# Silica Exposure and Scleroderma: More Bridges and Collaboration Between Disciplines Are Needed

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# Silica Exposure and Scleroderma:

# More Bridges and Collaboration Between Disciplines Are Needed

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Dear editor,

We have read with great interest Turner et al.'s correspondence concerning Connective Tissue Diseases (CTD) and silica exposure in artificial stone workers (1). We totally support their call for a new awareness on silica hazards and their broadening to CTDs. Indeed, silica hazards are too often, and almost systematically, narrowed to silicosis (2).

Although LD Erasmus was historically the first to link silica exposure with the occurrence of systemic sclerosis (SSc or scleroderma), B Bramwell, a Scottish physician, had described an outbreak of scleroderma among stonemasons fifty years before (3). Despite this ancient association, SSc is still largely considered today "of unknown cause". The Pasteurian paradigm (one cause, one disease) may have participated to an over-simplified vision of causality in diseases, leading to a dichotomous vision of aetiologies: either an obvious and single cause for some diseases (especially communicable diseases) or "complex diseases" with too many causal factors to be properly captured. Nonetheless, recent insights in the pathogenesis of SSc, including cancer-associated SSc, remind us that the search for a cause may not be totally in vain. Indeed, when silica exposure is properly explored - *i.e.* prospectively assessed through dedicated occupational questionnaires and/or evaluation by experts in occupational medicine and toxicology - this exposure appears to be strikingly frequent in male patients with SSc: at least half of them having occupational silica exposure in recent European studies (4). Therefore, crystalline silica exposure may be a decisive cause or trigger, and this would be especially relevant in males, more often engaged in occupations involving silica. Interestingly, recent insights in the pathogenesis of silica-induced autoimmunity in mouse models have highlighted that the production of autoantibodies after silica exposure was significantly higher in males in comparison with female littermates (5). In humans, sex/gender in SSc may be especially crucial, as SSc is frequently more severe in men.

The current outbreak of silicosis and CTDs after exposure to high silica content artificial stone dusts both demonstrates the specificity of the association of crystalline silica with

autoimmunity in comparison with other mineral dusts, and reminds us that silica exposure does not only concern mining industry but covers a wider range of sectors. In this regard, the call for systematic screening of patients for CTDs after silica exposure appears central, both in patients with and without signs of silicosis and/or pulmonary involvement. Concerning SSc, the systematic screening strategy proposed for a "very early diagnosis of SSc" (VEDOSS) (6) may be especially relevant for these silica-exposed patients. This "VEDOSS" strategy does not only include testing for antinuclear antibodies but also emphasises the central role of capillaroscopic findings and clinical detection of "puffy fingers", a manifestation of SSc that may precede the occurrence of sclerodactyly. Such a screening would therefore imply 1) a close collaboration of clinicians who have been trained to detect puffy fingers or other SSc early signs and who are familiar with capillaroscopic examinations with 2) specialists of occupational diseases and silica-associated respiratory disorders likely to detect the situations of silica exposure.

Beyond preventability and diagnosis, the lack of a proper understanding of the pathogenesis of silica-associated autoimmunity may also result from missing bridges between disciplines. From a toxicant viewpoint, this question of silica has been almost exclusively studied through fibrotic pulmonary diseases or cancer or, when addressing autoimmunity, has been based on mouse models of systemic lupus, whereas SSc has been considered for long as the CTD most frequently associated with silica exposure. The alarming recent outbreak of silica-associated CTDs may provide an opportunity to fill this gap and offer a timely lever to collectively better understand the pathogenesis of SSc.

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