CHAPTER XV

PYREXIA

MICROBIC DISEASES

WHEN a patient is suffering from some general or constitutional derangement, he complains of a vague "feeling of illness" (*i.e.*, malaise), or of "weakness" (debility, asthenia). He feels "generally" ill, and perhaps looks ill, but may be unable to mention any localising symptom, such as pain in the side or palpitation. Now, the first thing to do in such circumstances is to ascertain whether he is feverish or not, because all such conditions may be divided into two large clinical groups: A. **Debility with pyrexia,** which includes the Acute Specific Fevers and disorders in which there exists some localised inflammation; and B. **Debility without pyrexia,** which includes the different forms of Anæmia and various toxic and nutritional disorders. The latter will be dealt with in Chapter XVI. In this chapter we are concerned solely with the various conditions attended by elevation of the body temperature.

§ 465. Definitions.—The term **Acute Specific Fever** (or Specific Febrile Disease) has been applied to those fevers which are due to a specific or special poison, introduced into the body from without, and which run a definite course. If the poison was contracted from a previous case, but without contact with the patient, it was said to be an *Infectious* disease (*e.g.*, scarlatina); if the disease was produced only by actual contact with a person suffering from the malady, it was called *Contagious* (*e.g.*, syphilis); but these terms have always been used somewhat loosely and indifferently, and it would be better not to attempt any such distinction but to speak of them collectively as *Infective.* It would be out of place to enter here into the question of the nature of this poison; but there is direct or inferential proof in all the acute specific fevers that it is of microbic or parasitic origin. At first the organisms themselves were supposed to be the active agents of these diseases, but now in most cases the *causa vera* of the pyrexia and other symptoms is known to be a toxin or toxins which are produced by the microbe. This branch of knowledge has made enormous advances during the last three quarters of a century (*cf.* §§ 519 *et seq.*).

Bacteriology is dealt with in Chapter XXI. The chief **clinical characteristics** which cause us to suspect a disease of being **microbic in origin** are:

1. The occurrence of the disease in question in an *epidemic* form—*i.e.*, in the form of an outbreak, or as a series of cases which suggest that the patients contracted the disease either from one another or from a common source, the infection being conveyed to them through the air, the water or other ingesta, or by the bite of an insect.

2. Two features are common to all infective diseases: (i) *Pyrexia* is present at some time during the course [1]; and (ii.) in many cases the disease runs a more or less *definite course*—definite onset, gradual increase (fastigium) to an acme, defervescence, gradual or sudden, followed by complete restoration to health, or death.

3. The constant presence in the blood, tissues or excretions of the patient of a *microbe* or *protozoon*, which is not there normally.

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[1] Some diseases have become so attenuated (*e.g.*, rubella and chicken-pox) that pyrexia may at times be absent, although most of the other clinical features are present.

The *pathological proof* that a particular microbe is causally related to the disease consists in applying certain experimental tests (see § 519).

4. The fact that the attack is more or less protective against subsequent infection.

Epidemic, Endemic, and Sporadic are terms by which it is usual to express the relative prevalence of infectious diseases. A disease is said to be *Epidemic* when a large number of cases arise by infection from a common source or from one another at one time, followed by an interval in which relatively few arise. Thus epidemics of measles, scarlet fever, and diphtheria arise in the Metropolis and elsewhere from time to time. A disease is said to be *Sporadic* when it occurs only in isolated cases. Thus we speak of a sporadic case of mumps when no other cases of it have been known to occur about the same time and in the same district. An *Endemic* disease is one which is constantly present in a certain district. Thus measles is endemic in London, malaria in Central Africa, and cholera in India.

PART A. SYMPTOMATOLOGY

§ **466. Pyrexia and Symptoms which may attend it.**—Pyrexia may in some instances be unattended by any symptoms, but in nearly all cases the patient whose temperature is elevated complains of feeling "chilly," or he may have shivering or rigors; or perhaps he feels "burning hot." Headache, restlessness, and vague pains in the limbs and back are also common symptoms, in addition to the malaise or weakness. His skin is hot and dry to the touch, his pulse and respiration are rapid, his appetite is bad, tongue furred, and bowels constipated, his urine scanty and high coloured: in young children vomiting and convulsions may herald a pyrexial illness. In severe cases of fever there is great prostration, considerable mental dulness, and there may be delirium, or the "typhoid state." By these symptoms we suspect the presence of pyrexia, and the suspicion is confirmed, and the degree of fever ascertained, by the clinical thermometer (see below). Infective diseases pass through various STAGES which have many features in common: in severe cases, and often in association with high temperatures, RIGORS, DELIRIUM, and the "TYPHOID STATE" may occur.

§ **467. Incubation and other Stages of Acute Specific Fevers.**—Particularly in epidemics, the infective or specific fevers conform to a common pattern and run a *definite course* (*e.g.*, measles). However, it must be remembered that the same organism may at times give rise to dissimilar diseases: *e.g.*, the same strain of hæmolytic streptococci may produce acute tonsillitis, scarlet-fever or puerperal fever in three different individuals.

It is a curious fact that a person does not develop the disease directly after he has been exposed to infection. The interval is called the stage of *incubation*. The patient is usually quite well during this stage, but there may be transient fever ("illness of infection") for a few hours after exposure. The incubation period varies in different diseases (Table XXIIA). During at least part of this time a healthy person who has been exposed to infection needs to be isolated ("placed in quarantine"), to see if he will develop the disease. A glance at the first column in the table will show that a period of THREE WEEKS will cover the incubation of all the

TABLE XXIIA.—SHOWING INCUBATION, DATE OF ERUPTION, AND DURATION OF INFECTION OF THE PRINCIPAL INFECTIVE DISORDERS.

DISEASE.	INCUBATION PERIOD.	DAY OF DISEASE ON WHICH RASH APPEARS.	INFECTIOUS PERIOD, or period during which the *patient* need be isolated.
Varicella.	10 to 21 days, average 14.	The rash is usually the 1st symptom noticed.	Till all scabs have separated, or 14 days, whichever is the shorter.
Scarlet Fever.	2 to 4 days, average 2½.	**1st** or **2nd**.	From commencement of illness till an indeterminate date, which varies in different cases. Average 4 weeks. Rhinorrhœa, and possibly otorrhœa, may retain infection for 6 months or more.
Small-pox.	12 days.	**3rd.**	From commencement till not a trace left of scabs or desquamation. Most virulent during vesiculation, pustulation, and scabbing. 3 to 8 weeks.
Measles.	7 to 14 days, average 10.	**4th.**	*Great* in early period *before* rash out Till rash has faded : usually 1 week after rash appears.
Rubella.	14 to 19 days.	**1st** to **4th.**	5 to 6 days from commencement.
Typhus.	12 to 14 days.	**4th** or **5th.**	Probably 3 to 4 weeks.
Typhoid and Paratyphoid.	8 to 21 days, usually 10 to 14.	Average **2nd week.**	Several weeks after pyrexia has ceased. "Carriers" may retain their infection for many years.
Dengue.	2 to 6 days.	Initial rash 1st day. Terminal rash 4th.	
Diphtheria.	1 to 6 days, usually 2 to 4.	None.	Until 3 swabs from nose and throat, and any ear discharge, fail to grow the organism.

The period of incubation of the other microbic disorders so far as we know is given approximately below. This is important, as the duration of quarantine depends on the period of incubation. In cases with a relatively long incubation period, such as mumps, chickenpox, measles and rubella, it is not necessary to isolate contacts for the first week after exposure.

Malaria, 12 hours and upwards.
Erysipelas, 1 to 7 days.
Cerebro-spinal fever, 1 to 3 days.
Influenza, 1 to 3 days.
Pneumonia, 1 to 3 days.
Anthrax, 2 or 3 days.
Gonorrhœa, 2 or 3 days.
Plague, 3 to 7 days.
Glanders, 3 to 18 days.
Tetanus, usually 3 to 21 days.
Mumps, 3 to 28 days (average 17).
Relapsing fever, 4 to 10 days.
Glandular fever, 5 to 12 days.
Whooping-cough, 7 to 14 days.
Malta fever, about 9 days.
Cholera, under 14 days.
Yellow fever, under 18 days.
Syphilis, 15 to 25 days.
Hydrophobia, 40 days or more.
Tuberculosis, probably some weeks.
Infective Hepatitis, 17 to 35 days.

eruptive fevers. The actual *invasion* or development of the symptoms of the disease is usually more or less abrupt, except in typhoid fever, whooping-cough, and sometimes measles. *Prodromal symptoms* at the onset of the disease proper may indicate that a disease is commencing, but not permit an exact diagnosis. An *eruption* appears upon the skin within the next four days (except in typhoid fever) in those diseases which develop a rash, and which are called on that account the EXANTHEMATA. (Enanthemata are the lesions seen on the mucous membranes). The fever and other symptoms go on increasing until the *acme* is reached. *Remissions* indicate temporary diminution of symptoms, and *recrudescences* aggravation of the disease. Finally, the last stage—the stage of *defervescence* supervenes, and gradually the patient convalesces unless a *relapse* occurs.

