formative cells become much reduced in size, and finally lie in the characteristic openings in the homogeneous intercellular substance.

The process of new formation of bone is similar to the new formation of cartilage; the lime salts are finally deposited in the intercellular substance.

Mucous, lymphadenoid, and fatty tissues may all arise from embryonic connective tissue.

Fibrillated connective tissue may arise from any form of connective tissue that has suffered lesion, and has been converted into embryonic tissue.

From what has been said, it is evident that the stage which is preliminary to the new formation of permanent tissue after lesion is characterized by the appearance of embryonic tissue. The further development of this embryonic tissue is not the same in all cases; in some instances there is perfect reproduction of tissue in all respects like the original, or *restitutio ad integrum*. In many cases the restitution is only partial; in others again there is replacement of the original structure by connective tissue of a different type from the original. The replacement of the original structure by connective tissue of a different type from the original may occur in any kind of connective tissue, and is in truth a very common occurrence, constituting the formation of a scar, where the original structure is replaced by dense fibrous connective tissue, whose only function is to fill a gap. Where the original structure is endowed with any special function, the scar tissue is incapable of taking on this function. If, for example, the scar tissue is formed to fill up a defect caused by a lesion in a muscle, the scar tissue serves only to unite the divided ends of the muscle fibres, but is not itself capable of contraction. Scar tissue formed in the brain, in the liver, in the kidney, in the spleen, or in the lung does not perform the peculiar function of the tissues of these organs. The substitution of connective tissue of lower functional power than that originally present constitutes a form of degeneration, and is met with in cirrhosis of the liver and other organs. But although these processes are spoken of as degeneration, it would perhaps be more correct to regard them as hypertrophies of the connective tissue, for this is what they are in fact.

Regeneration of the formed elements of the blood does not differ essentially from regeneration of the other connective tissues. The leucocytes are reproduced in the lymphadenoid tissue in various parts of the body as well as in the circulating blood, as is shown by the fact that white corpuscles showing karyokinetic figures are met with abundantly in these situations. Direct nuclear division and fragmentation also occur, as is shown in the lobed and disrupted nuclei of the polymorphic nuclear leucocytes.

New Formation of Blood-Vessels.—A very important factor in regeneration is the new formation of blood-vessels. These are formed by sprouts arising from the vessels beneath the injured area. Each sprout is at first a solid arch, in reality a long cone or horn, of protoplasm projecting from the wall of the vessel (Fig. 3955, *a*) terminating in a long-pointed process. The solid arch may even send out several long processes (Fig. 3955, *b*, *c*). Sooner or later the solid arch becomes hollowed out by liquefaction of the interior, forming a cavity which finally opens into the parent vessel, or the arch may be hollow from the start and consist merely of a bulging of the wall of the parent vessel (Fig. 3955, *c*). In either case the arch next becomes a tube by the pressure of blood flowing in from the parent vessel, and this also causes the long processes to split and form hollow, conical tubes. Meanwhile nuclei formed by karyokinesis of the cells of the endothelium of the parent vessel wander into the walls of the hollow tube and convert it in this way into a capillary. The capillaries produced in this way have walls consisting of flat endothelial cells, but these cells are frequently quite thick; and when this is the case, the new-formed capillary resembles a tubular gland on cross section. The long, slender processes from the arches unite freely with the similar processes from other vessels (Fig. 3955, *b*) and even directly with the walls of other vessels, or they may unite with the parent vessel at a different point from the origin (Fig. 3955, *c*). In this way abundant anastomosis between the vessels is formed.

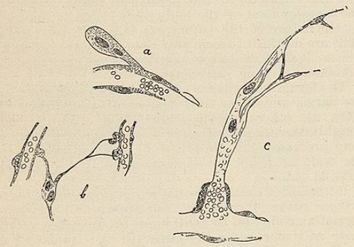

Fig. 3955.—New Formation of Blood-Vessels. (After Tillman.)

This is not the only origin of the new capillaries, for certain cells which at first have no connection with blood-vessels also take part in the process. These cells are spindle- or club-shaped masses of protoplasm which lie free in the tissue at first, but later become united with the long processes from the arches (Fig. 3955, *b*). After they become united with the processes from the arches they become perforated by a central canal and finally assume the character of capillaries.

Many of these new-formed capillaries subsequently change to arteries and veins by thickening of their wall through proliferation of the cells of the walls. The different coats finally become differentiated.

The account here given of the new formation of blood-vessels is that given by Ziegler, and is the one that has found universal acceptance. But some authorities claim that the blood-vessels are also formed in other ways. They maintain that the cells that wander into the area of the lesion unite to form capillary vessels, and that they also form new red blood corpuscles in a manner similar to the formation of vessels and blood in embryonic tissue. This method of new formation is not recognized by Ziegler in pathological regeneration.

Another process of new formation of blood-vessels claimed by some authorities is that certain spindle-shaped cells form in parallel rows, leaving a canal between them. Vessels apparently formed in this way may be seen in organizing blood clot, but Ziegler regards these as really deceptive offshoots from pre-existing blood-vessels.

