TREATMENT OF LEPRA REACTION AND LEPROMATOUS ULCERS BY ANTIMONY AND THE ARSPHENAMIDES

By Dr. R. C. Germond

Recently Medical Officer, Botsabelo Leper Asylum
Maseru, Basutoland

TREATMENT OF ACUTE LEPRA REACTION

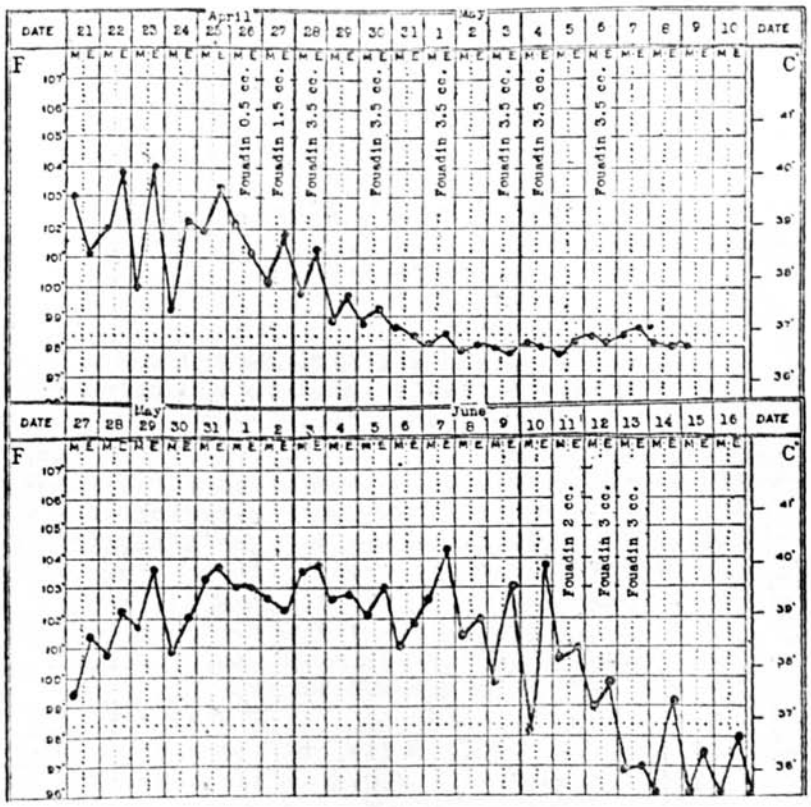
POTASSIUM ANTIMONY TARTRATE AND FOUADIN

Intravenous injections of potassium antimony tartrate in the treatment of acute lepra reaction were employed spasmodically at the Botsabelo Leper Asylum until the middle of 1932, when they were completely abandoned. It was then decided to renew the attempt to employ this drug but by a safer route, namely, by mouth. The effect produced in a first case was to provoke an intense congestion of the acutely raised macules, with blistering and general oozing of blood from their surfaces. This development was followed by a dramatic fall in temperature and a complete shrivelling up of the lesions. The result in this case was permanent, and the patient was subsequently discharged as arrested. The temporary subsidence of acute leprous lesions during an intercurrent attack of pneumonia is well known; the effect produced by the drug was similar but infinitely more pronounced and, in this case at least, permanent. Several other cases were subsequently treated by the same method with varying degrees of success, but the depressant effect of the drug was so alarming, and the gastro-intestinal symptoms that appeared were so distressing, that it was decided to discontinue the attempt.

The conviction remained, however, that antimony is a drug of definite potency in acute lepra reaction, and the question arose whether or not similar results could be obtained by the employment of less toxic organic compounds of that element. Fouadin, well known in connection with the bilharzia campaign in Egypt, was chosen for the attempt. The accompanying charts are reproduced (Text figs. 1 and 2) to illustrate the effects of this drug in acute reaction cases.

