Review

THE ASBESTOS DILEMMA: I. ASSESSMENT OF RISK

Fedor VALIĆ

Andrija Štampar School of Public Health, Medical Faculty, University of Zagreb, Zagreb, Croatia

Received March 2002

This paper gives a critical review of current problems related to quantitative health risk assessment of exposure to asbestos, and particularly to chrysotile, the only type of asbestos still available on the market. The paper reviews types, sources, uses and the main recognised health effects of asbestos, paying particular attention to the health-related properties of fibres and the role of their biopersistence. The main focus is on yet unresolved issues which introduce a large margin of uncertainty into the published quantitative risk assessments: 1) Are all asbestos types equally dangerous or is chrysotile asbestos less dangerous than amphiboles? 2) Are health effects of asbestos fibres threshold or non-threshold effects? 3) Are errors in mathematical modelling of risks so great as to make the risk evaluations worthless? Attention is also given to errors in estimates of past exposures, uncertainties and unspecificities of models and to the unfeasibility of practical application of some well recognized risk assessment models.

KEY WORDS: *amphiboles, biopersistence, chrysotile, risk assessment, thresholds*

In 1989, the US Environmental Protection Agency (EPA) issued the "Asbestos Ban and Phase-out Rule", which would have banned practically all uses of asbestos in the USA by 1996 (1). In 1991, however, a US Court of Appeals revoked the ruling. In 1991, the Commission of the European Communities enacted a Directive prohibiting the marketing and use of all amphibole fibres and the products containing them (2). It also prohibited the use of 14 categories of chrysotile products, permitting the continuation of use of the important chrysotile products - asbestos cement and friction materials. However, in 1999, the Commission enacted a Directive prohibiting the use of all asbestos types in EU member-states by the year 2005 (3). Thus in the two parts of the Western world developed an unusual situation of conflicting regulatory approach to the use of asbestos, an issue loaded with scientific controversies for years. The problem induces a dilemma for the responsible authorities in Croatia: Should the country follow the 'ban approach' of the EU or the 'controlled use' approach of the International Labour Organization (ILO) (4), the latter practically supported by the current regulatory situation in the US (official exposure limits)? If the former approach is selected, which is likely in view of the political interest of the country to join the EU, should the rule be applied by the year 2005, although Croatia will not yet have become the member of EU at the time?

TYPES OF ASBESTOS, THEIR SOURCES AND USE

My recent article "Asbestos and Health" describes the types, sources and the use of asbestos in detail (5). There are two basic

mineralogical groups of asbestos: serpentine and amphibole. Chrysotile (white asbestos) is now the only commercially important member of the first group which accounts for more than 98% of the current world consumption of asbestos. The main members of the amphibole group of minerals are amosite (brown asbestos), crocidolite (blue asbestos), and tremolite which mainly occurs as an impurity of chrysotile. Only the first three asbestos types have found commercial use. In general, asbestos minerals are characterised by high tensile strength, flexibility and durability, as well as heat insulation and flame retardant properties. In addition, they do not evaporate, burn or undergo significant reactions with chemicals. Asbestos has been used in thousands of products (see Table 1 for the brief list). Currently, asbestos is used principally in high-density products in which the asbestos fibres are embedded in a cementitious or resinous matrix. Asbestos-cement products, mostly pipes (for drinking water supply, sewage disposal and irrigation), shingles and sheets, account for about 85% of the total use of asbestos.

Natural erosion and many human activities are the sources of asbestos fibres. The latter range from ore recovery and processing, manufacturing, application and usage, to disposal activities. Fibres are also released during the construction and demolition of buildings and possibly during maintenance. Asbestos was produced in 24 countries in the world. In addition, the manufacture of asbestos-containing products took place in more than 100 countries. The world production peaked at over 5 million tonnes, but has been declining since the mid-1970's. The current production is about 2 million tonnes (6).

HEALTH EFFECTS

There is no consistent evidence that drinking or eating asbestos is associated with adverse health effects (7-11); only exposure to airborne asbestos fibres is a proven cause of disease. All types of asbestos, if inhaled at sufficient doses, can cause three main serious health disorders:

Table 1 *Main asbestos-containing products*

Product	Uses
Asbestos-cement products	Water supply and sewage piping Drain pipes and guttering Interior wall panels Casings for electrical wires Fire protection material Chemical tanks
Asbestos friction products	Clutch facings Brake lining for road and railway vehicles Industrial friction materials
Asbestos paper products	Table pads and heat-protective mats Heat and electrical wire insulation Industrial filters for beverages Underlining material for sheet flooring
Asbestos textile	Packing components Heat and fire-resistant clothing Fire-proof curtains
Asbestos felt products other asbestos products	Noise insulation Ceiling tiles Gaskets and packing Paints, coatings and sealants Patching tape Plastics

asbestosis, lung cancer, and mesothelioma. Significant overt clinical symptoms of asbestosis are unlikely to appear until approximately 20 years after the onset of exposure. No asbestosis has been found in the general population, except in populations living in the immediate vicinity of intense and uncontrolled sources of emission. It usually takes 20-40 years between the first exposure to asbestos fibres and the onset of lung cancer. Smokers are at a considerably greater risk of developing lung cancer than nonsmokers. Mesothelioma takes between 30 and 50 years to develop. This form of cancer is unavoidably fatal. Increased mortality rates have been observed in non-occupationally exposed subjects sharing the household with asbestos workers, or living in the vicinity of uncontrolled asbestos emission sources. It remains to be seen whether the observed and projected increases of mesothelioma mortality in the general population of the USA, New Zealand, and some European countries (12-19) are the effects of exposure to asbestos, and particularly to chrysotile, or not. Unlike in cancer, smoking does not contribute to the development of mesothelioma.

HEALTH-RELATED PROPERTIES OF FIBRES

Negative health effects are induced only by fibres which are inhaled, deposited and retained in the respiratory tract. Only fibres thinner than 3 μm, having an aerodynamic diameter of about 10 μm, can enter the conducting airways of the respiratory tract. Longer fibres are more dangerous. Therefore, in the regulations of many countries, as well as in some international recommendations (20), asbestos fibres to be measured in occupational environmental assessment are defined as those having a diameter ≤3 μm, length ≥5 μm, and length to diameter ratio at least 3:1 ("regulated fibres"). There is evidence that the most hazardous asbestos fibres are those longer than 5-8 μm and thinner than 1.5 μm. Early experimental results of *Stanton and Layard* (21) and *Pott* (22) indicated that implanted asbestos fibres of length to diameter ratio <5:1 are not carcinogenic, that the carcinogenicity of fibres of length to diameter ratio <10:1 is small, and that only fibres of length to diameter ratio >10:1 have significant carcinogenic properties. The conclusion is that it would be justifiable to measure fibres of length to diameter ratio >10:1 in the environmental health assessment (23, 24).

