a residual mass of protoplasm (*c*). Each of these sporoblasts surrounds itself with a firm membrane and becomes a sporocyst (*d*), while later within each sporocyst after nuclear division two sporozoites are formed and a residual mass of protoplasm is left unused. The sporozoites are characteristically sickle-shaped or crescentic, and abandon the sporocyst when this reaches the alimentary canal of the new host, and is opened by the action of the alimentary secretions. The entrance of the sporozoites into the epithelial cells and their growth to schizonts completes the life cycle.

This typical course of development is well represented by the tabular outline given by Lühe and reproduced here. The stages connected by a single vertical line (|) are successive generations in the life cycle; those connected by the sign of equality (=) are produced by growth or metamorphosis within the single generation.

is not in the interest of precision, and may evidently lead to serious misunderstanding. Henceforth the name coccidia can be used only in the more general sense.

The genus *Eimeria* is the best known of all. Its most important characteristic is the formation in each oocyst of four sporocysts, each with two sporozoites. A residual mass of protoplasm is always present in the sporocyst with the sporozoites, and a similar residual mass is sometimes formed in the oocyst with the growth of the sporoblasts. Of the many species assigned to this genus, the most important and better known forms which are pathologic to man and some domestic animals are included in the following key:

1. Oocyst with residual mass.......................... 2
1. Oocyst without residual mass........ 3
2. Oocyst oval, 33–49 μ by 16–28 μ; sporocyst spindle-shaped (rabbit, man).................*E. Stiedæ* (Lind.)

DEVELOPMENT OF EIMERIA.

Schizogony (oft repeated).
Sporozoite = Schizont.
Merozoite = Schizont. | Merozoite = Schizont.
Merozoite = Schizont | etc. (Schizogony soon ceasing).
Merozoite = ♀ Macrogametocyte. = ♀ Macrogamete.
Merozoite = ♂ Microgametocyte. | ♂ Microgamete.
Merozoite = ♀ Macrogametocyte. = ♀ Macrogamete.
Merozoite = ♂ Microgametocyte. | ♂ Microgamete.
Merozoite = Schizont | etc. (Schizogony soon ceasing).

Sporogony.
Copula = Sporont (Oocyst).
|
Sporoblast = Sporocyst.
|
Sporozoite = Schizont.

This general plan of development is modified in the individual species in various manner. The most striking modification is a simplification by suppression of the entire schizogonic cycle, so that the macrogametes and microgametocytes arise directly from the sporozoites which have penetrated epithelial cells.

The coccidia parasitize almost all groups of the animal kingdom, and are distributed over the entire world, although, as might be expected, the majority of reports thus far made concerning their presence come from European countries.

For the subdivision of the group Léger's proposal to use the number and form of the sporocysts and of the sporozoites has been generally adopted. The adjoined table gives a review of the common genera arranged according to Léger's scheme.

2. Oocyst spherical or cylindrical, 15–32 μ by 11–17 μ; sporocyst oval (mouse)........*E. falciformis* (Schuberg)
3. Simple forms. Oocyst oval to cylindrical, 24–35 μ by 13–20 μ..........................*E. hominis* (Riv.)
3. Twin forms.....................*E. bigemina* (Stiles)

Eimeria Stiedæ (Lindemann 1865).—(Syn.: *Monocystis Stiedæ* Lindemann 1865; *Psorospermium cuniculi* Rivolta 1878; *Coccidium oviforme* Leuckart 1879; *C. cuniculi* Raillet 1893; *Pfeifferia princeps* Labbé 1896; *Pfeifferella princeps* Labbé 1899. *Eimeria cuniculi* Lühe 1902.)

All stages are known. Oocyst (Fig. 5178) in the liver of rabbit, oval 0.033–0.049 mm. long, 0.015–0.028 mm. broad. Cyst wall heavy, smooth, with opening at one pole. The coarsely granular protoplasm completely fills the cyst, but later contracts to a spherical mass at the centre (0.017 mm. in diameter). Spore formation outside

Ripe oocyst contains......	Numerous sporozoites.....	No sporocysts. ASPOROCYSTIDEA		Legerella.
		Many sporocysts each with..... POLYSPOROCYSTIDEA.	One sporozoite	Barroussia.
			Two sporozoites	Adelea.
			Three sporozoites	Eucoccidium.
			Four sporozoites	Klossia.
	Eight sporozoites	Two sporocysts each with four sporozoites. DISPOROCYSTIDEA		Isospora.
		Four sporocysts each with two sporozoites. TETRASPOROCYSTIDEA		Eimeria.
	Four sporozoites	Two sporocysts each with two sporozoites.		Cyclospora.

