NOTES

Regional Immunosuppression Induced by *Plasmodium berghei yoelii* Infection in Mice

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*Plasmodium berghei yoelii* infection in mice severely depressed the splenic antibody response to sheep erythrocytes but had little effect on antibody formation in lymph nodes.

Speculation regarding the mechanism of malarial-induced immunosuppression has been focused primarily upon the afferent arc of the immune response. Greenwood et al. (2) suggested that malarial parasitemia depleted the lymphoid cells that carry immune complexes into germinal centers. On the basis of cell transfer studies, Loose et al. (5) concluded that malaria impaired the processing of antigen by macrophages.

If macrophage function is impaired during infection due to alterations in lysosomal enzymes incurred by the ingestion of parasite and cell debris as suggested by Loose et al. (6), it is possible that the immunosuppressive effects of plasmodial infection are most evident in the spleen where macrophages are exposed directly to the contents of the blood compartment. In contrast, macrophages in lymph nodes do not come into direct contact with blood-borne debris and, consequently, may not be adversely affected by the infection. To test this hypothesis, we compared antibody formation at the cellular level in the spleens and lymph nodes of normal and infected mice immunized with sheep erythrocytes.

Twelve adult female white mice from our closed colony were infected intraperitoneally with 10⁶ erythrocytes parasitized with *Plasmodium berghei yoelii* (17×). Thirteen days later, when parasitemias ranged between 10 and 43.5%, the mice were immunized with 0.01 ml of a 50% suspension of sheep erythrocytes in Dulbecco phosphate-buffered saline injected into the footpads of the fore paws of each mouse and 0.1 ml of a 25% suspension of sheep erythrocytes injected intraperitoneally. Twelve noninfected mice were immunized in the same way. Six mice injected with phosphate-buffered saline alone served as controls. Four days after immunization, the mice were sacrificed, and cell suspensions were prepared from the spleen and combined axillary and brachial lymph nodes of each mouse. The number of direct plaque-forming cells in each suspension was determined by a modification of the procedure of Jerne and Nordin (4).

Whereas the lymph nodes of infected mice were similar in weight to the lymph nodes of noninfected mice (58 versus 71 mg), infected mice showed marked splenomegaly. The mean spleen weight of the infected mice was 1.36 g and that for the noninfected mice was 0.16 g. Despite the approximate ninefold increase in spleen weight, relatively few plaque-forming cells were found in the spleens of infected mice when compared with those found in the spleens of noninfected mice after immunization with the same antigen (Table 1). Similar findings have been reported by others (1, 3, 7, 8).

In contrast, the lymph nodes of infected mice contained substantial numbers of plaque-forming cells. Although it is evident that the lymph nodes of normal mice possessed more plaque-forming cells than those of infected mice, the immunosuppressive effects of malarial infection are much less obvious in this respect. Histological examination of the lymph nodes of other mice infected with this parasite failed to reveal parasites or debris in the parenchyma of the nodes (J. Finerty, personal communication). These data clearly indicate that the severity of immunosuppression resulting from malarial infection is dependent upon the particular organ chosen for study. Further, they suggest that exposure of phagocytic cells directly to infected blood is more detrimental to the primary antibody response to sheep erythrocytes than when
### Table 1. Effect of malarial infection on the antibody response to sheep erythrocytes in spleen and lymph nodes

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatmenta</th>
<th>No. of animals</th>
<th>$\log_{10}$ PFC$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Spleen</td>
</tr>
<tr>
<td>A</td>
<td>Infected and immunized</td>
<td>12</td>
<td>$3.1721 \pm 0.4267$ (1,486)</td>
</tr>
<tr>
<td>B</td>
<td>Immunized</td>
<td>12</td>
<td>$5.0721 \pm 0.5348$ (118,060)</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>$1.7894 \pm 0.5437$ (62)</td>
<td>$&lt;1.6990$ ( &lt;50)</td>
</tr>
</tbody>
</table>

*a Mice were infected with $10^8$ *P. berghei* yoelii and immunized with 0.01 ml of a 50% suspension of sheep erythrocytes in phosphate-buffered saline in the foot pads of both fore paws, and 0.1 ml of a 25% suspension of sheep erythrocytes intraperitoneally.

*b Mean $\log_{10} \pm$ standard deviation. Geometric means are given in parenthesis. PFC, Plaque-forming cells.

Macrophages are protected against such exposure. The reason for the latter remains to be determined.

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### Literature Cited