Cement Eczema

An Epidemiological Intervention Study

By

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København Universitet, den 7. juli 1992
Jørgen Falck Larsen
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The present review is based on the following piblications:

I. Avnstorp C. Cementeksem blandt danske arbejdere beskæftiget på byggepladser og i industrien. Ph.D. afhandling Københavns Universitet 1983.

II. Avnstorp C. Follow-up of workers from the prefabricated concrete industry after the addition of ferrous sulfate to Danish cement. Contact Dermatitis 1989; 20: 365-371.

III. Avnstorp C. Risk factors for cement eczema. Contact Dermatitis 1991; 25: 81-88.

In the text these papers will be referred to by their respective roman numerals.

PREFACE

This thesis has been made possible through the co-operation and help of many persons and institutions not all of whom I have been able to mention by name, yet, I hope they will accept my heartfelt thanks for their kind support.

All of the studies upon which this thesis was based were carried out at the Department of Dermatology at Gentofte Hospital and hence, I am greatly indebted to the late Professor Niels Hjorth for his great interest and encouragement. None of this would also have been possible without the invaluable and persistant support of my friend and supervisor, Professor Torkil Menné. It was through his help that it was possible for me to test Dr Sigfrid Fregerts hypothesis which was the cornerstone of my studies.

A large amount of clinical testing was involved in the study, much of which was the result of patch-testing done in collaboration with Head Nurse Ella Ploug Petersen. Her calm professionalism was a constant encouragement.

The subsequent analysis of the large amounts of data gathered was carried out together with consultant Erik Henriksen from the Department of Data Processing, Copenhagen County Hospital. His excellent work facilitated the interpretation of the data greatly.

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Last but far from least, I would like to thank The working Environment Fund in Denmark, the Danish Medical Research Council, Knud Højgaards Foundation, Else and Mogens Wedell-Wedellborgs Foundation and Mrs Liv-Bryhns Foundation for their financial support.

To Eva, Magnus and Martin

CONTENTS

1. AIMS OF THE STUDY

This study was carried out for the following reasons.

1) to determine the status of cement eczema in Denmark in 1981.
2) to investigate the influence of water soluble chromates in cement on the development and severity of allergic cement eczema.
3) to estimate whether the addition of ferrous sulfate to Danish cement decreased the risk of developing allergic cement eczema in Denmark.
4) to evaluate if individual preventive measures were able to protect against development of cement eczema.
5) to evaluate the medical and social prognosis of workers with cement eczema after the addition of ferrous sulfate to Danish cement.
6) to study possible socio-economic benefits derived from the addition of ferrous sulfate to Danish cement.

2. DEFINITIONS

Allergic cement eczema:
cement eczema with a concomitant chromium hypersensitivity.

Irritant cement eczema:
Cement eczema without a concomitant chromium hypersensitivity.

Objective cement eczema:
Presence of the following skin changes found at the examination: erythema and/or vesicles and/or hyperkeratosis of the wrists and/or the palms and/or the dorsal aspect of the hands and/or the fingers.

Reported cement eczema:
Episodes of hand eczema previously and/or within the past year lasting at least 2 weeks and/or currently.

Chronic cement eczema:
Hand eczema currently and within the past year lasting for at least 2 weeks.

Chromium hypersensitivity:
A positive patch test to potassium dichromate.

3. INTRODUCTION

The association between cement eczema and cutaneous chromium hypersensitivity was established as early as 1950 (*Jäeger & Pelloni* 1950). The development of chromium contact sensitivity probably depends on the concentration of water soluble hexavalent chromate (Cr(VI)) in the cement. The exact concentration of water soluble chromate in the cement needed to induce hypersensitivity is not known. The threshold concentration for elicitation of hypersensitive reactions in occluded patch testing is approximately 1 ppm (*Pirilä* 1954, *Allenby & Goodwin* 1983).

Chromium hypersensitive workers may develop chronic hand eczema due to the ubiquitous occurrence of chromium compounds (*Nriagu* 1988) and the primary irritant effect caused by the alkaline, abrasive and hygroscopic properties of the cement itself (*Burrows* 1983). The hand eczema of some workers clears due to hardening (*Høvding* 1970, *Hunziker & Musso* 1960, *Peck et al.* 1945). Some workers have latent hypersensitivity without manifestations of hand eczema (*Høvding* 1970, *Avnstorp* 1991, III).

Fregert et al. (1979) suggested a method of reducing the amount of water soluble chromate in cement by adding ferrous sulfate. In 1981, Aalborg Portland A/S, the only manufacturer of cement in Denmark, patented a method whereby the amount of chromate in the cement could be reduced using this method. As of September 1981, ferrous sulfate has been added to all the cement produced by Aalborg Portland A/S for use in Denmark, thus reducing the content of water soluble chromate in cement to not more than 2 ppm at a cost of about 1% of the total value of the cement.

Legislation stating that the content of water soluble chromate in dry cement must not exceed 2 mg per kg (2ppm) was passed in Denmark in 1983 (Arbejdstilsynets bekendtgørelse 1983).

4. HISTORICAL REVIEW

4.1. The evolution of cement

The concrete used today is a mixture of Portland cement, sand, stones and water. Mortar consists of a mixture of Portland cement, sand, water and often also hydrated lime. The exact composition depends on the purpose for which the product is to be used.

More than two thousand years ago the Etruscans used calcined limestone to make concrete and mortar. In ancient Rome a mixture of calcined limestone, vulcanic ash, sand, stone and water was used in construction work (*Portland Cement* 1980). The Latin word, cementum, means crushed stone. In 1824 *Joseph Aspdin,* a British builder, patented a cement produced by firing a mixture of limestone and clay (Table 1) (*Bogue* 1949). He called his product Portland cement because it was similar in appearance to a building stone quarried on the island of Portland off the south coast of England. In 1845 the first Portland cement, in the modern sense of the term, was produced by firing such a mixture to temperatures from 1,200°C to 1,400°C (Portland Cement in the Making 1977). Joseph Aspdin heated his mixture in small, primitive, vertical kilns (*Bogue* 1949) in which no chromate formed (*Fregert* 1981). Chromate was not formed during the production of cement until the introduction of the modern horizontal kiln (*Fregert* 1981).

4.2. Cement eczema

Irritant dermatitis caused by cement was described as early as 1700 (*Ramazzini* cited in *Calnan* 1960), and in 1831 it was suggested

Table 1. *History of cement eczema.*

1824	Portland cement. Primitive kilns
1845	Portland cement. High temperatures
1908	Cement eczema
1939	Cement eczema. Chromium allergy
1950	Cement eczema. Chromium in cement
1979	Ferrous sulfate. Chromate reduction
1981	Epidemiological studies in Denmark
1981	Industrial chromate reduction
1987	Epidemiological studies in Denmark

that lime was harmful to the skin (*Thackrah* cited in *Calnan* 1960). In 1908, the first cases of cement eczema since the introduction of modern Portland cement were seen among workers building the Metro in Paris and were described as "la gâle du ciment" (Table 1) (*Martial* 1908). In 1925, 5 cases of "lime dermatitis" were seen among tunnel builders in the London underground (*O'Donovan* 1925). In 1939, *Bonnevie* described 7 cases of cement eczema in Denmark. He saw positive patch test reactions to potassium dichromate in some of the workers and thought that the sensitivity was caused by their chromium tanned leather gloves (*Bonnevie* 1939). In 1950, *Jäeger* and *Pelloni* brought to light the importance of the chromium content of cement as the cause of chromium allergy among workers with cement eczema (*Jäeger & Pelloni* 1950). In 1970, *Høvding* published an epidemiological study in which 20 of a group of 366 (5.5%) bricklayers and bricklayers' assistants had cement eczema; 17 of those workers with cement eczema (85%) reacted positively to patch tests with chromate (*Høvding* 1970).

Most authors have found the medical prognosis of those suffering from allergic cement eczema to be poor (*Høvding* 1970, *Hunziker & Musso* 1960, *Burrows* 1972, *Burrows & Calnan* 1965, *Dooms-Goosens* et al. 1980, *Reichenberg* 1972). In Denmark 46 men received permanent disability pensions because of chromium allergy from 1970 to 1976. This was approximately 21% of all those with allergic skin diseases causing permanent disability during that period (*Menné & Bachmann* 1979).

5. CHROMATE IN CEMENT

5.1. The origin of chromate

The potential source of Cr(VI) in cement is the trivalent (Cr(III)) compound (Cr_2O_3) in the raw materials from which it is produced. Cr(III) compounds are oxidized to Cr(VI) compounds (CrO_4^{--}) when heated in the kilns to temperatures of approximately 1,400-1,500°C. The content of chromium in cement is determined by the presence of chromium compounds in the raw materials, by the kiln lining and by chromium steel abrasion during the grinding processes (*Skomorowski* 1985). The Cr(VI) content of cement varies from country to country according to variations in the amount of chromium in the raw materials (*Fregert & Gruvberger* 1972).

5.2. Reduction and solubility

Ferrous sulfate reduces Cr(VI) in cement to Cr(III) (Fig. 1). In 1971, *Burckhardt* reported that 62 of 78 chromium allergic patients did not react to a solution of 40% cement in water to which 0.3% ferrous sulfate had been added (*Burckhardt et al.* 1971). In a study including 8 chromium hypersensitive individuals, negative reactions were obtained after patch testing with 1.76 ppm of potassium dichromate in water solution. Furthermore, no reactions were found from patch testing with buffered cement after iron sulfate was added (*Bruze et al.* 1990(a)).

