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EDITORIAL

The development and extension of the war is making the work of B.E.L.R.A. increasingly difficult fully to maintain. Several of our Toc H. workers have joined the military forces of our African possessions and although our activities have so far been little affected, yet extensions we had in view are being limited by lack of personnel. Fewer reports are reaching us and material for this review is thus being curtailed.

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Dr. Muir's tour to South America and the West Indies had to be cancelled owing to the dislocation of communications by air and by sea, but the receipt of a request to find a medical man to take charge of the important Chacachacare Leper Asylum of Trinidad led Dr. Muir to offer through the Colonial Office to take charge of that institution for a period, in order to enable him to renew his close connection with clinical work on leprosy. The Executive Committee agreed to the proposal on condition that facilities were granted to Dr. Muir to visit British Guiana and the leprosy infected West Indian Islands during his time in Trinidad, in accordance with the programme that had been postponed. The Colonial Office accepted this proposal and Dr. Muir has already left for Trinidad. During his absence the Honorary Medical Adviser will carry on the medical work of the London central office.

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We are fortunate in being able to publish in this issue a well illustrated paper by Dr. H. W. Wade of the Philippines on Tuberculoid Leprosy, regarding which he has done so much original histological work. He deals in a masterly way with the difficult question of the outlook of tuberculoid cases with special reference to the possibility of their passing into the much more dangerous lepromatous form. The appearance of many lepra bacilli during reactions of major tuberculoids may cause this stage to be taken for the lepromatous one; but Dr. Wade finds that on the subsidence of the reaction they revert to a typical tuberculoid condition and he has been unable to find any clear evidence in his own extensive experience or in the literature of lepromatous degeneration taking place in tuberculoid leprosy. On the other hand he records evidence to show that tuberculoid cases may

relapse after considerable periods of apparent subsidence, so they require watching.

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A paper by Dr. A. R. Davison on a trial of Grasset's tubercle endotoxin with inconclusive results is also published. Recent leprosy journals and reports are also reviewed.

RELAPSED AND BORDERLINE CASES OF TUBERCULOID LEPROSY

H. W. WADE

From the Leonard Wood Laboratory, Cutlon, Philippines

With the increased attention that has been given to the tuberculoid form of leprosy in recent years, the question of the ultimate outcome of cases of that class comes to the fore with increasing insistence. It is quite widely believed that their prognosis is particularly favorable, but because of the more or less frequent occurrence of relapse there is reason to inquire just how generally that is true. Some workers believe that occasional cases undergo transformation to the lepromatous form, but here again there is a question; others hold definitely that that change does not occur, while still others are uncertain because of lack of personal observation of the condition and the absence of convincing records in the literature. As will be seen, it is easy to be mistaken in this matter.

The conviction that tuberculoid leprosy is particularly benign is probably based largely upon experience with cases seen during what may be spoken of as the original phase of the process. In many of them, undoubtedly, the condition subsides permanently. In neural leprosy generally the outlook for patients with only one or a very few skin lesions is probably favorable. That, at least, has been the experience in the Philippines [12], as it has been that of Cochrane with early cases in children in Ceylon and sourhern India, [3, 5] and—with particular reference to tuberculoid leprosy of Souza-Campos in Brazil [18]. Furthermore the more active

(reaction) cases of tuberculoid leprosy, though often very marked and frequently bacteriologically positive and consequently liable to be diagnosed as of lepromatous type, generally respond more favorably to special treatment than any other form of the disease, and even without treatment they habitually subside remarkably within a few weeks or months, even to the point of apparent recovery.

RELAPSE IN TUBERCULOID LEPROSY

Perhaps because so many of the patients who have been observed in the original period drop from sight after they have improved, leaving behind them the impression of recovery, the question of relapse is seldom raised. Experience in the Philippines, however, indicates that it occurs not infrequently in cases that have been found bacteriologically positive, or " open." There is reason to believe that in Calcutta severe relapse must be a frequent occurrence.

Though tuberculoid cases are relatively less common in the Philippines than in some other places, there are always some of the more marked ones in the leprosaria, segregated because open. In 1936 the writer, with Rodriguez [24] took under observation the ten that were then at the Eversley Childs Treatment Station in Cebu, among a total of some 700 inmates, together with two others from another group of neural cases that had been under study earlier [22]. This small group affords no less than seven examples of relapse (more than 50 per cent) in cases that at one time or another enjoyed a period of apparent cure.

Case P. D. Hospitalized in 1935 with only a solitary but bacteriologically positive major tuberculoid plaque (right knee); a limited secondary papular eruption occurred later, after which improvement was steady. Paroled in 1937. One year afterward an eruption of " small, discrete, uniformly distributed macules " appeared, and the patient had to be rehospitalized. These lesions subsided but a new crop appeared later and the condition had not cleared up in 1939.

Case T. E. Essentially identical with the preceding case up to a certain point, with at first a solitary plaque (left elbow) and later a limited papular eruption. Admitted in 1934, paroled in 1937. Reactivation occurred two years later, with several rather small, torpidly spreading leprids (these of minor tuberculoid grade), but rehospitalization has not been necessary.

Case A. S. A very different condition, a particularly marked reactional development, in a boy aged only 10 (1936). Paroled in 1938. A few months afterward, and again in 1939, he was

found to have a limited number of new but minor-degree lesions, not necessitating rehospitalization.

Case P. M. A case of long duration, seen first in the Cebu clinic in 1931. Hospitalized in 1932 after a reaction, with very numerous lesions mostly of secondary, eruptive type. Paroled in 1935. Reactivation and rehospitalization two years later, but only for a year. In 1939 he was found to have several lesions, some new, but none positive.

Case T. S. This patient comes into this category because of her history or repeated generalized eruptions with intervening periods of subsidence before she was hospitalized in 1933, each outbreak following childbirth. After the fourth delivery and eruption the subsidence was less complete and she entered the leprosarium after still another reaction, with numerous conspicuous and extensive lesions. Not paroled until 1938 and not seen since; prognosis highly uncertain.

Case D. A. A particularly discouraging case, now "borderline." Hospitalized in Manila in 1927 with a solitary lesion (face), a few others developed later but subsided. Paroled in 1929. After five years of apparently complete recovery, in 1934 a reaction occurred and a few large leprids appeared, followed by a generalized papular eruption. With repeated reactions and multiple new lesions appearing and receding, he has remained in the Cebu leprosarium since then. For a time suspected of becoming lepromatous (Fig. 1), the case is actually in a peculiar state of unbalance [23].

Case T. C. An unusually active minor tuberculoid case in 1933, it became converted to marked major a few months later during a severe reaction. Recession was rapid, but parole was delayed until 1937. After quite two years of apparent recovery, relapse occurred abruptly in consequence of a pyogenic infection, the condition as a whole very suggestive of lepromatous transformation (Figs 2 and 3). This phase, and an extraordinary development that occurred later, have been reported [23], [13].

The group of cases from which these come was not a selected one except in that all had been bacteriologically positive, a more or less common occurrence among reaction tuberculoid cases everywhere. They are not, of course, necessarily representative as regards the frequency of relapse among tuberculoid cases elsewhere. Even for the Philippines they are too few to be statistically significant, and the course of events may be different among peoples of other races. They serve, however, to call attention to the uncertainty of absolute cure, at any given time, of a once open

case of tuberculoid leprosy. The last two cases bring up the problem of the worst possible development, namely, transformation to the lepromatous form.

