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SKIN CLEARANCE OF IONTOPHORETICALLY ADMINISTERED CHROMIUM (^{51}Cr) AND SODIUM (^{22}Na) IONS IN THE GUINEA PIG

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Abstract. An in vivo isotope technique (disappearance measurements) was used to compare, in the guinea pig, the skin clearance of chromate (^{51}Cr) and sodium (^{22}Na) ions after iontophoretic and epicutaneous administration. The effects of variations in the concentration of the ions, current strength and duration of current flow were especially studied. Disappearance from the skin occurred mainly during the first hour after iontophoresis. The maximal increase observed was up to 43 times greater than with epicutaneous administration for the lowest chromate concentration, and eight times greater for the sodium ions. A gradual increase in the current strength and the duration respectively, increased the skin clearance of the chromate ions, in contrast to clearance of sodium ions where it was already optimal at 2 mA at 5 min. It seems probable that iontophoretic administration can be used as a test method, complementary to ordinary patch testing, for the investigation of obscure cases of contact eczema.

When investigating patients with contact eczema where ordinary patch testing has shown negative results, sometimes other, supplementary, test methods have been used. Thus, when chromium allergy is suspected, the allergen has been introduced intracutaneously (inter alia 1, 2), or the test area has been pretreated with sodium lauryl sulphate and octylamine (5), or stripping ("Abriss" test) (4, 5, 9) has been applied. In other cases the chromium solution has been modified by adding detergents (6) or alkali (8). By these means it has been possible to detect further cases of allergic contact eczema.

The disadvantage of the traditional patch test procedure is that the patient has to wear the test strips for 24–48 hours; sometimes they become loose; sometimes the adhesive tape causes the patient subjective discomfort. In intracutaneous testing, too deep deposition of the test substances in the dermis can occur, resulting in unknown amounts reaching the epidermis from below.

The iontophoretic technique was previously used by Haxthausen (3) for studies on the influence of various physical and chemical agents on the eczematous allergic reaction, but not as a complement to ordinary patch testing. The advantage of iontophoretic administration in the investigation of contact allergy is that the test substances are administered rapidly on *one* occasion, and that they migrate through the epidermis down into the cutis and not vice versa.

Prior to an investigation of patients with suspected chromium allergy, isotope-labelled chromate and sodium ions have been administered iontophoretically in a pilot study on guinea pigs. The sodium ion was chosen as the substance for comparison since it lacks the protein-precipiating properties of chromium. A comparison (13, 14) is made with the results obtained by epicutaneous administration, i.e. the patch testing procedure. Moreover, the effect is studied on skin clearance of variations in concentration of the ions, current strength and duration of current flow. The method for studying the disappearance from the skin of the isotope-labelled ions (disappearance measurements) is the same as that in the previous experiments with epicutaneous administration (11).

MATERIALS AND METHODS

Experimental animals. White guinea pigs of both sexes were used in about equal numbers; weight 300–500 gm.

Sodium chromate ($Na_2CrO_4 \cdot 4H_2O$), analytical reagent (Mallinckrodt Chemical works, USA).

Sodium chloride (NaCl), analytical reagent (E. Merck, AG, Germany).

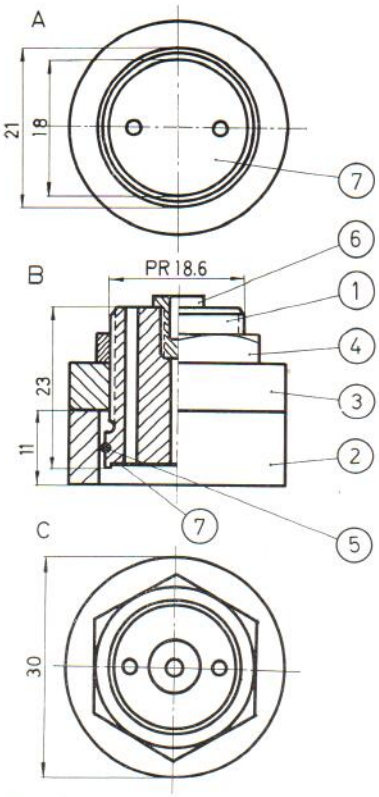

Fig. 1. Active electrode. Unit of measurement: millimeter.

