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Chromium in leather: is it a real health problem?

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- Trivalent chromium (CrIII) salts are used for tanning
- Hexavalent chromium (CrVI) is no longer present in modern tanning mixtures
- Small amounts of CrVI can be formed in certain conditions in CrIII-tanned leather goods



CrIII

- **Essential for the normal metabolism of glucose, lipids and proteins**
- **Daily requirement is 0.5-2 µg corresponding to a dietary intake of 0.03-0.13 µg/kg per day (equivalent to 2.1-9.1 µg per day for a 70 kg individual).**



CrIII

Toxicological data

- **Not genotoxic**
- **Inadequate evidence of carcinogenicity (IARC group 3)**
- **Animal studies did not show toxicological effects (oral administration)**

**Sources: ATSDR, 2012
EFSA, 2014
IARC, 2012**



CrVI

Toxicological data

- o Dermal, respiratory and gastrointestinal effects appear to be portal-of-entry effects for skin contact, inhalation and oral exposure, respectively
- o Systemic effects occur after very high exposures

Sources: ATSDR, 2012
EFSA, 2014
IARC, 2012



Allergic Contact Dermatitis (ACD)

ACD is due to allergic sensitisation to certain compounds, including Chromium

- **INDUCTION:** is the condition that leads to sensitisation.
 - This is generally associated with high level, prolonged contact with the agent
 - For certain compounds it has been shown that lower level, repeated exposures may cause induction

- **ELICITATION:** is the condition that leads to clinical signs of ACD in sensitised subjects



ACD

- About 20% of the general population is **sensitised** to at least one agent
- About 3% of these individuals are sensitised to CrVI
- Therefore about **0.6% of the general population** is sensitised to CrVI
- Among the CrVI sensitised subjects, 20-45% report skin reaction after contact with leather



Sources of Chromium

- Bleaches
- Chromated products
- Cosmetics
- Detergents
- Leather
- Medical implants
- Mobile phones
- Paints
- Tattoo ink



Chromium ACD

	INDUCTION	ELICITATION
CrVI	YES	YES
CrIII	NO	YES



Potency of CrVI and CrIII to elicit allergic skin reaction

	CrVI ($\mu\text{g}/\text{cm}^2$)	CrIII ($\mu\text{g}/\text{cm}^2$)	Ratio CrIII/CrVI
BMD₁₀	2.0	240	120
BMDL₁₀	1.1	134	122
MET 10%	0.089	>33	>370

BMC₁₀: BenchMark Concentration that causes allergic skin reaction in 10% of the tested sensitised subjects. Calculated on data pooled from 4 studies

BMCL₁₀: lower confidence interval (95%)

MET 10%: similar to BMC₁₀. Data from one study (Nethercott et al, 1994).



What is the evidence that chromium is the cause of allergic reactions to leather goods?

- Use of questionnaires and analysis of temporal trends
- Patch tests in subjects with reported “shoe-allergy” (or other leather-related allergy)
- Release of Cr from leather
- Patch tests with leather samples



Questionnaires

Increase of CrVI sensitised subjects reporting exposure to leather: from 24% during 1989-1994 to 45% during 1995-2007. (Thyssen et al., 2009)

However:

- Not confirmed by others (Caroe et al., 2010)
- Other allergens not taken into consideration (cross-reaction or co-exposure)
- Possible bias due to increased focus of dermatologists and patients on leather
- Temporal variability of sensitisation to various allergens not unusual