Some confusion has prevailed regarding the correct names of the various genera. The original cause of this difficulty rests on the fact that the two phases of the life cycle, schizogony and sporogony, were discovered and named separately, and that their relations as parts of the development of a single species did not become known until a much later date. All of the human parasites thus far recorded from this group fall within the limits of a genus named *Coccidium* by R. Leuckart in 1879, and this name has been generally incorporated into works on the subject. At a very recent date, however, Stiles and Lühe have independently called attention to the fact that the name *Eimeria*, introduced in 1875 by Aimé Schneider, has the right of priority, and must replace the more common form according to laws of zoological nomenclature. This is really fortunate from the general standpoint since the name coccidia has been very generally used for the entire group as well as heretofore for the genus; yet this

the host requires two to three weeks. The entire sphere divides into four sporocysts each with a thick covering and with a length of 0.012 to 0.015 mm. and a breadth of 0.007 mm. Two comma-shaped sporozoites are formed in each sporocyst, and a granular residual mass of protoplasm lies in the hollow between their enlarged ends (Fig. 5179). The sporozoites are set free by gastric digestion. They ascend the gall ducts, pene-

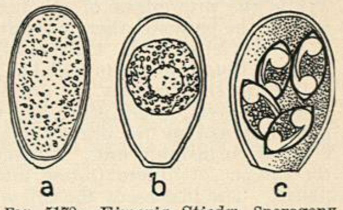

FIG. 5178.—*Eimeria Stiedæ*, Sporogony from Liver of Rabbit. *a*, Young oocyst; *b*, same with protoplasm contracted preparatory to division; *c*, same divided into four sporocytes, each containing two sporozoites which have already developed. Magnified. (*a*, *b*, after Leuckart; *c*, after Simond.)

trate the epithelial cells, and when fully grown measure 0.02–0.05 mm. in length by 0.02–0.039 mm. breadth. They divide into from 30 to 200 merozoites (Fig. 5176) which spread the infection. Ultimately the formation of macro- and microgametes leads to the fertilized sporont stage, the oocyst.

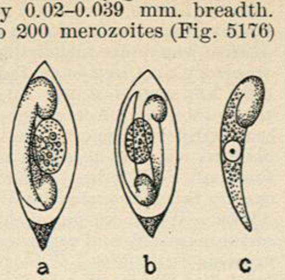

FIG. 5179.—*Eimeria Stiedæ*. *a*, *b*, Sporocysts each with two sporozoites and residual mass; *c*, a single sporozoite. Highly magnified. (From Railliet, after Balbiani.)

This species is an abundant parasite of the rabbit, in which it parasitizes in the epithelium of gall ducts and liver. According to the degree of infection sooner or later inflammation and proliferation of the epithelium lead to the formation of nodules of caseous matter, containing amid various remnants coccidia in all stages of development. These conditions may lead to severe sickness or even to the death of the host; in other cases the animal recovers as the process of schizogony appears to have distinct self-limitations. The infection is spread by the contamination of food with spore-infected fæces.

Several cases of human infection are on record. Evidently conditions favor such infection only rarely. To

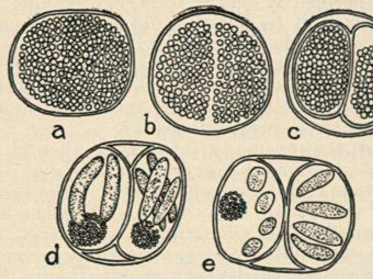

FIG. 5180.—*Eimeria bigemina*, Sporogony. *a*, *b*, *c*, Division into two masses; *d*, *e*, formation of sporoblasts with residual mass. Highly magnified. (After Stiles.)

the four positive cases cited by Leuckart, all in Germany and Austria, Silcock has added another from London. A number of doubtful cases are also included here by some authorities. The observations of Thomas in Boston, according to which this species was found in a small cerebral tumor surrounded by bone tissue, has little to support the diagnosis in view of the normal condition of the liver and intestine, and has been universally questioned by reviewers. In any event the supposed coccidia cannot belong to this species, or any other yet reported from man, on account of their size (0.014–0.022 mm. in length). They correspond, however, in size nearly to the coccidia reported by Stiles from sheep which belong to a species as yet unnamed. More probably they are not coccidia at all.

Eimeria hominis (Riv. 1878), nec. R. Blanchard 1895.—[Syn.: *Cytospermium hominis* Rivolta 1878; *Coccidium perforans* R. Leuckart 1879; *C. hominis* Railliet 1893; *Pfeifferella princeps* (Labbé 1899) in part.]

Oocyst (Fig. 5177) 0.024–0.026, or even 0.035 mm. long by 0.0128–0.014 or even 0.02 mm. broad, plumper than those of *E. Stiedæ*, from which also they differ in the constant presence in sporulation of a residual mass of protoplasm that is said to be constantly absent in the latter species. (Compare Figs. 5177 and 5178.) Here also only three to four days are necessary to bring the division of the contents of the oocyst into sporoblasts (sporocysts).

This species, which is so closely related to *E. Stiedæ* that many authors regard them as identical, parasitizes in the intestinal epithelium of the rabbit, where it evokes serious, often fatal epidemics. Railliet and Lucet have demonstrated that infection takes place by the ingestion of ripe spores, and rapid schizogony brings about in a few days serious auto-infection involving the epithelium and Lieberkühn's glands so as to occlude the latter. The forms found in horse, goat, cattle, sheep, pig, and other wild species are usually regarded as varieties, but the considerable differences in form and size make it more probable that some at least represent distinct species.