CHANGE OF FORM

In the reactivation that may interrupt a case in the course of improvement, or in the relapse that may occur after the stage of apparent recovery has been reached, the new or reactivated lesions may be essentially of the same type as before. On the other hand they may depart more or less markedly from the previous ones. Those which are of diminished severity, as the change from the major to the minor tuberculoid variety exemplified by two of the cases cited above, are not of concern here; only the more serious developments are to be discussed.

As has been said, there are differences of opinion as to whether transformation to the lepromatous form occurs or not. On the negative side Schujman, who alone has written especially on the subject of prognosis, expressed doubt in this matter in 1936 [16] and subsequently reached the conclusion that the change does not take place [17]; he holds that cases either recover or persist as such for long periods. He believes, probably correctly, that Querangel des Essarts and Lefrou [11] who reported the change in two cases, were simply dealing with the reaction tuberculoid condition that has caused so much confusion in the past.

Tisseuil [19] has also expressed the opinion that tuberculoid leprosy does not evolve toward the lepromatous form. He speaks of it as a manifestation of cutaneous resistance comparable to lupus, and especially to lupus erythematosus.

Cochrane [4] believes that the results of the lepromin test in tuberculoid reaction cases, generally held to be an indication of resistance, " makes unacceptable the view that tuberculoid leprosy may become lepromatous."* He speaks of " intermediate " cases with lesions that " simulate those of tuberculoid leprosy " but in which the lepromin reaction is negative. As a rule they recover after the manner of tuberculoid cases, he says, but occasionally one passes into the lepromatous form.

Mitsuda's group in Japan are especially convinced of the favorable significance of the positive lepromin reaction. So far as I am aware they have not reported lepromatous transformation of a tuberculoid case, the kind which they classify as " macular."

*It is generally agreed that, whereas the lepromin test is typically negative in leromatous cases, it is always positive in tuberculoid ones. The fact that the tissue-reaction found in the papule of a positive lepromin reaction is of tuberculoid nature, as is that reaction to the living infecting agent in tuberculoid cases, is regarded as significant in the present connection.

Indeed, in a recent follow-up study of certain cases which had been tested years previously, Igarashi and Hayashi [7] indicate special interest in the fact that an ordinary (Mitsuda-positive) neural case had become lepromatous.

On the affirmative side of this question Ryrie, who among his Chinese patients at Sungei Buloh, in Malaya, undoubtedly sees more severe tuberculoid reactions than anyone else, has expressed the conviction [14] that the tuberculoid condition is not a manifestation of resistance but a " potentially dangerous sensitization "—it represents tissue resentment to the presence of the infecting organism rather than tissue defence. The extreme ulcerative or sloughing reaction condition that he has described [15] he speaks of as a " tissue mania," adding that if the underlying factor in that condition is to be considered as resistance " it is resistance so violent and overdone that it damages the patient and often prepares the way for the transition to cutaneous leprosy." That change, he writes, has occurred in many of his cases, though it must be said that none of those that I biopsied with him in 1937, some of them old, had done so at the time though some of the specimens showed a mixture of tuberculoid and lepromatous histology.

Lowe, who in the Calcutta clinic sees more acute tuberculoid cases than anyone else, leads the affirmative, having touched repeatedly on this matter. He first said [8] that, on the whole, the existence of tuberculoid lesions is evidence of high resistance and comparatively few cases become lepromatous, though he wrote later [15] that the change happens in perhaps 25 to 30 per cent of tuberculoid cases. Recounting observations in Burma [9] he said that a considerable number of cases showed manifestations that " were either ' reacting ' tuberculoid lesions in which smears showed an abnormally large number of bacilli, or else were lepromatous lesions developing from a previously existing tuberculoid lesion "; and he also spoke of lepromatous cases that had lesions so peculiar in localization, distribution and otherwise that they must originally have been tuberculoid. These cases, difficult to classify, he like Cochrane speaks of as " intermediate," a term that has been used so commonly that it lacks particularity.

As for the morphology of converted lesions, he has said that sometimes the tuberculoid one forms the center of a lepromatous infiltration, the change starting at the margin and at first remaining localized here. When the process becomes marked, however, the original leprid subsides to remain as a depressed area in a " typical leproma " teeming with bacilli, and later the lepromatous condition may affect the skin of the whole body. This description might apply to the picture of a supposed leproma arising

from a residual tuberculoid leprid that Muir has recently published [10], except that he laid stress on a supposed lepromatous development in the flattened center of (as well as, it is gathered, around) the site of the original lesion. In that instance, he stated, there were also numerous lepromatous macules in previously unaffected skin. As will be seen, these descriptions and the picture referred to are, in the main, very similar to those of the " relapse tuberculoid " lesions that have been observed in Cebu [23] but that subsequent events proved not to be lepromatous.

Occasionally, here and there, I have run across cases with lesions of this general type—supposedly lepromatous ones abruptly delimiting sharply outlined flat areas but, in striking contrast, tending to taper off toward and to diffuse into the surrounding normal skin. Such a lesion is decidedly at variance with the typical leproma, which do not undergo central resolution and recession, and also with typical tuberculoid leprids, in which retrogression from the active marginal zone to the healed center is gradual while, in contrast, the outward limit is sharp.

A definite clue to the explanation of this peculiar formation came from the patient D.A. mentioned in 1938, in one of the four special annual examinations that have been made of that case, there were found several lesions of that description, two on the forearms and two on the wrists (Fig. 1). The patient, an exceptionally intelligent man, explained that the unaffected areas were the sites of previous (major tuberculoid) macules. Those areas were " immune " to the new development, but there was a striking and as yet unexplained peculiarity in their evidently intimate relation to the new, active lesion.

The nature of the active process was uncertain, but the patient refused biopsy. The bacteriological findings were not particularly suggestive, smears being reported as only 2+ (possible maximum 4+). Evidence was forthcoming when, four months later, the patient agreed to biopsy: the lesions referred to had all subsided most surprisingly, while others of similar nature had arisen elsewhere. One of the latter was biopsied, but as the specimen was lost in transit its histology remains unknown. Nevertheless, the rapid subsidence of the first lesions mentioned and development of new ones, they also to disappear completely within the next few months, is significant. Only lesions that are essentially of tuberculoid lepridic nature, whatever their actual histological structure may be, can come and go like that. The case, therefore, had not gone lepromatous, nor has it done so yet; in fact a specimen obtained in 1939, when a new eruption of quite different appearance was present, proved to be tuberculoid in structure.