§ **468. Rigors** often indicate the sudden onset of pyrexia. A rigor is an attack of shivering attended by elevation of temperature and great acceleration of pulse rate, rapidly followed (usually) by sweating and a fall in the temperature. Such an attack may vary widely in severity from a simple feeling of "chilliness down the back, like cold water," to a shaking of the whole body, so that the patient shakes the bed beneath him. Severe rigors occur typically and *regularly* in the course of malaria, also at frequent but *irregular* intervals throughout the course of septicæmia and pyæmia. In childhood, rigors are often replaced by convulsions.

1. First, ascertain that the shivering is not of purely nervous origin, because a trembling much resembling a rigor may occur as the result of pure fright or from slighter causes in nervous people.

2. Procure, if possible, a series of temperature records, because rigors occur in association with several conditions which can only be differentiated in this way.

Causes.—The causes of rigors are very numerous, but they are best approached in a general way as follows:

(*a*) Coming on in a person *previously healthy*, one should always suspect the advent of some acute illness. In children the eruptive fevers are sometimes ushered in with either convulsions or rigors. In adults, septicæmia, pneumonia, pyæmia, peritonitis, the eruptive fevers, malaria or influenza may be suspected.

(*b*) *Septic Infection.*—When rigors *supervene in the course of an illness* of any kind, abscess or pent-up pus in some position should always be the first thing thought of. *Before the days of the thermometer the doctor used to rely upon shivering and sweating as an infallible indication of the formation of pus.* For instance, in a case of pleurisy with an effusion, which has hitherto been serous, the occurrence of shivering indicates that the contents of the chest have become purulent (empyema). Similarly, a rigor occurring with otitis media suggests extension to the mastoid cells, or may point to lateral sinus thrombosis. Rigors occurring in a case of cardio-valvular disease indicate the occurrence of infected emboli, or the supervention of malignant endocarditis. Shiverings and sweatings may

occur during the course of tuberculosis and many other conditions mentioned under the Causes of Intermitting Pyrexia (§ 509). If no obvious cause for an attack of shivering appears, we may suspect some internal suppuration, such as appendicitis, or ulceration in some part of the urinary, biliary, or alimentary canals. If the rigor is due to a collection of pus, there will be found a definite leucocytosis.

(*c*) The *passing of a catheter* is often followed by a severe rigor, and sometimes the temperature goes suddenly up to 105° or 106° F., and as suddenly falls again. Sudden obstruction in the biliary or renal passages is often attended by rigors, followed by a feeling of heat and sweating, and the temperature may go up to 105° F ; these examples are probably due to bacterial invasion through minute abrasions. A rigor, too, may be set up by the intravenous injection of some chemical substance (*e.g.*, neoarsphenamine) or a therapeutic serum, such as diphtheria antitoxin, or after blood transfusion. Therapeutic use is made of this by injecting T.A.B. vaccine, sulphur and foreign proteins to produce pyrexia.

(*d*) *Neurasthenic* and *hysterical* patients often have shivering attacks, without pyrexia. An attack of shivering may also constitute a symptom of *vaso-motor disorder*. Thus it is a symptom of the reaction which follows, and often forms part of the " flush-storms " chiefly met with at the climacteric, without elevation of temperature.

(*e*) *Cholecystitis* may cause short attacks of shivering without pyrexia.

The *Prognosis* and *Treatment* belong to the several causal conditions, but in any case the patient should be kept warm in bed with a hot-water bottle to his feet : aspirin, bromide or morphia will soothe the nervous system.

§ **469. Delirium,** or incoherence of thought, is another symptom which frequently accompanies pyrexia. The older authors used to describe three varieties of delirium : (1) Delirium ferox, in which the patient is very violent and maniacal ; (2) typhoid delirium, in which the patient lies on his back muttering, with subsultus tendinum ; (3) delirium tremens, in which there is great sleeplessness, hallucinations and tremors, not necessarily due to alcohol. The nature of the delirium is not always constant in any given disease. For clinical purposes, the *causes of delirium* may be divided into two groups—FEBRILE and NON-FEBRILE. It is important, therefore, to take the temperature at once in every case of delirium. Alcoholic subjects and children, especially if neurotic, are predisposed to delirium when attacked with only slight fever.

a. Febrile Delirium may arise under four circumstances :

1. ACUTE LOCAL INFLAMMATION in some part of the body, such as pneumonia. It is advisable, therefore, to examine all the organs.

2. DISEASES OF THE BRAIN (Encephalitis), or OF THE MENINGES, such as tuberculous meningitis. The latter is accompanied by headache, vomiting, retraction of the head, intolerance of light, and paralysis of cranial nerves.

3. All the ACUTE SPECIFIC FEVERS are liable to be accompanied by

delirium. The tendency, however, varies considerably, though it is usually directly related to the height of the temperature and the nervous stability of the individual. It is important to bear this in mind, because, as a prognostic indication, delirium occurring in a disease like measles or acute rheumatism, in which it is rare, has a much more serious meaning than when it occurs in pneumonia, for instance, where it is more usual (see Table XXIII).

4. Certain cases of DELIRIUM TREMENS of a SEVERE KIND are accompanied by an elevation of temperature. Indeed, the prognosis in this affection may largely depend upon the temperature. We must be careful to exclude local inflammations in such cases, for they are apt to come on very insidiously. In the worst cases of ACUTE DELIRIOUS MANIA also the temperature may be considerably elevated (see *b* 6, below).

TABLE XXIII.—SHOWING THE RELATIVE FREQUENCY OF DELIRIUM IN THE VARIOUS INFECTIVE FEVERS.

Frequent in—	*Occasional in—*	*Rare in—*
Confluent Small-pox	Remittent Fever	Influenza
Typhus	Yellow Fever	Mumps
Lobar Pneumonia	Small-pox (modified)	Dysentery
Typhoid Fever (after 1st week)	Measles	Cholera
Meningitis	Relapsing Fever	Acute Rheumatism
Encephalitis	Scarlet Fever	Diphtheria
Erysipelas	Malaria	Rubella
Plague		Varicella
Malignant Endocarditis		
Septicæmia		

b. Non-febrile Delirium may arise under six conditions:

1. DELIRIUM TREMENS (Delirium e Potu) is, as just mentioned, usually unattended by a rise of temperature, and is undoubtedly the commonest cause of non-febrile delirium. It is recognised by the history, the muscular tremors, sleeplessness, and the characteristic hallucinations.

2. CHRONIC RENAL DISEASE, and especially chronic interstitial nephritis, gives rise in its advanced stages to a muttering delirium or incoherence, which thus becomes a symptom of the gravest import, and generally heralds coma and death. The delirium is due to uræmia, and occurs in other renal diseases.

3. POST-FEBRILE DELIRIUM (Post-Febrile Mania).—During the convalescence of pneumonia and other exhausting diseases, especially such as run a protracted course, and have been attended with a high degree of pyrexia, mental symptoms may develop. These symptoms, which usually make their appearance without any warning, give great uneasiness to the friends. Nevertheless, by means of good food, tonics, and fresh air, such mental symptoms will entirely disappear. Before venturing on a prognosis, however, inquiry should always be made for any family history of mental disease, for a hereditary tendency greatly

lessens the chance of recovery. The condition is recognised by the history of the previous malady. Sometimes the mental derangement consists simply of loss of memory, especially for the names of persons and things, but more often the mind "wanders" and there are delusions.

4. Reflex Delirium.—Trousseau mentioned cases of children with intestinal worms who had delirium, and described several cases which were caused by tickling the soles of the feet. The transient delirium connected with the severe pain of childbirth is possibly of the same nature.

5. Deliriant Drugs should always be suspected when delirium develops suddenly in a person in health, especially children in the country, in the absence of any of the foregoing causes. The most important are belladonna, hyoscyamus, hyoscine, cannabis indica, stramonium, and others of the solanaceæ, antipyrin, camphor in rare cases, œnanthe crocata, cocculus indicus (with which beer used to be adulterated), poisonous fungi, and sometimes salicylic acid and its salts, especially if adulterated, when given in large doses. Delirium may ensue when a patient is recovering from the effects of poisonous gases. Morphia in some people invariably produces delirium.

6. Acute Mania sometimes comes on very suddenly, and only differs from "delirium ferox" or maniacal delirium in not being referable to some bodily disease or toxæmia. Delirium occurs in the advanced stage of many mental diseases. We identify these conditions by (1) the temperature is not as a rule elevated; (2) it affects a person previously in good health; and (3) the exclusion of any organic lesion by a careful examination of the nervous and other systems. As regards the temperature there is an exception in the rare and serious condition known as "acute delirious mania," in which marked pyrexia is present (and see § 893).

Prognosis.—Febrile delirium is not necessarily a grave symptom when it is associated with a *disease in which its occurrence is usual*—*e.g.*, pneumonia—and especially when the cause is only temporary; but its presence adds considerably to the gravity of a case if the occurrence of delirium is unusual (see Table XXIII), for it indicates a very severe attack, or the occurrence of complications, or both. *Non-febrile* delirium is a grave symptom in chronic renal disease. The prognosis is serious as regards mental recovery in all patients who have a hereditary tendency to mental disorder. In acute mania the prognosis is grave.

