A STAGE IN THE MIGRATION OF THE ADULT TERTIAN MALARIAL PARASITE. EVIDENCE OF THE EXTRACELLULAR RELATION OF THE PARASITE TO THE RED CORPUSCLE.*

BY MARY ROWLEY-LAWSON, M.D.

(From the Laboratory of Dr. Mary Rowley-Lawson, New London.)

PLATES 51 TO 55.

In previous publications I have stated that I believe the malarial parasite to be extracellular and to migrate from corpuscle to corpuscle. To recapitulate:

I believe the malarial parasite to be extracellular throughout its existence; that is, except for brief periods when it is free in the blood serum, it is attached to the external surface of the red corpuscle.

The parasite attaches itself to the red corpuscle by means of delicate pseudopodia thrown out from the cytoplasm of the parasite. It encircles and squeezes up into a mound a portion of the hemoglobin (figures 1 to 17); thus it maintains its position on the outside of the red corpuscle.

From my observations I believe that each parasite in the course of its development, destroys several red corpuscles, migrating from one to another, thus giving a rational explanation of the anemia which occurs in the course of the malarial infections.

The evidence in favor of migration is as follows: 1. The great destruction of red corpuscles, which is usually out of all proportion to the number of parasites present in the peripheral blood, provided that each parasite destroys but one corpuscle. 2. Instances of multiple infection of red corpuscles by several young parasites,

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sometimes as many as seven. They cannot all grow on one corpuscle, and even if conjugation were amongst the possibilities, it would not account for odd numbers nor for infection of a corpuscle by parasites of varying stages of development. Therefore if these parasites are not to die, they must migrate. 3. What appear to be stages in parasitic migrations, which may be summarized as follows: (a) Pigmented parasites free in the blood serum. They may be seen in various stages of development, compact, ring-shaped, ameboid, and with protoplasmic pseudopodia, the pigmentation being evidence of previous attachments to red corpuscles. (b) Pigmented parasites in various stages of development, attached to red corpuscles the hemoglobin of which is apparently unaltered. Here, as in stage (a), the pigmentation is evidence of one or more previous attachments. (c) Pigmented parasites in various stages of development on decolorized red corpuscles and on corpuscular skeletons. (d) Pigmented parasites partly on and partly off degenerated red corpuscles, caught apparently in the act of abandoning them. (e) Corpuscular skeletons, which are the expanded, dehemoglobinized remains of red corpuscles, usually more or less semilunar in shape, granular, and staining a delicate pink. These skeletons are most frequently seen free from parasites.

This paper is intended principally as a description of stage (d), but it illustrates also the extracellular relation of the adult tertian parasite to the red corpuscle. In one specimen of blood from a series of smears taken consecutively, one after another, from a patient who had taken no quinine, I found over 100 thirty (?) hour parasites partly on and partly off expanded red corpuscles showing granular degeneration (figures 19 to 54, and 59 to 78). I have occasionally seen parasites partly off red corpuscles in other specimens; but never so many in any one smear as in this case. Free parasites, in the same stage of development as the parasites seen partly off the red corpuscles, were found in the same smear (figure 55). I believe that these parasites were preparing to migrate, for the infected red corpuscles, though retaining in general their contour, were undoubtedly degenerated, being more or less dehemo-

3 Segmenting parasites on red corpuscles showing similar granular degeneration (figures 55 to 58) were found in the same smear.
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globinized. Finding so many parasites in similar stages of development in this phase, in one smear, seems to me good evidence in favor of migration as against a condition caused by technique. I can think of no evidence in favor of technique that may be responsible for the phenomenon. The smear was made on a slide, with the blood spread only in one direction, yet the parasites were seen reaching away from the corpuscles in various directions. If rough smearing was the cause of the parasites being partly off the corpuscles, the parasites would be drawn off from the corpuscles all in one direction. And technique would not account for a condition where the corpuscle is distorted exactly at right angles to the direction in which the parasite reaches out from the corpuscle (figures 22 and 27).

In many instances that portion of the parasite which is off the red corpuscle, may be seen resting along the periphery of the infected cell (figures 20, 31, 32, 34 to 37, and 39), which would not be the case were technique responsible for its dislocation.

That the adult parasite is attached to the external surface of the red corpuscle and not submerged beneath its surface seems to me to be proved by figures 1 to 58.

