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AGENCE FÉDÉRALE DES RISQUES PROFESSIONNELS



**Advies van de
Wetenschappelijke Raad**

Systemesclerose

**Blootstelling aan oplosmiddelen
en aan formaldehyde**

19-10-2023



Systeemsclerose in verband met blootstelling aan oplosmiddelen en aan formaldehyde

Samenvatting van het advies van de Wetenschappelijke Raad van Fedris van 19 oktober 2023

De Wetenschappelijke Raad stelt op basis van het advies van de medische commissie Chemische en Toxische Agentia vast dat er momenteel onvoldoende wetenschappelijk bewijs bestaat voor een verhoogd risico op systeemsclerose bij de werknemers die blootgesteld worden aan oplosmiddelen en bijgevolg, onvoldoende elementen die het bestaan van een overwegend oorzakelijk verband kunnen aantonen. Het is ook niet mogelijk om de betrokken oplosmiddelen te identificeren en de blootstellingscriteria te bepalen. Aan de voorwaarden die noodzakelijk zijn om systeemsclerose veroorzaakt door blootstelling aan oplosmiddelen en aan formaldehyde in te schrijven in het lijststelsel van beroepsziekten wordt dus niet voldaan.

Systeemsclerose is een zeldzame ziekte van het bindweefsel, gekenmerkt door een hyperactiviteit en een vasculaire hermodellering, een activering van de fibroblasten en een synthese van de extracellulaire matrix. De prevalentie van deze ziekte werd geschat tussen de 7,2 en 33,9 per 100 000 individuen in Europa.

In 2023 heeft prof. T. Nawrot een studie van de epidemiologische literatuur van de laatste 20 jaar (2001-2022) uitgevoerd: *Solvent and formaldehyde exposure and systemic sclerosis, a systematic overview of the current evidence*.

Op basis van die studie heeft de medische commissie Chemische en Toxische Agentia vastgesteld dat de wetenschappelijke studies in het geheel significante associaties tonen tussen de systeemsclerose en de blootstelling aan oplosmiddelen. Het is echter onmogelijk om deze associatie toe te kennen aan specifieke oplosmiddelen of om dosis-responsrelaties vast te stellen. In de meerderheid van de geanalyseerde studies is de blootstelling gebaseerd op de beschrijving van de werkplek, de titel van de functie of de blootstellingen aangegeven via een vragenlijst; de gedetailleerde informatie over de duur en de intensiteit van de blootstelling of het verdachte oplosmiddel ontbreekt.

De commissie besluit dat er tot op heden nog onvoldoende elementen zijn in de literatuur om een duidelijk oorzakelijk verband aan te tonen, een drempel van verdubbeling van het risico vast te stellen en blootstellingscriteria te bepalen voor de verschillende organische oplosmiddelen en/of formaldehyde.

De Wetenschappelijke Raad heeft de studie van prof. Nawrot en de conclusies van de commissie Chemische en Toxische Agentia goedgekeurd.

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- Noot van de redacteurs: De volgende studie waarvan de resultaten publiek werden gemaakt in 2023 werden niet opgenomen in de studie, maar werd voorgesteld in de vergadering van de Wetenschappelijke Raad, die het dus kon analyseren alvorens zijn advies te geven: Muntyanu A., Milan R., Rahme E., Baron M., Netchiporouk E. Organic solvent exposure and systemic sclerosis: A retrospective cohort study based on the Canadian Scleroderma Research Group registry. *J Am Acad Dermatol.* 2024 Mar;90(3):605-607. doi: 10.1016/j.jaad.2023.04.062. Epub 2023 May 13.
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Solvent and formaldehyde exposure and systemic sclerosis, a systematic overview of the current evidence

Summary

Systemic sclerosis is a rare autoimmune disease with a multifactorial etiology. This document provides a systematic overview of the epidemiological evidence during the last 20 years, between systemic sclerosis and the possible occupational aetiologies due to solvent exposure.

In total we retrieved 10 studies of which 1 cohort, 7 case-controls and 2 descriptive studies of exposure prevalence in diseased populations. Seven of the eight analytical studies (1 cohort and 7 case-control studies) published in the last 20 years showed significant associations, with ORs ranging from 1.03 to 3.2. The most recent meta-analysis was published in 2016 and included 13 case-control studies and comprised 2107 patients. The combined Odds was OR 2.00 (95% CI 1.32–3.02; $p = 0.001$). Based on the reported literature and assuming a causal relationship we can estimate that in patients with SSc and proven occupational exposure to solvents, 65% to 50% (Attributable fraction of exposed) of SSc could be attributed to occupational exposure to solvents. However, to date the literature is not specific enough to establish dose-response relationships for different organic solvents and or formaldehyde as the majority of studies exposure is based on job description, job title or self-reported exposures via questionnaire, but not on actual dose-response associations in which exposure took into account the duration or intensity (with exception of 1 study for styrene).

Overall, there is consistency in the literature regarding the association between solvent exposure and scleroderma. However, is impossible to address this to specific solvents nor to provide a threshold for a doubling of the risk. While there is some consistency in the literature, the lack of comprehensive knowledge and a clear dose-response relationship limits our ability to establish causality.

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