# Technical Report

# No 45

# Nickel, Cobalt and Chromium in Consumer Products: Allergic Contact Dermatitis

## March 1992

ISSN-0773-8072-45

# TECHNICAL REPORT
# No 45

## Nickel, Cobalt and Chromium in Consumer Products:

## Allergic Contact Dermatitis

ISSN-0773-8072-45

Brussels, March 1992
©ECETOC copyright 1992

ECETOC Technical Report N° 45

© Copyright - ECETOC (European Chemical Industry Ecology and Toxicology Centre), 4 Av. E. Van Nieuwenhuyse (Bte 6), 1160 - Brussels, Belgium.

All rights reserved. No part of this publication may be reproduced, copied, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise without the prior written permission of the copyright holder. Applications should be made to ECETOC for the attention of the Director.

The content of this document has been prepared and reviewed by experts on behalf of ECETOC with all possible care and from the available scientific information. It is provided for information only. ECETOC cannot accept any responsibility of liability and does not provide a warranty for any use or interpretation of the material contained in the publication.

# Nickel, Cobalt and Chromium in Consumer Products: Allergic Contact Dermatitis

**CONTENTS**

# Nickel, Cobalt and Chromium in Consumer Products: Allergic Contact Dermatitis


## SUMMARY

Despite the improved awareness of the potential for nickel, cobalt and chromium to cause skin allergy, the incidence of sensitisation resulting from them is generally on the increase especially for nickel.

This report reviews data from the published literature and unpublished industry data on transition metal contamination of consumer products, and assesses the hazard to man. Consumer products are defined for the purposes of this report as personal care items and detergent/cleaning products used regularly in domestic work.

The analytical data demonstrate that consumer products are a relatively minor source of contact for nickel, cobalt or chromium. The trace levels of nickel, cobalt and chromium found in consumer products will not be the primary cause of sensitisation to these transition metals. Levels will be too low and exposure too brief. A person allergic to these metals has many other more significant sources of daily contact such as jewellery and metal objects. It is therefore necessary to focus on decreasing the high exposure to these transition metals from other sources rather than on possible trace amounts of metals found in consumer products.

Current good manufacturing practice ensures that nickel, cobalt and chromium concentrations in consumer products are less than 5 ppm of each metal. It is recommended that this should be accepted as a standard for maximum concentrations and that the target should be to achieve concentrations of no more than 1 ppm. Since it is recognised that consumer products manufactured to this standard are unlikely to give rise to allergic contact dermatitis, occasional minor deviations above 1 ppm are not seen as posing a significant risk. Even with the strictest controls it is recognised that some allergic individuals may show an elicited reaction. This situation is no different from that which applies to many chemicals known to elicit a reaction in exceedingly

sensitive people and to many foods known to cause problems in specific sub-populations. In all such cases the only solution is avoidance of the chemical (product) or food. In general, practical regulatory control of the use of sensitisers is aimed at the vast majority of people and not the population of sensitised individuals which is exquisitely sensitive.

## 1. INTRODUCTION

The transition metals nickel, cobalt and chromium are a major cause of allergic contact dermatitis in the general population (Fisher, 1986; Fowler, 1990). Recently, some groups have raised again the issue of whether trace levels of these metals in consumer products contribute to this disorder (Nava *et al*, 1987; Vilaplana *et al*, 1987; Angelini and Vena, 1989). To address this question a Task Force was convened with the following terms of reference:

to collect data on the concentrations of nickel, cobalt and chromium in consumer products and consider the forms of nickel, cobalt and chromium for which there is information on skin sensitisation;

to review the role of nickel, cobalt and chromium in the aetiology of allergic contact dermatitis in the light of the concentrations found;

to recommend an acceptable level for allergic individuals.

The definitions of the most important terms used in this report are given in Appendix 1.

