When the blood volume was first reduced by a large venesection, saline or serum injected in similar amounts and at similar rates caused little or no rise of venous pressure.

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SULPHONAMIDE SUNLIGHT ERUPTIONS

A CLINICAL STUDY OF 27 CASES

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The constant sunshine of the Middle East and the presence of considerable numbers of V.D. patients undergoing ambulant chemotherapy in an open-air tented hospital have recently given us unusual opportunities of observing cases of the light-sensitive type of sulphonamide dermatitis.

This form of dermatitis has been classified into two varieties (Tedder, 1939): generalized eruptions showing no predilection for the exposed parts, and light-sensitive eruptions. It is with the latter that this report is concerned.

Cases of sulphonamide photosensitivity were first recorded in 1937 (Newman and Sharlit, 1937; Menville and Archinard, 1937), rashes being described which appeared after from 3 to 5 days of drug therapy and which disappeared after 5 or 6 days of protection from light. Severe dermatitis has also occurred from artificial ultra-violet irradiation during sulphapyridine administration (Hallam, 1939). On the analogy of the sunlight eruptions in haematoporphyria, investigation has shown that sulphonamides cause an excessive urinary excretion of porphyrins, of which one, coproporphyrin I, is a recognized photosensitizer (Rimington and Hemmings, 1938). This occurs more often with sulphanilamide than with sulphapyridine (Wien, 1938). The porphyrinuria varies considerably with the individual, and by exposing unselected patients on sulphanilamide Eidinow (1939) has shown that by no means everyone becomes light-sensitive.

Case Reports

During the 12 months Oct., 1940, to Sept., 1941, 486 cases received sulphanilamide, of which 21 developed eruptions (4.3%); 309 cases received sulphapyridine, yielding 6 eruptions (1.9%). Of the 27 cases 8 occurred during July and 6 during August. As measured by the photo-electric cell, the intensity of visible light in this part of the Middle East in July is about four times that in January. We have divided our cases into two groups:

1. Eruptions Limited to Parts Exposed to Sun during Chemotherapy

There were 17 cases of this kind, 16 with sulphanilamide and 1 with sulphapyridine. In 5 cases the rash appeared on the eighth day of chemotherapy, in 5 on the ninth, and in 7 on the tenth. The eruption consisted of maculo-papules in a morbilliform or roseoliform configuration. It was confluent on the most exposed parts, being distinguished from sunburn only by the discrete lesions at the margins. The demarcation

was very sharp at places such as the singlet area or, where no shirt had been worn, the waist. The axillae were usually spared. The bronzed parts—face, neck, forearms, hands—suffered less than the upper trunk and upper arms, which had been exposed less in the past. Two patients admitted to unusually heavy sun exposure the day before the rash began. Only 5 of the 17 had always sunburned easily.

In addition to the above lesions there was in one case vesiculation and pustulation of the face, in 2 oedema of the hands, and in another oedema of the eyelids. Itching varied from severe to none at all. In one case—an eruption limited to the hands—an experimental exposure of the forearms to the sun was made for 3 hours on the third day of the rash. After an hour a maculo-papular eruption appeared in the exposed area, maximal on the non-bronzed flexor surfaces. In another case, in addition to a roseoliform eruption, the dorsum of the hands showed typical target patches of erythema iris at the sites of some old scars, and the face developed oedema and pustules, going on to extensive desquamation.

Constitutional disturbance was common, fever up to 102° and malaise occurring in half the cases and three rigors in one case. The eruptions faded rapidly—in 2 to 4 days in all cases except one, which lasted a week. Three patients continued chemotherapy for from 1 to 2 days after the rash appeared, with no ill effects, though they kept out of the sun. In one case the rash began 2 days after the drug had been stopped, and in the remainder cessation of the drug either coincided with or occurred on account of the rash.

Of these 17 cases 3 received further chemotherapy at later dates, varying from 1 week to 4 months afterwards. In no instance did the eruption recur, although there was no change in the amount of sun exposure.

2. Eruptions Maximal on Exposed Parts, but also Affecting Others

Case 1 received sulphanilamide for non-specific urethritis, 4 g. daily for 8 days, during which the patient went in the sun with only the face and hands exposed. He had always sunburned easily. On the eighth day an irritable morbilliform rash appeared on the arms, face, and trunk above the waist, principally on the upper part of the back. There was mild cyanosis but no fever.