Isotopes. ^{51}Cr (half-life 27.8 days) and ^{22}Na (half-life 2.6 years) were obtained from the Radiochemical Centre, Amersham, England.

Vehicle. Distilled water.

Concentrations were chosen that permitted direct comparison with the previous investigations (13, 14) with epicutaneous application.

Iontophoresis apparatus. This is principally a constant current source especially adapted for its purpose. It consists of a stabilised voltage supply, with sufficiently large serial resistances to the electrode connections, relative to the electrode resistance. Thus, variations in the electrode resistance can be disregarded while maintaining the same degree of accuracy.

In the Iontophoresis Apparatus used in this investigation, the electrode current is adjusted by a six-position switch control to 1.0, 1.5, 2.0, 3.0, 4.0 or 6.0 milliamps (mA). The source voltage is 260 Volts and the serial resistances vary between 40 kOhms at 6 mA and 235 kOhms at 1 mA. The external resistance, i.e. the electrode resistance, varies from approximately 6 kOhms to 30 kOhms for the range of current in question.

Active (driving) electrode. Fig. 1 (*A–C*) show the dimensions and shape of the chamber-type electrode used. No. 1 indicates the centre part of the electrode design. A platinum plate, no. 7 (Fig. 1 *A, B*), diameter 18 mm, is fastened to one end, and internally connected to a noninsulated banana jacket, no. 6, at the top end. The centre part has an outer screw thread made of PVC. No. 2 is a plexiglass ring, which, together with the centre part no. 1, forms the electrode chamber. No. 3 is a steering nut (PVC) locked in place by a brass nut no. 4. The height of the electrode chamber, and consequently its volume, can be set by means of these nuts. No. 5 is a rubber sealing ring.

The *indifferent electrode* is a 3.5×5.0 cm brass plate which is attached to one of the flanks of the experimental animal with a rubber band. An electrode ointment, containing 10% NaCl, is applied between the clipped skin and the concave surface of the brass plate.

Experimental procedure. The skin depot consists of a plexiglass cylinder, inner diameter 20 mm (exposure area: 3.1 cm^2) (11). 1.0 ml of the respective isotope-labelled solutions is put in the skin depot, that is to say, the same volume as in previous experiments (11). The active electrode (Fig. 1) is placed in the plexiglass cylinder and the indifferent electrode on the animal's flank. After that, the iontophoresis is started at the desired current strength (2.0, 4.0, or 6.0 mA, which corresponds to the current densities of 0.79, 1.57, and 2.36 mA/cm^2 respectively) and duration of current flow (5, 10, 15, or 30 min). Immediately after the completion of the iontophoresis the electrodes are removed, the cover glass glued on and recording started (11).

Disappearance measurements. (11). The radioactivity above the deposit of the isotope-labelled ions is continuously recorded for 5–25 hours by a scintillation detector. The decrease in activity indicates migration through the skin into the circulation, and is expressed mathematically in terms of a disappearance constant (k min^{-1}). For particulars of the scintillation detector, collimator, ratemeter, recorder, analysis of disappearance curves etc., see previous paper (11).

Statistics. Analysis of variance.

RESULTS

Disappearance curves

Fig. 2 shows 4 curves for the chromate ion (0.017 M). Curve 1 was obtained at epicutaneous administration, and curves 2–4 after iontophoresis for 5 min at 2, 4, and 6 mA respectively. The slope of the curves was more pronounced the higher the current strength at constant duration of flow. The analysis of the curves showed, moreover, that it was during the first hour $(J_0–J_1)$[1] that disappearance mainly took place. Consequently, in the tables and figures the k-values have been shown for this period, and for the subsequent 4 hours $(J_1–J_5)$[1]. In about half of the experiments, recording was continued for 20–25 hours (11). No

[1] J_0 = the initial in vivo counting rate from the deposit (at time t_0); J_1 and J_5 = the in vivo counting rate from the deposit at 1 hour (at time t_1) and 5 hours (at time t_5) respectively.