## 2. BACKGROUND

Allergic contact dermatitis (ACD) is a relatively common skin condition which is caused by a wide range of substances eg. perfumes, preservatives, plants, dyes, rubber chemicals, resins as well as transition metals (Cronin, 1980; Fisher, 1986). Nickel (Ni), cobalt (Co) and chromium (Cr) are often associated with ACD at specific skin sites (eg. the hands) and contribute significantly to occupational disease (eg. chromium in cement). Not infrequently the dermatitis resulting from contact with these metals is chronic, even when obvious sources of exposure have been eliminated (Burrows, 1983; Angelini and Vena, 1989; Adams, 1990; Fowler, 1990; Moeller, 1990).

At a dermatology clinic, when an individual presents with possible contact dermatitis, it is common for the medical history and examination to be supplemented by patch testing (cf. Appendix 2). By this means, a fairly high incidence of allergy to the transition metals has been identified (Cronin, 1980; Fisher, 1986; Fowler, 1990). Whilst in general the source of metal contact is well known (pierced ears, metal working/refining industries, cement etc), in a minority of cases it is not possible to identify a particular source of contact with the offending metal. Although there may be no direct correlation, the frequency of association with a possibly chronic condition such as hand eczema can be high (Wilkinson and Wilkinson, 1989). This leaves the physician to search for less obvious sources of metal contact. In this manner, the problem of chromium in household bleach was first identified (Rabeau and Ukrainczyk, 1939).

Nickel, cobalt and chromium are not components of modern formulations for the consumer products in question (see below for definition), but they are present as low level impurities in some of the raw materials. Modern analytical techniques can detect trace levels (low ppm range) of these metals in various consumer products. Consequently, several authors have suspected that impurity levels of nickel, cobalt or chromium in household products, whilst not a primary cause of allergy, could be sufficient to maintain the allergic

dermatitis (Nater, 1963; Malten and Spruit, 1969; Feuerman, 1971; Nava *et al*, 1987; Vilaplana *et al*, 1987; Angelini and Vena, 1989; Kokelj *et al*, 1989).

Clearly, it is essential that individuals with an existing contact allergy to these transition metals do not suffer episodes of dermatitis as a consequence of using consumer products contaminated with nickel, cobalt or chromium. The primary induction of allergy by this route would also be unacceptable.

This report reviews the published literature and unpublished industry data on transition metal contamination of consumer products, and assesses the hazard to man. Consumer products are defined for the purposes of this report as personal care items and detergent/cleaning products used regularly in domestic work. The Task Force realised that other products may contain nickel, cobalt and chromium in variable amounts but these products would be used in only a limited way such that exposure would be negligible. The Task Force has performed a hazard/risk assessment for the transition metals. Data were collected in order to provide an accurate measure of sensitisation potential, including dose response data, in both man and animal models. This information has then been assessed in relation to levels of the transition metals found in consumer products, and in relation to the known epidemiology of allergic contact dermatitis to these metals and in the context of the nature and extent of consumer exposure.

On the basis of the information generated guidelines are recommended which should minimise consumer risk in particular to the more sensitive individuals.

# 3. REVIEW OF ALLERGIC CONTACT DERMATITIS RESULTING FROM EXPOSURE TO NICKEL, COBALT AND CHROMIUM

## 3.1. DEFINITION OF ALLERGIC CONTACT DERMATITIS

Allergic contact dermatitis (ACD) or contact sensitisation is a common inflammatory skin disease caused by agents such as plants, chemical compounds and topical medications. It is defined as a delayed hypersensitivity response in a person's skin manifested as an eczematous reaction to contact between the epidermis and the sensitising agent. Several factors dictate the severity and persistence of the skin response including the sensitivity of the subject, the length of the exposure, the dose and the potency of the antigenic stimulus (Katz, 1990). The development of ACD is a two step process involving induction and elicitation. This process is described in more detail in Appendix 3.

It is necessary to distinguish between allergic and irritant skin reactions.