Biopersistence is also considered an important health-related property of asbestos fibres. It depends on the relative insolubility of the fibre, that is, on its retention in the respiratory tract. It is generally believed that the greater the biopersistence, the higher the probability of fibrogenic or carcinogenic effect (5, 25), although there are opinions that long retention of fibres in the respiratory tract is not the prerequisite for the formation of neoplasms (26).

UNRESOLVED ISSUES

In spite of years of studies of the effects of asbestos fibres and hundreds of scientific and other papers published, there remains a number of unresolved issues and unanswered questions.

Are all asbestost types equally dangerous?

Scientists and regulators are divided on this issue in two apparently irreconcilable groups. Some believe that the risk of exposure to amphiboles, particularly to crocidolite, is considerably higher than the risk of exposure to chrysotile. A minority disagree. In 1977, a group of experts of the Commission of the European Communities (CEC) concluded that there was general agreement that the risk of mesothelioma was fibre-related and decreased from crocidolite to amosite to chrysotile (27). The summary of a consultation of the World Health Organization (WHO) on occupational exposure limits for asbestos (28) says the following:

> *The human evidence suggests a lower risk of lung cancer from exposure to chrysotile than to crocidolite or amosite [...] Pleural mesothelioma has been produced by all types of asbestos fibre, but in general, the human evidence suggests a much lower risk from exposure to chrysotile than to crocidolite or amosite. Peritoneal mesothelioma can be produced by crocidolite and amosite, but has probably not been produced by chrysotile.*

A Working Group of the International Programme on Chemical Safety (IPCS) on the Reduction of Asbestos in the Environment (29) recommended as follows: "In any given situation, priority should be given to the control of air pollution by amphibole asbestos fibres (crocidolite, amosite, tremolite)". The 1996 CEC's evaluation says:

> *Recent studies have shown that amphibole-type fibres are more harmful than chrysotile... In general, epidemiologically, the risk levels seem to be, in descending order, crocidolite and amosite (two amphibole types of asbestos), followed by chrysotile and anthophyllite (another amphibole)* (30).

The latest evaluation of IPCS/WHO in 1998 (31) agreed with the previous evaluation of 1986 (7) that "the risk of mesothelioma in persons exposed to chrysotile is lower than the risk in persons exposed to crocidolite or amosite".

There are scientists and regulators who do not agree with the significant difference in the potency between fibres of different asbestos types. This is reflected in different approaches of the two groups in setting exposure limits. It is obvious that exposure limits for amphiboles must be lower than for chrysotile if the risks of exposure to the former are higher. Table 2 reflects the differences in the approach of authorities in a number of member states of EU (30); while the exposure limits are higher for chrysotile than for other types of asbestos in Belgium, France, Greece, Italy, Netherlands, Spain, United Kingdom and EU, there is no difference in Austria, Denmark, Finland or Germany. The prestigious American Conference of Governmental Industrial Hygienists (ACGIH) also differently evaluated chrysotile and amphibole asbestos (32). However, the US Occupational Safety and Health Administration (OSHA) (33) does not accept this approach - just like EPA which attempted to prohibit all the asbestos types (1). Under the influence of these US governmental agencies, the ACGIH, in its latest list of threshold limit values (34), adopted the OSHA limit of 0.1 f/ml for all asbestos fibres. It is surprising, however, that they included chrysotile among substances for which

Table 2 *Occupational exposure limits (f/ml) for chrysotile and amphiboles*

Source	Chrysotile	Amosite	Crocidolite
WHO (1989)	1	<1	<1
ACGIH (1995/1996)	2	0.5	0.2
EPA (1989)	ban	ban	ban
OSHA (1994)	0.1	0.1	0.1
Croatia (1992/1993)*	2	1	0.5
	Chrysotile	**Other asbestos types**	
	(Commission of the European Communities, 1996)		
Austria	0.15	0.15	
Denmark	0.3	0.3	
Finland	0.3	0.3	
Germany	0.15	0.15	
Belgium	0.5	0.15	
France	0.3	0.1	
Greece	1.0	0.5	
Italy	0.6	0.2	
Netherlands	0.3	0.1	
Spain	0.6	0.3	
United Kigdom	0.5	0.2	
EU	0.6	0.3	

*Exposure limits expressed as counts of fibres of undefined dimensions

information is being solicited, which suggests doubts about the TLV of this substance. Table 2 shows that Croatia has enacted different exposure limits for different asbestos types (35), but the fibres are not physically specified.

Table 3 shows the EPA's inconsistency in the approach to carcinogenic potency of different asbestos fibres. It shows modified values of the coefficient K_L, taken from an EPA publication (36), indicating considerable differences in the potency of different asbestos fibres. The coefficient K_L reflects the carcinogenic potential of the exposure to carcinogens; it is the estimated increase in lung cancer risk due to one-year exposure to the unit concentration of 1 f/ml. The values presented in Table 3 clearly show that the carcinogenic risk is by far the lowest in the exposure to chrysotile only, with the exception of chrysotile in textile production. Exposure to amosite fibres alone involves a much greater risk, as is the case with the combined exposure to amphiboles and chrysotile. The high K_L value in pure chrysotile textile production is attributed to a significantly higher content of more carcinogenic long chrysotile fibres in the textile production (37-40).