Treatment.—It is necessary to provide a nurse or attendant, and restraint may be called for. *Remedial Treatment.*—An ice-bag to the head for an intracranial inflammation; good nourishing food for mania and post-febrile delirium; a brisk purge for uræmia. *Symptomatic treatment* consists of the administration of sedatives, such as somnifaine, hexobarbitone (evipan), nembutal, chloral, calcibronat, the bromides and paraldehyde (injected). Opium and morphia require caution, especially if there is liver disease. In delirium tremens, it is most helpful in some cases by procuring sleep, but in others it only aggravates the maniacal condition. Periodical sponging with cold or ice-cold water often has a

steadying effect. In post-febrile delirium and other conditions where the brain is suffering from malnutrition, opium in small doses is a most valuable remedy, and may be given without fear if the liver and kidneys are healthy.

§ 470. The Typhoid State may be described as a condition of semi-consciousness or unconsciousness (coma) attended by elevation of temperature and muttering delirium, due to toxæmia. The name of this condition was derived from its frequent association with typhus, but it is met in many other fevers. With reference to the question of pyrexia, it should be stated that the comatose condition, due to renal disease (uræmia), advanced liver disease (cholæmia), and various poisons (particularly opium), has sometimes been described as the typhoid state, but these are apyrexial conditions, and it is preferable to include only those with pyrexia. In short, the typhoid state corresponds clinically to a state of coma *plus* pyrexia and muttering delirium.

Symptoms.—The typhoid state is always secondary to some febrile condition, in the course of which it arises: the height of the temperature and its persistence depend chiefly upon the nature of the primary disease. The first *mental symptom* usually noticed is sleeplessness with delirium, generally of the muttering variety, but by and by stupor supervenes, which gradually deepens. The mental faculties are obscured, but the unconsciousness is not always so complete as one would imagine. The profound disturbance of the nervous system is evidenced by prostration, restlessness, subsultus tendinum (muscular twitchings), floccitatio or carphology (picking at the bedclothes), unconscious evacuation of bladder and bowels, and, in extreme cases, convulsions. The *physical condition* is indicated by the pale and often cyanosed colour: the tongue is dry, brown, furred and tremulous: and sordes collects upon the lips and teeth. The pulse is rapid, feeble, and irregular, and the heart-sounds distant. The respiration is usually rapid, but shallow. The pupils are dilated, but the patient does not see. Nevertheless, he looks about at imaginary objects—"coma vigil." Dysphagia, diarrhœa and stertorous breathing are very serious indications of profound stupor.

Diagnosis.—(1) The "*typhoid state*," as above mentioned, may be distinguished from *coma* by the presence of pyrexia, and the absence of evidences of renal or liver disease, apoplexy, or other cause of the coma. (2) Certain acute *inflammations of the brain and meninges* are attended by pyrexia, and offer considerable difficulty—particularly with tuberculous meningitis (§ 727). The presence of papillœdema, head retraction, paralysis of the cranial nerves on the one hand, and the signs of the primary malady which has produced the typhoid condition on the other, are evidences upon which we can rely in many instances.

Causes.—Patients with an alcoholic history or with chronic nephritis are predisposed to the development of the typhoid state.

1. The Acute Infectious Fevers are the commonest causes, and particularly typhoid and typhus fevers. The Typhoid State occurs as an ordinary symptom of a grave attack in the course of these two diseases

and in some others (see Table XXIV). In another group of diseases it occurs only occasionally, and in others it is rare. If it arises in either of these latter groups, it indicates either (1) a very severe variety of the disease, or (2) some serious complications; and, in any case, that the patient is likely to die.

2. Certain other INFLAMMATORY or INFECTIVE DISORDERS with local manifestations may be attended by the typhoid state, such as acute lobar pneumonia, acute pulmonary tuberculosis, ulcerative endocarditis, acute meningitis, and encephalitis lethargica.

3. Certain acute IDIOPATHIC DISEASES may, in rare instances, be attended by the typhoid state, such as acute gout and very intense forms of delirium tremens. It is extremely rare in acute rheumatism, unless accompanied by peri- or endo-carditis.

TABLE XXIV.—RELATIVE FREQUENCY OF THE TYPHOID STATE IN DIFFERENT DISEASES. ALCOHOLIC SUBJECTS AND PATIENTS WITH CHRONIC NEPHRITIS ARE PREDISPOSED TO THE TYPHOID STATE.

Frequently met with, especially towards the end, in—	*Occasionally met with in—*	*Rare in—*
Typhoid (Enteric) Fever	Scarlet Fever	Cholera
Typhus	Measles with broncho-pneumonia	Variola (modified)
Confluent Small-pox (unmodified)	Cerebro-Spinal Fever	Dysentery
Erysipelas (severe)	Anthrax (Internal)	Malaria
Septicæmia (including Malignant Endocarditis and Osteomyelitis)	Remittent Fever	Relapsing Fever
Meningitis—especially tuberculous	Undulant (Malta) Fever	Acute Rheumatism
Encephalitis, especially E. lethargica		
Lobar Pneumonia		
Acute Miliary Tuberculosis		
Acute Glanders		
Acute Anthrax		
Remittent Fever		
Cerebral and Hæmorrhagic Malaria		
Yellow Fever		
Plague		

Diagnosis of the Cause.—The clinical investigation should be conducted on the same lines as in cases of pyrexia. Is it due to *local* or *generalised* inflammation? First, every organ in the body should be thoroughly examined so as to exclude local disorders. Secondly, we proceed to the diagnosis of the general fevers from one another, and, if possible, obtain a series of temperature records. In cases where the cause of the typhoid condition is obscure, septicæmia, especially with endocardial involvement, should always be suspected, and its origin carefully sought.

Prognosis.—The typhoid state, like delirium, has a less serious import in diseases such as typhoid fever, in which it is frequently met with. But it is always a grave condition, and indicates profound cerebral and general toxæmia. Occurring in the course of scarlet fever, erysipelas, or measles, it often indicates pulmonary or cardiac complications, and is proportionately serious. As regards symptoms, the profundity of the stupor is a measure of the intensity of the toxæmia, and dysphagia, uncontrolled diarrhœa, stertor, or convulsions are generally lethal signs.

The Treatment of a condition such as this arising in the course of so many diseases must necessarily vary, and our first duty is *to ascertain what disease is in operation.* The toxæmia is partly bacterial and partly the result of disordered metabolism and elimination. The indications are (1) to eliminate the toxins by diuretics, diaphoretics, and aperients; and (2) to stimulate and support the patient's strength by nutriment and stimulants. The use of alcohol in the treatment of fevers as in other branches of medicine has of late years considerably declined. As regards symptomatic treatment, if the delirium be very violent, sedatives such as chloral or bromide, in large doses, even up to 40 grains of each, are indicated. Opium should be avoided, as it prevents the elimination of the poison. For the treatment of Hyperpyrexia, see § 524.

PART B. PHYSICAL EXAMINATION

The clinical investigation of pyrexial disorders consists of (1) CLINICAL THERMOMETRY; (2) AN EXAMINATION OF THE ORGANS; and (3) BACTERIOLOGICAL INVESTIGATION.

§ 471. Clinical Thermometry and Types of Pyrexia.—The temperature is ascertained by means of the clinical thermometer: readings are usually taken in the mouth or the axilla. Mouth temperatures must be taken before meals, for food, drinks or mouth breathing cause false readings: a half-minute thermometer must be kept in the mouth for at least one minute, and in the axilla for ten minutes, to give accurate records. The temperature may also be taken in the rectum, where it may be ½° to 1° higher than in the mouth. In children the thermometer may be held in the groin, the thigh being flexed to the abdomen for the purpose. The normal temperature of the body varies between about 97·8° and 99° F.; average 98·4° F. It is lowest about 4 A.M. and highest about 8 P.M. It tends to be lower in old age and higher in infancy, especially after an attack of crying. The temperature is often subnormal after a loss of blood, during convalescence, in cardiac failure, and in all states of collapse. The latter is sometimes the direct result of toxæmia.

A temperature of 100° is regarded as slight fever.
„ „ 102° „ moderate fever.
„ „ 104° „ high fever.
„ „ 105° and upwards is regarded as hyperpyrexia.