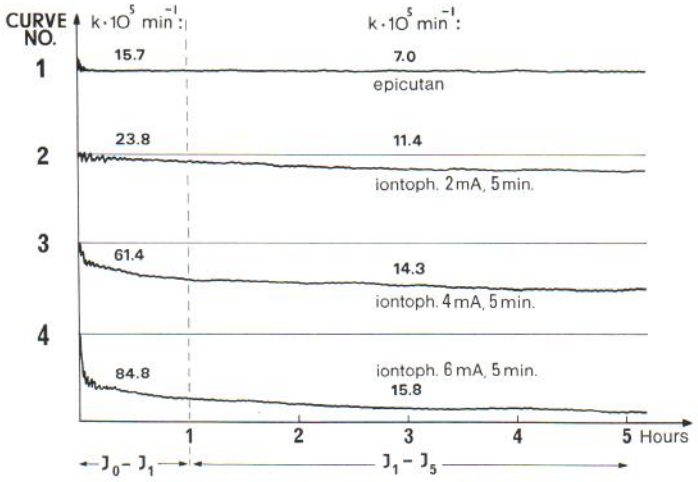

Fig. 2. Representative disappearance curves, obtained directly from the recorder, showing different degrees of slope. 0.017 M chromate.

difference was found for this period compared with the corresponding curves for epicutaneous administration.

Comparison between iontophoretic and epicutaneous administration

Tables I–III and Figs. 3–4 show the mean disappearance constants (k min $^{-1}$) for various concentrations of chromate and sodium ions after iontophoresis at 2, 4, and 6 mA and at duration of current flow for 5, 10, 15, and 30 min. The epicutaneous-administration series (1, 13, 20, 27, 35) have been previously published (13, 14). Tables I–III also give the ratios between the means of the disappearance constants when comparing iontophoretic and epicutaneous administration. For example, the mean disappearance constant for 0.017 M chromate was 17.0×10^{-5} min^{-1} (Table I, series 2, *iontophoresis* for 5 min at 2 mA, J_0–J_1), and 12.2×10^{-5} min^{-1} (Table I, series, 1, *epicutaneous*, J_0–J_1); a ratio of 1.4.

Chromate ion. Ratios were obtained between 9.4 and 43.2 (0.005 M, series 14–19) and 1.4 and 7.6 (0.017 M, series 2–8, 10–12) for the first hour. The observed differences compared with the epicutaneous administration were statistically significant ($P < 0.001$) with the one exception of series 2.

For the following 4 hours the ratios were 1.2–11.7 (0.005 M) and 0.9–3.4 (0.017 M). In series 12 and 19 the observed increase was statistically significant ($P < 0.001$). In series 7, 10, 14 there was a definite tendency to increase ($0.001 < P < 0.01$).

For 0.398 M the ratios were 1.1–3.4 (series 21–26) for the first hour. In series 24 the observed increase was statistically significant ($P < 0.001$), and in series 25 there was a definite tendency to increase ($0.001 < P < 0.01$). For the following 4 hours the ratios were 0.1–0.9, and the decrease in series 22 and 23 was statistically significant ($P < 0.001$).

Sodium ion. Ratios were obtained between 6.1 and 8.2 (0.005 M, series 28–33), and 3.9–6.0 (0.239 M, series 36–41) for the first hour. The observed differences were statistically significant ($P < 0.001$).

For the following 4 hours the ratios were 1.7–3.0 (0.005 M), and 1.4–4.3 (0.239 M). In the series 30, 32 and 37 the observed increase was statistically significant ($P < 0.001$), whereas in series 28, 31, 39, 41 there was a definite tendency to increase ($0.001 < P < 0.01$).

Effect of concentration of ions

The largest *relative* increases compared with the epicutaneous application were obtained with the lowest (0.005 M) chromate concentration (maximal 43 times); maximal 7 times (0.017 M) and 3 times (0.398 M). For the sodium ions the tendency was not as manifest, for the concentration 0.005 M the maximal increase was 8 times compared with 6 times for 0.239 M.