B. Meade Bolton.

REGISTRATION OF DISEASES. See *Vital Statistics*.

RELAPSING FEVER.—(Synonyms: Febris recidiva; typhus recurrens; famine fever; bilious typhoid; spirillum fever; epidemic remittent fever; remitting icteric fever; fièvre à rechute; fièvre récurrente; typhus à rechute; Hungerpest; Rückfallsfieber; Wiederkehrendes Fieber; Armentyphus; tifo recidivo, etc.)

Definition.—A specific, contagious fever, which may prevail as an epidemic among the destitute, and especially among those who live in overcrowded tenements, during seasons of unusual scarcity of food; hence the name famine fever. It is characterized by the presence of a mobile spiral filament in the blood—a spirillum or spirochaëte (*S. Obermeieri*)—which is found during the relapses as well as during the initial paroxysm, but is absent during the apyretic intervals. The first febrile paroxysm lasts for from five to seven, or even nine days, and is terminated abruptly in profuse perspiration; after an apyretic interval of a week or more a relapse commonly occurs, which is similar to the initial paroxysm, but of shorter duration; in some instances a second, a third, or even a fourth relapse occurs.

History.—The attempt has been made (Spittal, 1844) to show that some of the fevers described by Hippocrates correspond with relapsing fever. This view is considered by Hirsch to be quite erroneous. He says: "It is clear that Hippocrates speaks there of bilious remittent malarial fever." The first notice of the occurrence of relapsing fever in Europe is found in the writings of the Scotch and Irish physicians of the early part of the eighteenth century. Hirsch says: "I have searched in vain, in the descriptions which the physicians of the sixteenth and seventeenth centuries have given of the fever epidemics observed by them, for any indications of relapsing fever that would be in some measure precise." The fact that the disease was not recognized, and differentiated from other specific febrile affections, cannot, however, be taken as evidence that it did not exist prior to the date of the first clearly recorded epidemic in Ireland (1739). An account of this epidemic has been given by Rutty, who wrote in 1770. The earliest accounts of the disease in Scotland date from 1741 (Hirsch). But the literature relating to relapsing fever belongs for the most part to the past century. It prevailed in Ireland and in Scotland during the years 1799–1800, 1817–19, 1826–27, 1842–48, and in the latter year (1848) it invaded several of the larger towns of England. In 1868–70 it again prevailed in England and Scotland, and cases are reported to have occurred in London as recently as the year 1873. On the Continent the first accounts we have come from Russia—Odessa, in 1833; Moscow, 1840–41. In the autumn of 1863 the disease reappeared in Odessa; the following year it became epidemic over extensive areas in Russia, and extended to Livonia and Finland (1865), to Siberia (1866), and to Poland (1868). According to Hirsch, the disease continued to prevail in Russia over extensive areas during subsequent years, and was observed among the Russian troops as late as 1878–79. In Germany an extensive epidemic broke out in 1868, as a result of importation from Russia (Hirsch). A second, more restricted, epidemic occurred in 1871–72, and a third in 1878–79. In the west and southwest of Europe —Switzerland, France, Italy, Spain—the disease is as yet unknown. In India relapsing fever has, no doubt, prevailed for many years, but the differential diagnosis between it and remittent fever, or the specific continued fevers which prevail there so largely, was not clearly made out by the earlier observers. During the last forty years, however, numerous outbreaks of this disease in various parts of India have been recorded, and Carter has demonstrated that the disease, as it occurs in that country, is identical, as regards its clinical history, with relapsing fever as described by recent European authorities, and also that it is characterized by the constant presence of the spirillum discovered by Obermeier in blood drawn during a febrile paroxysm. Relapsing fever has several times been imported to the United States, but its prevalence has been limited to restricted areas in our largest seaport cities. In 1844 fifteen cases were received into the Philadelphia Hospital from an emigrant ship sailing from Liverpool; in 1848 a few cases arrived in New York, and in 1850–51 Dr. Austin Flint saw a number of cases, among recently arrived Irish emigrants, received into the Buffalo City Hospital; but no epidemic resulted from these importations, and it was not until some years later (1869–70) that the disease became epidemic in certain sections of the cities of New York and Philadelphia. Parry, who made a careful investigation with reference to the origin of the first cases in Philadelphia, was unable to trace it to importation; but this can scarcely be questioned in view of what is known of the history and etiology of the disease, and in consideration of the fact that Philadelphia is a seaport city which has constant communication with ports on the other side of the Atlantic which at that time were known to be infected. Parry and Pepper have given us admirable accounts of this epidemic in Philadelphia. We quote from a recent article by the last-named author the following statement, relating to its progress and extent: "In Philadelphia, of 1,176 cases in which the date of occurrence is known, there occurred in September (1869), 4 cases; December, 6 cases; January (1870), 5 cases; February, 13 cases; March, 124 cases; April, 209 cases; May, 325 cases; June, 293 cases; July, 115 cases; August, 19 cases; September, 28 cases; October, 15 cases; November, 1 case; December, 2 cases; January (1871), 2 cases; February, 1 case; March, 2 cases; May, 7 cases; June, 2 cases; September, ? cases; October, 2 cases.

