RISK ASSESSMENT OF NON-OCCUPATIONAL ASBESTOS EXPOSURE — CAN IT BE DONE?

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Because of a long latency period of asbestos-induced lung cancer and mesothelioma, all the published risk assessment models for risk assessment of non-occupational asbestos exposure are based on the mortality analysis at high-level occupational exposures of 20 — 40 years before, mathematically extrapolated to current, very significantly lower, asbestos exposures in the general environment. This paper deals with the errors involved in such extrapolations and illustrates the unfeasibility of practical applications of currently available models for asbestos risk assessment. The main weaknesses emphasized are wrong fibre types and sizes included in the models, the »non-threshold hypothesis« taken as proved, and the great errors introduced by conversion of weight or total particle concentrations measured in the past into fibre counts, the current standard measure of exposure levels. The calculations are performed of threshold limit values for ambient airborne asbestos fibres derived on the basis of some of the main published risk assessment equations which would bring about unfeasibly low values for practical application.

Cancer risk assessment is a two-step procedure involving a qualitative assessment dealing with the likelihood of an agent being a human carcinogen and a quantitative assessment of the cancer rates (incidence, mortality) the agent in question is likely to induce at given levels and durations of exposure. The available published risk assessments of non-occupational asbestos exposure of the general population apply information available from specific studies of occupational exposures in the past to the general population in order to calculate the latter's possible current or future risk. All of them are based on the results of cancer incidence or mortality analyses at high-level occupational exposures in the past and extrapolated to such low asbestos levels in the general environment at which no excess risk has actually been observed. These extrapolations have been made using so many dubious assumptions, conversion calculations and approximations, that the risks assessed must bear errors of several orders of magnitude. To make it even more uncertain, because of a long latency period

of both bronchial cancer and mesothelioma development, the mortality rates established today are the consequence of exposure 20—40 years ago. In other words, for setting up dose-response or exposure- response relationships at present quantitative estimates of asbestos exposure levels 20—40 years ago are necessary. This paper attempts to prove the errors involved and to illustrate that the practical application of quantitative assessments of asbestos cancer risk is not feasible.

FIBRE TYPE AND SIZE

The major asbestos fibre type in the ambient air is chrysotile with fibres very predominantly less than 5 mm in length, the majority of which with diameters that cannot be seen with optical microscope (1). Because of that such fibres have not been determined in work environments nor have they been considered in computing dose-response estimates for asbestos disease. That means that assessments of the risks to the general population have been made on the basis of exposure data obtained for fibre sizes not prevalent in the general environment and thus not sufficiently relevant for the general population.

In addition, there is evidence that fibres less than 5 mm in length are biologically less active than long fibres of the same type. For this reason alone, extrapolation of the incidence of disease in working population, derived on the basis of the exposure level to long fibres, to the incidence in the general population, exposed mainly to short fibres, is likely to introduce a major error in the estimate.

MECHANISM OF ASBESTOS CARCINOGENICITY

It is not yet quite certain whether asbestos acts as an initiator or a promoter of the carcinogenic process. Practically all the published risk assessment models assume the »non-threshold hypothesis« and use, therefore, the linear model to describe the relationship between the dose and the effect. This has never been proved or disproved. In fact, it is never possible to prove a no-threshold phenomenon. There may always exist a still lower level of exposure under which there will be no effect. *Browne* (2) has recently published evidence for asbestos acting as promoter rather than initiator of the carcinogenic process. If this epigenetic rather than genotoxic mechanism is to be assumed, the non-threshold hypothesis becomes less defendable.

CONVERSIONS

Currently, occupational exposure levels are determined most frequently by phase-contrast microscopy of fibres collected on membrane filtres (3). However, membrane filtration was introduced only in 1965 in U.S.A. and U.K. (4). Before that the determination of total airborne dust was used in the great majority of cases in the main published equations for asbestos risk assessment. In all these cases the authors of risk

assessment equations had to convert the concentrations originally determined into fibre counts expressed as fibres per unit volume.

Conversions of the results of measurements expressed in million particles per cubic foot by the midget impinger (mppcf) into number of fibres per unit volume (f/ml or f/m³) have introduced significant uncertainty factors. The experimentally determined ratios between particle and fibre concentration determinations at the same work places, obtained by *Robock* (5), varied from 0.5 to 47.4 introducing a variation source of about 95.