Calculated *absolutely*, the amount increased with increasing concentration. For chromium, the range was 23–105, (0.005 M, Table II, series 14–19), 56–305 (0.017 M, Table I, series 2–8, 10–12), and 824–2627 nM Cr cm^{-2} hr^{-1} (0.398

Table I. *Mean disappearance constants (k) after epicutaneous and iontophoretic administration of 0.017 M $^{51}CrO_4^{-2}$. For statistical analysis and ratios, see text*

Series no.	Mode of administration	Minutes	mA	Total number of experiments	J_0–J_1 $k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance	nM Cr cm^{-2} hr^{-1}
1	Epicutan.	—	–	10	12.2 ± 1.5	—	—	40
2	Iontoph.	5	2	10	17.0 ± 3.2	1.4	$0.05 < P < 0.2$	56
3	Iontoph.	15	2	10	42.8 ± 5.2	3.5	$P < 0.001$	141
4	Iontoph.	30	2	5	62.4 ± 4.5	5.1	$P < 0.001$	205
5	Iontoph.	5	4	5	47.8 ± 8.0	3.9	$P < 0.001$	157
6	Iontoph.	15	4	5	57.0 ± 8.3	4.7	$P < 0.001$	188
7	Iontoph.	30	4	5	74.3 ± 5.2	6.1	$P < 0.001$	244
8	Iontoph.	5	6	14	48.2 ± 6.3	4.0	$P < 0.001$	159
9	Iontoph.[a]	5	6	5	18.5 ± 4.6	1.5	$0.05 < P < 0.2$	61
10	Iontoph.	10	6	5	73.7 ± 4.4	6.0	$P < 0.001$	242
11	Iontoph.	15	6	10	77.1 ± 7.7	6.3	$P < 0.001$	254
12	Iontoph.	30	6	5	92.7 ± 5.3	7.6	$P < 0.001$	305

[a] Positive charge of the driving electrode.

M, Table II, series 21–26), and for sodium the range was 52–70 (0.005 M, Table III, series 28–33) and 1582–2415 nM Na cm^{-2} hr^{-1} (0.239 M, Table III, series 36–41).

Effect of variations in current strength and duration of current flow

Ratios were calculated between the mean disappearance constants to study the effect of increasing the current strength and the duration of the current flow. For example, the mean disappearance constant for 0.005 M sodium ion was 54.1 $\times 10^{-5}$ min^{-1} (Table III, series 29, iontophoresis for 15 min at 2 mA, J_0–J_1) and 57.6 $\times 10^{-5}$ min^{-1} (Table III, series 28, iontophoresis for 5 min at 2 mA, J_0–J_1); a ratio of 0.9. The corresponding statistical analysis showed that the differences in the magnitude of the disappearance constants between 5 and 15 min of iontophoresis were insignificant ($P > 0.2$).

Current strength 2 → 4 mA. For the sodium ion the ratios were 0.9–1.3 and the differences were not statistically significant. For the chromate ion the ratios were 0.7–3.2, and in two statistical ana-

Table II. *Mean disappearance constants (k) after epicutaneous and iontophoretic administration of 0.005 and 0.398 M $^{51}CrO_4^{-2}$. For statistical analysis and ratios, see text*

