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NECROTIC SKIN REACTIONS CAUSED BY 1 % GENTIAN VIOLET AND BRILLIANT GREEN

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Abstract. Three typical patients are described in whom a necrotic, painful and slowly healing skin reaction developed after topical treatment with 1% gentian violet in aqueous solution. The reaction could be reproduced in stripped but not in non-stripped skin in normal humans and in guinea pigs with both gentian violet and brilliant green. These adverse reactions to triphenylmethane dyes may be erroneously diagnosed as an exacerbation of the underlying skin disease for which the treatment was originally given. Treatment with 1% aqueous solutions of these dyes is not as harmless as has been supposed.

In the Department of Dermatology, Sahlgrenska sjukhuset, Gothenburg, Sweden, we have observed several cases with a characteristic necrosis of the skin following the application of 1% gentian violet in aqueous solution for mycotic infections caused by candida albicans and also dermatophytes. The submammary folds, the genitalia (in men and women), the gluteal fold and the toe-webs have been involved. Both children and adults of all ages have been affected. We report three typical patients with this reaction and also some experimental observations.

CASE REPORTS

Case 1. A 51-year-old man developed a fungus infection of the groins, axillae and feet caused by epidermophyton floccosum. He was treated with systemic griseofulvin and as a local application for the scrotum he was given a solution containing 0.5% gentian violet and 0.5% hydrocortisone. The lesions healed in all sites except on the scrotum. Here, after 10 days, intensely painful superficial ulcerations developed involving the whole area. No lesions were seen on the adjacent areas on the legs. The ulceration of the scrotum was sufficiently severe to necessitate admitting the patient to hospital for 19 days. The skin of scrotum was intensely reddened and swollen with a large number of small, partly confluent, superficial ulcerations with yellow necrotic bases. In some places black eschars were seen. After discontinuing the gentian violet a remarkedly rapid re-epithelialization occurred (Fig. 1). No growth of bacteria was demonstrated from the necrotic areas.

Case 2. A baby girl aged 7 months with a napkin dermatitis was treated with an aqueous solution of 1% gentian violet. After a few days the lesions were exaggerated and both labiae developed superficial ulcerations with yellow necrotic bases and surrounding erythema (Fig. 2). They were very tender. The dye solution was stopped, the skin was treated with a soothing application and the ulcerations healed rapidly.

Case 3. A 38-year-old woman was treated with 1% aqueous gentian violet for vaginitis and vulvitis caused by candida albicans. After a few days the patient returned because of increasing pain in the vulva. A large number of intensely painful, superficial and confluent ulcerations with yellow bases were seen in the red and swollen mucosa (Fig. 3). The gentian violet was stopped. After using wet dressing of boric acid the ulcers closed slowly and there was complete healing of the mucosa.

EXPERIMENTAL STUDIES

A. *Humans*

Patch tests on normal skin with 1% gentian violet (CI 42 555 batch uv.) and with 1% brilliant green (CI 42 040 batch uv.) in water. The back was chosen as the patch test site, the patches used were the Al-test (Fregert), they were held in place with Leucoplast (Beiersdorff) and left on for 48 hours. They were read at 48 and 72 hours.

Application to stripped skin

Two male volunteers were used and areas of skin approximately 1.5 × 8 cm were stripped on the flexor surfaces of their forearms. The stripping was done by the repeated application and removal of Scotch tape® until a glistening surface was obtained. No bleeding occurred. One-half of the stripped area was immediately painted with 1% gentian violet in water or 1% brilliant green, no applications were made to the other half, which served as a control. The dye was applied once daily for 2 days. The areas stripped and painted with gentian violet or brilliant