The coincidence of relapsing fever and typhus has been noted in many of the epidemics which have occurred in Europe, but the history of this coincidence does not justify the supposition that there is any etiological relation between these diseases other than that furnished by common predisposing causes, viz., the depressing effects of overcrowding, insufficient food, and filthy surroundings. This view is supported by the fact that either disease may occur alone, and by the circumstance that sometimes one and sometimes the other has the precedence in time in those epidemics in which coincidence has been observed.

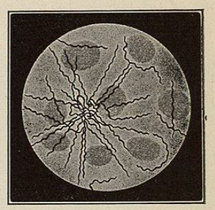

Fig. 3956.—Spirilla of Relapsing Fever. (After Soudakewitsch, *Annales de l'Institut Pasteur*, vol. v., 1890.)

Etiology.—The discovery by Obermeier, in 1873, of a minute vegetable parasite—*Spirochaëte Obermeieri*—in the blood of patients suffering from relapsing fever, and the subsequent demonstration, by numerous observers in various parts of the world, that this micro-organism is constantly present in the blood of relapsing-fever patients during the febrile paroxysms, has thrown a flood of light upon the etiology of this disease, and is one of the most significant facts with reference to the etiology of the infectious diseases in general which have been brought to light by modern microscopical researches. Conservatism suggests the possibility that the parasite may be simply an accompaniment of the disease, and not directly concerned in its etiology as the essential and specific cause. This hypothesis seems to us to be hardly tenable in view of what is now known of the pathogenic action of certain other micro-parasites of the same class, and of the following facts: (*a*) The parasite is constantly present in the blood during the febrile paroxysms, and in smaller numbers during the latter part of the period of incubation, and is absent during the apyretic intervals. (*b*) This parasitic organism is peculiar to the disease under consideration, *i.e.*, repeated researches by competent microscopists have failed to demonstrate the presence of a similar organism in any other disease. (*c*) The parasite is present in the blood in such numbers that its pathogenic power can scarcely be questioned. Carter says: "During specific fever several organisms (*e.g.*, five to ten) are visible in the field at one time; not seldom they are too numerous to count, and occasionally they are present in swarms, being apparently nearly half as common as the red discs themselves." (*d*) The disease may be communicated to man (Motschutkoffsky) and to the monkey (experiments of Koch and of Carter) by inoculations with blood containing the spirillum, and the parasite is found in great numbers in the blood of the inoculated individuals during the febrile paroxysm which results—after an incubation period of three or four days (Carter)—from such inoculations. The morphology of the relapsing fever "germ" is shown in Fig. 3956. The spiral filaments are exceedingly slender, their diameter being not more than 1 μ (0.001 mm., Lebert), or, according to Carter, $\frac{1}{50000}$ to $\frac{1}{40000}$ of an inch. The length varies from two to six times the diameter of a red blood disc (Carter). The motion of these spiral filaments, in blood recently drawn, is very lively, "rotary, twisting, and rapidly progressive, but soon ceases under the ordinary condi-

tions of microscopic examination" (Lebert). According to Carter, the movements may continue for from a few hours to one or two days or longer.

A good objective and a certain amount of skill in the use of the microscope are required for the detection of the spirillum in fresh blood. This is shown by the fact that Obermeier himself failed to recognize the presence of the parasite in the microscopic researches made by him some years prior to the date of his discovery; and by the failure reported by some of those who have since attempted to verify his observations. Carter says: "That, as regards the examination of fresh blood, obstacles do exist, is proved by the fact of the organism being originally found only after long-repeated scrutinies; and at Bombay I have met with observers, not unaccustomed to the use of the microscope, who could never clearly see the filaments." The demonstration is more readily made when a thin film of dried blood attached to a cover-glass is stained, *secundum artem*, with one of the aniline colors —an aqueous solution of methyl violet, or of Bismarck brown, or fuchsin.

It is not yet certain whether the spirillum of relapsing fever is reproduced by spores as well as by "spontaneous fission," but it seems extremely probable that this is the case. Carter supposes that certain short filaments which he has observed in the blood are germinating spores, and remarks that "the practical facts of contagion require the presence of fertile spores, since spiral filaments are absent in the *secreta* and *excreta* of the body, and propagation by blood inoculation is obviously not the rule in common life." The same author gives several instances in which an attack is supposed to have been due to accidental inoculation while making an autopsy. Other cases are ascribed to simple contact with the dead body, independently of any wound. That the disease may be transmitted from individual to individual by direct contagion, or indirectly through fomites, is demonstrated by a multitude of observations; and, indeed, we have no satisfactory evidence that it is transmitted in any other way, or that the specific infective agent—spirillum—is capable of multiplication in an external nidus, and thus of giving rise to an epidemic independently of direct contagion, as is undoubtedly the case in certain other diseases, *e.g.*, typhoid fever, cholera, yellow fever. On the other hand, the evidence on record shows that in well-ventilated apartments and hospital wards the attendants upon the sick and patients suffering from other diseases are not very liable to contract the disease. Where, however, the sick are massed together in insufficiently ventilated hospitals, or when cases occur in the overcrowded tenements of the poor, the transmission of the disease to attendants and others exposed to contagion is far more frequent.

