EDITORIALS

Lesions of the Testis

The report by Job and Macaden which appears in this issue, on the finding of tuberculoid lesions in the testes of borderline cases, we regard as a particularly noteworthy one.

In the first place it is, so far as we are aware, the first report of the kind. The author’s statement that the occurrence of such lesions is not well documented in the literature is decidedly an understatement. Nothing on that subject has been found in any textbook on leprosy published since the tuberculoid lesion has been generally recognized, not even in the exhaustive monograph on tuberculoid leprosy by Lauro de Souza Lima and Nelson de Souza Campos (1). An admittedly sketchy search of the periodical literature of the past thirty years has been equally unrewarding.

The fact that the author’s study material was obtained by biopsy is hardly less remarkable, at least to one who works in an institution where the patients are often reluctant to permit biopsy of skin lesions and not infrequently refuse, and where testicle biopsy is unthinkable. In an earlier article on testicle changes in cases with gynecomastia, Job (2) told of a total of 35 biopsy specimens, 21 of cases with gynecomastia and 14 “control” cases without it. Desire for hospitalization could not have always been the incentive, for the controls were all inpatients. Of the gynecomastia cases only 1 was borderline, whereas of the controls 6 were of that kind.

Only two other reports which tell of biopsies of the testes have been encountered. Grabstald and Swan (3), Carville, studied 29 specimens from lepromatous cases also in connection with gynecomastia; 3 had been obtained by biopsy. A report by Pedestran Editorials are written by members of the Editorial Board, and opinions expressed are those of the writers.

was a single nodule which had developed in a "probably" lepromatous case that had been bacteriologically negative for 3 years (but lepromin-positive for 7 years). Sections of the nodule showed fibrosis, with foci of lepromin cells and bacilli.

It would seem that it was not simply accidentally that Job and Macaden found these tuberculoid lesions only in borderline cases, and apparently seldom in them. That this is the fact is not specifically stated, but no such lesion was described for any of the 7 borderline cases in Job's earlier report, although he told of "focal collections of epithelioid cells" in some of the cases in the stage of invasion. Borderline cases in the ordinary sense begin as tuberculoid, the lepromatous elements developing secondarily as a result of subsequent reactional episodes (2). It seems probable that the testicular tuberculoid lesions were acquired in that earlier stage, perhaps in a reactional phase. Whether or not the secondary lepromatous changes had any influence in the matter cannot be said.

In reactional tuberculoid leprosy the small metastatic nodules, often abundant and widespread, obviously result from dissemination of bacilli by the blood stream. Since the testis is especially favorable to the location of the bacillus, one would expect that some degree of orchitis, observable clinically, would occur in at least an occasional case. Apparently, however, that condition has never been observed.

THE TESTIS IN NONLEPROMATOUS CASES

From the lack of any evidence to the contrary in the recent literature, it seems that the nonlepromatous cases—which term covers the indeterminate, the simple maculoanesthetic, and the frank tuberculoid forms of the disease—have been dismissed with regard to involvement of the testis. The only recent statements seen that are at all related to this matter are to the effect that gynecomastia does not occur in tuberculoid cases (5). Yet certain long-forgotten reports from Japan give an entirely different picture about both the finding of bacilli and of pathology changes. This refers to reports by W. Kobayashi, who in the 1920's studied the testis assiduously.

In 1924, Kobayashi reported (4) a method of demonstrating bacilli in the testis by

5. The possibility that the borderline condition may sometimes develop in cases of the indeterminate kind is admitted in the Madrid classification scheme, but we are not aware that the true borderline condition arising in such cases (not considering the "diminishing macular" cases, which clinically is very different) has ever been recorded.
6. Job (7) and Kiniura and Davison (1) found no tuberculoid cases to have gynecomastia. (They included 29 tuberculoid cases in their study of hormone excretion and liver function, a matter of interest for a comparison with lepromatous cases and normals.) Grabstald and Søre (8) had the "impression" that gross testis atrophy is far less common in tuberculoid than in lepromatous cases, but nothing is said of actual findings in the former group.
puncture. In 1925 (9), he reported his findings in 100 cases, only 1 of those leprosy tubercular. Of the 98 maculosa (tuberculoid) cases, 90 gave positive puncture sauces (36 of them 2+ or 3+); of 7 neural cases, 5 were positive; of 2 "suspect" cases, I was positive, a total of 72 positives in the 98 non-lepromatous cases. (The nodular case was 3+ positive.) In 1928 (10) Kobayashi published a monograph on the gross and microscopic findings in 35 autopsy cases, with a 2-page summary in German in which no figures are given. It is said that leprosy changes were found, although in lepra nerves they were sometimes slight.

"[Histologically] significant inflammatory granulations are recognizable in nearly all cases of leprosy nerves; the seminiferous tubules are hard to make out and their epithelium is hyalineized... In few cases (of nodular leprosy) is hyaline degeneration of the testicular tissue encountered."

In another monograph, published in 1929 (11), Kobayashi dealt at length with the visceral changes found at autopsy in 90 cases. Of the 49 males, 18 were non-lepromatous (15 nervous, 3 maculosa). Grossly, the consistence of the testes was abnormally hard in 33 of these 18 cases. The seminiferous tubules appeared normal in only 4; they were distinguishable here and there in 4, and quite indistinguishable in 8. Microscopically, the tubular lumens were normal in 4; in 5 they were narrowed or otherwise abnormal, while in the rest (as in the lepromatous cases) these were generally not to be seen. Spermatozoa were seen in only 3 cases of the entire 94, 2 of them non-lepromatous.

