clinical recurrence of the infection. If the dosage is diminished a sudden or progressive increase in the number of leucocytes may be noticed. To obtain this return of the cerebrospinal fluid to normal, which we consider indispensable, the minimum dosage varies from one patient to another; in certain cases the minimum effective dose is very close to or even exceeds the toxic dose. This is the eventuality to be dreaded most in practice, and though the situation may not be conclusive it is too soon to be certain on this point.

These are the broad outlines of the treatment which is at present being tried out at the Clinique Médicale des Enfants. The immediate results of the method are good. At the present moment 46 children who have been undergoing treatment for from 2 to 10 months are behaving like normal beings. The tuberculous meningitis ward is like a playroom, where the liveliness provides a constantly touching scene.

The problem arises, or will arise sooner or later, of when to stop the treatment, and this is the most difficult question of all. In every country doctors are asking themselves, When and on what indications can one stop the treatment? For our own part, forewarned by our early mistakes of the gravity of premature cessation of treatment followed by fatal relapses, we have not yet dared to make the decision. We are treating the children continuously, as diabetics are treated with insulin. Here, to be honest, we come up against an unfavourable factor in the occurrence of streptomycin resistance in the tubercle bacilli, but we have not arrived at any definite conclusions on this still very obscure problem; at the same time there is a favourable factor in the tendency shown by the lesions to heal by degrees as the duration of the tuberculosis increases. We have now decided not to cease treatment until we have the support of a large number of reassuring signs: absence of all clinical meningeal symptoms, an ascending weight curve, complete apyrexia, normal sedimentation rate, and a spinal lymphocyte count below 10 per c.mm. at repeated examinations. We would add to this, absence of tubercle bacilli in culture and, if possible, a normal quantity of cerebrospinal albumin. This last point is justified by an extremely important observation concerning the evolution of certain cases of meningitis treated by streptomycin.

Symptoms after Apparent Cure

A fourth group of patients develops in a very peculiar manner, and a knowledge of the facts involved constitutes an indirect advance in the streptomycin therapy of tuberculosis. Though apparently cured of meningitis in so far as they no longer present any clinical syndrome of the infection, are practically free from fever, and there is no longer any serious cellular reaction in their cerebrospinal fluid, these patients do not recover their liveliness like the others, and do not regain weight. Sometimes their neurological examination is not completely negative (there may be cutaneous hyperaesthesia, Babinski's sign, or slight tremor). In this case very careful attention must be given to the examination of the eye and of the cerebrospinal albumin. In these patients the possibility of a mechanical lesion, particularly the setting up of hydrocephalus secondary to meningeal adhesions, should be considered. This is where the neurosurgeon is called in to deal with the new situation; we are not yet certain whether this is the result of tuberculous meningitis or the consequence of a cerebral tubercle against which streptomycin does not seem so far to be as completely effective as against meningitis. The decision to operate was taken in 6 cases. In 5 of these the findings were widespread leptomeningitis or pachymeningitis of the cisterna pontis; in the sixth case there was a large

meningeal tubercle round the chiasma. In two of these cases the results were remarkable, one patient, who was comatose and blind at the time of operation, being one of those who are now giving us the greatest hope. In the new treatment of tuberculous meningitis the neurosurgeon is associated with the physician, as the chest surgeon is associated with the phthisiologist in certain cases of chronic pulmonary tuberculosis.

THE TROPICAL LICHEN PLANUS SYNDROME

BY

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An unusual disease with striking cutaneous manifestations has been observed in Australian, American, and New Zealand troops serving in widely scattered areas of the Pacific. Because of its geographical distribution, and from some clinical and histological resemblances, it has become commonly known as tropical lichen planus. The condition was briefly referred to by Myers (1944) in the course of a review of skin diseases affecting Australian troops in New Guinea. A detailed account of the findings in some American cases has been given by Bagby (1945).

The aetiology is not definitely established, but there is substantial evidence that the disease has some relation to the use of mepacrine as a malaria suppressive. The public revelation that an identical syndrome has been observed for some time in military forces using mepacrine suppression in Europe and the Middle East substantially confirms this belief (*Lancet*, 1945, 2, 711).