It is important to remark that the fall in temperature, whenever it occurred, was always accompanied by a corresponding improvement in the clinical aspect of the case. This was often

spectacular but at other times disappointing, the result apparently depending on the degree of acuteness of the condition. In other words the most acute cases, with high temperature and erysipelatoid swelling, were always more likely to respond than less acute and *a fortiori* subacute cases. It is interesting to note, moreover, that the subsidence of swelling which follows the



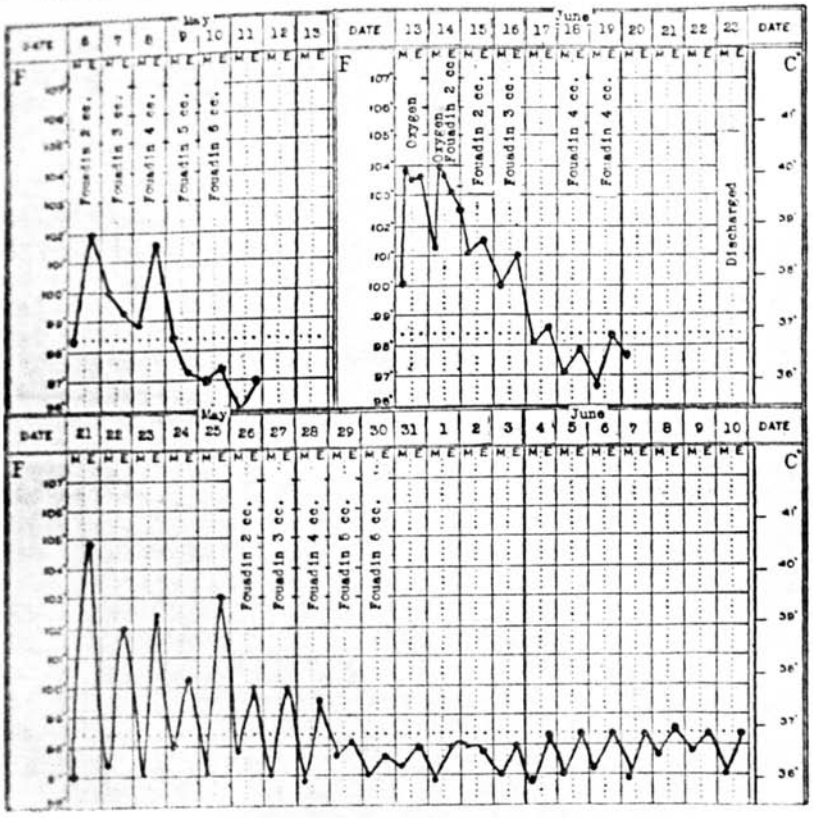
TEXT-FIG. 1. Case of acute lepra reaction (Ntsebo, female, aged 19 years) treated with fouadin. First reaction in April, 1934, with recurrence late in May.

intramuscular injection of fouadin occurs not only in spontaneous lepra reaction but also in the local reaction frequently produced by intradermal injections of iodized ethyl esters in the treatment of the disease.

PRONTOSIL AND SOLUSEPTASINE

Fouadin thus came to be considered as indispensable in the treatment of acute lepra reaction, and it remained my main stand-by at Botsabelo until certain new chemotherapeutic drugs ap-

peared. Prontosil was the first of these to be employed, its use being prompted by the growing conviction that the so-called acute lepra reaction is the result of a secondary infection. As will be seen in the accompanying charts (Text-figs. 3 to 6), the effects produced by injections of prontosil were if anything more dramatic than those following the use of fouadin. Moreover, the new drug proved to be effective in some cases which had

