# INACTIVATION OF CHROMIUM ION IN ALLERGIC ECZEMATOUS DERMATITIS*

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In previous studies (1) we reported that cysteine and glutathione showed a capacity to inactivate patch test reactions in chromate-sensitive patients. Protection against the chromate reaction afforded by glutathione and cysteine was based upon the protection of sulfhydryl groups which are inactivated by chromium salts. The instability and costs of these agents obviated their practical use.

We also showed that EDTA (edathamil calcium-disodium) did not inactivate the hexavalent chromium ion in patch tests performed on chromate-sensitive subjects. The reason is that hexavalent chromium does not react at all with EDTA; on the other hand $Cr_{III}$ can be easily joined with EDTA. There is little if any evidence that trivalent chromium is a sensitizing agent (2, 3, 4). We confirmed the incapability of trivalent chromium to sensitize a group of twelve patients with proved dichromate sensitivity. These patients were patch-tested with two trivalent chromium compounds, basic chromium sulfate‡ and chromium nitrate. All patients showed negative patch tests with the trivalent compounds while exhibiting positive reactions with the hexavalent compound (5). These results showed that no antigenic similarity exists between trivalent and hexavalent chrome and no cross-sensitivity occurs.

Since hexavalent chromium is the agent capable of producing specific epidermal sensitization, we thought that protection against the hexavalent chromium reaction could be accomplished if the $Cr_{VI}$ were reduced to the $Cr_{III}$ form. Since the latter could readily be chelated, complete inactivation of both $Cr_{VI}$ and $Cr_{III}$ would result. Although trivalent chromium ions are slow in their reactions with various complexing agents, once formed, the complexes are extremely stable.

Attention was directed to an agent which could convert hexavalent chromium to trivalent chromium with subsequent chelation without irritating the skin. Our studies have shown that sodium pyrosulfite was well suited as a reducing agent and that tartaric acid could serve as the chelating agent. In combination with glucose and ammonium chloride these chemicals have been compounded into an agent against chromium.

The anti-chrome reagent consisted of the following quantities:

| | |
|---|---|
| Sodium pyrosulfite | 2 parts/wt. |
| Tartaric acid | 1 part/wt. |
| Glucose | 1 part/wt. |
| Ammonium Chloride | 1 part/wt. |

1 gm. of the anti-chrome reagent contains sufficient sodium pyrosulfite to reduce 100,000 $\gamma$ of $Cr_{VI}$ to $Cr_{III}$; the tartaric acid in this amount of anti-chrome is sufficient to chelate the resultant $Cr_{III}$. For clinical use, the anti-chrome reagent was used in a 10% concentration either in ointment base (carbowax or hydrophilic ointment) or in aqueous solution.

The following formulas explain the reduction and chelation reactions with $Cr_{VI}$ and $Cr_{III}$.

1) $2\ Cr_2O_7^{--} + 3S_2O_5^{--} + 5\ H_2O = Cr^{+++} + 6SO_4^{--} + 10\ OH^-$

2) $Cr^{+++} + {}_3H_2C_4H_4O_6 = Cr\ (HC_4H_4O_6)_3 + {}_3H^+$

The chelation reaction of tartaric acid with trivalent chromium (6) may also be explained as follows:

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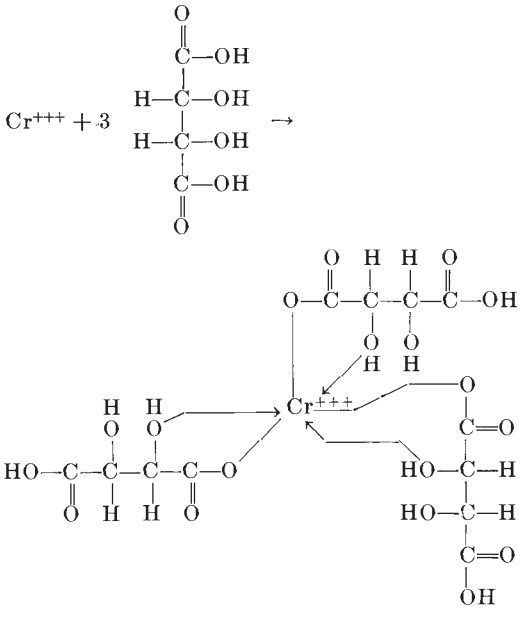

The function of the ammonium chloride is to render the system slightly acidic (pH = 4). The glucose aids in the reduction of hexavalent chromium.