Chromate is highly water soluble, and the solubility increases with the alkalinity of the cement (*Brun* 1964, *Fregert & Gruvberger* 1973). In ordinary Danish Portland cement, the chromium content is 40.5 ppm, and of this, 9.6 ppm is water soluble chromate

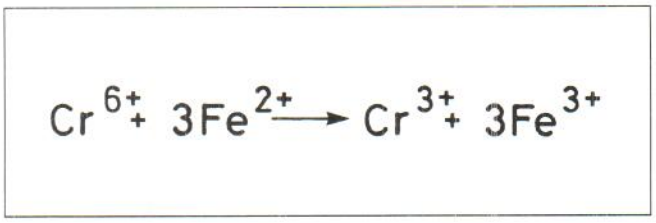

Fig. 1. *The main chemical reaction in the reduction of water soluble chromate by the addition of ferrous sulfate.*

(*Lund* 1977). Cr(III) compounds are precipitated in the alkaline environment as insoluble chromium hydroxide (*Fregert & Gruvberger* 1972). The addition of 0.35% (w/w) ferrous sulfate to cement reduces a water soluble chromate content of 20 ppm to undetectable concentrations (*Fregert et al.* 1979).

The chromium in both bagged cement and bulk cement will remain in a reduced state, as Cr(III) compounds, for 8 weeks. Storage conditions may be essential. Especially if bagged cement are stored in open sacks or exposed to moisture, the Cr(VI) will not be reduced when the cement is subsequently mixed with water (*Bruze et al.* 1990 (b)).

6. STUDIES BY THE AUTHOR

6.1. Populations and methodology

Status and case control study in 1981

Bricklayers and bricklayers' assistants were randomly selected from the files of the Danish Bricklayers' Federation and the Bricklayers' Assistants Federation in Copenhagen. A sub-group consisted of retired workers between the ages of 60 and 67; such early retirement is made possible by Danish law.

Concrete workers and workers employed in the manufacture of precast concrete building components were selected so that workers engaged at representative building sites and factories were included. The selection was done in collaboration with an advisory group including representatives of both workers and employers.

A total of 1,840 Danish workers who were representative of those workers who have daily contact with wet cement were selected for study. 1,538 (88%) of 1,749 accessible workers participated in the clinical and questionnaire investigations. 1,298 (74.2%) workers were examined clinically, and 1,230 (70.3%) were patch tested. The distribution of the population by specific occupation and type of examination is presented in Table 2 (*Avnstorp* 1983, I).

A control group composed of workers with no contact with wet cement was chosen from the same factories.

Prognosis study

In 1987 a follow-up study was carried out among a cohort of 143 workers who were engaged in the manufacture of precast concrete building components in 1981 and who had daily contact with wet cement at that time. The population was divided into two sub-groups; those who were and those who were not chromium hyper-sensitive in 1981 (*Avnstorp* 1989, II).

Risk factor study

Workers who had daily contact with wet cement and who were employed in five Danish factories manufacturing precast concrete

Table 2. *Distribution of the 1981 study population by specific occupation and type of examination.*

	Initially selected	Accessible for examination	Clinically examined	Questionnaire	Not examined	Patch tested
Bricklayers	777	738	525	145	68	499
Bricklayers' assistants	334	302	192	58	52	184
Retired bricklayers and assistents	157	157	113	37	7	105
Factory workers	238	232	196	0	36	190
Concrete workers	112	110	100	0	10	94
Control group	222	210	172	0	38	158
Total	1,840	1,749	1,298	240	211	1,230

building components participated in the studies in 1981 and in 1987 (*Avnstorp* 1991, III). Some of those workers from the 1981 study also participated in the prognosis study.

Cohort A

Cohort A consisted of 196 workers employed at the factories in 1981 at the time of the primary investigations (Fig. 2, cohort A). The workers in this cohort have therefore been exposed to cement containing 10 ppm water soluble chromate.

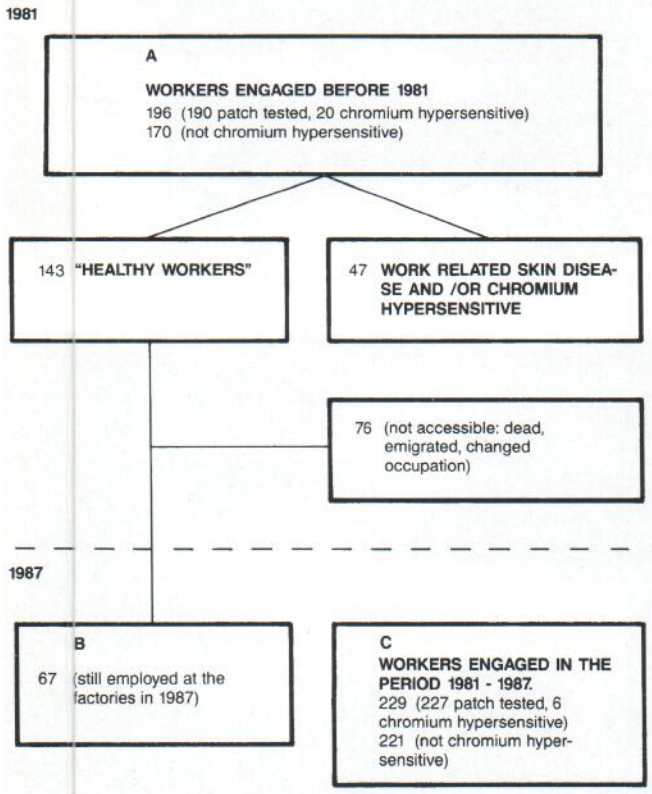

Fig. 2. *Composition of cohorts of workers participating in the risk factor study in 1981 and 1987.*

Cohort B

Cohort B consisted of 67 workers who in 1981 reported no episodes of hand eczema and who were still engaged at the factories in 1987 (Fig. 2, cohort B). Furthermore they were not chromium hypersensitive in 1981 or 1987 and had not changed work processes or preventive measures in the period 1981-1987.

Cohort C

Cohort C investigated in 1987, consisted of 229 new workers employed at the same factories after 1981 (Fig. 2, cohort C). 159 of those workers had been exposed only to cement with a chromate content of 2 ppm or less. While 70 workers had been exposed to cement containing 10 ppm before 1981 and since then to 2 ppm or less of chromate.

6.2. Description of work processes

Bricklayers

Bricklayers are skilled workers who lay bricks and stones using various bonding materials, especially cement (Fig. 3). They have contact with wet cement primarily on the hands and forearms. Their primary work sites are indoor or outdoor sites of new construction or renovation; there are often considerable concentrations of dust in the air at the latter sites due to the destruction of old walls. Bricklayers rarely use gloves and often put their hands into solutions of hydrochloric acid and water in order to neutralize the alkaline cement on their hands. For some work processes they use products containing epoxy resins.

Bricklayers' asistants

Bricklayers' assistants are semi-skilled workers who mix the mortar used by the bricklayers. The mixing is done with special tools and is typically performed once or twice a day.

Bricklayers' assistants also handle building materials and assist in the actual laying of bricks. They have contact with wet cement primarily on the hands, forearms and legs. Their work sites are the same as those of the bricklayers. Assistants, however, sometimes use leather gloves, but, like the bricklayers, they often put their hands into hydrochloric acid solutions.

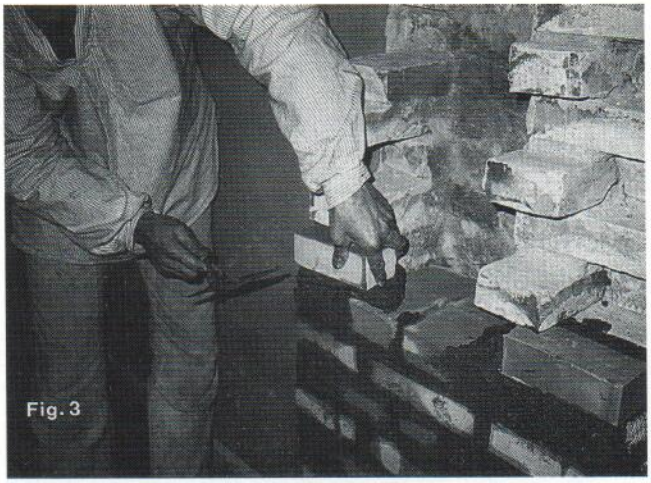

Fig. 3. *A bricklayer constructing a wall.*

Concrete workers

Concrete workers are unskilled workers engaged at the building sites. During construction they work largely out-of-doors where they pour the pre-mixed concrete into moulds containing steel reinforcements. The concrete is then vibrated manually. These workers often walk on newly poured concrete foundations while wearing rubber boots (Fig. 4). They have contact with wet cement primarily on the hands, forearms and legs. They often use leather or rubber gloves.

Precast concrete building component factories

Each factory is comprised of two separate areas. In one area the carpenters, painters, iron winders and moulding smiths who have no contact with wet cement carry out their work. In the other area, concrete prepared in the batch plant is transported by cranes to the moulding bays where it is poured into moulds and vibrated automatically or manually. The workers then level (Fig. 5) and sometimes also steam cure the concrete components. Finishing and repairing is done with mixtures of cement and epoxy resins (Fig. 6). The workers in the batch plant have contact with wet cement primarily on the hands, but the entire body can be exposed to cement when spills occur. Most of the work processes are carried out in large workshops, and those workers who have daily contact with wet cement often use leather or rubber gloves.

6.3. Compilation of test results

The clinical and questionnaire investigations

Medical and occupational histories which included all the variables listed in Table 3 were taken for each worker. The general condition of the skin and any sign of dermatitis on the hands or any other area of the body were recorded at the clinical examination, using the definitions listed above. Those workers who could not be present for a clinical examination were asked to complete a questionnaire in which the same definitions were used. There were no statistically significant differences with respect to exposure to wet cement or the reporting of skin changes between the group of workers actually examined and the group who were only examined by questionnaire.