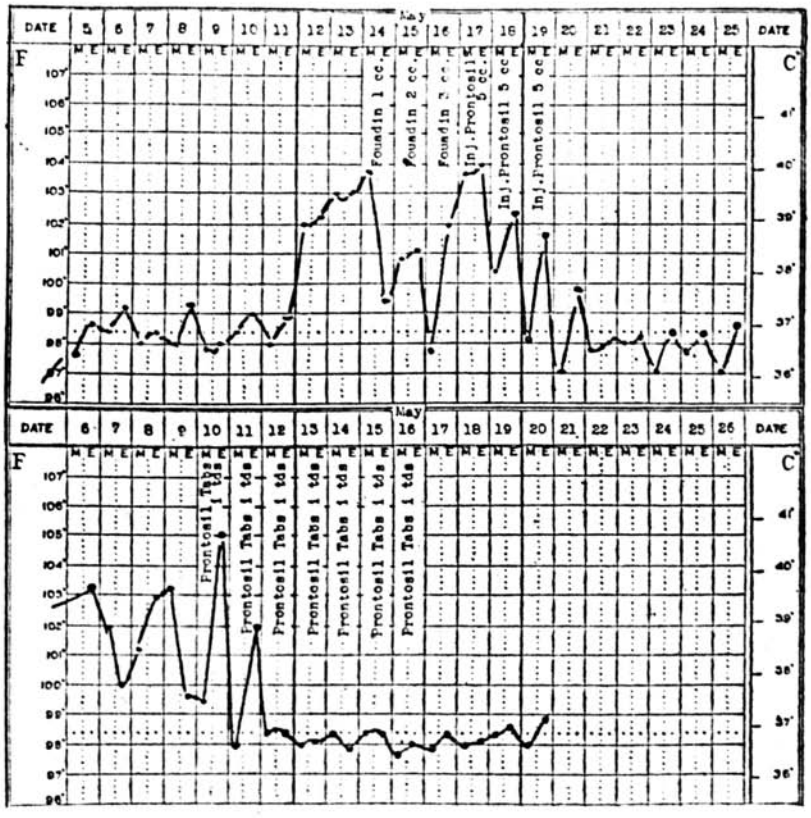


Text-fig. 2. Three cases of acute lepra reaction treated with fouadin. Upper, left (Mapaile, female, aged 6 years), in May, 1934; upper right (Mamasingdarang, female, adult) in June, 1936; and bottom (Kopano, male) in May and June, 1934.

persistently failed to respond to the other. Apart from this, the remarks already made with reference to fouadin are equally applicable to prontosil, namely, that the greater the degree of activity (acuteness) of the case, the greater the likelihood of success. Likewise whenever a fall in temperature occurred as a result of the administration of the drug, this was accompanied

by clinical improvement of corresponding degree. The rapid disappearance of swelling in the most favorable cases was followed by free peeling of the skin over the affected areas.

Unfortunately, for nonmedical reasons it was found impossible to continue the experiment and soluseptasine was decided



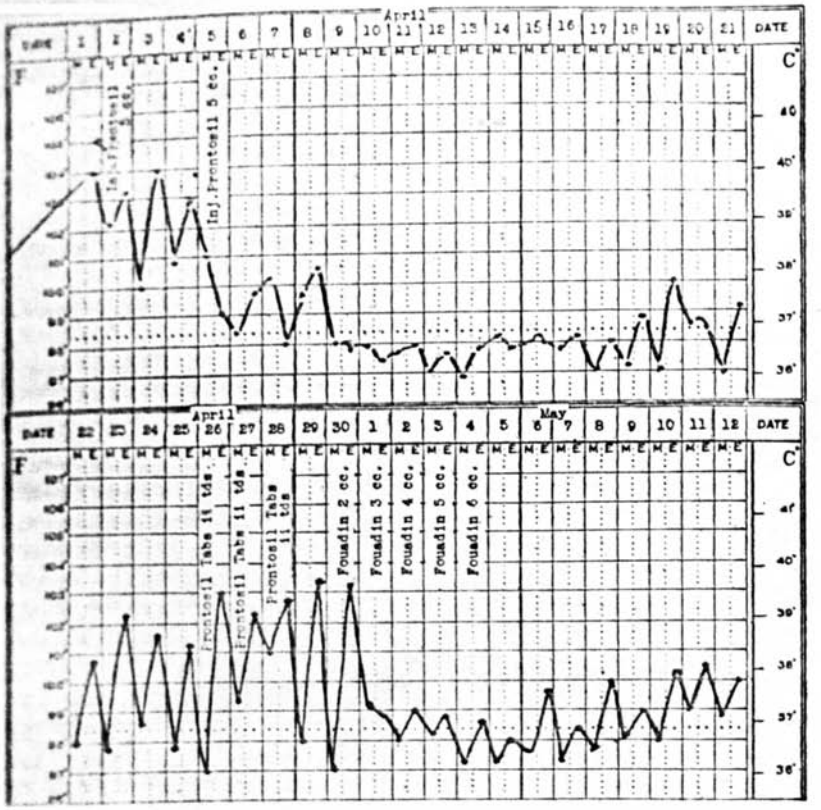
TEXT-FIG. 3. Two cases of acute lepra reaction. One (Nkhale, male, aged 20, upper chart) treated in May, 1936, first with fouadin with only temporary effect, then with prontosil by injection; the other (Ntaba, male, lower chart) treated in the same month with prontosil by mouth.

