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## Irritation and Staining by Dithranol (Anthralin) and Butantrone (10-Butyryl Dithranol): Further Short Contact and Tape Stripping Experiments

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Göransson A. Irritation and staining by dithranol (anthralin) and butantrone (10-butyryl dithranol): further short contact and tape stripping experiments. Acta Derm Venereol (Stockh) 1987; 67: 72–76.

Ten psoriatics were tested with three concentrations of butantrone (0.66, 2.0 and 3.9 %) on the healthy skin of the back and the irritant and staining reactions were compared with those produced by 0.1 and 0.5 % dithranol, both in white petrolatum. Of the three test areas one was stripped before exposure to simulate the penetration of a psoriasis lesion, one after exposure to simulate posttreatment washing and one was unstripped. The contact times were 20 and 60 min. The degrees of erythema and staining, and the increase in skin blood flow were measured 1, 2, 3 and 7 days after application. Both dithranol concentrations produced a markedly stronger increase of blood flow and erythema than any of the butantrone concentrations and a clear dose response when the concentration was raised from 0.1 to 0.5 %. Such a dose response was not clearly seen with butantrone. Staining with both dithranol and butantrone was minimal. Apparently, higher concentrations of butantrone than dithranol can be used in short contact therapy if cumulation of the drug can be excluded by a short contact time and careful removal of the surplus drug. *Key words: Psoriasis; Short contact therapy.* (Received May 30, 1986.)

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Dithranol (anthralin) has maintained a key place in the topical treatment of psoriasis (1). In conventional formulations like Lassar's paste, dithranol is effective but messy and unacceptable for continuous use by out-patients. Recently the use of high concentrations of dithranol for less than one hour daily, the so-called short contact or minutes therapy, has made possible the use of dithranol by out-patients also (2, 3).

Previous studies have shown that 10-butyryl dithranol (butantrone) retains antipsoriatic activity (4) but causes less irritation and staining of healthy-looking or stripped skin than

do equimolar concentrations of dithranol (5). Before clinical trials were planned this study was conducted to indicate, in terms of irritation and staining, the concentrations of butantrone and the exposure times suitable for short contact treatment of psoriasis.

## MATERIAL AND METHODS

Ten unselected in-patients with plaque psoriasis were tested on the unaffected skin of the back with 0.1 and 0.5 % dithranol in white petrolatum and 0.66 % (equimolar with 0.5 % dithranol), 2 % and 3.9 % butantrone in white petrolatum. Finn chambers® 8 mm in diameter were used for testing (6). The contact times were 20 and 60 min. Tape stripping was performed with Scotch Tape 810, and stripping was repeated 15 times to bring about the removal of at least one-third (cf. 5) of the horny layer. The test were divided into 3 groups: one unstripped, one stripped before exposure, and one stripped after exposure. The site stripped before exposure simulates the enhanced penetration of a psoriasis lesion and the site stripped after exposure simulates thorough washing.

Laser Doppler blood flow measurements (7) at the test sites and at corresponding unexposed sites and visual estimation of erythema and staining were performed 1, 2, 3 and 7 days after the start of the tests. One patient had to leave the hospital before the 7th-day reading. For the visual estimation of erythema, the following scale was used (cf. 7): 0=no erythema, 0.5=faint ill-defined erythema, 1=faint but more defined erythema, 1.5=precisely measurable slight erythema, 2=measurable moderate erythema, 2.5=marked erythema, 3=marked intense erythema.

The statistical methods used were Friedman's two-way analisis of variance and Willcoxon matched-pairs signed ranks test. The blood flow was compared with that in corresponding unexposed areas and was expressed as a relative change ($\Delta$ %). The $p \leq 0.05$ was considered statistically significant.

## RESULTS

### *Skin blood flow*

When the contact time of 0.1 and 0.5 % dithranol was 20 min there was an increase in blood flow at the before stripped or unstripped sites, but at the sites stripped after application no increase was observed. When butantrone was tested in the same way up to a concentration of 3.9 % only minor alterations could be seen (Fig. 1).

When the contact time of 0.1 and 0.5 % dithranol was prolonged from 20 to 60 min the blood flow was considerably increased. For both concentrations the increase was about 200 % (mean 203 %, range 71 to 358 %, $p<0.05$ on the second day). A similar but statistically not significant increase was observed when butantrone was tested. For the three concentrations of butantrone the increase was about 40 % (mean 36 %, range −26 to 80 %).

