

FORMATION OF LYMPHOCYTE AGGREGATIONS IN  
THE PERIportal SPACES OF THE LIVER  
AFTER REMOVAL OF CHIEF LYMPHOID  
ORGANS IN ADULT RABBITS\*

KORENOBU KARASAWA

*Department of Anatomy, Yamaguchi Medical School, Ube*

*Director: Prof. Dr. B. Osogoe*

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In the previous reports from our laboratory (Osogoe, 1950; Osogoe and Hitachi, 1950), it has been demonstrated that after homoiotransfusion of a large amount of lymphocytes in rabbits, there occurs a striking focal accumulation of lymphocytes in the periportal areas of the liver, with the formation of many lymphoid foci therein. A similar new formation of lymphocyte aggregations in the liver has been reported by Sanders and Florey (1940) after the nearly complete extirpation of the organized lymphoid tissues in rats. The experiments with rabbits similarly conducted by these investigators, however, failed to produce any lymphoid foci in the liver.

In the course of his earlier study on the effects of the removal of chief lymphoid organs on the blood counts in adult rabbits (Karasawa, 1954), the author observed a new formation of lymphocyte aggregations in the periportal space of the liver, which may be considered to be compensatory to the reduction in the mass of lymphoid tissue. It is worthy of notice that not only the introduction of a large amount of superfluous lymphocytes into the circulating blood but also the removal of a large part of lymphoid tissue leads to a new formation of lymphoid aggregations in the liver.

MATERIAL AND METHOD

The material was the same on which the preceding observations on the effects of the removal of chief lymphoid organs on the blood counts were based. As described in another paper (Karasawa, 1954), in a series of 8

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adult rabbits chief lymphoid organs such as the mesenterial mass of lymph nodes, vermiform appendix and spleen, as well as other several small lymph nodes, i.e., the anterior gastric, portal, pancreatic and mesocolic nodes, were removed at one seance under laparotomy. The popliteal nodes had been extirpated on the preceding day. The total weight of the removed lymphoid organs amounted to approximately 80 per cent of that of the entire lymphoid system. In another series of 7 adult rabbits either the mesenterial nodes or the vermiform appendix and spleen were extirpated without removing other lymphoid organs.

The tissues to be examined were fixed in Zenker-formol and stained routinely with hematoxylin and eosin or eosin-azur II.

### OBSERVATIONS AND DISCUSSION

As noted in another paper (Karasawa, 1954), simultaneous extirpation of the chief lymphoid organs and other several small lymph nodes produced a severe lymphopenia which persisted for several weeks. In association with such a severe and persistent lymphopenia, there appeared a variable degree of focal accumulation of lymphocytes in the periportal spaces of the liver in all of 6 rabbits that were examined later than 4 weeks after the operation. In 3 out of 6 examples this occurred to a great extent, as shown in Figs. 1 and 2. In such instances, almost all of the interlobular, periportal tissue spaces became occupied by large lymphocyte aggregations, and the picture was comparable to that observed after transfusion of an enormous amount of lymphocytes obtained from the mesenterial nodes of several adult rabbits into one (Osogoe, 1950). Accordingly, the total mass of newly formed lymphoid aggregations in the liver seemed to reach so great an amount that it might be responsible for compensating for the reduction in the mass of lymphoid tissue. Even in such instances, however, the pre-operative level of blood lymphocytes was not re-established until the end of the 6th post-operative week. This suggests that the lymphocyte aggregations newly formed in the liver do not actively participate in lymphocyte production until that time.

The lymphoid aggregations newly formed in the liver were composed for the most part of small lymphocytes with a few medium-sized ones. In some instances, there occurred small lymphocyte collections intravascularly on the wall of the interlobular portal vein, and all of the successive stages of the incorporation of accumulations of lymphocytes from the portal vein into the periportal spaces could be traced. This process is of great significance because it represents a mechanism for emigration of non-motile or slightly

motile cells, as has previously been emphasized by Osogoe (1950) and Osogoe and Ōmura (1950).