Eimer found in two bodies examined in Berlin the epithelium of the intestine filled with coccidia, and even in large part destroyed by them. These are probably referable to this species. Other authors have reported the discovery of coccidia in human fæces at various times without furnishing data for the determination of the species concerned.

Eimeria bigemina (Stiles 1891).—(Syn.: *Cytospermium villorum intestinalium canis et felis* Rivolta 1874; *Coccidium bigeminum* Stiles 1891.)

Oocyst (Fig. 5180) 0.012–0.015 mm. by 0.007–0.01 mm. (in dog), or 0.008–0.01 mm. by 0.007–0.009 mm. (in cat), or 0.008–0.012 by 0.006–0.008 mm. (in polecat). The oocyst divides into two parts, each of which encysts and forms four sporocysts. The oocysts occur not in the epithelium, but in the central tissue of intestinal villi (Fig. 5181).

The species was first seen as early as 1854 by Fink, who, however, misinterpreted the character of the objects. It has often been confused with *E. hominis*, from which the above characteristics easily distinguish it. A case of human infection, published by Virchow in 1860, and another by Grunow in 1901, very probably belong here. The description given by Railliet and Lucet of coccidia discovered in the fæces of a mother and child who had long suffered from chronic diarrhœa corresponds well with this species in the small size of the bodies found, and is also probably referable to it. The form is evidently only an occasional parasite of man, and infection probably results from lack of cleanliness or too intimate association with pet dogs or cats. It may be that the forms discussed as varieties from different hosts actually represent different species. Stiles has found this species in dogs killed in Washington, D. C.

It is not surprising in view of the imperfect acquaintance with this group that all sorts of questionable structures should be referred to it. They are all such as have been reported from man usually in connection with some abnormal condition, and frequently also on the basis of a single occurrence. In most cases only scanty data are given concerning the supposed coccidia, and even of the best known of these problematic structures too little can be said to determine their true nature or position in the zoölogical scheme. It is best to call attention to certain of these cases briefly, in order that if possible further data should be accumulated to elucidate their real character. Perhaps the most sporozoon-like of all are bodies described by Rixford and Gilchrist from two cases studied at the Johns Hopkins Hospital in 1897; their characters so far as known do not easily permit of their classification in the coccidia (s. str.).

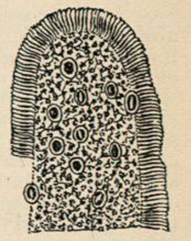
FIG. 5181.—*Eimeria bigemina* in Transsection of Villus from Intestine of Dog. Highly magnified. (After Stiles.)

Coccidioides immitis Rixford and Gilchrist 1897.—(Syn.: *C. pyogenes* Rixford and Gilchrist 1897.)

Unicellular spherical bodies from 0.007 to 0.035 mm. in diameter.* So-called capsule thick, doubly contoured, enclosing a finely granular protoplasm with a clear zone [ectosarc?], 0.002–0.003 mm. wide, between capsule [pellicle?] and contents. No vacuoles seen; nucleus not demonstrated. Position of parasites usually intracellular, sometimes, however, extracellular. Sporozoites [merozoites?] ap-

*The authors give the size of the adult (p. 229) as 15 to 27 μ; again in the diagnosis (p. 243) as 16 to 30 μ, and finally in their summary (p. 246) as 7 to 27 μ. In the second case the parasites are given as 20 to 35 μ in diameter.

proximately one hundred in a capsule, 0.001–0.002 mm. long.

Found primarily (?) in the skin, later generally throughout internal organs also. Reported from California and Buenos Ayres. All cases reported concern males of thirty to forty years of age.

In the first case the disease first appeared on the back of the neck and spread very slowly, causing death in

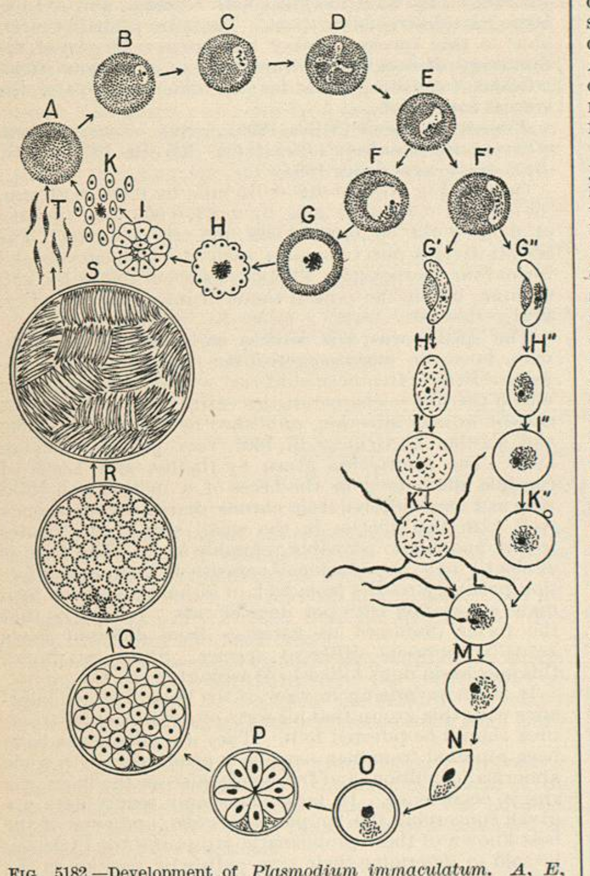

Fig. 5182.—Development of *Plasmodium immaculatum*. *A*, *E*, *G*, *K*, Schizogony in human blood; *F'*, *L*, formation of gametes and fusion of same; *M*, *S*, *T*, sporogony in mosquito. Somewhat diagrammatic. For further details see text. (After Neveu-Lemaire.)

