

COMMENTARY

The fibres with fluoro-edenitic composition in Biancavilla (Sicily, Italy): health impact and clues for environmental remediation

Pietro Comba^(a), Salvatore Scondotto^(b) and Loredana Musmeci^(a)

(a) Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Rome, Italy

(b) Dipartimento Attività Sanitarie e Osservatorio Epidemiologico della Regione Sicilia, Palermo, Italy

Abstract

Subsequently to the observation of a localized excess of mortality from malignant pleural neoplasms in the town of Biancavilla (Sicily), previously unknown amphibolic fibres with fluoro-edenitic composition were detected as naturally occurring soil contaminants. Less than two years after the initial report, ISS provided a set of public health recommendations that were complied by regional and local institutions. The recognition of Biancavilla as a National Priority Contaminated Site in 2002 opened the way to clean-up interventions. An up-dating of epidemiological studies, exposure assessment investigations and *in vivo* and *in vitro* mechanistic studies on fluoro-edenite fibres is provided in this issue. Scientific evidence can provide a sound foundation to public health action and environmental remediation. Finally, it is now necessary to properly tune the response of the health system to the community needs in terms of diagnostic procedures and medical treatment.

Key words

- fluoro-edenite
- mesothelioma
- asbestiform fibre exposure
- environmental clean-up

Environmental health requires a multidisciplinary approach apt to integrate exposure science, epidemiological investigations and mechanistic studies in order to throw light on the role of the environment in the causation of disease in humans, and to subsequently promote appropriate and effective remedial action. This approach requires, among else, cooperation between central and local institutions with responsibilities in the domains of both environmental protection and health prevention.

An example of the aforementioned approach is illustrated in the mini-monograph on the health impact of exposure to amphibolic fibres with fluoro-edenitic composition published in the present issue of *Annali dell'Istituto Superiore di Sanità*. In essence, subsequently to the observation of a localized excess of mortality from malignant pleural neoplasms, a proxy of pleural mesothelioma incidence, in the town of Biancavilla (Sicily), located at the slopes of Etna Volcano, in the absence of detectable occupational exposure to asbestos, three lines of research produced novel scientific knowledge that can be summarized as follows.

Epidemiologists, as reported in this issue by Bruno *et al.* [1] and by Conti *et al.* [2], soon after the initial observation published in 1996 [3], firstly described the case series of pleural mesothelioma among Biancavilla residents, characterized by a comparatively high presence of women, low age at diagnosis and lack of evidence on occupational asbestos exposure. They then provided quantitative estimates of the excess risk of mesothelioma incidence, mortality and hospitalization, and more recently estimated an excess mortality and hospitalization from non-malignant respiratory diseases, namely from pneumoconiosis, thus corroborating the notion of the occurrence of environmental lung fibrosis.

Exposure scientists detected previously unknown amphibolic fibres with fluoro-edenitic composition as naturally occurring soil contaminants. These fibres contaminated among else an area characterized by the presence of a quarry where building materials extensively employed in Biancavilla used to be caved. Exposure to these fibres could thus be determined both by outdoor and indoor sources (see Bruni *et al.* [4] in this same issue).



In vivo carcinogenicity of Biancavilla fibres was demonstrated in a study performed by the Ramazzini Institute in the Bentivoglio experimental laboratories [5] by means of intraperitoneal administration in Sprague-Dawley rats followed by a dramatic increase in peritoneal mesothelioma. *In vitro* studies mainly performed at Istituto Superiore di Sanità (ISS) concurrently documented the cellular and molecular mechanisms underlying the fibres' carcinogenicity, namely multi-nucleation, pro-survival activity and pro-inflammatory cytokine release, as discussed by Ballan *et al.* [6] in this issue.

Interestingly enough, less than two years after the initial report, when the Biancavilla fibre was still believed to be an intermediate phase between actinolite and tremolite, ISS provided a set of public health recommendations that were complied by regional and local institutions, and included termination of quarrying activities, removal of construction industry byproducts and waste from the newly urbanized Biancavilla districts, asphalt paving of roads originally covered by inert material originating from the quarry area. These recommendations were followed by local institutions, and some studies concerning the fibres' air concentration showed a consistent decrease over time [4]. The abovementioned recommendations by ISS were thus formulated on the basis of scientific evidence and at same time founded on a precautionary approach [7], considering the large amount of uncertainty unavoidably affecting the available evidence.