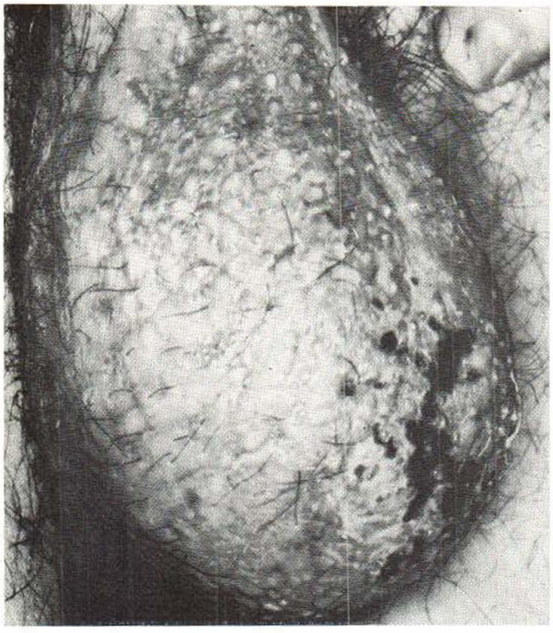

Fig. 1. Toxic reaction to 1% gentian violet in aqueous solution.

green were biopsied after 1 day (one application of the dye) and after 5 days (two applications).

B. *Guinea Pigs*

Applications on stripped areas

Albino guinea pigs were shaved with an electric razor. The skin on the side of the body was stripped with

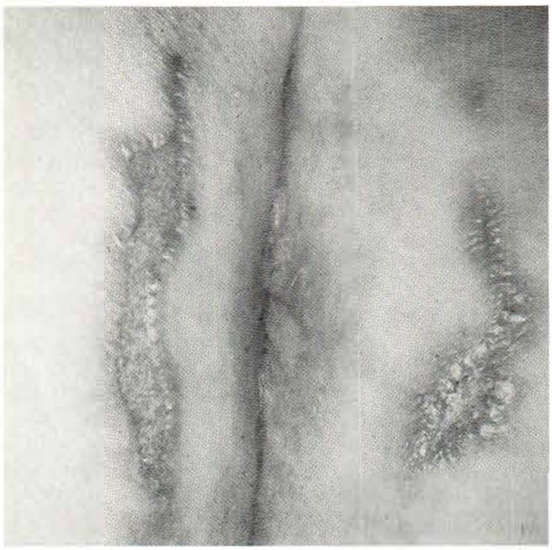

Fig. 2. Toxic reaction to 1% gentian violet in aqueous solution.

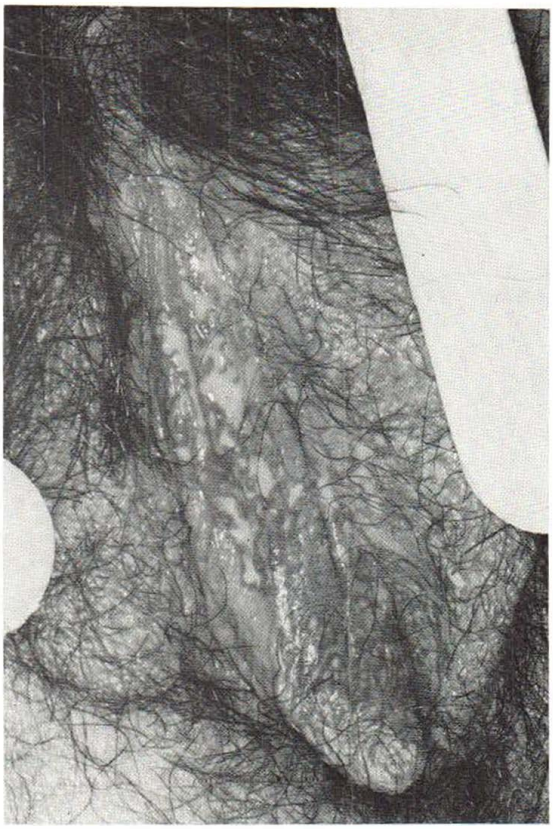

Fig. 3. Toxic reaction to 1% gentian violet in aqueous solution.

Scotch tape® until a glistening surface was obtained. Only a few strippings were necessary. The skin was stripped vertically and the dyes in saturated solutions (gentian violet 2% and brilliant green 2% in water) were painted horizontally across the stripped areas (Fig. 4). In this way one area in the centre was stripped *and* painted with the dye, two vertical control areas were stripped without dyeing and two horizontal areas were dyed without stripping. The application of the dyes was repeated daily for 3 consecutive days. Skin biopsies were taken 72 hours after beginning of the experiment.