about ten years. It was only very slightly contagious, if at all, as beyond the original sores new lesions appeared only in two spots on the patient's body, and none of those who came in contact with him are known to have become infected. Some inoculation experiments were successful, but no cultures. The cutaneous lesions resembled tuberculosis cutis in character, being the seat of genuine caseation or coagulative necrosis. Both to the naked eye and microscopically the nodules were indistinguishable from tubercles save that they contained the protozoa and did not contain tubercle bacilli. In the opinion of the discoverers this seems to indicate the power to produce toxic products which possess pyogenic properties, causing both the local lesions and general symptoms. From the fact that the whole alimentary canal and mesenteric glands remained normal throughout the course of the disease, the authors exclude the supposition that the parasites entered the system through the digestive tract. The parasites were particularly abundant in the caseous foci, and occurred in far greater numbers in the lesions of the internal organs than in the cutaneous lesions. Often these parasites were found in multitudes in giant cells. They were searched for in vain only in the membranes and substance of the brain.

Another case was reported by the same authors, and like the first occurred in a native of the Azores, who had been resident in California for a number of years. The disease was acute rather than chronic as in the first; and was very destructive as the patient lost both eyes, the nose, and much of the lip, and one ear in the course of three months. According to the authors the parasite was a different species, but the distinctions are insufficient to warrant a separation of the two in our present state of knowledge. The authors identify with their cases a third, reported by Wernicke in 1892 from Buenos Ayres. Wernicke gave only an incomplete description of the parasite, and regarded the cutaneous affection as a mycosis fungoides. The protozoa he found measured from 7 to 30 μ in diameter.

There are other reports of less definiteness than those just considered, and some of the questionable structures noted therein have found an explanation within recent times. Thus the psorospermcysts of Lubarsch and Ribbert, which were supposed to play a part in diseases of the urinary passages, are in reality metamorphosed nests of epithelial cells normally found in the urethra. The structures found by Künstler and Pitres in pleural exudate and interpreted by Blanchard as a sporozoon, *Eimeria hominis* R. Blanchard 1895, I have preferred to interpret as *Echinorhynchus* eggs (*Cf. Nematoda*, page 225). More uncertain still are Severi's "monocystic gregarines" from the lung parenchym of a still-born child. They are described as oval in form, exceedingly variable in size (0.003–0.03 by 0.0015–0.015 mm.), covered by a thin membrane, and either free or in epithelial cells; it is difficult to interpret them in any satisfactory manner. Some of these doubtful structures are discussed as appendices to the next sub-order, the Hæmosporidia, to which they show a certain similarity.

An error of the reverse type is that frequently made in the past of diagnosing eggs of parasites as coccidia. Thus nematode eggs have once been reported as coccidia, and eggs of trematodes many times. Were it not for the extremely small size of the structures described, the case of J. J. Thomas, noted above, concerning coccidia in a brain tumor would find its easy explanation in this same manner.

The Hæmosporidia, like the Coccidia, are characteristic cell parasites. The period of schizogony or multiplicative reproduction is passed in the blood cells, and only very exceptionally in the cells of other organs. These stages have long been known, and with them a few preparatory stages to the sporogonic cycle, although the latter have been entirely incorrectly interpreted as degenerative changes, etc. So far as is known this sporogonic cycle takes place only in the body of another host; and for the Hæmosporidia of mammals and birds this host is a blood-sucking insect in which the process of sporogony is carried out in the wall of the alimentary canal, and the sporozoites collect in the salivary glands, whence they are injected by the act of biting into a new host to start anew the schizogonic cycle. The close relationship of these forms to coccidia is evident from a study of the life history, as Doflein indicates most aptly in calling them coccidia adapted to parasitism in the blood system.

The life history may be outlined from that of the æstivo-autumnal parasite (Fig. 5182). The earliest stage of the parasite which occurs in the erythrocytes is a minute amœboid body (*A*) which increases rapidly in size, manifesting considerable amœboid activity (*B*–*E*). In connection with the growth of the organism particles of a black pigment matter, named melanin, are stored up in its protoplasm (*F*, *G*). The nucleus of the parasite, at first single, begins to divide rapidly when the organism has reached its maximum size and the daughter nuclei collect about the rim of the organism (*H*). Radial lines of division appear in the protoplasm (*I*), and the whole falls into a group of young germs or merozoites (*K*) about a central residual mass of protoplasm loaded with the pigment already referred to. The merozoites infect new blood cells, and the process of schizogony is repeated until conditions, as yet unknown, bring in a new set of changes,

the starting-point of another cycle, the sexual phase, or sporogony.

