well defined from the plasma of the host cell (compare Figs. 12-17). The light blue plasma of the parasites stands out well against the dark blue plasma of the lymphocyte. The reverse may be observed in forms against which the plasma of the lymphocyte does not stand out because that of the parasite appears to be of a dark blue colour. However, as I could not prove differences in the nuclei, I should not yet like to say that there are actually sexual differences.

Concerning the size of the agamogonous stages, we see from the above that it varies considerably. The youngest forms measure about 0.8–1 μ, the rest from 1–10 μ. The latter is quite an exception. Forms, as illustrated by Figs. 9 and 10, sometimes attain 12-15 μ.

The Gamogonous Generation.

There is a great deal of difference between the gamogonous generation and the agamogonous one. Biologically it is of special interest, as by means of this generation forms are called into existence with which the life cycle of *Theileria parva* in cattle has reached a definite point, and with its formation the disease likewise reaches its height. The animal must either succumb (which is mostly the case in South Africa) or recovers. Consequently the parasite inside the animal dies off and no other parasite will find a suitable medium to develop in.

As described before, the agamete produced by schizogony out of an agamont can again become an agamont, or, in other words, the agamogonous development repeats itself. However, the parasites, like all protozoa (after a certain time or rather after the agamogonous development) have to undergo a regulating process. This latter process will enable it to start a new life, which is due to fertilization. We are accustomed to a change of hosts in the protozoic blood parasite, which, in the course of its phylogenetic development has adapted itself suitably to its respective parasite. The parasite completes in one host its agamogonous and progamogonous stages until it has developed into gametocytes and in the second host finishes up with its sexual, gamogonous, and postgamogonous development. Besides this development we are aware of parthenogenesis, a process of fertilization which enables the female forms to obtain agamogonous forms by special metamorphosis of the nucleus. *Theileria parva* is an exception in this case. *Parthenogenesis does not occur, consequently there is no relapse and no possibility of infecting new ticks after the animal has recovered.*

The gamogonous forms come forth out of the agamogonous ones, viz., by means of schizogony the agamont produces young gamonts which differ from agametes by their nuclei. The nucleus generally has a round or oval shape during all its stages of development (Plate II, Figs. 20-41; Plate III, Figs. 42 and 43; Plate IV, Figs. 10-12; Plate V, Figs. 13-23), with the exception of the forms of division. In this respect the contrast with the agamogonous forms is so important that it may be considered to be a characteristic feature. The affinity of the gamogonous forms, in regard to staining material, is much stronger than is the case with the agamogonous ones. The structure of the nucleus of the gamont is denser and takes all the stains intensely, a deep black with haematoxylin mixtures, and a deep red with *Giemsa* stain. If the differentiation is successful, a still darker kernel is visible, the karyosom.

The agamont, before producing gamonts by schizogony, undergoes important nuclear changes. Frequent structures of chromidia are met with, especially in the intracellular forms. Undoubtedly this picture indicates a separation of vegetative and generative nuclear substance, as perceived in the cycle of development of many other protozoa. Sometimes it happens that the parasite, before dividing into gamonts, develops still further into gametocytes. The agamont becomes a gamont by transforming its vegetative nucleus into a generative one, and finally it is split up into gametocytes. Such a course of development is particularly conspicuous in the intracellular forms, which, by premature dying off of the host cell (Fig. 19, Plate I), break up into irregular, undeveloped agametes. The young forms of the parasite do not always die off, but continue their further development by turning into gamonts, showing soon stramonium and schizogonical forms. (Figs. 27 and 29, Plates II and V.)

I am not in favour of the expression "stramonium form", as it ought to be applied to the agamogonous generation as well, and as it is inappropriate for morphological distinction. With intracellular forms they are not found as a rule, except perhaps in the dry smear preparations after dry fixing; but the latter will often result in artificial products, and especially in stramonium forms, which will never be observed with the living object and moist fixing.

Generally, an agamont produces small gamonts (measuring from 0.7–1 μ) after having reduced its nuclei before the schizogony took place. These gamonts often show a second small kernel on the pole opposite to that of the principal nucleus. By successive division, similar to the above described mitosis, the number of the nuclei increases simultaneously with the size of the parasite to 12 μ and more. (Compare Plate II, Figs. 25, 30, 35.)

Schizogony does not always develop regularly (*vide* Fig. 35), but often small, undeveloped gametocytes cling together in groups of three, four, and more. Not seldom the latter infect the red blood corpuscles, in which the development into gametocytes takes place. Concerning the number of gametocytes brought forth by free, gamogonous forms, we may add that it is considerably smaller than that of intracellular forms (*vide* Plate III, Figs. 42 and 43, obtained by moist, fixed *Giemsa* preparations). As will be seen by the foregoing, this is connected with the power of resistance of the respective host cell. In some cases of East Coast fever I sometimes found a great number of lymphocytes which resisted infection until schizogony in the gametocytes had set in. The agamont divides into gamonts *within* the lymphocyte; the gamonts on their part continue to develop, and in this manner a great number of gametocytes is produced. Also the formation in groups of four is due to the schizogony of gamonts (as mentioned before, Plate III, Figs. 42 and 43; Plate V, Fig. 23).

