Letter to the Editor

After careful reading of the article of Kooij and Pepler “A Re-Evaluation of Tissue Reactivity to BCG, Tuberculin and Ink in Lepromatous Leprosy” (Dermatologica 122: 360 [1961]) I would like to add the following criticism since there are a number of inconsistencies in the paper.

Dr. Kooij and Pepler repeated some of the experiments which Waaler, Richter and ourselves have done independently, and in which we have come to the same conclusion, namely, that there exists a peculiar host reaction to various externally introduced substances similar to that in sarcoidosis as expressed in the Kveim test. In their experiments Kooij and Pepler used BCG, tuberculin and ink. Thirty five patients with lepromatous leprosy were injected with BCG. The results were given as follows:

1. “In 15 biopsies done between 30 hours and 9 days there was non-specific inflammation only in 3 of them and in 12 there was non-specific inflammation on a lepromatous background.”
   This lepromatous background is shown in an illustration depicting foam cell aggregates characteristic of lepromatous leprosy.

In the remaining 20 biopsies, which were taken between the 23rd and 65th day after the injection, epitheloid cell reactions with foreign body giant cells and without foam cells were noted.

Tuberculin was injected into 10 lepromatous patients. Again, in 6 of these 10 patients biopsies excised at various intervals, revealed a lepromatous background in addition to an inflammatory or tuberculoïd reaction.

In 10 additional patients ink was injected, and biopsies after 6 to 71 days revealed lepromatous infiltrates in only 2 cases.

The authors did control biopsies in 32 out of these 35 patients from normal-looking skin from a symmetrical site on the upper arm or from an area adjacent to the BCG papule. In 25 of the 32 cases a lepromatous appearance with bacilli was found. They therefore concluded that all these reactions were no more than lepromatous background in areas where the experiments were done. The main point of disagreement lies in the control experiments of these authors. In our own control experiments we have found some perivascular foam cell aggregates which we classified as -f- in 10 out of 41 control specimens taken from 34 patients (almost all of them)

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the same patients in whom the experiments were done). Larger lepromatous aggregates were present in only 4 additional specimens.

I do not believe that any pathologist examining leprosy patients will confirm the finding of about 75 per cent lepromatous leprosy in normal looking skin. If I am not mistaken, practically all of the biopsies in Dr. Kooij’s material were from the skin of negro patients, which may explain this high percentage. It may be that in these patients it is more difficult to recognise normal skin than in white patients. The biopsies may have been taken from slightly infiltrated plaques.

Also his and our patients were for various times under sulfone treatment and this seems not to be the main cause of differences in our findings. It should be pointed out that the first case in whom
we found this peculiar reaction was a “burnt out” case of leprosy in whom repeated biopsies have been done for years and in whom no lepromatous background could be found in the skin; until the biopsies of a tuberculin injection revealed a picture indistinguishable from lepromatous leprosy.

If we analyze the results of Kooij and Pepler on this background it seems strange that no lepromatous background was found in 23 out of 35 biopsies following the injection of BCG; and, furthermore, that when Indian Ink was injected, lepromatous background was found in only 2 out of 10 biopsies. If there is a lepromatous background even in apparently normal skin, as they state, the least we might have expected is, that this should also be present after any manipulation of such skin.

It is noteworthy that Kooij has actually invoked tuberculoid reactions by injecting normal tissue suspensions intradermally into patients with tuberculoid leprosy. “This could be considered as a kind of isopathic phenomenon.” This only strengthens our conclusion that in leprosy there is a peculiar tissue reaction to injected foreign materials; namely that in the lepromatous type a leproma develops, while in the tuberculoid type a tubercle develops.

A further point, incorrectly stated by Kooij, is that we found only a lepromatous reaction to the injection of living material such as BCG. In fact, after the injection of living organisms such as BCG and L. tropica we always observed the clinical course typical of the respective diseases. Histologically there was a tuberculoid arrangement following BCG and a leishmanial granuloma following the injection of L. tropica, but in both cases there was also a considerable aggregation of foam cells far exceeding the number which might have been present as “background” before inoculation. We also noted that in cases following BCG injections there were tubercles which consisted almost exclusively of foam cells and not of epitheloid cells as in tuberculosis. Furthermore L. tropica multiplied in foam cells and not in macrophages.

There is further a quantitative aspect in all our control cases in which some foam cell aggregates were found around the blood vessels or somewhere in the cutis. The 1 plus reactions were cell aggregates consisting of some dozens of cells. This certainly would not be apparent clinically. In the reaction following living or non-living materials the background was a granuloma which clinically would have shown up as an elevated papule of an infiltrated plaque. Therefore it is difficult to accept the lepromatous background of Kooij and Pepler. I believe if they were to re-examine their slides they might find a significant quantitative difference between biopsies taken from control sites and from those in which a lepromatous reaction was evoked by the introduction of foreign substances.

I further believe that they would find lepromatous material in some of their biopsies done following BCG after the lapse of 9 days.

Summary: In many respects the experiments of Kooij and Pepler confirm the idea of an isopathic phenomenon in lepromatous leprosy, despite certain inconsistencies in their results and conclusions, which may have been influenced by control experiments done in patients in whom the control site could not always be recognized as normal skin.

I therefore reaffirm the findings of Waaler, Richter and ourselves, in which patients with lepromatous leprosy have been shown to react in a peculiar manner to the introduction of foreign materials.

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