Patch testing

Patch testing was carried out at the work sites with 0.5% potassium dichromate in petrolatum (pet.) and in water, 5% nickel sulfate in pet., 1% cobalt chloride in pet., 25% balsam of Peru in pet., and 1% epoxy resin in pet. (Hermal Chemie, Reinbek, West Germany), as well as with a 3.85% rubber mix in pet. The rubber mix contained the following chemicals:

Tetramethylthiuramdisulfide	0.25%
Tetramethylthiurammonosulfide	0.25%
Tetraethylthiuramdisulfide	0.25%
Dipentamethylenethiuramdisulfide	0.25%
Mercaptobenzothiazole	0.50%
Cyclohexylbenzothiazylphenemide	0.50%
Morpholinylmercaptobenzothiazole	0.50%
Phenylcyclohexyl-p-phenylenediamin	0.25%
Isopropylaminodiphenylamine	0.25%
Diphenyl-p-phenylenediamin	0.25%
Dihydroxydiphenyl	0.10%
Total	**3.85%**

(*Hjorth & Fregert*, Personal communication 1979).

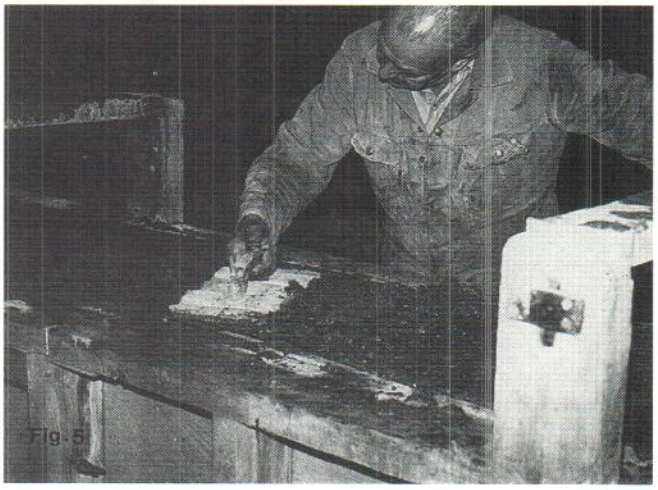

Fig. 5. *Leveling of a precast concrete building component.*

Fig. 4. *Concrete workers laying a floor.*

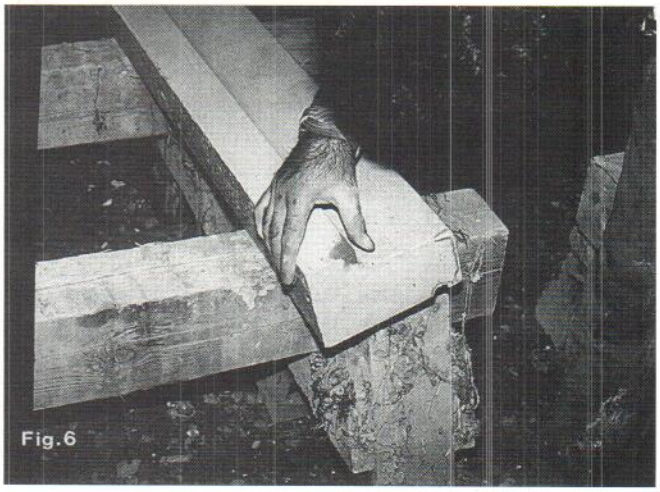

Fig. 6. *Repairing a precast concrete building component.*

Table 3. *Variables recorded at the clinical examination and from the questionnaire.*

Age
Duration of exposure to cement
Work processes (degree of exposure)
Eczema and other abnormal skin conditions:
a) previously
b) during the year prior to the examination
c) at the time of the examination
Itching, vesicles and fissures on the hands lasting at least two weeks within the past year or currently
Use of soaps, detergents, gloves and creams*)
Visits to physicians other than dermatologists or to dermatologists
Treatment with topical steroids
Sick leave due to eczema
State of employment
Change in occupation
Cause of change in occupation
Retired before the age of 67
Cause of retirement

*) Creams: emollient creams, barrier creams, protective creams.

The patch test substances were applied in Finn chambers (Epitest OY, Helsinki, Finland) which were fixed on the upper back with Scanpore (Norges Plaster A/S, Oslo, Norway). The patches were removed by the workers after 48 hours. Readings were made by the investigator after 72 hours in accordance with the guidelines of the International Contact Dermatitis Research Group (ICDRG) (*Wilkinson et al.* 1970). Any doubtful positive reactions and possible irritant reactions were read again after 96 hours and again after one week. A positive patch test reaction was defined as erythema plus infiltration and/or vesicles (++ and +++ reactions). The distribution of the patch test reactions to 0.5% potassium dichromate in pet. for the total group of patch tested individuals in 1981 is shown in table 4. There was no difference in the distribution of patch test reactions to potassium dichromate in pet. and in water.

One disadvantage with respect to the time of application of the patch tests was that the workers themselves removed the patches after 48 hours. If any of the workers had removed the patch before the scheduled time some reactions may have been missed. They may also have taken showers although informed about not to do so during the patch testing period. No exact information about these bias are given, but the workers were highly motivated for the investigation and the impression was that most followed the instructions carefully.

The most difficult part of patch testing is interpreting the results and especially determining when they are false positive or false negative (*Rycroft* RJG 1986, *Calnan* CD 1987).

In a high risk population few false positive reactions should be likely when standard patch testing procedures and concentrations are used (*Høvding* 1970, *Burrows & Calnan* 1965, *Coenraads* 1983 (b)). In the present study eight out of ten of the workers with positive patch test to 0.5% potassium dichromate had some skin damage. In the control group of workers without wet cement exposure 2% (2 of 172) were found to be chromium hypersensitive (*Avnstorp* 1983, I). This reactivity was equal to results reported from Finland where 2% (8 of 410) of a group of healthy volunteer males showed positive patch test reactions to potassium dichromate in pet. (*Peltonen & Fräki* 1983).

It is possible that an appreciable number of the truly positive reactions would have been missed had 0.25% or 0.375% potassium dichromate been used (*Burrows* 1983, *Burrows et al.* 1989). Sensitivity to chromate has been found to persist in workers with allergic cement eczema (*Czarnecki* 1979). In the present study some of the workers had a latent hypersensitivity to chromium. *Høvding* (1970) also found latent reactors in his study among bricklayers and bricklayers' assistants. These findings may reflect the dynamics in clinical manifestations of occupational hand eczema or the development of hardening (see also chapter 7.3). To increase the predictive value of the test, potassium dichromate was tested in both petrolatum and water as vehicles. It is not possible to judge about the specificity and sensitivity of the patch test since no other test procedures were performed. Further studies could include other patch test models and the comparing with in vitro tests.

Only ++ and +++ reactions were defined as positive patch test reactions. Thereby a high percentage of reactions ranging from doubtful and weak reactions to strong irritant reactions were excluded from the calculations (Table 4). If all patch test reactions had been included as positive the number of workers found to be chromium hypersensitive would have been about three times higher. By using the grading system shown in table 4, the present results are comparable to results made by other investigators. Furthermore the number of false positive reactions should have been brought to a minimum.

The conditions for the patch testing were equal in 1981 and again in 1987. Besides the finding of fewer positive reactions to potassium dichromate in 1987 the distribution of the reactions to the patch testing did not differ between the examination done in 1981 and again in 1987.

Patch testing with rubber chemicals was done especially to analyse if some work related hand eczemas were attributed to the use of rubber gloves and rubber boots and to exclude other frequent causes for work related hand eczema. The rubber mix used in this study was recommended for routine testing by *Hjorth* and *Fregert* (Personal communication 1979) and has previously been used in a patch test study (*Menné* 1981).

Epoxy resin was included for patch testing because the bricklayers and the workers engaged in the precast concrete building component factories were exposed to products containing epoxy resins.

Table 4. *The distribution of the patch test reaction to potassium dichromate 0.5% (in pet.) for the whole group of patch tested individuals in 1981.*

Negative reaction	1,028
Doubtful positive reaction (?+)	38
Weak reaction (+)	32
Positive reactions	
(++)	37
(+++)	31
Irritant reaction (IR?)	22
Follicular reaction	36
Hemorrhagic reaction	6
Total	1,230

Balsam of Peru was included because first aid boxes placed at the worksites previously contained ointments with balsam of Peru.

Results obtained from patch testing with epoxy resin and balsam of Peru were not included in the calculations since these allergens were not found to be of occupational importance in cement eczema.

Analysis of data

Prevalences were estimated. Non-parametric bivariable analyses were done using Chi-square, Wilcoxon-Mann-Whitney, Kruskall Wallis, and Goodman-Kruskal's gamma test (*Siegel* 1956). In general a 5% significance level was used. Multivariate analyses were carried out using multivariate contingency table analysis (*Bishop et al.* 1975) and logistic regression analysis (*Halperin et al.* 1971). A total of 150 variables were included.

7. CEMENT ECZEMA IN RELATION TO THE AUTHOR'S STUDIES

7.1. Chromium hypersensitivity

Immunology

Chromium allergy in patients with cement eczema represents a delayed type contact-hypersensitivity reaction (*Baer* 1986). In humans Cr(VI) compounds are more strong sensitizers than Cr(III) compounds (*Magnusson & Kligman* 1969), whereas the metal chromium itself is considered non-sensitizing (*Cronin* 1980). Chromium compounds are ubiquitous in the natural human environment, and elicitation may occur from skin contact not only with Cr(VI) compounds, but also with Cr(III) compounds (*Polak* 1983, *Zelger* 1964). In animal studies, Cr(VI) and Cr(III) compounds seem to have equipotency to induce sensitivity whereas Cr(VI) compounds have a superior elicitory capacity when applied epicutaneously or intradermally (*Haines & Nieboer* 1988). This is also the case in human studies where higher levels of Cr(III) than Cr(VI) compounds are required to elicit patch test reactions in chromium hypersensitive individuals (*Allenby & Goodwin* 1983). Different guinea pig sensitization assays have been used to evaluate the sensitization capacity of potassium dichromate. In such test systems the proportion of sensitized guinea pigs may vary from 50 to 100%. Genetical aspects may also influence the results. One guinea pig strain may respond well to potassium dichromate, while another strain may respond poorly (*Andersen & Maibach* 1985). With respect to the sex of the animal, the sensitization rates seem to be practically identical in males and females (*Ziegler & Süss* 1985).

