guished with difficulty. Fig. 3820 (19). A flagellum with a club-like enlargement at one end not infrequently separates from the parent body and floats away in the plasma with an active undulatory motion. It has been shown that the flagella contain part of the chromatin substance. All the extracellular bodies observable in freshly drawn blood do not undergo flagellation.

With the quartan infection a similar process is observable. Flagellate bodies, however, are encountered with much less frequency than in cases of tertian fever.

In cases of æstivo-autumnal fever it is the crescents

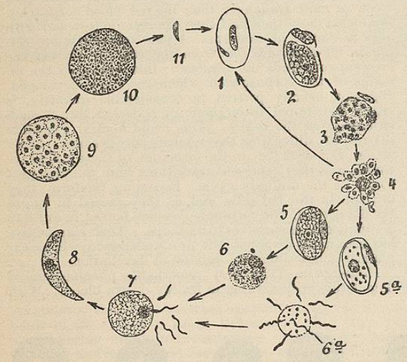


FIG. 3823.—Diagram Showing the Life History of the Avian Parasite, Proteosoma. 1 to 4, Development of the parasite within the blood of the bird; 4, merozoites; 5 and 6, macrogamete; 5*a* and 6*a*, microgametocyte; 7, fertilization; 8 to 10, formation and maturation of oöcysts; 11, sporozoite. (After Grassi from Lühe, *Cent. f. Bakt.*, 1900, xxvii.)

which undergo flagellation. In a specimen of fresh blood some of these bodies remain unchanged or merely assume a round or oval form; but others, after becoming spherical, extrude actively motile filaments which may become detached from the parent body.

The significance of this phenomenon has been explained by the study of a closely related parasite, Halteridium danilewsky, which occurs in the blood of many birds. This organism, which develops within the red blood corpuscles as a semilunar or halter-shaped body curved alongside the nucleus of the containing corpuscle, like the malarial parasites forms pigment granules from the hæmoglobin. Opie showed that the parasite may assume two distinct forms, either of which when fully grown becomes free in the plasma after the blood is drawn. With one form the protoplasm is granular and stains deep blue by the method of Romanowsky; the nucleus is small. The other form, somewhat larger than the first, is characterized by the possession of a very large nucleus and scant protoplasm which stains with difficulty. The supposition that this form alone undergoes flagellation has been confirmed by MacCallum, who has demonstrated the occurrence of a remarkable phenomenon. Flagella break from the parent body and make their way to the granular bodies which have become extracellular. Several flagella may collect about such a body and beat against it with active lashing movements. One flagellum finally projects itself into the substance of the body, with which it becomes merged. The process is to be regarded as one of fertilization; the granular body with small nucleus is the female element, or, according to zoological nomenclature, the macrogamete; the flagellum is the male element, or microgamete, its parent body being designated by the term microgametocyte. The fertilized body remains quiescent for from fifteen to twenty minutes, when it assumes an elongated form and becomes capable of very active progressive movement, constituting the pseudo-vermiculus described by Danilewsky.

Flagella-formation observable with the three varieties of malarial parasite doubtless represents a similar process of fertilization, though only in the case of the æstivo-autumnal parasite has the phenomenon been actually observed. With both the tertian and the æstivo-autumnal forms morphological differences have been established between the microgametocyte from which arise flagella or microgametes and the macrogamete which undergoes fertilization. With the æstivo-autumnal parasite those crescents which do not flagellate, like the analogous macrogamete of the halteridium, stain more deeply and are granular. The formation of a body similar to the pseudo-vermiculus of birds has not been observed.

Life History of the Malarial Parasites in the Body of the Mosquito.—Study of the parasites in birds has here again pointed the way to an understanding of the life history of the malarial organisms outside the human body. Ross, working in India, directed his attention to the extracorporeal development of the avian parasite, Proteosoma grassi, because at the time cases of malarial fever were not available. Observations of Manson upon the development of filaria in the body of the mosquito suggested the agency of these insects. Ross proved that the mosquito can act as an intermediary host in transferring infection from one bird to another, and showed that the parasite develops within the body of the insect. The process of flagellation occurs with much activity in the middle intestine of an insect which has fed upon the blood of an infected bird. The flagellum or macrogamete unites with the microgamete, and the so-called pseudo-vermiculus which results, endowed with active motility, makes its way into the wall of the mosquito's intestine, where it becomes encapsulated and divides into a great number of minute bodies designated sporozoites. The latter, after rupture of the containing capsule, finally reach the salivary glands of the insect and hence may be injected into a second bird, there to undergo asexual multiplication.