The merozoites develop to individuals differently formed from the schizonts and of two sorts, the one finely granular and opaque (*G"*), the other hyaline in appearance with a few conspicuous pigment granules (*G'*). These forms are shaped like a bean in the species under consideration, and are those previously designated as half-moon or crescentic bodies. When fully grown they desert the corpuscle (*H'*, *H"*) assume a spherical form (*I'*, *I"*). The macrogamete extrudes a portion of the nuclear substance (*K"*) and is mature. The nucleus of the microgametocyte divides, the parts migrate to the surface and form microgametes by a small accumulation of plasma about each (*K'*), leaving a large central residual mass. These two gametes copulate, their nuclei fuse, and the product (*M*) is the starting-point of the sporogonic cycle, the sporont.

The changes leading to the perfection of the sexual cells take place only after the blood has been drawn into the stomach of the new host, the blood-sucking insect. Abnormal stimuli may, however, bring about some of the changes, as in cultures of malarial blood. The copula acquires an amœboid form (*N*) necessary for its attainment of a location within the tissue of the new host. This motile stage, which has been denominated the ookinet, is a gregarine-like organism, and penetrates an epithelial cell, where it transforms itself into an immobile spherical oocyst (*O*). After nuclear division there are formed in the oocyst numerous sporoblasts (*P*, *Q*), which, however, never acquire a heavy membrane, *i.e.*, never become sporocysts as in the coccidia. Each sporoblast gives rise to a large number of sporozoites (*R*, *S*), which are set free into the body cavity of the insect host by the rupture of the wall of the oocyst. They collect as the result of an evident chemotactic influence in the salivary gland, and are injected into a new host when the insect bites. There they enter the erythrocytes and the life cycle begins anew.

The organisms included in this sub-order are the cause of serious diseases, and their number is being rapidly increased by the investigations of most recent times. Many doubtful forms have also been placed temporarily under this heading, so that it is impossible to give a synopsis of the genera, or to fix the precise limits of the sub-order itself.

Most prominent of the forms which are included here are the parasites of human malaria. Grassi still regards these all as merely varieties of one species. This is clearly doing violence to the ordinary zoological significance of the word. On the other hand, several investigators have grouped them into two genera, a plan which I myself followed in an earlier paper. Here they will be treated as three species of one genus in accord with a recently expressed view of Schaudinn, and with the known facts regarding their clinical manifestations, structural differences, and life histories.

The genus *Plasmodium* includes in addition to these species the parasite of avian malaria also. It was established in 1885 by Marchiafava and Celli, and although the name is employed here in a sense utterly at variance with its meaning as a term in general scientific use, yet the rules of zoological nomenclature call for its retention. The malarial organism was first seen and figured by Klencke in 1843 without any idea of the significance of the structures viewed. Laveran in 1880 was the first to attach etiologic significance to the structures he described from the erythrocytes in cases of malaria. A large number of investigators participated in the gradual elucidation of the schizogony of these parasites. It was 1896, however, before Manson set forth distinctly the agency of the mosquito in transmitting the disease. Just a year later Ross actually followed for the first time the fate of the parasites of avian malaria in the mosquito's stomach, and their development up to the infection of a new host by the sporozoites. Ross' observations on avian malaria were confirmed soon after by Grassi and other Italian investigators for human species of the malarial parasite.

The complicated terminology in this group, due to the continual changes introduced by various investigators, renders it advisable to give here for general information the table prepared with such success by Lühe, which shows the correspondence in the nomenclature of the chief investigators of recent date. The terminology of Schaudinn, which is followed in this article, has been more generally adopted than any other, and has much in favor of it from every standpoint. (See table below.)

The extensive consideration which the subject has received in previous articles in the Reference Handbook (compare *Malaria*, *Mosquito in Relation to Human Pathology*, *Plasmodium Malariæ*) renders it necessary here only to insert a brief diagnosis of the three species, and refer to the articles noted for further details.

Plasmodium malariæ (Laveran 1883).—(Syn.: *Oscillaria malariæ* Laverian 1883; *Plasmodium* var. *quartana* Golgi