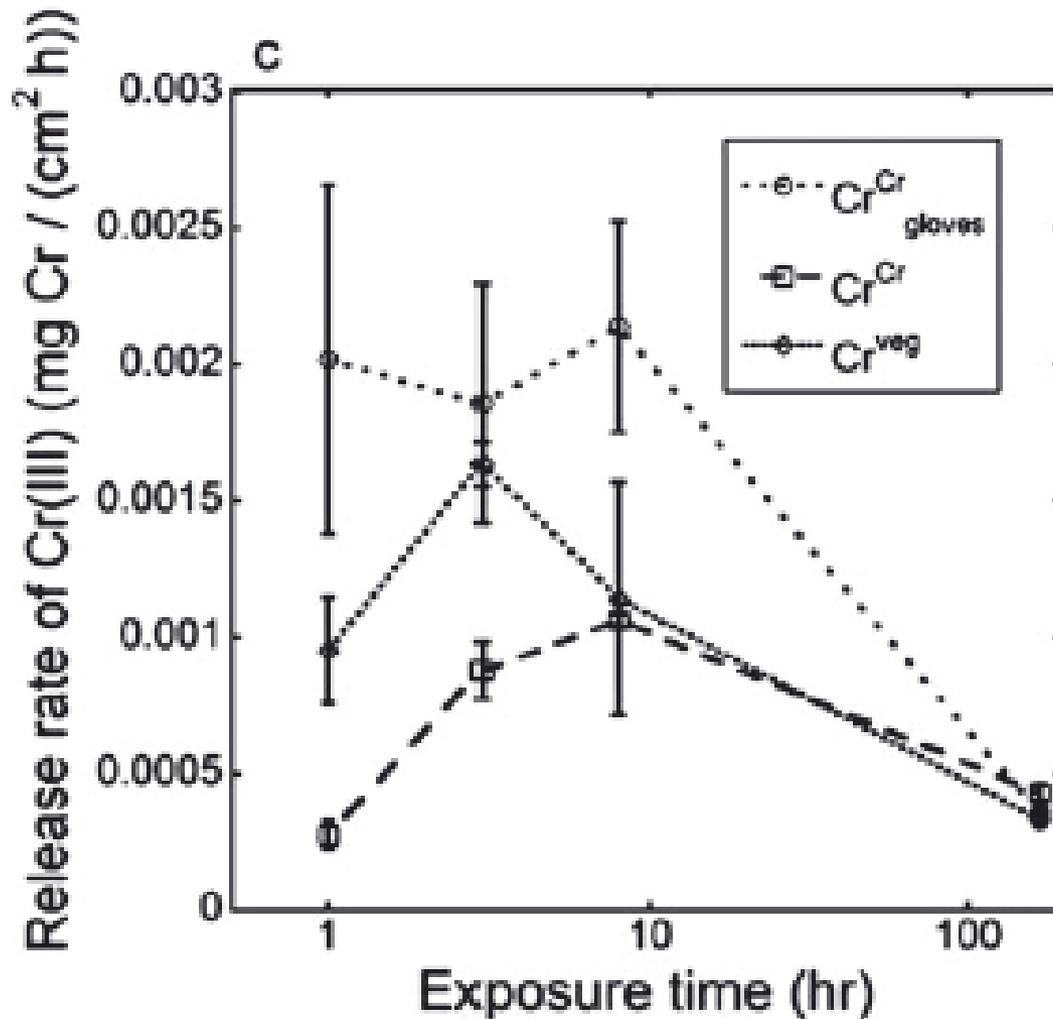


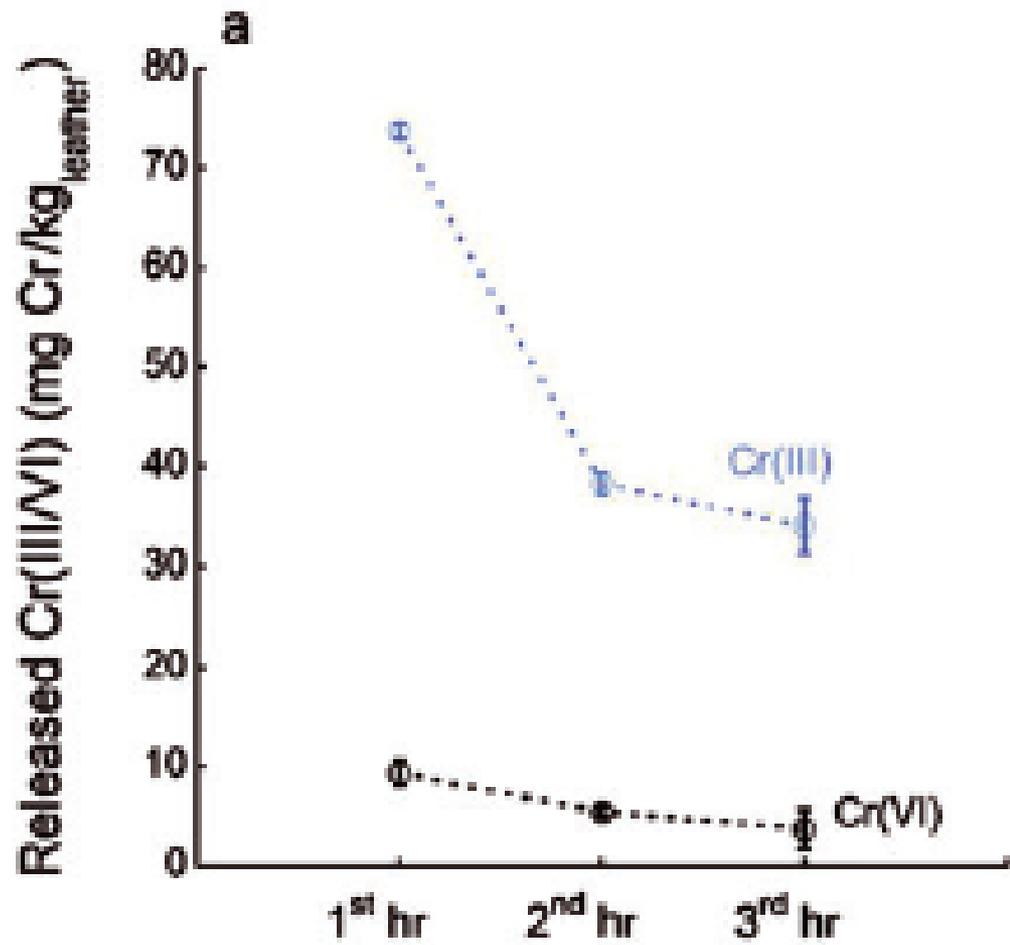
Patch tests in subjects with reported “shoe-allergy” (or other leather-related allergy)