An exceptional demonstration of relapse tuberculoid leprids

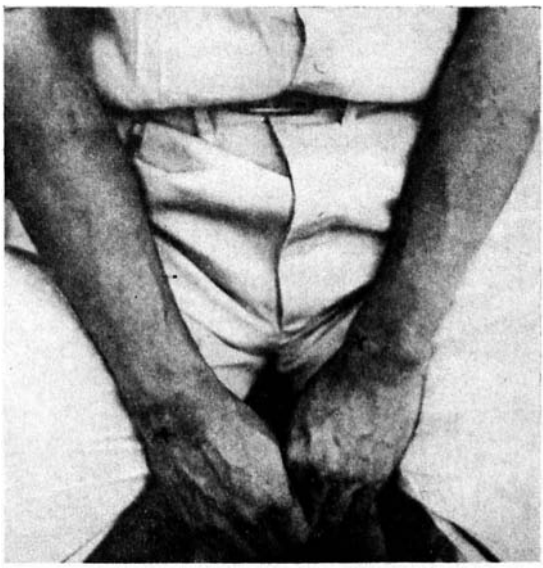
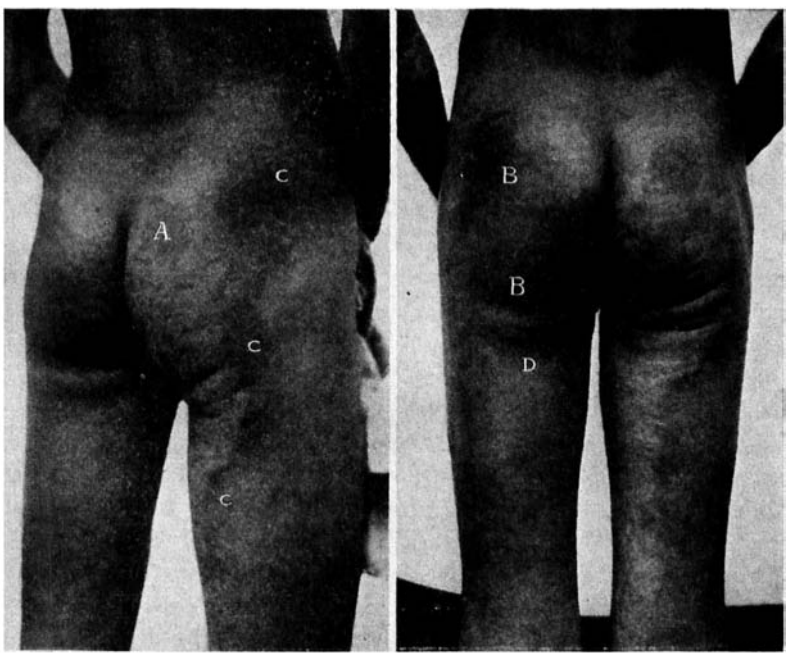


Fig. 1.
"Relapse tuberculoid" lesions on wrists and upper forearms, of suspicious appearance and generally sloping off like lepromata (Case D.A.). Each wrist lesion is indented at one place (X, X) by an "immune" area previously affected by an ordinary major tuberculoid leprid, and, less clearly demonstrated, there are central immune areas in the lesions on the forearms.



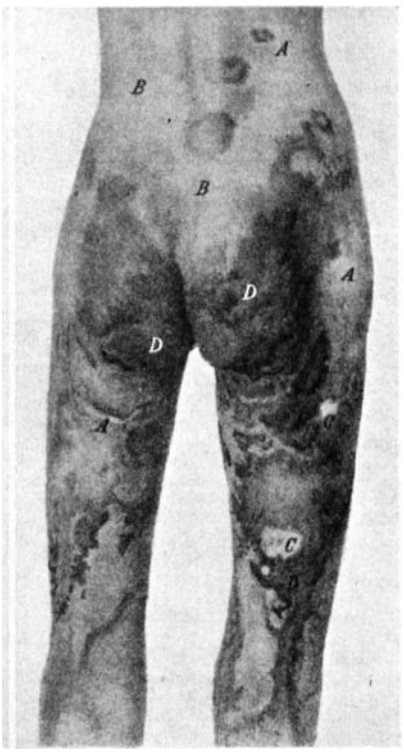
Figs. 2 and 3.
Remarkably extensive relapse tuberculoid lesions in Case T.C., showing the abrupt limitation against previously tuberculoid immune areas (A, B, C, D) and diffusion above.

was seen in the last of the cases of relapse detailed above (T.C.), when the disease suddenly became reactivated after a free period of two years [23]. The several extensive lesions are exemplified by those shown in Figs. 2 and 3. The characteristic diffusion into previously unaffected skin, present in the upper part of the region, is not well demonstrated, but the abrupt margination against immune areas is conspicuous. It is seen around the rounded flat area on the right buttock (A), and also around the much larger one that covers and extends below the left buttock (B, B). It is most striking on the right hip and thigh (C, C, C), where previously there had been a wide and very long tuberculoid plaque. The conspicuous elevated band below the left gluteal fold occupies a narrow zone upon which the previous lesions of the buttock above and the thigh below (D) had not encroached.

The clinical and histological evidence regarding the nature of this new development was conflicting. Though it was not definitely lepromatous in appearance, some of the smears were strongly positive (3+; one from the nasal septum 4+) and sections of a biopsy specimen showed what I can still only interpret as a non-foamy lepromatous granuloma. In spite of that finding however, subsequent events proved that the case itself had not undergone lepromatous transformation. When the patient was hospitalized some ten weeks later all of these lesions, except certain parts of them that had been reactivated later, had subsided. In a third reaction shortly afterward a very extensive bullous condition ("leprous pemphigus") developed that resulted in extensive scarring [13]. In 1939 none of the lesions showed any activity, and a biopsy specimen from one of the scarred areas showed slight but definite tuberculoid change.

In this connection note may be made of a case from the literature, reported by Arning and Nonne in 1893 [1], which they had studied with respect to nerve changes. The patient was a youth of Dutch parentage born in Sumatra. The disease had begun several years previously with "pemphigus," followed later by "typical rings and spots of lepra maculosa." Later "nodular infiltrations" developed, and when seen by the authors there were on all the extremities extensive "lepromas" of the appearance shown by pictures that are reproduced here (Figs. 4 and 5). On the trunk and parts of the extremities there were no "real lepromas" but leprids, dark liver-brown spots, in part elevated 3 to 5 mm. The thickest areas, on the buttocks and thighs (D), were spoken of as "large brown leprids." In spite of his condition the patient felt well and was of normal weight for his age. Significantly, the mucous surfaces were not involved.

This case is an example, the only one that I have found



Figs. 4 and 5.
A so-called "tubero-macular" case reported by Arning and Nonne in 1893 (reproduced from *Virchow's Archiv's*). Evidently a marked and chronic relapse tuberculoid case.