The inflammatory response in contact dermatitis involves specific immunological events activated by haptens and non-specific immunological events triggered by irritants (*Scheper et al.* 1989). The development of allergic contact dermatitis occurs in four different phases: refractory, induction, elicitation and persistence (*Haines & Nieboer* 1988). In the refractory period, an individual is exposed to the allergen but remains unaffected. During the induction period the individual develops sensitized populations of lymphocytes. Elicitation involves secondary challenge with the antigen and results in an inflammatory skin reaction. Persistence involves the continued presence of specific effector cells with the ability to produce inflammation.

There are few morphological differences between allergic and irritant reactions in the skin (*Avnstorp et al.* 1989). Antigen specific activation of the T-lymphocytes is dependent on the antigen presenting cells and the production of mediators (*Scheper et al.* 1989). The skin acts as an immunological unit, and the only barriers the hapten must cross in order to reach the immunoactive keratinocytes, Langerhans cells and other dendritic cells are the surface lipid layer and the stratum corneum (*Lidén* 1988).

Activated T-lymphocytes can be seen four hours after a challenge (*Avstorp et al.* 1987). Recently activated and antigen specific T-lymphocytes may enter sites of inflammation non-specifically (*Scheper et al.* 1983). This may in part explain the chronicity of cement eczema, since contact with chromate does not have to be constant, and contact with the alkaline cement itself could maintain the inflammation.

Concentration and exposure

The concentration of chromate in concrete and mortar is about 4 to 5 times lower than in dry cement. Because there can be great variations in the composition of the final product, the concentrations of chromate in the original dry cement are used here as the point of reference. Difficulties are obvious in comparing concentrations of chromium compounds between individual countries since no standardized method for the analysis exist. This fact has to be taken into account when comparing concentrations of water soluble chromate in cement from one area with another area (Table 5a). Standardized methods should be developed. In the European Community it is planned in the near future to co-operate in standardizing measurements of chromium compounds (*Molin* 1991). Standardized analyses results should further lead to a greater extent of comparability of results obtained from epidemiologic studies (see also chapter 7.3).

It could be that, in some areas, exposure to wet cement was more important for the prevalence of chromium hypersensitivity than other exposures. The use concentration of Cr(VI) being generally higher in cement than in the other substances (table 5a, b).

Dose-response relationships in chromium allergy might be difficult to establish since work processes and working conditions differ. Besides differences in chromium valencies and concentrations, differences in irritation and maceration may influence on the sensitization process. The chromate concentration in the cement and factors such as duration of exposure and workprocesses may influence on the development of chromium hypersensitivity in allergic cement eczema (see also chapter 7.3).

The risk of developing chromium hypersensitivity increases with the intensity and duration of exposure. Workers in the precast building component factories had the most intensive exposure to wet cement due to their work processes, while a group of retired bricklayers had had the longest exposure time. Both groups had higher prevalences of chromium allergy than the other groups examined (Table 6) (*Avnstorp* 1983, I). *Høvding* (1970) also found that there was an association between duration of exposure and the development of chromium allergy.

The bricklayers developed chromium allergy at a younger age than did the bricklayers' assistants. Bricklayers had a longer exposure time to wet cement since the mean age for starting work

Table 5a. *Chromate Cr(VI) concentrations in cement and prevalences of allergic eczema from various countries.*

Country	Concentration (μg/g) basic	use	Prevalence*) of allergic cement eczema (in percentages)	Author
Australia	<1-18.5	<0.2-4.6	–	*Ellis & Freeman* 1986
Denmark 1981	9.6	1.9-2.4	8.9	*Avnstorp* 1991 (III)
1987	<2	<0.4-0.5	1.3	
Germany normal	12.5-24	2.5-6	11.1	*Reifenstein et al.* 1986
(DDR) »low« chromate ..	<0.4	<0.08-0.1	0.7	
Italy	10-55	2-13.8	–	*Meneghini et al.* 1969
Norway	6-40	1.2-10		*Fregert & Gruvberger* 1972
			4.6	*Høvding* 1970
Sweden	2-15	0.4-3.8	3.0	*Fregert & Gruvberger* 1972
USA (California)	<0.1	<0.02-0.025	1.1	*Perone et al.* 1974

Use-concentrations are estimated and may vary further depending on final use.
*) Not uniformly defined in all studies.

Table 5 b. *Examples of other possible sensitizing exposures to chromium compounds Cr(III)/Cr(VI) than cement.*

Exposure	Chromium compound responsible	Concentration basic	use	Author
Bleaches	Cr(VI)	3.65-82.9	0.04-0.8 μg/ml	*Lachapelle et al.* 1980
Detergents	Cr(III)	5-15.5	0.05-0.16 μg/g	*Allenby & Goodwin*
	Cr(VI)	5-16.5	0.05-0.17 μg/g	1983
Cutting oils	Cr(III)/Cr(VI)	–	<0.1-1.17 μg/g	*Wahlberg et al.* 1977
Galvanized sheets	Cr(III)/Cr(VI)	–	0.03-0.44 $\mu g/m^2$	*Fregert et al.* 1970
Leather tanning	Cr(III)	<115-36.000	100-1.300 μg/g	*Fregert & Gruvberger* 1979
Cleaning water	Cr(III)	–	$2.6\text{-}35\times10^{-3}$ μg/ml	*Clemmensen et al.* 1983

Use concentrations are estimated and may vary further depending on the final dilution.

was 15 for bricklayers and 25 for bricklayers' assistants (*Avnstorp* 1983, I). Multivariate analysis showed that the risk of developing chromium allergy was not influenced by age and exposure time to the same degree as by exposure due to certain work processes (*Avnstorp* 1983, I). It seems that the influence of duration of exposure depends upon the precise type and degree of the exposure and cannot necessarily be predicted simply from the name of the occupation.

The minimal duration of chromate exposure leading to contact sensitization is unknown. Allergic cement eczema may develop already within 2 years of exposure (*Werdenbach & Kollmeier* 1989).

Cement burns, which usually occur among those working with cement as a hobby, rarely cause chromium allergy (*Rostenberg* 1962, *Vickers* 1976, *Hannuksela et al.* 1976, *Flowers* 1978).

Examples of other possible eczematogenic exposures of chromate than cement are found in the metal industry, and in washing and bleaching materials (table 5b). In cutting oils the chromium content might be higher after use, probably most as Cr(III) compounds (*Einarsson et al.* 1975). Mould oils are used in the manufacture of precast concrete components in factories. Oil dermatitis is largely of an irritant nature, but mould oils may contain chromium (*Anderson* 1960, *Wahlberg* 1977). Such oils may remove the lipids on the surface of the skin, thus facilitating the penetration of chromium compounds (*Fisher* 1979). Among the Danish workers, no direct association was found between the use of mould oils and chromium allergy (*Avnstorp* 1983, I). The total amounts of chromium (Cr(III)/Cr(VI)) washed off from the hands of workers

Table 6. *Prevalence of chromium hypersensitivity in the various occupations represented in the 1981 study population. Percentages are given in parentheses.*

	No. of workers examined	No. of workers patch tested	Chromium hypersensitive
Factory workers with daily contact with wet cement	196	190	20 (10.5)
Retired bricklayers and bricklayers' assistants	113	105	11 (10.5)
Concrete workers	100	94	5 (5.3)
Bricklayers	525	499	23 (4.6)
Bricklayers' assistants	192	184	7 (3.8)
Control group	172	158	2 (1.3)

who had worked with galvanized sheets has been found to be 1.04-5.00 mg per person. Of this, 42-51% was Cr(VI). In bricklayers the corresponding value was <0.007 mg total chromium (*Fregert et al.* 1970). In the metal industry an additive effect could be responsible since the workers are often exposed to cutting oils and chromium containing metal components at the same time during the work processes. Chromium allergy due to the use of bleaches and detergents has been claimed (*Feuerman* 1969, *Garcia-Perez et al.* 1973). The use concentrations of liquid bleach and detergents may be higher than indicated in table 5b, since these products are sometimes used undiluted. The removal of Cr(VI) compounds from liquid bleach, "eau de Javelle" has been claimed to be a good example of prevention against the development of chromium allergy among female domestic workers (*Garcia-Perez et al.* 1973, *Lachapelle et al.* 1980). For leather tanning high concentrations of Cr(III) derivatives are mostly used (table 5b). In contrast the Cr(III) content in cleaning water is not very likely to be high enough to induce or elicit chromium hypersensitivity.

Systemic reactions may occur in patients previously sensitized by the percutaneous absorption of chromium (*Veien et al.* 1991). Inorganic chromium compounds are poorly absorbed, and the amount absorbed from an oral dose varies from 1 to 25% (*Schroeder et al.* 1961, *Hansky & Connell* 1962). Chromium rich foods include brown sugar, animal fats and butter (*Love* 1983). Oral challenge with 2.5 mg potassium dichromate produced a flare of dermatitis in 21 patients with symmetric, vesicular hand eczema. In these patients the systemic exposure seemed to be more important than skin contact with the hapten since the dermatitis of 11 of these patients cleared or improved after all had followed a diet restricting the ingestion of chromate rich foods for 1 month (*Veien et al.* 1983). Systemic contact dermatitis to chromium may also occur after the inhalation of chromium in welding fumes (*Fregert & Övrum 1963, Shelley 1964*).