THE TEMPERATURE CHART.—*Very little information can be derived from a single observation of a patient's temperature, and in all cases of pyrexia one must know the course which it runs from day to day and hour to hour.* In most cases of fever it is hardly possible to come to any conclusion without seeing a "chart" of the case—*i.e.*, a series of records. In all cases of pyrexia the temperature should be taken **and recorded** morning and evening; and in all acute cases it should be taken four-hourly. In cases of suspected tuberculosis and some other affections it may be advisable to obtain hourly records throughout the day, otherwise slight eleva-

tions may be missed. The pulse, respiration and blood pressure should also be observed, especially in abdominal inflammations, extensive broncho-pneumonia, and after severe attacks of diphtheria, where the temperature alone does not give us a true idea of the amount of mischief which is going on. In broncho-pneumonia the rapidity of respiration is often the most reliable indication. The onset of pyrexia may be gradual, as in typhoid fever or diphtheria, but more often it is sudden and may be accompanied by a rigor, as is sometimes seen in pneumonia or small-pox. Remember that the *onset is apt to be very sudden* in scarlatina, erysipelas and small-pox ; it is *gradual* (taking perhaps two or three days) in measles, typhoid fever and pertussis. During the next few days the temperature

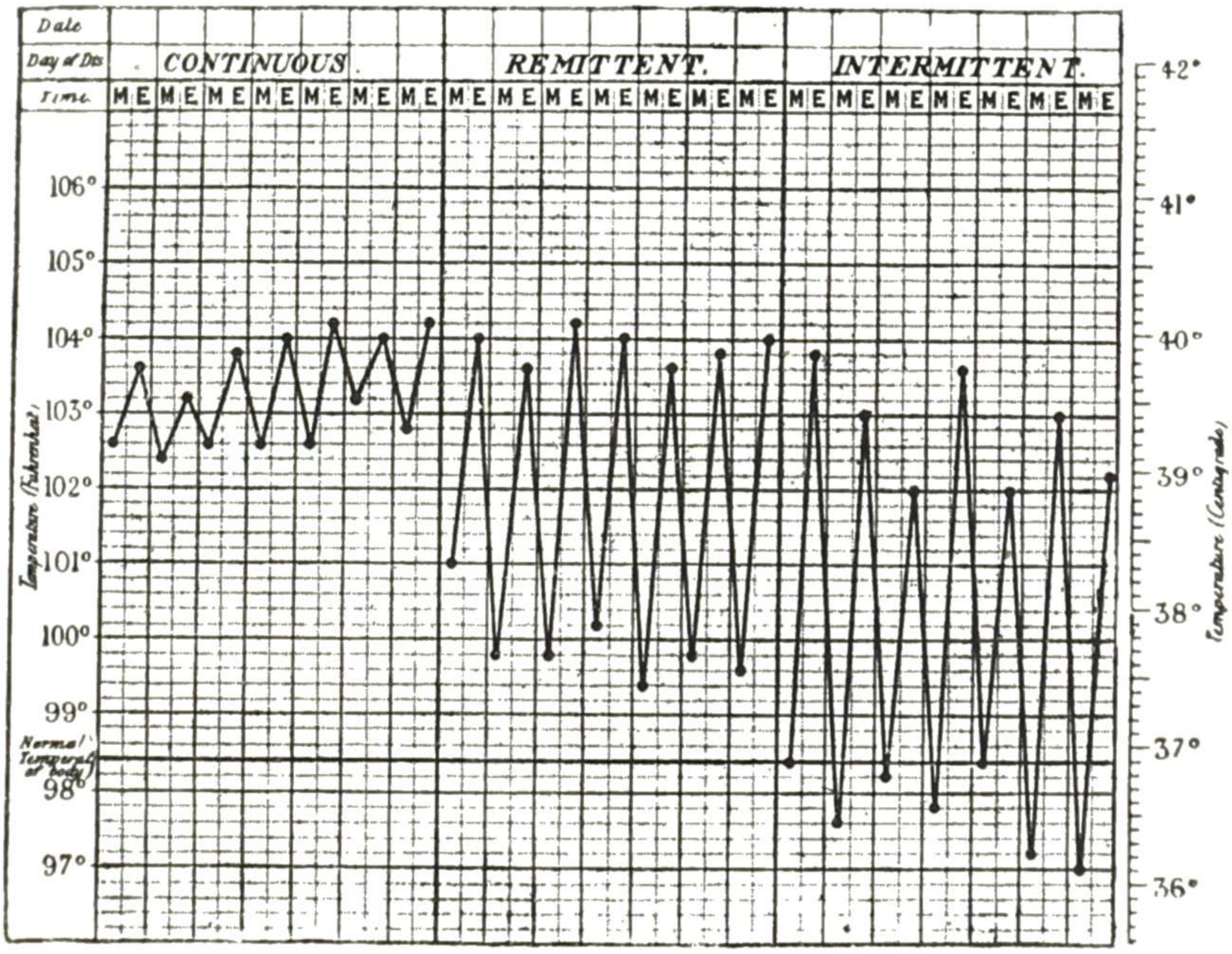

FIG. 110.—TYPES OF PYREXIA.—Continuous pyrexia showing only the normal variations in the morning and evening. Remittent pyrexia showing a drop of several degrees each day. Intermittent pyrexia where the temperature comes down to normal at some time every day.

generally increases until the *acme* is reached. The termination may be gradual, when it is said to terminate by *lysis*, as in typhoid ; or pyrexia may terminate suddenly by *crisis*, as in some cases of lobar pneumonia and relapsing fever.

Types of Pyrexia.—In the absence of any eruption, the COURSE OF THE TEMPERATURE is our best, and may be our only, guide. It is usual to describe three types of pyrexia, according to the course which the temperature pursues from day to day (Fig. 110) ; (i.) *Continued or Continuous Fever*, where the temperature remains elevated for a considerable period, and where the *diurnal variation often does not exceed the normal diurnal variation*—viz., one, or at most one and a half degrees ; (ii.) *Remittent Pyrexia*, when the diurnal variation is greater than the normal diurnal

variation, but where the temperature never comes down quite to normal; (iii.) *Intermittent Pyrexia*, where the temperature at some time of the day is normal or subnormal, and at another time of the day, usually in the evening, it is raised one, two, or more degrees. But for clinical purposes the two latter may be grouped together, and thus we have TWO GROUPS of fevers—one in which the pyrexia is practically CONTINUOUS, and another in which there is a remission, or INTERMISSION, once or oftener during the twenty-four hours, usually in the morning.

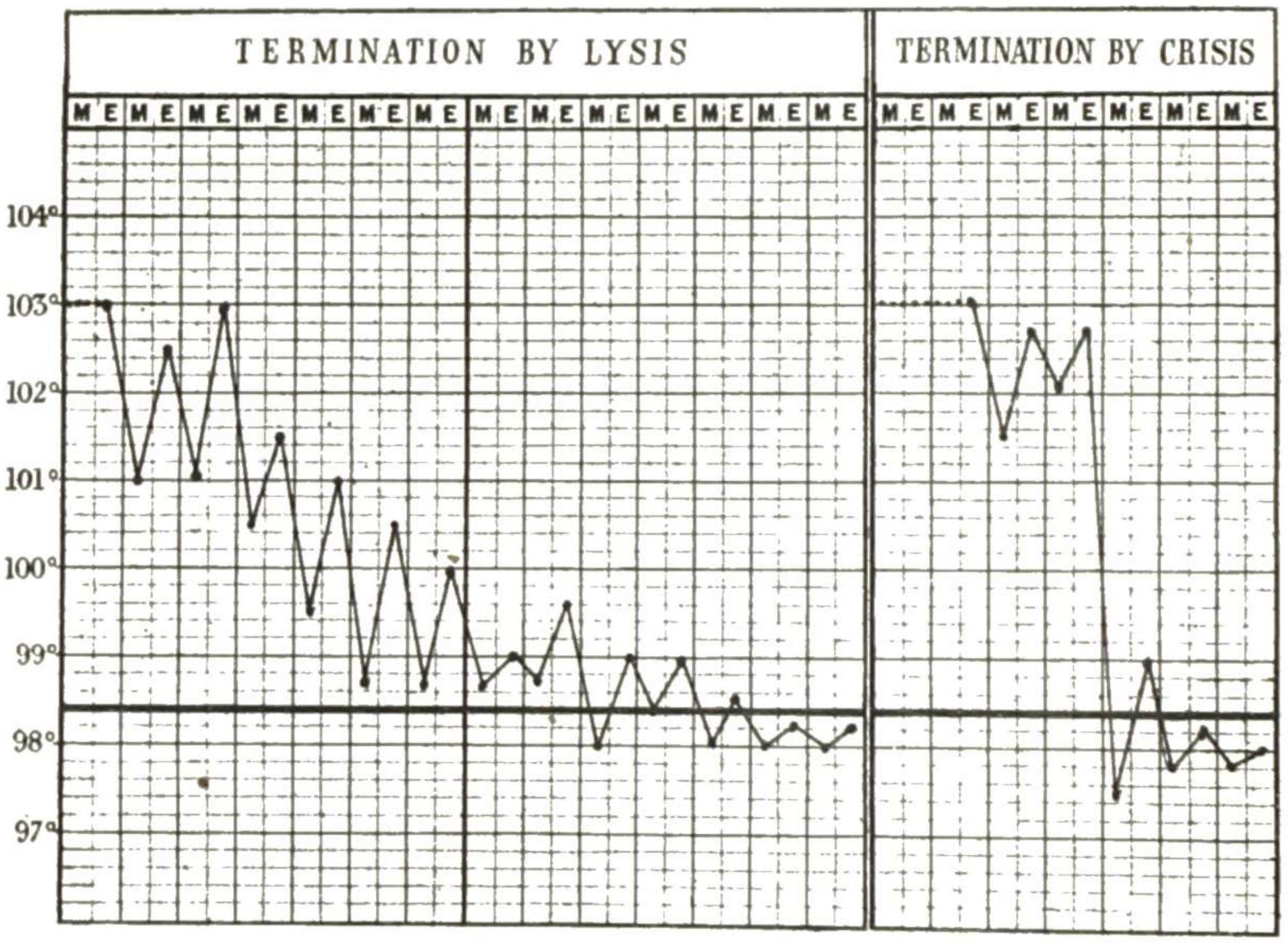

FIG. 111.—TERMINATION OF PYREXIA BY LYSIS AND CRISIS.

