but also other types of vascular or phagocytic cells. This was first shown to be true of *Plasmodium elongatum* by Raffaele[2] and shortly afterward by Huff and Bloom.[3] This species of avian plasmodium may be found in any type of blood or blood-forming cell, although it much prefers the erythrocytes. Since the work on this species, Raffaele,[4] Kikuth and Mudrow[5] and James and Tate[6] have been able to demonstrate that there are also exoerythrocytic stages in *Plasmodium praecox, (relictum), cathemerium* and *gallinaceum,* respectively; Kikuth[7] in a recent paper with Mudrow has given a good summary of our knowledge of such stages to date. He remarks, however, that although he has looked for stages of this sort in *Plasmodium circumflexum* infections he has not as yet been able to find them. It may be noted here that the three species last named differ from *Elongatum* in that the parasites occur in the cells of the reticulo-endothelial system and, of course, in the red cells also, rather than in all the blood and blood-forming cells.

The authors of the present paper have for some time been engaged in a study of the immunological characteristics of various strains of *Plasmodium circumflexum,* and as a somewhat incidental part of the study a number of infected birds (female canaries) have been examined for possible exoerythrocytic stages. As a result it is possible to say that such stages occur in at least four strains, and they have so far been found in the lungs, spleen, liver, heart muscle, bone marrow and brain, but not in all the birds examined. Of the thirty-six birds in which they have been looked for, they were seen in fifteen of twenty-one active cases, and not in any of the fifteen chronic cases. Of the four strains, one originated in Germany, one in Cape Cod and the other two in Syracuse. Our results suggest that stages in other than the red cells are most likely to be found soon after parasites first appear in the peripheral blood, and prolonged search may be necessary to find them. Once found, however, they are frequently found to occur in localized areas in great numbers.

The question has recently been raised by Hegner and Wolfson[8] as to whether, in certain cases at least, the parasites found in cells of the reticulo-endothelial system and interpreted as part of the asexual cycle of malaria, are not actually *Toxoplasma.* This is quite possible under some circumstances, for *Toxoplasma* may spread rapidly in the laboratory once it is present at all, and some stages strongly resemble what has been regarded and figured as exoerythrocytic schizogony in the avian malaria species mentioned above. It should be pointed out however that *Toxoplasma,* usually, if not always reproduces by binary fission. In our experience, *Toxoplasma* has occurred only once in laboratory canaries, and in this case it was apparently acquired from English sparrows. The infection spread very rapidly among the sparrows and killed a number of them, but it had no connection with malaria at all, since most of the sparrows had been previously shown to be free from malaria infection of any kind. We have seen no evidence of *Toxoplasma* in canaries since, although numerous birds have been studied and autopsied over a period of several years. For this reason and because the stages which we have found in the *circumflexum*-infected birds mentioned above are much like those seen by the other investigators already cited in connection with the work on *praecox, cathemerium* and *gallinaceum,* we believe that in *circumflexum* also it may be regarded as demonstrated that exoerythrocytic stages occur. From the evidence already existing it seems likely that similar stages will be found in the other species of avian malaria, and quite possibly in monkey and human malaria also. It also makes it probable that the biological relationship between the malaria parasites and *Hemoproteus* and *Leucotozoan* is closer than has been thought.

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[2] Raffaele, *Riv. di Mal.,* 13: 332–337 and 402, 1934.
[3] Huff and Bloom, *Jour. Inf. Dis.,* 57: 315–336, 1935.
[4] Raffaele, *Riv. di Mal.,* 15 (5), Sez. 1, 3–9, 1936.
[5] Kikuth and Mudrow, *Klin. Wschr.,* 16 (48): 1690–1691, 1937.
[6] James and Tate, *Nature,* 139: 545, 1937.
[7] Kikuth and Mudrow, *Zentralbl. Bakt.,* I Orig., 142: 113–132, 1938.
[8] Hegner and Wolfson, *Amer. Jour. Hyg.,* 27: 212–220.

THE PREVENTION OF TOXIC MANIFESTATIONS OF AN EXCESS OF VITAMIN B_1 BY SUPPLEMENTS OF MANGANESE TO THE DIET[1]

IN an earlier publication we reported that the addition of supplements, to our standard adequate diet, of vitamin B_1 in amounts of 50 international units per rat per day resulted after one generation in interference with lactation, loss of the maternal instinct, cannibalism and progressive loss of fertility.[2] Our standard diet contains rolled oats, meat scrap and bone meal, dried skimmed milk, fresh greens, fresh milk, salt, cod liver oil and brewer's yeast (in amounts equivalent to 2 or 3 international units per rat per day). With reduction in the excess amount of vitamin B_1 to 20 units or the elimination of the excess supplements of vitamin B_1 for short periods, normal lactation and normal interest in the young was restored. When the vitamin B_1 content was again increased the same toxic effects were observed. Further study completely confirmed our earlier findings. With supplements daily of 30 units of vitamin B_1, progressive decrease in

[1] From the Laboratory Division, Montefiore Hospital, New York City.
[2] D. Perla, *Proc. Soc. Exp. Biol. and Med.,* 37: 169, 1937.

fertility also occurred with a moderate incidence of loss of litters due to cannibalism. After five generations breeding markedly decreased.