By means of patch tests on chromate-sensitive subjects we have shown that in 10% concentrations our anti-chrome reagent in ointment or solution completely prevented the allergic reaction. The ointment bases and plain water were used as controls (Figs. 1, 2, 3, 4).

## METHOD

In order to determine the effect of the anti-chrome ointment and solution after the skin had been in contact with 0.25% potassium dichromate, the following procedure was performed on two chromate-sensitive patients:

Twelve closed patches of 0.25% potassium dichromate were applied respectively to the left and right sides of the back. After varying in

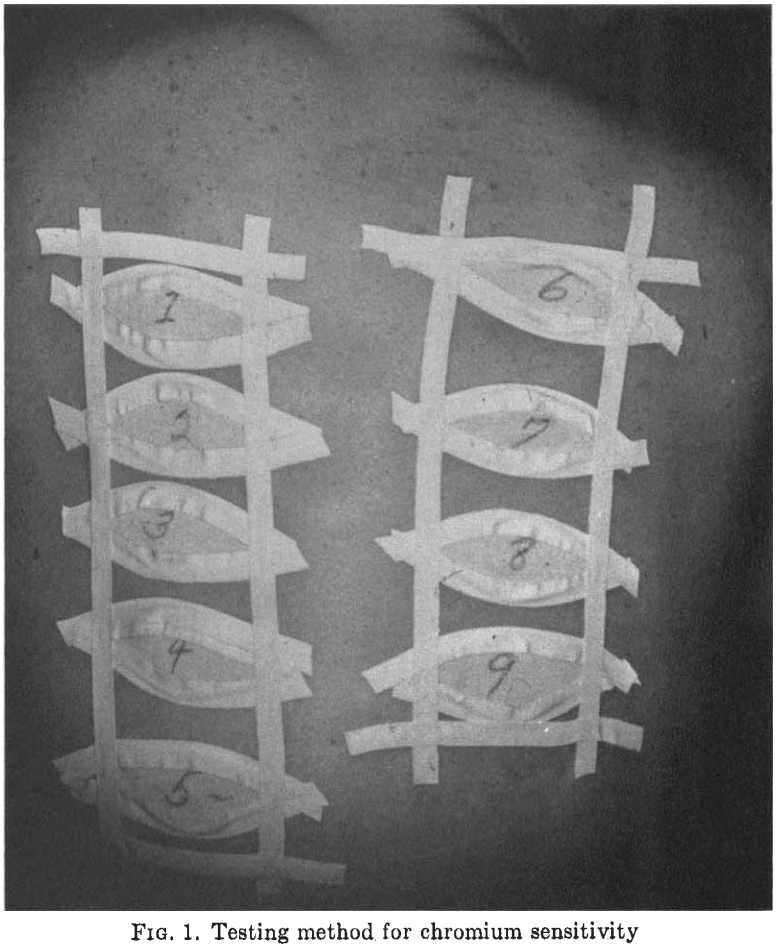

FIG. 1. Testing method for chromium sensitivity

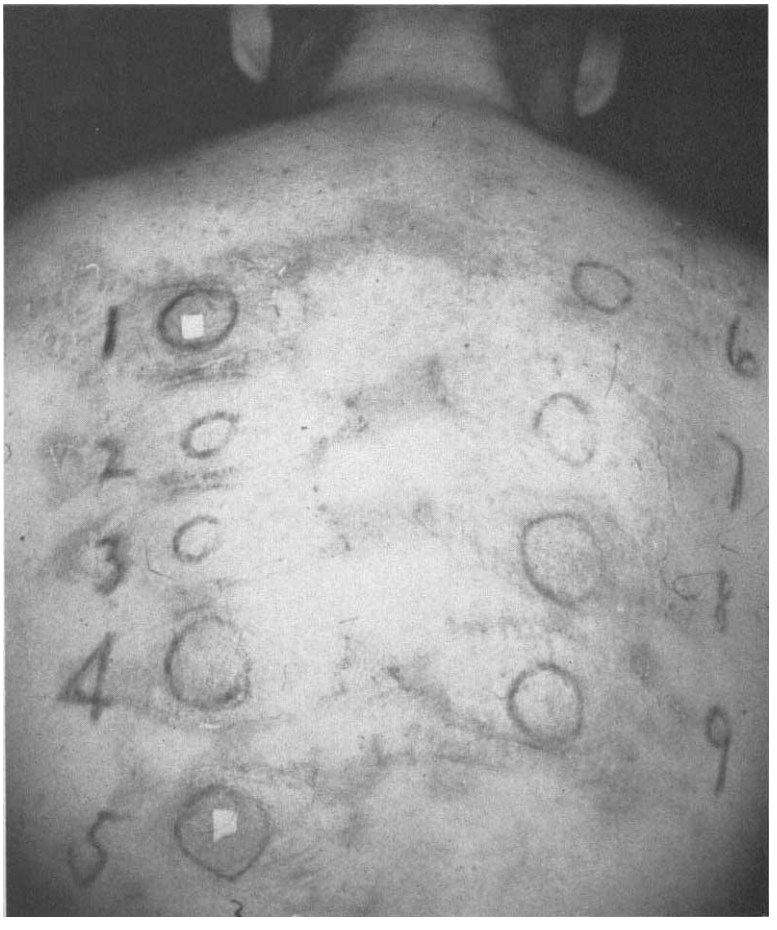

FIG. 2. (Patient F. K.) 48 hours reacing demonstrates the following:
Test 1: 3 plus reaction ($Cr_{VI}$: potassium dichromate 0.25%).
Test 2: Negative ($Cr_{III}$: chromium nitrate 0.25%).
Test 3: Negative ($Cr_{III}$: basic chromium sulfate 0.2%).
Test 4: plus reaction—control (carbowax) over which a patch test with 02.5% $K_2CrO_7$ was applied.
Test 5: 3 plus reaction—control base (hydrophilic ointment) over which a patch test with 0.25% $K_2CrO_7$ was applied.
Test 6: Negative—anti-chrome ointment (carbowax base) over which a patch test with 0.25% $K_2CrO_7$ was applied.
Test 7: Negative—anti-chrome ointment (hydrophilic ointment base) over which a patch test with 0.25% $K_2CrO_7$ was applied.
Test 8: 3 plus reaction—control of linen soaked in water over which a patch test with 0.25% $K_2CrO_7$ was applied.
Test 9: Negative—linen soaked in anti-chrome solution over which a patch test with 0.25% $K_2CrO_7$ was applied.
(There is a moderate amount of adhesive tape reaction in this case).

tervals of time, each horizontal line of patches was successively removed, the contact areas on the left side were rubbed with the antichrome ointment (a, b, c, d, e, f) and the control base (a′, b′, c′, d′, e′, f′) and left uncovered. The anti-chrome solution (g, h, i, j, k, l) and water (g′, h′, i′, j′, k′, l′) were used in a similar manner for the patches on the right side. The first group of four patches was removed after 15 minutes; the anti-chrome ointment and solution and their controls were applied; the second group of four patches after 30 minutes; the third group after an hour; the fourth group after two hours; the fifth group after three hours; and the sixth group after six hours. Readings were made after each successive removal of the patches and a final reading after 24–30 hours. In addition, 10 patches of 0.25% potassium dichromate were