In his account Bagby mentions that the total number of cases in American troops would be impossible to estimate. A reasonable assessment of the incidence, as well as some conclusions from the geographical distribution, can be made from an analysis of the figures for a New Zealand force which operated in the Pacific Zone. This was a relatively small force of some 18,000 men, and it maintained independent medical services. Divisional troops comprised about 12,000 men, and all evacuations from this group came ultimately to a single base hospital, where all skin cases were seen by me. Most of the men in the force had served for periods of six months to two years in Fiji prior to November, 1942. Individual battalions had been stationed also in Tonga and Norfolk Islands. In November, 1942, the force proceeded to New Caledonia. Although some of these islands are quite tropical in climate, none of them is malarious, and therefore no mepacrine suppression was employed. No case of tropical lichen planus, or any condition resembling it, was seen at that time, though the usual tropical dermatoses were prevalent.

In August and September, 1943, the combatant part of the force moved to Guadalcanal, one of the Solomon Islands, some units spending a few weeks on the New Hebrides en route. In the following 12 months they were divided into two groups, which operated independently on various islands in the Solomon region. All these islands are highly malarious, and suppressive mepacrine was started when troops left New Caledonia, being maintained continuously until their return. The rate of administration was 0.1 g. of mepacrine daily for six days in each week.

The first case of tropical lichen planus in this force was evacuated to the base hospital in early December, 1943, and five further cases were received in the following five months. This suggests, at first consideration, a steady trickle of cases, but examination of the histories shows that

in all six cases the initial symptoms and lesions appeared between eight and twelve weeks from the date of giving suppressive mepacrine. All cases seen were in divisional troops from malarious areas. No cases occurred in troops who did not enter a malarious zone.

The evolution of the clinical picture followed closely that described by Bagby (1945). Three representative case histories are given.

Case 1

The patient, a white soldier aged 24, had served in Fiji, New Caledonia, Guadalcanal, and Vella Lavella. Eight weeks after he entered the malarious area the toe-nails of both feet became diffusely opaque and thickened, and a patchy dry thickening of the skin started on his soles. This was followed shortly by cracking and peeling of the thickened areas. In the next month his finger-nails also became opaque and thickened, and a patchy keratosis followed by peeling appeared on the palms. About the twelfth week from the date of commencing mepacrine the whole of his trunk and limbs became very itchy, and a symmetrically distributed pink macular rash appeared on his lower legs and upper chest. Individual macules were up to 1/2 in. (1.25 cm.) in diameter. In the next four weeks similar lesions appeared thickly on his buttocks and sparsely over his back and limbs. His abdomen and upper thighs were almost free, and no lesions occurred on his head or neck. Within a few days of their appearance these pink macules, at first smooth and shiny, became dull and covered with thin scales. He was evacuated to base hospital in New Caledonia sixteen weeks after he had started to use suppressive mepacrine. No further mepacrine was given after his return to New Caledonia. On admission most of his body showed erythematous-squamous lesions up to half an inch in diameter, confluent on parts of the upper chest, buttocks, and lower legs. His palms and soles had completely peeled, and showed resultant irregular red scaly patches. All the nails of his fingers and toes were thickened, opaque, and crumbling at the ends, and there was much subungual proliferation. There were no lesions on his face or scalp, and his lips and tongue appeared normal. He was well nourished, felt well and alert, had a good appetite, and slept well. His only complaints were of slight itching of the back and buttocks and some tenderness of the feet. The erythrocyte count, haemoglobin estimation, white-cell count, sedimentation rate, and blood Kahn test gave normal findings. In the following fortnight a very few new macules appeared. The older lesions became increasingly scaly.

During the sixth month from beginning mepacrine the trunk and limb lesions lost most of their scalliness and some healed, to leave apparently normal skin. Others became gradually replaced by brown evenly pigmented macules. During this month a diffuse follicular keratosis appeared on his upper chest and most of his back. This prompted a further search for a convincing focus of cutaneous fungal infection. None was found. By the seventh month the spiky follicular plugs had all gone, and the areas of his palms and soles, which had been red and scaly, were covered with thin red shiny skin. Many of the macules had lost some pigment, to leave a reticulated patchy area at the site of a previously evenly coloured lesion. In the ninth month fading of the pigmented macules continued. In addition areas up to half an inch in diameter of the skin on his trunk, limbs, face, and forehead rapidly lost all their pigment. The resultant vitiligo appeared at sites previously apparently normal, as well as sometimes being superimposed on old pigmented lesions. This patient had shown no previous lesions on his scalp, face, or forehead.