Rich evidence of the significant difference in the potencies between fibres of chrysotile and amphiboles gave grounds for introducing "the chrysotile hypothesis" and "the amphibole hypothesis". The first says that the human risk becomes acceptable at a sufficiently low exposure level to chrysotile, and the second that the carcinogenic risk at low concentrations of chrysotile is present only if amphiboles are also present. These hypotheses are not generally accepted; they have particularly been rejected by the US regulatory agencies (1, 33) and by the Ramazzini Society (12, 41). The controversy about whether there is a difference in the carcinogenic potency between chrysotile and amphibole fibres is continued in more recent papers by most reputable authors in the field. While *Berry* (42), *Landrigan an co-workers* (43), and *Dement* (44) believe that chrysotile is less potent than amphiboles in its ability to cause mesothelioma, and *Hodgson and Darnton* (45) conclude that specific risks of mesothelioma from chrysotile, amosite and crocidolite are in the ratio 1:100:500, respectively, *Landrigan and co-workers* and *Dement* consider that the lung cancer risk from chrysotile is at least as high as that from amphiboles, and *Smith and Wright* (46) regard chrysotile as the main cause of pleural mesothelioma in humans. While *McDonald and McDonald* (50) and *McDonald* (53) state that the carcinogenic risk at present day levels of exposure to commercial chrysotile is vanishingly small and that the remaining risk is due to contamination of chrysotile by the amphibole tremolite, *Dement* (44) maintains that chrysotile should not be controlled differently than other asbestos types.

In the cohort of some 11,000 Quebec miners

Table 3 *Weighted values of unit exposure risk K_L (36)*

Asbestos process or use	Types of fibre	$K_L x 10^4$
Textile production	Predominantly Chrysotile	200
Friction products manufacturing	Chrysotile	2.3
Mining and milling	Chrysotile	9.8
Amosite insulation production	Amosite	430
All processes	Amosite Chrysotile Crocidolite	65
All processes except mining and milling	Amosite Chrysotile Crocidolite	100

and millers (47-53), 25 cases of mesothelioma were identified from miners in the Thetford Mines region and 8 from the large mine at Asbestos. The proportion of tremolite in the chrysotile was 3 times higher in the former than in the latter region. The analysis of deaths from mesothelioma in men employed in the Thetford Mines, with matched references, showed that odds ratios for work in the central mines, where the tremolite content was 3 times higher, were significantly elevated for mesothelioma and lung cancer. By contrast, in the peripheral mines, where the tremolite content was 3 times lower, there was little or no evidence of increased risk. The authors conclude that these long-term studies - including data from as early as 1970's - show that chrysotile rarely caused mesothelioma and was not a major cause of lung cancer, except at very high levels of exposure. They attribute the remaining risk to tremolite, because its biopersistence is much higher than that of chrysotile. However, the Mount Sinai group (54) in their analysis of the lung and mesothelial tissues taken from 151 human malignant mesothelioma cases, found asbestos fibres in almost all the lung tissues as well as in the mesothelial tissue, the most common asbestos types being an admixture of chrysotile and amphiboles, followed by amphiboles alone and chrysotile alone. The most common of asbestos types in the mesothelial tissues were chrysotile alone, followed by chrysotile plus amphibole, and amphibole alone. They conclude that chrysotile can induce human malignant mesothelioma without the presence of amphiboles, since, in some of the mesothelioma cases, the fibres detected in the lung or mesothelial tissues were exclusively chrysotile fibres.

The controversy continues.

Are health effects of asbestos fibres threshold or non-threshold effects?

All asbestos-related diseases are dose-related: the higher the concentration and duration of exposure, the higher the prevalence of the disease and mortality. However, the form of the dose-response curve at low doses, typical for the exposure of general population, is not known. There are contradictory opinions as to whether the dose-response relationship in the region of low doses is linear or not. It is practically impossible to measure the effects at such low doses either epidemiologically or experimentally. It is for this reason that mathematical extrapolations ("low-dose extrapolations"), which carry errors of several orders of magnitude, are used in the quantitative risk assessments. I criticised these extrapolations in 1988 (55) and again in 1991 (56) and 1993 (57). Recently, in 2001, *Berman* (58) reported that "the published dose-response coefficients for asbestos vary by more than a factor of 500 for lung cancer and more than a factor of 1,000 for mesothelioma". Extrapolation of the most frequently used linear relationship into the origin of coordinates means that there is no exposure threshold, i.e. that even the lowest exposure to asbestos may carry some risk of disease and death. Others, however, believe that there is an asbestos fibre exposure threshold for chrysotile below which there will be no pathologic effects (particularly asbestosis or lung carcinoma) or that the effects are so rare that they can not be epidemiologically detected. As negative effects can not be proven in practical risk assessment, the issue remains unresolved. An expert group of the CEC concluded the following in 1977 (27):

> *It is impossible to come to reliable quantitative assessment of the risk of malignancies for the general public. It is possible that there is a level of exposure (perhaps already achieved in the general public) where the risk is negligibly small.*

The evaluation of IPCS/WHO in 1986 (7) was:

> *In the general population the risks of mesothelioma and lung cancer attributable to asbestos can not be quantified reliably and are probably undetectably low. Cigarette smoking is the major etiological factor in the production of lung cancer in the general population. The risk of asbestosis is virtually zero.*

However, the latest IPCS/WHO evaluation in 1998 (31) stated that no threshold had been identified for carcinogenic risks from chrysotile asbestos. There is an almost general consensus that no threshold exists for amphiboles. There is still a controversy as to whether there is a threshold, or at least a practical threshold, for chrysotile. Studies are limited to only two industrial cohorts with relatively pure exposure

to chrysotile fibres containing sufficient high quality data for exposure-response analysis. These studies include the Quebec miners and millers (47-53, 59) and South Carolina textile workers (37-40). Table 4 shows standard mortality from lung cancer in Quebec miners and millers (48), 1976-1988, in relation to exposure accumulated up to the age of 55 years, and the lung cancer mortality by cumulative exposure in South Carolina workers (39) employed between 1940 and 1990. There is no indication of a trend in standard mortality over 7 lowest categories of exposure of miners and millers (<10-<990 f/ml yrs). The standard mortality was elevated at the three highest levels, i.e. at the cumulative exposure of more than 990 f/ml yrs. A completely different result was obtained in South Carolina textile workers. There was a consistent increase in the risk of lung cancer with increasing cumulative exposure in all the exposure categories of cumulative exposure more than 2.7 f/ml yrs. The proportional mortality from mesothelioma in the Quebec cohort was only 0.45% (33 deaths among 7,312 workers) by the end of 1988. Comparing the very high slope of 0.021 per f/ml yr in textile workers with the very low slope of 0.0005 per f/ml yr in Quebec miners and millers, the authors of the last exposure response analysis (40) attribute this large difference to the considerably higher proportion of carcinogenic long fibres in the textile production. It was on the basis of the results obtained in Quebec workers that the authors (48, 50, 53) concluded that chrysotile was not the cause of lung cancer, except at very high levels of exposure above 25-30 f/ml, well above current exposure even under poor conditions. Can the finding that there was no trend in standard mortality over 7 lowest exposure categories of miners and millers be taken as the basis for the conclusion that there is a practical threshold for chrysotile (49)?