If these intracellular, gamogonous forms undergo disintegration, the destruction of the host cell is closely connected with it. Naturally mistakes can easily be made as regards the breaking up of the lymphocyte nucleus or leucocyte nucleus into small chromatin masses which stain likewise. In stained preparations, however, the gametocytes are easily recognized by well stained protoplasma, which is absent in the decayed particles of the host nucleus.

These small gametocytes, if living, show jerky movements, which explains the comma shapes.

In the gamogonous forms (which attain about the same size as the agamogonous ones) the nuclei, if observed alive, are more prominent than is the case in agamogonous forms, and which is due to the more compact structure. When intracellular, they are distinguishable from granulations or chromidia of the host cell. Vital staining could only succeed when the parasite was about to die off.

The Gamogonous Forms in Red Blood Corpuscles.

The only men who have lately made observations regarding the parasites in the blood corpuscles are *Nuttall*, *Fantham*, and *Porter*. The result is as follows: *Theileria parva* increases in size in the erythrocyte, and is distinguished by its mobility. As to a reproduction, the above-named authors express themselves with reserve. They did not succeed in observing an actual division, but only an indication of this process in their larger forms, and they think it possible that a reproduction within the red blood corpuscles may take place.

As for my observations, I have already mentioned many items. I was only able to trace disintegration of gamonts, and I believe that *Nuttall* and his collaborators have observed these forms. The characteristic cross forms originate principally in the organs when the segmentation of gamonts in their gametocytes takes place. (Plate III, Figs. 42 and 43). It is possible that portions undergoing division, i.e. gametocytes not yet completely formed, or gamonts invade the blood corpuscles and that the further division is continued in or upon the erythrocyte. In one case of East Coast fever which showed an exceptionally large number of cross shapes, I observed in blood corpuscles a segmentation of multinuclear parasites (2-4 strongly refractile nuclei). This I must consider is quite an exception; I am also convinced that we had to deal with the above-mentioned portions of gamonts which occupied the blood corpuscles.

As to the movements of gametocytes within the erythrocytes I was unable to confirm the strong activity which *Nuttall* and his collaborators emphasized. On the contrary I found their movements to be slow. Undoubtedly there is a change in the shape. The small pear-shaped gametocytes assume another shape as soon as they have taken possession of the erythrocyte. It either grows into ring-shaped larger parasites, soon changing from a ring into a round or oval form, or it grows into long, narrow forms, stretched or bent (Plate III, Figs. 44 and 45). In any case, through this process the sexual difference becomes marked. However, a definite conclusion cannot be drawn until we have thoroughly studied the stages of development within the tick. In a second part of my work, I will report on the development in the transmitting host, and hope to deal with these forms more in detail.

With solutions of saponin (10 per cent.), sodium taurocholate (10 per cent.), and quinine (1 per cent.), parasites are rapidly destroyed. Saponin and sodium taurocholate dissolve almost completely all forms belonging to the cycle of development, Also the endoglobular blood stages will be destroyed as soon as the corresponding concentration is used. The harmful effect the parasites have upon erythrocytes is so slight that for their destruction the concentration required to destroy the normal blood corpuscles of a healthy bullock is just sufficient.

The foregoing described development of *Theileria parva* is observed principally in the lymphatic and haemolymphatic system. Concerning the pathological changes which the parasite causes in the system and the body of an animal generally, *K. F. Meyer*, at this Laboratory, has investigated the matter thoroughly, and I would now like to draw attention to it. At the beginning of my researches, *Meyer* was *not* convinced of the pathogenity of *Theileria parva*; he had, however, the same result as I, as far as concerns the schizogony of the gamogonous forms. Quite independent from me he detected the above-described schizogonical forms in dry preparations.

As the gamogonous development is preceded by an agamogonous one, which only takes place in the organs and in the haemorrhages, produced by the parasites (*K. F. Meyer*), the formation of gametocytes cause a rapid infestation of the blood with parasites. Experience teaches us that the parasites in the blood increase from day to day. And it is a striking fact that up till now no detailed observation on the living object concerning a further development hitherto considered to take place in the blood, could be made. Owing to the fact that there is no multiplication in the blood as seen by the cycle of development, this circumstance is explained. *Theileria parva* is not an exception in this respect.