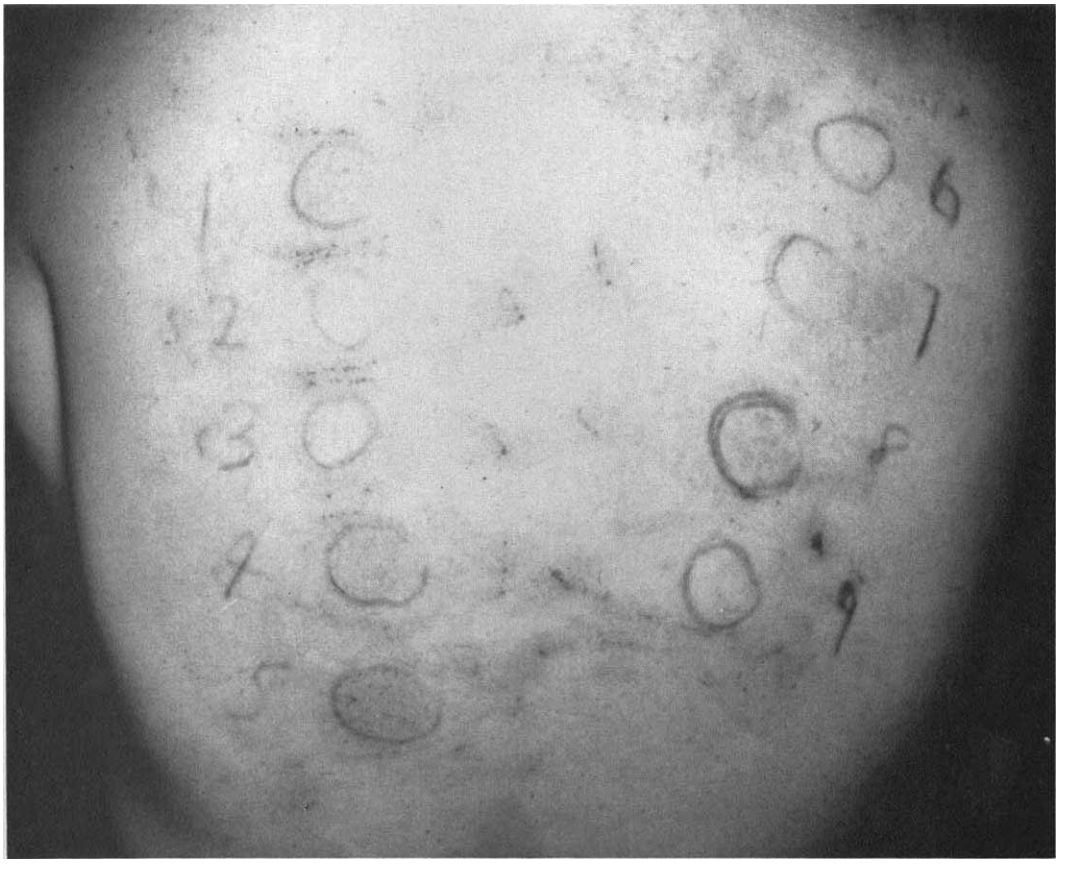

FIG. 3. Five day reading on same patient. Positive reactions have persisted; no change at the site of the negative reactions.

applied in a vertical line down the center of the back. These patches were removed after varying intervals of time and the sites of contact were washed with pledgets of cotton soaked in 1% sodium lauryl sulfate solution. The first patch was removed after 15 minutes, the second after 30 minutes, and the remaining 8 patches at 5 minute intervals. The results of this study are given in Charts 1, 2 and Figures 5, 6.

RESULTS

1. Trivalent chromium compounds caused no reactions on dichromate-sensitive patients.

2. An anti-chrome reagent of sodium pyrosulfite, tartaric acid, glucose, and ammonium chloride completely prevented patch test reactions in chromate-sensitive patients if applied to the skin before the application of 0.25% potassium dichromate.

3. In chromate-sensitive patients contact with 0.25% potassium dichromate for 15 minutes or less will elicit the eczematous reaction.

