FILE NAME: Quebec Asbestos Mining Association (QAMA)

DATE: 1969 Apr

DOC#: QAMA008

DOCUMENT DESCRIPTION: IOEH Report - Toward the Safe Use of Asbestos

TOWARDS THE SAFE USE OF ASBESTOS FIBRE

An analysis of the current status of the problem and suggestions for further systematic study and development of solutions.

By

The Scientific Committee of the

Institute of Occupational and Environmental Health

Montreal, Canada

APRIL 1969

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FOREWORD

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FOREWORD

The Institute of Occupational and Environment Health was brought about by the Quebec Asbestos Mining Association in 1965 so as to encompass and assess the factual health, as exactly as could be ascertained, of the asbestos worker, a worker surrounded by all the new procedures and methodology of the day, with a fibre of asbestos that has become associated, if not sometimes merged, with many other substances and this under changing modes of operation and changing conditions of circumstance time and place.

Although our mining association, we felt, had in the past done its share in the field of industrial health and hygiene it was nevertheless becoming evident that new health problems were mounting and this to a point that only the implementation of an adequate long range scientific research program could bring light to the question, a research program planned and evolved so that the needed points of comparison all over the world would be investigated, true as it is that the fibre of asbestos is reaching now into so many varieties of uses and commodities at the same time becoming more and more of strategic, if not of essential, value to humanity.

The fact is that imputations, rather suddenly and violently were now being levelled at the Asbestos Industry as a whole, in the field of mining, milling, manufacturing and processing or in some specific building trades (such as that of insulation materials sprayers.) Even the mere user of asbestos (the consumer) was being singled out as subjected to serious hazards of exposure.

Our association, a Canadian association already some thirty years old, groups together the world chrysotile asbestos mining producers (USSR excepted) our production having started a century ago and now totalling 3,800,000 tons a year (including USSR production, — a mining production located in Siberia —), the chrysotile asbestos production answering for some 95% of the overall world asbestos needs, the remaining 5% comprising other types of asbestos, belonging to the amphibole family such as crocidolite, amosite, anthophyllite etc.)

These imputations against the asbestos industry came primarily from South Africa where the aforesaid types of the amphibole family are also mined, save anthophyllite (which is mined in Finland.)

The gist of such imputations against the production and use of asbestos was that asbestos would constitute a factor in the causality of cancer, whether alone or in association with other factors and conditions. Carcinogenicity (relating to tumors of the lung as well as of the pleura and of the peritoneum) was becoming more and more, at times dramatically so, linked with the production of asbestos or the mere use of same.

The alarm was now spreading throughout the asbestos industry field and it was felt our association should take immediate steps so as to seek and coordinate all possible information and data over the whole world in connection with said problems, whilst establishing and maintaining contacts with (and sometimes enrolling into the study) such bodies or agencies which were already at work or susceptible of becoming constructive parts of the study.

Thus our association decided it should carry a substantial share of this responsibility and devote much of its resources, time and energy in that direction even if the etiology of the pathological conditions in point should not seemingly impugn chrysotile asbestos as much.

Hitherto our concern as to the health of the worker in our chrysotile mining industry had been confined to the development and maintaining of preventive industrial measures and safeguards as well as of medical services, all of which we thought were adequate, particularly as same were supported by organized industrial clinics the first one going back to the early thirties (at Asbestos, P.Q.) and our second, in the mid-forties, (at Thetford Mines, P.Q.) our consultants and advisors to same having been the Saranac Laboratory, at Trudeau, U.S.A. (under the direction of Doctor Leroy U. Gardner, the eminent pathologist and pioneer in industrial health) professor Anthony J. Lanza (New York University) professor J. A. Vidal, the Canadian pneumologist.

Whilst this association did not and still does not believe that asbestos problems threaten the general public (it being felt that same are rather occupational and not environmental) we could not but see that in our first line of duty did rest one avenue, (it seemed to us only one) that could lead to a sound and thorough quest into the possible causes and ways of redress in such a situation, such avenue being: the enlisting of a competent team the members of which would investigate, advise, recommend and SET IN MOTION a plan of scientific research, a worldwide plan.

This ambitious scheme we hope we may be able to achieve with such guidance as that of the Institute of Occupational and Environmental Health scientific committee, under the rigorous and enlightened direction of Dr. George Wright an authority in Labour Medicine and a foremost pioneer on this continent in the field of physiology.

Our chrysotile mines in Canada being responsible for some 85% of the world chrysotile mining production (USSR excepted) we could not, however, avoid the pursuit of research in those fields beyond mining and milling proper and we just had to embark into the fields adjunct such as manufacturing, processing and uses, even if our responsibility as such was not entailed for that use made of our fibre outside of the mines and mills. It is thus that our Association became involved in those other fields (manufacturing, processing, uses, etc.). In so doing we knew we would have to face problems which do not seem to exist in our mining operations, for instance the problem of mesothelioma, a problem which virtually does not exist according to our Clinic records, (thus no mesothelioma, verified as such, has appeared with us since 1960 and only four had appeared before 1960, two of which raising serious doubts as to their authenticity having not been, we feel, effectively investigated.)

It is with pride confidence that we submit to your good consideration this present study.

INTRODUCTION

We shall ever be most appreciative and thankful for the generous assistance and courtesy already extended to us in the preparation work and study which lead to the present scientific endeavour of the committee of the Institute under Dr. Wright, and we would address ourselves particularly to those distinguished institutions which participated to the two "Antigua Conference" meeting: the Pneumoconiosis Research Unit (Penarth, Wales), the United States Public Health Services, the Industrial Hygiene Foundation, at Pittsburgh, the Labour Medicine School at Milano, the Mount Sinai Occupational Sciences Laboratory at New York, the American Cancer Society, the Industrial Health Institute at Helsinki, and the many scientists of England, Canada, South Africa, France, Federal Republic of Germany, USSR, East Germany, who have so generously contributed with their knowledge, advice and data.

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INTRODUCTION

It has been known for nearly half a century that men employed in the production and use of asbestos fibre were, under circumstances of prolonged and intense exposure, liable to the development of a diffuse and at times fatal degree of lung fibrosis. Recognizing this, responsible components of industry instituted methods for reducing the concentration of asbestos fibre in the ambient air of the worker with a consequent lessening of the frequency and severity of pulmonary fibrosis in those exposed. Recent observations quite strongly indicate that even more stringent protection of the worker is needed in many situations if the problem of pulmonary fibrosis is to be entirely eliminated.

During the past twenty years it has been convincingly demonstrated that under some, but not all circumstances of human exposure to the inhalation of asbestos fibre, the frequency of occurrence of lung cancer (bronchogenic cancer) is higher than that expected in a similar but non-exposed population. This relationship, in a way similar to that with pulmonary fibrosis, appears to be dose and time dependent.

In the very recent past, there appears to have been demonstrated an epidemiologic relationship between the exposure of persons to substantial amounts of crocidolite asbestos and subsequent development of pleura and peritoneal mesothelioma; a fatal form of cancer in most instances. The role of chrysotile, amosite and anthophylite asbestos in this regard is still moot as is also the question of dose and time relationship between exposure and the occurrence of mesothelioma. Although it is a fact that the incidence of lung cancer and mesothelioma is higher in those who inhale substantial amounts of asbestos fibre than it is in the non-exposed population, the precise role of fibre in this relationship is still uncertain. Evidence suggests that one or more factors, such as cigarette smoking, must co-exist with fibre before the development of lung cancer is augmented. Less is known with respect to such a co-carcinogen action in the relationship between asbestos fibre and mesothelioma.