Parasites developed beyond the young ring-form stage (figures 1 to 11) may occasionally be seen to be attached to fairly healthy appearing red corpuscles, the bodies of the parasites resting on the periphery of the corpuscles (figures 13 to 16). These parasites are certainly not submerged beneath the surface of the red corpuscles, but have, I believe, only recently attached themselves, and are therefore coming rather than going. Occasionally a segmenting body may be seen extending beyond the periphery of a red corpuscle with unbroken contour (figure 18).

As to the parasites that are preparing to migrate (figures 19 to 54), to the trained eye those that are on the upper surface of the granular degenerated corpuscles can easily be differentiated from the parasites on the under surface; i. e., in figure 22, the parasite is partly off the upper surface of the red corpuscle, while in figure 33 the parasite is seen to be partly off the under surface of the corpuscle.

The unbroken contour of the majority of the infected red cor-
puscles showing portions of parasites extending beyond the periphery, as well as appearance of the adjacent cells, with the exception of a in figure 36, would seem to preclude any suggestion of unusual violence in the spreading of the smear. I use the adjective unusual, as it seems to me that it would require a very unusual violence to produce a condition as rare as that seen in the accompanying plates. I believe the infected red corpuscles were already too much damaged by the action of the parasites to regain their contour on the slide if the parasites had been forcibly squeezed or pulled out of them in spreading the smear, especially parasites of such advanced growth. I do not believe that in smearing the blood it would ever be possible to reach the parasite, if it were submerged beneath the surface of the red corpuscle, in order to pull or squeeze it out, without damaging that corpuscle beyond repair; for instance, in figure 20 the body of the parasite rests on the periphery of the corpuscle and only short pseudopodia are seen to be attached to the corpuscle, the contour of which is unbroken; and in figure 19 only a slender process extends beyond the periphery of a corpuscle with unbroken contour. If these parasites were submerged beneath the surface of the red corpuscles, could technique have produced the condition? I think not.

Healthy appearing red corpuscles may be damaged by technique when the blood is being smeared and not regain their contour. The healthy, uninfected, but distorted, red corpuscle seen at a in figure 35 did not regain its shape after being injured by obvious technique. In malarial infections, especially in the estivo-autumnal infections I have seen many red corpuscles which had not regained their normal contour after having been damaged by the parasites while in the circulating blood.\(^3\)

If the young parasite fastens itself to the external surface of a red corpuscle and proceeds with the destruction of the corpuscle while it is so attached (see young parasites encircling corpuscular mounds on the decolorized red corpuscles in figures 10 and 11), why should the adult parasite follow any other procedure? Indeed, peripheral mounds may be seen in connection with adult parasites.

\(^3\) An article describing and illustrating these damaged red corpuscles will appear later.
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(figure 17, a). And why should the adult parasite assume a more or less characteristic ring-form unless it be for the purpose of securing its attachment to the surface of the red corpuscle? For the ring shape, in connection with the adult parasite, may be explained, as it is explained in connection with the young parasite, as a result of the parasite encircling and drawing up into a mound a portion of the hemoglobin substance of the red corpuscle in order to secure its attachment to the surface of the corpuscle.

In fresh blood preparations, parasites may be seen to abandon red corpuscles which have not been entirely destroyed. Laveran,4 in referring to the external relation of the malarial parasite to the red corpuscle, says: "Osler noticed that the amoeboid bodies which adhere to the red blood corpuscles can be detached and become free in the blood," adding, that this was one of the arguments on which he relied in maintaining that the parasites were only attached to the surface of the red corpuscles. Marchiafava and Bignami5 and Monacho and Panichi6 have stated that quinine may cause certain parasites to abandon the red corpuscles. This being so, if the parasites were submerged beneath the surface of the red corpuscles, then the quinine would have to destroy the substance of the red corpuscles in order to release the parasites; but with the parasites attached to the external surface of the corpuscles, their detachment is more easily explained.

SUMMARY.

1. What appear to be certain definite stages in the migration of the malarial parasite from red corpuscle to red corpuscle may be demonstrated by thorough and persistent observations,—not minutes spent on each specimen, but many hours.

2. The migration of the malarial parasite from red corpuscle to red corpuscle gives a reasonable explanation of the loss of red corpuscles which cannot be accounted for by the destruction of the infected corpuscles at the time the parasites segment.