upon as a substitute. The results were so disappointing that I temporarily lost interest in the experiment. It is necessary to insist on the definite inferiority of soluseptasine as compared with prontosil in the treatment of acute lepra reaction.

TREATMENT OF LEPROMATOUS ULCERS WITH SOLUSEPTASINE

It is strange to remark that in spite of the striking results obtained by the use of prontosil in the treatment of acute lepra

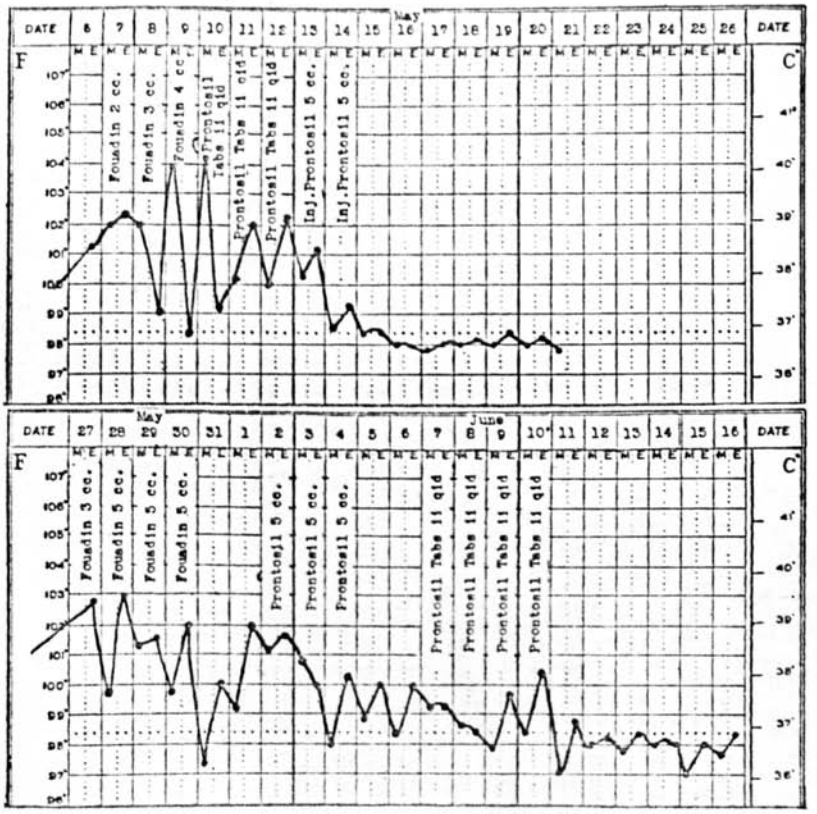
reaction, the equally remarkable results of chemotherapy on lepromatous ulcers completely escaped my notice until quite recently. The reason which prompted a trial of the intra-arterial route in treatment was the relative failure of soluseptasine in the acute reaction condition. It seemed obvious that, given intra-arterially, the drug would be supplied to the affected part in greater concentration. The original intention was to attempt the treat-



TEXT-FIG. 4. Case of acute lepra reaction (Jafeta, male) treated in April, 1928, with prontosil by injection, with recurrence and treatment with prontosil, ineffective, followed by fouadin.

ment of reaction cases with injections given into the external carotids, but before attempting to do that it was decided to test the method with a more easily accessible artery, as far as possible from vital centers. The choice of the femoral artery having been made, I was naturally led to consider the possible effects of soluseptasine on lepromatous ulcers.