Series no.	Conc. M	Mode of administration	Minutes	mA	Total number of experiments	J_0–J_1 $k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance	nM Cr cm^{-2} hr^{-1}
13	0.005	Epicutan.	—	–	10	2.5 ± 1.3	—	—	0.2
14	0.005	Iontoph.	5	2	10	33.0 ± 7.3	13.2	$P < 0.001$	32
15	0.005	Iontoph.	15	2	5	41.0 ± 3.6	16.4	$P < 0.001$	40
16	0.005	Iontoph.	5	4	5	23.5 ± 6.5	9.4	$P < 0.001$	23
17	0.005	Iontoph.	15	4	5	64.5 ± 8.4	25.8	$P < 0.001$	62
18	0.005	Iontoph.	5	6	5	66.1 ± 6.5	26.4	$P < 0.001$	64
19	0.005	Iontoph.	15	6	10	108.0 ± 7.9	43.2	$P < 0.001$	105
20	0.398	Epicutan.	—	–	10	9.9 ± 0.4	—	—	763
21	0.398	Iontoph.	5	2	5	14.3 ± 3.3	1.4	$0.05 < P < 0.2$	1102
22	0.398	Iontoph.	15	2	5	10.7 ± 2.2	1.1	$P > 0.2$	824
23	0.398	Iontoph.	5	4	5	13.1 ± 5.6	1.3	$P > 0.2$	1009
24	0.398	Iontoph.	15	4	5	34.1 ± 6.6	3.4	$P < 0.001$	2627
25	0.398	Iontoph.	5	6	5	19.3 ± 4.5	1.9	$0.001 < P < 0.01$	1487
26	0.398	Iontoph.	15	6	10	16.7 ± 3.7	1.7	$0.05 < P < 0.2$	1286

J_1–J_5		
$k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance
8.1 ± 1.6	—	—
8.0 ± 1.7	1.0	$P > 0.2$
7.0 ± 1.5	0.9	$P > 0.2$
15.5 ± 1.6	1.9	$0.01 < P < 0.05$
11.9 ± 1.2	1.5	$0.05 < P < 0.2$
11.4 ± 1.5	1.4	$P > 0.2$
27.9 ± 7.1	3.4	$0.001 < P < 0.01$
14.8 ± 2.4	1.8	$0.01 < P < 0.05$
7.7 ± 2.7	1.0	$P > 0.2$
20.6 ± 3.3	2.5	$0.001 < P < 0.01$
11.8 ± 1.7	1.5	$0.05 < P < 0.2$
27.4 ± 3.3	3.4	$P < 0.001$

lyses of seven there was a definite tendency to increase when the current strength was increased to 4 mA.

Current strength 2→6 mA. For the sodium ion the ratios were 0.9–1.3 and the differences were not statistically significant. For the chromate ion the ratios were 1.3–2.8 and in four statistical analyses of seven there was a definite tendency to increase when the current strength was increased to 6 mA.

Current strength 4→6 mA. For the sodium ion the ratios were 1.0–1.3 and the differences were not statistically significant. For the chromate ion the ratios were 0.5–2.8 and only for the concentration 0.005 M was there a definite tendency to increase when the current strength was increased to 6 mA.

J_1–J_5		
$k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance
2.2 ± 1.0	—	—
9.4 ± 2.2	4.3	$0.001 < P < 0.01$
5.9 ± 2.7	2.7	$0.05 < P < 0.2$
5.2 ± 2.2	2.4	$0.05 < P < 0.2$
9.0 ± 3.2	4.1	$0.01 < P < 0.05$
2.6 ± 0.9	1.2	$P > 0.2$
25.8 ± 4.9	11.7	$P < 0.001$
9.3 ± 1.2	—	—
1.9 ± 0.9	0.2	$0.001 < P < 0.01$
0.8 ± 0.5	0.1	$P < 0.001$
1.4 ± 0.9	0.2	$P < 0.001$
6.1 ± 1.7	0.7	$0.05 < P < 0.2$
6.3 ± 2.7	0.7	$P > 0.2$
8.4 ± 2.3	0.9	$P > 0.2$

Current flow 5→15 min. For the sodium ion the ratios were 0.9–1.5 and the differences were not statistically significant. For the chromate ion the ratios were 0.7–2.7, and for the concentrations 0.005 and 0.017 M there was, in four of seven statistical analyses, a definite tendency to increase when iontophoresis was prolonged to 15 min.

Current flow 5→30 min, chromate (0.017 M). The ratios were 1.6–3.7, and in two analyses of three the increase was statistically significant.

Current flow 15→30 min, chromate (0.017 M). The ratios were 1.2–1.5 and the differences were not statistically significant.