Schaudinn, 1899 and Lühe, 1900.	Ross, 1898.	Ross, 1899 and 1900.	Ray Lankester, 1900.	Harvey Gibson, 1900.	Koch, 1899.	Grassi, 1898–1899.	Grassi, 1900.
Schizogony....	....	....	....	....	Endogenous development.	Sporulation (fase asporulare).	Monogonia (generazione neutrale) per sporogonia conitomica.
Schizont	Sporulating form.	Sporocyst (young form: amœbula s. myxopod)	Oudeterospore .	....	Full grown parasite.	Amœboid form	Mononte.
Merozoite	....	Spore; becomes later after entrance into erythrocyte amœbula (s. myxopod).	Nomospore	....	Theilungskörper.	1898: amœbula .... 1899: sporozoite.	Sporozoito (monogonico).
Macrogamete..	....	Macrogamete (female gametocyte); young form: amœbula s. myxopod).	Gynospore.. ...	Ovum....	Female parasite	Macrogamete s. ooid.	Makrospora } gameti.
Microgametocyte.	Flagellated body.	Male gametocyte (young form: amœbula s. myxopod).	....	....	Male parasite ..	1899: mikrogametogen.	Anteridio } gameti.
Microgamete ..	Flagellum..	Microgamete	Androspore	Sperm ...	Spermatozoon..	Mikrogamet s. spermoid.	Microspora } gameti.
Ookinete (copula sporont).	Vermicule ..	Zygote	Gametospore ...	Oosperm .	Würmchen.....	1899: zygote	Vermicolo } amfionte.
Oocyst (copula sporont).	Coccidium..	Zygote	Gametospore ..	Oosperm .	Coccidienartige Kugel.	1899: zygote	.... } amfionte.
Sporoblast.....	....	1899: zygotomere...... 1900: mere, becomes blastophore.	....	....	....	....	Masse citoplasmatiche più o meno poligonale.
Sporozoite.....	Germinal rod.	1899: zygotoblast...... 1900: blast.	Gametoblast s. gametoclast s. filiform young	Zooid	Sichelkeim.....	1899: spore .... 1899: sporozoite....	Sporozoito (amfigonico). Young form: sporoblasto s. sporozoitoblasto.
Sporogony.....	....	....	....	....	Exogenous development.	Exogenous development.	Amfigonia (generazione sessuale) per sporogonia conitomica.

1890; *Hæmamœba malariæ* Grassi et Feletti 1892; *H. Laverani* var. *quartana* Labbé 1894; *Pl. malariæ quartanum* Labbe 1899.)

Young form in erythrocyte small, unpigmented; movement slow; pigment in coarse granules, first visible in about twenty-four hours, and peripheral in position. Movement decreasing until in sixty hours after the attack, or twelve hours before the next, the spherical *Plasmodia* fill almost the entire corpuscle. Having reached a diameter of about 0.007 mm. schizogony begins, and nine to twelve (rarely six or fourteen) merozoites are formed which are very regular (Fig. 5183, *e*). The melanin granules move in radial lines and collect in the central residual mass, from which the merozoites separate themselves in seventy-two hours. The synchronous release of these germs brings another paroxysm at this time, whence the name of quartan fever for the disease induced by this species, which is also often designated the quartan parasite. The gametes are few in number, spherical, and characterized by active streaming in the protoplasm. The sporogony of this species in *Anopheles* goes on at a minimum of 16.5° C., and stops before the maximum of 30° C. is reached. *Plasmodium malariæ* is found farther north than either of the other human malarial parasites, but does not extend into the tropics.

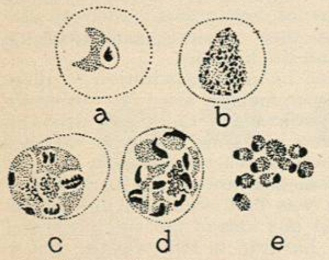

FIG. 5183. — *Plasmodium malariæ*, Schizogony. *a*, *b*, Growth of schizont; *c*, nuclear division; *d*, formation of merozoites; *e*, release of same by destruction of erythrocyte, residual mass at upper side of group. Magnified. (After Bastianelli and Bignami.)

Plasmodium vivax (Grassi et Feletti).—(Syn.: *Hæmamœba vivax* Gr. et Fel. 1892; *Pl.* var. *tertiana* Golgi 1889; *H. Laverani* var. *tertiana* Labbé 1894; *Pl. malariæ tertianum* Labbé 1899.)

Young stages in the erythrocytes are very active. Pigment granules are fine, and light brown in color. The fully grown schizont completely fills the red corpuscle, which is usually swollen and bleached in color. This stage measures 0.008–0.01 mm. in diameter, and produces fifteen to twenty merozoites in schizogony, which requires for its completion just forty-eight hours, whence the common names of tertian fever and tertian parasite. The pigment forms a solid mass in the centre, and the merozoites form a double ring about it, or more frequently an irregular mass. Schizogony occurs preeminently in the spleen. The gametes are abundant at a certain period, of spherical form, and distinguished from

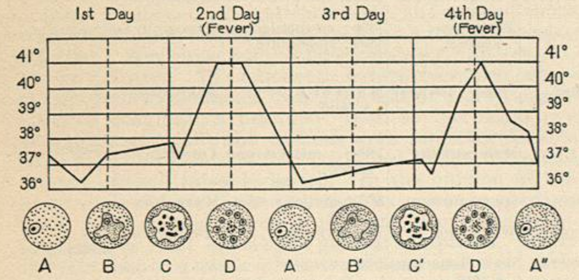

FIG. 5184.—Development of *Plasmodium vivax* in Relation to Temperature Curve of Patient. (After Doflein.)

the schizonts above all in the form of the pigment, which is in coarse granules or bacilliform masses. They reach two to three times the diameter of an erythrocyte. The sporogony in the body of *Anopheles* requires eight days at a temperature of 28°–30° C.; 17° C. is the minimum for this stage of development. This corresponds to the occurrence of the disease in the tropics and subtropics. The relation of the body temperature of the host to the development of the parasite is well shown in the accompanying diagram (Fig. 5184).

