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SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

Opinion on

RISKS TO HEALTH FROM CHROMIUM VI IN CEMENT

Opinion expressed at the 32th CSTEE plenary meeting

Brussels, 27 June 2002

CSTEE OPINION ON:

RISKS TO HEALTH FROM CHROMIUM VI IN CEMENT

June 27, 2002

Terms of reference

The Commission is currently considering a proposal for a Directive relating to restrictions on the marketing and use of cement containing chromium VI compounds in concentration higher than 2 ppm. Such a restriction in the framework of the Directive 76/769/EEC has been requested by several Member States. Because cement is neither an existing nor a new chemical which has been assessed and evaluated in the framework of Regulation 793/93 or Directive 67/548/EEC, a careful scientific consideration of the risk is necessary.

In order to go ahead and to decide on the appropriate risk reduction strategy the Commission has forwarded to CSTEE the following questions:

Is it scientifically justified to conclude that chromium VI in cement can cause serious skin diseases for construction workers?

Can chromium VI compounds in cement further increase the incidence of skin diseases resulting from high alkalinity of cement, or contribute to the development of more dangerous sensitizing diseases?

Is it scientifically justified to conclude that chromium VI compounds can penetrate human skin, and also the leather gloves usually worn as a protective measure?

Is it scientifically justified to conclude that cement containing less than 2 ppm of chromium VI compounds could substantially reduce the risk of skin sensitization in practice?

Background

Contact dermatitis is one of the most frequently reported disorders among construction workers who regularly work with cement (Halbert ert al 1992, Geier and Schnuch 1996, Diepgen and Coenraads 1999, Guo et al 1999, Kaufman et al 1998). Prevalence is usually associated with poor individual protective measures such as low use of gloves, duration of work as cement worker and direct manual handling of cement (Guo et al 1999, Halbert et al 1992).

Chromium, especially chromium VI, is a well-known skin sensitizer, and there is good reason to assume that sensitization reactions in cement workers are the result of its chromium VI content. Wet cement has a high pH of 12,5 so that it can alter the *stratum corneum* of the skin facilitating the penetration of water-soluble substances. Thus, skin contact with the alkaline cement-water suspension results in irritation, thereby enhancing absorption of chromium VI and its sensitizing effect and the elicitation of allergic reactions.

The content of chromium VI in cement depends on the Cr content, mostly chromium III, of the raw material but also from the kiln lining and by chromium steel abrasion during the grinding process (CSTE/93/12/COM). Oxidation of chromium III to chromium VI occurs during cement processing in the kiln at temperatures between 1400–1500 °C.

The obvious correlation between the content of water-soluble chromium VI in cement and allergic reaction of the skin has already been described in the opinion by the Scientific Advisory Committee to Examine the Toxicity and Ecotoxicity of Chemical Compounds (CSTE/93/12/COM) when evaluating the safety of ferrous sulfate regarding its mutagenic potential and reproductive toxicity.

Chromium dermatitis can also be induced by other causes particularly from chromium compounds in leather gloves (Zachariae et al 1996).

Measures to reduce exposure to chromium

Such measures include education and personal protective measures e.g. half-hourly sodium dithionite hand washes, water and alkaline protective gloves and barrier creams (Halbert et al 1992, Irvine et al 1994). It is to be mentioned that most leather gloves contain chromium compounds unless a non chromium tanning process has been applied (Nygren and Wahlberg 1998).

Reduction of chromium VI in cement is obtained by adding 0.35% (w/w) ferrous sulfate to the cement. As soon as the cement is wetted the ferrous sulfate reduces the water soluble chromium VI to less soluble chromium III.

As clinker, that is a major constituent of cement, became scarce, cement manufacturers in Canada, the US and Singapore have increasingly used slag from iron ore processing as a substitute. This results in lower chromium VI contents in the cement and a decrease of allergic contact dermatitis in Singapore has been reported (Goh and Gan 1996).

Efficacy of measures

The beneficial consequences of personal protection and reduction of chromium VI in cement are obvious. In several countries like Denmark, Finland, Sweden and partially in Germany ferrous sulfate has been added to cement reducing the content of water-soluble chromate to less than 2 ppm. In Denmark legislation was approved in 1983. Since that time in Denmark the prevalence of allergic cement eczema among cement workers decreased from 8.9% in 1981 to 1.3% in 1987 (Avnstorp 1989a,b, 1991, 1992). In these studies individual measures were not found to influence the development of irritant cement eczema. Avnstorp (1991) refers to a report by Goh and Gan (1990), who also found no protective effect from the use of barrier cream or an after work emollient in the development of occupational dermatitis in workers in the metal industry.