Penetration of the hapten and antigen formation

Cr(VI) compounds penetrates the skin more easily than Cr(III) compounds (*Mali et al.* 1963, *Mali et al.* 1964). In laboratory diffusion experiments with equivalent concentrations of different chromium compounds in phosphate buffers in the pH range 5-7, the order of diffusion through human skin has been found to be: Potassium dichromate Cr(VI) > Chromium chloride Cr(III) > Chromium sulphate Cr(III) > Chromium nitrate Cr(III) (*Samitz et al.* 1967).

As Cr(III) chromium compounds are not soluble in a mixture of alkaline cement and water, (*Fregert & Gruvberger* 1972) they are unlikely to induce hypersensitivity. In addition, Cr(III) salts have a strong affinity for the epithelium, thus reducing their ability to penetrate intact skin (*Mali et al.* 1963). Cr(III) compounds are more likely to penetrate damaged skin (*Flesch* 1965). Studies of penetration need to be reevaluated with newer methods to obtain more information about the bioavailability of the different chromium compounds.

The reduction of Cr(VI) to Cr(III) in the epidermis and the formation of protein-Cr(III) complexes is the possible first step in sensitization (*Mali et al.* 1963). A common antigenic determinant is probably involved in chromium contact sensitivity, rather than independent entities corresponding to each valency state. It has been suggested that this determinant can be formed by chromium in the trivalent form (*Siegenthaler* 1983).

The reduction of Cr(VI) to Cr(III) in the skin is probably caused by the sulfur-containing amino acids (*Samitz & Katz* 1964). Cr(III) then binds to skin proteins (*Samitz et al.* 1969) and to components of the Langerhans cells (*Shelley & Juhlin* 1976). Lactic acid, hemoglobin and gamma globulin have also exhibited chromium-reducing ability (*Samitz & Katz* 1964). The bricklayers and bricklayers' assistants who took part in the studies often applied a diluted hydrochloric acid solution to their hands. Although this may have protected some of them against developing cutaneous chromium hypersensitivity, this association was not found during the analysis of data (*Avnstorp* 1983, I).

Chromium concentrates at the dermoepidermal junction and in the upper dermis (*Lidén & Lundberg* 1979). Two months after the intracutaneous injection of a 51Cr labelled chromium compound, 3-5% of the compound could still be detected (*Pedersen et al.* 1969). Cr(III) has been found to persist in the skin as long as 4 years after intracutaneous injection (*Frégert* 1971).

7.2. Clinical patterns of cement eczema

Irritant cement eczema and risk factors

In general irritant cement eczema cannot be differentiated from allergic cement eczema clinically. The same efflorescenses may be present over time. Erythema and hyperkeratoses on the dorsal aspects of the hands and fingers, but also on the wrists are the most prevalent findings (*Avnstorp* 1983, I). Cement eczema may initially develop as a result of daily irritation of the skin by contact with wet cement (Fig. 7) (*Avnstorp* 1983, I, *Adams* 1983 (a)). The skin of those who have daily contact with wet cement becomes irritated by the hygroscopic and alkaline constitution of the cement (pH 12.6). The skin's barrier layer becomes more permeable, and repeated contact with abrasive materials may lead to irritant cement eczema (*Orris & Tesser* 1982, *Avnstorp* 1991, III). In hospital wet workers susceptibility to irritant hand dermatitis depends on the degree of exposure to chemicals, water, soil and wear, and individual predisposition to atopy. Co-existing or recently healed

Fig. 7. *The cement covered hands of a worker who has just finished making a precast concrete component.*

eczema may also make the skin more vulnerable (*Andersen et al.* 1987). By repetition of the same stimulus, or by a combination of varying stimuli, the degree of impairment surpasses a critical level, in consequence of which a clinical disease ensues (*Malten* 1981). Irritant cement eczema may therefore be due to the sum of various adverse reactions. In the current study, the influence of daily contact with wet cement was illustrated by the fact that cement eczema was more common among working bricklayers than among unemployed bricklayers (*Avnstorp* 1983, I).

Attempts have been made to distinguish endogenous eczema from exogenous eczema (*Rietschel* 1991). Combined influences from endogenous and exogenous factors have been found among hospital "wet workers". Trivial irritants and endogenous factors were found to play a greater role than contact sensitivity in the aggravation of current hand eczema (*Nilsson* 1985). Atopic eczema in childhood has been found to be a more important predictive factor for hand eczema than occupational exposure (*Meding & Swanbeck* 1990 (a)). *Rystedt* (1985) found that 57% of the individuals with atopic dermatitis in childhood developed sporadic or continuous hand eczema during concrete work. When compared with other occupations such as metal industry, cleaning and even among office workers, equal prevalences were found.

In the current study some of the hand eczemas categorized as irritant cement eczemas might therefore have been atopic hand eczemas. In contrast it should probably not have influenced the decrease in the number of workers with allergic cement eczema. Atopy was not included as a variable in the study because in a pilot study it was found that the workers had a poor memory of episodes of childhood eczema.

Non eczematous skin changes

Mild, reversible skin damage is commonly seen among workers who have daily contact with wet cement (*Avnstorp* 1983, I). Minor skin complaints are accepted as normal by these workers. Mechanical traumas from the handling of bricks, tools and machines, cause occupational stigmata in the form of hyperkeratosis with fissures on the palmar aspects of the hands and fingers. Workers often cover such fissures with plastic tape (Fig. 8).

In the present study it was the impression that during the winter months, many workers develop fissures on their hands and fingers. In winter, the cold outdoor air has a low relative humidity, and when this air is heated indoors, the moisture content is lowered further. This can cause a drying out of the skin of the hands (*Gaul & Underwood* 1952). Low humidity occupational dermatitis has been correlated to working environments with a relative humidity of 35% (*Rycroft & Smith* 1980).

Allergic cement eczema

Allergic cement eczema is primarily located on the hands, fingers and wrists (*Avnstorp* 1983, I, *Høvding* 1970, *Burrows & Calnan* 1965). Eczema on the dorsal aspects of the right hand, in particular, has been shown to be associated with chromium hyper-sensitivity (Fig. 9) (*Avnstorp* 1983, I). Furthermore allergic cement eczema has been found to have a greater extent of involvement than irritant cement eczema (*Avnstorp* 1991, III). Allergic cement eczema may also spread to the forearms, the feet and sometimes the face and parts of the trunk.

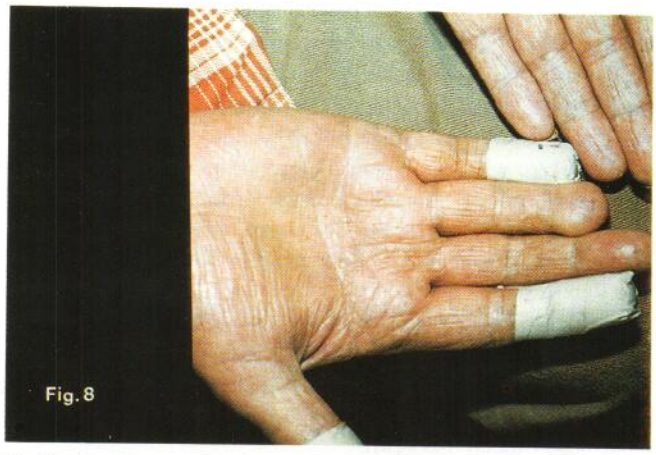

Fig. 8. *A worker covering fissures on the fingers with plastic tape.*

Heat and high humidity exacerbated allergic cement eczema among workers in Kuwait. This phenomenon was explained by the fact that excessive hydration of the skin could lead to increased leaking of chromium through the skin (*Kanan* 1972). In Singapore, where the climate is hot and humid year round, the number of heat related dermatoses was, nevertheless, lower than expected, possibly due to the use of air conditioning and good factory ventilation (*Goh & Soh* 1984).

Individual prophylaxis

The dynamics of the development of occupational hand eczema are not fully understood, but irritation and contact sensitivity, together with individual constitutional factors, influence its development. Theoretically, at least one of the triggering factors could be eliminated if the workers used individual preventive measures. Use of gloves, protective hand creams and hand washing were not found to influence the propensity to develop irritant cement eczema in the present study (*Avnstorp* 1991, III). Furthermore no additive effect

Fig. 9. *Allergic cement eczema.*

was found from the individual preventure measures. The absence of influence from individual preventive measures could be explained by the work processes being so hazardous that they overwhelm the protective effect. It could also be that the preventive initiatives were not conducted systematically or carefully enough.

In workers with chromium allergy, the use of leather gloves may deteriorate the dermatitis because of the chromium tanning (*Fregert & Gruvberger* 1979). The use of rubber gloves can cause secondary sensitization to rubber chemicals as described in chapter 7.3. Rubber gloves may contain chromium (*Conde-Salazar* 1980). Often gloves also contain the remains of cement spills and may be soaked with mould oil (Fig. 10). The moderate use of gloves may be advisable to protect against trauma from specific work processes, but prolonged occlusion of the skin with gloves should be avoided (*Adams* 1983 (b)).

Barrier creams and ointments containing chemicals such as ethylenediaminetetraacetate (EDTA), ascorbic acid and combinations of sodium pyrosulfite, tartaric acid and glycerine have been used in the attempt to reduce Cr(VI) to Cr(III) and to chelate Cr(III) on the skin (*Samitz & Pomeranz* 1958, *Samitz & Gross* 1962, *Samitz* 1970, *Shuppli* 1970, *Amphoux et al.* 1975, *Romaguera et al.* 1985). The effect of these measures under actual working conditions is, however, doubtful. A thin layer of cream can easily be rubbed and washed off, and it can hardly be thought of as an effective barrier for those carrying out manual work. The creams themselves do not inhibit the absorption of chromium (*Wahlberg* 1971).