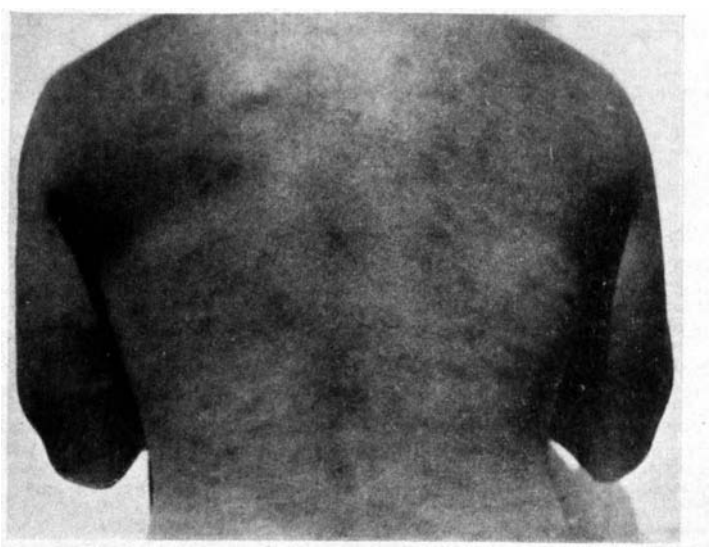


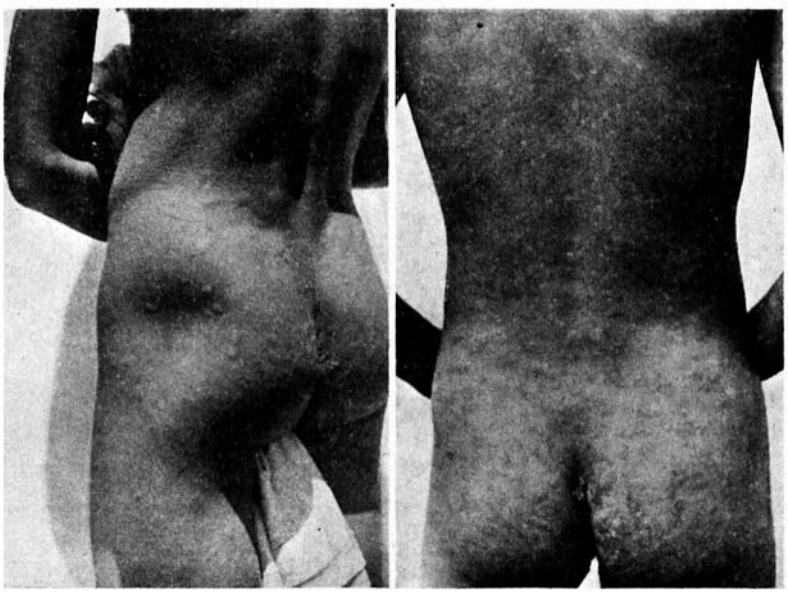
Fig. 6.
Multiple papular eruption of a persistently "borderline" case at Cebu (D.A.). Recent papules, pale residua of older ones, and areas of discoloration due to local injection of such lesions.

pictured, of what was then called the " tubero-macular " form. That class has long since been forgotten, but evidently it must be reinstated in the picture of leprosy but with a different concept of its nature. It seems obvious that it was one of " relapse tuberculoid " type, the lesions essentially like but more complicated and much more chronic than those in Case T.C., described. The authors recognized that certain uninvolved areas (marked C) had been affected previously, and it seems highly probable that other large areas that are sharply outlined by the new lesions had also been involved. Apparently a secondary eruption had developed inside some of these immune areas, as in Muir's photograph that has been mentioned.

Another report that may be mentioned is a recent one by de Castro Cerqueira [2] of so-called " mixed leprosy ", with inter-related—shown by photographs to be in places interlocking, like parts of a jig-saw puzzle as in Case T.C.—achromic macules and lepromas. Previous macular lesions had subsided, leaving pale residual areas; but new elevated ones had recently appeared on all parts of the body. These last were looked upon as lepromas and a biopsy specimen from one was so diagnosed, but they seem indubitably to have been of the relapse tuberculoid type. The most interesting finding in this case is that the lepromin test was positive in the flat macular areas but negative in the " nodular " lesions and in apparently healthy areas, leading the author to lay emphasis on local variations of reactivity of the skin.

The personally studied cases here cited certainly do not cover the field of atypical lesions that may be taken for leprids transformed to lepromata; it may be, perhaps, that their lesions are not representative of the most common that occur elsewhere. the peculiar papular eruption that has long dominated the picture of Case A.D. (Fig. 6) and that has for quite as long been the only important manifestation of the disease in a second borderline case (Figs. 7 and 8) cannot be discussed here. It may, however, be worth while to note a peculiar borderline case seen in South China with Fraser [20], though it does not exemplify the relapse tuberculoid condition.

There were lesions of three quite different aspects: (*a*) Conspicuous infiltrations of lepromatous appearance, particularly on the face and ears (Fig. 9). (*b*) A group of small, oval patches on the neck, sharply delimited and abruptly elevated, the surface level but coarsly granular, of tuberculoid aspect (Fig. 9). Bacilli in smears varied from absent to fairly numerous. (*c*) Multiple expanding lesions, evidently eruptive but of unusual appearance, on the thighs (Fig. 10) and elsewhere. Though merging had often produced complex figures, the typical unit



Figs. 7 and 8.
Multiple papular eruption of another borderline case, the first showing the typical flat tuberculoid papules early in the course (1936), the second showing the condition later (1938) with, among other lesions, many residual ones with hyperchromic halos resulting from local injections.

Figs. 9 and 10.
Showing the supposed lepromatous condition of the ears, the small tuberculoid plaques on the neck, and apparently intermediate lesions of the thighs in a borderline case seen in China.

lesion was a rather small round, moderately elevated, dully erythematous macule, soon becoming annular after the manner of ordinary leprids. In places, however, there were confluent areas that did not show this retrograde change but were highly suggestive of lepromatous infiltration (see Fig. 10, near knee). Furthermore, the outer edges of all of them sloped off to the normal skin (though not diffusing as completely as do lepromata); and smears were strongly positive, with occasional small globi. A biopsy specimen from one of the patches on the neck showed in part definite tuberculoid changes but mostly an atypical granuloma suggestive of a nonvacuolate leproma. One from the thigh showed only the latter condition.

Here, then, was a case with apparently lepromatous lesions (face and ears), a few that were clinically tuberculoid (neck), and many of a more or less intermediate appearance (as on the thigh). These manifestations, together with the bacteriological findings suggested that the condition was a mixed one, transitional from tuberculoid to lepromatous. The process did not continue in that direction, however, for a few months later the lesions had subsided markedly, the face returning to approximately normal appearance; the ultimate outcome is not known. The case may be looked upon as borderline, differing considerably from the persistent ones studied in Cebu but no less difficult to classify.

COMMENT

The cases cited serve to show, if nothing else, that transformation from the resistant, tissue-reactive ("allergic") tuberculoid form of leprosy to the anergic lepromatous form is a thing not easily accomplished, that the influences which determine the essential nature of the tuberculoid form are not easily abolished. A case may seem to have gone far in that direction, as regards the morphology of the lesions, their bacteriological content, and even their histology, to say nothing of the response to the lepromin test, yet will be proved by its subsequent course not to have become lepromatous in its actual character. That such cases may be mistakenly thought to have undergone transformation is not surprising, especially when it is considered that it has not been so long since we have come to recognize as tuberculoid, instead of lepromatous, the more ordinary bacteriologically positive major tuberculoid cases in reaction.

That transformation of such cases may occur it would be rash to deny. It is greatly to be hoped, however, that those who have the opportunity of observing the phenomenon will report in detail, with data on the clinical, bacteriological, histological and immunological changes, cases that have been followed through their

course. From the experiences here related it is obvious that follow-up observations are absolutely indispensable, for one thing to eliminate those borderline cases which subsequently clear up after the manner of ordinary reaction tuberculoid cases, for another thing to ascertain what those that persist indefinitely in the borderline state may come to look like, and yet again to learn if those that actually undergo transformation take on the aspect and follow the course of ordinary lepromatous leprosy. In the meantime, it is evident that caution is in order in pronouncing a case transformed. *

Summary

The question of the prospect for absolute cure, or on the other hand that of transformation to the lepromatous type, of active major tuberculoid cases, especially those that at one time or another have been found bacteriologically positive, is discussed.

