

Silica, silicosis and lung cancer: what level of exposure is acceptable?

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RIASSUNTO

«**Silice, silicosi e tumore polmonare: quale è il livello di esposizione accettabile?**». La recente Direttiva Europea 2017/2398 ha classificato la silice cristallina respirabile come cancerogeno, confermando la valutazione della IARC e di altre autorevoli agenzie ed organismi scientifici internazionali. L'Unione Europea (UE) ha contestualmente raccomandato un limite di esposizione professionale di 0,1 mg/m³ sulla base di valutazioni economiche e di fattibilità tecnica ma non di valutazione del rischio per la salute. Al di là della questione se la silice sia cancerogena di per sé, come suggeriscono alcuni studi, o se piuttosto la silicosi sia un prerequisito necessario per lo sviluppo del tumore polmonare, come altri sostengono, al livello di esposizione raccomandato dalla UE troppi lavoratori continueranno ad ammalarsi di silicosi, oltre che di tumore polmonare.

Silicosis is far from defeated and millions of workers are still affected worldwide today. Further concern comes from the more recent Directive (EU) 2017/2398 of the European Parliament and of the Council amending Directive 2004/37/EC on the protection of workers from the risk related to exposure to carcinogens or mutagens at work (CMD). In endorsing IARC classification of respirable crystalline silica (RCS) as a human carcinogen (7), the EC confirmed that there is sufficient evidence for the carcinogenicity of RCS, and stated that a limit value should be established, as well as for thirteen other chemical agents or groups of agents (6).

Indeed, several cohort and case-control studies and meta-analyses have consistently shown a higher, dose-dependent risk of lung cancer, of all main histologic types and by both cumulative exposure and duration of exposure (2), in workers exposed to silica in different countries and trades. Risk is generally, although not always, higher in subjects affected by silicosis compared to workers exposed to silica but

showing no evidence of silicosis. However, the carcinogenic role of silica *per se*, in the absence of silicosis, although supported by a number of studies (3, 9, 14) is still controversial and recent publications have not been able to shed light on this critical aspect (5, 11). Confounding factors such as cigarette smoking and exposure to ionizing radiation or other carcinogens might have modulated the results in some studies. In addition, in several meta-analyses the biophysical properties of RCS to which workers were exposed to in different work settings were considered to be the same; if it were not so, the different properties of RCS might explain the significant heterogeneity across the epidemiological findings.

An important issue to be solved, therefore, is whether RCS is a carcinogen *per se* and, if so, by what mechanism. Or whether, alternatively, the fibrotic process is a necessary prerequisite for the development of lung cancer, a conclusion not confirmed also by a more recent study (10). Further debate is expected following a re-evaluation of the

sensitivity and specificity of chest x-ray in respect to pathology in detecting the pulmonary tissue inflammatory reaction to inhaled silica (4). A definite answer to this crucial question is required, however, in order to improve both the risk assessment and the risk management of both occupational diseases. It would help, for instance, in solving the issue whether lower exposure limits are needed in order to protect workers not only against the risk of silicosis but also from that of lung cancer. In fact the values currently recommended may not be protective enough for the workers against silicosis, let alone lung cancer (15).

At present, different occupational exposure limits are proposed by the various agencies, which are based on different criteria and methodologies. The ACGIH recommends a Threshold Limit Value (TLV) of 0.025 mg/m³ for crystalline silica after applying a safety factor of 2 to a presumed No Observed Adverse Effect Level (NOAEL) for health effects (silicosis) of about 0.05 mg/m³ (1). The EU Scientific Committee on Occupational Exposure Limits (SCOEL), following a classification of carcinogens in four groups according to the mechanism of action and the presence or absence of a threshold dose, has classified RCS as a weak genotoxic carcinogen (group C) for which a threshold should be expected to occur. However, as a NOAEL has not yet been demonstrated convincingly, according to SCOEL the occupational exposure limit (OEL) should lie below 0.05 mg/m³ as based on a level of acceptable risk, *i.e.* the concentration at which silicosis occurs in 5% of the workers exposed (13). Similar, although not identical, quantitative risk assessment estimates have been published by other agencies, such as NIOSH and OSHA (12). Surprisingly, while endorsing the classification of silica as a human carcinogen, after extensive consultation with the social partners, the EC recently established an OEL of 0.1 mg/m³ for RCS (6).

So, while further work is needed to clarify the mechanism of silica carcinogenicity, the classification of RCS as a human carcinogen by IARC and more recently by the EU is based on robust epidemiological evidence and rigorous scientific risk assessment. The exposure limit values currently recommended, however, are not health-based as they are set primarily through risk management criteria.

At such exposure levels, considered acceptable by feasibility and economical standards, though, far too many workers will continue to develop silicosis and lung cancer following exposure to silica concentrations deemed less so by scientific judgement (8, 10) and occupational health practice and ethics.

CONFLITTO DI INTERESSE

The authors have no competing interests to declare concerning the issues discussed in the letter. MM, LL and GJ are current members of SCOEL.

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