COLLEGIUM RAMAZZINI

Comments on the causation of malignant mesothelioma: rebutting the false concept that recent exposures to asbestos do not contribute to causation of mesothelioma

The Collegium Ramazzini is an international scientific society that examines critical issues in occupational and environmental medicine with a view towards action to prevent disease and promote health. The Collegium derives its name from Bernardino Ramazzini, the father of occupational medicine, a professor of medicine of the Universities of Modena and Padua in the late 1600s and the early 1700s. The Collegium is comprised of 180 physicians and scientists from 35 countries, each of whom is elected to membership. The Collegium is independent of commercial interests.

Incidence of malignant mesothelioma, as approximated by death certificate diagnoses of mortality from pleural cancer, has been increasing constantly in Italy as well we in most industrialized countries in recent decades and is expected to peak around 2020. A large number of cases of mesothelioma have now been brought to the attention of the Italian courts as possible occupational diseases. According to the Italian law, exposures leading to an occupational disease not only determine liability for personal damage, but are also a potential criminal offence. In both civil and criminal trials, a key role is played by experts called to determine whether the relationship between exposure to asbestos and the occurrence of mesothelioma in a worker is a causal relationship.

The main strategy that the Italian asbestos industry and their expert witnesses have employed to rebut claims of asbestos causation in cases of malignant mesothelioma has centred on the thesis they have developed that brief exposures to asbestos are sufficient to induce mesothelioma. Therefore, in cases of prolonged or multiple exposures to asbestos, which are common, the defendants claim that only the earliest periods of exposure contributed to mesothelioma induction, while all subsequent exposures had no causal role.

A series of consequences stem from this thesis. Firstly, in a number of trials, only the firms that owned the factories where exposure occurred during the early years of the patients' work history have been considered liable for damage compensation. When those companies that employed workers many years ago were liquidated, as has often happened, no compensation has been awarded. Secondly, only the managers who were active during the early years of exposure could be indicted for the workers' deaths. But almost invariably those managers were already dead by the time of recent trials and could not be prosecuted. Managers in charge of the plants during subsequent, more recent years of employment (and exposure) have been acquitted.

This thesis that only early, brief exposures to asbestos are responsible for induction of mesothelioma has appeared in several different versions. A first, "hard" version postulated that a small trigger exposure to asbestos induces mesothelioma and does so only in susceptible individuals; subsequent exposures were considered to be ineffective. Professor Girolamo Chiappino, a respected professor of occupational medicine, presented this interpretation of the defendants' thesis to the Italian professional and scientific community in a 2005 paper. In his article, Chiappino largely misquoted Irving Selikoff's concept of "trigger dose"[1]. In the courts, Chiappino's paper has often been quoted by defendants' expert witnesses as providing scientific credibility to the trigger dose hypothesis.

A second, "soft" version of the thesis is now more often used. It is summarized in the following words presented in a review article by La Vecchia and Boffetta: "*for workers occupationally exposed in the distant past, the risk of mesothelioma is not appreciably influenced by subsequent exposures*"[2]. This review was submitted for publication in September 2011 and its content closely matched La Vecchia's examination as expert witness for the defense in the Montefibre asbestos trial in Verbania, Italy in March 2011. The proofs of this article were produced as defence exhibit

in the Montefibre appeal trial in Turin in November 2011.

La Vecchia and Boffetta's paper (and the thesis it promotes) have little scientific merit. It is based on a biased and highly selective review of the published literature[3].

In 2011, the Epidemiology and Public Health Working Group of the Second Italian Consensus Conference on Pleural Mesothelioma conducted an independent systematic review of the literature on the exposure-response relationship between asbestos and mesothelioma. It concluded that there is convincing evidence that mesothelioma incidence is proportional to cumulative asbestos exposure[4, 5]. "Subsequent" exposures cannot, thus, be considered without influence on mesothelioma risk on the basis of the available evidence, as they necessarily contribute to cumulative exposure".

Timing of exposure was recognized by the Italian Working Group to be important. The Working Group noted that any given increase in exposure is expected to be more effective when it occurring early during a prolonged exposure. There was, however, no mention in the Working Group's report of a time limit beyond which further increases in exposure would cause no further increases in risk of mesothelioma, nor was there any statement that such a limit should be set after a few years of exposure.

The concept that mesothelioma incidence is proportional to cumulative asbestos exposure was further confirmed in a 2015 review of published epidemiological studies which analyzed separately the role of intensity and duration of asbestos exposure[6]. This analysis found that both variables are determinant of mesothelioma risk.

In summary, the Collegium Ramazzini concludes that risk of malignant mesothelioma is related to cumulative exposure to asbestos in which all exposures—early as well as late—contribute to the totality of risk. The Collegium Ramazzini rejects as false, mendacious, and scientifically unfounded the claim put forth by the Italian asbestos industry and its expert witnesses that in cases of prolonged exposures to asbestos only the earliest periods of exposure contribute to mesothelioma induction, while all subsequent exposures have no causal role. The Collegium Ramazzini is deeply concerned that acceptance of this false claim will contribute to the unjust denial of workers' compensation and civil damages to affected workers, that it will hinder efforts to diagnose and prevent malignant mesothelioma, and that ultimately it will undermine the health of the public in Italy and in countries around the world.

References

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