Among the malaria plasmodia of apes we likewise distinguish agamogonous and gamogonous cycles; the forms known under the name *Plasmodium kochi* are very probably two species, one of which undergoes the above development described by *Von Ehrenberg*, *Gossler*, and myself; the development of the other, however, is similar to the tropical parasites of man. With the latter we only trace gametocytes in the blood, the agamogonous forms must consequently be looked for in the organs. These parasites, however, can be transmitted by means of blood, and we must, therefore, accept parthenogenesis. So far I did not succeed in transmitting *Haemoproteus columbae* artificially with large quantities of blood, but I had good results with minced lung pieces which contained agamogonous forms. Parthenogenesis, as known to occur in *Haemoproteus paddae*, I have likewise not been able to observe. A great similarity with *Theileria parva* has *Trichosphaerium sieboldi*, which, according to *Schaudinn*, has two cycles, agamogonous and gamogonous, well characterized by their nuclei.

With babesia infections we find the red blood cells having grave lesions, anisocytosis, basophilia, polychromatophilia, etc., and a typical increases of parasites. *Theileria parva* does not cause these changes, only towards the end of the disease anisocytosis is but slightly noticeable. According to observations by *W. H. Andrews*, assistant at this Laboratory, on the pathological changes in the blood corpuscles, the parasitism of *Theileria parva* influences the red blood cells to a very small extent only. The number of erythrocytes decreases only towards the end of the disease. This proves likewise that the parasite appears only in the blood corpuscles in order to get into the second host where it undergoes sexual development. It is the development in the organs which is responsible for the disease in the animal.

As mentioned before, an artificial transmission of East Coast fever with blood is impossible; as is known, experiments in this institute succeeded in conveying the disease from one animal to another by means of small pieces of organ or roughly minced parts of organ.

As we are always certain to trace the early stages of development in the organs which are subject to a further development, and in the blood the final stages which only continue their development in the tick, these facts find an explanation. There possibly may be a means of transmission with blood, although transfusion of 4-5 litres at the height of the disease had a negative result. Perhaps this transmission ought to be done at the beginning of the disease and before the agamogonous forms appear in the glands. Such experiments have yet to be undertaken.

In conclusion, I wish to refer briefly to the ookinetes (Plate III, Figs. 46 and 47). The parasites quit the blood corpuscles as soon as they enter the stomach of the tick, generally within a couple of hours. I was also able to trace an observation made by *Nuttall* and his collaborators, viz., an emigration of some parasites which invaded new blood corpuscles as soon as they came in contact with another medium or were brought into different physiological conditions. I believe that this invasion does not take place normally within the blood circulation of the animal. The parasites flock together in clusters within the tick; sometimes they cling close together, forming a large ball, in which case their morphological difference cannot be determined. Generally larger and broader forms can be discerned which hardly move and which are likely to represent macrogametes. The other forms are characterized by their mobility. The amoebal stages described by *Koch* and *Dschunkowsky* and *Luhs* I was never able to detect; however, sometimes forms were visible which seemed to die off by dissolving and sometimes under the protrusion of the plasma (pseudopodes). Forms destined to live in the tick, and which were of elongated shape, seemed to me to be the parasites referred to by the above-mentioned authors. Within these forms I sometimes found a second nucleus well developed. As I have not yet been successful in tracing copulation, I should not like to put forward a theoretical supposition. Undoubtedly the existence of ookinetes is assured. They are small, measure about five microns, and have the shape of a gregarine, which, in accordance with the ookinetes of the other blood parasites, are remarkable for their wriggling and jerky movements. Retort forms observed also which point to a further development not unlike that of malaria and other parasites.

Description of Plates.

All figures of Plates I-III were executed by means of the Abbe drawing apparatus, after moist fixed preparations stained with Giemsa. (Zeiss Micrasc. Apochr. Homog., 1 mm., 2mm., apochrom. comp. oc. 12.) Plates IV-V show microphotographs of dry preparations.

Plate I—

Figs. 1-19.—Agamogonous generation.
Figs. 1-11.—Free agamonts.
Fig. 11.—Agamont in schizogony.
Figs. 12-19.—Intracellular, agamogonous forms.
Fig. 19.—Schizogony of the agamont.

Plate II—

Figs. 20-35.—Free gamogonous forms.
Figs. 36-41.—Intracellular forms.

Fig. 36.—Double infection.
Fig. 37.—Division of nuclei.
Fig. 39.—Process of reduction in parasites.

Plate III—

Figs. 42-43.—Strongly infected lymphocytes. Gamonts in schizogony. Formation of cross forms.
Figs. 44-45.—Gametocytes in red blood corpuscles.
Figs. 45-47.—Ookinetes from stomach of tick.

Plate IV—

Figs. 1-9.—Agamogonous, free and intracellular forms.
Figs. 10-23.—Gamogonous, free and intracellular forms.
Fig. 24.—Ookinet.

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