Before describing in detail the cases treated by this method, it may be as well to state that no originality is claimed for the choice of the method. The idea of utilizing the intra-arterial route in the treatment of leprosy first occurred to me in 1933 or 1934. This route, I argued, would not only insure greater concentration of the drug in a part, but there was also the possibility that it would permit the injection of oily preparations without the



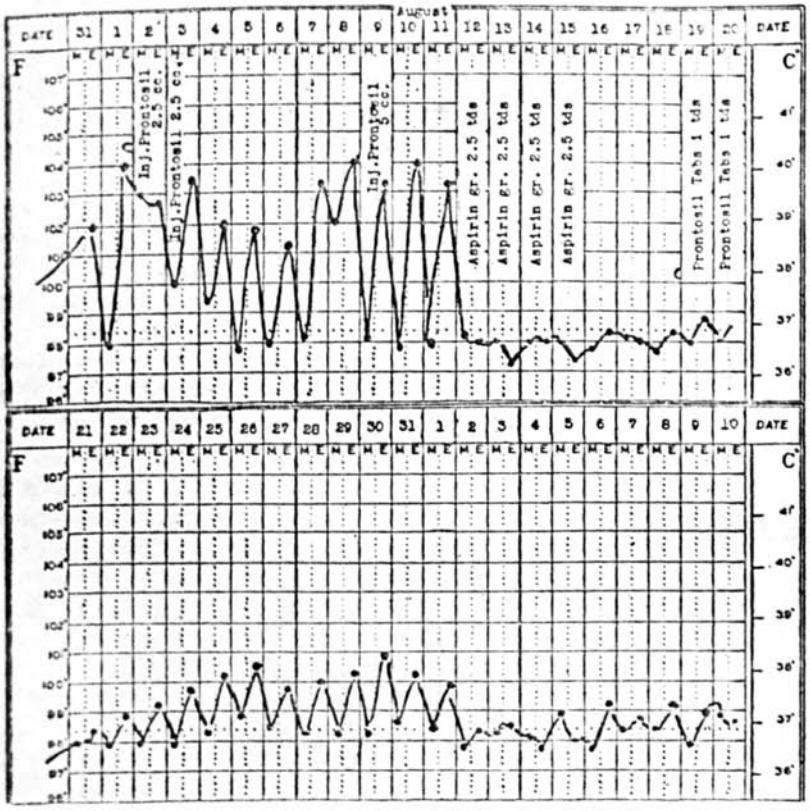
TEXT-FIG. 5. Case of acute lepra reaction (Koko, male) treated in May, 1936, with fouadin followed by prontosil; recurrence, controlled by prontosil.

risk of pulmonary embolus. Because of a slight accident in an attempt at self-experimentation, however, it was decided to abandon the route as too risky for our patients. The present observations are the result of the discovery that Leriche had employed the method ten years ago and that this route can be used with impunity.

DESCRIPTION OF CASES[1]

CASE 1. Makhokolotso, a young female, age 17, C2. Admitted to the hospital on May 9, 1939, with a dirty ulcer on the dorsum of the right foot. Injection of 5 cc. of soluseptasine into the right femoral artery. Within a few days the ulcer had completely cleaned up. (Observation interrupted.)

Subsequent condition.—On August 16 there was a large ulcer over the inner side of the foot and a small one on the dorsum, also one on left foot. They were clean but showed no evidence of healing.



TEXT-FIG. 6. Case of acute lepra reaction (Thai, male child) treated in August, 1936, with prontosil alone.

CASE 2. Lebea, a young adult male, C2. Admitted to the hospital in very poor condition, with a very large pale atonic ulcer on the external aspect of the right leg, swelling of foot and leg, pain and fever.

May 10th: 10 cc. soluseptasine injected into the right femoral artery. Local treatment, iodoform and dry dressings. *May 12th:* The ulcer presents a totally

[1]The notes on "subsequent condition" in these case summaries were kindly supplied me by Sir Walter Johnson after my departure from the asylum, which interrupted my own observations, and after the preparation of the manuscript of this article.

different aspect, with a complete coating of firm, bright red, healthy granulations. Swelling has almost completely subsided and temperature has fallen. *May 18th:* Swelling has completely disappeared, the ulcer now surrounded by a firm raised ridge. Patient very lively.