The asbestos related industries, at one time concerned only with preventing pulmonary fibrosis, are now faced with additional biological hazards associated with the fibre. The options available to the industry are apparent. 1) The production of this very useful material could be abandoned either voluntarily or by law. 2) Users of the fibre might minimize their responsibility by adopting substitutes of lesser biological activity. 3) If the precise nature of the injurious action of the fibre could be learned, it is conceivable that the fibre might be altered to remove this effect while retaining the desirable qualities of the fibre. None of these options are attractive or appear to be immediately feasible.

The remaining option is the one that industry has followed in the past and would likely find the most acceptable for the future. With the realization that asbestos fibre in sufficient concentration to produce tissue injury has and continues to exist in various operations, it becomes evident that we must determine what exposure patterns can be tolerated without the production of disease and adopt engineering methods capable of reducing the concentration to that which is consistent with good health throughout the life of persons who might be thus exposed. This objective must be achieved if the industrial use of asbestos fibre is to continue.

An additional objective, less directly related to safe utilization of asbestos fibre, is to learn how to manage the future of those persons who have already sustained a substantial exposure to the inhalation of these fibres. For example, should those persons who have had a known category of fibre exposure but have not as yet developed evidences of disease be removed entirely and forever from further exposure? If so, how are these persons to be identified? These two queries also can be applied to those persons now exhi-

biting "evidence" of biological effects of asbestos fibre. Is there reason to hope that removal from further exposure will prevent the disease or its progression once a certain level of exposure has been reached? Such queries and others of equal pertinence can be answered only by comprehensive, properly designed studies of the natural history of the biological effects of asbestos fibre. The combined medical, legal, and sociologic management of persons already exposed to asbestos fibre is dependent upon the information which can be gleaned from such studies. The factors discussed in Sections I and II of the following find their paramount importance as applicable to these two objectives.

There are those who believe that since the use of asbestos fibre saves lives, some risk to life in its production and use is acceptable. This compromise is not reasonable or necessary. Materials possessing more potential for injury than does asbestos are now being handled with greater safety than is asbestos. Examples of these are radiation emitters, explosives, and beryllium. With the cooperation of employer, employee and regulating agencies whose actions are based upon adequate knowledge, there is no reason to doubt that asbestos fibre can achieve safe utilization. Section III of this manuscript considers some aspects of this phase.

One may wonder why there has been a delay in the development of safe practices for using this material since its potential for fibrogenesis has been known for fifty years and the suspicion that it might play a role in neoplasia dates back to 1935. A paucity of knowledge has been and continues to be the major deterrent for the development of reliable and adequate safeguards. This in turn can be traced to several factors to which attention must be directed if the goal of safe utilization of the fibre is to be achieved.

The lack of study methods possessing sufficient reliability to convince all concerned has been a major deterrent to which considerable but still inadequate attention currently is being directed. A paucity of adequately trained persons willing to devote their energies to the problem is a second major deterrent. This in part has stemmed from the fact that the number of persons who might become interested in the problem has been diluted by the explosive broadening of the medical scientific horizon. Equally at fault is the lack of opportunity for study and insufficient funds for that purpose characteristic of past years. There is no reason to expect that these problems will disappear and adequate information be obtained spontaneously without directed effort. The industries involved, the workers with their organizations and the government regulating agencies either directly or indirectly might be expected to provide the opportunities for study and the funds for this purpose. Past experience of Government agencies suggests that they have difficulty in mounting an effort that must be sustained over several years and it is doubtful that the workers and their organizations can do so on a broad enough scale. This places the burden of developing the necessary information and putting into operation the required safeguards directly upon the shoulders of the industries involved.

The desired information falls into four major categories. These are:

1. Studies dealing with a maximum allowable concentration of asbestos fibre in the environment of man.
2. Studies dealing with the determinants and mechanisms of the biological action of asbestos fibre.
3. Studies dealing with reducing the concentration and numbers of inhaled asbestos fibres.
4. Studies dealing with the development and evaluation of methods used in the preceding considerations.

The material which follows proposes a systematic program for studying the problem in such a way as to provide the necessary information for the purposes set forth above. It is obvious that the

categories are inter-related and that there is some overlapping and reduplication. There is nothing that has not been expressed before, but it seems that a useful purpose might be served if the areas for study are recorded so that memories can be constantly refreshed and none of the important factors overlooked. Just how this material will be used is not entirely clear at the moment. It can act as a scaffolding upon which enlisted research can be structured. It may assist in minimizing overlap and reduplication. It is hoped that it may assist those who are designing pertinent studies to include the necessary components. It may also help to indicate the areas of study which would be the most productive in terms of a speedy development of safeguards. It should give an understanding of the size of the problem and hence avoid the staging of inadequate attacks. The outline may also assist in developing an orderly approach and thus reduce the chance that efforts will be dissipated by "popular" interests. It is apparent, too, from such an outline that the several major avenues can be worked upon simultaneously and each component will benefit by integration of effort. The time appears to have come for a concerted approach and a vigorous pursuit of the problem.

SECTION I

Studies Dealing with

The Maximum Allowable Concentration (MAC) of Asbestos Fibre in The Environment of Man

Here we are concerned with solving the essential question of what level of fiber concentration can be tolerated over one's entire life span without causing illness under those various circumstances of operation where man is exposed. The direct approach to the solution is by contrasting in terms of the total character of exposure two distinct populations, the one evidencing illness reasonably incriminating asbestos fibre and the other free of such evidences. The kind of exposure tolerated by the specific illness free population is the one which must be achieved and maintained.

The MAC for asbestos that has been followed in the U.S.A. during the past twenty-five years was designed to protect the worker against the development of pulmonary fibrosis and its sequelae. It had its data basis in the study of Sayers and Dreessen which was not proposed at the time as authoritative and was used rather as a tentative measure. It is not surprising that their study of persons exposed for less than fifteen years and whose environmental description utilized methods now known to be inadequate, should prove to supply an MAC which we have every reason to question seriously at this time. Moreover, we now have evidence that in addition to causing pulmonary fibrosis, "asbestos fibre" plays a role in pulmonary carcinogenesis and mesothelioma — conditions for which the current MAC made no allowance whatsoever. It can be said with little fear of contradiction that nowhere does there exist a body of scientifically sound data concerning the incidence of asbestos related disease arising out of a lifetime of employment in an *adequately* described environment. Hence, we have no ability to establish now a *proven* MAC for any single, much less for the multiple varied types of employment utilizing asbestos fibre. Reminiscent of the action of twenty-five years ago, a proposal is now being made as to a "safe limit" based on fibre count per cc. Admittedly this is tentative but unfortunately, again it is based on scant direct, plus much indirect, data from a small number of persons in a single type of employment. It is based also on the unproven assumption that the length of fibre to be counted is the one that causes disease while other lengths of fibre do not. While it may be prudent at this time to revise the MAC to a different value, the inescapable conclusion remains that properly designed studies of populations and environments adequately characterized must be started now so that twenty-five years hence we will at least have moved on a scientific basis from the position we currently occupy.

Because the kinds of fibre used vary as to nature and size and because coexisting materials present as airborne contaminants may vary greatly in different circumstances of employment, it is essential that the MAC be established for each of the broad categories of human exposure to fibre. The major sites of potential exposures to asbestos fibre are:

I. *Fibre production* exemplified by mining, milling, refining, conditioning, packaging and shipping.

II. *Manufacturing products* composed entirely or in part of one or more varieties of asbestos fibre. The major manufacturing users of fibre can be classified as textiles, friction materials, asbestos cement products, insulation, building materials, floor covering, fillers in many products of diverse character. Approximately 250 kinds of manufactured products utilize asbestos.