Out of twelve such cases observed at Cebu for several years, no less than seven have relapsed at one time or another after apparently complete recession of the disease. In one instance there had been a period of five years without trouble. It is suggested that the feature of relapse in tuberculoid leprosy is worthy of more attention than it has received.

Lepromatous transformation has not as yet occurred in any of these cases. Two of them, however, have persisted for three years and more in an unstable, " borderline " condition, the picture dominated by repeated papular eruptions, the lesions atypical clinically and histologically. Another borderline case of decidedly different aspect seen in China is cited; it presented at the same time apparently lepromatous, tuberculoid and intermediate lesions and was looked upon as transitional, yet later recession occurred as is common in ordinary tuberculoid leprosy.

At one time in one of the two persistently borderline cases at Cebu, and in a third one when it relapsed after two years of apparent recovery, there have been lesions of a kind designated " relapse tuberculoid," more or less suggestive of lepromatous development both morphologically and bacteriologically, and also histologically in the one specimen examined. These lesions look not unlike lepromata, especially with respect to their tendency to taper off to and diffuse into the adjacent normal skin; and in

* Since this manuscript was prepared there has come to hand an article by Davy 6 in which he emphasizes the need of careful and repeated clinical study of cases. He mentions borderline cases as a field for investigation and describes a condition, supposedly lepromatous, which seems very likely to be essentially of the nature of the persistently borderline cases studied at Cebu, though apparently the former condition differs in the progression of the eruptive lesions.

contrast with the gradual central recession of typical tuberculoid leprids they typically surround or adjoin, the infiltration ending abruptly, " immune " areas which are the sites of previous tuberculoid lesions. The subsequent course of the disease in both cases has shown conclusively that they had not undergone lepromatous transformation, but that the lesions were essentially of lepridic character.

Two reported cases of apparently similar nature are cited, one recent and one old, of the form then called " tubero-macular ". Such reports, and other evidence from current literature, afford reason to believe that lesions of this atypical " relapse tuberculoid " kind have at times been accepted as evidence of lepromatous change.

Experience indicates that there may exist the paradoxical situation of a case with lesions that, so far as can be identified by known criteria, are histologically lepromatous but that may behave clinically like ordinary tuberculoid lesions. Therefore, disconcerting as it may be, the histological findings cannot always be regarded as diagnostic in atypical cases of the kind under consideration. The situation is further complicated if, as seems to be the case, the lepromin reaction may be negative.

The conclusion is obvious that transformation of a tuberculoid case is not readily accomplished, and that caution must be exercised in diagnosing it. This matter, especially, calls insistently for careful investigation.

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LEPROSY TREATMENT WITH GRASSET'S TUBERCLE ENDOTOXOID

INTERIM REPORT

A. R. DAVISON

On the supposition that there may be a group antigen for the mycobacterium leprae and the mycobacterium tuberculosis it was decided to try the effect of " Grasset's Tubercle Endotoxoid " on a series of cases of leprosy. This was prepared and presented to us by the South African Institute for Medical Research, Johannesburg.

Clinical results on the treatment of human tuberculosis have been exposed in several papers by E. Grassett:—

1. C. R. Acd. Sci. Paris 1935, t.200, 1889.
2. C. R. Intern. Congress Pediatrics, Rome, 1937. Acta Paediatr. 22, p. 364.
3. Tubercule; 1939; vol. 22. p. 397.
4. Proc. Tranv. M. Med. Off. Ass. 1940. vol. 19, p. 239.

Principles and methods of préparation :

According to the method described by E. Grasset (1935; 1939) tubercle endotoxoid consists of the antigenic, water soluble fractions obtained from tubercle bacilli by an extraction process of repeated freezing at low temperature. By submitting the resulting antigen to the detoxicating action of formol at incubator temperature, after the addition of hydrolyzed peptic medium, an atoxic stable vaccine " tubercle endotoxoid " is obtained, which has retained the antigenic properties of the original endotoxin. It can be injected in doses of several c.c. without giving rise to toxic or allergic symptoms in either normal or tuberculous subjects.

The following types of cases were selected for treatment with Grasset's tubercle endotoxoid. Where possible similar cases were selected as controls. They were left on routine anti-leprotic treatment and their condition was noted in November and again in June.

		Classification
1.	Advanced nodular leprosy with failing vision ...	L.3
2.	Maculo anaesthetic tuberculoid minor (acute) ...	Nt.2
3.	" " " " (chronic) ...	Nt.2
4.	" " " major (acute) ...	Nt.2
5.	" " " major (chronic) ...	Nt.2
6.	Lepromatous infiltration with discrete nodules ...	L.3
7.	" " " lepromatous ulcers ...	L.3
8.	Neural case with positive nasal smears and no macules	N.1

9.	Early maculo-anaesthetic with new macules	N.1
10.	Diffuse lepromatous infiltration	L.2
11.	Lupus vulgaris	

The injections were given subcutaneously bi-weekly commencing at 0.05 c.c., and rising each week until 2.0 c.c. were given at each injection. The cases were treated for 6 months.

Local reactions were experienced in several instances in the first two weeks. These varied from tenderness at the site of the injection to brawny swelling of the arm which passed off in 48 hours. Case No. 2 was not satisfied with his progress and asked to have daily intradermal injections as well.. This was done in 1 c.c. doses during the month of June, with no obvious beneficial effect.

In November, 1939, each case was Mantoux tested, the sedimentation index and the weight were recorded. A clinical description of the lesions was recorded and the case was photographed. Treatment was commenced in December, 1939.

CASE RECORDS

Case 1. Vision very weak, eyes not painful but watery. As a result of iritis and keratitis the oculist reported " Narrow stiff pupil and cataract on right side, vision being 2/60. Fundus cannot be observed any more. His vision will gradually but slowly deteriorate a little more. The left eye is atrophic."

November, 1939: Clinically he was noted to have erythematous nodular infiltration of face and limbs with occasional ulcerating nodules. Back and chest covered by infiltration varying in colour from red to brown.

Sedimentation index 42. Weight 135 lbs. Mantoux positive.

June, 1940: The report was—" Vision weaker. States he eats and sleeps better. Ulcerating nodules generally healed but have recurred on left hand and flank. No change in infiltration.

Sedimentation index 44. Weight 139 lbs.

Conclusion—no improvement.

Case 2. November, 1939: Clinical condition—dusky heavy spongy maculae on forehead, limbs and abdomen; erythematous and thickened left ear, healing macule back of neck but active (raised and erythematous) where it extends into scalp. Black desquamating border and spreading erythematous margin to macule on buttock.

Sedimentation index 40. Weight 145 lbs. Mantoux negative.

June, 1940: Lesions definitely less raised, not spreading, but erythema persists.

Sedimentation index 2. Weight 145 lbs.

Conclusion—slightly improved.

Case 2 (a) : (Control of Case 2.)

November, 1939 : Raised red pea-sized maculae on face, abdomen and back. Flat centres on shoulder.

Sedimentation index 32. Weight 150 lbs. Mantoux negative.

June, 1940 : No clinical change.

Sedimentation index 3. Weight 145 lbs.

Conclusion—has not responded as well as Case 2.

Case 3. November, 1939 : Clinical condition—active maculae with granular erythematous margins and erythema on chest. Isolated patches of residual erythema in sites of old maculae on back and legs.

Sedimentation index 1.5. Weight 165 lbs. Mantoux negative.

June, 1940 : Internal zone of erythema on chest maculae had faded but margins are still raised and erythematous. Other maculae unchanged.