In mosquitos which had fed upon the blood of individuals infected with tertian and æstivo-autumnal malaria, Ross found pigmented bodies similar to those which he had discovered in mosquitos. Bignami, Bastianelli, and Grassi have extended these observations and have shown that the tertian, quartan, and æstivo-autumnal parasites pass through similar changes within the body of mosquitos of the genus Anopheles.

An insect of this genus confined in glass test tubes is allowed to feed upon the blood of patients infected with malarial fever. The mosquito is so voracious that it stings when the mouth of the tube is applied to the skin of the patient. It is then kept confined in a larger vessel at a temperature of 20°–30° C., and is supplied with abundant moisture and vegetable matter for food. The parasite in the insect is studied after varying periods, in the intestinal wall and in the salivary glands, prepared by delicate teasing and examined in salt solution. Sections of the insect hardened and stained for microscopic examination give additional information.

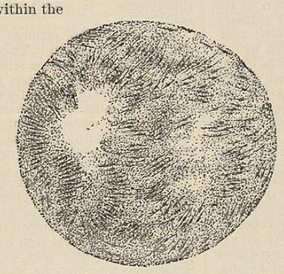
With the tertian parasite fertilization of a macrogamete by a flagellum (microgamete) doubtless occurs, though the process has not been actually observed. During the second day after the insect has fed on malarial blood pigmented bodies can be found in the muscular walls of the intestine. Grown to twice the size of a red blood corpuscle, they are sharply outlined and possess homogeneous or vacuolated protoplasm. In stained specimens the chromatin substance is found to have increased in amount and may have undergone division into several small masses. Increasing in size, the parasite acquires a refractive capsule, and on the third day its contents have divided into a varying number of small bodies, each containing a part of the chromatin substance; between these lie the pigment and a small amount of undivided cytoplasm. This cyst-like body

increases in size and within it is formed an increasing number of small bodies. Finally, on the sixth day, the parasite, which has grown to such size that it projects into the body cavity of the insect (compare Fig. 3825 showing Proteosoma of birds), contains a great number of slender bodies with pointed extremities, sporozoites, Fig. 3825 (*C*) each containing a particle of nuclear substance demonstrable only in stained specimens; they are arranged in groups side by side. The containing capsule ruptures and the sporozoites are set free in the body cavity, whence they make their way to the salivary glands of the insect. Should a mosquito so infected sting a human being, parasites are injected with the irritant fluid secreted by the gland. Developing within the red blood corpuscles, the organism now begins in its new human host the asexual cycle of development with which is associated tertian malarial fever.

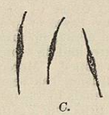
A few observations have shown that the quartan parasite passes through a series of phases corresponding to those just described, but when mosquitos are allowed to sting patients suffering with quartan fever, in only a small proportion of the experiments are developmental stages of the parasite obtained. The small number of flagellate forms observable in the blood of patients suffering with quartan infection may explain this fact as well as the relative infrequency of this type of malarial fever.

The development of the æstivo-autumnal parasite in the mosquito may be readily observed. On the seventh day after the mosquito has stung a patient infected with the disease, cyst-like bodies project into the body cavity of the insect and are filled with sporozoites, which, though more numerous, resemble those of the tertian parasite. Even before sporozoites are formed, the æstivo-autumnal parasite is recognizable by the character of its pigment and by the high refraction of its cytoplasm.

A.



B.



C.

FIG. 3824.—*A*, Parasite of Æstivo-autumnal Fever in the Wall of the Middle Intestine of Anopheles; *B*, formation of sporozoites within the oöcyst; *C*, ripe sporozoites. (After Grassi from Lühe.)