By the tenth month the earlier pigmentation was no longer detectable, his nails were normal, all scaly lesions had disappeared from his body, and the skin of the palms and soles looked normal. He was entirely symptom-free. However, there were many scattered areas of vitiligo, and patches of scalp, eyebrow, and beard hair were quite white. The remaining hair was a diffuse grey colour. He indulged a good deal in sun-bathing at this time. The vitiliginous areas were unchanged, but appeared more prominent because the skin between tanned normally. His condition was reported to be unchanged eight months later—i.e., 18 months after he began taking mepacrine. It is possible that the vitiligo is permanent.

Case 2

A quarter-caste Maori, aged 37, who had served in New Caledonia and Vella Lavella, found that ten weeks after he began the use of suppressive mepacrine the skin of his palms became dry, with patches of thickening and some cracking and peeling. Two weeks later his tongue and lips became tender, and a number of reddish scaly patches about half an inch in diameter appeared on his limbs. Patches of hyperkeratosis were noticed also on his feet. His nails, both of fingers and of toes, became opaque and brittle. He was much troubled by what he called prickly heat, though no lesions were present on his trunk. In the next few weeks further scaly patches appeared on his buttocks.

Five months after he had started mepacrine he was evacuated to New Caledonia and mepacrine was stopped. He felt quite well and was well nourished. Examination showed irregular patches of hyperkeratosis on his palms, with some red scaly areas where peeling had occurred. Almost the whole of both palms was involved to some degree. A similar patchy keratosis with peeling was present on his feet. The nails of fingers and toes were brittle and showed much subungual proliferation. Dark, petechia-like spots, visible through the nails, were present in profusion. There were slightly raised bluish-purple areas, mostly about half an inch in diameter, with a powdery surface, on the dorsal aspect of some toes, a few on his legs, a big crop on his buttocks, some on his arms, and one or two on his face. These lesions had originally been a dark-red colour. A striking specimen on one forearm was a vivid blue raised lesion an inch (2.5 cm.) in diameter. His lips showed a patchy bluish pigmentation, which was present also on the buccal mucosa. Irregular areas of the tongue and lips were superficially ulcerated. There was much tenacious white material on his lips, tongue, and palate. The erythrocyte count, white-cell count, haemoglobin estimation, and blood Kahn reaction were within normal limits. His blood sedimentation rate was 8 mm. in one hour.

Change in this patient was very slow. The mouth lesions gradually cleared, and by the eighth month there was appreciable healing of the red scaly areas on his palms, with the production of a thin shiny scar, associated with a good deal of brown pigmentation. There were also several small areas of vitiligo on his hands and arms. By the end of the ninth month he showed red atrophic scarring of large areas of his palms, with much brown pigmentation. There were also scattered, scaly, almost healed areas of a purplish colour on the soles of his feet. There were purple-pigmented areas on his hips, buttocks, toes, and limbs. There was some interspersed loss of pigmentation on his buttocks, but it did not amount to complete vitiligo. He still showed much bluish pigmentation of the lips and buccal mucosa.

In the next three months his condition showed no change. His general health remained good, and he felt thoroughly well at all times.

Case 3

A white soldier, aged 26, who had served in Fiji, Norfolk Island, New Caledonia, Guadalcanal, and Mono, had suffered occasional mild attacks of seborrhoeic dermatitis of his chest for ten years, but had been quite free for the previous two years. Twelve weeks after he started taking mepacrine he complained of sore lips, which he attributed to sunburn. His lips rapidly became dry and fissured, and within a week he became aware also of some roughening and cracking of the skin in his fingers and palms, large areas of which peeled. In the following week his feet became tender, and whitish "empty blisters" appeared on the soles. They contained no fluid, and were shed in a general desquamation of the soles of both feet. About this time the nails of his fingers and toes became brittle and there was a marked increase of the subungual tissue. The distal parts of the nails assumed a dusky hue, and dark spots like petechiae could be seen through the nail substance. In his fourteenth week on mepacrine he was admitted to a medical unit, and at that time a pink macular rash erupted on his wrists, arms, back, toes, and legs.

