and during convalescence the greatest care must be taken to provide only the most digestible articles of food. In chronic dysentery, diet is perhaps the most important element in the treatment. The number of stools can frequently be reduced from ten or twelve in the day to two or three, by placing the patient in bed and restricting the diet. Many cases do well on milk alone, but the stools should be carefully watched and the amount limited to that which can be digested. If curds appear, or if much oily matter is seen on microscopical examination, it is best to reduce the amount of milk and to supplement it with beef-juice or, better still, egg-albumen. The large doses of bismuth seem specially suitable in the chronic cases, and the injections of nitrate of silver, in the way already mentioned, should always be given a trial.

XXI. MALARIAL FEVER.

Definition.—An infectious disease characterized by: (*a*) paroxysms of intermittent fever of quotidian, tertian, or quartan type; (*b*) a continued fever with marked remissions; (*c*) certain pernicious, rapidly fatal forms; and (*d*) a chronic cachexia, with anæmia and an enlarged spleen.

With the disease are invariably associated the hæmatozoa described by Laveran.

Etiology.—(1) **Geographical Distribution.**—In Europe, southern Russia and certain parts of Italy are now the chief seats of the disease. It is not widely prevalent in Germany, France, or England, and the foci of epidemics are becoming yearly more restricted. In America it is now rare on the Atlantic coast above the latitude of Philadelphia. From New England, where it once prevailed extensively, it has gradually disappeared, but there has of late years been a slight return in some places. In the city of New York genuine malaria is rare except as an imported disease. In Philadelphia and along the valleys of the Delaware and Schuylkill Rivers, formerly hot-beds of malaria, the disease has become much restricted. Except in the low-lying southern portions of the city it rarely develops, and the majority of cases admitted into hospital are of the poorer class, who have returned from picking cranberries and peaches in Delaware and New Jersey. In Baltimore a few cases develop in the autumn, but a majority of the patients seeking relief are from the outlying districts and one or two of the inlets of Chesapeake Bay. Though prevalent in certain regions on this bay, the disease is yearly becoming less widespread and less severe. In the Southern States there are on the seaboard many isolated regions in which malaria prevails; but here, too, there has everywhere been a marked diminution in the prevalence and intensity of the disease. W. W. Johnston states that in the Gulf district there are places in which the disease is increasing. The percentage of cases admitted to the Marine Hospital Service in 1876 was 18·4, and 23·4 in 1887.

But this may be due to the development of the shipping trade and to the greater number of sailors who carry the infection from the West Indian ports, and those of Mexico and Central America.

In the interior of Louisiana, Mississippi, Arkansas, and Texas malaria is endemic, and the severe types are not infrequent. At irregular periods epidemics of the most severe forms occur.

In the Western and Northwestern States malaria is almost unknown. It is rare on the Pacific coast. In the region of the Great Lakes malaria prevails only in the Lake Erie and Lake St. Clair regions. It has practically disappeared from Lake Ontario, whereas in the upper Huron and Lake Superior basins it is unknown. The St. Lawrence River region remains free from the disease. In Montreal a patient with malaria is invariably questioned as to his latest residence.

(2) **Telluric Conditions.**—The importance of the state of the soil in the etiology of malaria is universally recognized. It is seen particularly in low, marshy regions which have an abundant vegetable growth. Estuaries, badly drained, low-lying districts, the course of old river-beds, tracts of land which are rich in vegetable matter, and particularly districts such as the Roman Campagna, which have been allowed to fall out of cultivation, are favorite localities for the development of the malarial poison. These conditions are most frequently found, of course, in tropical and subtropical regions, but nothing can be truer than the fact that reeking marshes of the most pestilent appearance may be entirely devoid of the poison, and the disappearance of the disease from a locality is not necessarily associated with any material improvement in the condition of the marshes or of the soil. Thus, in New England and in parts of western Canada, in which malaria formerly was very prevalent, the increased salubrity is usually attributed to the clearing of the forests and the better drainage of the ground; but these improvements alone can scarcely explain the disappearance, since in many districts there are marshy tracts and low-lying lands in every respect like those in which, even at the same latitude, the disease still prevails. Compare, for example, a swampy tract on the northern shore of Lake Erie and a similar tract on the southern shore of Lake Ontario; the flora and fauna of the two districts are practically identical, but in the former the conditions under which the malarial virus develops still exist, whereas in the latter they have gradually disappeared. In short, it is impossible to ascertain from the nature of the soil and climate in any given place whether it is malarial or not. In the absence of accurate knowledge as to the habitat of the hæmatozoa, the only means of deciding this point is by noticing the effect of residence in such a place on the human subject, preferably one of the Caucasian race.