Reduction of chromium VI to chromium III in cement significantly reduces prevalence of chromium allergy. Burckhardt et al (1971) reported that 62 of 78 chromium-allergic patients did not react to a solution of 40% cement in water to which 0.3% of ferrous sulfate has been added. Zachariae et al (1996) investigated 79 patients with a positive patch test to potassium dichromate observed in the Dermatology Clinic of the University of Copenhagen. Of 34 patients (19 males, 15 females) the source of chromate exposure could be established. Out of the 19 men 10 had a previous contact with cement, 7 of them had been sensitized before 1981 either by full-time construction work or in hobby/spare time-bricklaying. Only one had occupational cement contact since 1981. He

also reported the experience of the Danish Working Environmental Service during the construction of the combined tunnel and bridge over the Great Belt between 1992-1993. About 3000 workers have been involved in full-time jobs at the different construction sites, only 4 of them claimed skin diseases, 2 of them having contact dermatitis, 1 a follicular eczema due to contact with hydraulic oil, 1 an eczema due to contact with machine oil. Although not specifically addressed the authors relate this to the lower chromium VI levels in cement used in Denmark.

Workers exposed to cement with high chromium VI concentrations show a higher prevalence of cement eczema. During the Channel Tunnel project the British drive employed 5900 underground workers (Irvine et al 1994). These authors described skin problems in 1138 construction workers between January 1990 and January 1992. In 332 of them an occupational dermatitis has been diagnosed. Of the 180 patch tested patients 96 had a positive reaction to chromate, with a number of patients also having a positive reaction to cobalt and nickel. Most cases improved with regular medical supervision, education and personal protective measures, and relocation to less exposed work. In their conclusion the authors stress the beneficial effects of individual protective measures together with education in hygiene and "good housekeeping" at work. However they point to the Danish experience that reduction of chromium VI in cement considerably reduced morbidity and expenditure and recommend to follow the Scandinavian initiative.

A more recent report from the Dermatology Clinic of the University of Copenhagen confirmed previous findings. There was an overall decrease in chromate allergy, from 3% in 1985-86 to 1.2% in 1997-98 primarily among those of working age between 19 and 60 years (Johansen et al 2000).

By contrast, in a London Contact Dermatitis Clinic there was no appreciable difference in the prevalence of chromate sensitivity between 1982-3 and 1992-3 (Olsavszky et al 1998) during which addition of ferrous sulfate was not introduced in the UK. For females Patch-test-positive rates were 1.59% and 1.99%, and for males 3.99% and 4.25% in the early 1980s and 1990s, respectively.

In Switzerland a decrease of cement eczema from about 1000 cases in 1963 to about 100 in cases in 1993 is reported although no measures to reduce chromium in cement are taken (Hunkeler and Jacobs (1996). This is seen as the result of education and personal protective measures.

Skin sensitization of Cr^{III} and Cr^{VI}

Immunologically the trivalent chromate appears to form the hapten of concern in chromate sensitization. It binds strongly to proteins most of which might be of less immunological relevance. However, hexavalent chromium readily penetrates the skin and the membrane of Langerhan´s cells where it is transformed into trivalent chromate which then binds to proteins and forms a hapten-carrier complex which acts as an antigen (Burrows 1987).

Direct skin contact with chromium compounds elicits an allergic response leading to eczema or dermatitis in sensitized individuals. Numerous animal studies and patch testing studies in humans have been conducted to evaluate the sensitizing effects of chromium VI and chromium III. After repeated intradermal injections of chromium VI and chromium III compounds subsequent patch testing with chromium VI and chromium III compounds resulted in the same erythmatic reactions. The response was greater when chromium VI was used as the sensitizer (Gross et al 1968, Jansen and Berrens 1968). Polak (1983) showed that guinea pigs sensitized with

chromium VI reacted with chromium III and vice versa. This indicates that chromium hypersensitivity is not directed against chromium of specific valency.