7.3. The epidemiology of cement eczema

Prevalence and incidence

Most data concerning prevalences and incidences of hand eczema and contact hypersensitivity are obtained from patch test clinics. This may give inaccurate information due to selection bias.

Contradictory results about frequencies of chromium hypersensitivity have been published. Some authors have found decreasing numbers of chromium hypersensitive individuals (*Färm* 1986, *Von Gailhofer & Ludvan* 1987, *van Ketel* 1984, *Estlander* 1990), while others have found unchanged (*Edman* 1988), high (*Wall & Gebauer* 1991), or increased numbers (*Gollhausen et al.* 1988).

In Heidelberg, Germany (*P. Frosch*, personal communication), in Erfurt, Germany (*HJ. Schubert*, personal communication) and in London, England (*I. White*, personal communication) the incidence of chromium allergy appeared to be stable from 1981 to 1987. 20-70% of the chromium hypersensitive patients were thought to have allergic cement eczema, but no exact data was available.

The prevalence of chromium hypersensitivity in men in Finland has been shown to vary from 2% in a healthy group of men to 15.5% among male patients engaged in the building industry, who were examined at a hospital dermatology out patient clinic. A high prevalence was also found among female workers in the leather tanning industry where 15.4% were found to be chromium hypersensitive (*Peltonen & Fräki* 1983).

Recently published data from Sweden found that the prevalence of chromium hypersensitivity was low for both sexes but higher for females than for males (*Meding & Swanbeck* 1990 (b)). The same trend was found by *Edman & Møller* (1982) with respect to the distribution among the sexes.

Studies carried out at work sites provide more accurate epidemiological information. Such studies have previously been done in Norway (*Høvding* 1970), Sweden (*Wahlberg* 1968), The Netherlands (*Coenraads* 1983 (a)) and Germany (*Reifenstein et al.* 1986) (Table 5a). These studies gave attention to the high prevalence of irritant dermatitis among workers in the building and construction industries and to the importance of hypersensitivity to chromium. In the present study the epidemiologic design was composed of a prevalence and case-control study (*Avnstorp* 1983, I), a historical cohort (*Avnstorp* 1989, II, *Avnstorp* 1991, III) and a prevalence study of two different populations (*Avnstorp* 1991, III) (see also chapter 6.1). The ideal epidemiologic design would probably have been a parallel longitudinal study of two different cohorts, who were primarily examined at the same time and who in the following years only differed with respect to exposure to the amount of water soluble chromate in cement.

The prevalences of chromium allergy in the study carried out in Denmark in 1981 is shown in Table 6 (*Avnstorp* 1983, I). The prevalences differ between the occupations. Workers with most intensive exposure to wet cement such as factory workers and workers with the longest duration of exposure such as retired bricklayers having the highest prevalences of chromium hypersensitivity (see also chapter 6.2 and 7.1).

Among workers with daily contact with wet cement at the factories covered by the study the prevalence of allergic cement eczema decreased statistically significant from 1981 (cohort A fig. 2, exposed to 10 ppm water soluble chromate) to 1987 (cohort C, fig. 2, exposed to 2 ppm since 1981). A concomitant decrease was not found with respect to irritant cement eczema (table 7) (*Avnstorp* 1991, III). The risk for developing irritant cement eczema was therefore unchanged. The decrease in allergic cement eczema may be associated with the reduction of the content of water soluble chromate in Danish cement. In a previously published paper (*Avnstorp* 1989) it was postulated that the decrease followed the addition of ferrous sulfate. This might not be true since the results could have been influenced by confounding factors. Especially problems

Fig. 10. *Leather gloves soaked with mould oil.*

Table 7. *Prevalence of allergic and irritant cement eczema in 1981 and 1987 among factory workers with daily contact with wet cement. Percentages are given in parentheses.*

	1981	1987	p-value*)
Allergic cement eczema.....	17 of 190 (8.9)	3 of 227 (1.3)	<0.001
Irritant cement eczema.....	30 of 190 (15.8)	25 of 227 (11.0)	N.S.

*) Yates' correction applied to p-values (χ^2-test).

with obtaining matched groups of workers with respect to duration of exposure might have influenced the results (see also chapter 7.4).

If the development of allergic cement eczema is the result of a dose-response effect a decrease could be expected as a consequence of lowering the exposure to water soluble chromate. As seen in table 5a the prevalence of allergic cement eczema is low among workers exposed to low concentrations of water soluble chromate in cement in contrast to higher prevalences among workers exposed to higher concentrations. The prevalence values given in table 5a are not directly comparable since the patch tested group of workers in each study not have been equally selected. Furthermore, differences in exposure to wet cement are probably due to different working conditions and differences in duration of exposure (see also chapter 7.1).

In a study from the German building industry it was found that fewer workers developed cement eczema if they were processing cement containing low concentrations of water soluble chromate (Table 5a) (*Reifenstein et al.* 1986). Five out of 690 workers developed allergic cement eczema after 3-15 years of exposure to cement with a Cr(VI) content < 0.4 ppm. The corresponding value was 85 out of 765 after 2-6 years of exposure to cement containing 12.5-24 ppm of Cr(VI). Work processes are not well defined in this paper and therefore selection bias may have influenced the results.

In a study in San Francisco, California, among workers exposed to cement containing no more than 0.1 ppm water soluble chromate (table 5a), one out of 95 workers was found to be hypersensitive to chromium although more than one-third had evidence of mild to moderate cement eczema (*Perone et al.* 1974). More than 50% of the workers examined were exposed to cement for 15 years or longer. The patch test concentration of potassium dichromate used in this study was 0.25% in water. More positive reactions might have been obtained if 0.5% was used (see also chapter 6.3). On the other hand cement filtrates containing 4.7 ppm Cr(VI) that were used in supplementary for patch testing gave the same result.

Automatization of work processes could probably bring the risk for developing allergic and irritant cement eczema to a lower level, whereas individual preventive measures do not seem to have significant influence on the development of irritant cement eczema (see chapter 7.2) (*Avnstorp* 1991, III). Furthermore the use of gloves did not seem to influence on the development of allergic cement eczema to the same degree as the chromate content of the cement (*Avnstorp* 1989) (see also chapter 7.4).

In Denmark mechanization of workers' processes was performed in the late 50's and early 60's. Up to the early 70's further modifications in working practices took place. Since then and during the study period in the present study, no essential changes in the performance of the concrete pouring occurred.

Medical prognosis

Allergic cement eczema seems to be more severe than irritant cement eczema (*Avnstorp* 1991, III) (see also chapter 7.2). *Meding* and *Swanbeck* (1989) also found that allergic dermatitis had a higher score of extent of involvement than irritant dermatitis. Workers with allergic cement eczema had more frequent hand eczema episodes and requirements of topical steroid treatment (*Avnstorp* 1989, II). *Høvding* (1970) found that the duration of cement eczema was short among bricklayers and bricklayers'assistants without a concomitant chromium hypersensitivity in contrast to the year-lasting symptoms among those hypersensitive to chromium. None of the 11 workers with irritant cement eczema who participated in the prognosis study (*Avnstorp* 1989, II) had changed occupation, but one worker had retired earlier. Ten of the eleven workers were therefore still employed at the factories. The eczema of eight of the workers had cleared although they stayed in the same occupation. Therefore the difference between the medical course for allergic and irritant cement eczema was not caused by change in occupation among those with irritant cement eczema. Chromium hypersensitivity therefore seems to be an important factor for the severity and prognosis of cement eczema. The addition of ferrous sulfate to the cement did not influence the status of hand eczema in already chromium sensitive workers (*Avnstorp* 1989, II).

The three main contending explanations for the chronicity of allergic cement eczema could be that inapparent sources of contact with the original cause of the eczema continue, or that contacts with other causes of hand eczema (to which the workers' skin is rendered more susceptible by the original allergic cement eczema) maintain the eczema, or that there is some inherent chronicity to hand eczema (see also chapter 7.1 and 7.2).

In workers already hypersensitive to chromium, the concentration of water soluble chromate in cement needed to elicit allergic cement eczema is probably lower than the concentration needed to induce sensitivity. Elicitation from even very low concentrations of chromate would also be likely if the skin is damaged as a result of irritation from wet cement. When used as a filler in repair work, cement in which the chromate content has not been reduced may represent a source of the hapten (*Lück & Jentsch* 1988).

The persistence of allergic cement eczema would also, in part, be associated with daily irritation of the skin by wet cement. If a worker is advised to change occupations or to be retrained, it is therefore essential that the new job should not involve contact with abrasive "wet" work processes or contact with other irritants such as, for example, cutting oils.

Whether or not allergic cement eczema can be improved by a change in occupation is not clearly shown in the literature. Some authors have found the medical prognosis to be poor in spite of a change (*Dooms-Goossens et al.* 1980, *Fregert* 1975), while others have found that a job change has a favourable influence on the course of the disease (*Geiser and Girard* 1965, *Peter* 1968).

If the worker remains in his original occupation, the prognosis may be favourable. In his cohort study of chromium allergic

bricklayers and bricklayers' assistants in Bergen, Norway, *Høvding* (1970) found that 4 of 15 eczemas cleared after five years. The cement eczema of 8 of 17 bricklayers in Geneva, Switzerland, cleared although the workers continued to have the same jobs (*Hunziker & Musso* 1960). No reduction was made in the chromate content of the cement used by the workers in either of these studies. No conclusive explanation has been given for this adaptive phenomenon seen in some workers. It may be that some workers develop immunological tolerance (*Peck et al.* 1945), and some may experience hyporeactivity induced by repeated irritation of the skin (*Lammintausta et al.* 1987).