Case 2 received sulphanilamide for chancroid, 4 g. daily, until it was stopped on the eighth day because of a morbilliform and roseoliform rash, resembling the cases in group 1 except that patches appeared on both thighs over the trochanters. It was slightly itchy, and less pronounced on the bronzed parts. The patient had not previously been sensitive to sunlight. The rash lasted 4 days and was accompanied by a fever up to 103°.

Case 3 received sulphanilamide for chancroid, 4 g. daily for 10 days, during which he went in the sun wearing an open-necked shirt, elbow-length sleeves, long trousers, and rubber shoes. He has always sunburned easily. On the ninth day he developed a slightly itchy morbilliform rash, confluent on the necklace area, back, and outer upper arms. It was also present on the bronzed parts to a lesser degree. Except for a small patch over each great trochanter no rash appeared below the waist. There was no fever or malaise. The rash lasted 3 days.

Case 4 received sulphapyridine for gonorrhoea, 26 g. in 7 days. He had always sunburned easily. On the fifth day he took an open-air shower-bath in the sun, but was otherwise in bed until the seventh day, after which he went out in an open-necked shirt, long trousers, and shoes without socks. On the tenth day a morbilliform and roseoliform rash began. It was confluent on the face, forearms, and dorsum of the feet; discrete on the knees and trunk above the waist; and scanty on the trunk below the waist, upper arms, thighs, and legs. The bronzed parts suffered equally with the others. Itching was slight. The patient was afebrile, but complained of backache. The rash faded in 5 days.

Case 5 received sulphapyridine for gonorrhoea, 26 g. in 7 days. There had been no previous sensitivity to the sun. On the ninth day a dusky-red morbilliform eruption appeared, maximal on the shoulders and outer arms, less marked elsewhere, and especially scanty on the bathing-drawers area and in the axillae. The face was unaffected, but the other bronzed parts suffered equally with the remainder. There had been exposure during chemotherapy. The rash faded in 3 days. A low fever, malaise, vomiting, and headache occurred for 2 days with the rash.

Case 6 received sulphapyridine for gonorrhoea, 26 g. in 7 days. Sun exposure during this time was slight. He had never been sensitive to the sun. On the eighth day a morbilliform

rash appeared; this was not itchy. It was confluent on the back, chest, and outer upper arms. Below the waist it was scantier, with a cluster of lesions over each trochanter. There was little if any involvement of the bronzed parts—face and forearms—or of the legs. It faded in 3 days. On the seventh, eighth, and ninth days he had a fever up to 103°, with headaches, backache, anorexia, and conjunctivitis. This was considered to be phlebotomus fever, an epidemic of which was raging at the time.

Case 7 received sulphapyridine for non-specific urethritis, 4 g. daily for 8 days, most of which time he was in bed, but sometimes up in a shirt with elbow-length sleeves and long trousers. He denied being in the sun without a shirt in the past 2 months. He had never sunburned easily. On the eighth day an itchy maculo-papular rash appeared, lasting 3 days. It was generalized—being maximal on the back above the waist and the forearms, and minimal in the axillae. The temperature rose to 99.4°.

Case 8 received sulphapyridine for gonorrhoea, 26 g. in 7 days. Sun exposure and previous sun sensitivity were denied. On the eighth day the patient developed a roseoliform eruption, very itchy, and confluent on the outer upper arms and the trunk above the waist. It also involved the trunk below the waist, the arms and legs, most of the lateral pelvis, and thighs, ankles, and dorsum of the feet. Accompanying this was a suspected attack of phlebotomus fever.

Case 9 received sulphanilamide for non-specific urethritis, 3 g. daily for 10 days. There had been little exposure to the sun. Previously he had always sunburned easily. On the eighth day a rash appeared, consisting of maculo-papules running together into an erythema with wheals in it. The configuration was morbilliform and in places circinate. There was itching. The rash was maximal on the face, neck, upper trunk, forearms, and dorsum of the hands. It was present on the lower trunk, palms, legs, and thighs over the trochanters; but was absent from the bathing-drawers area and the left wrist, where a watch was worn. The exposed parts were not spared. The rash faded in 8 days, desquamation occurring on the face from the fifth day onwards. For 5 days he had malaise, fever up to 101°, and a distinct air-hunger.