(3) **Season.**—Even in the tropics, where malaria constantly prevails, there are minimal and maximal periods; the former corresponding to the summer and winter, the latter to the spring and autumn months. In temperate regions, like the central Atlantic States, there are only a few

cases in the spring, usually in the month of May, and a large number of cases in September and October, and sometimes in November. In the tropics, too, the cases are most numerous in the autumn months.

(4) **Meteorological Conditions.**—(*a*) *Heat.*—A tolerably high temperature is one of the essential conditions for the development of the virus. It is more prevalent after prolonged hot summers.

(*b*) *Moisture.*—In the tropics the malarial fevers are most prevalent in the rainy seasons. In the temperate climates the relation between the rainfall and malaria is not so clear, and cases are more numerous after a dry summer; but if either heat or moisture is excessive, the development of the virus is checked for a time.

(*c*) *Winds.*—Many facts are on record which seem to indicate that the poison may be carried to some distance by winds. The planting of trees has been held to interfere with the transmission by prevailing winds. Possibly, however, the quickly growing trees, such as the *Eucalyptus globulus*, have acted more beneficially by drying the soil.

(5) **Specific Gravity.**—That the distribution of the poison of malaria is influenced by gravity has long been conceded. Persons dwelling in the upper stories, or in buildings elevated some distance above the ground, are exempt in a marked degree.

The Specific Germ.—As Hirsch correctly remarks, the late J. K. Mitchell "was the first to approach in a scientific spirit the nature of infective disease and particularly in malarial fever." Many attempts were made to discover a constant and characteristic organism. Klebs and Tommasi-Crudeli in 1879 announced the discovery of a *bacillus malariæ*, but their observations have not been confirmed. In 1880 Laveran, a French army surgeon, now professor at the Medical School at Val de Grace, announced the discovery of a parasite in the blood of patients attacked by malarial fever. During the next three years he published nine additional communications, but for a time these observations attracted little attention. The Italian observers Marchiafava, Celli, and Golgi corroborated Laveran's statements. Councilman carefully studied the question in this country, and Laveran's statements were confirmed by myself in Philadelphia, by Walter James in New York, and more recently by Dock in Galveston. In India, Vandyke Carter has published an elaborate monograph on the parasites. In France, Germany, and England, owing in great part to the absence of cases of malaria, the value of Laveran's observations has been overlooked, but recently the confirmation has been published from many of the German clinics. So far as I know, not a single observer, who has had the necessary training and the material at his command, has failed to demonstrate the existence of these parasites.

The bodies which have been found invariably associated with all forms of malarial fevers, belong to the protozoa and to a group of organisms known as the *hæmatozoa*, the precise affinities of which have not yet been definitely determined. In some respects they closely resemble the monads,

in others the sporozoa. Parasites of the red blood-corpuscles have been met with abundantly in the blood of fish, turtles, and many species of birds. One of the best and most readily studied examples is the *Drepanidium ranarum*, a common parasite in the red blood-corpuscles of the frog.* In the blood of patients with malarial fevers the following forms may be seen: (1) an unpigmented hyaline body within the red blood-corpuscles which displays active movements; (2) a pigmented amœboid body within the red blood-corpuscles, which, under certain circumstances, may increase in size and form (3) a segmenting body, in which the protoplasm divides into a variable number of definite small spheres; (4) crescentic bodies, the so-called *crescents*, which develop within the blood-corpuscles and form characteristic and distinctive structures; (5) flagellate organisms, which may be seen to develop from the intercellular pigmented forms, or from ovoid bodies which are altered crescents; (6) free flagella. To the amœboid from within the red blood-corpuscles Marchiafava and Celli gave the name *plasmodium malariæ*. The following statements may be made with reference to these bodies:

The highest living authorities on protozoa, such as Bütschli, of Heidelberg, acknowledge that they are truly parasitic organisms. The testimony is now unanimous in France, India, America, Italy, and Germany that these bodies are always present in the malarial fevers. There is no evidence to show that they are ever present in any other disease. I can speak on this point with some confidence, having for years been in the habit of making blood examinations.

The relation of the parasites to the symptoms of the disease has been worked out in part by Golgi, who has shown that corresponding to the paroxysm there is a process of segmentation.

The relation of the different phases of growth to the varieties of malarial fever has not yet been thoroughly established, but the following points may be referred to: The typical intermittents are associated with large forms of the parasites, of which several varieties have been described. Golgi has described two distinct forms which he considers the causes of tertian and quartan fevers, and makes all other types depend on combinations of these. This probably holds good for a large proportion of intermittents. With the remittents, Marchiafava and Celli have described a distinct species, and look upon the crescents as representing a phase in its development. The pernicious malarial fevers are also associated with this variety, which the Italian observers call the "small plasmodium." The crescents may occur also in acute cases, but are most constant in malarial cachexia. The flagellate bodies do not appear to have any definite relation to the different forms of the disease.

The general symptoms and the morbid anatomy of malaria are in har-

* For an excellent account of these hæmatozoa and their development, see *Celli*, in Fortschritte der Medicin, 1891.

mony with the changes which this parasite induces. The destruction of the red blood-corpuscles by it can be traced in all stages. The presence of the pigment in the blood and the viscera, so characteristic of malaria, results from the transformation of the hæmoglobin by the plasmodia. The anæmia is a direct consequence of the wide-spread destruction of the corpuscles by the parasites. The constancy of their presence, the fact of their causing rapid destruction of the red blood-corpuscles, and the remarkable coincidence of their disappearance contemporaneously with the symptoms on the administration of quinine, are points strongly in favor of their etiological relation with the disease. There are still many gaps in our knowledge. We do not know how the parasite enters, or how or in what form it leaves the body; how and where it is propagated; under what outside conditions it develops, whether free or in some aquatic plant or animal. No record of its successful cultivation has been published.

Meantime, awaiting further knowledge, advantage may be taken of its constant presence in malaria. This alone, without reference to the true nature of the organism, is a fact of the highest importance. To be able, everywhere and under all circumstances, to differentiate between malaria and other forms of fever is one of the most important advances which has been made of late years in practical medicine, one which will revolutionize the study of fevers in tropical and subtropical countries, and should, within a short time, bring some order out of the chaos which at present exists regarding the different forms which there prevail.*

Morbid Anatomy.—The changes result from the disintegration of the red blood-corpuscles, accumulation of the pigment thereby formed, and possibly the influence of toxic materials produced by the parasite. Cases of simple malarial infection, the ague, are rarely fatal, and our knowledge of the morbid anatomy of the disease is drawn from the pernicious malaria or the chronic cachexia. Rupture of the enlarged spleen may occur spontaneously, but more commonly from trauma. A case of the kind was admitted under my colleague, Halsted, in June, 1889, and Dock has recently reported two cases.