The increase in blood flow caused by dithranol at a concentration of 0.5 % was significantly higher than that caused by butantrone at the different concentrations used ($p<0.05$ %; Fig. 1). For unstripped skin peak values were seen on the third day and for the sites stripped before application they were seen on the second day.

When the dose of dithranol was raised from 0.1 to 0.5 % there was a clear increase registered in blood flow. With the butantrone concentrations used (0.66, 2.0, 3.9 %) no such dose related increase could be observed.

### *Erythema*

The erythema reactions after contact for both 20 and 60 min showed a similar pattern to that of the blood flow measurements. With 20 min contact time the 0.5 % dithranol concentration caused significantly more intense erythema than any of the butantrone concentrations ($p<0.01$ on the second and third day after application). With 60 min contact time both dithranol concentrations (0.1 and 0.5 %) were significantly more irritative than 0.66 % and 3.9 % butantrone (at least $p<0.05$; Fig. 2).

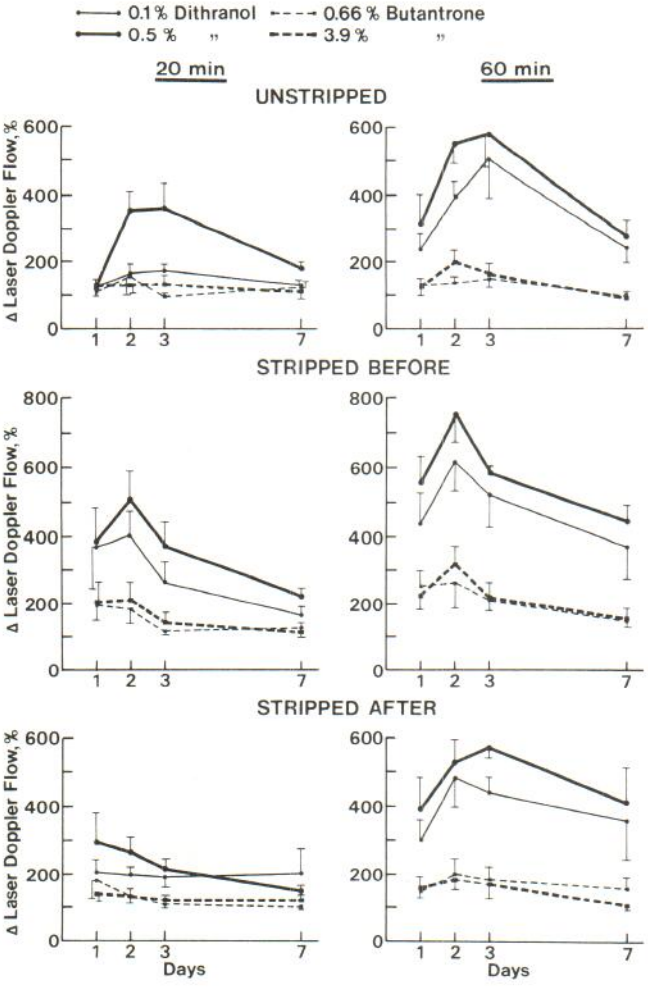


*Fig. 1.* Relative increases in superficial blood flow during 7 days after contact for 20 and 60 min with 0.1 and 0.5% dithranol (DP) and 0.66 and 3.9% butantrone (BP). The values are given as means of Δ%±SEM. Because the results with 2% butantrone were similar to those with 3.9% butantrone, this set of values was omitted.

*Staining*

When the contact time was 20 min, practically no staining was to be seen with either dithranol or butantrone. When the contact time was 60 min dithranol gave a faint staining.

## DISCUSSION

In a previous study we have shown that butantrone causes less irritation and staining of both normal and stripped skin than dithranol at equimolar concentrations (5). The present study shows that butantrone can be applied in concentrations six times as high as dithranol without any appreciable increase in irritation or staining.

The inflammatory response to dithranol was related to the dose applied, and the same was noted by Lawrence et al. (8). This was not seen with butantrone in the concentrations used. In fact, when tested with single 24 h exposures on unstripped skin, butantrone required a 20-fold concentration to be equi-irritant with dithranol (7).