Sedimentation index 1.5. Weight 156½ lbs. (possibly due to playing football).

Conclusion—slightly improved.

Case 3(a) : (Control of Case 3).

November, 1939 : Active maculae with raised dusky red margins.

Sedimentation index 1.5. Weight 150 lbs. Mantoux negative.

June, 1940 : Maculae active and coalescing.

Sedimentation index 2. Weight 150 lbs.

Conclusion—not improved.

Case 4. November, 1939 : Face is one erythematous slightly raised blush with suggestion of infiltration but smears show only occasional bacilli. Spongy maculae with silvery desquamation on trunk. Maculae more erythematous but not desquamating on limbs.

Sedimentation index 56. Weight 85 lbs. Mantoux positive.

June, 1940 : Lesions on face completely resolved leaving tissue papery skin. Erythema faded from maculae of trunk and limbs. Lesions now flat.

Sedimentation index 48. Weight 81 lbs. (plays football). Smears negative.

Conclusion—very marked improvement.

Case 4(a): (Control of Case 4).

November, 1939: Face is diffusely erythematous around multiple flat dusky healing maculae (tuberculoid major). Small erythematous maculae on back have coalesced into plaque on right flank.

Sedimentation index 1.5. Weight 150 lbs. Mantoux negative.

June, 1940: Infiltration absorbed in right flank. Erythema faded from face. Less erythema in other macule.

Sedimentation index 3. Weight 160 lbs.

Conclusion—improved but not to same extent as Case 4.

Case 5. November, 1939: All maculae on trunk and limbs have raised margins which are blackened and desquamating. There is diffuse erythema in a tuberculoid macule on buttock. Some isolated patches of raised erythema are present in one macule.

Sedimentation index 10. Weight 122 lbs. Mantoux negative.

June, 1940: Lesions show less elevation of the margins but erythema persists. There has been no spread of the maculae.

Sedimentation index 2. Weight 112 lbs.

Conclusion—slight improvement.

(No similar case available as control.)

Case 6. November, 1939: Discrete nodules on face project above diffuse infiltration. Ears not pendulous. Diffuse erythematous infiltration on abdomen. Nodules above kidney and on arm are ulcerating. Mottled maculae on chest and back.

Sedimentation index 45. Weight 130 lbs. Mantoux negative.

June, 1940: Treatment cancelled owing to oedema forearms, hands and feet. Trace albumin in urine. New erythematous maculae slightly raised on chest, abdomen and arms. No change in nodules.

Sedimentation index 45. Weight 118 lbs.

Conclusion—worse.

Case 6(a): (Control of Case 6).

November, 1939: Diffuse infiltration face with discrete nodules on nose and chin.

Sedimentation index 26. Weight 145 lbs.

June, 1940: No change clinically.

Sedimentation index 60. Weight 145 lbs.

Case 7. November, 1939: An advanced lepromatous case showing heavy infiltration of face with ichythotic margins to maculae on trunk. Very weak—has to be carried. Selected to

see the effects on ulcers of legs which are very deep with grey anaemic sloughs.

Sedimentation index 60. Weight 115 lbs. Mantoux positive.

January, 1940: Ulcers improving—now are red, granulating and closing in from sides.

February, 1940: Ulcers deeper with punched out margins. Granulations pale.

March, 1940: Too ill to disturb.

Conclusion—Case unsuitable for investigation.

Case 8. November, 1939: An old-standing maculo anaesthetic case. The maculae have faded leaving traces on shoulders and front of thighs. Perforating ulcers both feet. Gynaecomastia. Has been clinically arrested for two years but every routine monthly smear is positive.

Sedimentation index 59. Weight 125 lbs. Mantoux negative.

June, 1940: Ulcers on foot healed. Routine monthly smears continued positive until February. Scanty bacilli found in March. Negative in April, May and June.

Sedimentation index 42. Weight 127 lbs.

Conclusion—satisfactory progress but conclusion now would be premature.

Case 8(a): (Control of Case 8).

This case is healed to all clinical appearances, but monthly nasal smears are consistently positive.

Sedimentation index 10. Weight 165 lbs.

June, 1940: New maculae with pink puffy margins on chest. All smears from November to June have been positive except the one of May month.

Sedimentation index 2. Weight 145 lbs.

Conclusion—not so satisfactory as Case 8.

Case 9. November, 1939: Maculae on face raised and red with margins which fade into normal skin. Faint erythema on forearms. Maculae are plaque-like around left elbow. Multiple raised new maculae on left buttock. He is husky and well-formed but posture is bad, abdomen protrudes and chest is hollow.

Sedimentation index ½ (Repeated 1). Weight 140 lbs. Mantoux negative.

In April developed crepitations of apex and large pleural effusion. Pulmonary tuberculosis was diagnosed despite negative sputum.

June, 1940: Marked improvement in all leprotic lesions which are less erythematous and less raised. This is what we would

expect in any patient with active tuberculosis even without anti-leprotic treatment.

Sedimentation index 27. Weight 127 lbs. Mantoux negative.

Conclusion—not possible to evaluate effect of treatment.

Case 9(a) : (Control of Case 9).

November, 1939 : Dusky margins with raised erythematous centres to maculae on face. Margins becoming granular but still erythematous on abdomen. Multiple new maculae on back with raised margins.

Sedimentation index 53. Weight 150 lbs. Mantoux positive

June, 1940 : The erythema and raised margins have subsided on face. The maculae are flat and inactive on trunk.

Sedimentation index 1. Weight 139 lbs.

Conclusion—improvement more marked than in control.

Case 10. November, 1939 : Diffuse infiltration face, slightly more thickened over eyebrows. Ears slightly pendulous. Diffuse erythematous infiltration chest and arms, heavier infiltration down spine.

Sedimentation index 40. Weight 135 lbs. Mantoux negative.

June, 1940 : No change in clinical condition.

Sedimentation index 60. Weight 128 lbs.

Conclusion—no improvement.

Case 10(a) : (Control of Case 10).

November, 1939 : Diffuse infiltration of face with coalescing plaques on trunk and limbs.

Sedimentation index 28. Weight 120 lbs.

June, 1940 : Infiltration of face, flanks and forearms worse.

Sedimentation index 38. Weight 131 lbs.

Conclusion—disease has advanced more rapidly than in control Case 10.

Case 11 : This case was admitted in April, 1939, as a certified leprosy patient. On the face and left buttock were identical large lesions. The margins were elevated and described as " blackish fungating irregular edge which bleeds easily ". The centres were of healed and glistening scar tissue. There was no anaesthesia of the face and only slight impairment of sensation in one portion of the scar on the buttock. No other nerves were involved. No leprosy bacilli could be found. Cultures on three media, Dorset, Sabourand and Harold were negative. Dr. Muir saw the case in July and agreed that it was probably lupus vulgaris as a

tuberculoid macule showing such destruction of tissue would certainly have shown more nerve involvement.

In November, 1939, there had been no change in the clinical condition despite anti-leprotic treatment. He was placed on T.B. endotoxoid and the lesions commenced to resolve.

In March, 1940, he was examined by the Annual Leprosy Board and was discharged. The lesion on the face was almost completely flat but on the buttock some elevation of the edge was still present in certain parts.

Conclusion—Lupus vulgaris responded to treatment by T.B. endotoxoid.