Wrong polarity

In series 9 and 34 the electrodes were changed, so that the active electrode and the ions that were investigated had the opposite polarity. This resulted in only a minimal increase (ratio 1.5) compared with epicutaneous administration ($0.05 < P < 0.2$). On comparing series 8 (correct polarity) with series 9 (wrong polarity), but identical strength and flow of current, the mean disappearance constant for the chromate ion was reduced from 48.2×10^{-5} min^{-1} to 18.5×10^{-5} min^{-1} ($0.01 < P < 0.05$). For the corresponding comparison with the sodium ion (series 33 and 34) the mean disappearance constant was reduced from 72.7×10^{-5} min^{-1} to 13.4×10^{-5} min^{-1} ($P < 0.001$).

DISCUSSION

With the method used (disappearance measurements) a decrease was recorded in the counting rate above the administered isotope, i.e. they disappeared from the field of vision of the scintillation detector (11). This disappearance is made up of at least two components, a rapid component with reference to the ions which were introduced into the skin by means of iontophoresis and which are being transported away via the circulation, and a slow component with reference to the ions absorbed from the epicutaneous depot.

The analysis of the disappearance curves (Fig.

Table III. *Mean disappearance constants (k) after epicutaneous and iontophoretic administration of 0.005 and 0.239 M $^{22}Na^{+1}$. For statistical analysis and ratios, see text*

Series no.	Conc. M	Mode of administration	Minutes	mA	Total number of experiments	J_0-J_1 $k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance	nM Na cm^{-2} hr^{-1}
27	0.005	Epicutan.	—	–	10	8.9±0.1	—	—	9
28	0.005	Iontoph.	5	2	5	57.6±8.6	6.5	$P<0.001$	56
29	0.005	Iontoph.	15	2	5	54.1±9.2	6.1	$P<0.001$	52
30	0.005	Iontoph.	5	4	5	55.3±8.0	6.2	$P<0.001$	54
31	0.005	Iontoph.	15	4	5	57.9±4.1	6.5	$P<0.001$	56
32	0.005	Iontoph.	5	6	5	67.9±7.1	7.6	$P<0.001$	66
33	0.005	Iontoph.	15	6	5	72.7±10.1	8.2	$P<0.001$	70
34	0.005	Iontoph.[a]	15	6	5	13.4±4.6	1.5	$0.05<P<0.2$	13
35	0.239	Epicutan.	—	–	12	8.7±0.1	—	—	402
36	0.239	Iontoph.	5	2	5	34.2±6.6	3.9	$P<0.001$	1582
37	0.239	Iontoph.	15	2	5	52.2±7.1	6.0	$P<0.001$	2415
38	0.239	Iontoph.	5	4	5	44.9±9.8	5.2	$P<0.001$	2077
39	0.239	Iontoph.	15	4	10	45.6±7.1	5.2	$P<0.001$	2109
40	0.239	Iontoph.	5	6	10	45.2±5.7	5.2	$P<0.001$	2091
41	0.239	Iontoph.	15	6	10	45.3±8.9	5.2	$P<0.001$	2095

[a] Negative charge of the driving electrode.

2) and the statistical analysis (Tables I–III) showed that it was during the first hour after iontophoresis that the main disappearance from the skin occurred. Subsequently, it took place essentially from the epicutaneous depot, since the difference in the size of the disappearance constants was, as a rule, small during the period t_1–t_5, when comparing iontophoretic with epicutaneous administration. Nor were there any differences for recording periods up to 25 hours. Zankel et al. (16) also found that the main disappearance occurred during the first hour after iontophoresis.

A disadvantage of the method employed is, that at present it is not possible to record the radioactivity while the iontophoresis is in progress. Thus, only a minimal increase was observed when comparing iontophoresis for 30 and for 15 min, probably because recording was started after 30 min when part of the transport via the circulation had already occurred.