(1) **Pernicious Malaria.**—The condition depends upon the duration of the infection and upon whether the patient has had previous attacks. The blood is hydræmic and the serum may even be tinged with hæmoglobin. The red blood-corpuscles present the endoglobular forms of the parasite and are in all stages of destruction. The spleen is enlarged, often only moderately; thus, of two fatal cases recently in my wards the spleens measured 13 × 8 ctm. and 14 × 8 ctm. respectively. If a fresh

* One rises from the perusal of the recent *Traité des Maladies des Pays Chauds*, by Kelsch and Kiener, with a feeling that the key to many of the complex problems there discussed and a totally different conception of many of the features of malaria would have been obtained had they studied the disease from the standpoint of their countryman Laveran.

infection, the spleen is usually very soft, and the pulp lake-colored and turbid. In cases of intense reinfection the spleen may be enlarged and firm. The amount of pigment in the spleen elements is enormously increased. The liver is swollen and turbid. In very acute cases there is not necessarily any macroscopic pigmentation, though microscopically the capillaries may be stuffed with degenerating red blood-corpuscles deeply pigmented. Perivascular (portal) infiltration has been found in a very acute case in a young man (Dock). The brain usually shows interesting changes. In severe cases of some duration the tissue is stained, sometimes chocolate-colored. In mild cases the discoloration is present, but less marked. The blood-vessels, especially the arterioles and capillaries, contain large numbers of parasites, with partial or total destruction of red blood-corpuscles, and pigmented leucocytes. Occlusions of arterioles by means of parasites are often seen. Anæmia and œdema are commoner than congestion. The kidneys show analogous conditions.

(2) **Malarial Cachexia.**—A patient, the subject of chronic paludism, usually dies of anæmia or of hæmorrhage associated with it. The most characteristic cases of the kind which have come under my observation have been in the workmen returning from the Panama Canal, victims of the so-called Chagres fever

The anæmia is profound, particularly if the patient has died of fever. The spleen is greatly enlarged, and may weigh from seven to ten pounds. If the disease has persisted for any length of time, it is firm and resists cutting. The capsule is thickened, the parenchyma brownish or yellowish-brown, with areas of pigmentation, or in very protracted cases it is extremely melanosed, particularly in the trabeculæ and about the vessels.

The liver may be greatly enlarged; but, as a rule, the increase in size is moderate in proportion to that of the spleen. It may present to the naked eye a grayish-brown or slate color due to the large amount of pigment. In the portal canals and beneath the capsule the connective tissue is impregnated with melanin. Varying with the duration of the disease, the shade of color of the liver ranges from a light gray to a deep slate-gray tint. The texture is firm, but there is not necessarily any great increase in the connective tissue. Histologically, the pigment is seen in the Kupffer's cells and the perivascular tissue.

The kidneys may be enlarged and present a grayish-red color, or areas of pigmentation may be seen. The pigment may be diffusely scattered and particularly marked about the blood-vessels and the Malpighian bodies, or it is often abundant in the cells of the convoluted and collecting tubules. The peritonæum is usually of a deep slate-color. The mucous membrane of the stomach and intestines may have the same hue, due to the pigment in and about the blood-vessels. In some cases this is confined to the lymph nodules of Peyer's patches, causing the shaven-beard appearance.

(3) The Accidental and Late Lesions of Malarial Fever.

(*a*) *The Liver.*—Paludal hepatitis plays a very important *rôle* in the history of malaria, as described by French writers. Kelsch and Kiener devote over sixty pages to a description of the various forms, parenchymatous and interstitial, describing under the latter three different varieties. The perusal of this section of their work by no means carries conviction that all the forms which they describe are associated definitely with malaria. Many of the patients were the subjects of chronic alcoholism, and the most important diagnostic point upon which they seem to have placed reliance was melanosis of the spleen, sometimes with pigmentation of Glisson's sheath. The existence of a cirrhosis dependent upon the irritation of large quantities of pigment in the liver is unquestioned, but only those cases in which the history of chronic malaria is definite, and in which the melanosis of both liver and spleen coexist, should be regarded as of paludal origin. The affection in this country is of extraordinary rarity. In the post-mortem room of the Philadelphia Hospital I have frequently seen, in subjects in whom the spleen was deeply pigmented, the portal sheaths of the liver stained, and a slight increase in the connective tissue; but it is begging the question to say that in such patients, who have almost certainly been habitual consumers of bad whisky, the condition of the liver was due to malaria. No instance of malarial cirrhosis has been shown at the Philadelphia Pathological Society since its foundation. Welch tells me he knows of but one specimen which has been shown in New York, and that was from an Algerian.