RESULTS

Clinical picture. On the basis of the clinical features the following observations may be made:

After a few days to some weeks of repeated applications of 1% gentian violet in aqueous solution on usually mycotic skin lesions, the patient may complain of increasingly painful local discomfort. Some parts of the bluish painted area become a more intensely dark blue colour and appear somewhat swollen. After a few more days

these dark surfaces begin to exude slightly. Later, a slough occurs leaving superficial ulcers which are small and irregular and have characteristic yellow, and in a few cases black, surfaces. They are surrounded by a narrow erythematous border. The individual ulcers are a few millimetres in diameter but may merge to form large denuded areas. The clinical picture is very characteristic, rendering the diagnosis easy. The reactions may be severe, necessitating admission of the patients to hospital. After cessation of gentian violet treatment, re-epithelialization is remarkably rapid.

Healing occurs without scars, though pigmentary disturbances may be seen.

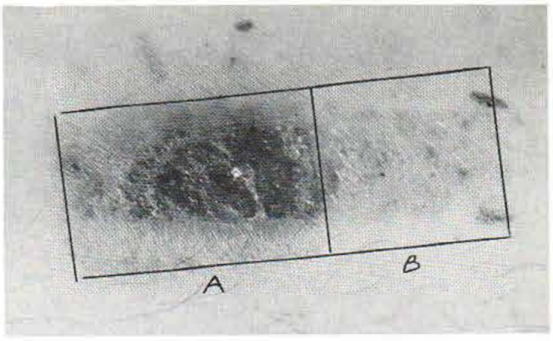

Fig. 5. Toxic reaction in human 5 days after stripping and application of 1% gentian violet in aqueous solution (area A). In area B only stripping without painting with the dye.

Experimental Studies

A. *Humans*

Patch tests with 1% gentian violet and with 1% brilliant green gave no reactions in 2 patients who had had necrotic reactions to gentian violet.

Application to stripped skin

On the second day the painted area was slightly tender in both subjects. The pain increased during the succeeding days. Five days after the stripping, superficial ulcerations developed in almost the whole painted area (Fig. 5). On the preceeding days, prior to ulceration, these areas became a darker blue colour and so contrasted with the rest of the field which did not ulcerate. In the control areas rapid epithelialization occurred without any untoward reactions. Healing of the necrotic lesions occurred after 2 or 3 weeks leaving some scars together with hyperpigmentation. The test procedure on stripped area was repeated with a 1% aqueous solution of brilliant green. Exactly the same necrotic reactions were obtained as with the gentian violet.

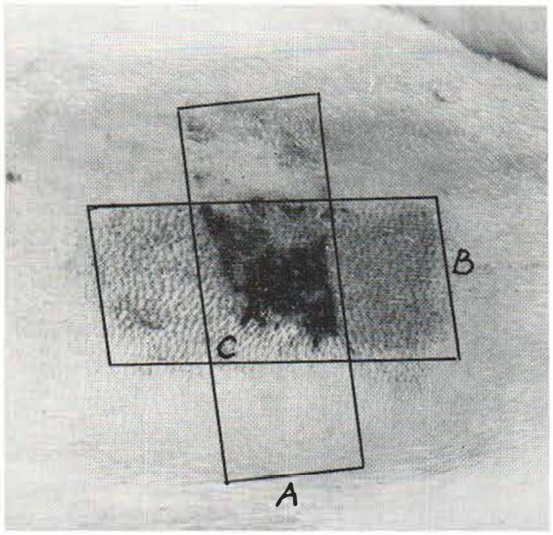

Fig. 4. Skin reaction in guinea pig to 2% gentian violet in aqueous solution. Area A stripped, area B painted, area C stripped *and* painted.

