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ON THE CURRENT EXISTENCE OF A COCCIDIAL LINE OF DEVELOPMENT IN THE MALARIA PARASITES: A THEORY

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Most opinion favors the origin of the malaria parasites from a coccidial ancestor. It is assumed that whatever the process through which the coccidia differentiated into a Plasmodium *this phenomenon very probably occurred millions of year ago, and during that differentiation process the original coccidia vanished. Therefore it has never been repeated. At the light of some experiments the existence, at the present time, of a coccidial cycle of development in the malaria parasites, is proposed. The connection routes and mechanisms through which the malaria parasite changes to a coccidial life, and the routes in reverse are exposed. Transmission of the malaria-coccidial forms is suggested.*

Key words: coccidia – *Plasmodium* differentation – *Plasmodium* evolution and development

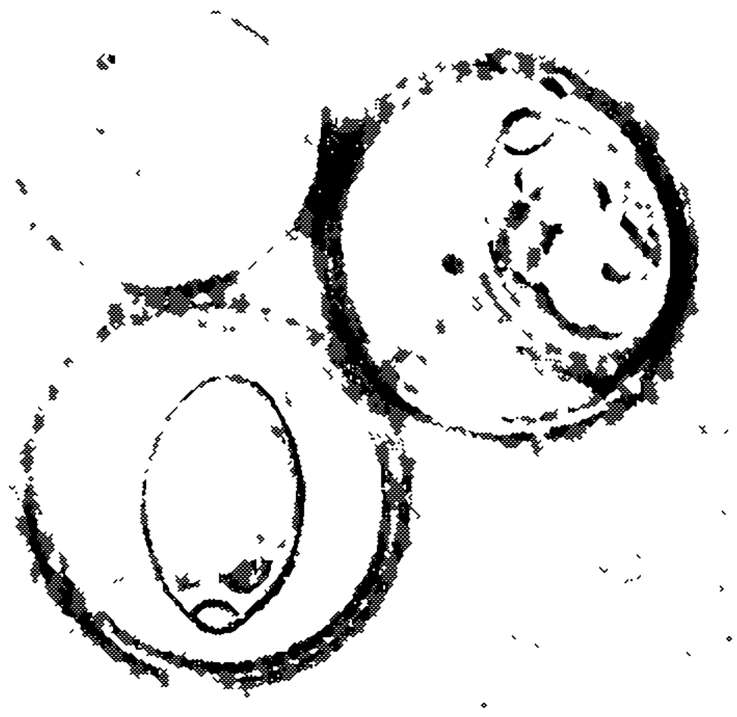
According to our present knowledge on the life cycle of the malaria parasites, two different hosts are required for that cycle to be completed, one vertebrate, reptile, bird or mammal and one invertebrate, mosquito or sand fly. When studying the possible development and evolution of these parasites, discussion arises on whether they originated from a parasite already established in the vector or in the vertebrate host. Current opinion on this matter favors an origin of the malaria parasites from other parasites present in the gut of the vertebrate, and subsequently acquired by the vector, rather than from parasites present in the vector and acquired by the vertebrate (Mattingly, 1983). There are entomological evidences to support this opinion (Mattingly, 1977).

Being the malaria parasite an Apicomplexa, we may assume they originated from another existing Apicomplexa, so that, the parasite of the vertebrate intestine from which the plasmodia could be differentiated, can just only be a coccidia, because it is the only one Apicomplexa infecting vertebrate intestine. In support of this ideas Manwell (1955) argued the probability that reptiles and birds had appeared before hematophagous diptera did, so that, primary evolution of the plasmodia could have taken place in the absence of vectors. To Bray (1963) the present cycle corresponding to a coccidial origin started in the vertebrate gut, because if evolution had started in the insect, schizogony and gamctogony now would occur in the mosquito and sporogony in the vertebrate. Baker (1965) pointed out the tendency of some intestinal coccidia of vertebrates to migrate and to develop tissue forms, in support of the coccidial origin of plasmodia.

Differentiation of the ancestral coccidia into *Plasmodium*, possibly started with the passage of coccidial forms from the gut to the portal vein system, and through it to the liver. After adaptative forms established in hepatocytes, in a second step they got adapted to invade erythrocytes and use hemoglobin as substrate. Blood forms when sucked by mosquitoes accomplished the third step of adaptation-differentiation, in the mosquito gut and salivary glands. In short, this putative route of adaptation-differentiation of the ancestral coccidia depicts the present life cycle of the malaria parasites. Probably this parasite evolution process occurred for the first time in reptiles, and later in birds and mammals, millions of years ago. Apparently during the coccidia-*Plasmodium* differentiation process the original parasite vanished, so that this phenomenon probably has not occurred again, and the pre-*Plasmodium* coccidia never observed.

EXPERIMENTAL INSIGHTS

During electron microscopy study of axenically cultivated malaria parasites, performed some years ago, it was observed that some of the



Three *Isospora* oocysts passed by chickens fed on *Anopheles albimanus:* two of them mature, oine showing sporozoites the smaller degenerated.

forms grown in the culture could be interpreted as being similar to the sporocyst of a coccidia. To find out whether cultivated forms actually behaved as a coccidia, some experiments of infectivity in cats were done. New born cats after weaning and checked free of coccidial infection were daily fed with one seven days old culture, and controls fed with sterile medium. All cats fed with cultivated forms shed oocysts in faeces, 8 to 15 days after the first inocula. All control cats were oocysts negative. Shed Oocysts were immature with one or two sporoblasts, oval or spherical in shape with 14 to 16µm in diameter, and showing, when mature, two tetrazoic sporocysts, typical of *Isospora* genus (Malagon & Tapia, 1985).

