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COMMENTARY

Comments on the 2014 Helsinki Consensus Report on Asbestos

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Abstract

BACKGROUND The Finnish Institute of Occupational Health (FIOH) convened an Expert Committee in 2014 to update the 1997 and 2000 Helsinki criteria on asbestos, asbestosis, and cancer.

METHODS The Collegium Ramazzini reviewed the criteria for pathological diagnosis of the diseases caused by asbestos presented in the 2014 Helsinki Consensus Report and compared them with the widely used diagnostic criteria developed in 1982 by the College of American Pathologists and the National Institutes of Occupational Safety and Health (CAP-NIOSH).

FINDINGS The sections of the Helsinki Consensus Report dealing with pathological diagnosis are based on a biased and selective reading of the scientific literature. They are heavily influenced by the outdated and incorrect concept that analysis of lung tissue for asbestos bodies and asbestos fibers can provide accurate information on past exposure to asbestos. Five specific problems are :

1. Over-reliance on the detection of "asbestos bodies" as indicators of past exposure to asbestos.
2. Over-reliance on asbestos fiber counts in lung tissue as an indicator of past exposure to asbestos.
3. Use of the scanning electron microscope (SEM) at low magnification as a tool for evaluation of asbestos-related disease.
4. Failure to recognize that chrysotile is the predominant type of asbestos fiber found in pleural mesothelioma tissue.
5. Postulating the existence of a threshold for development of an asbestos-related lung cancer.

CONCLUSION Accurate diagnosis of the diseases caused by asbestos must be based on a carefully obtained history of occupational exposure. An accurate exposure history is a far more sensitive and specific indicator of asbestos exposure than asbestos body counting or lung fiber burden analysis.

ETHICAL NOTE The sections of the 2014 Helsinki Consensus Report on asbestos, asbestosis, and cancer dealing with pathologic diagnosis of the diseases caused by asbestos appear to have been influenced by members of the Expert Committee with undisclosed financial conflicts of interest.

KEY WORDS asbestos, asbestosis, Helsinki consensus report

The Collegium Ramazzini recognizes the work of the 2014 expert committee convened by the Finnish Institute of Occupational Health (FIOH) to update the 1997 and 2000 Helsinki criteria on asbestos, asbestosis, and cancer in light of new advances in research. The published Consensus Report of the Helsinki Committee[1] and its more extensive online version[2] provide a valuable synthesis of many aspects of current knowledge of the hazards of asbestos.

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The Collegium Ramazzini is, however, very concerned about the sections of the 2014 Helsinki Consensus Report that discuss criteria for pathological diagnosis of the diseases caused by asbestos.

The sections of the Helsinki report dealing with pathology diagnosis are based on a selective reading of the medical literature. They rely too much on certain published articles[3-5] while omitting references to other important and highly relevant information. They are heavily influenced by the outdated and incorrect concept that analysis of lung tissue for asbestos fibers and asbestos bodies can provide data to contradict exposures that are documented in a reliable occupational history. Further, without any explanation the most accepted College of American Pathologists—National Institutes of Occupational Safety and Health (CAP-NIOSH) 1982 asbestos definition, which underwent extensive review and endorsement by NIOSH, is now replaced in the 2014 Helsinki criteria by the more restrictive CAP/pps modification, which differs especially in the early histological stages of asbestosis and in the higher numbers of asbestos bodies needed to make the pathological diagnosis of asbestosis.[6] These sections of the Helsinki report appear to have been influenced by members of the Helsinki committee with undisclosed financial conflicts of interest.

Applying the 2014 Helsinki report recommendations on pathology diagnosis will lead to the following:

- Missed diagnoses of cases of disease caused by asbestos.
- Failure of workers' compensation systems to properly compensate workers who have been exposed to asbestos.
- Lost opportunities for public health authorities to recognize asbestos hazards and to prevent asbestos-related disease.

For these reasons, relying on lung tissue analysis for the diagnosis and compensation of asbestos-related disease—while ignoring the history of occupational exposure—is unacceptable. Application of these recommendations will cause harm to the health of workers and their families in countries around the world.

The Collegium Ramazzini has identified 5 specific problems with the pathology sections of the 2014 Helsinki Consensus Report:

1. *Over-reliance on the detection of "asbestos bodies" as indicators of past exposure to asbestos.*

Chrysotile asbestos, the predominant form of asbestos in use today, is now recognized to rarely form asbestos bodies. Therefore, failure to detect asbestos bodies cannot be used as a criterion for excluding exposure to chrysotile asbestos. Reliance on the detection of asbestos bodies as an index of past exposure to asbestos may lead to false negative diagnoses.[6,7]

The Collegium Ramazzini is particularly critical of the suggestion in the 2014 Helsinki Consensus Report that a finding of "over 1000 asbestos bodies per gram of dry tissue (100 asbestos bodies per gram of wet tissue) or over 1 asbestos body per milliliter of bronchoalveolar lavage fluid as measured by light microscopy in a qualified laboratory" can be used as a guideline "to identify persons with a high probability of exposure to asbestos dust." This suggestion is not consistent with the current recognition that chrysotile asbestos rarely forms asbestos bodies. It omits any mention of what defines a "qualified laboratory." It fails to address the well-documented variability across laboratories in both counting procedures and standards[8,9] and may lead to unethical, unnecessary, and risky surgical procedures (see later). The Collegium Ramazzini has no concern about using a finding of asbestos bodies as an indicator of past exposure to asbestos. However, there is no reliable basis for the proposed thresholds that must be met before such a conclusion is allowed, and the failure to find asbestos bodies cannot be used to contradict a reliable occupational history of exposure, particularly to chrysotile.