4. Washing with sodium lauryl sulfate up to 15 minutes will prevent the reaction; no inhibition occurs if the washing procedure is used at later time intervals.

5. The application of anti-chrome ointment on two chromate-sensitive patients after 15 and 30 minutes blocked reactions over sites of contact with 0.25% potassium dichromate; application of the control ointment base produced minimal blockage at 15 minutes and no effect at 30 minutes. After 30 minutes, all blocking attempts proved ineffective.

6. Anti-chrome solution and the water control prevented a reaction if applied within 15 minutes after contact with 0.25% potassium dichromate; neither showed any blocking effect by 30 minutes.

7. The earliest clinical manifestation of

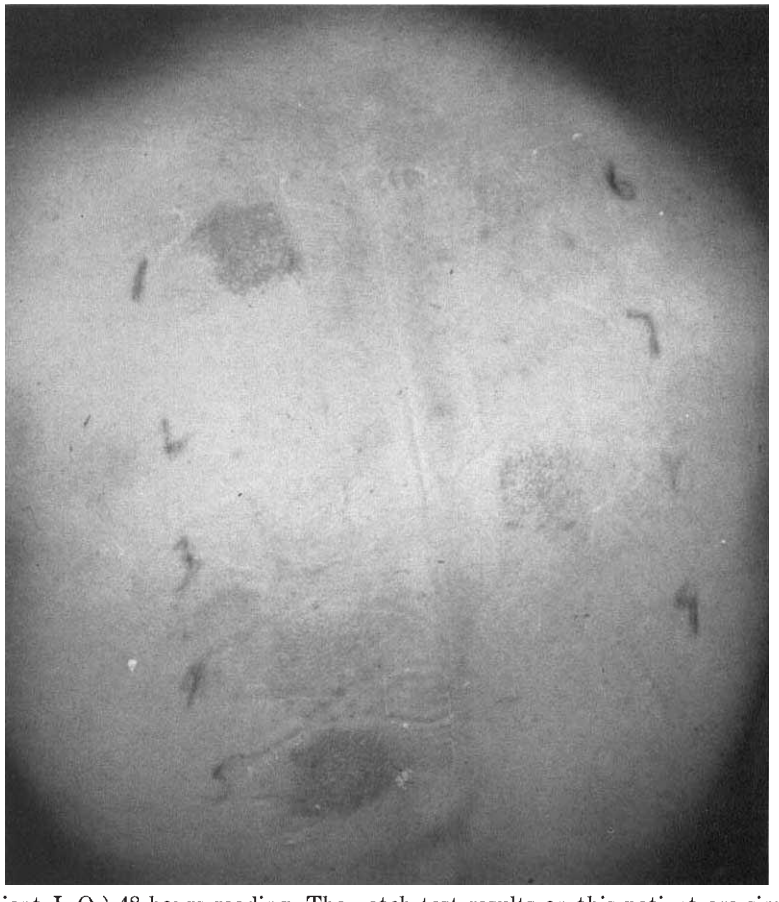

FIG. 4. (Patient J. O.) 48 hours reading. The patch test results on this patient are similar to those described in Fig. 2.

| Time Intervals for Reading Test Sites | a | a′ | b | b′ | c | c′ | d | d′ | e | e′ | f | f′ | g | g′ | h | h′ | i | i′ | j | j′ | k | k′ | l | l′ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15* minutes | − | − | | | | | | | | | | | − | − | | | | | | | | | | |
| 6 hours | − | − | | | | | | | | | | | − | − | | | | | | | | | | |
| 30* minutes | | | − | − | | | | | | | | | | | − | − | | | | | | | | |
| 6 hours | | | − | ± | | | | | | | | | | | + | ± | | | | | | | | |
| 1* hour | | | | | − | − | | | | | | | | | | | − | − | | | | | | |
| 6 hours | | | | | + | + | | | | | | | | | | | + | + | | | | | | |
| 2 *hours | | | | | | | − | − | | | | | | | | | | | − | − | | | | |
| 6 hours | | | | | | | + | + | | | | | | | | | | | + | + | | | | |
| 3* hours | | | | | | | | | − | − | | | | | | | | | | | − | − | | |
| 6 hours | | | | | | | | | + | + | | | | | | | | | | | + | + | | |
| 6* hours | | | | | | | | | | | + | + | | | | | | | | | | | + | + |
| 24-30 hours | − | ± | − | +/+2 | +2 | +2/+3 | +3 | +3 | +3 | +3 | +3 | +3 | − | − | + | ± | +/+2 | + | +2 | +2 | +2/+3 | +2/+3 | +2/+3 | +2/+3 |