Within the next few days a thin blue epidermal film had appeared all around the ulcer, along the base of the raised edge. Although there was no apparent need for it, the patient requested a second injection, and on May 19th another 10 cc. dose was given into the same artery. On the next day the ulcer had the same beautifully healthy aspect, progress continuing. (Observation interrupted.)

Subsequent condition.—On August 17 there were five ulcers on the right leg, small, clean, shallow, showing signs of healing. The intervening skin was dark and unhealthy looking.

CASE 3. Likou, an adult male, C3. Admitted to the hospital in extremely poor condition, with recent breaking down of chronic ulcers on arms and hands, legs and feet, the condition very painful. The patient's chances of recovery seemed very poor. Local treatment: Dakin dressings.

May 12th: After a week of this treatment, the condition is worse than ever: swelling of hands and feet, deep gray slough over dorsum and external aspect of right foot, very offensive odor. Injection of 10 cc. soluseptasine into right femoral artery. *May 13th:* No visible improvement; same foul necrotic ulcers. *May 14th:* Perhaps slightly improved. *May 15th:* Pale pink granulations forming over center of ulcer.

Thereafter the whole surface cleaned up rapidly, with formation of healthy granulation, so that on the 22nd the slough had completely disappeared. The granulations, however, were not as bright red as in Case 2. The present case was a much more serious one; unfortunately patient refused a second treatment, claiming that the injection had increased the size of the ulcer, whereas the truth of the matter was that it had merely revealed the extent of the damage, by removing the slough. (Observation interrupted.)

Subsequent condition.—On August 15 the lesion was almost completely healed. Similar ulcers that had appeared later on the left leg were now small and covered with healthy granulations. No special treatment since the soluseptasine injection.

CASE 4. Masimphane, an elderly male, C1-N2. Seen at the dispensary on May 13th, he presented a very considerable swelling of left foot and great toe. A small plug of gray slough protruded from the crease at the base of this toe; no necrosed bone, trouble obviously articular. Patient very ill and "septic." Immediate disarticulation of the great toe was advised "to save life and limb." Patient refused treatment or admission to hospital. Two days later (May 15th) the foot and leg were enormously swollen. Slough extended around base of toe to dorsum of foot, as far as the interspace between the 2nd and 3rd toes; a probe met articular cartilage. Patient reluctantly accepted removal of the toe, but it was then almost certain that nothing could save him. It was therefore decided to try the effect of an injection of soluseptasine and to postpone disarticulation until the morrow. The patient gladly accepted this proposal and was admitted to the hospital, where unexpectedly the temperature was found to be normal. Injection of 10 cc. soluseptasine given into the left femoral artery.

May 16th: Contrary to expectation, considerable subsidence of swelling of foot and leg. Slough remains unchanged. *May 17th:* Ulcer definitely cleaning up. Part of the slough has come off. First appearance of healthy granulations. A second injection of 10 cc. soluseptasine into left femoral artery made at patient's request. *May 21st:* Ulcer has now completely cleaned up. It forms a deep and irregular but clean and healthy trench. Swelling of foot has practically completely subsided. Progress would probably have been still more rapid if patient had remained in bed as ordered. (Observation interrupted.)

Subsequent condition.—On August 17 there was a shallow clean ulcer, the size of a shilling, on the end of the big toe, and edema of the lower half of the right leg.

CASE 5. Sebonang, a young female adult. Admitted to the hospital on May 20th with an extensive septic but shallow "ulcer," black and green as to surface, on dorsum of right foot. This lesion was almost certainly the result of a burn. Intra-arterial injection was attempted but found to be unexpectedly difficult and had to be abandoned. The 10 cc. of soluseptasine was therefore given intramuscularly, into the left thigh. It was thought that it would be interesting to compare the result of this injection with that which would probably have been obtained by the intra-arterial route. On the following day the whole surface was completely modified and was definitely turning pink. It is difficult to imagine that a more rapid result would have been produced if the injection had been intra-arterial. It must be remembered, however, that the lesion in this case was very shallow, actually a giant blister. (Observation interrupted.)

Subsequent condition.—On July 4 the foot was noted as swollen and painful, with no evident collection of pus. Intra-arterial injection again tried, without success, and 10 cc. of soluseptasine was given intramuscularly. On August 16th the dorsum of the foot was completely healed. A small clean trophic ulcer present on the sole.