Thus, by means of iontophoresis the absorbed amount of an ion can be increased up to about 40 times compared with epicutaneous application. The largest relative increases were obtained with the lowest chromate and sodium concentrations respectively. Calculated absolutely, the amount increased with increased concentration of the re-

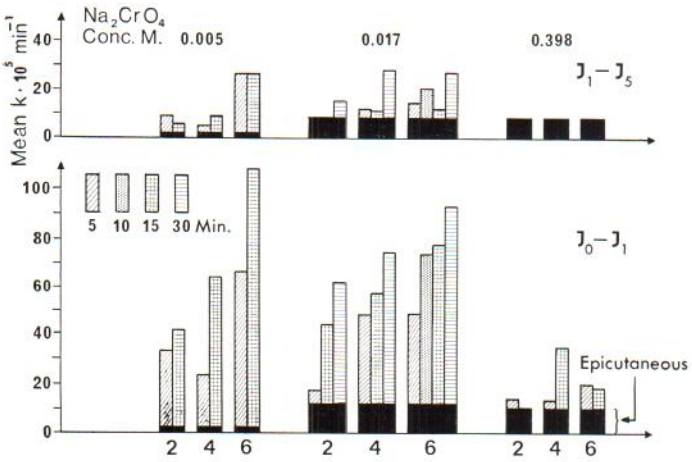

Fig. 3. Mean disappearance constants (*k*) after iontophoretic administration of chromate ions (3 concentrations) at varying current strengths (2, 4, and 6 mA) and duration of iontophoresis. J_0–J_1 (*bottom*) represents the *k*-values for the first hour after iontophoresis; J_1–J_5 (*top*) represents those for the following 4 hours. The shaded areas represent the *k*-values after epicutaneous administration.

J_1–J_5		
$k \cdot 10^5$ min^{-1} ± S.E.	Ratio	Analysis of variance
7.3 ± 0.8	—	—
17.6 ± 4.3	2.4	$0.001 < P < 0.01$
12.2 ± 3.6	1.7	$0.05 < P < 0.2$
19.2 ± 6.0	2.6	$P < 0.001$
21.6 ± 6.6	3.0	$0.001 < P < 0.01$
14.3 ± 3.1	2.0	$P < 0.001$
19.3 ± 6.3	2.6	$0.01 < P < 0.05$
16.2 ± 3.1	2.2	$0.001 < P < 0.01$
8.0 ± 0.9	—	—
18.9 ± 6.3	2.4	$0.01 < P < 0.05$
34.2 ± 7.5	4.3	$P < 0.001$
20.4 ± 10.3	2.6	$0.05 < P < 0.2$
19.6 ± 4.0	2.5	$0.001 < P < 0.01$
11.4 ± 2.4	1.4	$0.05 < P < 0.2$
16.9 ± 2.8	2.1	$0.001 < P < 0.01$

spective ions. Consequently, there is experimental support for the hypothesis that by means of iontophoresis sufficient amounts of a test substance can be administered to elicit a reaction.

For absorption through stripped skin (10), [which is most closely comparable to "Abriss" tests (4, 5, 9)], for 0.239 M NaCl the mean disappearance constant was 41.8×10^{-5} min^{-1} for the first hour (J_0–J_1). The corresponding values for iontophoresis were higher (Table III), indicating that this method yielded a higher degree of absorption. Calculated for the first 5 hours (J_0–J_5) the mean value through stripped skin, however, was 42.7×10^{-5} min^{-1}, and the corresponding values for iontophoresis were lower. It would be desirable to be able to record absorption during the usual period of 48 hours that the patch strips are worn, but it is not possible experimentally to keep the animal's circulation, etc. constant for such a long time. In previous experiments with prolonged exposure (guinea pigs, in vivo, 20 hours, (11) and human skin respectively, in vitro, 48 hours (12)), it was observed that absorption gradually decreased with time, despite constant temperature.

It was shown (7) that after iontophoresis, the distribution of ^{32}P in the tissues was proportional to current density, duration of iontophoresis and concentration. Zankel (15) found that prolonging the time of iontophoresis was less effective in promoting Ra ^{131}I absorption into the circulation than was increasing the current. The differences observed in the present investigation are probably due to the lack of tissue irritation by the sodium ion and the resulting free diffusibility, whereas the chromate ion was irritative (13), especially in higher concentrations (Table II). With regard to the chromate ion it was observed that prolonging the iontophoresis from 5 to 15 and 30 min respectively had a definite increasing effect. Increasing the current strength from 2 to 4 and 6 mA respectively had, for the two lowest concentrations, in most cases the effect of augmenting skin clearance. For the sodium ion the conditions were entirely different. After iontophoresis for 5 min at 2 mA optimal disappearance had already occurred, and the gradual increase in the strength and duration of the current had only a minimal effect.