The situation with mesothelioma is somewhat different. The standard mortality rates in several countries show an increasing trend. The results of some evaluations caused panic. British (14, 19), French (17), New Zealand (15), and the US (12, 18) data projected thousands of deaths per year of mesothelioma in the decades to come. As a considerable proportion of diagnosed mesothelioma was believed to be the consequence of exposure to asbestos fibres, there is a tendency to attribute all these deaths to the effects of these fibres without an objective proof and without differentiating the type of fibres. It is worth noting that the description of mesothelioma in literature preceded the exploitation of asbestos (59) and that other causes of mesothelioma have also been described (60). The role of Simian virus SV40 in the development of human mesothelioma has recently received more attention. Some authors (60) assume that SV40 may contribute to the development of human mesotheliomas that occur in people not exposed to asbestos.

Table 4 *Lung cancer mortality in relation to cumulative exposure (39,48)*

MINERS			TEXTILE WORKERS		
Exposure (f/ml x yrs)	Deaths O/E	Standard mortality	Exposure (f/ml x yrs)	Deaths O/E	Standard mortality
<10	36/31.4	1.14	<1.4	7/7.6	0.92
10<33	28/25.3	1.11	1.4-2.7	4/5.5	0.73
33<99	33/31.3	1.05			
99<198	39/24.4	1.60	2.7-6.9	15/6.2	2.4
198<330	26/22.8	1.14	6.9-27.0	10/5.1	1.96
330<660	32/28.3	1.13	27-110	16/5.2	3.08
660<990	20/7.3	1.15	110-274	18/2.2	8.18
			>274	2/0.2	10.00
990<1320	16/10.7	1.50			
1320<3300	42/25.4	1.65			
>3300	22/7.2	3.04			

O - observed; E - expected

However, they state that the available epidemiologic data are insufficient to explain the role that SV40 may have played in contributing to the increased incidence of mesothelioma currently recorded. Other authors (18, 61, 62) propose that asbestos and SV40 may be cocarcinogens.

The latency period for the development of mesothelioma is between 30 and 50 years, so that the current mesothelioma deaths are predominantly the consequence of exposure to mixtures of chrysotile and amphiboles in the far past when the exposure levels were incomparably higher than those of today. It is impossible to evaluate whether the current (considerably lower) exposures to pure chrysotile would bring about similar consequences.

UNCERTANTIES IN RISK ASSESSMENT

Errors in estimates of past asbestos exposure

The current mortality from asbestos-related cancer is the consequence of exposures of 20-50 years ago, or even longer. There is no doubt that the exposure levels in the distant past were considerably higher than those of today. As an example, Table 5 shows the concentrations measured in mines and towns of Canada in the period 1973 to 1995 (63).

In the distant past, the techniques of exposure measurement did not specify asbestos fibres, but referred to either gravimetric concentration of total particles in the air, expressed in grams or mg per m^3 or, later, to count concentrations of particles (not fibres) expressed in million particles per cubic foot of air (mppcf). Thus, the early methods measured all particles, of which fibres constituted only a minor fraction. As exposure levels in the past must be taken into account in the quantitative risk assessment, various authors estimated assumed specific concentrations of airborne asbestos fibres converting the measured gravimetric or count concentrations of total particles to the currently defined fibres using a number of mathematical conversions. These conversions relied on many dubious assumptions and approximations, and included errors of several orders of magnitude into the mathematical estimates of historical airborne fibre concentrations. This is one of the main reasons why I cautioned - quite early - that the quantitative risk assessment equations and particularly low dose extrapolations used for predicting mortality or morbidity in populations exposed to considerably lower exposure levels were very uncertain (56,57). Table 6 shows some errors in the conversion of such concentrations. The first part of the table shows the relationships between asbestos fibre diameter and length and the concentration expressed in fibres per ml for the gravimetric concentration of 10 ng/ml air [based on calculations by Pott (22)]. The table shows that the same air with weight concentration of 10 ng/ml may contain 32 f/ml if the fibre diameter

Table 5 *Concentrations in mines and towns of Canada: 1973-1995 (63)*

	Mines			Towns
Year	Mean value	Highest value	Lowest value	Mean value
1973	15.9	52.2	4.3	0.08
1974	11.4	24.7	3.3	0.08
1975	8.7	16.7	2.7	-
1977	2.6	5.4	1.5	0.04
1979	1.1	2.0	0.7	0.05
1981	1.0	1.5	0.6	0.02
1983	0.8	1.0	0.5	<0.01
1985	0.7	1.4	0.3	<0.01
1987	0.5	0.9	0.1	<0.01
1989	0.7	0.9	0.5	<0.01
1991	0.6	0.7	0.3	<0.01
1993	0.4	0.5	0.3	<0.01
1995	(0.4)	(0.5)	(0.2)	<0.01

Results in parentheses - personal communication

Table 6 *Variations in concentration conversions*

No. of asbestos fibres in ml of air corresponding to weight concentration of 10 ng/ml (22)

Diameter (μm)	Length (μm)	f/ml
2.0	40	32
1.0	10	500
0.25	5	16,000
0.03	0.63	8,200,000

Conversion of weight concentration to no.of fibres per unit volume (36)

$\mu g/m^3 \rightarrow f/ml$	0.5-150 (from 6 studies)
	30 (geometric mean)

Conversion of particles per unit volume into no. of fibres per unit volume (64)

mppcf→f/ml	0.5-47.4

is 2.0 μm and the length 40 μm, while it may contain 8,200,000 f/ml of fibres with the diameter 0.03 μm and the length 0.63 μm. The errors involved in the conversion of weight concentrations of total particles of unknown size distribution into the count concentrations of fibres of a defined size fraction are so great that the obtained results may be complete nonsense. Table 6 also shows an example of EPA's conversion in 1986 (36). EPA took 30 (the geometric mean of conversion factors ranging 0.5-150 obtained in six studies) as the conversion factor to be used, introducing a possible error of more than 200 in the conversion. *Robock* reported in 1984 (64) that the conversion factor for converting mppcf into f/ml obtained in a large number of samples was between 0.5 and 47.8, which introduces a hundredfold error into conversions.

