THE HEALTH EFFECTS OF CHRYSOTILE ASBESTOS: CONTRIBUTION OF SCIENCE TO RISK MANAGEMENT DECISIONS

SUMMARY OF SCIENTIFIC WORKSHOP. SEPTEMBER 14-16, 1997¹

Science and Decision Making: Should We Use Chrysotile Asbestos?

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Thank you Mr. Chairman. I have been asked by the conveners of this meeting to present a general overview of papers given at our workshop and to share with you some of the opinions expressed by the scientists concerning important issues. I believe that many of these have already been touched upon by various speakers this morning. Jean Dupéré has told that there may be a practical threshold concerning the exposure-response to chrysotile asbestos. This may be so, and such evidence appears to exist at least in some chrysotile-using industries. He stated that there are marked differences in the biological potential among the asbestos fiber types. This is definitely so especially for mesothelioma. He also intimated that science occasionally falls prey to political agendas. Somehow, I believe that no one requires the input of scientists to gauge the accuracy of such a statement. Mr. Clément Godbout suggested that there may be health problems associated with exposure to untested asbestos substitutes. He told us that substitutes convey a false sense of security to the workforce. Precautions which have been used in the past with asbestos in general, and chrysotile asbestos specifically, may no longer be observed. Of course, he could have stated that any adverse health effects will not become evident for new substitutes until a time has elapsed which may be 25 or 30 or more years from onset of exposure. Clinical latency periods for carcinogens tend to be very long. We will not know the effects of inhaling new substitutes today until the year 2025 or later. Our colleagues in the Labor Movement have stated that they would rather work with a known hazard, with proper controls and work practices, than with a substance for which health-effects data are unavailable, or controls for which are non-existent. A cautious and prudent approach.

Our workshop was called the *Health Effects of Chrysotile Asbestos: Contribution of Science to Risk Management Decisions*. The Québec government asked for the latest data concerning the health effects of chrysotile asbestos which would allow various governmental agencies, and for that matter governments themselves, to decide on whether or not to use this material in the future. We

¹ Based on remarks presented at the *International Conference on the Safe and Responsible Use of Chrysotile*.

were to provide the data and you were to make the decisions. Decisions like these are reached through consortium agreement by the labour movement, by the private sector and by various government agencies. As scientists we are no better equipped morally than any one else in making such decisions. It is your collective risk; it is your collective decision. Our charge and responsibility was to review the current data upon which all of our knowledge is founded. We were to review the biological potential of the different asbestos types, to compare the experience of workers exposed to chrysotile fiber with the experience of workers exposed to the amphibole asbestos types, and to determine the risks associated with current chrysotile use. We were to explore what had been done in the past to control these risks and what could be done in the future to reduce them further. You were to have the data for use in the decision making process. The technical issues were addressed by 31 scientists from 7 countries. Disciplines included medicine, pulmonology, pathology, engineering, statistics, chemistry, epidemiology, experimental biology, molecular biology, mineralogy, economic geology and crystallography. A list of the organizers and the participants is included at the end of this paper.

There were a number of subjects which were presented and discussed at this meeting. Here are some of the major points:

Legacy of Past Exposures. Chrysotile or Amphiboles?

With my colleague Dr. Nolan we reviewed the experience of the past. Exposure to asbestos dust in the past has produced the diseases that we see today. The epidemiological studies of cohorts of man exposed to amphibole asbestos or mixed fiber types are frequently cited in asbestos risk documents. The health experience of workers exposed to crocidolite and amosite are commonly used as indices of "asbestos risk". However, we stated that asbestos is a generic term and the use of the generic name can be misleading. Chrysotile is but one of the varietal types of asbestos. Asbestos minerals have different physical and chemical properties, and different surface properties, and therefore exhibit different biological potentials. The risk associated with one fiber type need not be the same as risks associated with another. Drs. Johnson and Mossman described the well established factors of dose, durability, and dimension, in controlling fiber activity. For example they described the lack of durability of chrysotile in a biological host as one crucial factor in reducing its biological potential. In addition to increase in removal kinetics, the loss of magnesium from the structure has been shown to blunt the fiber's action on cells.

We concluded that the mesothelioma risk model used today by regulatory agencies and governments was developed from cohorts exposed to amphibole and mixed-fiber types. The amphibole-exposed cohorts have produced many mesotheliomas; there are few mesotheliomas following exposure to chrysotile asbestos only. The mesothelioma risk model, generally attributed to Peto and colleagues (1982) is based almost entirely on the experience of the US Insulators (amosite-chrysotile-crocidolite exposed), the crocidolite-exposed workers from Wittenoom Gorge in Australia, the amosite-crocidolite exposed workers in the Barking plant in London and amosite-exposed workers in Paterson, New Jersey.