An **allergic** (contact sensitisation) reaction is an inflammatory reaction which is a consequence of an immunological process. It is characterised by itching, erythema, papules, oedema and possibly vesicles. The reaction boundary is often diffuse and the response usually lasts for several days. Another common feature is that the skin reaction can also increase in strength after removal of the test substance (Fregert, 1981).

An **irritant** reaction (Irritant Contact Dermatitis) is an inflammatory reaction which is provoked by direct cell damage and not by an immune process. Characteristically the erythema is limited to the damaged contact area, the reaction area being sharp. In mild, acute cases there is no itching, oedema, papules or vesicles and the erythema appears within one day and disappears rapidly after removal of the irritating substance. Some irritants can cause the skin to swell without erythema and strong irritants can produce erosions or bullae (Fregert, 1981).

It is, in practice, difficult to distinguish clinically between contact dermatitis caused by irritant and allergic reactions. Studies of healthy

individuals using patch tests may clarify whether a substance is likely to produce responses which are irritant or allergic in nature but the difficulty in diagnosis may persist due to the great variation among individuals in susceptibility to irritants (Fregert, 1981; Fowler, 1990).

## 3.2. ALLERGIC CONTACT DERMATITIS TO NICKEL, COBALT AND CHROMIUM IN MAN

### 3.2.1. Introduction

The metals nickel, cobalt and chromium are ubiquitous in the environment. Despite the improved awareness of the potential of these metals to cause skin allergy, the incidence of sensitisation resulting from contact with them is generally increasing (Fowler, 1990). The prevalence of metal allergy in the population prompts the search for metal releasing objects with which the individual comes into contact.

In this section, epidemiological and human patch test data will be considered separately. A summary of information gathered from the literature on the epidemiology of ACD to nickel, cobalt and chromium can be found in Tables 1 and 2. It must be remembered that the incidences of ACD reported almost always relate to patients attending dermatology clinics and are not representative of the general population.

### 3.2.2. Epidemiology

Epidemiology is the scientific discipline used to describe disease occurrence in a population and to assess the nature and distribution of risk factors. Thus, epidemiological research provides the basis for prevention of disease and planning of health care.

The prevalence of metal allergy varies with the population tested, the geographic location and patch test techniques, vehicles and concentrations employed.

3.2.2.1. Epidemiology, Nickel. Nickel is the most frequent contact allergen (Menné *et al*, 1989; and Tables 1 and 2). Although the majority of cases are non-occupational, work related nickel dermatitis is a predominant diagnosis in reports on permanent disability due to skin disease. Nickel dermatitis was first clinically recognised as "Das Galvanizierekzem" in 1889 (Blasko, 1889). Occupational nickel dermatitis was common in the 1920's and 1930's (Bulmer, 1926; Jadahssohn and Schaaf, 1929; Du Bois, 1931), while nickel dermatitis was first reported in consumers in the early 1930's and recognised as a large scale consumer problem in 1936 (Bonnevie, 1936).

The intimate contact of metallic nickel and nickel alloys with the skin is the main reason for the high incidence of nickel allergy in the population. Most cases in women are non-occupational and result from ear piercing or intimate contact with metal objects such as clips, buttons, zippers, buckles, and clasps (Peltonen and Terho, 1989; Menné *et al*, 1987; Emmet *et al*, 1988; Widstroem and Erikssohn, 1989).

Schubert *et al* (1987) stated that costume jewellery, wrist watches and metal clothing buckles are not only the most important sources of primary nickel sensitisation but also of relapses and persistence of allergy. Santucci *et al* (1989) asked 730 schoolgirls (mean age 17 years) about the incidence of contact dermatitis at the sites of direct contact with earrings, 92% regularly wore earrings, 70% daily, 17% weekly, 13% monthly; 438 girls (67%) described symptoms of itching, erythema or eczema and a clear relationship was found with the repeated use of cheap (67%), gold (2%) or silver (1%) earrings, or more than one of these. The schoolgirls were not patch tested and thus the authors could not say if they were truly sensitised.