III. *Appliers or assemblers of asbestos* or products containing asbestos. In this category are insulation workers, carpenters,

plumbers, electricians, pipe fitters, and a large number of additional and commonly unrecognized operations dealing with asbestos fibre. In some instances removal of previously installed asbestos or asbestos-containing products constitutes the source of a not-always-recognized exposure.

IV. *Solid waste disposal* affords a potential exposure because of the subsequent use for other purposes of bags previously containing fibre and also because of the use of rejected material such as asbestos cement products as land fill or for roads or for other surface construction.

V. *Public exposure* may occur via several mechanisms. The processes involved in production of fibre and in the manufacture and use of materials containing asbestos may disseminate fibres which are subsequently carried via air currents into the neighborhood where adjacent workers may be involved or into more distant adjacent areas which may be occupied by residents or by other workers not directly involved in the plant giving rise to the fibre dissemination. The solid waste disposal of materials containing fibres may also act as a source of public exposure. Workers exposed to fibre in the course of their occupation may bring it home on clothing and thus expose members of their family including children at a very young age and thus expose the public at distances quite far removed from the site of origin of the fibre. The use of talcum powders containing easily disseminated fibres of "asbestos" causes exposure throughout the life span.

With regard to the requirements for an adequate MAC, it is likely that such a limit may be different not only for specific kinds of exposure pattern as suggested in the foregoing, but also for different *kinds* of fibre and proportions in a mixture thereof. The inherent structure of asbestos fibre in its various forms, its length and diameter and contaminants or coexisting potentially injurious agents may cause one environment to be more or less injurious than another.

For purposes of learning the biologic MAC of each kind of fibre, exposures limited to one variety of material will be required. These would most likely be found in a fibre production environment. Since mixed exposures are common and asbestos plus other biologically active agents coexist in some types of exposure, it will be necessary to study examples of these variations of exposure in order to set a meaningful MAC for each such class of operations. The studies required for establishing the MAC of a specific environment will of necessity be of an epidemiologic character embracing various categories of exposure and will look at the role of asbestos fibre as it is related to neoplasia and to tissue injury and consequent alterations.

Recognition of the biological end result of exposure to fibre poses difficulties both qualitative and quantitative but with sufficient effort and care it appears reasonably possible. Evaluation of the "exposure" in terms of quality and quantity is much more difficult, even at present, let alone in those periods of the past 25-30 years which are so essential to our understanding of the import of biological end results of the present. This seemingly insurmountable task may delay arrival at a reliable MAC but should not deter us from our task. We possess, even now, exposure data which can be useful for our purposes, though with no pretense of desired accuracy. If contemporary data can be obtained on a broad scale, it will be found very useful at a later date.

An outline of desired information pertinent to establishing a reliable MAC follows. No single study is apt to embrace all of the factors noted.

I. Fibre Production

A. Chrysotile

1. Mining

a. Nature of exposure

1) Duration and lapse time

2) Class of fibre

3) Fibre count

4) Fibre size pattern

5) Material adherent to fibre — trace metals — waxes — etc.

6) Coexisting particles

7) Coexisting carcinogens

8) Smoking history

9) Hobbies or homework or second job

b. Recognition of tissue reaction

1) Pulmonary physiology

2) Roentgenogram

3) Clinical

4) Biopsy

5) Autopsy

6) Ferruginous bodies

c. Type of tissue reaction

1) Inflammation and granuloma

2) Fibrosis

3) Pleura plaque

4) Bronchogenic cancer

5) Mesothelioma

6) Gastrointestinal

7) Chronic bronchitis

d. Nature of population

1) Case studies — retrospective and prospective

2) Current employees — one time survey

3) Cohort — retrospective and prospective

2. Milling and shipping

a — d as under mining

B. Amosite

C. Crocidolite

D. Anthophylite

E. Asbestos like materials: talc, tremolite, Wollastonite, brucite,

Study B, C, D, and E by scheme for A

II. Manufacturing

a — d as under mining for

Textiles

Insulation

Brake lining

Asbestos cement products

Floor tile

Roofing

Building materials

III. Appliers, assemblers and users

a — d as under mining for

Insulation workers

Plumbers

Steam fitters

Ship builders

Carpenters

IV. Solid waste disposal neighborhood — workers and residents

V. Public — family of workers exposed, resident neighbors of plants and solid waste disposal, general public (water, talcum powder)

Study IV, and V by a-d under mining

The following outline lists the individuals actively engaged in studies directed towards determining the maximum allowable concentrations of asbestos fibre in the environment of man. We are confident that others, as yet unknown to us, are working in this area and regret that they are not included. The abbreviations (appendix II) indicate the nature of evidence under study. In appendix I further details of each study will be found.

Immediately following the outline of work in progress is an analysis of the relative need for initiating new or additional studies.

STUDIES DEALING WITH MAXIMUM ALLOWABLE CONCENTRATIONS OF ASBESTOS FIBRE IN THE ENVIRONMENT OF MAN

I. *Fibre Production* (Mining and Milling — Pure exposure)

A. Chrysotile

McDonald, Can — bc,me,fb,pf,pp,dc
Vigliani, It — bc,me,fb,pp,dc
Zolov, Bu — fb,pp
Webster, S. Afr — bc,me,fb,pp,ab
Sluis-Cremer, S. Afr — di,pf

B. Crocidolite

McNulty, Australia — fb,pp
Webster, S. Afr — bc,me,fb,pp,ab
Sluis-Cremer, S. Afr — di,pf

C. Amosite

Webster, S. Afr — bc,me,fb,pp,ab
Sluis-Cremer, S. Afr — di,pf

D. Anthophylite

Noro, Fin — bc,me,fb,pp
Kaski, Fin — bc,me,pp
Meurman, Fin — bc,me
Buminovich, SU — fb,pf

E. Talc

Kleinfeld, US — bc,me

F. Other

Kacnelson, SU — (mixed exp.) fb
Zolov, Bu — (mixed exp.) fb,pp,pf

II. *Manufacturing*

A. Textiles

Cralley, US — bc,me,fb,pf,dc,pp
Mancuso, US — bc,me,fb
Enterline, US — bc,me,fb
Wolfsie, US — fb,pf
Newhouse, GB — bc,me,fb,pp,dc
Hunt, GB — fb,pf,dc
Lewinsohn, GB — fb,pf,dc
Avril, F — me,pp
Navratil, Cz — bc,me,fb
Enterline, US — (J-M — retiree) fb,me,bc,other
Bristol, US — (J-M — x-ray) fb
Anspach, EG — bc,me,fb
Bohlig, WG — bc,me,fb
Ashcroft, GB — me
Roach, GB — tx,fb
Kacnelson, SU — fb
Einbrodt, WG — ab

B. Insulation

Cralley, US — bc,me,fb,pf,pp,dc
Enterline, US — (J-M — retiree) fb,me,bc,other
Bristol, US — (J-M — x-ray) fb

C. Brakelining

Cralley, US — bc,me,fb,pf,pp,dc
Enterline, US — (J-M — retiree) fb,me,bc,other
Bristol, US — (J-M — x-ray) fb

D. Asbestos Cement

Lepoutre, B — bc,me,fb
Navratil, Cz — bc,me,fb
Enterline, US — (J-M — retiree) fb,me,bc,other
Bristol, US — (J-M — x-ray) fb