Uncertainties and unspecificities of models

Table 7 shows the estimation of lifetime risk due to lethality from mesothelioma (L: excess deaths per million population) induced by the asbestos concentration of 0.0004 f/ml for an age of 73 years, calculated by the well known equation of the National Research Council of the US National Academy of Sciences (NRC/NAS) $L = C (conc.) (age)^K$ (65). Using the values of the coefficients C ($0.85\text{-}7.22 \times 10^{-8}$) and K (2.6-5.0), obtained in epidemiological investigations, the number of calculated excess deaths ranges from 0.2-60,000 per million population, yielding a ratio of up to 300,000 in estimated mortality per million population and rendering the risk assessment meaningless (56).

In 1991, I criticised (56) those EPA's uncertainties in risk assessments which led to their proposal of the asbestos ban. Table 8 shows the number of cancer cases expected by EPA to be

Table 7 *Lifetime risk estimates of mesothelioma death in seven studies (65) based on equation L = c (0.0004) (73)^k*

c	k	2.6	3.0	3.2	3.5	3.8	4.0	5.0
0.85×10^{-8}		0.2	1.3	3.0	11	41	97	7000
2.53×10^{-8}		0.7	4	9	34	120	290	21000
7.22×10^{-8}		2	11	26	96	350	820	60000

(exposure level 0.0004 f/ml, lifetime 73 years)

Table 8 *Cancer cases predicted by EPA to be avoided by the ban of asbestos use in the future period of 13-15 years (56)*

Product	1986 (36)	1988 (66)	1989 (1)
Vinyl-asbestos floor tiles	468	0.0	-
Friction products	386	282.0	99.39-143.7
Asbestos-cement pipes	82	6.0	2.10-4.38
Asbestos-cement plates	31	0.9	0.70-1.51
Gaskets	-	14.0	6.68-42.54
Others	33	12.9	39.13-9.87
Total	**1,000**	**315.8**	**148-202**

avoided in 13 years following the proposed asbestos ban, as set forth by three consecutive EPA proposals. The very fact that the number of cancers varied from 1,000 in 1986 (36) to 315.8 in 1988 (66), ending with 148-202 in the Final Rule of 1989 (1), sheds strong doubt on EPA's risk estimates.

I wish to single out the problem of asbestos-induced cancers due to exposure to friction materials. In the Final Rule of 1989 (1), EPA attributes up to 144 projected cases of cancer to the exposure to friction materials. These risks account for the majority of all the risks in the Final Rule. These risk assessments were obtained using exposure-response relationships for cancer in different industries and in populations exposed to different asbestos materials of which the friction material is only one. In their study of more than 13,500 workers manufacturing friction materials in the period 1942-1980, *Berry and Newhouse* (67) found little excess cancer, and the only excess mortality comprised 10 deaths from pleural mesothelioma, out of which 8 at least partly due to exposure to crocidolite. The slope for increased lung cancer risk was only 0.00058 fibres/ml years. *McDonald and co-workers* (68) found practically no lung cancer risk and no mesothelioma in the group of long-term workers and in higher exposure categories in their study of more than 3,500 men employed in the manufacturing of friction products in the period 1938-1958. The slope for increased lung cancer risk was practically zero. The authors interpreted the results as "doubtful whether there was any significant lung cancer excess". I strongly disagreed (57) with the approach to the estimation of the projected number of cancers using the mean of slopes derived in all studies, of which only two (by far the lowest) were obtained in the friction products exposures. The population with expected exposure to asbestos fibres are garage mechanics, because of their work on the maintenance and repair of automobile asbestos-containing brakes and clutches. In a large case-control survey of all cases of mesothelioma diagnosed by pathologists in the USA and Canada during a defined period, *McDonald* (69) observed a substantial excess risk of mesothelioma in many occupations with exposure to asbestos, and particularly to amphiboles, but no excess was observed in the category of garage mechanics. In 1988 (70) I analysed all the available literature regarding asbestos risk in vehicle manufacture, maintenance and repair, and concluded that, provided good work practices are followed and no amphiboles are used, detectable risks in vehicle maintenance and repair are not to be expected. As in 1991 (56) and 1993 (57), I still disagree with the EPA's approach to the estimation of the projected number of cancers due to exposure to friction materials by using a mean slope of 11 studies (1, 36), of which only two (having by far the lowest slopes) were obtained in the friction products exposure. It is hardly justifiable to estimate risks due to exposure to one type of fibre population by using the slopes obtained in exposure to completely different fibre populations, while being fully aware of the large variations among the slopes. This approach has resulted in an ungrounded overestimation of the projected number of cancers in exposure to friction materials.

Unfeasibility of practical application of risk assessments

As early as in 1988 and later in 1993, I pointed to the implications and practical unacceptability of the results of some well-known published asbestos risk estimates (55, 57). Table 9 shows my calculations of exposure limits for asbestos in the atmosphere derived from some of these risk assessments.

A 1986 WHO Expert Meeting proposed the lifetime risk estimate for smokers (mesothelioma: $12x10^{-5}$, lung cancer: $16x10^{-5}$ as upper limits of the number of expected deaths per 100,000 population) at an assumed airborne asbestos fibre concentration of 500 f/m^3 (71). Assuming that the acceptable risk, used for carcinogens in the WHO Water Quality Guidelines (72), is $1x10^{-5}$, the calculated exposure limit is 18 fibres per cubic meter of air. Taking the risk estimate of $13.5x10^{-5}$ for nonsmokers and using the same acceptable risk ($1x10^{-5}$), the obtained exposure limit is 37 fibres per cubic meter. Confronted with prevalent concentrations found in the air of rural areas with no specific asbestos sources (up to 100 f/m^3) (7), these exposure limits seem to suggest that in areas without any specific source of asbestos emission, a nearly 6-fold reduction of current asbestos levels would be required, which is practically impossible to achieve.