Plasmodium immaculatum (Grassi et Feletti).—(Syn.: *Laverania malariæ* Gr. et Fel. 1890; *Hæmamœba malariæ præcox* Gr. et Fel. 1892, nec. *H. præcox* Gr. et Fel. 1890. *Hæmamœba immaculata* Gr. et Fel. 1892; *Plasmodium præcox* Doflein 1901.)

This is the smallest of all human malarial organisms. Fully grown schizonts measure only 0.005 mm. in diameter. Young form very active; pigment moderate in amount, very fine in peripheral zone. The schizont may also remain unpigmented, and this form has been regarded as a separate variety. Multiple infection of an erythrocyte is not rare, and the assumption of a signet-ring form is very common. The erythrocyte shrinks during the growth of the parasite. In schizogony seven, ten, or twelve merozoites are formed, rarely twelve to fifteen, and these are small, being only 0.001–0.0015 mm. in diameter. The length of the schizogonic cycle is not well determined, as the process takes place in internal organs, especially the spleen. It is apparently irregular, though forty-eight hours seems most probable. The gametes are crescentic or reniform, and originate especially in bone marrow. Further changes have been most carefully followed in this species. In the stomach of *Anopheles* these crescents become spherical (Fig. 5185) and the microgametes are formed and set free. The fertilization is completed by the fusion of a single microgamete with a macrogamete; and the resulting motile ookinet (Fig. 5186, *a*) penetrates the wall, entering first

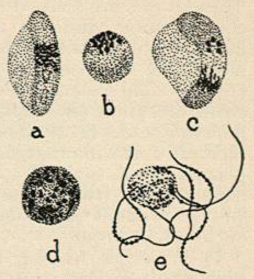

FIG. 5185.—*Plasmodium immaculatum*; Development in Stomach of *Anopheles claviger*. *a*, Macrogamete with remnant of erythrocyte; *b*, same one-half hour after ingestion by mosquito; *c*, microgametocyte with remnant of erythrocyte; *d*, same one-half hour after ingestion, the nucleus has divided several times; *e*, microgametes still attached to residual mass (so-called polymitus stage). Highly magnified. (From Braun, after Grassi.)

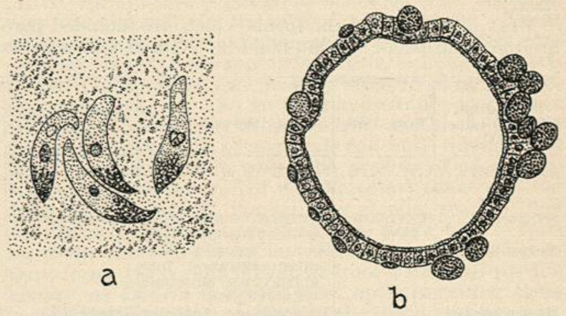

FIG. 5186.—*Plasmodium immaculatum*. *a*, Ookinet in stomach of *Anopheles claviger* thirty-two hours after ingestion; *b*, transsection of stomach with partly developed oocysts several days later. Magnified. (From Braun, after Grassi.)

an epithelial cell and coming later to lie between the layers of the wall (Fig. 5186, *b*). The oocyst forms no special covering, but increases rapidly in size. Sporoblasts and then sporozoites are formed; the latter have a length of 0.014 mm. and a thickness of 0.001 mm., and are produced to the number of ten thousand in a single oocyst. After the rupture of the latter they accumulate in the salivary gland, lying in the secretion either within the cells or in the duct itself, whence they are expressed in the act of biting (Fig. 5187).

The sporogony requires eight days at a temperature of 28°–30° C., and 18° C. is the minimum temperature for the infection of *Anopheles*. This species gives rise to the

malarial fever designated as æstivo-autumnal, perniciosa, tropica, etc., and is epidemic only in the tropics and subtropics. This is the form which has been rated as a representative of another genus, *Laverania malariæ*, by

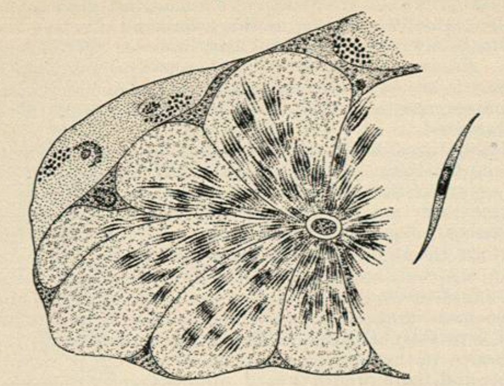

FIG. 5187. — Section Through Dorsal Sac of Salivary Gland from *Anopheles* with Groups of Sporozoites of *Plasmodium immaculatum* both in gland cells and in duct. Isolated sporozoite at right more highly magnified. (From Lang, after Grassi.)

many observers. While its separation from the genus *Plasmodium* is perhaps a convenience, it seems hardly justifiable on scientific grounds, as the differences between it and the other species are not of generic rank.

Uncertain Species.—According to the work of certain investigators, particularly Celli, there exists a true quotidian malarial parasite, which is related to *Plasmodium immaculatum*, although smaller and completing the schizogony in twenty-four hours. The supposed species is found in Italy particularly in summer and fall, and is regarded by most authors as at most a variety of *Pl. immaculatum*. Still other forms from tropical regions have been regarded as distinct species without sufficient evidence as yet for this opinion.