E. Floor tile

F. Roofing

G. Building material

Cralley, US — bc,me,fb,pf,pp,dc
Enterline, US — bc,me,fb
Enterline, US — (J-M — retiree) fb,me,bc,other
Bristol, US — (J-M — x-ray) fb

H. Unknown type of fibre and mfg.

Linell, Sw — me

III. *Appliers*

Vigliani, It — bc,me,fb,pf,pp,dc
Selikoff, US — bc,me,fb,pf,pp
Balzer, US — bc,me,fb,pp,dc,gi
Kleinfeld, US — bc,me,fb,gi
Harries, GB — bc,me,fb,pp,dc
Sheers, GB — bc,me,fb,pp (Neighboring workers)
Elmes, GB — bc,me,fb,pf,pp
Sturm, EG — pp
Stumphius, Ne — me
Cowle, Can — fb,me,bc

IV. *Solid Waste Disposal*

V. *Public Exposure*

Selikoff, US — ab,fb
Selikoff, US — bc,me,fb (amosite, neighborhood)
Harries, GB — me
Wagner, GB — me
Wells, GB — bc,me,fb,pp,dc (important if being done)
Bell, GB — ab
Gibson, GB — me,ab
McDonald, Can — me
Cartier, Can — bc,me,fb (neighborhood)
Saucier, Can — ab (animals)
Avril, F — ab
Roitzsch, EG — me,ab
Burilkov, Bu — bc,me,tbc.
Cooper, US — me,bc,fb,pp,dc,gi
Selikoff, US — me,fb
Smith, GB — bc,ab,pp,fb (Nottingham) ab
Cralley, US — talcum powder
Noro, Fin — dc
Kotin, US — North Carolina, pp
Bohlig, WG — me
Ashcroft, GB — me
Zolov, Bu — fb,pp
Kaski, Fin — bc,pp
Linell, Sw — me

Comments

I. It would appear that the exposures to pure chrysotile and anthophyllite currently are being looked at in sufficient depth to make the maximum use of data derivable from past exposures. Some serious thought, of course, should be given to making certain that data for the future will be obtained properly. In this respect we think mostly of proper environmental hygiene studies and methods adequate to recognize the biological aspects of fibre in humans. Membrane filter collection and fibre counting will be needed. Personal medical follow up of cohorts with accurate knowledge of what diseases develop and autopsy confirmation must be provided.

We need to look into the question of whether or not anyone is obtaining the desired information with respect to crocidolite and amosite and talc. The first two of these are being used in conjunction with chrysotile and probably with anthophyllite. It might be added that talc is not only being used in conjunction with asbestos fibres but also may be creating situations in the absence of asbestos exposure for which asbestos might be blamed if one utilizes ferruginous bodies or pleura plaques as the marker for previous asbestos exposure.

II. While it is true that quite a few names appear under studies in Manufacturing, it should be pointed out that some are of rather limited utility for determining a proper MAC. The studies of Mancuso, Enterline, Wolfsie, Avril, and Navratil lack industrial hygiene data. The studies of Cralley may have considerable utility because he does have some industrial hygiene data, but the medical studies remain to be done. The two Johns-Manville epidemiologic studies (Enterline and Bristol) may ultimately develop into usable information, but at this point should be considered predominantly as exploratory studies to set the stage for later more specific studies. The studies of Newhouse, Hunt, and Lewinsohn (successor to Knox) should lead to quite useful data. It can be readily seen that information regarding insulation, brakelining, asbestos cement, floor tile, roofing, and building material is almost devoid of specific approach at this time. In this category we need the following. 1) A study of available cohorts in *each type* of manufacturing going back as far as there are usable records and where data is not available in the records of the company with respect to the cause of death an effort should be made to do this through Social Security data. 2) Truly prospective studies with direct follow-up to the time of death should be set up and pursued in a) populations going back as far as we still have appreciable numbers of living members, b) employees who have begun work after known improvements in industrial hygiene, c) employees now being started. With respect to these groups we should have adequate data concerning their total employment and hobbies, clinical histories and smoking records, physical examinations, chest films, sputum for ferruginous bodies, appropriate pulmonary function tests, and adequate data concerning the environment to which there has been exposure. This study should also include every effort to look at the progression in those who have been removed from exposure and also the question of regression. These studies need to be done in:

1. A textile exposure.
2. Insulation manufacturing.
3. Asbestos cement products.
4. Brakelining — especially personnel used in testing.
5. Building material.
6. Floor tile.
7. Roofing.

Every effort should be made to try to make these studies in populations where there is relatively little crossover of type of employment involving asbestos exposure. Of these groups, *floor tile* and *roofing* might be delayed until information from the J-M (Bristol) study is finished.

III. With respect to stimulating and pursuing studies in the group of appliers of asbestos products, there would appear to be a rather intensive effort in this direction at this time by various groups. This research should be encouraged by any means at our disposal. It is apparent that the question of what concentration and type of fibre the applicators are exposed to should be studied in detail. The importance of learning what kinds and concentrations of substances *other* than asbestos the insulation workers may be exposed to is also of paramount importance.

IV. Insofar as we can determine no one is specifically directing attention to solid waste disposal other than what each specific industrial plant or operation is doing. These efforts range all the way from burying the material at sea or bulldozing it under-

ground to using it for paving of roads and parking lots.

V. There are numerous investigators looking into the question of public exposure but for the most part they look at only one feature, namely, the presence of asbestos bodies or the frequency of mesothelioma in populations not classed as workers in the asbestos-using industries. The weakest part of the program relating to public exposure would appear to be the absence of knowledge with regard to the presence and numbers of asbestos fibres in the ambient air near building projects, asbestos-using industry plants, solid waste disposal depots, and the city streets or farmers' fields. There can be little question of the importance of this part of the overall program and it would seem that the hang-up has to do with the questions of accuracy and the feasibility of making such studies. The U.S. Public Health Service considers asbestos to be a pollutant of second importance, (ozone, SO_2, and oxidants are of primary importance at this moment) and they will perhaps do something about the question of asbestos in about two years. It would seem that along with the development of adequate methods of in-plant industrial hygiene monitoring some extra dollars from a pooled resource might be used to encourage the personnel of industry to make some outside-the-plant studies. We would think the desirability of this is beyond question and the feasibility from several aspects should be looked into.

SECTION II

Studies Dealing with

The Determinants and Mechanisms of The Biological Action of Asbestos Fibre

In addition to the easily appreciated contribution of such studies to science, there are cogent reasons of a practical nature for a vigorous sustained effort to learn all that we can about the mechanisms whereby asbestos fibre may cause disease. There are reasons to believe that at this moment there are persons who have had exposure in the past years sufficient to cause illness at some time in the future even though further exposure now is reduced to a safe limit. Although one cannot be too optimistic, there is the hope that new knowledge might provide the key to interrupting the process in such persons.

Another reason is to be found in the fact that from an exposed population some develop evidences of illness attributable to asbestos fibre whereas co-workers exposed in a similar manner over the same interval of time remain free of evidences of injury. Unevenness of exposure among the population and variations between individuals as to the amount of fibre retained may be important factors. The possibility of a variation between individuals with respect to tissue sensitivity may also play a role. In any event, the answer to this riddle would bear upon methods for prevention of injury.