SUMMARY

1. Ten cases of leprosy and one case of Lupus Vulgaris were treated for six months with Grasset's Tuberculosis Endotoxoid.
2. The Lupus Vulgaris was markedly improved (Case 11).
3. One case (Case 4) of leprosy—an acute tuberculoid major—was markedly improved.
4. Cases 2, 3 and 5 were slightly improved. These were neural cases of the tuberculoid type.
5. Case 8 who had persistently positive nasal smears has now been negative for three months.
6. No beneficial effect was obtained in the cutaneous type (Cases 1, 6, 7 and 10).
7. Case 9 developed signs of presumable pulmonary tuberculosis while undergoing the treatment.
8. The greatest improvement was obtained in a Mantoux positive case.

DISCUSSION

The improvement obtained in all the neural cases of the tuberculoid type, particularly Case 4, points to the fact that Grasset's endotoxoid has some beneficial effect on tuberculoid lesions. We are satisfied that the improvement in Case 4 is greater than we have previously obtained with any other medicaments. It is our intention to select other cases of this type for further study.

I have to thank the Secretary for Public Health for the Union of South Africa for authority to conduct these experiments at the Pretoria Leper Institution. Also I have to thank Dr. Grasset and the South African Institute for Medical Research for the material as well as the interest and help which was given me.

REVIEWS

International Journal of Leprosy, Vol. No. 2, April-June, 1940.

Familial Susceptibility as a Factor in the Propagation of Leprosy in North America, by W. L. Aycock. Three areas of leprosy frequency in North America are dealt with in this paper. The first area includes Wisconsin, Minnesota, Manitoba and Saskatchewan, where Norwegian, Swedish and Russian immigrants with leprosy, either active or latent, are described. In the second two areas, viz. New Brunswick and Louisiana, the disease is supposed to have originated with French settlers expelled from Nova Scotia some 150 years ago.

"The studies of these two foci, which are recorded in this paper, indicate that leprosy tends to recurrence in successive generations in certain family lines in which intermarriage is common. Moreover, though the two localities are widely separated, the same family lines have been involved in both places. In another small focus the records of cases show a high frequency of relationship to previous cases in the same and in distant localities. In still other groups, where family studies have not been carried out, the restriction of the disease to certain minority groups, originally from areas of prevalence, are indicative of the operation of the same familial factor in the occurrence of the disease."

[The fact that intermarriage is common in a community may indicate that the community is exclusive, and either unwilling or unable to mix with surrounding communities. The opportunity of spreading infection to its own members would be increased in proportion as that of spreading it to surrounding communities was diminished. Therefore, while considering special susceptibility as a cause of familial leprosy, the effect of social customs in exclusive families should be kept in mind. E.M.]

The Lepromin Test in Lepra Reaction, by J. O. Nolasco.

This paper is summarised as follows:—

"Of forty-eight hospital patients with lepromatous leprosy in various states of lepra reaction that were tested with lepromin, only four, or 8.3 per cent, gave clear-cut positive reactions—one 3+ and three 2+. The 1+ reactions are considered not significant, a point to be discussed in a subsequent paper. Irrespective of whether the patients were in the reaction state or not, retests made from two to four months after the original ones tended to give from slightly to moderately stronger lepromin reactions in twenty-four out of forty-eight patients (including the controls) that were retested. No apparent relation in the intensity of the lepromin test to the presence of lepra reaction can be shown in the different groups into which the cases had been arbitrarily classified. Similarly, no deductions can be made concerning the intensity of the lepromin test in relation to the time of the injection after the onset of lepra reaction in the mild, or mild brief and mild recurrent cases. From the results of these studies, no apparent conclusion can be drawn to support the hypothesis that lepra reaction is a manifestation of allergy. Lepra reaction remains an obscure condition."

[In lepromatous reacting cases almost the whole surface of the body is infected, though visible lesions may not show in certain parts of the skin. The injection of lepromin, a bacillary

suspension, into such skin is only like "sending coals to Newcastle", and an allergic reaction in such cases cannot be hoped for, especially as a non-reacting part of the skin would naturally be chosen for the inoculation. This does not mean that an allergic reaction is not taking place in other parts of the skin where perhaps the *gloea* surrounding large masses of bacilli has given way, bringing these bacilli in contact with the surrounding tissues. E.M.]

The Histopathology of the Reactive Phase of Lepromatous Leprosy, by N. I. Ermakova.

"The histopathology of the leprous process in the reactive stage warrants the conclusion that lepra fever represents an allergic state. The degenerative and necrotic changes of the collagenous element and of the smooth muscles (fibrinoid swelling), noted in the reactive nodules are the morphologic expression of the hyperergic reaction of tissue sensitization. In some instances of lepra fever the hyperergic reaction passes with hemorrhages and necrosis analagously to the Schwarsman phenomenon. The changes in the reactive capacity of the organism are reflected in the cellular picture of the specific leprous tissue. There appear numerous lymphoid, plasma and polymorphonuclear cells. In the reactive nodules in which suppuration develops there occurs considerable degeneration of the bacilli, even to the loss of acid-fastness. The polymorphonuclear leucocytes which invade the leprous infiltrations exercise a fermentative action upon the cells of the specific granuloma and the bacilli."

The paper is illustrated with several excellent photo-micrographs.

Leper Colonization of Kengtung State, Burma, by R. S. Buker. The author describes antileprosy work among the primitive people of the Shan States in the corner between Burma, Thailand and China, where it is calculated there are 4,000 lepers among 230,000 people. First a central colony was started at Kengtung, the chief town. The people were trained to help with treatment and were fed with a minimum of expense. Later other colonies were begun to which trained workers were drafted from the central institution. The latter were on a self-supporting basis, free treatment and a little help in building houses being all that was given.

"With a budget of less than one rupee per month per leper, which amount has been increased by one half, or in some cases doubled, we have established nine colonies in which 900 lepers are receiving treatment."

Murine Leprosy and Carotinoids, by F. Ribeiro. This paper is summarised as follows:—

"In this study of the effect of substances of the carotinoid type in the treatment of murine leprosy, it has been observed that there is a difference in the distribution of the Stefansky bacillus in the organism of mice according to whether the germs used in the inoculation are alive or have been killed by heat (autoclaving at 120° C for 20 minutes). Within the period of 80 days after inoculation pieces of the liver were always negative when the inoculated germ was dead, and positive in the majority of cases when the germ was alive. Similar though less clear-cut

findings were obtained with regard to the spleen. With infected animals treated with a crude substance of carotinoid type it was observed that the distribution of bacilli was the same as if they had been inoculated with dead germs, and that was also true when the treatment was with one of the fragments (fraction A) of the primitive substance. Two other fractions (B and C) were inactive, although it would appear probable that the active substance (fraction A) originates through the oxidation process from fraction C. A substance obtained in the laboratory through oxidation of raw carotinoid (fraction D) showed activity in a small number of observations.

International Journal of Leprosy, Vol. VIII. No. 3, July-Sept., 1940.

Skin Reaction Tests with Tuberculin-type Extracts of Leprous Spleens. This is a report by the Joint Committee on Leprosy Skin Tests in the Philippines working with a view to discovering a reliable test for leprosy on the lines of tuberculin in tuberculosis. Extracts were made from the spleens of three fatal cases of leprosy in which numerous acid-fast bacilli were present, together with control tests of similarly prepared antigens from healthy spleens. Three different preparations were tried, but the contact and control healthy groups of patients gave more positive reactions within twenty-four hours than did leprosy patients. They therefore conclude that the protein extracts of leprosy spleens used in the tests did not contain any substance giving a specific response in leprous patients.