Table 9 also illustrates that an exposure limit of 45 asbestos fibres per cubic meter can be derived from the asbestos risk estimate published in the asbestos concentration of 400 fibres per cubic meter, the respective calculated exposure limits are 9 and 22 fibres per cubic meter. In other

Table 9 *Estimated lifetime risks from exposure to asbestos at 500 f/m³ and calculated threshold limit values at the assumed acceptable risk of 1x10⁻⁵ (57)*

Expert meeting (71) (upper limit)	Risk (smokers): $12x10^{-5}$ (mesothelioma) + $16x10^{-5}$ (lung cancer) = $28x10^{-5}$
	TLV on the basis of accceptable risk $1x10^{-5}$: 500/28 ~ 18 f/m³
	Risk (non-smokers): $12x10^{-5}$ (mesothelioma) + $1.5x10^{-5}$ (lung cancer) = $13.5x10^{-5}$
	TLV on the basis of accceptable risk $1x10^{-5}$: 500/13.5 ~ 37 f/m³
Air Quality Guidelines (73)	Risk (30% smokers): $1x10^{-4}$ (mesothelioma) + $1x10^{-5}$ (lung cancer) = $11x10^{-5}$
	TLV on the basis of accceptable risk $1x10^{-5}$: 500/11 ~ 45 f/m³
Prevalent asbestos concentrations: rural areas<100 f/m³, urban areas<100-10000 f/m³,indoor 400-500 f/m³	

WHO Air Quality Guidelines in 1987 ($11x10^{-5}$ for a population with the hypothetical proportion of 30% smokers) (73). This value is lower or as low as the concentrations found in rural areas without specific asbestos emission. The table also shows prevalent asbestos fibre concentrations in urban areas (from fewer than 100 to 10,000 per cubic meter) (7).

Table 10 shows the same calculations on the basis of the risk assessment by the NRC/NAS (65). Applying the same level of acceptable risk ($1x10^{-5}$) and using the number of estimated deaths from mesothelioma and lung cancer for male smokers and nonsmokers at the assumed

words, these limits require a nearly 10-fold reduction of asbestos fibre levels in rural areas without specific asbestos emission!

It is obvious that mathematical extrapolations of asbestos risk lead to unfeasible threshold limit values.

CONCLUSIONS

There is no doubt that fibres of all the prevalent forms of asbestos can cause lung cancer and mesothelioma. The weight of evidence convincingly suggests that amphiboles are more

Table 10 *Estimated lifetime risks* from exposure to asbestos at 400 f/m³ and calculated threshold limit values at the assumed acceptable risk of 1x10⁻⁵ (57)*

Mesothelioma	$15.6x10^{-5}$
Lung cancer — male smoker	$29.2x10^{-5}$
Lung cancer — male non-smoker	$2.7x10^{-5}$
Lung cancer — female smoker	$10.5x10^{-5}$
Lung cancer — female non-smoker	$1.4x10^{-5}$
Risk — male smokers: $15.6x10^{-5} + 29.2x10^{-5}=44.8x10^{-5}$	
TLV on the basis of accceptable risk $1x10^{-5}$: 400/44.8 ~ 9 f/m³	
Risk — male non-smokers: $15.6x10^{-5} + 2.7x10^{-5}=18.3x10^{-5}$	
TLV on the basis of accceptable risk $1x10^{-5}$: 400/18.3 ~ 22 f/m³	

*National Research Council of the US Academy of Science, 1984 (65)

potent carcinogens than chrysotile. No threshold has been identified for any of the types of asbestos except possibly for chrysotile; a practical threshold was found in chrysotile mining operations, in the manufacturing of chrysotile friction products and in some cohorts of workers in asbestos-cement production. The unit risks, estimated in studies acceptable as regards the number of examinees, the duration of follow-up and the quality of data vary by several orders of magnitude. To a large extent, this is the consequence of considerable uncertainty in the estimates of past exposure levels due to errors in conversion from weight ($\mu g/m^3$) or count (mppcf) concentrations of total particles to the currently used count concentrations of defined fibres. The practical application of unit risks of such uncertainty leads to unachievable exposure limits. In spite of hundreds of papers published on asbestos health effects, there are still important unresolved issues. The effects seen today are the consequence of uncertain exposure of 20-50 years ago. It cannot be predicted with any degree of certainty what will the consequences of the current, incomparably lower exposure levels be in the future. Yet, there is no doubt that it is advisable to replace any potential carcinogen with noncarcinogenic or less carcinogenic material whenever possible. At this point in time, however, there are few materials of known toxicity/carcinogenicity and at least equal technological performance. There is a potential for the development of such materials, but their toxicological properties have not been evaluated sufficiently. This is the main problem the world is facing on the eve of the possible worldwide asbestos ban, which will be considered in the second part of this paper: "The Asbestos Dilemma: II. The Ban".

REFERENCES

1. US Environmental Protection Agency (EPA). Asbestos manufacture, importation, processing, and distribution in commerce prohibitions. Final Rule. Federal Register 1989; 54/132:29462-29513.
2. EU Commission Directive 91/659/EEC. Official Journal L.363.31/12/1991, p. 36-38.
3. EU Commission Directive 1999/77/EC. Official Journal L.207.06/08/1999, p.18-20.
4. International Labour Organization (ILO). Asbestos recommendation, No. 172. Geneva: ILO, 1986.
5. Valić F. Asbestos and health. Local authorities, Health and Environment Briefing Series 25. Copenhagen: WHO Regional office for Europe, 1998.
6. Landrigan PJ, Nicholson WJ, Suzuki Y, Ladou J. The hazards of chrysotile asbestos: a critical review. Industrial Health 1999;37(3):271-80.
7. International Programme on Chemical Safety/ World Health Organization (IPCS/WHO). Asbestos and other natural mineral fibres. Environmental Health Criteria 53. Geneva: WHO; 1986.
8. IARC Monographs on Evaluation of Carcinogenic Risks to Humans. Suppl. 7. Lyon: International Agency for Research on Cancer; 1987.
9. Commission of the European Communities (CEC). Official Journal of the European Communities, 1995;(C326/38).
10. World Health Organization (WHO). Guidelines for drinking water quality. Vol.2. Geneva: WHO; 1996.
11. Valić F, Beritić-Stahuljak D. Is chrysotile asbestos exposure a significant health risk to the general population? Central Eur J Publ Health 1993;1:26-30.
12. Collegium Ramazzini. Updating the epidemiology of asbestos disease. Proceedings, Annual Ramazzini Days. Med Lav 1995;86(5):388-500.
13. Peto J, Henderson BE, Pike MC. Trends in mesothelioma incidence and the forecast epidemic due to asbestos exposure during world war II. In: Peto J, Schneiderman M, editors. Quantification of occupational cancer. Banbury Report 9. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory; 1981. p. 51-72.
14. Peto J, Decarli A, La Vecchia C, Levi F, Negri E. The European mesothelioma epidemic. Br J Cancer 1999;79:566-672.
15. Kjellstrom T, Smartt P. Increased mesothelioma incidence in New Zealand: the asbestos-cancer epidemic has started. New Zealand Med J 2000;113:485-90.
16. Bourdes V, Boffetta P, Pisani P. Environmental exposure to asbestos and risk of pleural mesothelioma: review and meta-analysis. Eur J Epidemiol 2000;16:411-7.
17. Banaei A, Auvert B, Goldberg M, Gueguen A, Luce D, Goldberg S. Future trends in mortality of Frenchmen from mesothelioma. Occup Environ Med 2000;57:488-94.
18. Carbone M, Rizzo P, Pass H. Simian virus 40: the link with human malignant mesothelioma is well established. Anticancer Res 2000;20:875-7.
19. Coggon D. Occupational cancer in the United Kingdom. Environ Health Perspect 1999;107 (Suppl.2):239-44.