Histopathology

After 1 day a darker blue colour was seen in some parts of the gentian violet treated area (a dark green colour in the brilliant green area) but there was no macroscopical necrosis. In biopsies taken from these areas the deeper layers of the epidermis were mainly affected being partly necrolytic and spongiotic. Hydropic degeneration of the basal layer formed subepidermal vesicles. In the upper part of the dermis, especially around the vessels, there was infiltrate of polymorphonuclear leucocytes showing karyorrhexis (Fig. 6).

After 5 days necrosis was observed macroscopically. The microscopic picture too was more pronounced than after 1 day with total necrolysis of the epidermis leaving large erosions. The slight or severe infiltration in the corium consisted of neutrophilic leucocytes with karyorrhexis and of lymphocytes (Fig. 7).

B. *Guinea pigs*

Forty-eight hours after the stripping a necrotic reaction was observed in the central field in each of the 5 animals painted with gentian violet and

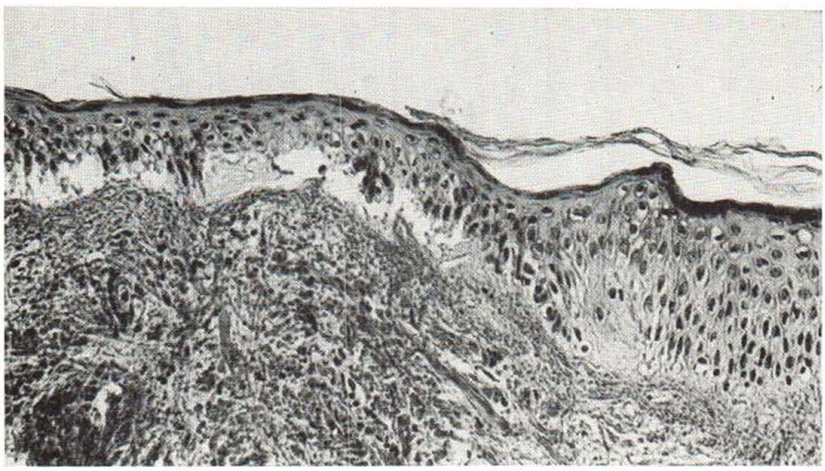

Fig. 6. Microscopic picture in human 1 day after application of 1% gentian violet to a stripped area.

also each of the 5 painted with brilliant green. The control fields showed no reaction (Fig. 4).

Histopathology

After 72 hours most of the epidermis had disappeared. In some places severe hydropic degeneration of the basal layers caused the formation of vesicles. Small infiltrates in the dermis consisted of leucocytes and lymphocytes (Fig. 8). The control areas of stripping without dyeing and of dyeing without stripping had only a very slight inflammatory reaction of lymphocytes in the corium.

COMMENTS

Triphenylmethane dyes (gentian violet, brilliant green, malachite green, fuchsin) are widely used by otologists, gynecologists, dermatologists, stomatologists and surgeons as topical antibacterial and antifungal agents. The usual concentration is 1% in aqueous solution. These substances are recommended in standard textbooks of medicine as being innocuous.

There are in the literature rare case reports of contact sensitization to triphenylmethane dyes (2, 4, 5). Tissue necrosis has also been observed. Hosford & Smith 1952 (7) described corneal damage from gentian violet in an indelible pencil after an accident to the eye. In 1957 and 1966 Slotkowski (11, 12) published observations on 2 children with oral thrush who were treated with 1% aqueous solution of gentian violet. Both children developed erosive lesions of the mucous membranes. He was able to reproduce the lesions with gentian