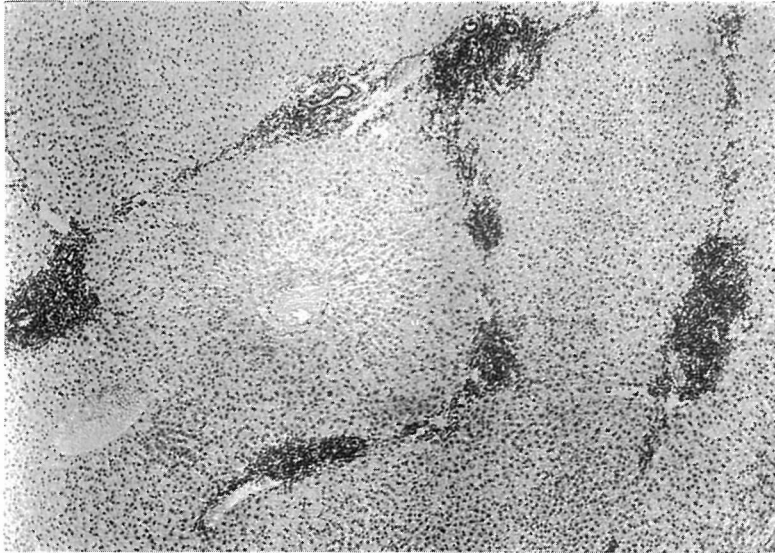


Fig. 1. Periportal lymphocyte aggregations in the liver. Five weeks after the removal of the mesenterial nodes, popliteal nodes, vermiform appendix and spleen.  $\times 40$ .

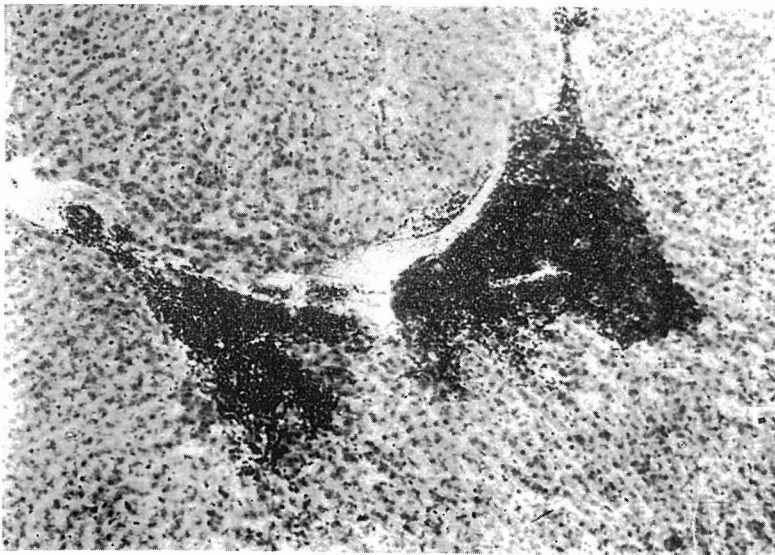


Fig. 2. Two large periportal aggregations of lymphocytes from the same section of the liver illustrated in figure 1.  $\times 80$ .

It should be noticed here that small lymphocyte aggregations also appeared in the femoral bone marrow in 4 out of 6 examples that were killed later than 4 weeks after the operation. They were composed of small lymphocytes with a relatively large number of medium-sized lymphocytes (see Fig. 3). Such lymphoid aggregations are usually absent in the femoral bone marrow of normal adult rabbits.

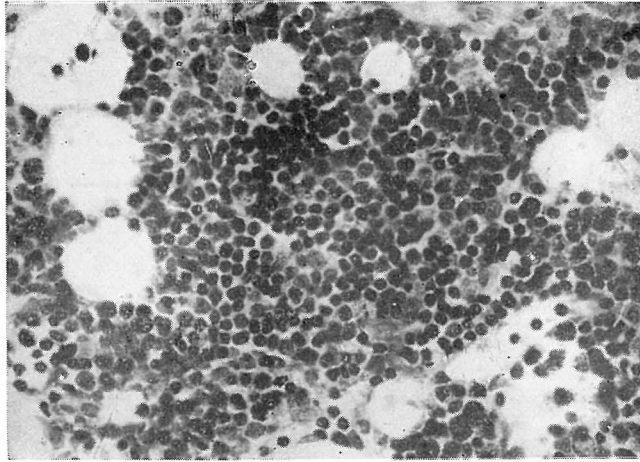


Fig. 3. Small nodule-like aggregations of lymphocytes in the femoral bone marrow. Four weeks after removal of the mesenteric nodes, popliteal nodes, vermiform appendix and spleen.  $\times 400$ .

When the animals were killed before the 4th post-operative week, no lymphoid aggregations occurred either in the liver or in the bone marrow. Likewise, no alterations in these organs were observed at any period when the mesenteric, mesenteric nodes or the vermiform appendix and spleen had been extirpated without removing other lymphoid organs.