In view of the fact that Williams[3] stated that as much as from 160 to 1,000 γ of vitamin B_1 daily could be given without any toxic effects when rats were fed a Sherman breeding diet (one third whole milk and two thirds whole wheat), it seemed probable to us that interference with some other essential factor in the diet may have induced the manifestations observed in our experiments.

It is known that deficiency of manganese in the diet presents similar toxic effects on the maternal instinct and reproduction.[4] It was reasoned that perhaps manganese is essential as an oxidative catalyst in the utilization of vitamin B_1 in the tissues. If this is so the available manganese in the tissues may be exhausted by an excess of vitamin B_1, and analogous manifestations would occur as is observed with a deficiency of manganese.

To test our hypothesis we added small amounts of manganese to the diet. Rats which had shown loss of maternal instinct and cannibalism now bred and raised normal litters. The studies were then extended. Rats were raised on the normal diet and given parenterally 200 units of vitamin B_1 daily. Others were given the same diet and vitamin B_1, but the diet was supplemented with 2 mg of manganese as $MnCl_2$ per day per rat. In those receiving the vitamin B_1 alone, cannibalism and interference with lactation occurred in a high percentage in the P and F_1 generation in successive litters (13 of 22 litters). In those receiving in addition supplements of manganese in the diet, none of these toxic symptoms were apparent and the normal maternal instinct and normal lactation were preserved (in a total of 25 litters). In our normal stock observed during the same period no loss of litters occurred.

These results demonstrate that manganese is essential in the utilization of vitamin B_1 in the tissues and is intimately bound up with the role of vitamin B_1 in the physiology of the organisms. It also suggests that variations in certain constituents of the diet, such as manganese, may greatly affect the vitamin B_1 requirement. With the use of large amounts of vitamin B_1 in therapy, an adequate supply of manganese must be made available. As yet it is not known whether the protective effects observed with manganese are specific for manganese as such or would be obtained with other oxidative catalytic metals such as cobalt or copper.[5]

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE USE OF THE NEON GLOW LAMP IN THE PHYSIOLOGICAL LABORATORY FOR THE ELIMINATION OF MAKE INDUCTION SHOCKS

IN the use of an induction coil as a source of electrical stimuli for living tissue, in the physiological laboratory, it is often desirable to prevent the "make shocks" (the E.M.F. induced in the secondary coil when the primary circuit is closed) from passing through the tissue, and various devices are in use for short-circuiting the secondary coil while the primary circuit is being closed. While entirely satisfactory in performance, such devices, if arranged to operate automatically, are generally complicated and expensive.

While seeking a simple means of automatically eliminating make shocks, that would be suitable for use in the students' laboratory, we hit upon the idea of connecting a neon glow lamp in series in the secondary circuit. It happens that the Harvard coil and some of the other coils manufactured for physiological use in this country when used with one or two dry cells give make shocks that are too weak to ionize the gas in the lamp and are, therefore, not conducted through it; the break shocks, however, are readily conducted.

Since there is some loss of energy in the lamp, due to resistance, a high capacity lamp without auxiliary resistance gives best results. We have provided our students with two-watt glow lamps without resistance in the base. For convenience and sturdiness of mounting, lamps with radiatron base were obtained on special order from the General Electric Vapor Lamp Company of Hoboken, N. J. The sockets are recessed in small cast-iron blocks; suitable binding posts are provided for making connections.

The method has but one serious disadvantage. Since the secondary is not short-circuited and is open-circuited only for low voltage impulses, chatter or vibration of the key used to control the primary circuit must be avoided at the make; otherwise a succession of rapid makes and breaks occurs which induces a high enough potential in the secondary to pass through the lamp. Chatter is easily avoided with hand-operated keys, and electrically operated keys or relays should, in any case, be so designed as to close without chatter. Inciden-

[3] R. R. Williams and T. D. Spies, "Vitamin B_1 and its Use in Medicine," p 286. Macmillan Company, New York, 1938.

[4] E. R. Orent and E. V. McCollum, *Jour. Biol. Chem.*, 92: 651, 1931.

[5] The vitamin B_1 for these experiments was kindly furnished by the Department of Medical Research of the Winthrop Chemical Company.