Still another reason for such studies will also bear upon preventive methods. It is customary to think of reducing or interrupting all contact with a potentially hazardous agent as being the chief or only method of preventing injury. It is conceivable, however, that alteration of the agent in such a manner as to convert it to a non-injurious one might be achieved. Examples of this occurred in the use of lead compounds in the pottery industry. One might also alter the host, the method of vaccination being an elegant though not entirely appropriate example.

The factors determining the relationship between the physical and chemical nature of an agent and its potential to cause tissue injury are complex. Among these relationships one can see the relevance of the following. Intensity and duration of contact with tissue are important factors in determining the effect of an agent on the tissue. For this reason the biological dynamics of asbestos fibre with respect to its deposition, removal, and transfer or storage within the body needs thorough study. For a biological reaction to occur, the individual cells of the tissue, both fixed and mobile, are the basis of the reaction. In addition via humoral mechanisms reaction in a more distant portion of the tissues may occur. For these reasons, the intimate details of the way in which individual cells react to asbestos fibre deserve the most thorough study. In addition to reacting individually, the cells also act in a more organized fashion and express this in what might be termed a tissue reaction. Virtually all of the ways in which tissue can react is known to occur in response to asbestos fibre. These include inflammation and granuloma formation, fibrogenesis or scar formation, and neoplastic reaction. It is possible also that asbestos fibre influences the immunological state of the body both locally and in a more general way. Much has been learned about these reactions from a study of human tissue but for obvious reasons this kind of approach to the overall problem is somewhat limited because one lacks the ability to manipulate the conditions under rather controlled requirements. Because of this, extensive work utilizing animal models will be required as well as a continuation and more detailed study of human material.

Our attention should not be directed entirely to the host's reaction to the fibre. To understand the cellular reactions one must also consider asbestos fibre as being of a highly diverse character with respect to its chemical and physical makeup and

as to materials which may be adsorbed or bound to it. The fact that in all sorts of human exposures to asbestos fibre there exists an opportunity for simultaneous exposure to other materials which may influence the fibre or vice versa in a peculiar way so as to vary its biological potential further complicates the entire problem. For these reasons the simple term "asbestos exposure" or "asbestos worker" is a colossal oversimplification and leads to confusion rather than enlightenment. The enormity of the task required for full understanding of the biological effects of this unusual material as it is actually utilized in world affairs staggers the imagination and tends to paralyze one's will to embark upon the effort. It is probable, however, that a full understanding of all aspects of the total problem are not actually required in order to develop the safe utilization of this important material and the enormity of the task should in no way interfere with our pursuit of the matter.

An outline of some of the approaches to this part of the total problem follows. That it is only a partial development will, of course, be obvious.

I. Biological dynamics of asbestos fibre

A. Deposition
   1. Anatomical location*
   2. Effect upon muco-cilliary apparatus*
   3. Effect upon macrophages*

B. Removal
   1. Bulk removal*
   2. Muco-cilliary mechanism* (rapid removal)
   3. Macrophages* (slow removal — transfer — storage)
   4. Chemical reaction*
   5. Influence of various agents and conditions upon the removal mechanism.

C. Transfer and storage of fibre within the body
   1. Location in organs and tissues*
   2. Recirculation of fibres*
   3. Influence of various agents and conditions upon this mechanism

D. Influence of alteration of asbestos fibre upon its biological dynamics.

II. Biological reaction of tissue to asbestos fibre

A. Inflammation and granuloma
   1. Anatomical location*
   2. Reversibility*
   3. Dose patterns and time lapse*
   4. Influence of other agents upon the reaction* (PVPO — steroids — infection — gases — etc.)
   5. Effect of altering fibre upon the tissue reaction

B. Fibrogenesis
   1. Anatomical location* (where in parenchyma — pleura — peritoneum) (why not lymph nodes?)
   2. Mechanism of formation* (macrophages — fibroblasts — mechanical — chemical — immunologic)
   3. Reversibility*
   4. Time and pattern sequence related to inflammation*
   5. Dose and time lapse*
   6. Influence of other agents to prevent, arrest, or reverse process
   7. Effect of altering fibre upon tissue reaction

C. Neoplasm
   1. Bronchogenic cancer and metaplasia
      a. Anatomical location*
      b. Association with other manifestations of asbestos exposure* (ferruginous bodies — fibrosis — plaques — etc.)
      c. Association with agents other than asbestos
      d. Dose and time lapse*
      e. Asbestos as a *tool* to study carcinogenesis*
      f. Effect of altering fibre upon the reaction
      g. Effect of altering host (cancer prone animals — animals altered by radiation or by hosting another cancer)
   2. Mesothelioma
      a. Anatomical location*
      b. Pathways of fibre transport*
      c. Association etc. as in b above*
      d. Association etc. as in c above*
      e. Dose and time lapse
      f. Asbestos etc. as in e above*
      g. Effect of altering fibre upon the reaction
   3. Gastrointestinal*
      a. Why not manifested in experimental animal
      b. Pathway and dynamics of fibre transport in GI system
      c. Is fibre altered in some way by chemical reaction in GI system so that it behaves differently than it does in the lung*

III. Biological reaction of cells to asbestos fibre

A. Mechanism of fibre handling*
   1. Cells in vivo (in situ)
   2. Cell culture
   3. Isolated cells

B. Reaction of cells to fibre*
   1. Pre-mitosis (isolated, cell culture, in situ)
   2. Post-mitosis (isolated, cell culture, in situ)
   3. Chemical alterations (isolated, cell culture, in situ)

C. Immunologic reactions*
   1. Immediate
   2. Delayed
   3. Competent vs incompetent animal

D. Reaction of cells from other than mammals

IV. Physical and Chemical aspects of asbestos fibre which may influence its biological activity

A. Oils and waxes
B. Other carcinogens
C. Properties for adsorption of pertinent materials
D. Rigidity
E. Divisibility
F. Surface

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* Possibility of different effects being caused by specific kind, physical nature or contaminants of fibre must be considered.

The following outline lists the individuals actively engaged in studies dealing with the determinants and mechanisms of the biological action of asbestos fibre. We are confident that others, as yet unknown to us, are working in this area and regret that they are not included. The abbreviations (appendix II) indicate the nature of evidence under study. In appendix I further details of each study will be found.

Immediately following the outline of work in progress is an analysis of the relative need for initiating new or additional studies.

STUDIES DEALING WITH THE DETERMINANTS AND MECHANISMS OF THE BIOLOGICAL ACTION OF ASBESTOS FIBRE

I. *Biological Dynamics of Asbestos Fibre*

A. Deposition

Timbrell, GB — mo
LeBouffant, F — mo

B. Removal

Thomson, GB — cl

C. Transfer and Storage

Timbrell, GB — fsb,fsr
Botham, GB — ab
Reimann, US — gi
Swinburne, GB — gi
Holmes, GB — (radioactive asbestos)
Rubnitz, US — gi

D. Influence of alteration of fibre

II. *Biological Reaction of tissue to a fibre*

A. Inflammation & Granuloma

Holt, GB — fb (P.204)
Webster, SA — fibre length (Monkey)
Klosterkötter, WG — fibre length, (P.204)
Dumont, Ca — (Pouch)
Schlipköter, WG — (P.204-EDTA)
Jacob, EG — (bronchoscopy)
Friberg, Sw
Helsinki, Fin
Goldstein, S. Afr — ab

B. Fibrogenesis

McIver, US — fb,ab (dogs)
Leathart, GB — fb,pf (steroids-human)
Szymczykiewicz, Po — fsb
Kogan, SU — fb
Zwi, S. Afr — fb,pf

