CORRESPONDENCE

This department is provided for the publication of informal communications which are of interest because they are informative or stimulating, and for the discussion of controversial matters.

THE ISOPATHIC PHENOMENON IN LEPROMATOUS LEPROSY

To The Editor:

This communication is in reply to questions about the experience of our group in provoking, in cases of lepromatous leprosy, what we call the isopathic phenomenon; that is, reaction lesions which histologically are of lepromatous structure in some degree, regardless of the nature of the inoculum—tuberculin, milk, peptone, living BCG, or killed or living leishmania flagellates. [For references to the several reports on the subject, see an editorial in this issue.]

1. I believe that the lesions produced are an *imitation* of lepromatous tissue, that they do not represent local activation of the lepromatous process. In the first place, the same results have been obtained regardless of whether the patient had bacteriologically positive lesions in other regions or had long been recovered and bacteriologically negative. Furthermore, there is no accumulation of leprosy bacilli in the induced lesions, as would be the case were they actual lepromas. In general, the sections show bacilli—when any at all—in numbers corresponding to those found in other places in skin of the same appearance in the same patients.

The striking facts are (*a*) that the injection of living parasites, either BCG or leishmania flagellates, always brought about *clinical* lesions of the kind to be expected of them, but in most cases the *histologic* changes were similar to lepromas and were not the characteristic ones produced in the controls; and (*b*) that a considerable proportion of these induced lepromas, even those which we graded at 3+, showed no bacilli in the sections. So the answer seems "no" to the question of whether or not the changes found in the injection sites may possibly represent activation of invisible, "inapparent," lepromatous foci that might have been present where the injections were made. I do not know what other proof could be obtained that our findings were or were not due to such a process.

2. The possibility that we were simply finding old foamy collections and infiltrations that had been there before, was also given thought in our work. To begin with, each of the two cases of our first report had had two previous skin biopsies—from other areas, of course—which revealed no such foci. Then, early in the work, we did what we could to check on the point by a control series of 41 biopsies from 34 of the experimental cases. These control specimens were taken from sites very close to those of original ones, or from corresponding areas of normal-appearing skin. Among these 41 specimens, small foamy-cell islands (corresponding to our 1+ grade) were found in 10, and larger infiltrations (corresponding to our 2+ and 3+ grades) in 4; whereas 27, two-thirds of the lot, were quite negative. These control examinations were reported in our third article, and it did not seem worth while to repeat the findings in the later reports.

It is possible that in some proportion of cases the findings in the experiments with various dead materials could have been mistaken for inapparent lepromatous structures which were present before and were happened upon accidentally. Control specimens from nearby sites would not completely eliminate that possibility, for it is a

fact that sections from one level of a given specimen may show slight foamy-cell infiltrations while others from a different level would show none. However, the injection of living organisms caused macroscopic lesions, and these were histologically "leproma-like," of the most marked degree. We saw no way of proving directly that the phagocytic macrophages involved had accumulated under the influence of the inflammatory process and had undergone the foamy change secondarily.

3. It is true that in two or three reports we spoke of the foamy cells of the isopathic lesion as "sudanophilic," without elaboration. Early in our work we felt it necessary to eliminate the possibility that the structures we were finding might be due to some artifact occurring while excising the specimens or during fixation. We therefore made frozen sections, for fat staining, of a few specimens (about 6 or 8) and found Sudan-positive material in some of the foamy cells. We could not do that regularly, because there was not enough material. The cells of this reaction should certainly be studied more thoroughly.

4. We cannot say what kind of tissue reaction would result from such inoculations in tuberculoid or indeterminate cases because, apart from healthy controls, we have worked practically entirely with lepromatous cases, treated or untreated. We have very few tuberculoid cases available, and have not wished to say anything about reactions in that type of the disease.

In continuation of the work reported, I have been systematically studying all our contacts bacteriologically and by means of histological examinations of tuberculin reactions after 48 hours and lepromin reactions after 3 weeks. Tuberculin is used because in most patients it causes positive clinical reactions, especially since a large part of the population has received BCG inoculations. I do not yet know whether 48 hours is the best interval, or if it should be longer, but the tuberculin reaction generally disappears after some days. In further work I also expect to find out from early cases if, for whatever reason, the patient's phagocytes will go foamy before the leprosy infection becomes generalized. This will be a long-term job before definite conclusions can be reached.

Hadassah University Hospital
Jerusalem, Israel

FELIX SAGHER, M.D.