There are yet other hæmatozoa of which it may be said that their exact relationship has not been sufficiently demonstrated to give them a definite place in the system, but which in all probability will be included in this suborder, though evidently not in the same genus with the malarial organisms just described.

In this connection should be noted the parasite of the spotted fever or tick fever of the Rocky Mountains, a new disease especially virulent in the valley of the Bitter Root River in Montana, where it has been known for twenty years, but present apparently also, though in milder form, in other parts of Montana, Idaho, Wyoming, Nevada, and Eastern Oregon.

Wilson and Chowning were the first to note ovoid intracapsular bodies in stained blood preparations, and to determine that in fresh blood these bodies manifest amœboid movements. These observations have been confirmed by later investigators, and the hæmatozoon is regarded by all as probably the cause of the disease. A brief description of the organism may be given here.

The smallest forms, or the first phase of Wilson and Chowning, are intracellular, ovoid bodies and measure 0.0015–0.002 mm. in length by 0.0005 to 0.001 mm. in thickness. They resemble slightly young schizonts of malaria, and more strongly the organism of Texas fever of cattle. These bodies occasionally change position in the corpuscle, and according to Anderson project pseudopodia quite rapidly. Two such bodies may lie in a single corpuscle. In the second phase the bodies are solitary in the erythrocytes, oval, ellipsoidal or spherical in form, and from 0.002 to 0.003 mm. thick by 0.003 to 0.005 mm. long. This phase is actively amœboid with the formation of pseudopodia in various directions. The third phase is seen in pyriform bodies arranged in pairs with the pointed ends approximated, and in rare cases distinctly united by a fine thread. This form is not amœboid.

Though the parasites are not found in large numbers in the circulating blood, only a few being present in each field of a preparation of freshly drawn blood, yet in the capillaries of tissues removed at autopsies from one to five per cent. of the erythrocytes are infected. This is marked in the lung, spleen, liver, and kidney, where also are found many red cells included in phagocytes, being faintly outlined within the protoplasm of the latter, and each containing a large parasite. In tissues taken some hours after death, the organisms are almost all spheroidal. They are present in the blood at least twenty-four days after recovery.

The organism is apparently transmitted by ticks, and all cases of the disease show a history of tick bites about one week before the onset. Stiles made a provisional determination of some ticks from the region as *Dermacentor reticulatus* but in correspondence later expressed the view that certain differences though slight justify placing these forms in a new species. Some facts point to the existence of another normal mammalian host for the parasite, and the gray gopher has been indicated as the most probable form. Further study is necessary to establish the character and development of this parasite, its exact systematic position, and its positive relation to the disease. Its superficial resemblance to *Piroplasma bigeminum*, the cause of Texas fever in cattle, has already been mentioned.

Myxococcidium Parker, Beyer, Pothier 1903.—Schizogony unknown; sporogony in *Stegomyia fasciata*. Only one species, thus far imperfectly known.

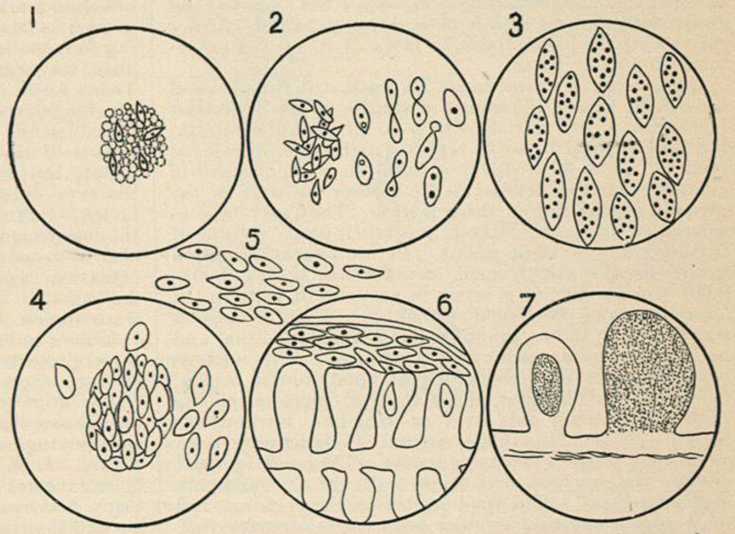

FIG. 5188.—*Myxococcidium stegomyiæ* from sections of mosquito killed (1) three days, (2) four days, (3) five days, (4) six days, (5) six to twelve days, (6) twelve days, (7) fourteen days after feeding on blood of yellow-fever patient. (Unpublished sketches, by courtesy of J. C. Smith.)

Myxococcidium stegomyiæ Parker, Beyer, Pothier 1903 (Fig. 5188).—A fusiform body (ookinet?) 0.003–0.004 mm. long by 0.0015–0.002 mm. broad in lumen of stomach and œsophageal diverticulum, about three days after mosquito has bitten yellow-fever patient; this body is provided with a nucleus. A spherical body (oocyst?) in