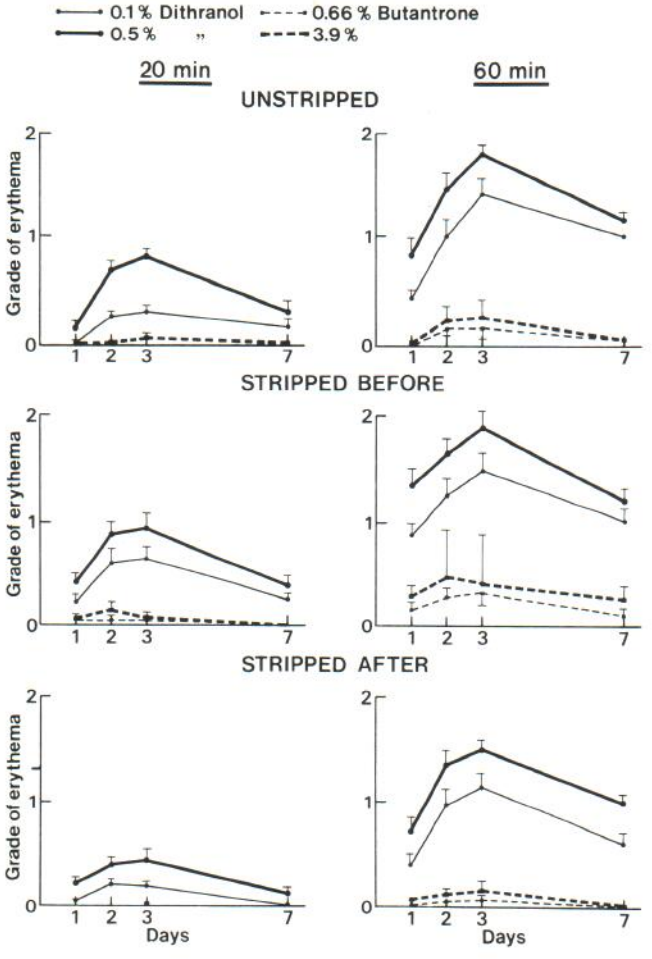


*Fig. 2.* Course of erythema during 7 days after contact for 20 and 60 min with 0.1 and 0.5 % dithranol (DP) and 0.66 and 3.9 % butantrone (BP).

With both dithranol and butantrone staining was minimal when the contact time was 60 min or less. In practice, when short contact therapy was used daily, staining with dithranol usually appeared after two weeks of treatment and was relatively weak. The staining with butantrone appeared about one or two weeks later and was somewhat weaker (unpublished results).

Stripping after application reduced the irritation caused by dithranol, when the contact time was 20 min. Almost no reduction was seen after contact for 60 min. This suggests that by 60 min irritating amounts of dithranol have already penetrated the skin. With butantrone the effect of stripping was not so clear. To reduce the side effects in short contact therapy it would be advisable to use contact times shorter than one hour.

This study shows that in the test conditions used, butantrone causes less irritation and staining than dithranol, irrespective of concentration. Therefore it should be possible to use comparatively high concentrations of butantrone in short contact therapy of psoriasis. However, in daily use butantrone may cumulate and cause delayed irritation. Therefore, the surplus of butantrone must be thoroughly removed, presumably within 30 min of application.

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## Amiodarone Photoreactions

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Roupe G, Larkö O, Olsson SB. Amiodarone photoreactions. Acta Derm Venereol (Stockh) 1987; 67: 76–79.

Four patients with photoreactions after Amiodarone therapy are described. The action spectrum for photosensitivity was found in the UVA region. Pigmentation seems to be due to wavelengths below 360 nm. (Received May 30, 1986.)

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Amiodarone is a potent cardiac antiarrythmic agent. Photosensitivity is a common skin complication to Amiodarone therapy but so is also a facial slate-grey pigmentation. These side effects were documented in 57% and 1.4% respectively in a recent review (1). The drug has been shown to possess phototoxic properties in the mouse (2). This is a report of four patients phototested during treatment with Amiodarone.

### MATERIAL AND METHODS

*Patients*

*Patient 1 (J.-B. T.)*

This patient is a man who was born in 1938. Due to attacks of atrial fibrillation which remained unaffected by conventional antiarrythmic drugs he was in 1983 given Amiodarone in a dose of 200 mg three times daily for one week, thereafter 200 mg daily. After three months, the dose was increased to 300 mg daily with good antiarrythmic effect.

The patient belongs to skin type II. Four months after starting Amiodarone therapy he experienced side effects in the form of burning and itching sensations in his skin already one hour after sun exposure. In addition, sunexposed skin regions became swollen and red. After the summer of 1984, after having taken Amiodarone for one year, he noticed a slight grey bluish discoloration in the skin of