In the present study the status of workers who had continuous contact with wet cement containing no more than 2 ppm was almost equal to the status of workers who had no contact with wet cement (*Avnstorp* 1989, II). Among those 12 workers with allergic cement eczema in 1987, six workers were still engaged at the factories, 3 had taken early retirement and 3 had changed occupation.

During the study period from 1981 to 1987 the number of statement of claims for occupational injury benefits due to cement eczema was unchanged (table 8). Statement of claims include both workers with irritant cement eczema and workers with allergic cement eczema. In contrast the number of approved claims of chromium allergy from exposure to cement decreased statistically significant (P=0.033, chi-square) while the number of approved claims of chromium hypersensitivity due to other exposures, as for example chromium for leather tanning, was unchanged (table 8). These data may reflect that the workers had an unchanged risk for developing irritant cement eczema. The decreased number of approved claims of allergic cement eczema may reflect the decreased risk of developing chromium hypersensivity from exposure to wet cement.

Concomitant sensitivities

The chronicity of allergic cement eczema may also be attributable to co-existing contact allergies (*Avnstorp* 1989, II, Förström et al. 1969). Concomitant sensitivities to cobalt and rubber chemicals were found significantly more often among chromium hypersensitive workers than among those not hypersensitive to chromium (*Avnstorp* 1983, I). This is in agreement with the findings of *Høvding* (1970), *Fregert & Rorsman* (1966) and *Fregert* (1975).

Cobalt occurs in cement as non-water-soluble oxides but forms complexes with amino acids in eczematous skin, thereby possibly forming haptens (*Fregert & Gruvberger* 1978). In cement eczema cobalt sensitivity is therefore probably secondary to the chromium hypersensitivity. Nickel is a contaminant of cement in the form of insoluble NiO which, in contrast to the cobalt oxides, is not allergenic (*Wahlberg et al.* 1977). This was confirmed in the present studies since no statistically significant association between nickel allergy and cement eczema was found (*Avnstorp* 1983, I, 1989). Sensitization to rubber chemicals is thought to be a secondary sensitization because workers with hand eczema use rubber gloves to protect their hands from the wet cement. A similar correlation has been described among workers from a factory in Singapore manufacturing precast concrete building components (*Goh & Gan* 1987).

Table 8. *Statement of claims and approved claims of cement eczema and chromium hypersensitivity in Denmark in the period 1981-1987. Number of workers. 5 mill. population.*

	I	II	III	IV
1981.....	not computerized	25	21	46
1982.....	not computerized	18	29	47
1983.....	26	12	20	32
1984.....	21	12	16	28
1985.....	25	13	13	26
1986.....	33	7	18	25
1987.....	38	5	14	19

I) Statement of claims of occupational injury due to cement eczema.
II) Approved claims of chromium hypersensitivity due to exposure to wet cement.
III) Approved claims of chromium hypersensitivity due to other exposures (leather tanning, metal industry).
IV) Total number of approved claims due to chromium hypersensitivity.

Social prognosis

The social prognosis of workers with chromium allergy may depend on whether or not they are skilled or unskilled. Bricklayers, for example, are skilled workers who may find it difficult to change occupations. Employed and unemployed bricklayers in Denmark had an equal prevalence of chromium allergy, thus illustrating that chromium allergy itself had no influence on their employment status (*Avnstorp* 1983, I). *Høvding* found that healthy bricklayers and bricklayers' assistants changed occupation to a greater degree than did workers with eczema and that workers with eczema did not lose their jobs more often than those without eczema (*Høvding* 1970).

Chromium allergy in unskilled workers had no significant influence on whether or not they changed jobs, nor was it a cause of unemployment (*Avnstorp* 1989, II). Unskilled chromium sensitive workers are sometimes given the opportunity to change to a job within the factory where they will have no contact with wet cement (*Avnstorp* 1989, II, *Coenraads* 1983 (a)). This initiative enables them to remain employed.

The social prognosis of chromium hypersensitive workers is influenced by their age, with workers below the age of 40 having the best opportunity to change jobs or be successfully retrained (*Avnstorp* 1989, II, *Hjorth & Avnstorp* 1986). In a German study, most workers experienced a loss of social standing upon entering a retraining programme, especially if they were 50 years of age or older (*Carrie & Kühl* 1968). In the present study, the fact according to Danish legislation, that older workers could retire with little loss of income from the age of 60 may have enabled them to maintain their social standing. Social standing is here considered to be the sum of earnings as well as the maintenance of employment status in the peer group (*Avnstorp* 1989, II).

Economic aspects

Fewer workers consulted a dermatologist in 1987 than in 1981, and the need for topical steroid treatment decreased over the same period (*Avnstorp* 1989). Concomitantly the number of approved allergic cement eczemas decreased (table 8). If the decreased numbers of allergic cement eczema are thought primarily to result from

the reduction in the chromate content of cement (*Avnstorp* 1991, III) these benefits may result from the same reason.

In Singapore, allergic cement eczema was the only dermatosis severe enough to result in sick leave among workers in the construction industry, where absence due to occupational dermatoses was generally low (*Goh* 1986 (a)). Studies in The Netherlands (*Coenraads* 1983 (b)) and the UK (*Burrows & Calnan* 1965) have shown that the loss of working days in the building and construction industries due to occupational dermatitis, has had significant financial consequences for these industries. These findings were not confirmed in the present study. The number of Danish workers who took sick leave due to hand eczema was low even before reduction of the chromate content (*Avnstorp* 1983, I). The number decreased further after the reduction in chromate, but this decrease was not statistically significant (*Avnstorp* 1989).

Approximately 10% of the total amount of cement used in Denmark in the study period contained more than 2 ppm of chromate. This cement was imported, and, possibly to keep the cost low, the chromate content had not been reduced. This type of cement was used at small building sites and fabrics, but not in the factories making precast building components. The cost of reducing the content of water soluble chromate in Danish cement is about 1% of the total price of the cement, or approximately 10 million DKK (1 million £, 1.7 million $) per year (*Avnstorp* 1989). Calculations of the cost-benefit of the intervention were not included in the present study.

7.4. Bias

Selection

One disadvantage of the risk factor study (*Avnstorp* 1991, III) is that it does not take into account that some workers with hand eczema may have changed occupation because of the eczema. Some of those workers with chromium hypersensitivity may have left the occupation with wet cement exposure before 1981 due to severe allergic cement eczema. Older workers with allergic cement eczema retired earlier (*Avnstorp* 1989, II), and a high percentage of retired bricklayers and bricklayers' assistants were chromium hypersensitive (*Avnstorp* 1983, I). Older chromium hypersensitive workers who left their jobs before 1981 could therefore have influenced the results of the risk factor study and the prognosis study. If withdrawal due to chromium hypersensitivity was more pronounced before 1981 than in the study period from 1981 to 1987, the number of workers with allergic cement eczema found in 1981 was lower than the real number of sensitized workers. Previous studies among workers in the building industries have found such withdrawal to be of relatively little importance (*Høvding* 1970, *Goh* 1986 (a), *Coenraads* 1983 (a)). In the present study, some of the workers with cement eczema were assigned to other jobs within the factories (*Avnstorp* 1983, I). In the prognosis study (*Avnstorp* 1989, II), chromium hypersensitive workers were not found to have changed occupation to a higher degree than workers not chromium hypersensitive (*Avnstorp* 1989, II).

Although such a selection effect might have been pronounced before 1981, the results in the current study with respect to the development and severity of allergic cement eczema and the prognosis for workers with allergic cement eczema, would have been further confirmed if more chromium hypersensitive workers had participated in 1981.

In contrast, more workers over the age of 40 than under this age participated in the study. This tendency has also been seen by *Agrup* (1969) and could be explained by the fact that younger workers were not motivated to participate, as they had no skin complaints. A primary selection of workers done by the employers should not be very likely. A certificate of health was not requested and industrial doctors or nurses were not involved in the employment.

As the examination was carried out at the work sites, the number of workers who refused to participate was low. This was true for both the population at risk and the control group.

A secondary healthy worker effect was not found to be prominent in a study of construction workers in The Netherlands (*Coenraads* 1983 (a)), while it was supposed to be of some magnitude in Singapore (*Goh* 1986 (a)). Migration among the study populations was pronounced during the period covered by the current study, but this may have been due more to the difficulty in getting a job in the building and construction industries in some geographical areas than to the health of the workers. More of the workers who had skin complaints in 1981 participated in the follow-up study than workers who had no skin damage in 1981 (*Avnstorp* 1989, II). This was in agreement with *Meding* (1990), who in a population study found that persons with more severe hand eczema probably participate to a higher degree in dermatological examinations than persons with mild or cleared hand eczema. If this reflects a general tendency, it should lead to conservative estimates of the relevant parameters.

Information

In order to ensure the similarity and equal quality of the information gathered, workers who had daily contact with wet cement and workers in the control group were examined in the same way. The results obtained from the questionnaire completed by workers who were not present for a clinical examination were found to be valid since there was good correspondence between the answers given by those only examined by questionnaire compared to those workers examined both by questionnaire and by clinical examination.

With respect to the used definitions of objective cement eczema as the presence of just one of three skin changes (erythema, vesicles, hyperkeratosis) at the time of examination, the biology of hand eczema was respected (*Avnstorp* 1991, III). Hand eczema varies in its clinical expression over time, the individual effluorescenses fluctuating and not being permanently present. Furthermore by specifying the extensions of the objective skin changes, the results in the present study should be comparable to studies made by other investigators (*Avnstorp* 1991, III).