The Tremolite Issue

Professor Williams-Jones presented his mineralogical study (carried out with his graduate student, Mr. Normand) of a major chrysotile producing pit in the Eastern Townships of Quebec. He focussed on tremolite fiber as it is associated with chrysotile ore. His data showed that tremolite does not occur within the ore zone but rather among the associated (barren) rocks. The geology and geochemistry were well described and the physical-chemical conditions required for the formation of tremolite were outlined. His data show that it is both feasible to mine chrysotile and to avoid the barren zones which contain tremolite. What may have been inadvertently incorporated into processed chrysotile in the past may be eliminated from chrysotile ore in the future. The ore body must be mapped in detail and the barren zones avoided during mining and thereby eliminated from the milling process. The significance of the tremolite issue was broadly discussed in reference to the asbestos diseases, especially mesothelioma. There exist some broad relationships which reinforce the association between mesothelioma proportional mortality and tremolite content of ore.

Dr. Wicks led a discussion on methods of mineral detection and identification using such standard techniques such as x-ray diffraction. He warned that the standard data files commonly used may contain flawed data sets. Mineral characterization of chrysotile specimens must be carried out carefully.

Fibers in Human Tissues; Risk Associated With Low-Level Exposure

Drs. Nolan, Pooley, Wagner and Churg discussed the occurrence, fiber types, their quantities and dimensions, found in lung tissues of persons who die in the general population. It appears that virtually everyone who lives in industrial countries today has chrysotile asbestos fragments in their pulmonary tissues. It was noted that the presence of these fibers is not associated with the presence of asbestos-related lesions or diseases. Dr. Pooley reported that in many occupational settings the amphibole content of lungs correlates better with malignant disease than does chrysotile.

Dr. Wilson addressed on the issue of asbestos risk in the general population. We were reminded by Dr. Price that "hazard" and "risk" carry two distinctly different meanings. Materials may be hazardous. A hazardous material is one which is capable of causing disease. Risk is the probability of unwanted outcome. Dr. Wilson stressed the need to use comparative risks to place in perspective risk at low-level exposure to chrysotile. A risk of asbestos disease of 1 in 100,000 deaths takes some meaning when expressed in terms of well-known risks, e.g., those associated cigarette smoking. The latter risk in heavy smokers is approximately 30,000 tobacco associated deaths per 100,000 smokers. The asbestos-associated risk of 1 in 100,000 is the same as smoking about 1.5 packs of cigarettes over a 50-year time period (less than 1 cigarette per year). Comparative risk answers the question "What does it really mean?" We were reminded by Dr. Hoskins that Paracelsus, in the 16th century, stated that "dose makes the poison."

Dr. Hoskins spoke about possible thresholds. Although hazardous, a material which is a human carcinogen does not necessarily produce cancer. These substances display thresholds. Chrysotile may possess a practical threshold. That is, an exposed person may require a latency which exceeds the human lifetime. In some of ensuing discussions the phenomenon of chrysotile degradation was discussed. Some thought this degradation was a possible detoxification event. If so, the dose-response slope of chrysotile would lessen markedly and result in a physical threshold. This would follow relationships established for organic compounds which are metabolized.

Discussion focused on the existence of risk among occupants of buildings in which asbestos-containing materials were in place. Dr. Nolan's data on asbestos in buildings indicated that building occupants in the US are exposed to very low levels of fiber. The levels found inside buildings are often the same as found in outdoor air. The asbestos concentrations in buildings in the United States are low, and the risk small. Professor Wilson cited a paper published in the United States which calculated the total risk to students exposed to asbestos in New York City school buildings was approximately the equivalent of smoking 12 cigarettes in a 72-year life time. This risk was regarded by many as a "phantom risk". Both Drs. Wilson and Price addressed the linear dose-response model and everyone accepted it as the most "protective" model in use.

Mesothelioma Trends in the General Population

Dr. Price presented the most recent data concerning mesothelioma mortality in the United States. The mesothelioma rate for females has remained level for approximately the past 20 years (about 2.5-3.0 per million). During this same time period the rate has slightly increased in males (about 5-15 per million) apparently reflecting the presence of asbestos dust in workplaces in the past. Some evidence suggests that the male rate may have begun to level off in about 1990. The ambient air in the US contains chrysotile fibers. A discussion followed concerning the apparent increase in mesothelioma incidence among younger birth cohorts in the United Kingdom. Evidence was brought forward suggesting that perhaps the reported trend was based upon extrapolation from a few data points. Further, statistical analysis of the data project a mesothelioma peak in 2010-2020, rather than in 2035. Amphibole asbestos application was acknowledged to be more widely used in the U.K. than in the US. Amosite and crocidolite were more widely used.

Mesothelioma and Other Agents

The workshop participants discussed agents other than asbestos which have been etiologically linked with appearance of human mesothelioma. The zeolite mineral erionite is implicated as an agent in the induction of mesothelioma in Central Turkey (the Karain area on the Cappadocian Plateau); the use of the diagnostic medium Thorotrast was implicated as the agent in the production of peritoneal mesotheliomas in Germany some 30 years ago; the use of the drug isoniazid in the first trimester of pregnancy was implicated in pediatric mesothelioma some years ago.