(*b*) *Pneumonia* is believed by many authors to be common in malaria, and even to depend directly upon the malarial poison, occurring either in the acute or in the chronic forms of the disease. I have no personal knowledge of such a special pneumonia It certainly does not occur in the intermittent or remittent fevers which prevail in Philadelphia and Baltimore. The question was formerly warmly discussed in this country, and I may refer to the attempt on the part of Manson to distinguish special forms depending upon the malarial poison. The exhaustive and critical review of the subject by W. T. Howard, in 1859, put a check to many of the speculations on the subject. The French authors quoted above recognize as common in chronic paludism a form distinguished by an irregular course, an absence of many of the characteristic symptoms, by a rapid swelling of the liver and spleen, and a special tendency to the formation of necrotic foci. On two occasions in the Philadelphia Hospital I had an opportunity of seeing the development of pneumonia in convalescents from malaria—one of a quotidian, the other of a quartan type. They developed in a ward with several other cases of pneumonia, and the disease ran a perfectly normal course. In about four hundred cases of malaria which have been under observation at the Johns Hopkins Hospital and Dispensary bronchitis has been frequent as an early symptom, but we have seen no indication of any special form of inflammation of the lungs.

(*c*) *Nephritis.*—Acute inflammation of the kidneys is rare in the milder forms. Albumen in the urine is not infrequent during the chill, and in the course of the continued or remittent fevers. Kelsch and Kiener describe several forms of nephritis. No instance of acute or chronic Bright's disease resulting directly from paludism has come under my notice.

Clinical Forms of Malarial Fever.—(1) **Intermittent Fever.**—This form is characterized by recurring paroxysms of what are known as ague, in which, as a rule, chill, fever, and sweat follow each other in orderly sequence. The stage of *incubation* may be very short. Attacks have occurred within twenty-four hours after exposure. Usually the time of incubation is from seven to fourteen days. On the other hand, the ague may be, as is said, "in the system," and the patient may have a paroxysm months after he has removed from a malarial region, though I doubt if this can be the case unless he has had the disease when living there.

Description of the Paroxysm.—The patient generally knows he is going to have a chill a few hours before its advent by unpleasant feelings and uneasy sensations, sometimes by headache. The paroxysm is divided into three stages—cold, heat, and sweating.

Cold Stage.—The onset is indicated by a feeling of lassitude and a desire to yawn and stretch, by headache, uneasy sensations in the epigastrium, sometimes by nausea and vomiting. Even before the chill begins the thermometer indicates slight rise in temperature. Gradually the patient begins to shiver, the face looks cold, and in the fully developed rigor the whole body shakes, the teeth chatter, and the movements may often be violent enough to shake the bed. Not only does the patient look cold and blue, but a surface thermometer will indicate a reduction of the skin temperature. On the other hand, the axillary or rectal temperature may, during the chill, be greatly increased, and, as shown in the chart, the fever may rise during the chill to 105° or 106°. Of symptoms associated with the chill, nausea and vomiting are common. There may be intense headache. The pulse is quick, small, and hard. The urine is increased in quantity. The chill lasts for a variable time, from ten or twelve minutes to an hour, or even longer.

The *hot stage* is ushered in by transient flushes of heat; gradually the coldness of the surface disappears and the skin becomes intensely hot. The contrast in the patient's appearance is striking: the face is flushed, the hands are congested, the skin reddened, the pulse is full and bounding, the heart's action is forcible, and the patient may complain of a throbbing headache. The rectal temperature may not increase much during this stage; in fact, by the termination of the chill the fever may have reached its maximum. The duration of the hot stage varies from half an