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Life History and Immunity Studies of the Avian Malaria Parasite, *Plasmodium circumflexum.*

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Six strains of *circumflexum* were used. These were secured from 5 different species of hosts, 3 of which were from widely separated localities (Syracuse, N. Y., Cape Cod, Mass., and Germany). The technic consisted in inoculating chronic infections (infections which had been made 2 or more months previously) of a given strain with parasites of another strain. The results indicated that a chronic infection with one strain protected against subsequent infection with another in most cases, although in general the degree of immunity to infection with another strain was somewhat less than when superinfection with the same strain was done. It was found, however, that the 4 strains originally isolated from birds caught in Syracuse (although they were isolated from 3 different host species) conferred much higher immunity against reciprocal or cross-infection with some other of the 4 than toward the strains derived from Cape Cod or German hosts. Of all 6 strains, that derived from a Cape Cod blackbird proved most able to break down the resistance conferred by chronic infection with some other strain, but previous infection with it conferred strong protection against the other five strains.

These results show that at least in this species of avian malaria immunity ("premunition") is more a matter of strain than previous work with other species had indicated (Gingrich,[1] Manwell[2]), and it was thus more like the monkey and human malaria parasites in this respect. Indeed the degree of immunity exhibited by a chronic infection of one strain towards another may be less than that occasionally observed between species. As an example, *Plasmodium rouxi* may be mentioned. This species has been found to confer a strong immunity towards subsequent infection with *circumflexum,* but the relationship is not reciprocal.

The results of the experiments to test whether immunity could be artificially conferred by the repeated injection of serum from chronic cases showed that this could be done quite successfully, thus

[1] Gingrich, W., *J. Prev. Med.*, 1932, **6**, 197.

[2] Manwell, Reginald D., *Am. J. Hyg.*, 1938, **27**, 196.

demonstrating that avian malaria is like that in monkeys in this respect (Coggeshall and Kumm[3]). A total of 20 birds were used in these experiments, of which 14 were treated and 6 were controls. Six of the former group received 8 injections of immune serum before inoculation with parasites and one injection afterward. No infection developed in any of the 6, and this was confirmed by successful infection later. Inoculation of clean birds with the blood of these birds also gave negative results. The other 8 treated birds received 10 injections of immune sera after inoculation with parasites but in this case protection was less effective. However, all showed a definite degree of immunity as compared with the controls. It may be noted, however, that immunity was greater in those birds which received parasites of the same strain as originally used to infect the donors of the immune serum. When parasites of strain "E" (from the Cape Cod redwing referred to above) were given to birds immunized with serum from birds carrying chronic infections with one of 3 strains of Syracuse origin more severe infections developed, although still considerably milder than in the unprotected controls. It is thus clear that other factors than the reticulo-endothelial system are involved in the development of immunity.

The final portion of the work herein reported concerned the possible occurrence of exoerythrocytic stages in *Plasmodium circumflexum.* Such stages have been reported for 4 other species of avian malaria *(gallinaceum, praecox, cathemerium, elongatum).* It was found that stages very similar to those said to exist in the species just listed also occur in *circumflexum,* and are most numerous in the large monocytes of the lungs, liver, spleen, and bone marrow, more or less in the order named, They may also be found in other situations, such as the heart muscle, and they may occur in large numbers in the endothelial cells of the brain. Reproduction in these forms seems always to be by schizogony, and in this respect these parasites differ from *Toxoplasma.* The latter is said to reproduce by binary fission in all the species so far worked on (although the number of these is still very small). We have confirmed this observation for the strain worked on by Sabin and Olitzky of the Rockefeller Institute, from preparations furnished through the courtesy of the former. It may also be noted that although *Toxoplasma* is a very common parasite, at least among English sparrows in this vicinity, it differs considerably from the exoerythrocytic stages seen in *Plasmodium circumflexum* infections, and also from those seen on slides of *Plasmodium cathemerium* sent by Dr. Kikuth

[3] Coggeshall, L. T., and Kumm, H. W., *J. Exp. Med.*, 1937, **66**, 177.

of Elberfeld, Germany. It is only fair to admit, however, that the question of the significance of what have been regarded as exoerythrocytic stages by others, and are so regarded by the authors in the *Plasmodium circumflexum* infections mentioned here, will not be altogether conclusively settled until typical malaria infections are transferred to clean birds by inoculation of these stages alone. It is of interest that these stages have so far been observed only in acute cases, and not in all of these. Fatal cases are most likely to exhibit them.

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Failure of Ascorbic Acid to Influence Albuminuria and Hematuria in Nephritis.*

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Following the isolation and identification of Vitamin "C" in 1932, several reports on the effectiveness of ascorbic acid on hematuria of acute nephritis and from other causes appeared in the European literature. Szent-György[1] reported favorable results in cases of hemorrhagic nephritis following 150-200 mg of ascorbic acid on alternate days. Koranyi and Bentsath[2] also noted a hemostatic effect in nephritic hematuria. Engelkes[3] described 2 cases of hematuria and albuminuria in which the red blood cells in the urine disappeared in 10 and 6 days, respectively, after administration of 100-200 mg daily. Ceruti and Costanzo[4] stated that in 2 patients suffering from nephritis and essential forms of hematuria, 50 mg were given daily for 10 days with satisfactory results verified by microscopic studies of the urine. These favorable reports prompted Murphy[5] to advocate routine administration of ascorbic acid in cases of acute nephritis with hematuria. On the other hand, Parsons,[6] Wilbur,[7] and Abt and Farmer[8] in reviewing the subject of Vitamin

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1 Quoted in Wright, I. S., and Lilienfeld, A., *Arch. Int. Med.*, 1936, **57**, 241.

2 Koranyi, A., and Bentsath, A., *Orvosi hetilap.*, 1935, **79**, 378.

3 Engelkes, H., *Lancet*, 1935, **2**, 1285.

4 Ceruti, G., and Costanzo, F., *Riforma Medica*, 1937, **53**, 1770.

5 Murphy, F. D., *International Clinics*, 1938, **2**, 231.

6 Parsons, L. G., *Lancet*, 1938, **1**, 123.

7 Wilbur, D. L., *Arch. Int. Med.*, 1937, **59**, 512.

8 Abt, A. F., and Farmer, C. J., *J. A. M. A.*, 1938, **111**, 1555.