3. Migration to other red corpuscles is a satisfactory explana-

5 Marchiafava, E., and Bignami, A., in Twentieth Century Practice of Medicine, New York, 1900, xix, 461.
tion of the ultimate fate of the young parasites seen in instances of multiple infection of single corpuscles.

4. In the light of the facts here presented, it would seem impossible to explain the instances of the parasites partly on and partly off degenerated red corpuscles as the result of technique. A stage in the migration of the parasite seems to me to be the probable interpretation of the phenomenon.

5. A corpuscular mound encircled by an adult parasite, when seen at the periphery of the red corpuscle, should have the same significance and interpretation in reference to the extracellular relation of the parasite to the corpuscle, that it has when it is seen in connection with a young parasite.

6. The adult ring-form parasite should have the same interpretation as the young ring-form parasite.

7. Attachment to the external surface of the red corpuscles seems to me to be the only possible interpretation of the appearances of the parasites pictured in this article.

EXPLANATION OF PLATES.

PLATE 51.

TERTIAN MALARIAL PARASITES.

Magnification, × 1,750.

Figs. 1 to 3. Young parasites attached to the external surface of the red corpuscles. Those attached to peripheral mounds may be seen at a; the other parasites are attached to surface mounds.

Fig. 4. The nucleus of the young parasite attached to the peripheral corpuscular mound at a is distorted by technique.

Fig. 5. A young parasite attached to a peripheral corpuscular mound at a, which is almost entirely dehemoglobinized.

Fig. 6. A young parasite attached to the red corpuscle. The body of the parasite rests on the periphery of the corpuscle.

Fig. 7. A young parasite attached to the periphery of a peripheral corpuscular mound. The mound is almost entirely dehemoglobinized.

Figs. 8 and 9. Young parasites encircling peripheral corpuscular mounds.

Fig. 10. A young parasite encircling a surface corpuscular mound; the entire corpuscle is much dehemoglobinized.

Fig. 11. A young parasite encircling a peripheral corpuscular mound. The corpuscle is much dehemoglobinized.

Fig. 12. A pigmented parasite attached to the surface of a red corpuscle. The mounds to which it is attached can be seen at a.

Fig. 13. A pigmented parasite attached to the surface of a red corpuscle, the hemoglobin of which appears to be unaltered. As a large part of the parasite
rests on the periphery of this corpuscle, I believe that the parasite has only recently attached itself to it, hence the unaltered appearance of the hemoglobin.

Fig. 14. A parasite attached to the external surface of the corpuscle. The body of the parasite is seen to be off the corpuscle, having been dislocated by technique.

Fig. 15. A pigmented parasite on the periphery of the red corpuscle, the appearance of the pseudopodia suggesting that the parasite is starting to encircle a corpuscular mound. The slightly degenerated appearance of the infected corpuscle is probably due to the action of the young parasite.

Fig. 16. A pigmented parasite, the body of which rests on the periphery of the corpuscle. This parasite is attached to the under surface of the red corpuscle. There is another parasite attached to the upper surface.

Fig. 17. An adult pigmented parasite attached to the external surface of the red corpuscle. The peripheral mound to which it is attached can be seen at a.

Fig. 18. Young parasites resulting from a very recent segmentation; the red corpuscle has not been entirely destroyed. One of the segments can be seen to be partly off, and two entirely off the corpuscle at a.

Fig. 19. An adult pigmented parasite on the upper surface of a granular degenerated red corpuscle. A pigmented protoplasmic process arising from the parasite can be seen extending beyond the periphery of the corpuscle at a.

Fig. 20. An adult parasite resting on the periphery of a granular degenerated red corpuscle. With the exception of three short and delicate pseudopodia, the parasite is free from attachment to the corpuscle.

Fig. 21. An adult parasite on the upper surface of a degenerated red corpuscle, with a portion of its protoplasm extending beyond the periphery of the infected corpuscle.

PLATE 52.

TERTIAN MALARIAL PARASITES.

Magnification, X 1,750.

Fig. 22. An adult parasite partly on and partly off the upper surface of a degenerated red corpuscle. Note that the parasite is lying off the corpuscle at right angles to the way the cell is distorted.

Fig. 23. An adult parasite partly on and partly off the upper surface of a degenerated red corpuscle. The mound to which the parasite is attached shows less of the granular degeneration than the rest of the corpuscle.