Up to the present time attempts to reproduce the spirillum of relapsing fever in a series of *cultures* have not been successful. Carter has, however, observed a growth of the spirilla in length, and the development of a tangled network of long filaments in a culture cell containing aqueous humor, kept in a warm chamber at a temperature of 40.5° C. (105° F.).

Predisposing Causes.—There is no evidence that *climate* or *season* has any marked influence upon the prevalence of relapsing fever; the disease has prevailed in Siberia as well as in India, and its preference for certain localities is quite independent of climatic conditions, relating rather to circumstances connected with the mode of life and hygienic surroundings of the population. No *age* is exempt, and *sex* has no apparent influence; but children are more subject to be attacked than adults, and susceptibility seems to diminish to some extent with advancing age. According to Murchison, only 195 out of 2,111 cases received into the London Fever Hospital, in twenty-three years, were over fifty years of age. To appreciate the value of these figures it would evidently be necessary to know how large a proportion of the exposed population were over fifty years of age.

Insufficient food is generally recognized by medical writers as a potent predisposing cause, and epidemics have so frequently been observed to coincide with periods of unusual scarcity that the name "famine fever" has been applied to the disease. Some authors have even gone so far as to ascribe to starvation and its accompaniments, overcrowding and filthy surroundings, an essential rôle in the development of the disease. But, as in the case of other specific contagious diseases, there seems to be very little foundation for the idea that relapsing fever may be developed *de novo* in times of famine, and its epidemic prevalence at such times is to be ascribed rather to increased vulnerability, on the part of the starving population, to the action of the specific exciting cause of the disease. We know that under favorable hygienic conditions the disease has but little disposition to spread, and that in the severest epidemics it finds its victims almost exclusively among the destitute. On the other hand, in the numerous instances in which shipwrecked mariners, Arctic explorers, etc., have been subjected to absolute starvation, we have no account of the development of any such disease as relapsing fever. *Overcrowding* is considered by Parry to be a more potent predisposing cause than starvation, and his careful study of the circumstances of those who were taken sick during the prevalence of the disease in Philadelphia (1870) seems to justify this conclusion—which is, moreover, supported by the observations of Muirhead, Bennett, Lebert, and others.

One attack of relapsing fever does not protect the individual from subsequent attacks, and second, or even third, attacks during the same epidemic have been noted.

Carter's experiments upon the monkey have led him to the conclusion that "the human virus becomes intensified in its passage through this animal." It is noticeable that, with one or two exceptions, there was but a single febrile paroxysm in the numerous successful inoculation experiments made by the author quoted. This does not invalidate the value of the evidence furnished by his experiments as to the identity of the disease produced in the monkey with the specific infectious disease of man known as relapsing fever, for this single paroxysm was characteristic in its origin, duration, and termination, and in the constant presence of the blood parasite which is peculiar to this disease. Moreover, in man the relapse is not an essential feature of the disease. Thus Carter, out of a total of 411 cases, found that in 98 (23.8 per cent.) there was but a single febrile paroxysm. Pepper has recorded the fact that in 10 out of 181 cases observed in Philadelphia there was no relapse; and Murchison, in a series of 2,425 cases collected from various sources, found that there was but a single paroxysm in 30 per cent.

Clinical History.—As a rule, the primary febrile paroxysm begins abruptly, without noticeable *prodromes*. In certain cases, however, the patient experiences a certain amount of malaise, loss of appetite and headache, for a day or two prior to the sudden access of fever. The *period of incubation* has usually a duration of from five to seven days (five to nine days—Murchison), but instances of a longer or shorter incubation are not infrequent. In several cases of accidental inoculation, at autopsies, which came under the observation of Carter, the period of incubation was from three and a half to seven days; and in the successful inoculations in the monkey, made by the same author, the mean duration of this period was about ninety hours. Speaking of these experiments, the author referred to says: "My experiments showed conclusively that prior to the onset of the fever there always occurs a more or less prolonged period of visible blood contamination; and hence that the interval between infection and fever is divisible into two parts, viz., an earlier and usually longer non-spirillar stage, and a final stage of spirillar manifestation during which the body heat, so far from being augmented, is often rather depressed."

The *initial paroxysm* of fever is commonly inaugurated by a decided chill, or at least by slight chilly sensations, accompanied by headache, pain in the back and limbs, and a feeling of weakness, with indisposition to exertion.