As noted in another paper (Karasawa, 1954), no new formation of lymph nodes occurred at the sites where they had been completely extirpated. Although small portions of the mesenteric mass of nodes remaining behind the portal vein showed a marked hyperplasia with the formation of many active secondary nodules of Flemming type, no indication of such hyperplasia was observed in the other remaining lymph nodes and lymphoid tissues until the end of the 6th week, with the exception of the peribronchial lymph node that showed a slight degree of hyperplasia. Thus, compensatory hyperplasia on the part of the remaining lymph nodes and lymphoid tissues took place only to a small extent.

The findings noted above indicate that new formation of lymphocyte aggregations in the liver and bone marrow represents a compensatory mecha-

nism for marked reduction in the mass of lymphoid tissue. The fact that such a compensatory reaction takes place to the greatest extent in the liver deserves special attention. In connection with this, the following facts are of particular interest: (1) The transfused lymphocytes accumulate preferentially in the periportal spaces of the liver (Osogoe, 1950; Osogoe and Hitachi, 1950); (2) likewise in the lymphoid leukemia, lymphoid cells accumulate in the same places of the liver; (3) in some lower vertebrates such as birds and reptiles, lymphoid aggregations or nodules are very common in the periportal spaces of the liver (Osogoe, 1953). On the basis of these facts Osogoe has suggested that the periportal space of the liver is to be regarded as potential lymphoid tissue (cf. Osogoe, Karasawa and Awaya, 1953).

Lastly, some mention should be made of the question whether the lymphocyte aggregations newly formed in the liver and bone marrow may produce lymphocytes or not. It is suggested that they do not actively participate in lymphocytopoiesis until the end of the 6th post-operative week, because the pre-operative level of blood lymphocytes was not re-established until that time. This, however, does not exclude the possibility that such lymphoid aggregations may acquire lymphocytopoietic activity in later period, because Sanders and Florey (1940) observed no definite reduction of blood lymphocytes in a period later than 3 months after the extensive extirpation of lymphoid tissue in rats. Further experiments extending for a longer period will answer this question.

#### SUMMARY

After the removal of chief lymphoid organs such as the mesenteric mass of nodes, vermiform appendix and spleen as well as other several small lymph nodes in adult rabbits, there appeared new formation of lymphocyte aggregations in the periportal spaces of the liver to a large extent and, though to a lesser extent, also in the femoral bone marrow. This phenomenon is considered to be compensatory to the reduction in the mass of lymphoid tissue.

In contrast with this, compensatory hyperplasia on the part of the remaining lymph nodes and lymphoid tissues took place only to a small extent. There was no local regeneration of lymph nodes when they had been completely removed.

The fact that a compensatory reaction in response to a marked reduction in the mass of lymphoid tissue takes place to the greatest extent in the liver was stressed.

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#### LITERATURE CITED

- KARASAWA, K. 1954. Experimental studies on the chief source of blood lymphocytes in adult rabbits. *Okajimas Fol. anat. jap.*, **26**: 309-325.
- OSOGOE, B. 1950. Transplantation of hematopoietic tissues into the circulating blood. I. Experiments with lymph nodes in normal rabbits. *Anat. Rec.*, **107**: 193-220.
- OSOGOE, B. 1953. Phylogenetical study of bone marrow. *Symposium of Hematology* (Matsumoto), **5**: 1-18. (Japanese.)
- OSOGOE, B. and T. Hitachi. 1950. Über die Lymphocytennatur der Thymocyten. (Das Verhalten der in die Blutbahn transplantierten Thymocyten im Vergleich mit dem der Lymphocyten.) *Okajimas Fol. anat. jap.*, **23**: 51-56.
- OSOGOE, B. and K. Ōmura. 1950. Transplantation of hematopoietic tissues into the circulating blood. II. Injection of bone marrow into normal rabbits, with special reference to the histogenesis of extramedullary foci of hematopoiesis. *Anat. Rec.* **108**: 663-686.
- OSOGOE, B., K. KARASAWA and K. AWAYA. 1953. Experimental morphological studies on the lymphatic tissue. *Kaibo Z.*, **28** (Supplement): 36. (Japanese.)
- SANDERS, A. G. and H. W. FLOREY. 1940. The effects of the removal of lymphoid tissue. *Brit. J. Exp. Path.*, **21**: 275-287.
- SELYE, H. 1937. Studies on adaptation. *Endocrinology*. **21**: 169-188.