Drs. Carbone and Mutti and Dr. Giordano presented some fascinating research findings concerning the ability of a specific virus to cause mesothelioma in laboratory animals. This finding prompted an investigation of human mesothelioma tissues. In the late 1950's through the early 1960's, polio vaccines utilizing live polio viruses were prepared in monkey tissues. Some of these tissues contained animal viruses, including a virus which was later found to be oncogenic, now called SV-40 (simian-virus 40). Their hypothesis is that this virus may play a role in the induction of some human mesotheliomas. The SV-40 virus is a DNA virus which contains a 76 base-pair sequence (which has been described as a small-t antigen) which binds to a tumor suppressor gene site (p53). Recently analysis of a number of human mesothelioma tissues revealed, upon DNA signal amplification by PCR, the presence of the small-t antigen of SV 40. This has been interpreted as the SV-40 "footprint". This area of study requires further investigation.

Asbestos, Cigarette Smoking, and Co factors

Agents which have been identified that exacerbate asbestos effects. In this regard cigarette smoke and ethyl alcohol are the two which are most important. Among a cohort of insulation workers, those who continue to smoke cigarettes as they work die of lung cancer ten time more frequently than their workmates who do not smoke cigarettes. They also die more frequently of asbestosis. For all asbestos workers in general, and for chrysotile-exposed workers specifically, those who smoke should stop; those who do not now smoke cigarettes should never start. Dr. Rao told us that his workforce in an asbestos-cement plant in Hyderabad, India, is paid a premium not to smoke in the workplace. The cessation of cigarette smoking has been shown to bring with it a dramatic lowering of disease risk.

New Products and Risk

Dr. Ross indicated the chrysotile production in the West has declined over the past decade, but that sources in, e.g., Brazil have experienced increase in production. Amosite and crocidolite production is thought to approach near zero worldwide. Dr. Ross also commented on environmental contamination by chrysotile. Natural water run off from serpentines (the host rock for many chrysotile ore deposits) carries chrysotile into the water supplies. Chrysotile fiber has been found in the ice caps of Greenland and Antarctica. Dr. Rickards reflected that only some 650-odd workers worldwide now engage in chrysotile textile manufacturing, a well-known risky trade. Rather, asbestos cement and friction products manufacturing account for over 95 percent of current chrysotile asbestos production worldwide. He also presented data which indicated that analysis of 23,000 work area samples, and 5400 personal air samples, showed that 97.3% of area samples produced values less than 1 f/ml of air.

Dr. Dunnigan commented on the possible contribution of high density composites such as chrysotile cement construction products and friction materials as a source of environmental burden. These non-friable materials have been found to be stable, and do not emit fibers at levels in excess of 0.004 f/ml; many achieve values of 0.0002 f/ml of air. Dr. Higashi stated that study of asbestos in

air following the Kobe earthquake indicated a level of about 0.008 f/ml was reached, but quickly returned to ambient concentrations over a short period of time. Dr. Rickards indicated that manufacturing of chrysotile products in AIA reporting countries is now achieved at levels of exposure which are historically associated with little or no risk. He shared his concern of point-sources of exposure in manufacturing sites, apparently related to poorly-trained workers who do not follow established work practices or procedures. These, he indicated, need to be addressed by plant owners and Unions. The shop steward needs to be involved. These point sources appear to account for 4% of all air measurements, those in excess of 2 f/ml of air.

Export Expertise as well as Technology

The members of the workshop firmly support the principle of exporting technology along with fiber. Dr. Bragg's work showed that implementation of modern control technologies has been effective in allowing industry to meet regulatory statutes. In addition to technological control of dust, the enormous expertise of the older producing countries should be used by consumer nations as well. This should include both training in handling and use of chrysotile products and the introduction of good work practices. Education of workers is of paramount importance. Dr. Bragg was quick to point to producers in some countries which continue to engage in dusty, operations. These must cease operation. The control of cigarette smoking, alcohol consumption, introduction of good work practices, and the use of modern technological advances to control dust all come under the rubric of risk management.

Acceptable Risk

The other day my colleague Dr. Jacques Dunnigan made coffee in his hotel room. On the package of the sugar substitute the following label appeared: "USE OF THIS PRODUCT MAY BE HAZARDOUS FOR YOUR HEALTH. THIS PRODUCT CONTAINS SACCHARIN, WHICH HAS NOW BEEN DETERMINED TO CAUSE CANCER IN LABORATORY ANIMALS." I don't mean to belittle or cavalierly dismiss risk with chrysotile usage, but what I would like to illustrate is that we all accept risks in our every day life. I am not asking a working population to embrace my idea, or Dr. Dunnigan's concept, of personal risk. The acceptance of risk is for the various countries, the various memberships and constituencies which are exposed to asbestos, to consider. The risk associated with use of saccharin is so minuscule that I would consider it to be a phantom risk. Perhaps some of you also support that characterization. I also believe that use chrysotile asbestos comes with an acceptable risk; If this material is used properly it will be associated with vanishingly small, undetectable risk. Should we use chrysotile asbestos? That is your decision.