He was evacuated to base hospital in his fifteenth week, and then showed almost complete peeling of the palms and soles,

to leave a rough red surface. Many of the earlier pink macules had become scaly. There were some fresh pink lesions. His lips displayed patches of a thick whitish exudate and some fissuring. Similar exudate was present on the palate, and the tongue showed some small ulcers. He had no signs of seborrhoea. His general condition was good, he felt alert and active, and he slept and ate well. The erythrocyte count, haemoglobin estimation and white-cell count were normal. His blood sedimentation rate was 27 mm. in one hour. His urine was normal and he was apyrexial. A Kahn test was negative.

There was no notable change till three weeks later, when he became troubled with diarrhoea, having three or four loose bowel motions daily. This continued for several weeks and subsided gradually. Stool examinations were negative, and he remained apyrexial. When the diarrhoea began an extensive fresh crop of pink macules appeared, most thickly on the thighs and buttocks, the latter being almost covered. There was at this period a further shedding of skin from his feet, and over the heels this was so severe as to produce two raw exuding areas $1\frac{1}{2}$ in. (3.75 cm.) in diameter.

In the sixth month from the date of starting mepacrine there was a gradual change. The trunk lesions lost their scaliness and were replaced by pigmented macules. His lips and tongue healed. Subsequent change was slow. By the ninth month some chest lesions had vanished. The remainder were deeply pigmented. The healing areas on his palms were very atrophic. During this month he developed some typical seborrhoeic lesions on his sternal area. They responded rapidly to routine treatment.

By the tenth month there was irregular depigmentation of some of the back lesions, but marked pigmentation of the healed atrophic palmar areas. There was much horny accumulation on the lesions grouped about his wrists. The granulating areas on his heels had remained virtually unchanged for four months (Fig. 1). Elsewhere on his feet there was atrophic pigmented scarring. The Kahn reaction remained negative. The erythrocyte sedimentation rate was 30 mm. in one hour. The patient felt well and ate well.

FIG. 1.—Case 3; ulcers of feet unchanged for four months. Condition at time of the second injection of neoarsphenamine.

FIG. 2.—Condition of ulcers in Case 3 three weeks later.

Although there was no proof of a spirochaetal cause, the general resemblance of this and the other cases to pinta had been noted. As this patient remained bedridden from the state of his heels, it was felt that a course of organic arsenic injections was worth a trial. He showed no untoward effects from the first two injections of 0.3 and 0.45 g. of neoarsphenamine, and epithelization of the granulating areas on his heels had started before the third injection of 0.6 g. (Fig. 2). However, a few hours after this injection he suffered a severe reaction, was pyrexial for a week, and had generalized limb and joint pains, sore throat, enlarged lymph glands, albuminuria, and a leucocytosis. There was no cutaneous reaction. This acute disturbance subsided rapidly, and two weeks later he was symptom-free, apyrexial, and passed normal urine. The granu-

lating lesions on his heels were almost covered with epithelium by this time; and there was rapid improvement in all the early lesions of his feet and wrists. No more neoarsphenamine was administered.

He was later permitted to sun-bathe, in graduated doses, to determine his response to light. There was no recrudescence, and he tanned normally except for some areas of vitiligo on his buttocks.