Mathematical conversion of the results of gravimetric determinations to fibre counts theoretically may introduce an uncertainty factor of up to 400,000. Table 1. shows that one nanogram of asbestos, assuming an average density of 2.5, may contain 1.6 to 409,600 fibres of cylindrical shape (6), depending on their length and diameter, for size

Table 1

Numbers of fibres per nanogram (density 2.5)

Diameter (µm)	Length (µm)					
	1.25	2.5	5	10	40	80
0.03	409600	204800	102400			
0.13	25600	12800	6400	3200		
0.25	6400	3200	1600	800	200	
0.5	1600	800	400	200	50	25
1.0		200	100	50	12.5	6.3
2.0			25	12.5	3.2	1.6

categories between 2.0 mm in diameter and 80 mm in length and 0.03 mm in diameter and 1.25 mm in length. The EPA, in their risk assessment of 1985 (7), quote the range of conversion factors µg/m³ into f/ml in seven studies 0.007 — 1.4, and use in their further calculations the geometric mean of these factors. It can be estimated that an uncertainty factor of over 200 has been introduced into their quantitative risk assessment only by this procedure of interconvertibility of mass concentrations and fibre counts.

ERRORS IN RISK ESTIMATES

An analysis of the very reputable *National Research Council of the U.S. Academy of Sciences* (8), made in 1984, of the sensitivity of estimates for lifetime risks of asbestos-induced mesotheliomas to values of coefficients c and k of the estimation equation used ($L = c\,(0.0004)(73)^k$) is presented in Table 2. The analysis showed that the estimate per million population for a lifetime of 73 years at a continuous concentration

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Table 2

Lifetime risk estimates of mesothelioma death in seven studies* based on equation $L = c\ (0.0004)\ (73)^k$
(exposure level 0.0004 f/ml, lifetime 73 years)

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	11	41	97	7.000
2.53×10^{-8}	0.7	4	9	34	120	290	21.000
7.22×10^{-8}	2	11	26	96	350	820	60.000

* National Research Council of the US National Academy of Sciences, 1984.

of 400 fibres/m^3 in seven very serious studies varied with different k values from 0.2 to 7,000, from 0.7 to 21,000 and from 2 to 60,000 for three different respective values of c. This yields a difference of up to 300,000 in estimated mortality per million population, making a quantitative risk assessment meaningless. The later admission by NRC of an error in the calculation of mesothelioma risks (9, 10) has accounted for too low calculated risks but did not change the uncertainty of estimates caused by their strong dependence on the values of coefficients c and k.

UNFEASIBILITY OF PRACTICAL APPLICATION OF RISK ASSESSMENT

In order to show the practical implications and practical unacceptability of the results of some very reputable published risk estimates, the threshold limit values for

Table 3

Estimated lifetime risks from exposure to asbestos at 500 f/m^3 and calculated threshold limit values at the assumed acceptable risk of 1×10^{-5}

Expert meeting (11) (upper limit)	Risk (smokers): 12×10^{-5} (mesothelioma) $+ 16 \times 10^{-5}$ (lung cancer) $= 28 \times 10^{-5}$
	TLV on the basis of acceptable risk 1×10^{-5} : $\frac{500}{28} \sim 18$ f/m^3
	Risk (nonsmokers):
	12×10^{-5} (mesothelioma) $+ 1.5 \times 10^{-5}$ (lung cancer) $= 13.5 \times 10^{-5}$
	TLV on the basis of acceptable risk 1×10^{-5}: $\frac{500}{13.5} \sim 37$ f/m^3
Air Quality Guidelines (13)	Risk (30% smokers): 1×10^{-4} (mesothelioma) $+ 1 \times 10^{-5}$ (lung cancer) $= 11 \times 10^{-5}$
	TLV on the basis of acceptable risk 1×10^{-5} : $\frac{500}{11} \sim 45$ f/m^3

Prevalent asbestos concentrations:
  rural areas < 100 f/m^3
  urban areas $< 100 - 10000$ f/m^3
  indoor $400 - 500$ f/m^3

asbestos in the atmospheric environment that would be derived on the basis of such estimates are calculated and presented in Table 3. The lifetime risk estimate for smokers (mesothelioma: 12×10^{-5}, lung cancer: 16×10^{-5} as upper limits of the number of expected deaths per 100,000 population) at an assumed airborne asbestos fibre concentration of 500 f/m³ has been derived by a WHO Expert Meeting in 1986 (11). Assuming an acceptable risk of 1×10^{-5}, as used in the *WHO* Water Quality Guidelines (12), a threshold limit value of 18 asbestos fibres per cubic metre of air is obtained. In the same way, taking the risk estimate of 13.5×10^{-5} for non-smokers and assuming the same acceptable risk (1×10^{-5}), a threshold limit value of 37 asbestos fibres per cubic metre is obtained. Comparing these threshold limit values with prevalent concentrations found in the air of rural areas (up to 100 fibres per cubic metre), the application of the results of the quoted risk assessment would require an up to 6-fold reduction of current asbestos levels in areas without any specific source of asbestos emission, a requirement practically unachievable.

