

to a lymph node, and thus a reduction in oxygen supply to the node, reduces the sensitivity of the lymphocytes therein to irradiation (1). Reduced oxygen tension, however, does not "stimulate" lymphocyte production. The production of anemia in the experimental animal by phlebotomy or phenylhydrazine administration by virtue of reducing the oxygen supply to the bone marrow produces a stimulus, an optimum condition, for the proliferation of erythroblasts. The mechanism for the reduced radiosensitivity in the lymphatic tissue with O<sub>2</sub> deprivation is probably different from that operating in erythropoietic tissue in the presence of an anemia.

#### Reference

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## Alterations in the Development of *Plasmodium gallinaceum* Following Passage Through Tissue Culture

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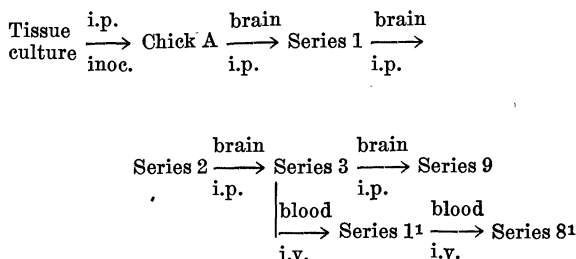
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A series of tissue culture experiments<sup>2</sup> have been carried out in which exoerythrocytic stages of *Plasmodium gallinaceum* have been maintained in continuous culture by the roller tube technique of Gey and Gey (1). The cultures were tested for the presence of parasites by inoculating chicks intraperitoneally with material from the cultures. The majority of the experiments involved colonies of cells derived from the pia mater of blood-infected, quinine-treated chicks. Some of the cultures, however, had been derived from heart muscle of such birds. Each of the cell strains was subcultured at intervals which varied with the rate of growth of the tissue-cultured host cells. Microscopical examination of such cultures failed in most instances to reveal extensive development of parasites. Nevertheless, young chicks receiving inoculations from cultures which had been maintained for four or five subcultures, and which were as much as 70 days old, became infected with *P. gallinaceum*.

The primary purpose of this preliminary paper is to emphasize the peculiar character of the resulting infection in chicks, since this has been exclusively of an exoerythrocytic nature. Chicks infected as indicated above ranged from 7 to 32 days old. They invariably developed an overwhelming exoerythrocytic infection which terminated fatally 10-17 days after their inoculation with

material from culture. No pigmented erythrocytic stages developed in any of the birds, although, in several instances, at the time of death a low percentage (1-3%) of the erythrocytes were parasitized with minute, unpigmented, uninuclear forms. With the exception of a more rapid onset and an apparently greater severity, this infection is almost identical with that encountered in blood-infected, quinine-treated chicks (3, 4).

In a number of instances the parasites obtained from chicks infected from culture have been maintained by serial passages in other chicks. The nature of this exoerythrocytic infection has remained unchanged in one experiment through 9 serial passages (note diagram below) accomplished by means of intraperitoneal inoculation (i.p.) of brain suspended in saline. The infection in birds 2-35 days old continues to be acute, with exoerythrocytic parasites readily demonstrable in the capillary endothelium of the brain as early as 4 days after inoculation. Death from exoerythrocytic parasitism has occurred as early as 6 days after inoculation with infected brain material.



In contrast to the above, serial passage of the infection by intravenous inoculation of blood from such birds resulted in a somewhat different picture of parasitism. For example, blood taken from chicks of the previously mentioned series (see diagram) was used to initiate a blood inoculation series. Parasitism of the birds of the first and second inoculations of this series was again almost exclusively of the exoerythrocytic type. However, after the third blood passage pigmented erythrocytic stages were found. Continued blood passage seemed to increase the number of the pigmented blood stages. Nevertheless, even at the end of the 8 serial blood passages, the infection continued to be preponderantly exoerythrocytic in most of the infected birds.

Since completion of this work, a report of similar alteration in the development of *P. gallinaceum* has been made in which passage through chick embryos, rather than tissue cultures, was a contributing factor (2).

#### References

1. The author wishes to express his appreciation for the assistance and advice which G. F. Otto, of the Department of Parasitology, and G. O. Gey, of the Division of Cellular Physiology, have given during the course of this investigation.
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