The following are useful facts to remember regarding temperatures: (i.) The sudden advent of high fever in a previously healthy person without other symptoms indicates, in England, Scarlet Fever, Influenza, Small-pox, or Erysipelas, and sometimes Pneumonia. A very gradual advent is suggestive of Typhoid Fever. (ii.) A fresh rise after the temperature has begun to fall indicates a complication or a relapse. (iii.) A sudden fall in the course of a fever (especially Typhoid Fever) may indicate internal hæmorrhage, perforation of one of the viscera, or profuse diarrhœa. (iv.) A considerable rise in diseases usually non-febrile, such as tetanus, delirium tremens, cholera, cancer, epilepsy, apoplexy, etc., generally indicates a fatal termination.

§ 472. Subnormal Temperature.—The temperature of the surface of the body, as indicated in the mouth or axilla, is rarely more than one or two degrees below normal. When it is below 96° the condition usually amounts to collapse. Subnormal temperature is not so important, for purposes of diagnosis, as elevation of temperature; but in the first four instances given below it may aid us in their differentiation. Subnormal temperature adds to the gravity of the prognosis in most wasting disorders. With regard to treatment, temperature readings below the normal are indications for the administration of stimulants, nourishment, and the application of external warmth.

Causes.—1. Subnormal temperature as an indication of *lowered vitality* occurs in normal circumstances in the aged, in whom the temperature is habitually several fractions of a degree below normal.

2. The temperature drops suddenly in *internal hæmorrhage* and in *abdominal rupture* or *perforation*: rupture of an abdominal cyst, traumatic rupture of the liver, spleen or kidney, or perforation of a peptic ulcer or of an ulcer of the bowel are usually attended by other and more distinctive signs (§ 243). In typhoid fever this sudden fall may be the only indication of these serious complications.

3. In all severe *abdominal inflammations* prostration and collapse are marked features, and the temperature may in some cases be subnormal, although there may be considerable constitutional disturbance, as shown by the prostration, and the rapid pulse (§ 239).

4. Subnormal temperature occurs in several other disorders in which it is not of much diagnostic significance, because we depend upon other signs for their identification. Thus, the temperature of the body is lowered (i.) when there is an excessive withdrawal of heat from the body, as in cases of inanition or exposure combined with privation, or with extensive weeping skin eruptions; or when large quantities of fluid are evacuated, as in severe diarrhœa or cholera (when the temperature may be 90° in axilla, though 105° in rectum); (ii.) in states of inanition or cachexia—*e.g.*, during convalescence from fevers, Addison's disease, cancer (especially of the alimentary canal), diabetes, and chronic mental disorders; (iii.) when there is deficient oxygenation, as in cases of congenital heart disease, cardiac failure, alcoholism, jaundice, uræmia, and myxœdema; (iv.) in some diseases of the central nervous system, such as tuberculous meningitis, the onset of cerebral hæmorrhage, or cerebral tumour; and (v.) in poisoning by phosphorus, morphia, phenol, and other drugs.

5. In all states of COLLAPSE the temperature is considerably lowered (2° or more). Indeed, this is one of the chief means by which it may be distinguished from syncope.

§ **473. Examination of Organs.**—All the viscera must be carefully examined in accordance with the Scheme of Case-taking, pp. 6 and 7, so that local causes for the pyrexia may be excluded. Examination of the urine or the stools may reveal an unsuspected cause of pyrexia. For *clinical* purposes there are two large groups of causes of pyrexia: (*a*) **local inflammation**: such as pleurisy, appendicitis, abscess of the liver, etc., and (*b*) **general bacteræmic** or **toxæmic conditions,** like scarlet fever, rheumatic fever, and streptococcal or coli infection.

If any local inflammation is found, turn to the chapter dealing with the disease of that part. But it must still be remembered that some constitutional disease (*e.g.*, some specific fever) *may* be present, of which the local disease is a complication. Thus pneumonia, which would be discovered in the course of our examination, is a frequent complication of typhoid fever; and endocarditis of rheumatic fever. There are two features which may lead us to suspect a combination of disorders such as this: (1) The signs and symptoms of the local disorder may be of an aberrant type (*e.g.*, see Aberrant Types of Pneumonia, § 122); and (2) the constitutional disturbance presented by the patient would be greater in degree or different in kind than would accompany the local disease if it were the only disease present.

§ **474. The Examination of the Blood** often affords most valuable information, and it may be useful to make a complete blood-count or stain a film (§§ 530 and 531), to take blood for the purpose of culture or to determine the Widal and Wassermann reactions (§§ 922 and 924). In certain cases the sedimentation rate test (§ 927) is also useful.

PART C. THE DIAGNOSIS, PROGNOSIS, AND TREATMENT OF PYREXIAL DISORDERS

§ 475. Routine Procedure and Classification.—In cases of pyrexia we must investigate, as in other cases, three points:

First, THE LEADING SYMPTOM complained of by the patient will be one or more of those mentioned in §466.

Secondly, THE HISTORY OF THE ILLNESS. The *date* when the symptoms commenced—*i.e.*, the PRECISE DURATION OF THE ILLNESS—is a most important matter. A few of the fevers—*e.g.*, typhoid fever and diphtheria—commence insidiously; but the majority are ushered in suddenly, very often with an attack of shivering (a rigor). Throughout the entire course of every case of fever the physician should have constantly in mind the "day of the disease,"[1] so that he may know what events to expect at that particular period of the case. In typhoid fever, for instance, on the fourteenth day, or a little later, the diurnal range of the temperature should commence to be more marked, and during the next few days special care should be exercised to avoid hæmorrhage or perforation.

Thirdly, THE EXAMINATION OF THE PATIENT comprises three important matters: (1) Physical examination; (2) is there, or has there been, an eruption? and (3) the temperature and its course.

(1) EVERY ORGAN must be systematically examined (Scheme of Case-taking, pp. 6 and 7), and as carefully and thoroughly as the patient's condition will allow, in order that we may DETECT OR EXCLUDE ANY LOCAL DISEASE. This is important, because all cases of pyrexia are associated with or due to some **local inflammatory disease,** or some **generalised febrile disorder** (*e.g.*, **typhoid fever**), or both.

(2) WHETHER THERE IS OR HAS BEEN ANY ERUPTION is the next question. The first of the groups (*vide infra*) into which all fevers may be divided comprises those in which a rash distinctive of the disease appears within the first four days (with one exception) after the illness. The day on which it appears in each disease should always be in mind (Table XXIIA).

(3) THE TEMPERATURE **and its course** is the next thing to investigate; and it is of the greatest importance to obtain a CHART or succession of readings, after the manner described in § 471. The DURATION of the fever is of assistance in diagnosis, especially when it has lasted longer than two or three weeks.[2]

The **classification** of pyrexial disorders may conveniently be based upon

[1] The fourth day of a disease is the third day *after* its commencement. Thus the eruption of measles appears on the fourth day, and, supposing the patient were taken ill on a Monday, the eruption would appear on Thursday.

[2] Excluding diphtheria and the exanthemata, it is found that the majority of short fevers, of a few days' duration, are due to "common colds," "rheumatism," "constipation," and "influenza." "Colds," including bronchitis, influenza, tonsillitis and pharyngitis, 4,164; acute appendicitis, 1,504; acute arthritis, 1,016; salpingitis, 871; pneumonia, 803; lymphangitis, 365; sinusitis, 259; erysipelas, 241; poliomyelitis, 227.—R. C. Cabot, "Differential Diagnosis." London, 1919.

the results of our examination—namely, the eruption, if present, and the course of the temperature.

GROUP I.—ACUTE EXANTHEMATA or ERUPTIVE FEVERS—*i.e.*, fevers which are characterised by AN ERUPTION (*i.e.*, a RASH) distinctive of each disease appearing on one of the first four days of the illness (§ 476).

GROUP II.—CONTINUED FEVERS—*i.e.*, fevers in which the temperature runs a more or less continuous course, and which present NO ERUPTION during the first four days (§ 492).

GROUP III.—INTERMITTENT FEVERS—*i.e.*, fevers in which the temperature runs an intermittent (or remittent) course, and which present NO ERUPTION (§ 509).

If the physical examination reveals signs of disease of some particular organ, reference should be made to § 473, and to the chapter on diseases of that organ.

GROUP I. THE ACUTE EXANTHEMATA OR ERUPTIVE FEVERS

In all the diseases in this group the onset of the pyrexia is more or less abrupt, and in the majority a well-marked GENERAL ERUPTION appears during the *first four days* of the illness.[1] The course of the pyrexia varies considerably in the disorders in this group.