3.2.2.2. Epidemiology, Cobalt. Cobalt is an essential trace element. It is ubiquitous in foods (Schrauzer, 1984). Many metal alloys contain cobalt together with nickel.

Cobalt is a metal which also causes allergic reactions in man (Cronin, 1980; Dooms-Goossens *et al*, 1980; Fisher, 1986; Fowler, 1990; Shehade *et*

*al*, 1991). The latter reported on 4,721 subjects of whom 5.7% were patch test positive to cobalt. Simultaneous allergy to nickel and cobalt is frequent and cobalt has been considered of significance in persistent hand eczema in patients with positive patch tests to nickel and cobalt (Menné, 1980).

Menné (1980) performed patch tests on 168 subjects with pure cobalt salts and few reacted. Since isolated cobalt allergy is very rare, it has been suggested that positive results could occasionally be due to nickel impurities in cobalt (Rystedt and Fischer, 1983; Fisher, 1986; Eady *et al*, 1991).

3.2.2.3. Epidemiology, Chromium. Chromium metal, alloys (eg. stainless steel) and chrome plating are not soluble and in this form its sensitisation potential cannot be realized. Nevertheless the corrosive action of sweat must be borne in mind as this might cause solubilisation of chromium and thus realize its potential.

The sensitising capacity of chromium salts depends on their concentration, valency, solubility, pH, and presence of organic matter. Hexavalent soluble salts in an alkaline medium have the greatest sensitising potential (Burrows, 1983) and there is a good correlation between the solubility of chromium salts and their sensitising potential.

Organic material has the ability to reduce hexa- to trivalent chromate (Burrows, 1983). Hexavalent salts, which are more soluble than trivalent salts, penetrate more easily through the skin where they are reduced to $Cr^{3+}$ which is considered the sensitising agent (Polak, 1983).

The occurrence of chromate allergy in cement workers was first described by Bonnevie (1939) and Stauffer (1939) but was thought to be due to chromium compounds in leather gloves. Pirila and Kilpio (1949), reported that 10 patients with cement dermatitis were sensitive to chromate. Jaeger and Pelloni (1950) demonstrated that 32 patients with cement dermatitis all had a positive patch test to potassium bichromate

but of the 168 other patients with eczema from other causes, only 5% reacted. This was first proof of the relation between cement dermatitis and chromium allergy. Subsequently cement was recognised as the most common cause of primary sensitisation to chromate (Cronin, 1971, 1980). Recently there has been a decrease in the number of cases of cement dermatitis probably due to changing patterns of handling cement, such as increasing use of ready-mixed cement, increased automation in the building industry, addition of ferrous sulphate (a complexing agent for chromium) and the improved facilities for personal hygiene.

Bleaches and liquid detergents containing chromates were reported to be a cause of "housewives dermatitis" in Belgium, France, Spain and Italy. Garcia-Perez *et al* (1973) quoted a high incidence in Spain. Lachapelle *et al* (1980) showed that liquid bleach in Belgium contained up to 83 ppm (mg/l) chromate. A correlation between the use of these bleaches and the frequency of chromate allergy in Belgium was suggested (Dooms-Goossens *et al*, 1980). Lachapelle *et al* (1980) showed that removing chromate from bleaches reduced the incidence of dermatitis. In other countries bleaches had only trace levels of chromate, which were no different from other consumer products (Hostynek and Maibach, 1988).

Feuermann (1970, 1971) reported that in two groups of housewives with eczema in Israel, a high proportion (34% in 1970; 91.6% in 1971) were patch test positive to potassium bichromate. This high incidence has never been reported by others. All detergents analysed contained traces of chromates. There is no evidence that the detergents used in Israel have a higher chromate content than those used elsewhere.

In general, the problem of chromate allergy associated with household products has resulted from deliberate addition of chromate salts to the product. Cessation of this manufacturing practice resolved the outbreak of ACD (Burrows, 1983).