The tongue is coated; nausea and vomiting are of common occurrence; and there is usually a certain amount of tenderness on pressure in the epigastric region. Enlargement of the spleen occurs early in the attack, and usually a certain amount of enlargement of the liver may also be detected after the second or third day. Jaundice is of frequent occurrence in certain epidemics, and in others is quite rare. The abrupt seizure usually occurs during the daytime, and is marked by a rapid rise of temperature and a correspondingly rapid pulse. The pyretic movement exhibits a somewhat remittent character, the evening temperature being one or two degrees higher than the morning temperature, and attaining a maximum of 103.5° to 105° F. during the first twenty-four hours—a maximum which may be exceeded by a degree or two during subsequent evening exacerbations. The distinctive character of the pyrexia is its sudden termination by crisis, as a rule on the fifth or seventh day—more rarely as early as the third or as late as the twelfth day. This sudden termination of the febrile paroxysm is commonly attended with profuse perspiration, and occasionally by a critical diarrhœa, or hemorrhage from the nose, rectum, or vagina. The temperature frequently falls, during this termination of the paroxysm by crisis, as much as 10° or 12° F. in a few hours, and, as a rule, a subnormal temperature is quickly reached, and may persist at the morning observation for two or three days. *Defervescence* may occur at any time during the twenty-four hours, but the observations of Carter indicate that in a majority of the cases (66.6 per cent.) it happens between the hours of 4 P.M. and 7 A.M., or in other words, that it is most likely to occur during the night. It is attended by a complete relief of the distressing symptoms which marked the febrile paroxysm, and with the exception of a feeling of lassitude the patient has nothing to complain of, his tongue cleans up, his appetite returns, and within three or four days he might be considered convalescent, were it not for the known tendency of the disease to relapse after an apyretic interval of about a week. In one hundred and ninety cases analyzed by Carter the mean duration of the *apyretic interval* was 7.4 days, the extreme range being from three to twelve days.

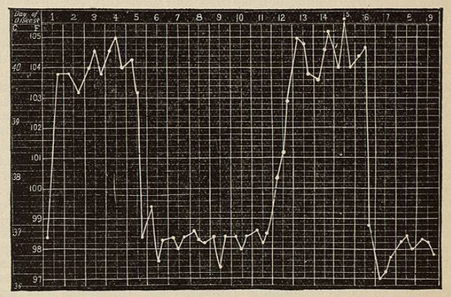

Fig. 3957.—Temperature Curve in a Case of Relapsing Fever.

The *relapse*, occurring commonly on the fourteenth day from the date of seizure, resembles the initial paroxysm in its sudden onset and abrupt termination, but is usually of shorter duration—three to seven days. The temperature not infrequently attains a higher point than during the initial paroxysm, and there is a correspondingly rapid pulse, but with the exception of increased debility the other symptoms are, for the most part, of a milder character. Defervescence is attended with profuse perspiration, and, as in the first apyretic interval, a subnormal temperature is quickly reached. After a *second apyretic period*, of from six to fourteen days, a *second relapse* of still milder character and briefer duration may occur, and, in exceptional cases, this may be followed by a third or even a fourth relapse.

Special Symptoms.—The characteristic features of the *pyrexia* are shown by the accompanying chart (Fig. 3957) of a case reported by Murchison, which, however, cannot be taken as entirely typical, inasmuch as the initial paroxysm and the relapse are of about the same duration, whereas the rule is that the relapse is not so protracted, and the date of its occurrence is more commonly the fourteenth rather than the twelfth day, as in this case. Variations from the typical form are, however, the rule rather than the exception, and the most we can say is that there is a tendency to crisis on the seventh day, and to relapse on the fourteenth day. The remittent character of the pyretic movement is often more marked than in this case, and especially so in the relapses. We remark, also, that the subnormal temperature which follows crisis and sudden defervescence is less marked than usual in this case, after the first febrile paroxysm, although shown very well in that part of the chart which represents the second apyretic interval. This is a very noticeable feature of the disease, although not peculiar to it, a subnormal temperature being quite common during the "calm stage" of yellow fever. We have the authority of Murchison for the statement that the temperature may fall as much as 14.4° in the course of twelve hours, reaching as low a point in certain cases as 94°, 93°, or even 92° F.

Pepper has observed a fall from 107.2° to 95°, and states that this is as low a point as is commonly reached. The observations of Carter, also, indicate that a fall below 95°, in non-fatal cases, must be extremely rare. The acme of temperature is commonly reached during the twenty-four hours immediately preceding the crisis, and in certain cases a sudden rise of several degrees has been noted to occur just before the abrupt fall which terminates a paroxysm. In a typical series of cases analyzed by Carter the maximum temperature observed during the initial paroxysm was 108°, on the evening of the sixth day; the maximum temperature noted during the relapse in the same series of cases was 106° F. Pepper has recorded a temperature of 107.5° as having come under his observation, and in a typical case, of which he gives a chart (*op. cit.*, p. 380), a temperature of 107° was reached at the termination of the initial paroxysm, and also during the relapse. In this chart a slight febrile movement is seen to follow the subnormal depression after the relapse. "Reactionary fever" of this kind, of moderate degree and irregular in its course, is commonly seen to follow the febrile paroxysm and subsequent subnormal depression of temperature in yellow fever. In relapsing fever it is not perhaps so common, but is sufficiently so to have attracted the notice of Carter, who speaks of it as the "rebound" or "secondary fever," and states that it was observed in about one out of six of his cases. "Its duration is brief, and the blood spirillum is invariably absent."