Mitamura and Ogawa (12), in 1937, contributed a study of 150 autopsies. They stated—and reported in the summary—that the visceral changes described for leprosy leprosy are not to be found in cases of the neural type; "except for those of the testis..." (italics added.) They also stated that "the tuberculous change is found only in the skin and nerves"—this being before such lesions were found in lymph nodes by Schulman (13), and others, and in biopsy specimens of the liver by Okada (14), Galván (15), and others. These statements are not necessarily contradictory; apparently it was meant that the tubercular lesions of neural cases are essentially similar to those of lepromatous cases. In Mitamura's Atlas (11), all of the seven pictures of testicular lesions are specified as of the lepromatous kind.

Beyond these references nothing on changes of the testis in non-lepromatous cases has been turned up. Kobayashi's remarkable findings appear to have been ignored, at least outside of Japan. With regard to them, it may be asked, were none of the changes in such cases of tuberculous nature? Did the changes in any of the cases consist solely of atrophy of the seminiferous tubules, with or without hyalinization, and in the absence of leprous infiltration or at a distance from it?

11 KOBAYASHI, W. Uber die tuberkulose Leprosen. Monograph Acta Dermatologica, Series Dermatologica, 1929, No. 4, Institut Dermatologisch, Kyoto Imperial University, 267 pp. (In English; abstract in German, and in Japanese; English abstract).
15 OKADA, S. Pathological studies by means of biopsy on the changes in the livers of leprosy patients and marine leprosy rats, Report I. Tuberculoid granuloma found in the livers of non-lepromatous cases by puncture. Le Lepro. 22 (1953) 299-308 (in Japanese; English abstract).
The last question is asked because, in our autopsy work at Culion in the 1920's, testes with such lesions in sections were occasionally encountered. The only thing that can be said of the case type is that only bacteriologically positive cases, supposedly lepromatous, were admitted to this institution; the tuberculoid conditions were not recognized at that time. The only photomicrograph that was made of the condition referred to is reproduced here. There is no specific infiltration of the area shown, although of course it cannot be said that there was none elsewhere in the organ.

At about that time we became aware of the findings of Long (19) of allergic sensitivity of the testis in tuberculous guinea-pigs, due to some substance liberated at the site of infection. Injection of very small amounts of tuberculin into the testis of infected animals caused profound degeneration and later complete atrophy of the tubules. The spermatocyte was the cell chiefly injured, and the reaction was therefore called the spermatocyte reaction (19). It was found by Stewart (20) that this reaction could be obtained earlier than that in the skin. With respect to the quantity of tuberculin required, the spermatocyte reaction was produced by 0.1 c.c. of a 1:10,000 solution of tuberculin, whereas the skin reaction required 0.5 c.c. of a 1:5,000 solution of tuberculin.

reaction is about 10 times as delicate as the skin reaction, in which the cell chiefly injured is the endothelial cell of the blood vessels.

Similar results were later obtained in guinea-pigs infected with Bacillus abortus (21). Finally, these observations were extended to experimental blastomyecosis in the guinea-pig (22). In that condition, it had been reported, skin hypersensitivity is not demonstrable; Skin tests of the animals involved in Long's experiment showed that they were not sensitive to a "blastomycen" made from cultures, or to the whole dead microorganisms. When the antigen was injected into the testis, however, it caused a reaction, milder in degree than but identical in type with that of the tuberculin reaction. Photomicrographs show the lack of any change after one month in a normal guinea-pig, the acute reaction in an infected animal at two days, and the profound atrophy of the tubules after a month (20).

It has been learned (personal communication) that in 1961 this type of experimentation had been revived by W. H. Feldman and associates, who had made related observations with another mycobacterial infection (23).

Now, to apply—speculatively—what may be called the "Long phenomenon" to leprosy. Lepromatous leprosy is a notoriously nonreactive form of the disease, being regularly negative to the lepromin test. Yet that is not to say that the testis may not be sensitized. Acute reactions, presumably of allergic nature, are a common occurrence but anomalous and unexplained. As a rule the testes are badly involved by lepromatous lesions before the patient comes to autopsy, and the Long phenomenon—if it occurs in such cases—may be overwhelmed by the other changes. The tubular atrophy, we venture to say, is exemplified by the photomicrograph reproduced here.

Lepromatoid leprosy is an entirely different matter. It is reactive to lepromin, and sensitivity is frequently observed in the tuberculin-like 48-hour Fernandez reaction. It would be strange, to say the least, if the testis were not equally hypersensitized if not more so. Presumably the antigen, the infecting agent, will reach it sooner or later. It certainly should in reactional tuberculoïd leprosy, in which there are more or less numerous metastatic skin lesions obviously due to the dissemination of the bacilli by the blood stream, and presumably the highly receptive testis gets its share of them.

What may result cannot be said with any assurance; such cases are seldom seen at autopsy. The effect may be like one of the photomicrographs shown by Long (21), in which there appears a small hematoogenous tubercle in the testis, with a zone of tubular atrophy around it.

**Experimention**

As for animal experimentation, the possibilities seem limited. Only in the dog are strong responses to lepromin elicited, with marked sen-

sitization shown on reinjection. Intratesticular injections of small amounts of lepromin, or of a lepromin filtrate (a "lepromin"), might give significant results. The guinea-pig also offers possibilities, although the skin is normally nonreactive to lepromin, as with blastomycosis. It would be interesting to see whether, after one or more intracutaneous injections of lepromin, the testes would be specifically sensitized.

The same is to be said of the monkey, the skin of which is not sensitized by human lepromin. Observations of specificity of the sensitivity might be made in that animal, which becomes actively sensitized by a Steffansky lepromin made of the nodules of rat leprosy (25).

It is to be hoped that someone, somewhere, will undertake the observations and experiments indicated (26).—H. W. W.

25 Wade, H. W. Unpublished observations.
26 Not all of the references to the reports of this work have been seen personally. They are all given here for the benefit of anyone who may wish to look them up.