A major breakthrough, in this frame, was represented by the previously quoted *in vivo* experiment [5], that demonstrated the carcinogenicity of fluoro-edenite fibres in rats. It is noteworthy to emphasize the proactive role of Ramazzini Institute that designed and realized the experiment, responding to a request by ISS, in the absence of any financial support from public institutions.

The recognition of Biancavilla as a National Priority Contaminated Site in 2002 opened the way to clean-up interventions whose effectiveness in reducing fibre exposure is well documented [4]. This act was a cornerstone, not only for environmental remediation, but also in terms of environmental justice. The Biancavilla municipality was recognized as a community deserving support by the national and regional governments, in terms of prevention, health care and further epidemiological monitoring.

Several detailed mortality and morbidity studies (the latter performed through the analysis of hospital discharge records) were produced by the Epidemiological Observatory of Sicily. The most recent release reports an analysis of mortality from 2004 through 2011 and analysis of hospitalization from 2007 through 2011. The only neoplastic disease in excess is pleural mesothelioma. Circulatory and respiratory diseases show excess risk in terms of both mortality and hospitalization [8].

Sicilian Region Health Authorities have recently designed an *ad hoc* plan of health intervention in the National Priority Contaminated Sites of Biancavilla [9]. The plan first of all recommends fostering epide-

miological surveillance with special emphasis on mesothelioma, pneumoconiosis, other asbestos-related radiological alterations and CO diffusion alterations. Health promotion will concurrently be pursued by anti-smoking campaigns and health education. Improvements of diagnostic and therapeutic interventions in the domain of chronic respiratory disease will also be ensured.

The health profile of Biancavilla community, as discussed in this issue [1, 2] and briefly summarized in the present commentary, shows similarities with the corresponding health profile of other populations characterized by environmental asbestos exposure due to residence in contaminated sites [10]. Tremolite-induced pleural plaques and mesothelioma were consistently reported in South Eastern Europe [10], including Italy [11, 12], New Caledonia [13], and the well-known case of Libby, Montana [14, 15].

The section concerning Biancavilla in the last report of SENTIERI study, the national epidemiological surveillance project on the population resident in National Priority Contaminated Sites, recommends to focus further epidemiological studies on the prevalence of lung fibrosis and pleural plaques, and to pursue a better characterization of exposure to fibres with fluoro-edenitic composition [16]. In the meanwhile, environmental clean-up must proceed, and its efficacy in terms of exposure mitigation has to be monitored as extensively discussed in this issue [4].

The improvement in exposure assessment should lead to three main goals: a better understanding of the location and characteristics of major sources of fibres in the Biancavilla territory, a better appreciation of activities and circumstances that may determine elevated, even if short-term, airborne fibres levels, and a better insight into indoor sources of fibres. This issue can benefit from innovative approaches, like the use of sentinel animals as biological indicators of fibre exposure, following the pilot study by De Nardo (17) on fluoro-edenitic fibres concentration in sheep lung samples. Progress in these domains may contribute to priority setting in environmental remediation by optimizing resource allocation in a health prevention perspective.

With respect to epidemiological surveillance, the top priority is completing the collection of residential and occupational histories of mesothelioma cases, since the proportion of missing data is still much too high. Subsequently to this achievement, it will be possible to perform etiologic studies aimed at testing hypotheses of causal interest, such as the contribution of outdoor vs indoor exposure to the overall mesothelioma risk, or the weight of exposure in specific time-windows, namely in childhood.

A further comment concerns the perspective of a permanent scientific cooperation between national and regional institutions in charge of environmental protection and health promotion. This goal is pursued by ISS as shown, among else, by the qualified presence of colleagues from Sicilia Region Environmental Protection Agency, Epidemiological Observatory and



Operational Centre for the National Mesothelioma Registry among the Authors of this mini-monograph.

As stated at the start of this Commentary, advances in causal reasoning require integration of epidemiology, exposure science and understanding of biological mechanisms. As a second step, scientific evidence as a whole can provide a sound foundation to public health action and environmental remediation. Finally, it is now necessary to properly tune the response of

the health system to the community needs in terms of diagnostic procedures and medical treatment. In order to be effective, preventive, diagnostic and therapeutic interventions will have to be characterized not only by sound scientific background, but also by well-designed communication strategies, in order to actively involve the whole community in a participatory process.

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