Common.		*Rare.*	
I. Chicken-pox (first day) ..	§ 476	VIII. Dengue (first day) ..	§ 483
II. Scarlet fever (second day)	§ 477	IX. Classical Typhus (fourth or fifth day)	§ 484
III. Erysipelas (second day) ..	§ 478	X. Rocky Mountain fever	§ 485
IV. Small-pox (third day) ..	§ 479	XI. Scrub typhus (rash fifth to seventh day)	§ 486
V. Measles (fourth day) ..	§ 481	XII. Q Fever	§ 487
VI. Rubella (first to fourth day)	§ 482	XIII. Trench Fever	§ 488
VII. Typhoid fever (usually eighth to tenth day), influenza, cerebro-spinal meningitis, plague, and other members of Group II, occasionally present early rashes.	§ 493	XIV. Rickettsial Pox	§ 489
		XV. Anthrax	§ 490
		XVI. Acute glanders	§ 491

In each of the acute exanthemata the ERUPTION has special and DISTINCTIVE CHARACTERS, which, together with the DAY OF THE DISEASE on which the eruption appears, may enable one to differentiate the members of this group from one another. SCARLET FEVER may be regarded as the type, but it will be convenient to take them in the order in which the eruption appears. TYPHUS is hardly ever seen, and DENGUE is not met with in England. ANTHRAX and GLANDERS are, like hydrophobia, derived from animals.

Some DRUGS IN COMMON USE may give rashes and pyrexia ("drug fever"): common examples are the sulphonamides and the barbiturates which at times can mimic the eruptive fevers closely.

§ 476. I. Varicella (synonym: **Chicken-Pox**) may be defined as an

[1] Incomplete forms (formes frustes), in which the rash or other characteristic symptoms are absent, may occur especially during an epidemic.

acute contagious disease, manifested by an eruption of successive crops of limpid vesicles, usually accompanied by slight exacerbations of fever. It is in most cases a trivial disorder of childhood. It was differentiated from small-pox by Heberden in 1767, but its autonomy was disputed for nearly a hundred years later.

Symptoms.—Especially in young children the characteristic rash is generally the first sign noticed. In older children and in adults *prodromal symptoms* precede this rash for the first twelve to twenty-four hours and give rise to a temperature even to 101°–102°, malaise, headache, backache and sometimes a prodromal scarlatiniform, morbilliform or urticarial rash. In any case within twenty-four hours the *characteristic eruption* appears: this consists of dark pink, slightly raised, ovoid, or somewhat pyramidal papules, which in the course of a few hours become vesicular. The typical vesicle is at first a thin-walled, translucent, unilocular, glistening bleb, which contains a clear fluid in the most superficial layer of the skin: some of the lesions are ovoid and in the direction of the folds of the skin. After a day or so the fluid is invaded by staphylococci, causing the fluid to become opaque: the vesicle meanwhile loses its tension and dries into a scab which within ten to fourteen days separates, leaving a pigmented scab but rarely extensive scarring. Some of the papules do not proceed to vesiculation at all, but dry up. The essential feature of this eruption is that it *comes out in successive crops*, and so we see different stages of the rash on the same area of skin: this process rarely exceeds four days and is often less. The earliest lesions often appear on the mucous membranes of the palate and cheeks, which should always be inspected: on the skin, first the back, and then the front of the chest and abdomen are invaded: soon the whole body is affected, including the face and limbs, but as the lesions spread away from the centre, so they become much less numerous. Hence the density of the lesions is much less on the forearms and hands than on the upper arms, is less on the lower legs and feet than on the thighs, and is less on the upper face and scalp than on the lower face and neck. On the arms and legs, the *flexor* rather than the *extensor* surfaces are affected. The number of lesions can be very variable: in some the whole body seems to be covered, in others only isolated vesicles are to be seen.

The whole disease seldom lasts longer than ten days, and may be so trivial as to pass unnoticed by the patient. The temperature rarely exceeds 103° F., and mild cases may be afebrile throughout. A case ceases to be infectious after the primary scabs have separated. The incubation period is usually about a fortnight, with limits from ten to twenty-one days (see Table XXIIA, p. 557). A *quarantine period* is unnecessary, but child-contacts should be kept under regular observation for twenty-one days.

Varieties.—A *non-eruptive form* (varicella sine varicellis) may occur, but abortive lesions may have been missed in some of these cases. *Varicella bullosa* and *V. ulcerosa* occur most commonly in children with a concomitant infection with virulent streptococci as in those who have

simultaneous impetigo contagiosa or scarlet fever. *V. gangrenosa* occurs when the lesions are infected by hæmolytic streptococci or by C. diphtheriæ. *V. hæmorrhagica* in which bleeding occurs into and between the vesicles, and from the mucous membranes, is very rare but usually fatal.

Diagnosis.—Modified Variola is the chief disease from which it has to be differentiated, although this should not be difficult, because in small-pox (i.) the rash comes out definitely on the third day; (ii.) it does not appear in successive crops; (iii.) its favourite situations are the distal extremities; (iv.) the evolution of the pock is much less rapid; and (v.) the constitutional symptoms are very definite and characteristic; and see p. 571. *Herpes zoster* is distinguished by the limited area, and grouping of the vesicles (§§ 635, 826). *Pemphigus* is identified by the size and chronic character of the blebs, but a bullous or pemphigoid form of varicella may occur. *Dermatitis Herpetiformis* is very chronic, its vesicles occur in groups, and irritation is severe. In *Scabies* the chest and abdomen are not the most affected areas, and oral lesions are never seen.

Etiology.—Varicella is essentially a disease of childhood, but adults are not exempt; even elderly persons may be attacked.[1] It occurs in epidemics, for the most part of limited extent, though it is endemic in London. One attack usually confers immunity, but there are many reported cases of second and even third attacks. Other infectious fevers predispose to it; attacks following scarlet fever are apt to be severe. The disease is transmitted mainly by droplet infection, but can be carried by feeding utensils and by the hands and clothing of contacts. The disease can be inoculated, though not so constantly as small-pox. The vesicle fluid has been found by C. R. Amies and others to contain elementary bodies which are much smaller than those of small-pox and which are agglutinated by the serum of patients convalescent from varicella.

There is a close relationship between the virus of chicken-pox and of herpes zoster, and the elementary bodies of the two appear identical (Amies). A patient with herpes zoster can cause contacts to develop chicken-pox after the usual incubation period, and more rarely the reverse occurs. Yet an individual who has had chicken-pox is not protected against herpes zoster.

Prognosis.—An attack is usually over in a week or ten days, but it is apt, particularly in adults, to be followed by weakness which indeed may be more troublesome than the disease itself. Death is very rare apart from the hæmorrhagic form and secondary infection (see *varieties*). Rare *complications* include encephalitis, meningitis, myelitis, neuritis, arthritis and fibrositis, from all of which recovery is usual.

Treatment.—The itching is generally the chief trouble. The child should be prevented from scratching the pocks. The early application to each crop of papules or vesicles of 2–3 coats of a paint (cresol 0·5, tannic acid 12·5, collodion flexile 100) decreases the amount of pustulation and subsequent scarring (Mitman). The oral lesions need frequent mouth washes. Quinine and arsenic are the best remedies for the resulting

[1] J. D. Rolleston, "Varicella in Old Age," *Brit. Med. Jour.*, 1932, ii, 1007.

weakness. When the lesions are infected by hæmolytic streptococci or by C. diphtheriæ, give full doses of penicillin and diphtheria antitoxin. Isolation need not be maintained for more than fourteen days from the first appearance of the eruption.

§ **477.** II. **Scarlet Fever** (synonym: Scarlatina) used to be one of the most serious, and one of the commonest, of the eruptive fevers. It is still very prevalent, especially in those under ten years of age, though its severity has undergone remarkable mitigation in this country during recent years. It may be defined as an infective febrile disease due to a hæmolytic streptococcus, attended by inflammation of the tonsils, a punctiform eruption on the skin, and followed by desquamation. There are six characteristic *Symptoms.* (1) After a period of incubation which varies from one to seven days, though usually two to four, there is a *sudden advent of high fever* to 100°–103°, reaching a maximum on the second or third day (Fig. 112). As with other hæmolytic streptococcal infections, the pulse is rapid, 120 or over: headache and muscular pains are usual. *Vomiting* with the initial rise of temperature occurs in 80 per cent. of cases. In the absence of complications, the temperature gradually subsides to normal about the fifth or sixth day. It does not, as in small-pox, subside when the rash comes out. (2) A *sore throat*, with enlarged lymph glands at the angles of the jaw, is complained of or seen on the first day. The tonsils are inflamed and often develop a follicular exudate on both sides, which can be removed without causing bleeding: the fauces become uniformly red or scarlet in colour, whereas the palate shows a punctate redness. Sore throat occurs with several of the exanthemata. In scarlet fever it is the tonsils and pharynx that are affected (rarely the larynx); in measles the larynx is chiefly affected; in small-pox both the larynx and pharynx are involved. The inflammation may become very severe, and is always attended with more or less glandular swelling. (3) The *eruption* is the next symptom and is remarkably regular in its appearance, twenty-four to thirty-six hours after the advent of the pyrexia. It has two elements—a generalised red blush, disappearing on pressure, and a number of minute points (punctate erythema) slightly raised and redder than the surrounding skin. The flush is first seen on the face, and is rapidly followed by the punctate rash which starts on the neck and quickly spreads to the chest, trunk and upper arms. The forearms and hands, and the legs are not affected at first, but within the first twenty-four hours the whole body is covered. There are certain special points to notice: (*a*) the face is flushed, but has no punctiform rash. (*b*) In contrast to measles and German measles, the face in scarlet fever usually shows a *circumoral pallor.* (*c*) Punctate hæmorrhages may be seen, especially in the flexures of the elbows (Pastia's sign). (*d*) Miliary sudamina may occur if the rash is severe. The rash continues to be well marked until the fourth or fifth day of the disease, but disappears earlier if antitoxin has been given: slight staining may remain. (4) In the early stages the *tongue* becomes reddened along the edges, and covered with a thick white fur—"Straw-