C. Br. Cancer & Metaplasia

Stanton, US — in
McIver, US — in (dogs)
Wagner, GB — in (brucite)
Smith, US — in,cc
McIver, US — in,cc
Peacock, GB — in (fowl)
Gross, US — in,cc
Wagner, GB — in

D. Mesothelioma

Stanton, US — in
Graham, US — in (ovary)
Massey, Ca — in
Smith, US — in,cc
McIver, US — in (dogs)
Wagner, GB — in
Schmähl, WG — in (long fibre)
Davis, GB — in

E. Gastrointestinal

Spjut, US — gi,cc

F. Pleural Plaques

Irmsher, EG — calcification

III. *Biological reactions of cells to asbestos fibre*

A. Mechanism of fibre handling

Botham, GB — ab

B. Reaction of cells to fibre

Suzuki, US — la
Pernis, It — ma (size & kinds of a.)
Allison, GB — ma
Davis, GB — oc
Barrett, GB — ma (serum)
Szymczykiewicz, Po — fsb
Harrington, GB — ma (a & sil)
Holt, GB — fb, P.204, ab

C. Immunologic reactions

Szymczykiewicz, Po — fsb
Turner-Warwick, GB — (Human)

D. Chemical alteration of lung

Dodgson, GB

E. Reaction of cells from other than mammals

IV. *Physical and chemical aspects of fibre relative to biological activity*

A. Oils and waxes

Gibbs et al, Can — cc

B. Co-carcinogens

Crailey, US — trace metals
Smith, US — Benzopyrene
Hammond, US — cigarettes
Stanton, US — methylcholanthrene
Wehner, US — cigarettes

C. Adsorption

D. Rigidity

Massey, Can — in

E. Divisibility

F. Surface

G. Trace Metals

J-M Research Inst.
Michailova, Bu — cc

V. *Non or altered asbestos fibres*

Gross, US — fb,in,cc,ab — synthetic C.
Gross, US — fb,in,ab — brakedrum dust
Gross, US — ab — other materials
Wagner, GB — in (neoplasia) (brucite)
Davis, GB — me,fb

Comments

A survey of the number of individuals working in this general area reveals a disappointingly small number. In addition, it can be safely assumed that a good proportion of those who do work in this area have other responsibilities and additional interests. If we are to obtain the needed information, we will have to encourage and promote specific research studies in this general area.

With respect to studying the determinants of biological action, we urge the pursuit of practical questions, the study of which would come under one or more of the areas indicated in the outline. These are as follows.

1. The question of just what length of fibre causes the biological reaction remains unanswered. Is there an innocuous length of fibre? Current recommendations for MAC propose counting only fibres greater than 5 microns in length. Those shorter than this are lumped with particles. Are we in fact monitoring the proper and specific agent for this general problem? Insofar as we know, the definite study with respect to fibre length remains to be done even though several studies do exist suggesting that only fibres greater than 5 microns in length are biologically active.

2. The practical questions of removing workers from exposure and other medical-legal considerations hinges on a determination of whether or not biological reactions to asbestos progress, remain static, or are reversible after cessation of exposure. Small bits of information gleaned from studies having other purposes are at times cited in this regard but insofar as we know there has been no systematic study of this question.

3. In a vein similar to item 2, there is the question of whether or not there is a dose of specific asbestos fibre which can be tolerated with safety or which can be tolerated with no recognizable reaction. The question might be raised as to whether or not there is a "critical mass" needed in order for biological reaction of recognizable degree to occur. It is recognized, of course, that the definition of "biological reaction" would determine how one might try to answer this question. Nevertheless, in terms of those matters of significance to human beings, namely granuloma, fibrosis, and malignancy, the problem should be explored.

4. There is a strong suggestion of intra-species variation of response to some kinds of irritant and the question can be raised as to whether or not asbestos is one of this type of irritant. If there is an intra-species variation, can a method be designed to determine in advance those individual members who will respond and those who will not? This is a very practical question in employment.

5. There is very little being done about the *biological* dynamics of fibre, the studies having thus far been confined almost solely to mathematical models. A substantial amount of work with respect to biological dynamics of non-fibrous materials is currently in progress and it is worth considering that we might encourage these groups to add fibres to their study. The AEC has interest in this and perhaps those working on that problem might add fibres of various kinds to their studies. Information of this kind would go towards answering the question of whether or not there is an innocuous length of fibre. The strange story of pleural plaques might be further elucidated by such studies.

6. Closely allied to 5 is the question of the fate of asbestos fibre after it has been lodged in the lung. Does it persist indefinitely and what are the quantitative aspects of this. Some promote the concept that every fibre which enters the lung stays there and persists forever and thus it becomes of increasing importance to know whether or not this is true.

7. While there is an increasing amount of information concerning the role of inorganic materials as carcinogens, it has been disappointing. There has been insufficient interest in such studies. The genuine possibility that trace metals associated with asbestos fibre play a strong role in carcinogenesis almost demands that the role of these metals unaccompanied by other agents be completely explored and this should be supported.

8. The clinical data suggests in an overwhelming way that cigarette smoking plays a very dominant role in the increased frequency of bronchogenic cancer among those heavily exposed to asbestos fibre. The quantitative aspects of this could very well be explored in the experimental animal. A new technique developed by Battelle at the Hanford Complex might be employed in this regard.

9. The fate of ingested chrysotile and other types of asbestos fibre is almost totally unexplored. Pundsack believes that the gastric juice has a sufficiently high pH to dissolve chrysotile. The transit time would

of course play a considerable role. The quantitative aspects of this problem are approachable and should be encouraged.

10. The use of ferruginous bodies as a marker for both public and industrial exposure to asbestos fibre is prone to all manner of immoderate statements because we have relatively little reliable quantitative data with respect to these objects and their relationship to biological reaction in tissue. A full exploration not only of the relationship between the total of ferruginous bodies and the biological reaction, but also with respect to the number of ferruginous bodies arising out of known quantitative exposures and also the question of destruction and removal of bodies is quite urgently needed.

11. The role of the physical aspects of fibre in fibrogenesis and malignancy is being explored to some degree but probably not to a sufficiently intensive degree for the importance of the question.

12. As long as pleural plaques are as great a mystery as they are (with respect to their formation and the paucity of asbestos fibres associated with them, plus the fact that the plaques are primarily in the parietal pleura) there will be great difficulty in determining the significance of these structures with respect to past exposures and the future developments. Can these structures be examined in the experimental animal? To do so would be very useful since in man our only chance is to see the end stage and not the developmental processes.

13. There are a host of general problems of a somewhat less directly applied nature but which may be even more important from the point of view of their indirect application. These are too numerous to list.

The listing of the above problems should in no way be interpreted as minimizing the importance of the many other problems that could be suggested for study. The purpose in listing the above was to indicate at this very moment there are numerous directly applicable studies of an almost pragmatic nature that need pursuit. In fact, the *direct* applicability might suggest that they are somewhat pedestrian and therefore are not as desirable for spontaneous study by scientists. Efforts to overcome this will need to be made.

SECTION III

Studies Dealing with

Reducing the Concentration and Numbers of Inhaled Asbestos Fibres

As was pointed out in the first paragraph of the Introduction, there is evidence that protection of workers and perhaps of the general public from the potentially injurious effects of asbestos fibre has been inadequate during the past twenty-five years. In Section I it was stated that in part this may be the result of reliance upon an untrustworthy MAC. In addition, however, there can be little doubt but that engineering methods for reducing the airborne fibre concentration have been and remain inadequate both in design and application. While some of this may have stemmed from apathy, most of it must have arisen from inadequate knowledge with regard to many factors. Among these one might list; 1) Dependence upon methods of counting dust which do not reflect accurately the fibre concentration, 2) The untested assumption that generation, dispersion, and other particle dynamics are the same for fibre and non-fibre particles, 3) Ignorance of effects of coexisting particles upon the airborne fibre, 4) The lack of knowledge concerning the behavior of filters with respect to fibres.

