New substances responsible for contact dermatitis due to clothing or footwear

In 2008, dimethyl fumarate (DMFu) was responsible for cases of allergic and irritative contact dermatitis in several European Union countries. It had been used as an antifungal agent on furniture (sofas, armchairs, etc.), footwear and clothing during maritime container transport or storage in warm and humid places.

French poison control centres (PCCs) were alerted to the first cases in 2008 by the French Institute for Public Health Surveillance (InVS), which became *Santé Publique France* on 1 May 2016. Following this alert and at the request of the Directorate General for Health (DGS), several studies of the cases recorded by the PCCs were carried out, in collaboration with the dermato-allergology vigilance network (Revidal-Gerda) and the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P) in 2009, 2011, 2012 and 2015. Each of these studies found around a hundred cases of contact dermatitis associated with the wearing of clothing or footwear. However, it was difficult to link them to DMFu exposure because analyses of the articles had rarely been carried out, mainly because of their cost and the difficulty in identifying a testing laboratory able to perform them. Moreover, patch testing, which might have demonstrated the patient's allergy to one or more substances contained in the incriminated article, had rarely been performed, because the patient did not consult an allergist or dermatologist-allergist once cured, or because the specific patch test for a substance was not available or was too expensive for a general practitioner.

The last study by the PCCs carried out in 2015 showed that despite the inclusion of DMFu in Annex XVII of the REACH Regulation in May 2012[1], which prohibited its use and marketing in articles at concentrations above 0.1 mg/kg, cases of allergies and/or skin irritations were still being reported to the PCCs (see photos). The symptoms observed may have been related to another, unidentified substance, but this could not be confirmed in the absence of analysis of the articles and patch tests on the patients concerned.

This led the DGS and the General Directorate for Competition, Consumer Affairs and Fraud Control (DGCCRF) to ask ANSES to identify the skin irritant or sensitising chemicals, regulated or non-regulated, liable to be found in footwear and textiles, and in particular to propose a method for investigating cases of skin allergy or irritation reported by medical specialists, in order to improve knowledge of the substances in question.

ANSES therefore set up a ground-breaking biomedical research study in France to link the presence of one or more substances contained in clothing or footwear with the symptoms of patients having worn these articles. To do this, ANSES mobilised a group of volunteer hospital doctors specialised in dermatology-allergology and toxicology: 18 dermatologist-allergists from the Revidal-Gerda network, toxicologists from eight PCCs and specialist doctors from four occupational disease consultation centres (CCPPs). ANSES also organised the collection and analysis of suspect articles by two specialised laboratories, in order to identify and characterise the chemicals found in them.

Each clinical case was reviewed by a steering committee of toxicologists, dermatologist-allergists and chemists. The committee compared the results of the medical diagnosis (which included patch tests performed by the physician participating in the study), the results of chemical analyses by the testing laboratory and, if applicable, the results of additional patch tests not included in the standard batteries.

Between January and September 2017, 31 patients including 21 women (between 24 and 68 years of age) and 10 men (between 27 and 64 years of age) were recruited. One patient was unable to take part, living too far away from the dermatologist-allergists participating in the study. These 31 patients were matched with 42 articles to be analysed (one patient provided several articles suspected of being responsible for their contact dermatitis).

This study, which is currently being finalised, has already identified the imputable chemical in six articles causing symptoms. Some of these substances, in addition to their skin sensitising or irritant property, have carcinogenic, mutagenic or reprotoxic (CMR) potential, such as chromium VI, nickel and 4-aminoazobenzene. Substances not screened for by the dermatologist-allergists were found in the chemical analysis of the articles: this was the case with benzidine and the dyes CI Disperse Orange 37/76 and CI Disperse Yellow 23.

1. Commission Regulation (EU) No 412/2012 of 15 May 2012 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

For two articles, it was concluded that the symptoms were related to another cause than the suspect article. For five suspect articles, it was not possible to reach a conclusion due to cross-contamination with cosmetics or paint, or intensive washing of the article that may have caused the contact dermatitis.

It should also be noted that DMFu was never detected in the articles analysed.

This study also identified articles that did not comply with the regulations in force, leading ANSES to report them to the DGCCRF. In addition, it showed that, as with chromium VI, the regulatory thresholds currently recommended do not provide sufficient protection against elicitation, i.e. a new allergic reaction in people already sensitised to this substance.

All these results led ANSES to recommend revising the regulatory threshold for chromium VI in leather articles and setting regulatory thresholds for sensitising or irritant substances currently without a threshold, such as 1,4-paraphenylenediamine in clothing or drometrizole in leather. ANSES is also taking part in and supporting the European regulatory actions under way, designed to restrict the presence of sensitising, irritant and CMR substances in textiles and footwear.

Because of these initial results, ANSES has decided to extend this study in 2018, by increasing the number of patients recruited and doctors participating, in order to improve its territorial coverage and representativeness of clothing and footwear placed on the market in France.

Photos: Foot injuries from wearing shoes (CCTV, 2018)

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TO FIND OUT MORE, VISIT:

ANSES. 2018. Safety of footwear and textile clothing. Request No. 2014-SA-0237 "Textiles". ANSES Collective expert appraisal report and Opinion on the assessment of the skin sensitising/irritant effects of chemicals found in footwear and textile clothing.

Toxicovigilance Coordination Committee (CCTV). 2009. Risks associated with the presence of dimethyl fumarate. http://www.centres-antipoison.net/CCTV/Rapport_CCTV_DMFU_2009.pdf

CCTV. 2011. Diméthylfumarate ou articles susceptibles d'en contenir : recensement des cas symptomatiques notifiés entre janvier 2009 et février 2010 [Dimethyl fumarate or articles that may contain it: identification of symptomatic cases notified between January 2009 and February 2010]. http://www.centres-antipoison.net/CCTV/Rapport_CCTV_DMFu_2009-2010_VFINALE.pdf

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CCTV. 2018. Cas d'intolérance aux textiles et articles chaussants susceptibles de contenir des substances allergisantes et irritantes telles que le diméthylfumarate [Cases of intolerance to textiles and footwear that may contain allergenic and irritant substances such as dimethyl fumarate]. Retrospective study of cases of accidental exposure recorded by the French poison control and toxicovigilance centres from 01/01/2015 to 31/12/2015 http://www.centres-antipoison.net/CCTV/Rapport_DMFu_2015_GT_VPC_VFINALE.pdf