berry and cream tongue." Soon the brilliant red papillæ show through, and as the fur separates leaves a bright red denuded surface, resembling a ripe raspberry. Some confusion has arisen from the term "strawberry tongue" having been applied to both these conditions. (5) *Desquamation* ("peeling") is apt to occur with any severe skin inflammation, but it is more characteristic in this than in any other fever. It begins about the fourth day, and continues for four to six, or eight weeks—first on the face, and, following the order of the rash, *last on the palms and soles*, the complete desquamation of which may be very tedious. In the latter position the flakes are large; elsewhere they are small and shreddy. (6) The *blood*

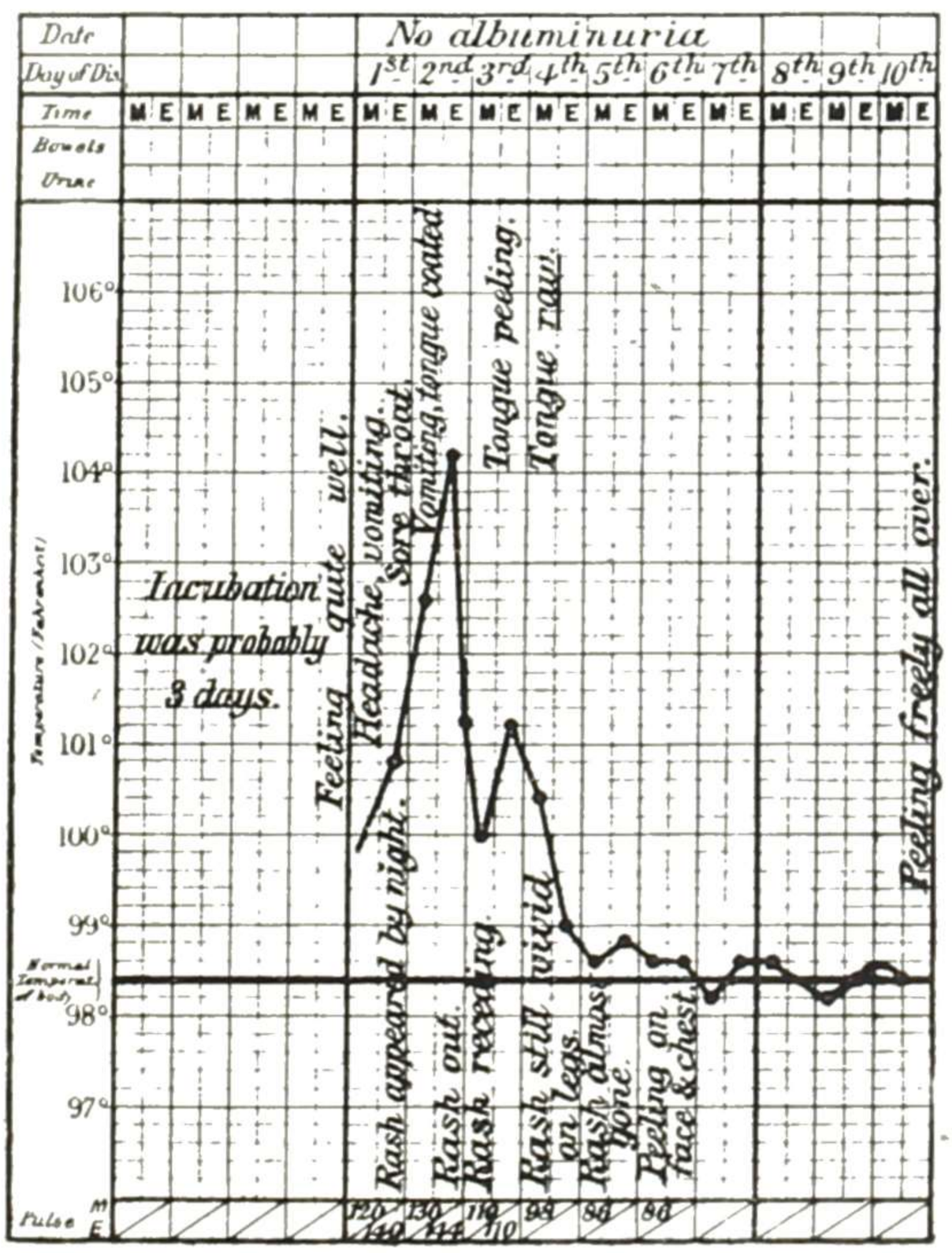

FIG. 112.—SCARLET FEVER.—Arthur M——, æt. 5. A typical mild case, especially as regards the initial symptoms, the rash, the tongue, and the desquamation. The various incidents are shown on the chart.

shows a polymorphonuclear leucocytosis and moderate eosinophilia. According to some observers, the Wassermann reaction is positive during the acute stage, though this is denied by others.

The primary cause is a hæmolytic streptococcal infection, usually of the throat, and sometimes arising from wounds (surgical scarlatina) or from the uterus (puerperal scarlatina). The rash indicates the production of an erythrogenic toxin by the infecting organism. Thus additional signs of the disease are available for (7) a hæmolytic streptococcus can be isolated from the primary source of infection (usually the throat and nose). A positive result may be obtained in non-scarlatinal cases, but a reliable negative report excludes the disease. (8) The *Schultz-Charlton* reaction or

Extinction Sign consists of a blanching of the eruption within eight to twenty-four hours of intracutaneous injection of 0·2 c.c. of a 1 in 10 dilution of scarlatinal antitoxin. It is absent in non-scarlatinal eruptions. (9) A *positive Dick test* (§ 656) becomes negative after an attack of scarlet fever.

Varieties.—There are four chief varieties: (1) The *Benign*, simple or ordinary type as above described. Various symptoms—*e.g.*, rash, fever or sore throat—may be absent and these cases are spoken of as *latent* or *formes frustes*. (2) *Modified* scarlet fever follows the administration of scarlatinal antitoxin within the first one to two days. Within forty-eight hours of the serum the temperature settles to normal, the intensity of the sore throat and rash is considerably lessened and desquamation may not occur. (3) In *Septic Scarlet Fever*, Scarlatina Ulcerosa or Anginosa, the ordinary symptoms are aggravated by a septic infection of the throat, with an exudate which may spread beyond the tonsils and may produce local ulceration even of the fauces and palate. From this focus septic material is absorbed, the upper cervical glands may suppurate and the middle ears become involved. The rash is often faint, but a blotchy or gyrate eruption frequently appears on the face and limbs in the second or third week. (4) In the *Toxic* form the patient is seized with high fever, delirium, and marked cardio-vascular weakness; the vomiting persists, the rash is very intense, but the throat symptoms often ill-marked, and the patient dies during the first week. Toxic scarlet fever of such intensity as to deserve the name *Malignant*, with low muttering delirium, usually a marked rash, and death without complications in a few days, is a very rare variety.

Diagnosis.—The diagnosis of scarlatina is not difficult in typical cases. The abrupt advent of high fever, accompanied by vomiting and sore throat in a child who has not had the disease, is always extremely suggestive, and if the disease is prevalent the diagnosis is almost certain. During the first few days the greatest difficulty is sometimes experienced in the diagnosis from *tonsillitis*, and especially that variety due to other strains of hæmolytic streptococci. Vomiting is more common in scarlatinal cases, and a careful watch must be kept for the rash and for subsequent desquamation. *Diphtheria* has no punctate rash, though a flush may be seen on the chest and arms, but the characteristic membrane appears on the throat and the tongue remains coated. In doubtful cases it is best to act as if the graver disease were present (see Table X, § 156). *Measles* is associated with marked catarrhal symptoms in the eyes, nose and bronchi, and Koplik's spots are usually present. The characteristic differences between the rashes of the two diseases are best seen on the limbs. *Dengue* (*q.v.*) is accompanied by severe articular pains and a morbilliform eruption on the fourth day; the diagnosis is easier when the eruption is present. The scarlatinal rash is distinguished from the diffuse prodromal erythema of *small-pox* by the fact that the latter starts in the groins or axillæ, and invades the oral circle if the rash is diffuse, and lumbar pain is usually complained of. *Enema rashes* and *Epidemic*

Exfoliative Dermatitis are sometimes mistaken for scarlatina. A *septic rash* may be scarlatiniform, but is distinguished by fever of a pyæmic type, the presence of a septic focus, and the absence of characteristic punctation. The erythema of *belladonna poisoning* is accompanied by great thirst, dryness of the fauces, and dilatation of the pupils. *Copaiba* or *Sulphonamide rashes* and those due to so-called "*ptomaine poisoning*" may be a source of confusion.