Clinical Features of the Disease

Analysis of the histories revealed the following details: (i) It is a disease confined to persons who had used mepacrine as a malaria suppressive in a tropical climate. (ii) There was a singular absence of constitutional disturbance throughout except in one case. (iii) The initial signs appeared between eight and twelve weeks after mepacrine was started. (iv) Fresh lesions continued to appear so long as mepacrine was used, and ceased within a few weeks of its discontinuance. (v) In all cases some degree of palmar and plantar hyperkeratosis as a primary or early lesion was present. (vi) There was a fairly generalized pink macular eruption, the individual lesions of which became scaly and sometimes markedly infiltrated. (vii) Striking pigmentation, producing a wide range of colours. (viii) A variable degree of horny follicular plugging on back and shoulders. (ix) Involvement of the tongue, lips, and buccal mucosa in most cases, the lesions being suggestive of syphilitic mucous patches. (x) Early and destructive but not permanent nail changes. (xi) Fading of pigmented lesions, which was sometimes arrested, to leave a reticulated or variegated appearance. (xii) Ultimately the development of vitiligo in scattered areas. This deformity seemed likely to be permanent. (xiii) Marked atrophy of the skin in some healed lesions.

Discussion

These cases provided a rich field for diagnostic speculation. That they were a spectacular form of "id" eruption associated with a fungal infection was the first suggestion. Thorough search failed to confirm this belief, though the discovery of what at first appeared to be a veritable tangle of fine hyphae in the skin of the back raised high hopes. It was later realized that the suspected mycelium was elastic tissue obtained by cutting into the corium. That there was a dietary basis for the disorder seemed most unlikely in view of the general well-being and absence of the distinctive stigmata. Substantial dosage with vitamins A and D, thiamin, nicotinamide, and riboflavin produced no notable change.

The possibility of an infective cause peculiar to the Solomon Islands was considered. It was not then known that the condition was more widespread. Yaws is endemic in the native populations of the Pacific. Pinta, also clearly proved to be a spirochaetosis, which is a common disease of tropical Central America and the West Indies, produces a clinical picture in many ways very much like these cases (Stitt and Strong, 1945). Especially is this true of the Cuban variety of pinta, in which the primary lesion is said often to be a palmar keratosis. With yaws common in a native community a lesser spirochaetal disease like pinta might well exist unrecognized. The method of transmission of pinta is not known with certainty. Insect vectors have been suggested. Thus an insect-borne spirochaetosis such as pinta could perhaps make its appearance in troops even if their association with natives was not close enough to allow of contact transmission of yaws.

Searches for spirochaetes and Kahn and Wassermann tests were therefore carried out at regular intervals, with consistently negative results. Cerebrospinal-fluid Kahn and Wassermann findings were negative. Attempts to transmit the disease by inoculation of a volunteer with serum from scarified lesions were unsuccessful. Kahn and Wassermann tests repeated eighteen months after the onset

of the original symptoms were reported to be negative. Although positive serological findings develop relatively late in pinta it was felt that this diagnosis need no longer be entertained. The improvement in one case following neosarsphenamine was presumably a non-specific effect.

The world-wide distribution of this disorder, its involvement of different racial types, its independence of climate, and its invariable association with the use of mepacrine seem to leave no doubt of that drug's causative role. It also raises the question whether less typical cases may have escaped detection. Out of a profusion of ordinary tropical dermatoses only one other patient seen at the same time as the above group warrants brief description:

Sapper E., when admitted, displayed infiltrated erythematous plaques on the dorsum of both feet, on the extensor surface of his arms, on the back of the hands, ears, face, front and back of the neck, and a few in the axillae. He showed also some patchy loss of scalp hair. He had been taking mepacrine for eight months. The lesions had appeared ten weeks after he started taking the drug, and had advanced slowly thereafter. He had no symptoms. Shortly after his admission, at which time his case was tentatively diagnosed as subacute lupus erythematosus, a peculiar gross patchy hyperkeratosis of his palms appeared, with similar but smaller lesions on the feet. It was identical with that displayed in the typical tropical lichen-planus cases. He had no constitutional symptoms. His lesions gradually improved over the next two months, and he was then lost sight of.

Review of the history of Case 3 reveals a considerable resemblance to disseminated lupus erythematosus. Suggestive of this disease were the onset following unusual exposure to sunshine at a picnic—he was an orderly-room clerk and mostly kept indoors—the period of diarrhoea associated with an exacerbation of his rash several weeks after he had stopped taking mepacrine, and the persistently raised sedimentation rate. Against this, and supporting its classification as tropical lichen planus, were the relation to mepacrine, the complete absence of lesions of the face, and the extensive and severe involvement of the palmar and plantar regions.