Case 10 received sulphanilamide for a tonsillitis of 2 days' duration. The last exposure to sunlight had been 3 days previously, in shirt and shorts. He had never sunburned easily and was accustomed to going about in singlet and shorts. For 2 days 1 g. of the drug was given 4-hourly. On the evening of the first day a rash appeared on the upper trunk and upper arms, and then spread all over. Seen for the first time on the fourth day, the eruption consisted of erythema, vesiculation, and, in the worst places, profuse weeping and desquamation. Behind the ears a typical streptococcal intertrigo had supervened. Itching was severe. Its distribution was maximal on the face, the neck and shoulders where left uncovered by a singlet, the outer upper arms, the forearms, thighs, and legs. It was less marked on the chest and back, inner upper arms, and the feet. It was completely absent from the bathing-drawers area. At this stage the patient also showed an intense catarrhal stomatitis, glossitis, and pharyngitis, considerable prostration, and a fever of 102° for 10 days. The rash finally subsided in 2 weeks.

Discussion

Sulphanilamide was responsible for most of the milder cases (16 out of 17). The more severe cases were caused by sulphanylamine and sulphapyridine in equal numbers (5 of each). This greater incidence with sulphanilamide has been reported before, but in our cases it may have been due to the fact that only sulphanilamide patients were ambulant. In the largest series of cases in the literature at our disposal—that of Erskine (1939)—eruptions usually appeared at the eighth to tenth day, lasted 1 to 7 days, and were irritable in 20 out of 36 cases: although the majority of his cases were not described as light-sensitive, these features are in close agreement with our own observations.

Case 10 above merits separate discussion. It differs conspicuously from the remainder in its onset on the first day of chemotherapy, without sunlight exposure. Yet its distribution left no doubt as to its photosensitive character, affecting sites in order of their previous exposure to light. This early onset suggests an allergic origin. Epstein (1939) has described two types of photosensitivity from sulphonamides. Irradiating with ultra-violet light the site of an injection of sulphanilamide, he obtained an erythematous reaction. In the same subject 9 days later, irradiation of another injection site produced a more severe, prolonged, and exudative reaction, to which he

gave the name "photo-allergy." Our own case was also atypical in its exudative nature.

Summary and Conclusions

In their power to cause an eruption in parts previously exposed to the sun sulphonamides resemble pellagra.

In all, 27 cases of light-sensitive sulphonamide eruption are described, 21 due to sulphanilamide and 6 to sulphapyridine. These represent 3.4% of the total cases treated with these drugs, under conditions favouring considerable exposure to constant strong sunlight. About half the cases occurred during July and August.

Photosensitivity occurs from the eighth to the tenth day of administration. Two cases were found to be photosensitive 2 days after stopping chemotherapy. It therefore appears that patients given sulphonamides for more than 6 days are possible victims of sunlight eruptions.

In many cases the presence of melanin is a protection against these eruptions. Three observations support this: (1) about one-third of the cases are subjects who sunburn easily; (2) the bronzed parts of the body tend to be affected less than the others; (3) no eruptions have ever been seen in Maoris, who comprised about 100 of the 800 cases treated during the 12 months.

The following parts are affected in order of severity: (a) parts exposed to the sun during chemotherapy; (b) parts exposed in the past; (c) pressure points, such as the great trochanters; (d) least of all, parts always kept covered, such as the bathing-drawers area.

The commonest lesions are erythematous papules in a morbilliform or roseoliform pattern, becoming confluent. Itching varies (severe in 5, moderate in 7, slight in 9, absent in 6). Less common lesions are oedema, urticaria, vesication, pustulation, and desquamation.

Drug fever and other toxic effects are common accompaniments (12 cases).

Most rashes subside in 2 to 4 days.

Further chemotherapy.—Avoiding exposure to sunlight, 6 cases completed their courses of chemotherapy and 3 had further courses later without ill effects. In the milder cases, at all events, a rash is no indication for discontinuing the drug.

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CHRONIC LEG ULCER IN PURPURA HAEMORRHAGICA

REPORT OF TWO CASES

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The association of chronic ulcer of the leg with splenomegaly seems too frequent to be a mere coincidence, though the reason for it is not known. It has been described in sickle-cell anaemia, acholuric jaundice, Gaucher's disease, splenic anaemia, and Algerian splenomegaly. Last December I had two patients with essential thrombocytopenia, both of whom had had chronic ulcers of the leg. Although I had previously seen patches of purpura break down and ulcerate in patients who were acutely ill, the occurrence of chronic ulceration of the legs was new to me. The spleen was not palpable in either of these two patients, but in view of the important part which the spleen plays in purpura haemorrhagica, the cases seem worth reporting as a further contribution to this odd chapter of medicine and surgery.