* Denotes removal of patch.

CHART 1. The effects of anti-chrome mixtures and their controls used after varying periods of time following contact with 0.25% potassium dichromate. Sites a to l treated with anti-chrome preparations; a′ to l′ controls.

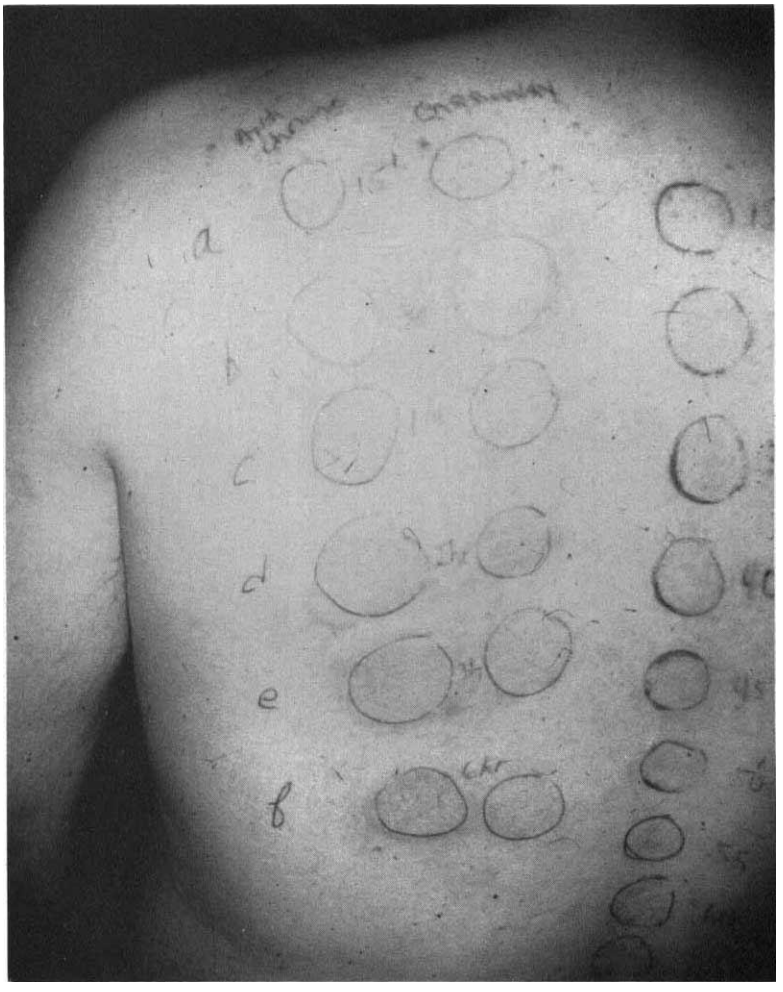


FIG. 5. The application of anti-chrome ointment blocked reactions at sites of contact at 15 and 30 minutes (a and b), control ointment base produced minimal blockage at 15 minutes (a′) and no effect at 30 minutes (b′). After 30 minutes, all blocking attempts proved ineffective (c to f). Anti-chrome solution and the water control prevented reaction at sites of contact with 0.25% potassium dichromate when applied within 15 minutes (g and g′); neither showed any blocking effect by 30 minutes (h and h′).

