

Monday December the 20th, 2021 Eternit bis Hearing

by Silvana Mossano

The question is whether there is a hereditary predisposition to mesothelioma: in a small percentage of individuals, there might be, but had these people not been exposed to asbestos, they would never have developed the disease. These are the results from a 2017 study, by a group of Piedmontese researchers - including Professor Irma Dianzani, Professor Corrado Magnani, Doctor Dario Mirabelli and others -. Prof Dianzani, expert witness for prosecutors Gianfranco Colace and Mariagiovanna Compare illustrated the research results to the Court of Assizes, at the hearing on Monday 20 December of the Eternit Bis trial. Stephan Schmidheiny, the defendant, is accused of voluntary murder, with possible intent, of 392 people from Casale who died as a result of the asbestos fibres.

Professor Irma Dianzani is a genetic pathologist and a full professor at the School of Medicine of the University of Eastern Piedmont. She commented: of all people exposed to high doses of asbestos, between 10 and 17 per cent develop mesothelioma. In addition, in some families, there have been several cases of mesothelioma among relatives: parents, children and grandchildren. Hence the question: is there a genetic predisposition? Or are the clusters of cases in the family merely due to a shared exposure to asbestos?

THE AMERICAN STUDY

A group of American researchers first investigated the issue in 2011. Studying two families, they found that many relatives had suffered from mesothelioma and other cancers. It was found that they all had a genetic disorder known as '*Bap1 syndrome*', which causes no visible malformations but increases the risk of certain cancers, including melanoma and mesothelioma.

In addition to *Bap1*, there are other types of syndrome that determine a predisposition to develop cancer. In order to facilitate understanding, Professor Dianzani referred to the case of the famous actress Angelina Jolie: she herself had reported a specific genetic predisposition to breast and ovarian cancer.

THE ITALIAN STUDY

What did the 2017 Italian research show? Professor Dianzani explained that 93 patients (including several from Casale) with mesothelioma were studied and their DNA was sequenced for 96 genes involved in cancer predisposition. In 10 per cent of the patients observed, hereditary cancer syndromes were found, i.e. they had a predisposition to cancer in their genes.

However - and this is the important thing - 'none of the cases in which this tumour syndrome was found (e.g. *Bap1* syndrome, and also others) developed mesothelioma without exposure to asbestos,' the prosecutor's expert witness stated with certainty. In other words 'the genetic factor alone is not enough'. Even where there is a hereditary predisposition, if you don't breathe in asbestos fibres you don't develop the disease because what exposure to asbestos is what triggers the onset of mesothelioma. All the patients examined, the majority of whom (90%) had no genetic predisposition, died as a result of breathing the fibre. None of the Casale patients examined in the 2017 study and subsequent studies had the *Bap1* syndrome.

The prosecutor's expert witness also described what is now known about the development of mesothelioma and how the tumour genome is structured. While predisposition factors are in the DNA of every cell in the carrier's body, cancer cells have their own modified genome, unlike from that of normal cells, which determines their aggressiveness. The mesothelioma genome is shaped by exposure to asbestos, which caused the tumour transformation.

Prof Dianzani illustrated the various features of the mesothelioma genome induced by the carcinogenic effects of asbestos. 'Chromotripsis' or chromosomal catastrophe is one of the alterations: this is an error that occurs in the mechanism of DNA reconstruction after multiple breaks. Based on this, some have argued that this 'catastrophe' can accelerate the onset of cancer. Professor Dianzani, on the other hand, argues that, in the cancers where chromotripsis has been studied, the 'catastrophe' often represents a late event in the cancer's history, due to characteristic genetic instability. "It is therefore not possible that mesothelioma develops very quickly (as the defence consultants claim), but it is true instead that it develops slowly over many years."

THE *MEDICINA DEMOCRATICA* (DEMOCRATIC MEDICINE) EXPERT WITNESS

On Monday morning, occupational physician Edoardo Bai, an expert in epidemiology and a consultant appointed by *Medicina Democratica*, which is a plaintiff in the case with lawyer Laura Mara, was also heard.

Doctor Bai took spoke about a subject already debated of the Public Prosecutor's expert witnesses, Prof Corrado Magnani and Doctor Dario Mirabelli ("with whom I fully agree") concerning the validity of epidemiological results applied to individuals: a thesis the Swiss businessman's defence lawyers disagree with.

Doctor Bai insisted: "As confirmed by a recent study by the Aie (Italian Association of Epidemiology, ed.) published in the authoritative journal 'Epidemiologia & Prevenzione', the results of epidemiological studies based on the observation of behaviour in homogeneous groups hold for single individuals too. This is our method in medical research'. Drugs are a case in point: they are tested on a certain number of animals or people to assess their effectiveness and tolerability. Repeated positive responses to that substance means that the drug is deemed suitable for administration to individuals. Similarly, Doctor Bai insisted, epidemiological studies have looked at cohorts of asbestos-exposed and non-exposed people.

Medicina Democratica's expert then agreed with the prosecutor's on the dose-response issue: "We have consolidated scientific consensus in favour of the 'multistage theory' for pleural mesothelioma: that is, all the phases of exposure to asbestos count, from the early stages to the diagnosis: the theory - he reiterated - that is known as the 'trigger dose', according to which it is the first exposure that counts, and, once the tumour has started, the fibres inhaled subsequently no longer have any effect, is incorrect". On the other hand, Doctor Bai pointed out that 'the more you are exposed, the greater the risk of falling ill, as well as anticipating the onset of disease by shortening life expectancy'.

Finally, the doctor addressed the issue of 'cell duplication' to calculate the duration of the so-called induction phase (time elapsing between the moment when the first cell in the body develops the cancer and the moment when the tumour is present but not yet visible and diagnosable). Using a

mathematical calculation, Medicina Democratica's expert argued that it is possible to calculate the duration of the induction period and the period in which it took place.

NEXT HEARING

The first hearing after the Christmas break will be on Monday, 10 January: experts Doctor Pietro Gino Barbieri, Professor Mauro Giulio Papotti and Doctor Edoardo Bai will be cross-examined. The cross-examination of Irma Dianzani is scheduled for Monday 17 January.

<https://www.silmos.it/mesotelioma-casi-di-predisposizione-ereditaria-ma-nessuno-si-ammala-senza-esposizione-allamianto/>