2. *Over-reliance on asbestos fiber counts in lung tissue as an indicator of past exposure to asbestos.*

Asbestos fiber counts obtained from human lung tissue are now recognized to be a highly insensitive measure of past exposure to chrysotile asbestos. Chrysotile asbestos fibers are now well documented to have only a short residence time in lung tissue, and therefore their measurement in the lung cannot be used as a measure of cumulative past exposure.[8,10-18] As with asbestos bodies, the Collegium Ramazzini has no concern about using a finding of asbestos fibers in lung tissue as an indicator of past exposure to asbestos. However, there is no reliable basis for the failure to find asbestos fibers in lung tissue to be used to contradict a reliable occupational history of exposure, particularly to chrysotile.

Short asbestos fibers, <5 microns in length, are a further issue here and are not discussed in the Helsinki Consensus Report. These fibers were originally not counted by most laboratories because they were below the visibility limits of the phase contrast microscope. Today they are readily visible under the electron

microscope and are counted by some laboratories and not by others. The Helsinki report considers neither short asbestos fibers nor their possible contribution to the pathogenesis of asbestos-related diseases,[7,8,16,19] nor does it consider the well-documented wide intra- and interlaboratory variability in procedures for the counting of short fibers.[8,9,11]

3. *Use of the scanning electron microscope (SEM) at low magnification as a tool for evaluation of asbestos-related disease.*

The SEM at low magnification should not be used for causal attribution in diagnosis of the diseases potentially caused by asbestos because it is incapable of detecting most chrysotile fibers.[11,15,20,21]

An additional problem with microscopic screening of lung tissue for asbestos bodies and asbestos fibers by SEM at low magnification is that there is wide intra- and interlaboratory variability in these procedures, with no standardization of diagnostic procedures across laboratories.[8,9]

For all of these reasons, use of low-magnification SEM as a diagnostic instrument will lead to false-negative diagnoses, particularly in the case of individuals with a history of exposure to chrysotile. The Collegium Ramazzini recommends instead that analytical transmission electron microscopy should be the diagnostic instrument of choice for fiber analysis in cases of suspected exposure to asbestos.[22]

4. *There is no recognition that chrysotile is the predominant type of asbestos fiber found in pleural mesothelioma tissue.*

Multiple studies have demonstrated that chrysotile fibers are the predominant type of asbestos fiber found in pleural mesothelioma tissue. The relative abundance of chrysotile fibers in mesothelioma tissue contrasts with their relative scarcity in lung tissue.[8,10,12-14,16,17]

5. *Postulation of a threshold for the development of an asbestos-related lung cancer.*

The 1997 Helsinki report states: "The relative risk of lung cancer is estimated to increase 0.5-4.0% for each fiber per cubic centimeter per year (fiber-years) of cumulative exposure." The 2014 Helsinki report[1] states on pages 6 and 7: "Using an estimate of 4% increase of risk for each fibres per cubic centimeter per year (fibre year) of cumulative exposure: 'A cumulative exposure of 25 fibre-years is estimated to increase the risk of lung cancer 2-fold, clinical cases of asbestosis may occur at comparable cumulative exposures.'" Setting aside the fact that published studies support a linear dose-response relationship without a threshold,[23-26] the 2014 consensus statement ignores its previously acknowledged range of risk estimates and chooses the upper end of the range without comment or explanation. This compounds the error of its failure to acknowledge and reference studies indicating a linear dose-response relationship and instead embraces a statement that implicates a specific threshold. This error is not mitigated by its sop to chrysotile: "Occupational histories (fibre years of exposure) are probably a better indicator of lung cancer risk from chrysotile than fibre burden analysis…because of the higher clearance rates for chrysotile." It is the rare occupational history that provides information about fiber-years of exposure.

These concerns are not new or novel. Rather, they have been recognized for at least the past 25 years.[11,15] Because chrysotile has always been the vast majority of the asbestos used globally and for at least the past 20 years has essentially been the only form of asbestos used, these concerns are all the more significant going forward.

In conclusion, the Collegium Ramazzini emphasizes that a carefully obtained history of occupational exposure to asbestos is the cornerstone of an accurate diagnosis of the diseases caused by asbestos.[27] An occupational history taken by an experienced clinician and supplemented as necessary by an exposure assessment conducted by an experienced industrial hygienist is a far more sensitive and specific indicator of lung cancer risk from chrysotile asbestos than asbestos body counting or lung fiber burden analysis.[27,28]

The Collegium Ramazzini recommends against any requirement for lung biopsy or for the use of lung tissue histopathological examination or fiber counts from lung tissue as procedures for the diagnosis of pulmonary fibrosis, including asbestosis, in medicolegal or compensation cases because of the invasive and potentially risky nature of the lung biopsy[29] and because the procedure is medically unnecessary. It is the opinion of the Collegium Ramazzini that such invasive diagnostic procedures are *never* ethically justified solely for medicolegal or compensation purposes, given that asbestos exposure can reliably be ascertained through a properly obtained occupational history.

The Collegium Ramazzini notes that a diagnosis of idiopathic pulmonary fibrosis is a diagnosis of exclusion. This diagnosis should never be made until exposures to asbestos and to other known exogenous causes of lung fibrosis have been carefully excluded; therefore, in a setting of exposure to a

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fibrosing agent, the diagnosis of idiopathic pulmonary fibrosis cannot be made.[29]

Professor Irving Selikoff, the Founder of the Collegium Ramazzini, stated in a letter 35 years ago that "patients should be compensated if there is documented history of occupational exposure to asbestos." This principle applies also to environmental exposures to asbestos. It still holds true today.

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