Information on chromium salts as skin sensitizers in humans has been repeatedly reviewed (Burrows 1987, Syracuse Research Corporation 2000). In 812 healthy volunteers patch testing with a chromium VI compound revealed chromium sensitivity in 1.7% of the test population (Peltonen and Fraki 1983). In chromium sensitive workers chromium VI was found to elicit reactions more frequently than do Chromium III compounds (Mali et al 1966). However, patch-testing of chromium VI sensitive patients with chromium III compounds revealed that high concentrations of chromium III compounds can also elicit an allergic reaction (Fregert and Rorsman 1966, Mali et al 1966). The higher concentrations of chromium III compounds needed to elicit an allergic reaction is attributed to a relatively greater degree of permeation of the hexavalent form than the trivalent form through the skin.

As for the elicitation potential for skin allergic reactions of chromium VI a threshold in patients that are allergic to chromium has been investigated. The study indicated, on normal skin, the patch test threshold was 10 ppm chromium. In the presence of an irritant (sodium lauryl sulfate) the threshold was closer to 1 ppm. It should be mentioned, however, that this study was based on a small sample of 17 patients, most of them females that were allergic to household products (Basketter et al 2001). Since elicitation levels are generally lower than induction levels it is likely that a level of chromium VI below 1 ppm must be reached before protection from sensitization is obtained. Since the concentration of chromium VI in mortar is 4 to 5 times lower than in dry cement, cement containing less than 2 ppm of chromium VI compounds would thus reduce skin sensitization and elicitation in practice.

Skin penetration of chromium III and chromium VI

In vitro and in vivo studies clearly indicate that chromium VI in contrast to chromium III is relatively well absorbed. In human skin in vitro uptake of chromium VI into the epidermis was more than ten times higher than that of chromium III even when chromium III was applied at twofold higher concentrattions. The amount of chromium VI in recipient phase and skin layers increased with increasing pH which was ascribed to the decreased skin barrier function. (Gammelgaard et al 1992). In humans application of chromium III to the skin did not increase urinary excretion of chromium III (Aitio et al 1984). Low skin penetration of chromium III agrees with the observation that much smaller amounts of hexavalent chromium than of trivalent chromium are required to elicit a positive reaction in hypersensitive persons (Fregert and Rorsman 1966, Mali et al 1966, Bagdon and Hazen 1991).

In cement, addition of iron sulfate reduces chromium VI to chromium III which in the alkaline cement water mixture precipitates as chromium hydroxide of very low water solubility. This is why chemical analysis showed no demonstrable water soluble chromium in cement when iron sulfate had been added (Fregert et al 1979). The hydroxide is virtually insoluble in human sweat (Bruze et al 1990).

Response of CSTEE to the questions

1. Is it scientifically justified to conclude that chromium VI in cement can cause serious skin diseases for construction workers?

On the basis of the available information CSTEE concludes that chromium in cement induces sensitization and causes serious allergic reactions in construction workers.

2. Can chromium VI compounds in cement further increase the incidence of skin diseases resulting from high alkalinity of cement, or contribute to the development of more dangerous sensitizing diseases?

The high alkalinity of the cement-water suspension results in irritation, thereby enhancing absorption of chromium VI. In the skin chromium VI is transformed into chromium III which readily binds to proteins and forms the hapten-carrier complex, that acts as an antigen. Thus, chromium VI compounds in cement enhance the severity of skin eczema of cement workers. Reduction of chromium VI to the less bioavailable chromium III is achieved by adding 0.35% ferrous sulfate to the cement which reduces the concentration of chromium VI to less than 2ppm. The bioavailability of chromium III is further reduced by formation of insoluble precipitates of chromium hydroxide in the alkaline cement water mixture.

3. Is it scientifically justified to conclude that chromium VI compounds can penetrate human skin, and also the leather gloves usually worn as a protective measure?

Water-soluble Chromium VI compounds have a higher penetration rate than the less water-soluble chromium III compounds. Due to the better water-solubility of chromium VI it is also assumed that chromium VI readily penetrates wet leather gloves.

4. Is it scientifically justified to conclude that cement containing less than 2 ppm of chromium VI compounds could substantially reduce the risk of skin sensitization in practice?

The available information clearly demonstrates that reduction of chromium VI in cement to less than 2 ppm of chromium VI compounds will reduce the prevalence of allergic cement eczema in workers. Since elicitation levels are generally lower than induction levels it is likely that this concentration will also reduce the risk of sensitization in practice. Educational and personal protective measures also contribute to the lower frequency skin sensitization. Without protective measures reduction of chromium VI in cement alone will reduce but not eliminate prevalence of chromium allergy but not the prevalence of irritative cement eczema.

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