Factors other than ignorance doubtless contribute to the delay in developing the required degree of protection from airborne fibre. Failure of earlier designs to provide the expected suppression of dustiness probably discouraged subsequent efforts embodying newer types of equipment. Reluctance to accept alterations in the "style" of the product consequent to protective measures may also have contributed. The persistent use of old equipment and housing which makes dust control difficult to achieve doubtless was a factor. The changes in the intimate character of the raw fibre as it left the production site over the past years may also have played a part. The manner in which fibre is handled in the manufacturing process, especially with regard to the level of energy used in order to augment production may have determined the number of fibres that became airborne. The economic influence of competitive materials has been far from a negligible factor. All of these things have held back the application of methods which now appear available for the control of airborne fibre.

One is tempted to predict that with an energetic and unrestricted application of contemporary dust control expertise in the way of complete fibre containment and point source exhaust, the inplant and neighborhood dispersal of fibre could be brought to zero per cubic centimeter. Whether it is necessary or economically feasible to do so is quite another matter.

Even if one controls "inplant" fibre completely, there are still the large areas of exposure represented by users and appliers, solid waste disposal and public exposure from other sources which are not so amenable to correction.

One is forced to conclude that studies relating to dust abatment have a high priority. The following scheme indicates areas for investigation.

I. Information with regard to fibre populations in the actual "breathing zone" of the exposed person

A. Fibre production
1. Concentration — duration pattern
2. Kinds of fibre
3. Physical nature of fibre (size — rigidity — flocs)
4. Origin of fibre at BZ
   a. Unincorporated — pure fibre
   b. Incorporated — mixed with or bound to other materials
5. How is air-borne fibre created
6. Pathway of fibre to BZ

B. Manufacture of products
1,2,3,4,5 and 6 as under A.

C. Appliers and assemblers of asbestos products
1,2,3,4,5 and 6 as under A.

D. Solid waste disposal
1,2,3,4,5 and 6 as under A.

E. Public
1,2,3,4,5 and 6 as under A.

II. Aerodynamics of asbestos fibre

A. Variations caused by size and shape

B. Influence of coexisting material
1. Free materials
2. Attached materials

C. Flocculation

D. Can suppressants be added

III. Launching or dispersal of fibre

A. Effect of way in which energy is applied

B. Effect of wetting or compacting agents

C. Aerosol with fibre droplet nuclei

IV. Dynamics of fibre filters

V. Methods of reducing air-borne concentrations of fibre

While these methods will vary according to the circumstances both general (fibre production, etc.) and local (old vs new plants, etc.) there are broad classes of procedures to be used.

A. Prevention of dispersal
1. Total enclosure from primary bulk handling to finished product — this whenever possible or if only way of doing it.
2. Suction ventilation with filter capture of fibre. Abolishing exhaust to outside air
3. Packaging
   a. Fibre tight and strong
   b. Automatic handling
   c. Reduce handling
   d. Exhaust with filter capture of fibre
   e. Utilize container that can be incorporated in finished product
4. Reduce local applications of energy
5. Wetting, oiling, or compacting of fibre not totally enclosed

B. Prevention of re-dispersal
1. All exhaust properly filtered
2. Immediate vacuuming of spills
3. Frequent vacuuming of settled dust
4. Handle re-processing as carefully as primary
5. Exhaust aerosols (droplet nuclei fibre) to filters
6. Completely enclosed air transport of fibre

C. Dust suppression
1. Humidity — droplet nuclei

D. Dust dilution
1. Large volume exchange — outside exhaust?
2. Large volume with removal of fibre

E. Personnel protection
1. Masks
   a. Question effectiveness
   b. Design better ones regarding comfort and vision
   c. Question primary and secondary filters
   d. More frequent change
   e. Disposable
2. Positive pressure devices
   a. Local or fixed places of work
   b. Mobile or self-contained
3. Operator in enclosed booth
4. Change of clothes
5. Water repellant clothes — changed and washed
6. Special time schedules for workers
   eg: rotation through jobs of varying exposure, limit as to hours per day, days, weeks, years based upon data regarding deposition and removal of fibre and also dose/injury relationships obtained in other studies.
7. Requirement that workers in certain jobs refrain from exposure to other agents eg: cigarette smoking

F. Solid waste disposal
1. Handling of filtered material
   a. Plastic containers and buried
   b. Slurry → settling ponds — buried
2. Rejects — buried or bonded
3. Used materials eg: insulation — buried or bonded

The following outline lists the individuals actively engaged in studies dealing with reducing the concentration and number of inhaled asbestos fibres. We are confident that others, as yet unknown to us, are working in this area and regret that they are not included. The abbreviations (appendix II) indicate the nature of evidence under study In appendix I further details of each study will be found.

Immediately following the outline of work in progress is an analysis of the relative need for initiating new or additional studies.

STUDIES DEALING WITH REDUCING THE CONCENTRATION AND NUMBER OF INHALED ASBESTOS FIBRES

I. *Fibre populations at breathing zone*

A. Mining and milling

du Toit, S. Afr — dc

B. Manufacturing

Holmes, GB — tx

Kesting, WG — tx

Muglich, EG — tx

J-M, US — tx, is, asb. cem. build. prod. production

C. Appliers

Harries, GB — is

Selikoff, US — is

D. Solid waste disposal

Harries, GB — is

Selikoff, US — is

E. Public

Selikoff, US — is

II. *Aerodynamics of asbestos fibre*

III. *Launching and dispersal of fibre*

IV. *Dynamics of fibre filters*

V. *Methods of reducing airborne fibre concentration*

A. Prevention of dispersal (enclosure, packaging, reduce energy, wetting)

Holmes, GB — tx

Kesting, WG — tx

Harries, GB — is

J-M, US — tx etc.

Selikoff, US — is

B. Prevent redispersal (cleaning, filtered exhaust, enclose transport)

J-M, US — tx

Selikoff, US — is

Holmes, GB — tx

C. Dust suppression

D. Dust dilution (ventilation)

Holmes, GB — tx

Muglich, EG — tx

J-M, US — tx, etc.

Selikoff, US — is

E. Personnel protection (masks, clothes, time schedules, smoking)

Harries, GB — is

J-M, US — tx, etc.

Selikoff, US — is

F. Solid waste disposal

Comments

While most, including member companies of the QAMA, of the operating industrial units utilizing asbestos fibre maintain some observation and control of the "dustiness" at various working places, few can be thought of as actually *studying* the problem. For such a purpose, precise determination of the concentration and nature of airborne particles in an environment being deliberately manipulated by efforts designed to influence it are required. A glance at the outline for III indicates the lack of systematic effort in this regard. Our Committee considers no other facet of the asbestos problem to be more important than this one At the same time, we do not believe ourselves at this moment sufficiently informed and we would like more information and guidance before proposing specific studies in this area. With this in mind, we plan to enlist the help of one or more experts in this field via either enlargement of our Scientific Committee or by ad hoc consultation. After further study, we plan specific suggestions. We realize that some of the immediately applicable facets of the problem are receiving attention as indicated in outline III and possibly most of the studies could be done "in house" by the industry. If this mechanism for obtaining the desired information is to be pursued, we strongly urge 1) the use of personnel for these purposes that have such studies as their only or primary responsibility, 2) pooling of resources — personnel, equipment, sites of study, finances — by industries having identical or similar problems. We further urge recognition that some facets of this problem would best be pursued outside the industry proper, as for example a study of "filter dynamics for fibres."