- Shoes (and other leather goods) may contain other allergens:
 - Rubber antioxidants from rubber adhesives, innersoles, elastics
 - Cobalt
 - Nickel
- Not all subjects with “shoe-allergy” tested positive to CrVI patch test (in certain studies <30%)
- Certain subjects with “shoe-allergy” tested negative to all most common allergens



Release of Cr from leather





Release of Cr from leather

(from Hedberg et al., 2015)

$\mu\text{g}/\text{cm}^2$	CrIII		CrVI	
	Phosphate buffer	Artificial sweat	Phosphate buffer	Artificial sweat
release	2 in 3 hours	10-20 in 10 hours	0.3 in 3 hours	Not measurable
BMCL ₁₀	134		1.1	

For comparison, Cr deposition on hands of locksmiths, carpenters and cashiers is up to 7 $\mu\text{g}/\text{cm}^2$ per hour (Van Linden et al., 2008)



Patch tests with leather samples

Lack of correlation between the content of soluble CrIII and/or CrVI in 14 leather samples and allergic skin reaction in 15 Cr-sensitised subjects.

The total number of subjects who tested positive was 4/15.

	CrIII (ppm)	CrVI (ppm)	Patch test (+) (48 hours)
9 samples	93-209	< 3-16.9	0/15
1 samples	112	9.2	1/15
3 samples	90-591	<3-4.6	2/15
1 sample	12	< 3	3/15

(Hansen et al, 2006)



Comments to Hansen et al (2006)

- **No correlation CrIII and CrVI content and allergic skin reaction**
- **Quality and source of leather not specified**
- **Only 1 control of vegetable-tanned leather**
- **Content of other potential sensitisers not considered**



What is the evidence that chromium is the cause of allergic reactions to leather goods?

- Use of questionnaires and analysis of temporal trends: **EQUIVOCAL**
- Patch tests in subjects with reported “shoe-allergy” (or other leather-related allergy): **NOT ALWAYS CONCLUSIVE**
- Release of Cr from leather: **POSSIBLE; PRESENTLY, AMOUNT UNLIKELY TO BE ENOUGH**
- Patch tests with leather samples: **INCONCLUSIVE**



Other important factors

- o Quality of leather
- o Skin hyperhydrosis
- o Wearing socks or other barrier
- o Humidity



Quality of leather

Most of the time not assessed in the publications that estimated release of Cr, role of leather contact in ACD etc....

BUT QUALITY IS IMPORTANT!

Many authors report resolution/improvement of ACD following use of “good quality, new leather shoes”



Conclusions

- CrVI induces sensitisation
- CrVI and CrIII elicit ACD
- CrVI is >100 time more potent than CrIII
- CrIII (and CrVI) **was** probably responsible of some ACD cases associated with leather contact
- Modern tanning systems unlikely cause the release of CrIII and CrVI in sufficient amounts to cause ACD
- In any case, this problem involves a small minority of the population and there are mitigating measures



Thank you for your attention and patience

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