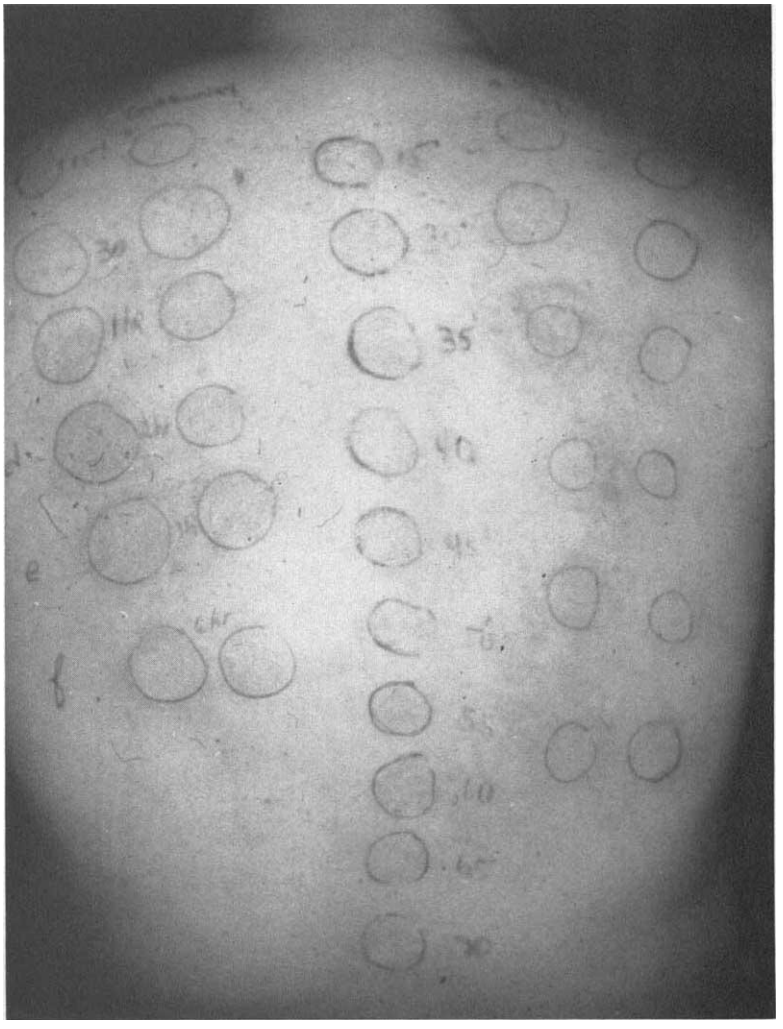

FIG. 6. Washing with sodium lauryl sulfate within 15 minutes after contact prevented allergic reaction; no inhibition of allergic reaction occurred if washing with sodium lauryl sulfate solution is applied after 15 minutes.

| Time Intervals for Removal of Patch | Reaction at Time of Removal of Patch | Reaction After 6 Hours | Reaction After 24 Hours |
|---|---|---|---|
| 15 minutes | − | − | − |
| 30 minutes | − | − | +/+2 |
| 35 minutes | − | − | +2 |
| 40 minutes | − | − | +2 |
| 45 minutes | − | ± | +2 |
| 50 minutes | − | ± | +/+2 |
| 55 minutes | − | ± | +/+2 |
| 60 minutes | − | ± | +2 |
| 65 minutes | − | ± | +2 |
| 70 minutes | − | − | +2 |

CHART 2. Effect of sodium lauryl sulfate washing at varying intervals of time following contact with 0.25% potassium dichromate.

eczematization was observed after 6 hours following contact with the sensitizer.

## CONCLUSIONS

An anti-chrome reagent based on the reduction of hexavalent chromium to the trivalent state with subsequent chelation, capable of inactivating patch test reactions in chromate-sensitive patients, was described.

These findings open a practical approach to the prophylactic management of chromate dermatitis. Current studies are being conducted in various industries to determine the usefulness of this reagent under actual working conditions.

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