SECTION IV

Studies Dealing with

Development and Evaluation of Methods in the Preceding Considerations

While there is evidence that asbestos fibre can produce pulmonary fibrosis with its sequelae; play an undetermined role in pulmonary and mesothelial carcinogenesis; is related also to pleural plaques and is the central fibre of ferruginous bodies in many instances, the *quantitative* aspects so crucial to the full understanding of these relationships and thus to their prevention is greatly hampered by inadequate methods of study. In some instances the procedures are themselves at fault and in others they have not been applied properly. As examples one might mention; 1) At this time there is no agreement with respect to the criteria upon which a diagnosis of "asbestosis" is to be made either during life or upon histologic examination of the lungs. The same can be said with respect to "mesothelioma." 2) Continuous measurement of airborne fibre concentration, thus giving full meaning to the character of exposure, it practical only upon a very limited scale and meaningful data of this kind is virtually absent up to the present. 3) Reliable identification of the central fibre in ferruginous bodies is still not possible and obscures our understanding of the meaning of these structures in terms of Public exposure.

A major and deliberate effort to promote better methods is urgently needed so that as little activity as possible be wasted in compiling further data of questionable value. While some of this effort in the direction of methodology will doubtless be made by those directly interested in the problems of the biological effects of asbestos fibre, it will likely be necessary to enlist the help of those whose major interest may not be along the lines of biology and fall more nearly in the field of chemistry or physics.

The following is a list of some of the areas and procedures that need better designed and understood methods of study.

I. Characterization of ambient air

A. A practical method for continuous sampling of airborne fibre concentration at the breathing zone.

B. A rapid method for "sizing" the fibres and expressing each as a percentage of the whole.

C. A rapid and reliable method for identifying asbestos as opposed to other kinds of fibres and also quantitatively differentiating between various kinds of asbestos fibres.

II. Recognition of human exposure to asbestos fibre

A. Identification of asbestos bodies as differentiated from other fibrous ferruginous bodies.

B. Development of a "marker" which by examination of urine, blood, sputum, or lung tissue would indicate specific asbestos exposure qualitatively and quantitatively. Can some agent be added to fiber for this purpose?

III. Recognition of biological effects of asbestos fibre

A. Radiologic manifestations of the biologic effects of asbestos.

1. X-ray classification.
2. Contrast between exposed and non-exposed persons with respect to items in x-ray classification.
3. Techniques of radiography for lung and pleura.
4. Use of "standard" films.

B. Criteria for early recognition of inflammation and fibrosis of lung

1. X-ray evidence.
2. Pulmonary function evidence.
3. Histology evidence.
4. Can other evidences be obtained from blood, urine or sputum?

C. Criteria for recognition of neoplasia.

1. Standards for diagnosis of bronchogenic ca.
2. Standards for bronchial metaplasia.
3. Standards for mesothelioma.
4. Value to be placed upon cytology studies.

D. Standards for epidemiologic studies.

1. Standard approaches based on retrospective and prospective methods as to the type of data which is required in order to make study worthwhile.
2. Relative weight to be given mortality data derived from death certificate, hospital records, autopsy, and also from personal examination during life and its termination.
3. Methods of evaluating exposure on the basis of data now extant. Can this be done? Can a standard procedure be set?

The following outline lists the individuals actively engaged in studies dealing with development and evaluation of methods used in the preceding considerations. We are confident that others, as yet unknown to us, are working in this area and regret that they are not included. The abbreviations (appendix II) indicate the nature of evidence under study. In appendix I further details of each study will be found.

Immediately following the outline of work in progress is an analysis of the relative need for initiating new or additional studies.

STUDIES DEALING WITH DEVELOPMENT AND EVALUATION OF METHODS

I. *Characterization of ambient air*

A. Dust sampling

Addingly, GB — tx
LeBouffant, F — tx
Lynch, US — tx
Rendall, S. Afr — mines
Chamber of Mines, S. Afr — mines

B. Sizing fibers

Keenan, US — tx
Speil, US — tx
Walter, WG — tx

C. Identification of fibres

Speil, US — tx
Berkley, US — is
Swettenham, GB — tx
Heron, GB
"Institute of Occ. Health", Netherlands (Joosting) — is
Tousimis, US
Werner, EG
Grimshaw, GB

D. Public

Elfenberger, WG
Heron, GB

II. *Recognition of human exposure to asbestos fibre*

A. Identification of fibre

Einbrodt, WG — ab
Swettenham, GB
Berkley, US
Netherlands group — Joosting
Baden et al., US

B. Development of "marker" of exposure

Bader, US — ab
Gold, GB — ab (quantitative)

III. *Recognition of biological effects of asbestos fibre*

A. Radiology

Gilson (UICC), GB
Viikeri, Fin — ultrasound
Hennig, EG — scintigraphy

B. Criteria for early recognition of inflammation and fibrosis of the lung

Andreeva, SU
Regan, GB — pf,ra,cli
Bader, US — pf
Otto, WG — fb & total dust
Champeix, F — pf,ra
Galy et al., F — pf
Worth et al., WG — pf
Stolbun et al., SU — pf, ballisto

C. Criteria for recognition of neoplasia

Thomson, SA — me
Naylor, US — me
Kotin, US — (mesothelioma registry)
Webster, S. Afr — (mesothelioma registry)

D. Standards for epidemiological studies

Comments

One of the major deterrents to controlling human exposure to asbestos fibre is the lack of a readily usable method of quantitating and sizing "fibre" in the air at the breathing level of the worker. Current methods are cumbersome and time consuming and do not encourage the desired frequency of sampling at the working place. This problem is also faced by others studying industrial and public environments and likely will not be solved by "in house" efforts. Since much of the effort of both sections I and III, dealing with maximum allowable concentration is dependent upon a usable method for monitoring dust, the importance of this facet of "methods" can be readily appreciated.

It seems likely that enough workers are now being attracted to methods for identifying asbestos fibre.

The desirability of a "marker" of the presence and quantity of asbestos fibre retained in the body is obvious. The measurement of urine lead or porphyrin as a marker of lead retention is an example. At this point in time, there are no very logical suggestions for a method applicable to asbestos but the matter should be thoroughly explored. The possibility of an immunological reaction based upon titre is suggested.

The use of radiologic evidence to recognize the biological effects of asbestos fibre is receiving adequate effort at this time. We now know that the radiologic evidence is not the first or earliest discernable manifestation of biological activity of asbestos. McDonald has confirmed the findings of others that abnormality of oxygen transfer across the alveolar membrane precedes radiologic abnormality. This opens the possibility for recognizing hyper-reactors and removing them from exposure. Further exploration of this in both humans and animals is urged at this time. Other efforts to develop methods for earliest recognition of biological reaction to asbestos should be pressed. Here, too, the role of an immunologic response might be explored.

At this time there appears to be sufficient effort being devoted to criteria for neoplasia, especially mesothelioma, and also the methods of epidemiologic study. The problem in this regard is largely that of a failure to apply what is now known.

APPENDIX I

SECTION ONE

Each item sets forth a resumé of work in progress. For each of the four sections (see index) the specific project is arranged alphabetically according to the first letter of the last name of the principal investigator.