THE MORPHOLOGY OF THE ACTIVE AND INHIBITORY PHASES OF IMMUNITY IN GUINEA PIGS IMMUNIZED WITH HEATED PARATYPHOID VACCINE

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Many descriptions have been given [4, 5, 6, 8] of the variations in the immunological reactions of experimental animals receiving repeated antigenic stimuli. It has been shown that under these conditions there is a periodicity in which phases of excitation and depression of antibody formation alternate. Under the influence of the immunization, immediately after the phase of maximal immunity excitation, there follows a phase of depression during which the animals lose the power of producing antibodies, although stimulated by further antigenic stimuli. The refractory phase disappears slowly over a long period.

The reports of this condition do not refer to the morphological changes. The exception is the work of G. A. Gurvich and G. V. Shumakova [1], who describe the immunological changes of the plasmocyte reaction. They showed that during the phase of immunological excitation, there is a considerable increase in the number of transitional forms of plasma cells in a regional lymphatic node, and during the inhibitory phase the regional node responds by a much weaker plasmocyte response, i.e., a condition of fatigue occurs quite frequently.

The object of the present investigation has been to study morphological changes in lymphatic nodes in the spleen of experimental animals, during excitation and inhibition of the immunological processes.

EXPERIMENTAL METHODS

Groups of 25 guinea pigs were immunized with a subcutaneous injection of B. paratyphi A into the left inguinal region, as follows.

Animals of the first group received 1.3 milliard bacterial cells in 1 ml of fluid; the second group were immunized in precisely the same way, but after 26 days they were revaccinated; the third group received 100 million bacterial cells each, in small portions; 13 injections were given at intervals of 2-3 days.

The degree of immunological change was determined from the amount of agglutinins in the blood, which was collected on the days when the antigen was injected. To construct the graph, and also to consider the immunological response, we used mean values obtained by determining the titres of the agglutinins in the blood of 5-10 animals.

For the morphological studies, two guineapigs of the first group were killed on the 2nd, 6th, 12th, 18th and 24th days after immunization, and animals of the second group were killed at the same times after revaccination. In the third group, animals were taken for morphological study after 5, 8, 10, and 13 injections and 15 days after the last injection.

Studies were made of the spleen, of the regional and cervical lymph nodes. The organs were fixed in Zenker-formol, and were embedded in paraffin. Sections 5 μ-thick were stained with azure II-eosin.

Microscopically, there was some increase in the size of the regional lymph nodes and spleen in the animals of the first and second groups. In the third group the regional lymph nodes were enlarged in some of the guinea pigs, and in some they were reduced while in all of them, the spleen had enlarged 1½-2 times.

EXPERIMENTAL RESULTS

A single immunization with heated paratyphoid vaccine caused a marked production of agglutinins, which was maximal on the 11th day (mean titre 1 : 167) and was gradually reduced towards the 27th day. A second injec-
tion of the antigen after an interval of 26 days caused a more intense production of agglutinins, and the concentration in the blood reached a maximum after 7 days, when the mean titre was 1:290; subsequently the level was greatly reduced.

Microscopically, regional morphological changes were found as early as two days after the injection. Large numbers of lymphocytes were rapidly liberated into the sinuses of the cortical and medullary zones, and then, a moderate hyperplasia of the cells of the reticular tissue and of the lymphoid follicles. There were a few plasma cells. There were no noticeable changes in the cervical lymph nodes.

On the sixth day, in the regional and cervical lymph nodes there was a marked hyperplasia of the cells of the reticular tissue, although the change was more marked in the regional lymph nodes. The reticular tissue was noticeably bereft of lymphocytes.

A large number of eosinophils and eosinophilic promyelocytes, metamyelocytes, and plasma cells appeared. Among the latter there was a preponderance of young forms.

On the 12th day, in the regional lymph nodes there was a marked hyperplasia of the cells of the reticular tissue, although the change was more marked in the regional lymph nodes. The reticular tissue was noticeably bereft of lymphocytes.

On the 18th day, and still more on the 24th day after immunization, the lymphoid tissue had recovered: between the cortical and medullary zones, and in the medullary cords there were a large number of plasma cells, among which there were mature and occasional degenerate cell forms. There was still a hyperplasia of the cells of the reticular tissue, which remained swollen, and as before there were a large number of eosinophils.

After revaccination, on the 6th day, there were dense hemorrhagic infiltrations at the site of the injection, and a great increase in size of the regional lymph nodes and of the spleen. By the 24th day, these changes were only weakly shown.

It was found microscopically that all the changes in the regional and cervical lymph nodes after revaccination showed a still greater accumulation of plasma cells than there had been after the first immunization (Fig. 1).

The response of the spleen was essentially the same as that of the lymph nodes. In the red pulp there was a rapid increase in the number of plasma cells. After revaccination the increase in these cells was still more marked, and practically the whole of the red pulp was thickly filled with them. At the end of the period of observation, i.e., on the 24th day after revaccination, the plasma cells of the spleen were not diffusely scattered, but were gathered in pockets around the trabeculae, beneath the capsule, and along the periphery of the lymphoid follicles. The greater portion of the red pulp contained no plasma cells at this stage.