Biopsy of a fresh macular lesion of the trunk in this case showed a non-specific histology resembling acute solar dermatitis. A hypertrophied scaly papule from the wrist appeared like typical lichen planus in most of its details. It showed hyperkeratosis, increase of the granular layer, acanthosis, liquefaction degeneration of the basal layer, and a diffuse infiltration of the upper cutis by lymphocytes and plasma cells merging with the basal cell layer. In the deeper part of the corium this infiltration was associated with vessels and hair follicles, and there were also some oedema and proliferation of the endothelium of the smaller vessels.

Summary

In a group of troops serving in scattered tropical areas, both malarious and non-malarious, tropical lichen planus was noted only in those who had taken mepacrine for malaria suppression. The incidence was approximately 1 per 2,000 troops. The initial symptoms appeared when mepacrine had been used for between two and three months. Some of the residual lesions seemed to be permanent. Some resemblance to disseminated lupus erythematosus is noted.

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POLIOMYELITIS: A SECOND ATTACK

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It is generally believed that second attacks of poliomyelitis are very uncommon, and this seems to be borne out by the small number of such instances reported in the literature. Quigley (1934) collected 12 cases, while Bridge *et al.* (1946) reported 6 among approximately 1,100 cases of poliomyelitis in and around Buffalo during the summer of 1944. In all some 37 cases have been reported in various American publications.

We feel, therefore, that it would be of interest to record the following case of a second attack which came to our notice recently. This was one of the 21 cases admitted to hospital in the Swansea area.

Clinical Summary

First Attack.—A girl aged 3½ was admitted to Hill House Isolation Hospital on Aug. 28, 1938, at the height of a poliomyelitis epidemic. The child had been generally out of sorts and listless for a few days, later becoming feverish, with occasional twitching of face and body. There was no history of obvious contact with infection, but her father worked in close association with a man whose child had been admitted to the same hospital on Aug. 19 suffering from poliomyelitis. On admission the child was pyrexial—temperature 102° F. (38.9° C.)—and showed left-sided facial paralysis and weakness of the abdominal muscles. C.S.F. findings were: colourless slightly granular fluid; 39 cells per c.mm. (all lymphocytes); globulin, faint trace; protein, 30 mg. per 100 ml.; glucose, 74 mg. per 100 ml.; chlorides, 702 mg. per 100 ml.; Lange curve, 0012210000. A facial hook was fitted and the child kept in bed for five weeks. She was discharged a week later with the hook still *in situ*. Subsequently she was seen at regular intervals by an orthopaedic specialist, and at the end of six months the facial muscles showed complete recovery of power and the facial hook was discontinued.

Second Attack.—During the current epidemic of poliomyelitis the child, now aged 12, was admitted to Hill House Hospital on Oct. 9, 1947, with a definite attack of the disease. She had had a cold a week previously, followed later by aches and pains "like 'flu'." On the day of admission she became feverish, developed a stiff neck, and had some difficulty in moving her right leg. Again there was no definite history of contact with infection, but a month previously two young children living opposite the patient had been admitted to hospital with poliomyelitis, and the parents of the two families had had frequent contact. On admission the temperature was 100.4° F. (38° C.); there was stiffness of the neck and spine, and a sluggish knee-jerk on the right side. Next day there was paresis of the right gluteus medius and quadriceps with loss of the knee-jerk on the same side and weakness of abdominals. C.S.F. findings were: clear fluid; 89 cells per c.mm. (90% lymphocytes); globulin, trace; protein, 100 mg. per 100 ml.; glucose, 80 mg. per 100 ml.; chlorides, 731 mg. per 100 ml.; Lange curve, ½12110000.

It will be noted that the following factors were common to both attacks: (1) A fairly typical history in the presence of an epidemic; (2) muscle paralysis and weakness; (3) changes in the C.S.F.—namely, increased cell count and raised protein content—which are consistent with a diagnosis of poliomyelitis. These, we feel, serve to demonstrate the true nature of the illness in both instances.

Discussion

The occurrence of a clinically recognizable second attack of poliomyelitis, in the ratio of one such case to a total of