20. World Health Organization (WHO). A recommended method by phase-contrast optical microscopy (membrane filter method). Geneva: WHO; 1997.
21. Stanton MF,Layard D. The carcinogenicity of fibrous minerals. In: Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods. Special publication 506. Washington (DC): US National Bureau of Standards; 1978. p. 143-151.
22. Pott F. Some aspects of the dosimetry and of carcinogenic potency of asbestos and other fibrous dusts. Staub-Reinhalt Luft 1978;38:486-90.
23. Walton WH. The nature, hazards and assessment of occupational exposure to airborne asbestos dust - a review. Ann Occup Hyg 1982;25:117-247.
24. Valić F, Skurić Z. Metodologija ocjenjivanja profesionalne izloženosti vlaknima azbesta [Methodology of the evaluation of occupational exposure to asbestos fibres, in Croatian]. Arh Hig Rada Toksikol 1988;39:169-81.
25. Kane AB, Boffetta P, Saracci R, Wilbourn JD, editors. Mechanisms of fibre carcinogenesis. IARC Scientific Publication No. 140. Lyon: International Agency for Research on Cancer; 1996.
26. Nicholson WJ, Landrigan PJ. The carcinogenicity of chrysotile asbestos. In: Mehlman MA, editor. Advances in modern environmental toxicology. Volume XXII. Princeton (NJ): Princeton Scientific Publication; 1994. p. 407-23.
27. Commission of the European Communities (CEC). Public health risks of exposure to asbestos. Bruxelles: CEC; 1977.
28. World Health Organization (WHO). Occupational exposure limits for asbestos. Geneva: WHO; 1989.
29. International Programme on Chemical Safety/ World Health Organization (IPCS/WHO). Reduction of asbestos in the environment (ICS/ 89.34.). Geneva: International programme on Chemical Safety; 1989.
30. Commission of the European Communities (CEC). Communication 426. Bruxelles: CEC; 1996.
31. International Programme on Chemical Safety/ World Health Organization (IPCS/WHO). Chrysotile asbestos. Environmental Health Criteria 203. Geneva: WHO; 1998.
32. American Conference of Governmental Industrial Hygienists (ACGIH). Occupational exposure limits 1995/1996. Cincinnati (OH): ACGIH; 1996.
33. Occupational Safety and Health Administration (OSHA). Occupational exposure to asbestos; Final Rule. Federal Register 1994;59:40964-41158.
34. American Conference of Governmental Industrial Hygienists (ACGIH). 2001 threshold limit values for chemical substances and physical agents & biological exposure indices. Cincinnati (OH): ACGIH; 2001.
35. Pravilnik o maksimalno dopustivim koncentracijama štetnih tvari u atmosferi radnih prostorija i prostora i o biološkim graničnim vrijednostima [Threshold limit values of hazardous materials in the air of work premises and biological threshold limits, in Croatian]. Narodne novine 1992/1993; (92):2088-111.
36. US Environmental Protection Agency (US EPA). Airborne asbestos health assessment update. EPA/600/8-84/003F. Washington (DC): Environmental protection Agency; 1986.
37. Dement JM, Wallingford KM. Comparison of phase contrast and electron microscopic methods for evaluation of occupational asbestos exposures. Appl Occup Environ Hyg 1990;5:242-7.
38. Dement JM, Brown DP, Okun A. Follow-up study of chrysotile asbestos textile workers: cohort mortality and case control analyses. Am J Ind Med 1994;26:431-47.
39. Dement JM, Brown DP. Lung cancer mortality among asbestos textile workers: a review and update. Ann Occup Hyg 1994;38:525-532.
40. Stayner L, Smith R, Bailer J *et al*. Exposure-response analysis of risk of respiratory disease associated with occupational exposure to chrysotile asbestos. Occup Environ Med 1997;54:646-652.
41. LaDou J, Landrigan P, Bailer J, Foa V, Frank A on behalf of the Collegium Ramazzini. A call for an international ban on asbestos. Can Med Ass J 2001;20:489-490.
42. Berry G. Models for mesothelioma incidence following exposure to fibers in terms of timing and duration of exposure and the biopersistence of the fibers. Inhalation Toxicol 1999;11:11-30.
43. Landrigan PJ, Nicholson WJ, Suzuki Y, LaDou J. The hazards of chrysotile asbestos: a critical review. Indust Health 1999;37:271-80.
44. Dement J. Differences in carcinogenicity between asbestos types. 2001 EPA Asbestos Health Effects Conference; May 2001; Oakland (CA) [cited 10 March 2002]. Available from URL: http:// www.epa.gov/swerrims/ahec/summary.htm
45. Hodgson JT, Darnton A. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. Ann Occup Hyg 2000;44:565 601.
46. Smith AH, Wright CC. Chrysotile asbestos is the main cause of pleural mesothelioma. Am J Ind Med 1996;30:252-66.
47. McDonald JC, Liddell FDK, Dufresne A, McDonald AD. The 1891-1920 birth cohort of Quebec chrysotile miners and millers: mortality 1976-1988. Br J Ind Med 1993;50:1072-81.
48. Liddel D. Cancer mortality in chrysotile mining and milling: exposure-response. Ann Occup Hyg 1994;38:519-23.