An Attempt to obtain Specific Antigens from Leprosy Spleens, by Howard J. Henderson. This is a research on similar lines to the above which also yielded negative results.

The Lepromin Test in Lepra Reaction. II. Histology of the Reaction Lesions and Persistence of the Injected Bacilli, by J. O. Nolasco. This paper, which is illustrated by micro-photographs, reports a study of biopsy material from thirty-five of forty-eight lepromatous cases during lepra reactions following the lepromin test. The specimens in the cases giving three-plus reactions both showed histological tuberculoid pictures, as did four of five of the two plus reactions, but only three of nineteen one-plus reaction cases showed such changes. In the two three-plus reactions the test sites suppurated and in one of them numerous bacilli were found in the necrotic focus. Leprotic foci were found in 33 of the 37 lepromatous cases in the healthy sites of the lepromin tests.

Specific Affections of the Folicular Apparatus in the Skin in Leprosy, by A. A. Stein. The writer has found no records of a peculiar affection of the follicular structure of the skin which he

has met with in 33 per cent of his cases. The lesions appear clinically as yellowish-brown, somewhat sunken follicular spots with atrophic epithelium. Histologically specific granuloma with lepra cells and bacilli are found, which rapidly destroy the hair follicles and hairs. The skin of the lower extremities is principally attacked and the follicular lesions form starting points for the formation of lepromatous granulomata.

Borderland Tuberculoid Leprosy, by H. W. Wade and J. N. Rodriguez. This is a detailed account of three cases illustrated by photos. Two for long periods remained in a " borderline " condition repeatedly suspected of becoming lepromatous, and the other was of a " relapsed tuberculoid " type.

Bullous Tuberculoid Leprosy, by J. N. Rodriguez and H. W. Wade. In this case the sudden appearance of numerous bullae, followed by ulceration and finally leading to the formation of pigmented, achromic and spotted scars, suggests that it was one of the so-called " lazarine leprosy."

The History and Distribution of Leprosy in Formosa, by Yutaka Kamikawa. The island of Formosa is peopled by the descendents of Chinese immigrants of the seventeenth century, who largely displaced the aboriginals. Little is known of the early prevalence of leprosy here, but the author now records the results of a recent survey. This showed an average rate in samples of seven localities of 2.2 per mille, or double the number previously known to the police. This would bring the 1936 police figure of 827 cases in the island up to 1,241. An examination of 500 cases in government or private leprosaria showed the following differences from the conditions met with in Japan. In Formosa leprotic alopecia was comparitively rare, but ulcers and nodular cases were more frequent. The Government propose to establish a leper asylum for the 1,000 open cases they estimate to be present " to the end that the disease may be eradicated within the next few decades."

" Alfon " treatment.—In *Leprosy Review,* Vol. XI. Apr., 1940, pp. 114-115 appeared an English abstract by Dr. J. W. Lindsay from the report in Portuguese of the Sao Paulo Leprosy Association on the " Efficacy of the Alfon Treatment of leprosy " which appeared in the *Revista Brasileira de Leprologia* VII., 4 Dec. 1939, p. 456, which was not favourable to the claims of the originator of the method. A letter has been received from Dr. Gomes maintaining and defending the findings as to the value of

the " Alfon " treatment, and asking for further trials of the method. During the last few months Dr. Muir has had a voluminous correspondence on the subject with the advocates of the method, and has maintained a sympathetic attitude and arranged to look further into the question during a visit to Brazil. That visit has had to be postponed for a time owing to the war conditions, but Dr. Muir has already proceeded to the West Indies on leprosy work. The controversy can only be decided by further trials by competent authorities in different parts of the world, which must be awaited. Advantage will be taken of any offers by British workers to carry out carefully controlled tests of this and any other methods which appear to be worthy of trial.

Leprosy in India, Vol. XII, No. 3, July, 1940.

Leprosy in Kengtung, Southern Shan States, Burma, by Richard S. Buker. This state has a scattered population of 300,000 and it borders on China and Siam. During 1939-40 groups of villages inhabited by different races have been surveyed with the following results. Among slightly less than 10,000 people examined, 609 cases of leprosy were found, or 6.1%. The Lalu race showed the high rate of 14.2%, the Kachins came next with 8.3 and the Shans and Kaws respectively had 3.6% and 3.3%. The one Chinese village showed no cases. In the Shan valley the disease is said to have increased after a famine. It was noticed that the incidence of leprosy in the different races was in inverse proportion to the numbers showing enlargement of their spleens. Inquiry also showed that all the affected races eat forms of colocasia. The conclusion was come to that leprosy is an increasingly serious problem in Kengtung State, in which ten leper colonies now accommodate a total of 1,100 patients.

Tuberculoid Leprosy affecting the Palpebral portion of the Lachrymal Gland, by R. G. Cochrane and T. B. M. Sloan.

This short note records a case of this rare complication, illustrated by a photomicrograph showing giant cell formation and also the clinical appearance.

This number also contains a review of *Leprosy* by Sir Leonard Rogers and Ernest Muir. Unfortunately it consists essentially of a statement of the points in which the reviewer's personal opinions differ from those of the authors. We would suggest that the readers of *Leprosy in India* would be well advised to read one of the more instructive reviews in the *British Medical Journal, The Lancet, The Bulletin of Tropical Diseases* and the *International Journal of Leprosy* before forming their opinions on this work.

The remainder of this issue is taken up with Notes on Early Leprosy Institutions in India, a reprinted article, abstracts and reports of local interest.

REPORTS

Annual Report of the Indian Council of the British Empire Leprosy Relief Association, 1939.

This report shows steady progress with the campaign against leprosy in our densely populated Indian Empire. The Madras branch has been re-organized as a separate entity from the Provincial Public Health Department, which had previously held charge of its administration. Under the present arrangements the routine propaganda, survey and treatment work is carried out by the Government, while our provincial branch concentrates on the special work of epidemiological and other research under the general supervision of Dr. R. G. Cochrane of the Lady Willingdon Leper Settlement, Chingleput. One result has been increased demand for special training in the subject of leprosy.

Research has been continued under Dr. Lowe in the Leprosy Department of the Calcutta School of Tropical Medicine, where 1,347 new cases of the disease were examined, 1,054 of which were neural cases and 293 lepromatous ones. About 300 cases attend for treatment every week and the rest are referred to other centres. The previously reported rise in the clinical and bacillary infection between April and September has been confirmed during 1939. During epidemiological studies in a rural area of Western Bengal and in a Santhal colony the very high proportion of 20 neural to one lepromatous case has been observed. Methylene blue was found to have no action on the staining properties or on the pathogenicity of the rat leprosy bacillus in vitro, contrary to some previously published findings of French authorities. In hamsters splenectomy was not found to influence their susceptibility to infection with human leprosy bacilli. These experiments made it very doubtful if the organisms actually multiply in the tissues of the inoculated hamsters, although they do persist for a long time and in large numbers in the implanted nodules.

The usual training of leprosy workers has been carried on. The major part of the report is taken up with the activities and accounts of the provincial branches which are mainly of local interest.