Terms in general use by zoologists have been introduced to designate various phases of the asexual generation of the malarial parasite in man and of its sexual generation in the intermediate host, the mosquito. Some of these have been mentioned. The microgamete or flagellum, derived from the microgametocyte or flagellate body, unites with the more granular macrogamete, and as the result an oöcyst is formed within the stomach wall of the mosquito. Division of cytoplasm preceded by nuclear division gives rise to a great number of nucleated bodies known as sporozoites. The latter, injected by the mosquito, are capable of transmitting malarial infection, since they are capable of development within the red blood corpuscles of their human host. Reaching a certain size, the intracorpuscular parasites divide without preceding fertilization into a variable number of bodies, which may be termed merozoites, each capable of re-entering a red blood corpuscle and undergoing the same process of multiplication. A certain number of merozoites, however, are not destined to multiply by such asexual division, but give rise to macrogamete or microgametocyte as already described. By union of the male and female elements within the stomach of the mosquito is formed a body which is capable of development in the intermediary host. An analogous alternation of asexual and sexual generation occurs with other protozoan micro-organisms, notably those belonging to the order Coccidia. Asexual reproduction is the means by which a few parasites which

FIG. 3825.—Oöcysts of Proteosoma in the Wall of the Middle Intestine of the Mosquito. (After Ross from Lühe.)

have gained entrance multiply in the new host. In the case of the malarial parasite, relatively few organisms injected by the mosquito multiply to form the great number characteristic of the malarial fevers.

Eugene L. Opie.

PLASMOLYSIS is the term used in a general sense to denote the disorganization of the achromatic part of the cell, in opposition to *karyolysis*, which is applied to the complete disorganization of the nucleus. *Achromatolysis* is, accordingly, used as a synonym for plasmolysis. The word plasmolysis, having been introduced by a number of investigators working along special lines, is frequently used in a more narrow sense to indicate the destruction or degeneration of the protoplasm of certain forms of cells. Thus, for example, plasmolysis is by a large number of writers applied only to such changes in the red blood cells, and is used interchangeably with *erythrocytolysis*. In this condition the soluble substances of the red cell escape into the plasma so that the red cells become smaller (microcytes) or come to consist only of the outer envelope (red cell shadows). Through the imbibition of fluids such cells may become swollen. Grawitz uses the term to indicate solution of the red blood cells and the production of hæmoglobinæmia. In the case of nerve cells, plasmolysis is applied to the simplest disorganizing changes in the achromatic part of the cell. In the case of bacteria, plasmolysis is used to indicate the formation of clear spaces beneath the capsule, due to the shrinking of the plasma, as may be observed in bacteria held in a salt solution.

Aldred Scott Warthin.

PLASMORRHEXIS is the term applied to processes of disorganization in the protoplasm of the cell, in opposition to *karyorrhexis*, which is used to denote similar processes in the nucleus. By the majority of writers plasmorrhexis is applied to these changes as occurring in the red blood cells alone, and the word is used as a synonym for *erythrocytorrhexis*. The process is characterized by the formation of small granules or globules in the protoplasm of the red cell, and the escape of these from the cell; or the formation of minute prickles or globules over the surface of the cell, giving it an appearance of a gooseberry or mulberry; or the formation of variously shaped

processes. Plasmorrhexis may be regarded as the stage immediately preceding plasmoschisis.

Aldred Scott Warthin.

PLASMOSCHISIS.—The partial or total disorganization of the cell through fragmentation or splitting of its protoplasm. It is characterized by the snaring off of the processes developed through plasmorrhexis, and the formation of round, oval, disc-like, angular, or thready bodies, which may be homogeneous or granular; or by the separation of the protoplasm from the nucleus. The term is used, particularly with reference to the disintegration of the red blood cells, as a synonym for *erythrocytoschisis*. It is believed by many investigators that the blood plates are nothing more than specially formed products of the plasmorrhexis and plasmoschisis of the red blood cells. *Aldred Scott Warthin.*

PLASTIC SURGERY. See *Reparative Surgery*.

PLETHORA. See *Circulation, Pathology of*.

PLEURISY.—The pleura may be the seat of various forms of inflammation, some of which are only a part of a general inflammation involving the tissue of the lung, as in pneumonia, tuberculosis of the lung, and emphysema of the lungs, and some of which involve the pleura without disease of the lung.