The *pulse* in relapsing fever presents no distinctive character. During the pyretic movement it is very frequent, and at the outset is commonly full and tense; but with defervescence there is a rapid reduction in its frequency, and during the first portion of the apyretic intervals, when the temperature is subnormal and the patient is in a state of partial collapse, it becomes small and feeble, and occasionally extremely slow—as slow even as in the corresponding stage in cases of yellow fever. Thus, Obermeier has seen it as low as 44, and other observers have seen it even lower than this—Muirhead 34, Stillé 30. While, in general, the rapidity of the pulse corresponds with the pyretic movement, yet this is not an invariable rule, and according to Murchison is less true as regards the relapse than in the initial paroxysm; thus, he has seen a pulse of 90 when the temperature was 106°. On the other hand, Carter has noted that in the

Bombay epidemic the sudden fall of temperature marking the crisis was not attended with a corresponding decline in the frequency of the pulse. During the height of the fever the number of pulsations per minute, in adults, may be stated as from 110 to 140, while in children it often reaches 160 or even 170. After the crisis, an irregular or dicrotic pulse is not infrequent, and as a rule it is feeble and compressible. At this time there is danger of sudden death from syncope. A soft systolic murmur heard over the base of the heart and along the large vessels is frequently discovered, both during the primary paroxysm and during the relapse.

Pain in the back and limbs is complained of during the first days of the primary attack, and to a less extent during the relapse. Articular pains, unaccompanied by swelling, may also persist during the apyretic interval. But the most distressing pain is felt in the head. *Headache* is usually frontal; it is an early and often very persistent symptom, disappearing only with the crisis, and recurring with less severity with the relapse. Other symptoms referable to the nervous system are: *Vertigo*, induced by assuming an erect position; especially common at the outset of the attack, and often persisting throughout the paroxysm; *delirium*, usually of an hysterical character, and most common among the victims of chronic alcoholism; or the low muttering delirium which accompanies suppression of urine, and which, in the absence of relief, passes into stupor and coma; *convulsions*, the result of uræmic poisoning or of extreme nervous irritation due to severe and protracted pyrexia; *insomnia*, due largely to the distressing pains, and not readily controlled by hypnotics; *paralysis*, limited to single muscles or to groups of muscles—of rare occurrence. Of these symptoms vertigo and insomnia are the only ones which are so common as to constitute a characteristic feature of the disease.

The symptoms referable to the *digestive system* are those common to febrile complaints generally, viz., thirst, loss of appetite, a coated tongue, torpid bowels, and nausea, with vomiting of ingesta and bilious matters. The *tongue* usually remains moist and is coated with a thick white fur which may become yellowish or, in cases having a typhoid tendency, brown and dry. It is usually somewhat swollen and indented at its edges by contact with the teeth. This appearance, together with the frequent absence of coating upon the edges and over a triangular space at the tip, which remains bright and red, has been regarded by some authors as of diagnostic value. Occasionally the tongue is red and glazed, and it may become deeply fissured, or in severe and protracted cases dry and brown. The tongue quickly clears up and appetite returns when the febrile paroxysm has terminated by crisis, and when a relapse occurs it again becomes coated and there is a return of anorexia and gastric disturbance. *Nausea* and *vomiting* are almost constant symptoms at the outset of the attack, and, less frequently, recur during the relapse. Occasionally a considerable quantity of bile is ejected; more commonly the vomited matters consist of ingesta or glairy mucus tinged with bile. "Black vomit," due to the presence of blood in the vomited matters, has been seen by several observers, and in certain epidemics seems to have been not very infrequent. It is a symptom of grave import. Three cases out of four in which it was noted by Pepper terminated fatally. This author observes that, "judging from the frequency with which in fatal cases we find ecchymoses of the gastric mucous membrane, with blood-stained mucus in the cavity of the stomach, we should expect black vomit to be more often observed than is the case." More or less tenderness and pain on pressure in the epigastric region is a common symptom during the early part of the febrile paroxysm; in this particular, as in several others, there is a noticeable resemblance to yellow fever.

The *bowels* are commonly constipated at the outset of the attack, but later diarrhœa is not infrequent, and this may be profuse and of a critical character, occurring at the close of a febrile paroxysm, and to a greater or less extent taking the place of the usual critical sweating.

Enlargement of the liver may usually be demonstrated by careful percussion, and in some instances this organ extends to three inches below the margin of the ribs toward the close of the febrile paroxysm. Pressure in the hepatic region causes pain, and occasionally hepatic tenderness is quite a constant cause of distress. *Jaundice* is a prominent symptom in certain epidemics, occurring in from twenty to twenty-five per cent. of the cases. At other times it is comparatively rare. It appears toward the close of the primary paroxysm, or in one of the succeeding febrile paroxysms, and usually disappears after the crisis. According to the observations of Pepper and of Stillé, it is more frequent in the negro than in the white man.