3.2.2.4. Incidence Trends and Sex Differences. Historically the incidence of positive patch test reactions to chromate and nickel remained remarkably constant (9% in 1937; 12% in 1970) (Baer *et al*, 1973). During the last

two decades a clear increasing trend was observed for nickel ACD and to a lesser rate for cobalt ACD, but a decreasing incidence was found to chromate (Gailhofer and Ludvan, 1987; Kiec-Swierczynska, 1990) (cf. Table 1). There are clear sex differences in the incidence of positive patch test reactions to these metals.

**Nickel**: Studies of the trends over a long period indicate that nickel allergy is increasing, particularly in the female population (Table 1) (Angelini and Vena, 1989; Kiec-Swierczinska, 1990).

Several studies have been conducted which examined the incidence of patch test reactions to nickel in the general female population. These have been summarised and show approximately 10% of women may have a nickel sensitivity (Menné *et al*, 1989), although the figure was only 0.67% in a group of male soldiers (Seidenari *et al*, 1990).

In all reports from dermatological departments in industrialised countries, nickel is the most frequent contact allergen. The increasing incidence has continued and in Sweden one in four women patch tested was positive to nickel (Moeller, 1990). In former times, most cases of female nickel dermatitis were ascribed to suspenders. It would be expected that changes in female clothing habits should have been followed by a marked decrease in nickel sensitisation. This has not been the case. Instead, ear piercing and the wearing of cheap jewellery have maintained the intimate metal/skin contact leading to nickel allergy. The higher frequency of nickel allergy among young girls with pierced versus non-pierced earlobes was impressive (Larsson-Stymne and Widstroem, 1985). Female reactors do not predominate in all countries, although the exposure may be the same as in Kuwait, Japan and Nigeria (Kanan, 1969; Sugai *et al*, 1979; Olumide, 1985). Local dressing habits and varying occupational exposure may explain these differences. In Nigeria, nickel plated wrist watches and watchbands are the main sources of nickel sensitisation in men. The hot and humid climate increases corrosion from nickel plated articles and alloys (Menné *et al*, 1989). Some men are increasingly decorating themselves by ear piercing and wearing jewellery, as well as being exposed to metal in jeans, etc.

This results in an increasing ACD incidence in males, but on a significantly lower level than in females (cf. Table 2).

Romaguera *et al* (1988) investigated the sources of contact allergy from nickel. They tested 964 patients who complained of metal intolerance and compared the results to those of 200 controls. The authors noted an increasing incidence of positive patch tests to nickel from 13.8 to 26.1% over the past ten years and also a corresponding increase for cobalt, from 4.5 to 10.5%. Of the 26.1% positive to nickel, 5.5% were occupational and 20.5% non-occupational. The increase was assumed to be due to contact with metals or alloys containing nickel, above all with imitation jewellery sometimes worn from a very young age.

In a study population of 1,158 adult volunteers the prevalence of positive patch tests to nickel was 5.8% of which 9% women reacted compared with 0.9% men (Prystowsky *et al*, 1979). There was a strong correlation of nickel allergy with a history of pierced ears, earlobe rash, and jewellery rash. Women appeared to have higher rates of exposure to nickel than men which was reflected in their allergy incidence.

**Cobalt:** Most comparative studies demonstrate that the incidence of positive patch tests to cobalt has increased in the last twenty years, but not with such a clear effect as nickel (Table 1). In Poland, an increasing positive patch tests to cobalt were found in women, but with the opposite tendency in men (Kiec-Swierczynska, 1990).

**Chromium:** In contrast to nickel and cobalt the incidence of chromate allergy seems to be decreasing. The North American Contact Dermatitis Group (NACDG) has seen a decline in the prevalence of positive patch tests from 7.6% in 1972 to 2.1% recently (Fowler, 1990). One possible reason for this may be better workplace protective habits which decrease the contact with construction materials and this is supported by data from Finland (Estlander, 1990). Avnstorp (1989) reported the rate of chromate allergy in cement workers has decreased from 10.5% in 1981 to 2.6% in 1987. Likewise, hand eczema prevalence in these workers dropped