As result of these observations the existence of a coccidial form of *Plasmodium* occurring at the present time was proposed, which means that one of the *Plasmodium* stages of development, at least, can deviate its differentiation process into a coccidia. For this phenomenon to occur two conditions have to be fulfiled, first, the malaria parasites have to get in contact with the gut cells of a suitable host and second, the stage of that parasite has to be an invasive form. Theoretically then merozoites from erythrocytic and exoerythrocytic schizonts, ookinetes, and sporozoites might be involved.

During development of the *Plasmodium* life cycle there is not an instance of parasite exposure to the environment, on the contrary its entire life is confined to its hosts. Therefore liver or blood parasites of the vertebrate host and, gut and salivary glands parasites of the vector have to reach the intestine of the suitable host to start invasion and coccidial differentiation.

In the vertebrates in which exoerythrocytic development takes place in the liver, there is certain possibility that merozoites released by the exoerythrocytic schizont might get a bile canal instead of blood, and be secreted with the bile into the same host intestine and so entering in contact with gut cells if they survive the bile lytic action. Blood merozoites could reach the intestine of its own host if blood vessels rupture and shed infected blood into the lumen of the digestive tract. In mammals, infected mothers may transfer parasites to their babies during breast feeding if milk is contaminated with infected blood also by blood vessel rupture. Intestine contact of invasive forms may also occur when a vertebrate eats a *Plasmodium* infected pray. Invasive stages developing in the vector might get to the gut of a vertebrate only if the insect is eaten by it. From the former three possibilities, in the first the survival of a merozoite submerged into pure bilis seems very improbable, and the second and third could be much infrequent. The last two seem to be much suited to get a place in nature through food chains.

The malaria parasites are present in a wide spectrum of vertebrate hosts among reptiles, birds and mammals. Predator mammals may pray on other mammals, birds, reptiles and insects. Predator birds may feed on birds, small mammals, reptiles and insects, and reptiles may feed on other reptiles, insects and small mammals, therefore, reptiles, birds and mammals may pray on *Plasmodium* infected animals belonging to these taxas and, on hematophagous insects. Malaria parasites going through the alimentary canal of a vertebrate, whatever the stage of the parasite be, could get destroyed, but as result of the new physico-chemical conditions, they may also get prepared to invade gut cells. Invasion could follow, provided the vertebrate receptor is the correct one.

Thinking on these possibilities an experiment was performed with a model of *P. vivax* sporogonic forms in the mosquito *Anopheles albimanus* and new born red Rhode Island chickens. Mosquitoes were twice infected by feeding them on *P. vivax* infected person showing sexual forms in peripheral blood. Chickens were fed with the infected mosquitos and control chickens with uninfected ones. Five days after mosquito feeding, chickens that received infective mosquitoes shed *Isospora* oocysts in faeces while the controls did not. Spheric oocysts from 26-28µm in diameter, were mostly shed mature, showing a discrete micropile and two spheric, oval or elon-

gated sporocyts with prominent stieda body and four sporozoites inside each one (Malagon et al., 1988) (see figure).

THE THEORY

As result of the above observations the current existence of a coccidial line of development of the malaria parasites is proposed. On this theoretical trend, it can be assumed that the ancestral coccidia from which malaria parasites originated, had not disappear, it is among us now, and still connected to its life cycle.

A malaria-coccidia parasite produce a very versatile creature, with a double cycle, one carried out only in the vertebrate, and other alternating a vertebrate with an hematophagous insect host. However, even when each cycle can develop independently, as we are used to see them, routes of connection have to exist in nature, so that the parasite may pass from one cycle to another.

The putative route of differentiation from coccidia to *Plasmodium* could be the same as that already mentioned through which the plasmodia were originated. Following the route: epithelial gut cell-hepatocyte (in mammals) erythrocyte-mosquito.

The malaria parasites in its coccidial form might infect different types of hosts, those that support coccidal growth and multiplication for at least several cycles, and those which do not. Hosts belonging to the first group may be either, those which are susceptible to malarial infection and permit the entrance of the coccidial forms to tissues and its differentiation into *Plasmodium*, and those unsusceptible ones that only permit the growth and dispersal of the coccidial forms. Hosts of the second group susceptible to malaria, when eating oocysts of the malaria-coccidial forms would develop malaria but not a coccidial infection.

Once a malaria infection is established and cycling, it would leave the malaria cycle and enter to its coccidial one when a malaria infected host, either vertebrate or arthropod, were eaten by an adequate predator. Adequacy would be shown by development of a malarial, or coccidial infection or both, by the predator as result of the entrance of asexual or sporogonic invasive forms to its gastrointestinal tract. Parasite dispersal in one case is, as we know, by means of mosquitoes, and by means of faeces the other case would be. Transmission of malaria is through the skin by the bite of an infected mosquito, and through the mouth by ingestion of either faeces with malaria oocyst forms, or tissues of malaria infected animals.

Despite the fact the these theoretical thoughts are much unfinished, I hope they would be enough to stimulate research work in those who share the idea that the malaria, for many epidemiological reasons, may well be transmitted by other means apart from the mosquito.

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