Enlargement of the spleen is a constant and early symptom, and it is not unusual for this organ to attain from three to four times its normal bulk. It may be detected as early as the second day, projecting below the margin of the ribs, and toward the close of the febrile paroxysm it often forms a visible tumefaction on the left side of the abdomen. During the apyretic interval its volume rapidly diminishes, to increase again during the relapse.

The *skin* is free from any characteristic eruption, but occasionally an eruption of pinkish or rose-colored spots has been observed (Carter), and "true petechiæ have been quite common in some epidemics" (Pepper). Sudamina and herpetic eruptions about the mouth and nostrils are of common occurrence. Desquamation of the cuticle, especially from the hands and face, is not infrequent. Several observers have noted a peculiar odor, exhaled from the body of the patient, which is said to resemble that given off by "burning straw with a musty odor."

The *urine* is somewhat scanty and high-colored during the febrile paroxysms, and, as is usual in such cases, has a higher specific gravity than normal; its reaction is usually acid, and it deposits, on standing, a more or less copious sediment of urates, associated sometimes with crystals of oxalate of lime. The amount of urea present is subject to considerable variations, but the general rule seems to be that it is increased during the paroxysms, and decreased at the time of the crisis, to increase again during the first part of the apyretic interval. In certain cases the critical sweating is replaced by an abundant discharge of light-colored urine of low specific gravity, but under ordinary circumstances the amount of urine is greatly reduced at the time of crisis; subsequently the quantity is increased and the specific gravity is reduced to a minimum, and this may persist for some time after convalescence is established. Thus, Carter reports a case in which the daily amount, for two weeks after the relapse, was one hundred and thirty ounces, while the specific gravity was only 1002.6. Slight *albuminuria* has been noted by several observers as commonly occurring toward the close of the febrile paroxysm, or shortly after its termination. According to Carter, other evidence of acute renal congestion, such as blood discs and tubular casts, is almost never found. Other observers, however, have reported the presence of tube casts in those cases in which the urine is albuminous, and Obermeier has claimed that acute desquamative nephritis is one of the ordinary phenomena of the disease under consideration.

Epistaxis is of rather frequent occurrence in relapsing fever, and hemorrhage from the stomach, from the bowels, and from the kidneys, has been noted in rare cases. Pepper reports fifteen cases in which very profuse epistaxis occurred at the crisis, evidently as a critical discharge, replacing to some extent the usual perspiration.

Convalescence is usually rapid in the absence of any complication, but, after very severe and prolonged attacks, a considerable interval must elapse before the emaciated patient regains his usual strength. The average duration of the period included between the date of seizure and complete convalescence is about six weeks (Wilson).

Varieties.—At least one relapse, occurring after an apyretic interval, is necessary to constitute a typical case of relapsing fever. But in a certain proportion of the

cases occurring during an epidemic, there is but a single febrile paroxysm—*abortive form* (Carter)—which, however, is undoubtedly due to the same specific cause, as is shown by the constant presence of the spirillum of Obermeier in blood drawn during the pyrexia. These cases are often mild in character, and in the absence of a microscopic examination of the blood, and demonstration of the presence of the spirillum, the diagnosis would remain uncertain. The form of fever denominated *bilious typhoid* by Griesinger and other German authors is undoubtedly a variety of relapsing fever. It is characterized by intense jaundice, a tendency to suppression of the urinary secretion, to hemorrhages from mucous surfaces, and to those grave symptoms which constitute the typhoid state, viz., great prostration, muttering delirium passing into stupor and coma, hypostatic congestion of the lungs, a dry and brown tongue, etc. These symptoms may be developed during the primary febrile paroxysm in such a manner as to interfere with the termination of this paroxysm by crisis, and to render obscure the apyretic interval which, in typical cases of relapsing fever, distinctly separates the initial paroxysm from the relapse.

Complications.—One of the most frequent and fatal complications of relapsing fever is *pneumonia*. It commonly occurs after the crisis of the primary paroxysm, but may also follow the relapse, or may occur as a more remote sequel of the disease—three or four weeks after the close of specific pyrexia. In 97 autopsies Carter found evidence of pneumonia in 27 instances. Out of 23 autopsies, Pepper found the lesions of this complication in 8. It is more frequent in adult males than in females and children. *Pleurisy* was found by Carter to coexist with pneumonia 13 times in 21 autopsies in which inflammation of the lungs was verified. Deaths from pneumonia commonly occur within a week or ten days after the first crisis. The onset of this grave complication is marked by the usual symptoms and physical signs, and by pyrexia, which may be confounded with that of the relapse due to specific blood contamination. The pyrexia attending this complication is, however, distinguished from that of the preceding or subsequent specific febrile paroxysm by the absence of spirilla from the blood. The same is true of the "secondary" or "reactionary" fever, which in severe cases sometimes follows the critical defervescence, and which is independent of any recognizable organic complication.