Taking the risk assessment published in the *WHO* Air Quality Guidelines in 1988 (13) (11×10^{-5} for a population with a hypothetical proportion of 30% smokers), a threshold limit value of 45 asbestos fibres per cubic metre would be derived, as shown in Table 4. This value is still lower or as low as the concentrations found in rural areas without specific asbestos emission. The Table also shows asbestos concentrations found in urban areas (from fewer than 100 to 10,000 asbestos fibres per cubic metre).

Table 4

Estimated lifetime risks from exposure to asbestos at 400 f/m³ and calculated threshold limit values at the assumed acceptable risk of 1×10^{-5}*

Mesothelioma	15.6×10^{-5}
Lung cancer — male smoker	29.2×10^{-5}
Lung cancer — male non-smoker	2.7×10^{-5}
Lung cancer — female smoker	10.5×10^{-5}
Lung cancer — female non-smoker	1.4×10^{-5}

Risk — male smokers: $15.6 \times 10^{-5} + 29.2 \times 10^{-5} = 44.8 \times 10^{-5}$

TLV on the basis of acceptable risk 1×10^{-5} : $\dfrac{400}{44.8} \sim 9$ f/m³

Risk — male non-smokers: $15.6 \times 10^{-5} + 2.7 \times 10^{-5} = 18.3 \times 10^{-5}$

TLV on the basis of acceptable risk 1×10^{-5} : $\dfrac{400}{18.3} \sim 22$ f/m³

* National Research Council of the US National Academy of Sciences, 1984 (8), corrected by Breslow and co-workers, 1986 (10).

It is doubtful whether a concentration as low as 18 asbestos fibres per cubic metre is at all achievable in the majority of urban areas, but if it is, it could be achieved only at an economic cost hardly bearable to the majority of countries.

Table 4 shows the same calculations on the basis of results of the well-known risk assessment by the *National Research Council of the U.S. National Academy of Sciences*

(10). Taking their estimated deaths from mesothelioma and lung cancer for male smokers and non-smokers at the assumed asbestos concentration of 400 fibres per cubic metre, and applying the same level of acceptable risk (1×10^{-5}), threshold limit values of 9 and 22 asbestos fibres per cubic metre, respectively, are derived. That would lead to a requirement of a 10-fold reduction of asbestos levels found in rural areas without specific asbestos emission.

CONCLUSIONS

Not only do the currently published extrapolated asbestos risk estimates, for the same exposure level, vary over many orders of magnitude, depending on the assumptions, conversions, cohorts used, and validity of exposure data, but their application would bring about unfeasible threshold limit values for the air in rural and particularly urban areas.

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Sažetak

JE LI MOGUĆE OCJENJIVANJE RIZIKA OD NEPROFESIONALNE EKSPOZICIJE AZBESTU

Gotovo sve dosad objavljene kvantitativne ocjene rizika od neprofesionalne ekspozicije aerogenim vlaknima azbesta temelje se na rezultatima analiza incidencije ili mortaliteta od karcinoma uzrokovanih visokim razinama bivše profesionalne ekspozicije koje se matematičkim modelima ekstrapoliraju na niske ekspozicije opće populacije. Uz tako niske ekspozicije prekomjerni rizik se epidemiološki uopće ne može ocijeniti. Zbog niza dvojbenih pretpostavki i aproksimacija rizici izračunati tim modelima neminovno uključuju pogreške nekoliko redova veličina. U članku su analizirani izvori pogrešaka takvih ocjena. Autor dokazuje da se dosad objavljenim modelima ne mogu dobiti u praksi primjenjivi standardi. Kao glavne izvore pogrešaka navodi modele izračunate na osnovi učinaka neodgovarajućih tipova i veličina aerogenih vlakana, zatim općenito prihvaćen stav da se pri ocjenjivanju karcinogenih učinaka ne može pretpostaviti razina ekspozicije bez zdravstvenih učinaka (»non-threshold hypothesis«), a posebno pretvorbe gravimetrijskih koncentracija ukupne prašine, koje su se u prošlosti jedino mjerile, u brojčane koncentracije aerogenih vlakana koje se danas primjenjuju u ocjenjivanju izloženosti.

U članku su navedeni rezultati izračunavanja maksimalno dopuštenih koncentracija za aerogena vlakna azbesta u vanjskoj atmosferi dobiveni upotrebom glavnih u literaturi objavljenih jednadžbi za ocjenjivanje rizika. Na temelju tih izračunavanja dobivaju se neprihvatljivo niske vrijednosti maksimalno dopuštenih koncentracija koje se ne bi u praksi mogle realizirati osim uz potpuni prestanak primjene azbesta.

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