A pleurisy may be primary, or it may be secondary to disease of the lung, or to some general disease, as chronic nephritis or rheumatism.

The different forms of pleurisy may be conveniently classified as follows:

1. Pleurisy with the production of fibrin, or acute pleurisy, or dry pleurisy.
2. Pleurisy with the production of fibrin and serum, or sero-fibrinous pleurisy, or pleurisy with effusion, or subacute pleurisy.
3. Pleurisy with an excessive production of fibrin.
4. Pleurisy with the production of fibrin, serum, and pus, or empyema, or suppurative pleurisy.
5. Chronic pleurisy with adhesions.
6. Tuberculous pleurisy.
7. Cancerous pleurisy.
8. Traumatic pleurisy.

Etiology.—Pleurisy occurs at all ages and in both sexes. Pleurisy may be *primary* or *secondary*, but there is at the present time considerable difference in opinion as to the relative frequency of true primary pleurisy, as well as to the frequency of tuberculous infection as the essential factor in the production of so-called primary pleurisies. Thus Strümpell states that we know positively of but two forms which may be regarded as primary, viz., the traumatic and the rheumatic; while others regard exposure to cold and wet and individual predisposition as frequent exciting causes. Of late years, under the lead of the French and German writers, the tendency of a large number of the profession has been to regard the majority, if not all, of acute and subacute pleurisies as tuberculous. There seems, however, good reason to reject so sweeping an assumption. That the tubercle bacillus is a frequent cause of pleurisy is, of course, well known, but many cases of pleurisy with effusion have been observed in which no tubercle bacilli have been found in the exudate, and in which tuberculosis has not subsequently developed. Moreover, an exactly similar pleurisy with effusion has been produced experimentally in the lower animals by chemical agents, as is shown by Delafield. By injecting a saturated solution of chloride of zinc with a hypodermic syringe into the pleural cavity of the dog he was enabled to excite a pleurisy exactly resembling that which is seen in the human subject. By varying the amount of fluid injected he was able to obtain pleurisies of different degrees of intensity, and with different amounts of products of inflammation.

Pleurisy may be secondary to changes in the lungs, notably tuberculosis of the lungs and lobar pneumonia, or to the infectious diseases, especially la grippe, to rheumatism, to peritonitis, to abscess of the liver, to carcinoma of the stomach, liver, or chest wall, or to nephritis.

Bacteriology.—Cultivations from the exudate give in the larger proportion of cases negative results, but, as stated by Netter, we may recognize three groups of acute or subacute pleurisy, caused by the tubercle bacillus, the pneumococcus, and the streptococcus respectively.

The tubercle bacillus is very difficult to find in the exudate. It has been demonstrated that a large amount of the exudate must be taken to make the test complete, either in cultures or in the inoculation of animals.

The pneumococcus pleurisy is almost always secondary to a focus of inflammation in the lung. It may, however, be primary. The exudate is usually purulent, but the prognosis of this form is very favorable. The streptococcus pleurisy is the typical septic form which may occur either from direct infection of the pleura through the lung in bronchopneumonia or in cases of streptococcus pneumonia; in other instances it follows infection of more distant parts. This is the most serious and fatal of all forms. The exudate is usually purulent.

These, then, are the important groups, but other bacteria have been found, as the staphylococcus, the typhoid bacillus, the bacillus coli communis, the gonococcus, the pneumobacillus of Friedländer, and the influenza bacillus.

Pleurisy with the Production of Fibrin (Dry Pleurisy).—*Morbid Anatomy.*—The inflammation may begin on the pulmonary, costal, or diaphragmatic pleura according to the cause which produces it. That beginning in the pulmonary pleura is always secondary to changes in the lungs. That which begins in the costal pleura is often independent of any inflammation of the lung. Usually only a circumscribed portion of the pulmonary, costal, mediastinal, or diaphragmatic pleura is involved, but the entire pleura of one side of the chest may be inflamed. The inflammation always extends to the portion of the pleura opposite to it. The inflamed pleura is coated with a more or less thick layer of fibrin, and bands of fibrin extend between the opposite pleural surfaces. As most persons recover from dry pleurisy, but little is known of its bacteriology.