CASE 6. Mamohlokoane, an adult female, an advanced nodular (C3) case with chronic laryngeal obstruction. Three years ago that condition necessitated daily intubation for a fortnight. On May 20 the patient was obviously very ill. She explained that three days before the strips of old blanket with which she envelops her feet had caught fire, a fact which she did not notice until her attention was attracted by the smell of burning flesh. There were almost exactly symmetrical burns of the dorsa of the two feet extending as far as three fingers' breadth back from the base of the toes and exposing the joints and phalanges of the 2nd and 3rd toes of each foot. The whole surface was converted into a thick gray slough of horribly offensive odor. As the condition was so symmetrical, it was decided to inject the right femoral artery alone and to note the effect produced as compared with the condition of the left foot; 10 cc. of soluseptasine injected. No local treatment other than boiled water compresses. On the following day the ulcers were already beginning to clear up; pink granulations were discernible here and there, and swelling had partly subsided, with fine wrinkling of the skin surrounding the burns. The improvement was absolutely symmetrical. (Observation interrupted.)

Subsequent condition.—On August 16th, extensive ulceration of the right leg and dorsum of foot, present since the burn occurred. Left leg completely healed except for a small area between the second and third toes.

INTRA-ARTERIAL SOLUSEPTASINE IN OTHER CONDITIONS

In laryngeal leprosy.—It is regrettable that during the short period under review there was no opportunity to study the effect of the above treatment in acute laryngeal obstruction. It was thought that the inflammatory element (secondary infection) in these cases would probably respond to chemotherapy, more especially if buccal or pharyngeal ulcerations existed. The only two available cases presented partial aphonia due to laryngeal leprosy without symptoms of acute exacerbation. Injections of 5 cc. soluseptasine were given into the external carotid arteries at intervals of a few days, but apparently with no result whatsoever. Laryngoscopy was not performed either before or after treatment.

In other conditions.—Attempts were made to ascertain the effects of the intra-arterial injections of soluseptasine in tuberculoid leprosy and for leprotic infiltration, leprous nodules and perforating ulcers. In all of the cases the object was to influence secondary infection; no effect whatsoever on the leprotic condition itself was expected. Nine cases were treated by the injection of from 5 to 10 cc. into the femoral or external carotid arteries. The results in all cases were completely negative. It is important to note that none of these cases was acute.

SUMMARY

1. Intramuscular injection of fouadin in acute lepra reaction causes a fall in temperature with simultaneous clinical improvement in a large proportion of cases, provided they are definitely acute.

2. The same results are obtainable by the injection of prontosil. The action of this drug appears to be more constant and more pronounced than that of fouadin.

3. Intra-arterial injection of 5 to 10 cc. of soluseptasine in septic leprotic ulcers and burns results in their rapid cleansing with corresponding improvement in the general condition. Growth of healthy granulations is promoted and dead tissue is rapidly eliminated.

4. Despite the presumably greater concentration of the drug on the injected side, the effect does not seem to be more pronounced than on the noninjected side.

5. The results obtained by the intramuscular injection of soluseptasine do not seem to be inferior to those obtained by the employment of the intra-arterial route.

6. The hypothesis that acute lepra reaction is due to secondary infection is rendered more plausible by the success of prontosil in the treatment of this condition.

7. Neither fouadin nor the arsphenamides appear to possess the least curative value on leprosy itself. Their virtue lies in their action against the inflammatory element (secondary infection).

8. The treatment of burns and lepromatous ulcers is greatly simplified by chemotherapy. Their rapid cleansing is insured without active local treatment, and elastoplast can be applied at a much earlier date than ordinarily.

9. In neural cases chemotherapy does not dispense with surgical treatment in the presence of necrosed bone. When, on the other hand, the septic condition originates in the tendon sheaths or small articulations, chemotherapy may render surgical measures unnecessary.

10. Further experimentation to determine the value of chemotherapy in acute laryngeal obstruction and ulcerations of the mouth in advanced lepromatous cases is desirable.

11. Should the results obtained in the present series be confirmed by other authors, the treatment of septic conditions in leper asylums will be revolutionized.