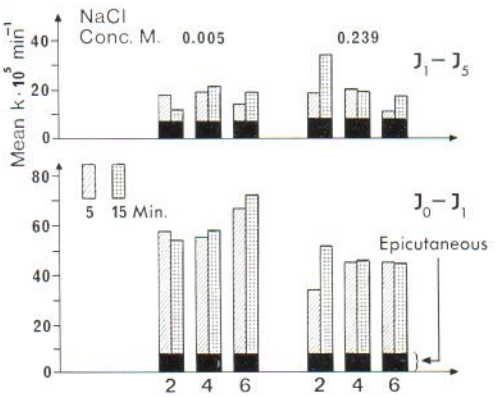

Fig. 4. Iontophoretic administration of sodium ions (2 concentrations). For key to signs, see Fig. 3.

REFERENCES

1. Darabos, L.: Beiträge zur Bichromat-Allergie. II. Die Modifizierung der Bichromat-Probe. Hautarzt *11*: 408, 1960.
2. Fregert, S. & Rorsman, H.: Allergic reactions to trivalent chromium compounds. Arch Derm (Chicago) *93*: 711, 1966.
3. Haxthausen, H.: Some experiments with electrophoretic patch tests. J Invest Derm *24*: 211, 1955.
4. Jung, E. G.: Nachweis der beginnenden Bichromat-Sensibilisierung von Zementekzematikern mittels des Abrisstestes. Berufsdermatosen *11*: 93, 1963.
5. Kligman, A. M.: The SLS provocative patch test in allergic contact sensitization. J Invest Derm *46*: 573, 1966.
6. Kvorning, S. A. & Svendsen, I. B.: A synthetic deter-

gent as a provocative agent in patch tests. J Invest Derm *26*: 421, 1956.
7. O'Malley, E. P. & Oester, Y. T.: Influence of some physical chemical factors on iontophoresis using radioisotopes. Arch Phys Med *36*: 310, 1955.
8. Skog, E. & Wahlberg, J. E.: Patch testing with potassium dichromate in different vehicles. Arch Derm (Chicago) *99*: 697, 1969.
9. Spier, H. W. & Natzel, R.: Chromatallergie und Zementekzem. Gewerbedermatologischer und analytischer Beitrag. Hautarzt *4*: 63, 1953.
10. Wahlberg, J. E.: Some attempts to influence the percutaneous absorption rate of sodium (^{22}Na) and mercuric (^{203}Hg) chlorides in the guinea pig. Acta Dermatovener (Stockholm) *45*: 335, 1965.
11. — "Disappearance measurements", a method for studying percutaneous absorption of isotope-labelled compounds emitting gamma-rays. Acta Dermatovener (Stockholm) *45:* 397, 1965.
12. — Percutaneous absorption of sodium chromate (^{51}Cr), cobaltous (^{58}Co), and mercuric (^{203}Hg) chlorides through excised human and guinea pig skin. Acta Dermatovener (Stockholm) *45*: 415, 1965.
13. Wahlberg, J. E. & Skog, E.: Percutaneous absorption of sodium chromate (^{51}Cr) in the guinea pig. Acta Dermatovener (Stockholm) *43:* 102, 1963.
14. — Percutaneous absorption of trivalent and hexavalent chromium. Arch Derm (Chicago) *92*: 315, 1965.
15. Zankel, H. T.: Effect of physical modalities upon Ra ^{131}I iontophoresis. Arch Phys Med *44:* 93, 1963.
16. Zankel, H. T., Cress, R. H. & Kamin, H.: Iontophoresis studies with a radioactive tracer. Arch Phys Med *40:* 193, 1959.

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