This form of pleurisy is regularly seen with lobar pneumonia, less frequently with bronchopneumonia. It is very frequently associated with tuberculosis of the lungs, and may be the first or only sign of such tuberculosis. It is frequently found in connection with la grippe, and it may develop at any time in the course of this disease. It may develop simply from exposure to cold.

Symptoms.—The rational symptoms are usually few and not well marked. There may be more or less pain over the affected side, a slight dry cough, a little fever, and some malaise. Often these symptoms are absent. Though the pain is usually referred to the seat of inflammation, it must be remembered that this pain may be referred to a distant point, and thus the error may be made of regarding the case as one of lumbago or of appendicitis, of renal colic, or, in cases of diaphragmatic pleurisy, of peritonitis.

The physical signs are characteristic. Over the inflamed area are heard crepitant or subcrepitant râles. With these there may be a little dulness on percussion and some little diminution in the intensity of the breathing, but the essential sign is the presence of fine pleuritic râles. These râles may be scanty or very abundant. Sometimes they may be so faint as to be heard with the greatest difficulty. They are usually brought out best by causing the patient to cough. It must be remembered that these râles—contrary to the usual impression—are not necessarily constant; they may come and go in the same manner as a bronchial râle. If the pleurisy be diaphragmatic or mediastinal, no râles may be heard.

With acute or subacute miliary tuberculosis of the lung a dry pleurisy may either mark the invasion of the tuberculous inflammation of the lungs or it may be repeated from time to time as the tuberculosis goes on. Recent

pleuritic râles, pain in the chest, and a rise of temperature regularly accompany these attacks.

So well is it recognized that fine pleuritic râles may be the only symptom of a beginning tuberculosis that such evidence of localized dry pleurisy, especially if primarily at the apex of the lung and attended with afternoon fever, is always a source of great anxiety to the physician, unless he can be sure that he has to do with an acute pleurisy due to other cause than tuberculosis, as, for example, one occurring in the course of an attack of influenza. In primary dry pleurisies involving the costal pleura there is a great variation in the extent of pleura involved. The inflammation may involve only a small area of the pleura; there are râles heard over a circumscribed area only, the patient has but little fever, and the pleurisy runs its course in a week. In other cases the pleuritic râles are heard all over the front or back of the chest, the pain is quite severe, there is considerable fever, and the patient may be confined to bed or to the house for two weeks.

The *prognosis* is good. Most cases end in recovery after a short time, but the patient is often left with permanent thickenings and adhesions of the pleura. Such adhesions may give no further trouble, or they may form the starting-point for a chronic pleurisy with adhesions, or the process may go further and cause chronic interstitial pneumonia and chronic bronchitis.

Rarely, dry pleurisy is succeeded after several days by a pleurisy with effusion.

In a moderate number of cases one or more attacks of dry pleurisy are followed by pulmonary tuberculosis.

Treatment.—Many of the milder cases are never seen by the physician and need no treatment, although it would seem wise to keep them in the house till the pleuritic râles have disappeared. The more severe cases should stay in the house or go to bed till the attack has run its course. There is no especial drug treatment. The pain in the chest may be relieved by poultices, strapping the chest, opium, phenacetin, or the like. Most physicians either paint the affected chest with iodine or employ wet or dry cups, but it is doubtful if anything is gained by these counter-irritants.

Pleurisy with the Production of Fibrin and Serum (Pleurisy with Effusion).—This is a much more serious form of pleurisy, and is the type which is most commonly seen by the general practitioner, since many persons with acute dry pleurisy never consult a physician.

Morbid Anatomy.—The essential lesion is the inflammation of the greater part of the costal and pulmonary pleuræ on one side, and the accumulation of a considerable or large amount of serous fluid in the pleural cavity. Sometimes, however, the extent of the inflamed pleura is small, and the serum is shut in by adhesions (sacculated pleurisy).

Rarely, the pleuræ of both sides of the chest are inflamed, and when this is the case there is apt to be *pericarditis* also.