Diarrhœa, in certain epidemics, is rather common as a complication or sequel, and may be the immediate cause of death. It occurred in 33 per cent. of the cases observed by Pepper in Philadelphia, and in 50 per cent. of the cases in the Königsberg epidemic. *Parotitis* occurred in from 2 to 3 per cent. of the cases collected by Carter, and was observed by Pepper in 3 cases out of 185. It may result in resolution, or more commonly in suppuration. As a rule, it is developed during the first apyretic interval. *Hiccough* is a distressing complication which frequently occurs in severe cases, especially in those attended with jaundice. It is most common toward the end of a febrile paroxysm, and usually disappears after the termination of the paroxysm by crisis. *Bronchitis* of a moderate degree of intensity is a frequent complication which is developed, for the most part, during the febrile paroxysms, as a result of congestion of the bronchial mucous membrane, and disappears, or is greatly modified in degree, during the apyretic intervals. *Acute laryngitis*, with œdema, is an occasional complication. *Enlargement of the spleen* is so constant that it may be considered an essential feature of the disease, rather than a complication. In certain cases the enlargement persists for many weeks, and is attended with marked debility and anæmia. *Rupture of the spleen* has been reported by several authors, and *splenic abscess* has been noted in certain rare cases. The former accident is marked by suddenly developed pain and collapse, and is quickly fatal; the latter commonly gives rise to pyæmia, or may induce acute peritonitis or pleurisy, by discharging into the cavity of the abdomen or the left pleural cavity. Other complications which have been noted as events of rare occurrence are: hemorrhage from the stomach; metastatic abscesses of the lung; suppuration of the mesenteric glands; general peritonitis; thrombosis of veins, and cerebral hemorrhage. When pregnant women are attacked with relapsing fever, *abortion* is almost sure to occur; and in those cases in which menstruation occurs during the attack, it is usually profuse, and sometimes dangerously so. Among the sequelæ of the disease, we may mention as most prominent: diarrhœa, dysentery, anæmia, neuralgic pains, local palsies, keratitis, and inflammation of the deeper tissues of the eyeball, mental hebetude, mania, and in rare instances gangrene of the feet, nose, or ears, as a result of arterial thrombosis (Wilson).

Diagnosis.—The early diagnosis of relapsing fever is made easy by the discovery of Obermeier, and by the fact, now verified by numerous observers, that the spirillum peculiar to this disease is found in the blood during the entire period of pyrexia—including the relapses—and usually for a short time in advance of the febrile paroxysms. Without this test the diagnosis must always remain somewhat uncertain for some days, inasmuch as there are no pathognomonic symptoms marking the outset of the attack. The sudden termination of the initial paroxysms by crisis, and the relapse after an apyretic interval of five to twelve days, will, however, be sufficient to establish the diagnosis in typical cases; but, as in other specific febrile diseases, there are many atypical cases in which the diagnosis might remain uncertain if it depended upon the clinical history alone. This is especially true of the so-called "abortive form," in which there is but a single paroxysm, in that form which has been denominated bilious typhoid, and in cases in which the typical character of the pyrexia is masked by complications of one kind or another. In countries where severe forms of malarial fever prevail there can be no doubt that cases of relapsing fever, especially at the outset of an epidemic, before the prevalence of this disease has been generally recognized, are often ascribed to malarial poisoning, and fall under the denomination "remittent fever"—a term which in former years, and in the absence of precise knowledge, has been made to do duty in tabular statements of disease and mortality for more than one specific disease, *e.g.*, typhoid fever, yellow fever, relapsing fever. The investigations of Carter make it appear probable that relapsing fever is by no means a new disease in India, yet it has been only recognized during recent years, and the available records of an epidemic which prevailed in Bombay so recently as 1863–64–65 do not permit the author mentioned to decide positively whether the enormous mortality from "fever termed remittent" was in truth due to relapsing fever or to typhus, as was claimed by some of the local practitioners. The differential diagnosis between relapsing fever and true malarial remittent presents no serious difficulties, although there are many symptoms—such as headache, vomiting, epigastric tenderness, enlargement of the spleen, and jaundice—which are common to both diseases. The character of the pyretic movement, the sudden termination by crisis, the failure of quinine favorably to influence the course of the disease, the protracted apyretic interval, and the relapse, will suffice. But in addition to these facts relating to the clinical history, there are various circumstances relating to the epidemic prevalence of the disease which will aid greatly in its recognition. Thus, relapsing fever is transmitted from individual to individual by contagion, and is a disease of towns, and especially of the overcrowded portions of such towns where the poorer classes of the population are congregated under unfavorable sanitary conditions; whereas remittent fever is especially a disease of the country, the prevalence of which depends upon circumstances relating to locality, climate, and season, and not upon personal intercourse and social condition. As a rule, it may be said that a fatal epidemic disease which prevails among the crowded population of a large city is not remittent fever, whatever else it may be.