49. Gibbs GW, Valić F, Browne K, editors. Health risks associated with chrysotile asbestos. Ann Occup Hyg 1994;38:399-426.
50. McDonald JC, McDonald AD. Chrysotile, tremolite, and carcinogenicity. Ann Occup Hyg 1997;41:699-705.
51. McDonald AD, Case BW, Churg A *et al*. Mesothelioma in Quebec chrysotile miners and millers: epidemiology and aetiology. Ann Occup Hyg 1997;41:707-19.
52. Liddel FDK, McDonald AD, McDonald JC. The 1891-1920 birth cohort of Quebec chrysotile miners and millers - development from 1904 and mortality to 1992. Ann Occup Hyg 1997;41:13-36.
53. McDonald JC. Carcinogenicity of fibrous tremolite in workplace and general environments. 2001 EPA Asbestos Health Effects Conference; May 2001; Oakland (CA) [cited 10 March 2002]. Available from URL: http://www.epa.gov/swerrims/ahec
54. Suzuki Y, Yuen SR. Asbestos tissue burden study on human malignant mesothelioma. Indust Health 2001;39:150-60.
55. Valić F. Risk assessment of non-occupational asbestos exposure - can it be done? Arh Hig Rada Toksikol 1988;39:499-505.
56. Valić F. Some health aspects of environmental asbestos exposure. Proceedings of the AIA/NIOSH International Colloquium on Dust Measurement Techniques and Strategy. Budapest: National Institute of Occupational Health; 1991. p. 24-45.
57. Valić F. Influence of exposure conversions and activity-specific exposure- response relationships on the chrysotile asbestos risk assessment. In: Gibbs GW, Dunnigan J, Kido M, Higashi T, editors. Health risks from exposure to mineral fibres: an international perspective. North York (NY)-Ontario: Captus Press Inc., 1993. p. 129-35.
58. Berman DW. Assessing asbestos-related risk: new thinking/new protocol. 2001 EPA Asbestos Health Effects Conference; May 2001; Oakland (CA) [cited 10 March 2002]. Available from URL: http://www.epa.gov/swerrims/ahec
59. McDonald JC, McDonald AD. The epidemiology of mesothelioma in historical context. Eur Respir J 1996;9:1932-42.
60. Carbone M, Fisher S, Powers A, Pass HI, Rizzo P. New molecular and epidemiological issues in mesothelioma: role of SV40. J Cellul Physiol 1999;180:167-72.
61. Mayall FG, Jacobson G, Wilkins R. Mutations of p53 gene and SV40 sequences in asbestos associated and non-asbestos-associated mesotheliomas. J Clin Pathol 1999;52:291.293.
62. Bocchetta M, Di Resta I, Powers A, Fresco R, Tosolini A, Testa JR, et al. Human mesothelial cells are unusually susceptible to simian virus 40-mediated transformation and asbestos cocarcinogenicity. Proc Nat Acad Sci 2000;97:10214-9.
63. Lebel J. Review of fibre concentrations in asbestos mines and Quebec asbestos mining towns. Sherbrooke: Quebec Asbestos Mining Association; 1995.
64. Robock K. Comparison of different measuring procedures in relation to conditions at the work place. In: Fischer M, Meyer E, editors. Assessment of the cancer risk from asbestos. BBA Schriften No2. 1984.
65. National Research Council, US National Academy of Sciences. Asbestiform fibers: non-occupational health risks. Washington, DC: National Academy Press, 1984.
66. US Environmental Protection Agency (US EPA). Regulatory impact analysis of controls on asbestos and asbestos products. Technical Report Vol.1. Washington, DC: US EPA; 1988.
67. Berry G, Newhouse ML. Mortality of workers manufacturing friction materials using asbestos. Br J Indust Med 1983;40:1-7.
68. McDonald AD, Fry JC, Wooley AJ, McDonald JC. Dust exposure and mortality in an American chrysotile asbestos friction products plant. Br J Indust Med 1984;41:151-7.
69. McDonald JC. Health implications of environmental exposure to asbestos. Environ health Perspect 1985;62:319-28.
70. Valić F. Asbestos risk in vehicle manufacture, maintenance and repair. In: Reduction of asbestos in the environment. Geneva: International Programme on Chemical Safety/World Health Organization, 1989, 73-99.
71. World Health Organization Regional Office for Europe (WHO/Europe). Asbestos. Final meeting on air quality guidelines for the European region. Copenhagen: WHO/Europe; 1986.
72. World Health Organization (WHO). Guidelines for drinking water quality, Geneva: WHO; 1984.
73. World Health Organization (WHO). Air quality guidelines for Europe. WHO Regional Publications, European Series No. 23. Copenhagen: WHO/Europe; 1987.

Sažetak

DILEMA O AZBESTU I OCJENA RIZIKA

Kritički su prikazani današnji problemi u vezi s kvantitativnom ocjenom zdravstvenih rizika izloženosti azbestnim vlaknima, a posebno vlaknima krizotila, jedinog preostalog tipa azbesta u komercijalnoj uporabi. Dan je pregled izvora, tipova i uporabe, uloge bioperzistencije vlakana te odnosa njihove duljine i promjera važnih pri ocjeni rizika. Glavna je pozornost dana nekim još nerazriješenim pitanjima koja uvode velike granice nepouzdanosti u objavljene kvantitativne ocjene rizika: 1. Jesu li svi tipovi azbesta jednako opasni ili se prihvaća pretpostavka da je krizotil manje opasan? 2. Jesu li zdravstveni učinci izloženosti azbestnim vlaknima učinci s pragom izloženosti ili bez praga? 3. Jesu li pogrješke u matematičkome modeliranju rizika tako velike da ocjenjivanje postaje bezvrijedno? S time su u vezi analizirane pogrješke ocjenjivanja razina izloženosti u prošlosti te nesigurnosti i nespecifičnosti objavljenih matematičkih modela kvantitativnog ocjenjivanja rizika. Primjerima je upozoreno na nemogućnosti praktičke primjene nekih priznatih modela ocjenjivanja.

KLJUČNE RIJEČI: *amfiboli, bioperzistencija, krizotil, ocjenjivanje rizika, prag rizika*

REQUESTS FOR REPRINTS:

Professor Fedor Valić, Ph. D.
Andrija Štampar School of Publich Health
Rockefellerova 4, HR-10000 Zagreb, Croatia
E-mail: *fvalic@andrija.snz.hr*