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CONCLUSIONS

Silica and lung cancer: what next?

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As the papers in this dedicated issue of *La Medicina del Lavoro* suggest, there is now a general consensus that silicosis is a predictor of a roughly doubling risk of developing lung cancer (3-6). Whether it would result from exposure to a high cumulative silica level, incidentally also associated with silicosis through different mechanisms, or from a necessary silicosis-mediated pathway, is the matter of the debate. In fact, although more consistent from an epidemiological perspective and reassuring in terms of the effectiveness of current standards in preventing lung cancer risk among silica exposed workers, the silicosis-mediated hypothesis still does not account for some elevated risks among silicosis-free silica exposed workers: in the nested case-control analysis of lung cancer in dusty trades in China a dose-response trend of lung cancer for the same categories of cumulative silica exposure was observed even after excluding cases and controls with a radiological diagnosis of silicosis, as well as those with the dubious borderline radiological features of a tightening of the parenchymal design, but no clear nodular aspects (2). It is worth noting that extending the follow-up and increasing the number of cases and controls, and using different methodologies, other authors came to opposite conclusions (1). Opposite conclusions based on roughly the same data were also featured in independent analyses of the Vermont granite workers cohort: we should acknowledge that the association with low cumulative doses of silica is overall weak; it is influenced by a number of variables and methodological techniques as well as the study design; and it does contradict the fifth Bradford Hill principle of causation, as it does not replicate wherever silica exposure occurs. On the other hand, heterogeneity in risk according to the various circumstances of occupational exposure to silica was cited in the 1997 IARC conclusion; it might reflect a true biological phenomenon, for which there is clear experimental support (6); but, it has not clearly emerged thus far with meta-analytic procedures (5).

The first conclusion is that technology is now available that can better characterize the surface properties of crystalline silica in dust samples from specific workplaces and test their specific bioreactivity towards cytokine induction and adducts formation. The NIS program of workplace inspections and measurements in the Tuscany and Emilia

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Romagna regions might provide a very useful background to identify cohorts, including workers in small factories and workshops, with detailed information on the specific size and bioreactivity of the silica particles they are exposed to, as well as their lifestyle habits, such as smoking, and other concurrent workplace exposures. Acquiring the necessary statistical power for a profitable analysis might require extending the programme to other regions and perhaps accessing important research funding, which is so difficult to obtain, particularly when Occupational Health is concerned. Perhaps greater opportunities might be offered by extending the surveillance programme to Eastern Europe and developing countries, to where most mining companies have moved their businesses and where silica exposure levels are at present far more elevated. To do so, different opinions and different perspective should be brought together in a common multidisciplinary effort. The scientific consortia created by the NCI are an example of an effective way of creating synergy and achieving important advances in knowledge.

The second conclusion is that, if lung cancer risk actually varied by workplace depending on the specific mineralogical, crystallographic, granulometric, and chemical/physical features of silica particles, as suggested by experimental work, the binary yes/no approach of the IARC classification of human carcinogens would not effectively describe its carcinogenic properties, and the fifth Bradford Hill criterion should be amended. However, although the semantic contradiction between silica exposure and silicosis definitely makes sense from a regulatory perspective, it does not change the fact that no silicosis develops without silica exposure; therefore, a wise decision would be to classify silica for its carcinogenic potential and assign to it the H350i label, maintain the current exposure standards and promote research to identify those trades and work situations that pose elevated risks at airborne silica concentrations lower than the current standard, thus independent of silicosis, if confirmed.

This leads to my third conclusion, which is not a conclusion, i.e. what standards should currently be applied? The precaution principle would suggest a general introduction of the proposed ACGIH standard of 25 mg/m^3, under the assumption that more protection is always better. However, who could enforce compliance with such low levels when not even all the available methods are able to detect them, as the NIS experience suggests? Regulatory agencies might set lower standards, but reality requires keeping under control small factories and workshops where no monitoring programme has ever been implemented, and therefore even compliance with the current standard is at best uncertain. One thing would be to set a lower standard, which would make many of us happier; enforcing it would be quite another story. A long and thorough discussion would follow in this regard, which is outside the scope of this already provocative and stimulating set of papers. Ethical and forensic issues are at stake, as well as advances in industrial hygiene methods, with measurements of nanosized particles and particle surface analyses. More than ideological disputes, there is a need for renewed international collaboration.

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