Confounding factors

It is questionable whether age itself is a confounding factor in occupational hand eczema (*Goh* 1986 (b)). In a German study of workers with dermatitis, who were engaged in the manufacture of precast concrete building components, allergic cement eczema was manifest in 50% (14 of 28) of the workers between the ages of 18 and 25 (*Lück & Jentsch* 1988). Multivariate analysis showed that varying exposure to cement in different occupations had a

greater influence on the development of allergic cement eczema than age (*Avnstorp* 1983, I). Although no direct relationship has been found between the time of onset of cement eczema and the duration of exposure to cement, it has been found that the duration of exposure is an important factor in the development of chromium hypersensitivity (*Høvding* 1970). In the present study, differences in the duration of exposure in the two compared groups in the risk factor study (*Avnstorp* 1991, III), could be a confounding factor. The fewer number of chromium hypersensitive workers found in 1987 could be the result of a shorter duration of exposure and not a result of exposure to a lower concentration of water soluble chromate. When comparing matched groups of workers with respect to duration of exposure from the two different populations the same trend was found that the number of chromium hypersensitive workers in the group of workers decreased if the workers had been exposed to lower concentrations of water soluble chromate (*Avnstorp* 1989). The number of matched workers were too small to give a statistically significant value. On the other hand no difference was found in the distribution of the duration of exposure in the two populations (*Avnstorp* 1991, III).

The time interval between the first examination in 1981 and the reexamination performed in 1987 was chosen in collaboration with the advisory group (see also chapter 6.1). The group found that it was not advisible to wait more than six years. By waiting longer, the motivation from the workers to participate would probably decrease. Bias due to migration should also be expected to be more pronounced. By waiting more than six years the performance of matched analyses of larger groups of workers should probably therefore not have been possible, although from a statistical point of view it would have been very attractive.

Workers in 1987 used gloves to a greater degree that did workers in 1981. Stratified analysis removed the influence from this confounding factor (*Avnstorp* 1989): Those workers from the 1981 and 1987 populations who frequently used gloves were selected for this analysis. In 1981, 93 of 190 workers had frequently used gloves during the past year prior to the examination. Of these 93 workers, 13 were found to be chromium hypersensitive. In 1987, 144 of 227 workers had frequently used gloves during the past year prior to the examination. Of these 144 workers, 5 were found to be chromium hypersensitive ($p=0.006$, chi-square with Yates correction). Since the statistically significant decrease in chromium hypersensitivity found in the study remained unchanged for these matched workers, the decrease should probably not be the result of changes in habits of using gloves by the workers.

8. CONCLUSIONS AND SUGGESTED ADDITIONAL STUDIES

Water soluble chromate in cement may cause allergic cement eczema in workers in the building and construction industries who have daily contact with wet cement. The addition of ferrous sulfate to the cement reduces the amount of water soluble chromate in it.

During the study period the prevalence of allergic cement eczema decreased. Concomitantly the number of approved claims of allergic cement eczema decreased. It can not be proven from the current study that the decrease was a result of reducing the content of water soluble chromate in cement. Especially differences in duration of exposure could be a confounding factor. On the other hand no other explanation for the decrease was found. Individual preventive measures such as using gloves and creams were not found to have an influence on the development of cement eczema.

Allergic cement eczema seems to be more severe, with a greater extent of involvement than irritant cement eczema. The medical prognosis of workers with irritant cement eczema can be assumed to be good. Most of those suffering from irritant cement eczema in 1981 did not have it 6 years later. Those with allergic cement eczema have a poorer prognosis as their status was generally unchanged by the addition of ferrous sulfate to the cement. Allergic cement eczema is chronic and is characterised by persistent or recurrent hand eczema. Concomitant sensitivities to cobalt and rubber chemicals may in part explain the unfavourable prognosis of those with allergic cement eczema. Neither a change of occupation nor retirement changed the medical prognosis significantly in comparison with remaining in the original occupation.

Minor skin complaints, such as dry skin with fissures and itching of the hands and fingers, are frequently seen in workers who have daily contact with wet cement. Such mild skin damage is largely reversible and is not influenced by the chromate content of the cement.

Further studies should be performed to determine the influence of individual prophylaxis on the development of occupational hand eczema. Also of special interest for additional study are the mechanisms which trigger the onset of occupational hand eczema.

Additional epidemiologic studies done in other countries where chromate-reduced cement is now used, should also be of value in the discussion of the results found in the present study.

If the decrease in number of workers with allergic cement eczema found in the present study was a consequence of lowering the exposure to water soluble chromate in cement the development of allergic cement eczema may be dose-response dependant. Concentrations of water soluble chromate in cement not exceeding 2 ppm could be near or below the minimal threshold concentration needed to induce hypersensitivity in workers with daily exposure to wet cement, whereas concentrations of 2 ppm or lower could elicit allergic cement eczema.

As standard testing procedures and methods of data analysis have been used, the results presented here can be compared with those obtained in other countries.

The dynamics of and association between constitutional differences and allergy and irritation of the skin could be examined by statistical methods based on multivariate analysis, but even sophisticated statistical methods cannot compensate enherent weakness of the data.

The sources of chromium exposure in females should be examined since more women seem to develop chromium hypersensitivity.

If the decreased numbers of allergic cement eczema are thought primarily to result from the reduction in the chromate content of the cement, the economic benefit of the intervention can be seen in the reduced need for the services of dermatologists and treatment with topical steroids. Concomitantly the number of approved claims of allergic cement eczema decreased, reducing the costs for the insurance agencies. Also, a reduction in the chromate content of

cement could lead to a reduction in sick leave taken because of allergic cement eczema.

The addition of ferrous sulfate increases the price of the cement by about 1%. Ferrous sulfate should be added when the cement is manufactured, using an industrialised method to ensure that the final product contains standard concentrations of water soluble chromate which do not exceed predetermined levels.

9. DANISH SUMMARY

Allergisk cementeksem viser sig oftest som et vedvarende håndeksem hos arbejdere og håndværkere med daglig kontakt med våd cement i beton eller mørtel. Sammenhængen mellem cementeksem og kromallergi blev fastslået allerede i 1950. Allergien overfor krom skyldes cementens indhold af vandopløseligt kromat. Sidst i 1970erne var cementeksem et tiltagende arbejdsmiljøproblem, idet cementeksem var blandt de hyppigst anmeldte arbejdsbetingede hudsygdomme hos mænd i Danmark. Det vides ikke nøjagtigt hvilke koncentrationer af vandopløseligt kromat i cementen, der er nødvendige for at fremkalde allergi hos arbejdere med daglig kontakt med våd cement. Det naturlige indhold af vandopløseligt kromat i dansk cement er ca. 10 mg pr kg cement (10 ppm).

I 1979 viste en gruppe svenske hudlæger en mulig praktisk løsning på problemet. De viste, at tilsætning af jernsulfat til cementen nedsatte indholdet af vandopløseligt kromat. Den danske cementfabrik Aalborg Portland A/S videreudviklede metoden til industrielt brug, hvilket sikrede et lavt kromatindhold i cementen allerede ved levering fra fabrikken. Metoden blev patenteret og indført i 1981.

Undersøgelsen viste, at hyppigheden af allergisk cementeksem faldt statistisk signifikant fra 1981 til 1987. Samtidig faldt antallet af allergiske cementeksemer anerkendt i Arbejdsskadestyrelsen. Antallet af irritative cementeksemer var uændret. En væsentlig fejlkilde i undersøgelsen var forskelle i ekspositionstiden for de undersøgte arbejdere. Faldet i antallet af allergiske cementeksemer i Danmark kan derfor skyldes andre forhold end lavere koncentrationer af vandopløseligt kromat i cementen. På den anden side syntes brugen af personlige værnemidler ikke at have haft indflydelse. Personlig beskyttelse med handsker syntes således ikke at have indflydelse på udviklingen af allergisk cementeksem. Udviklingen af irritativt cementeksem syntes samtidig at være upåvirkelig af individuelle profylaktiske foranstaltninger som håndvask, forsøg på at undgå kontakt med våd cement samt handske- og cremebrug. En mulig forklaring på faldet i antallet af allergiske cementeksemer, var indførelsen af kromatreduceret cement. Faldet synes ikke at være begrundet i øget automatisering af arbejdsprocesserne.

Forløbet af det allerede udviklede allergiske cementeksem er dårligt, selv efter tilsætningen af jernsulfat til cementen. Forløbet er præget af vedvarende eller tilbagevendende håndeksem. Tilstødende allergier overfor kobolt og gummikemikalier forværrer formentlig forløbet. I modsætning hertil er forløbet af det irritative cementeksem godt, idet de fleste irritative cementeksemer svinder efter en vis tid.

Erhvervsskift påvirker ikke sikkert forløbet af det allergiske cementeksem i forhold til forbliven i det oprindelige erhverv. Den sociale prognose vurderet ved den beskæftligelsesmæssige udsigt er formentlig god for yngre arbejdere med allergisk cementeksem, hvad enten de bliver i deres oprindelige erhverv eller skifter til et andet uden kontakt med våd cement. Risikoen for at ende i arbejdsløshed synes ikke at være større for de kromallergiske end for de ikke-kromallergiske. Efterlønsordningen medfører at ældre arbejdere kan opretholde deres sociale status på trods af cementeksemet.

Såfremt faldet i antallet af allergiske cementeksemer skyldes indførelsen af kromatreduceret cement er der opnået en arbejdsmiljømæssig gevinst for de arbejdere og håndværkere, som har kontakt med våd cement. Den samfunds-økonomiske gevinst er et nedsat behov for lægelige ydelser og behandling med hormoncremer. Mistede arbejdsdage viser samme tendens. Da antallet af anerkendte tilfælde af allergisk cementeksem i Arbejdsskadestyrelsen samtidig er faldet findes en yderligere gevinst i form af færre udbetalte mén-erstatninger.

Undersøgelsen er baseret på standardiserede undersøgelses- og testmetoder. Kromatreduceret cement anvendes nu i bl.a. Sverige og Finland. Epidemiologiske undersøgelser fra disse lande vil yderligere kunne belyse resultaterne i nærværende studie.

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