Fig. 24. An adult parasite partly on and partly off the upper surface of a degenerated red corpuscle. The surface mound to which the parasite is attached is almost entirely decolorized by the action of the parasite. This mound can be seen at a.

Figs. 25 and 26. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles. The mound to which the parasite in figure 26 is attached can be seen at a.

Fig. 27. An adult parasite partly off the under surface of a degenerated red corpuscle. The granular outline of the infected corpuscle can be traced across the upper surface of the parasite between o and o. The mound to which the parasite is attached can be seen at a. Note that the distortion of the corpuscle is at right angles to the way the parasite lies off the corpuscle.
FIGS. 28, 29, and 30. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles. The mounds of attachment of the parasite in figure 30 can be seen at a.

FIGS. 31, 32, and 33. Adult parasites partly on and partly off the under surfaces of degenerated red corpuscles. In figures 31 and 32, the part of the parasite that is off the corpuscle can be seen resting on the periphery of the infected corpuscles.

PLATE 53.

FIG. 34. An adult parasite partly on and partly off a degenerated red corpuscle; the part of the parasite that is off the corpuscle may be seen resting on the periphery of the corpuscle.

FIG. 35. An adult parasite partly on and partly off the upper surface of a red corpuscle which is less dehemoglobinized than the other corpuscles shown which are infected by parasites partly off and partly on. At a is a red corpuscle that has been injured by technique and has not regained its normal shape.

FIGS. 36 to 39. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles. In figures 36, 37, and 39 the part of the parasite which is off the corpuscles can be seen resting on the periphery of the infected corpuscles. In figure 37 a young parasite is seen attached to the infected corpuscle.

FIG. 40. An adult parasite partly on and partly off the under surface of a degenerated red corpuscle. Another adult parasite can be seen on the under surface of the infected corpuscle.

FIGS. 41 and 42. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles.

FIG. 43. An adult parasite partly on and partly off the under surface of a degenerated red corpuscle. The mound of attachment is seen at a.

FIGS. 44 and 45. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles. In figure 44 a young parasite is seen attached to the infected corpuscle. The mound to which the adult parasite is attached can be seen at a.

PLATE 54.

FIG. 46. An adult parasite partly on and partly off the under surface of a degenerated red corpuscle.

FIGS. 47, 48, and 49. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles.

FIG. 50. An adult parasite partly on and partly off the under surface of a degenerated red corpuscle.

FIGS. 51, 52, 53, and 54. Adult parasites partly on and partly off the upper surfaces of degenerated red corpuscles.

FIG. 55. An example of the free parasites found in the same smear with, and in the same stage of development as, the parasites seen partly on and partly off the degenerated red corpuscles.
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Figs. 56, 57, and 58. Segmenting parasites on corpuscles which are in a similar stage of degeneration to many of the corpuscles which show the parasites partly off them, and which came from the same smear.

Plate 55.

TERTIAN MALARIAL PARASITES.

Magnification, $\times$ 1,750.

Fig. 59. (Corresponds to figure 18.) A segmenting parasite showing some of the separate segments beyond the periphery of the infected red corpuscle.

Fig. 60. Two young parasites attached to the surface of a red corpuscle; the body of one of the parasites is on the periphery of the corpuscle with the attaching pseudopodium arranged in the form of a loop overlying the corpuscular substance; the other parasite is attached to a decolorized surface mound.

Fig. 61. (Corresponds to figure 12.) A pigmented parasite attached to the surface of a red corpuscle. The mounds to which the parasite is attached can be seen.

Fig. 62. (Corresponds to figure 15.) A pigmented parasite on the periphery of a red corpuscle, with the pseudopodia overlying the corpuscular substance.

Figs. 63 to 78. (Correspond to figures 25, 28, 23, 24, 37, 26, 30, 22, 29, 33, 32, 31, 21, 20, 19, and 36.) Adult pigmented parasites partly on and partly off granular degenerated red corpuscles. Some of the parasites may be seen to be on the upper surfaces of the corpuscles, others on the under surfaces. In figure 18, with the exception of three short and delicate pseudopodia, the parasite is free from attachment to the corpuscle. In figure 19 only a delicate pseudopodium extends beyond the periphery of a red corpuscle with unbroken contour.
(Lawson: Migration of the Adult Tertian Malarial Parasite.)
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