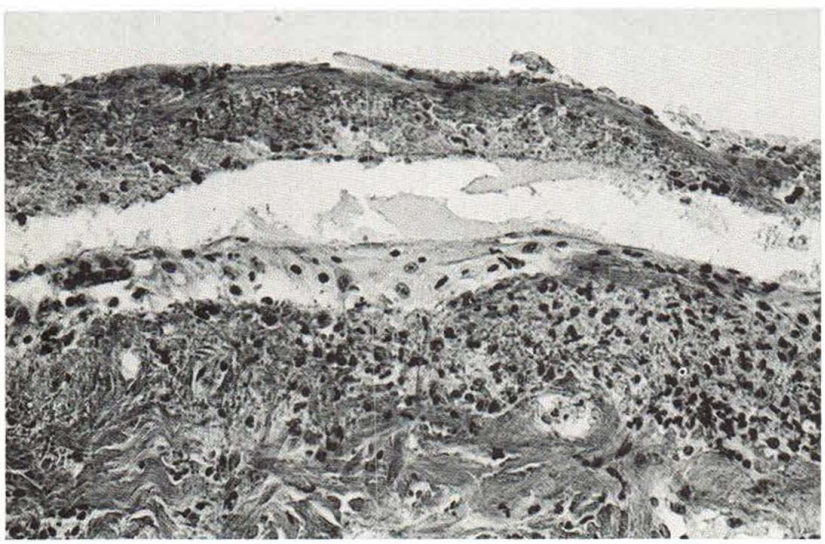

Fig. 7. Microscopic picture in human 5 days after application of 1% gentian violet to a stripped area.

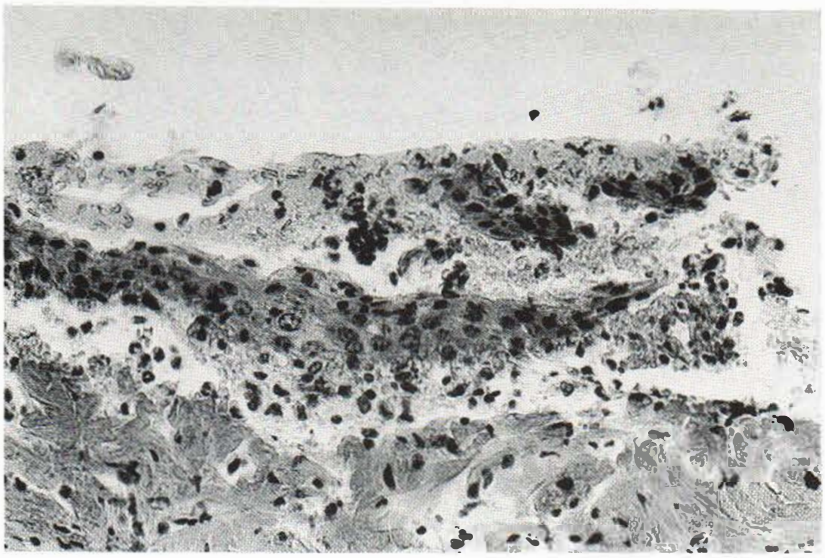

Fig. 8. Microscopic picture of guinea pig 3 days after application of 2% gentian violet to a stripped area.

violet by applying it to the normal mucosa of the mouths of rabbits. In 1968 John (9) reported 2 children treated with gentian violet for oral thrush, who also developed the same type of ulcerative lesions. Jennison & Llywelyn-Jones in 1957 treated 36 patients with monilial vaginitis with 1% aqueous solution of gentian violet. Of this series 6 developed a severe local reaction which necessitated stopping the treatment (8). In a new method described by Clabaugh (3) to remove tattoo-marks, gentian violet is used in 2% concentration after dermabrasion. It may give rise to a very intense local necrotic inflammatory reaction (6). When used as a vermifuge, gentian violet has also been described as a direct irritant of the gastro-intestinal mucosa (1, 10).

These reactions may be classified as primary irritant on the basis of the early onset of the experimental necrotic reaction to gentian violet and brilliant green without any previous exposure to the dyes, the negative patch test, the macroscopic appearance and the histology together with the fact that the reaction could regularly be provoked in 2 out of 2 humans, and in 10 of 10 guinea pigs. The experimental results in human subjects and in guinea pigs are in agreement with our clinical findings of necrotic reactions in patients treated with gentian violet. The observations are also supported by the few reports in the literature. Our clinical and experimental experience stresses the importance of using 1% aqueous solutions of gentian violet and brilliant green with caution. This treatment is neither as safe nor as harmless as it is usually considered to be. The typical necrotic skin reactions caused by triphenylmethane dyes may be erroneously diagnosed as an exacerbation of the underlying skin disease, for which the treatment was originally given.

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