The surface of the inflamed pleura is coated with fibrin, and bands of fibrin join together its opposed surfaces. In the pleural cavity is found clear or turbid serum of a straw or amber color, containing a few leucocytes. Red blood cells are so rarely found that a bloody effusion is usually regarded as a sign of a tuberculous or a cancerous pleurisy. The blood, however, may be due to an injury. There are, moreover, a few cases which do not differ from ordinary cases except that the fluid is bloody. Thus bloody fluid may be found in pleurisy in connection with cirrhosis of the liver and with infectious diseases. The quantity of fluid varies from a few ounces to a quantity sufficient completely to fill and distend the pleural cavity. The fluid is, of course, found in the most dependent part of the pleural cavity, unless shut in by adhesions, in which case it may be found anywhere, but most commonly at the base of the lung and in the neighborhood of the axillary region. If the effusion be of any considerable quantity the lung is compressed upward and backward against the vertebræ, the degree of compression of the lung depending upon the amount of fluid. In extreme and long-continued cases the lung is almost unaërated. If the amount of fluid be great the adjacent viscera may be displaced. After the inflammation has subsided the serum and fibrin are absorbed and the pleura is left thickened by connective tissue and with connective-tissue bands between the two layers. The compressed lung expands again either completely or partially; if the latter, more or less retraction of the affected side of the chest is left.

The causes of pleurisy with effusion have been already stated.

The behavior of the acute cases is such as to make it probable that infection by the pneumococcus is the cause of the inflammation; and this belief has been confirmed in a considerable number of cases, but, as before stated, in a large number of cases the fluid is found to be sterile.

The *diagnosis* is made by the symptoms and physical signs.

The essential symptoms are *pain* in the chest, *cough* with little or no expectoration, *dyspnœa*, and *fever*.

The essential physical signs are *absent*, or greatly diminished, *vocal fremitus*, *flatness* on percussion, *feeble* or *absent breathing*, *feeble* or *absent voice*.

With this combination of symptoms and physical signs the diagnosis is one of the simplest problems in medicine, but there are so many variations from these conditions of the problem that a more extensive discussion of the subject is advisable.

First, as regards the symptoms and course of the disease. We may conveniently divide the symptoms of pleurisy with effusion into three groups:

1. Pleurisy with an acute invasion.
2. Pleurisy with an insidious invasion.
3. Pleurisy with a subacute invasion.

In the first group the symptoms may very closely resemble the invasion of lobar pneumonia.

In the second group the pleurisy may be entirely overlooked by the unwary, and "malaria" or some equally indefinite diagnosis may be made.

In the third group the conditions are more regular and the diagnosis more simple.

First Group.—In pleurisy with an acute invasion the patient is suddenly taken ill with the symptoms of an acute infection. Sometimes there is an initial chill, as in pneumonia; more often there are chilly feelings, and then the patient is taken with a sudden pain in the chest, with a high fever, 103°–104° F., a dry cough and immediate prostration. The pulse is full, 100–120, and the face is flushed. In a few hours dyspnœa appears, and this may increase so greatly that the patient cannot lie down in bed. The breathing is from 28 to 35. The pain is apt to be very great and referred to the affected side, but it may be also felt throughout the muscles of the body. The pain, on the other hand, may be very slight over the inflamed pleura, but is referred to the opposite side of the chest, or to the abdomen. In the latter case, if it be on the right side, the rigidity of the abdominal muscles and the situation of the pain may lead to the erroneous diagnosis of appendicitis, an error which of course would be corrected by a proper physical examination of the chest. As the fluid accumulates in the pleural cavity this pain becomes much less.

While the constitutional symptoms are going on the fluid accumulates rapidly, and within two days it may fill the pleural cavity; but the quantity of fluid varies greatly in different cases.

The patient continues to have a high temperature and all the appearances of a severe illness for about two weeks; then the temperature subsides, leaving only a moderate afternoon fever, which continues as long as the fluid remains in the chest. These cases make us think of an infection of the pleura by the pneumococcus.

The prognosis is usually good, but sometimes death occurs, and some of these patients die suddenly.

In the *second group*, that of insidious invasion, we have a picture which is just the opposite. The disease begins so gradually that the patient hardly knows when