Etiology.—The disease is highly infectious, especially at the onset and during the early stages. It is due to a hæmolytic streptococcal infection with an organism belonging to Lancefield's Group A, and capable of producing a toxin which causes the characteristic skin rash. The infection is propagated through the air for short distances as a droplet-infection from other cases, from healthy carriers, or from an infection derived from a case recently discharged from hospital ("return cases"). More rarely the organisms are conveyed by dust, or by direct contact with an infected spoon, fork or the nurse's fingers: outbreaks due to infected milk have been recorded.

The patient used to be regarded as infectious until desquamation had ceased, a period averaging four to six weeks, or even longer. There is no evidence that the desquamation of scarlet fever is ever infectious, traditional belief notwithstanding. On the other hand, the infection may survive in the mucous discharges from the throat and nose, and possibly the ears, for many weeks, long after the peeling has completely finished. One attack usually gives immunity for life. *Relapses* or second attacks are believed to arise in those who have developed a poor immunity from the first attack (shown by a persistently positive Dick test), and who are infected by a different serological type of hæmolytic streptococcus.

A hæmolytic streptococcus has been proved to be the causal organism, on the following grounds: (1) inoculation of an apparently pure culture has produced scarlet fever in volunteers; (2) intracutaneous injection of a filtrate of the culture gives a strongly positive reaction in susceptible subjects (Dick test); (3) preparation of a serum by immunisation of a horse with the scarlatinal type of *Streptococcus hæmolyticus* has a curative effect. The presence or absence of a rash depends on the susceptibility of the individual and the capacity of the organism to produce a highly active erythrogenic toxin.

The *Dick Test* is performed by injecting intradermally one skin test dose of scarlatinal exotoxin, contained in 0·2 c.c. of fluid. In eight to twelve hours, there appears a small circular erythematous area which reaches its maximum in eighteen hours after injection, then rapidly fades. To avoid pseudo-positive reactions, a control test should be carried out simultaneously. A true positive result is found in 70 to 100 per cent. of cases of scarlet fever in the first three days of the disease, as well as in susceptible persons. The test possesses some diagnostic value: conversion of a positive reaction in the acute stage into a negative reaction at the end of the week or fortnight indicates that the disease is scarlet fever.

Prognosis.—The disease has become very much milder in Great Britain, and during the last seventy years the case fatality in the London Fever Hospitals has fallen from 13·5 to under 1 per cent.: it still remains serious in other parts of the world. The danger is greater in those under five

years: untoward symptoms arise when the throat infection is severe, the temperature above 105°, when cardio-vascular toxæmia is marked and with persistent vomiting. Delirium at night is more or less usual in severe cases, but violent delirium or stupor is a bad sign. The septic, toxic, malignant and hæmorrhagic forms always cause anxiety. Otherwise the disease is noteworthy chiefly for its *Complications* and *Sequelæ*. These may cause death even after slight attacks. (1) Some degree of upper cervical adenitis is usual: more marked changes and even abscess formation occur in about 5 per cent. (2) Otitis media is regarded as one of the most important complications, attacking 2–3 per cent. of all cases, and leading occasionally to permanent deafness, while mastoiditis and its complications may follow. (3) Acute nephritis (1–2 per cent.) appears usually at the end of the third week, very rarely after the fourth. It is much less common if children are kept strictly in bed from the commencement of the disease: it usually shows itself by slight pyrexia, albuminuria and the presence of casts. This may soon clear up or may proceed to more severe acute nephritis and occasionally to uræmia: chronic nephritis may follow. (4) Scarlatinal rheumatism occurs in the third week, and is due to supervening acute rheumatic fever, often with carditis. (5) Acute sinusitis, ulcerative stomatitis and broncho-pneumonia are relatively rare. Among the *sequelæ* subacute rheumatism and chorea are occasionally found.

Treatment.—With the milder cases now prevailing, it is no longer necessary to insist on treatment in a fever hospital, so long as the patient can be isolated and nursed at home (*Hygienic* treatment is considered in §§ 522 *et seq.*). Strict bed rest for at least three weeks is necessary even in the mildest cases, to prevent complications: a well-ventilated room is essential. Aspirin is useful as a gargle and to swallow in the initial stages: kaolin poultices form a useful application to the cervical glands. *Serum treatment* by the injection of 3,000–12,000 units (intramuscularly) of scarlatinal antitoxin, shortens and lessens the initial toxic symptoms: the dose may be repeated after twenty-four hours with advantage. Penicillin and the sulphonamides have no effect on the toxæmia but are of great value for the septic complications of the disease: they may be given in addition to the antitoxin. If an abscess forms in the neck, or in the middle ear, incision will be necessary. For the treatment of acute nephritis or acute rheumatism, see §§ 397, 582. *Isolation* should be carried out for a period not exceeding four weeks, in uncomplicated cases. The occurrence of return cases, *i.e.*, cases of scarlet fever arising in the same family within a month of the patient (primary case) being sent back to it, is most frequent in the cold months of the year, between the ages of 8 and 10, and within the first fortnight of the patient's return, especially if the primary case has suffered from rhinitis or otitis while in hospital.

Prophylaxis can be promoted by three methods: (1) *Chemotherapy.* A daily dose of sulphadiazine (G. i) for twelve days has stamped out an epidemic among naval recruits. (2) *Passive immunisation* by the injection

of 3,000 units of antitoxin (intramusc.) produces temporary immunity for ten to fourteen days. (3) *Active immunisation* consists in administering to Dick-positive persons five graduated doses of scarlatinal toxin at weekly intervals, after which immunity has usually been conferred. Unfortunately reactions to these injections are common. A Dick test one month after the last dose should have become negative.

§ **478.** III. **Erysipelas** may be defined as an acute febrile contagious disease, characterised by a progressive marginated redness and tumefaction of the skin, usually attacking the face, or the neighbourhood of wounds. (1) *The Stage of Invasion.*—After an incubation period of one to seven days the advent is abrupt, as in scarlet fever and small-pox. The temperature on the evening of the same day may be 103° to 104° F., or more. Vomiting is very common, and so also are muscular pains, especially pain in the back,[1] like that of small-pox. (2) The *Eruption* begins about twenty-four to thirty-six hours after the advent of fever, as a tense red spot on the face (facial erysipelas) or at the site of an abrasion (which may be microscopic). It often commences just within the external nares on one side at the junction of the skin and mucous membrane. It enlarges, spreads, becomes bright red and tender: where the skin is loose as in the eyelids or the scrotum, œdema is well marked. Thin-walled bullæ may form in the centre of the inflammatory area. The advancing edge is sharply defined and raised, the receding edge indefinite. The eruption may vary in duration from three or four days to a fortnight: it is materially shortened by chemotherapy. Delirium at night is not unusual. Convalescence becomes established, and desquamation occurs in the course of one to three weeks. During this last stage albumen may appear in the urine, if it has not appeared before.

Diagnosis.—Erysipelas is to be diagnosed from *erythema* complicated by cellulitis, in which the margin is less raised, and there is less fever. In *herpes* of the first division of the fifth nerve vesicles occur in groups, are limited to one side of the face, and are unattended by fever.

Varieties.—(i.) Although erysipelas and cellulitis are often classified as separate diseases, spread of the infection from the skin to the subcutaneous tissues may give a combination of both (erysipelo-cellulitis). (ii.) Phlegmonous erysipelas or gangrenous erysipelas are severe varieties with suppuration or extensive sloughing. (iii.) Erysipelas neonatorum is a very fatal variety; death may be due to peritonitis by inflammation spreading along the umbilical cord. (iv.) Erysipelas of the fauces is a severe variety, the eruption spreading to, or starting in, this situation. The disease may spread to the larynx and cause fatal dyspnœa.

Etiology.—It is a highly contagious malady due to a local infection with a hæmolytic streptococcus. Persons are predisposed to it, especially alcoholics, by wounds and unhygienic conditions. Infants and persons

[1] This is not usually mentioned as characteristic of erysipelas, and the first case I was called to I mistook for small-pox on this account. I have never met with a case in which it was absent, excepting in second or third attacks of the disease.

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abdomen and thighs and indicates a very severe attack. After two or two and a half days, these initial symptoms disappear, the temperature drops, and on the third day the true small-pox eruption appears. (2) During the *Eruptive stage*, the temperature at first remains much lower—the patient, indeed, may feel comparatively well. The earliest lesions are often visible in the mouth and involvement of the larynx and pharynx causes a sore throat. On the skin, for the first few hours (of the third day) there is a macular eruption which rapidly gives place to a crop of papules of *shotty hardness* which can be felt even more readily than they can be seen, like small shot beneath the skin (Plate I) : each papule is surrounded by a pink areola. They first appear on the forehead and on the fronts

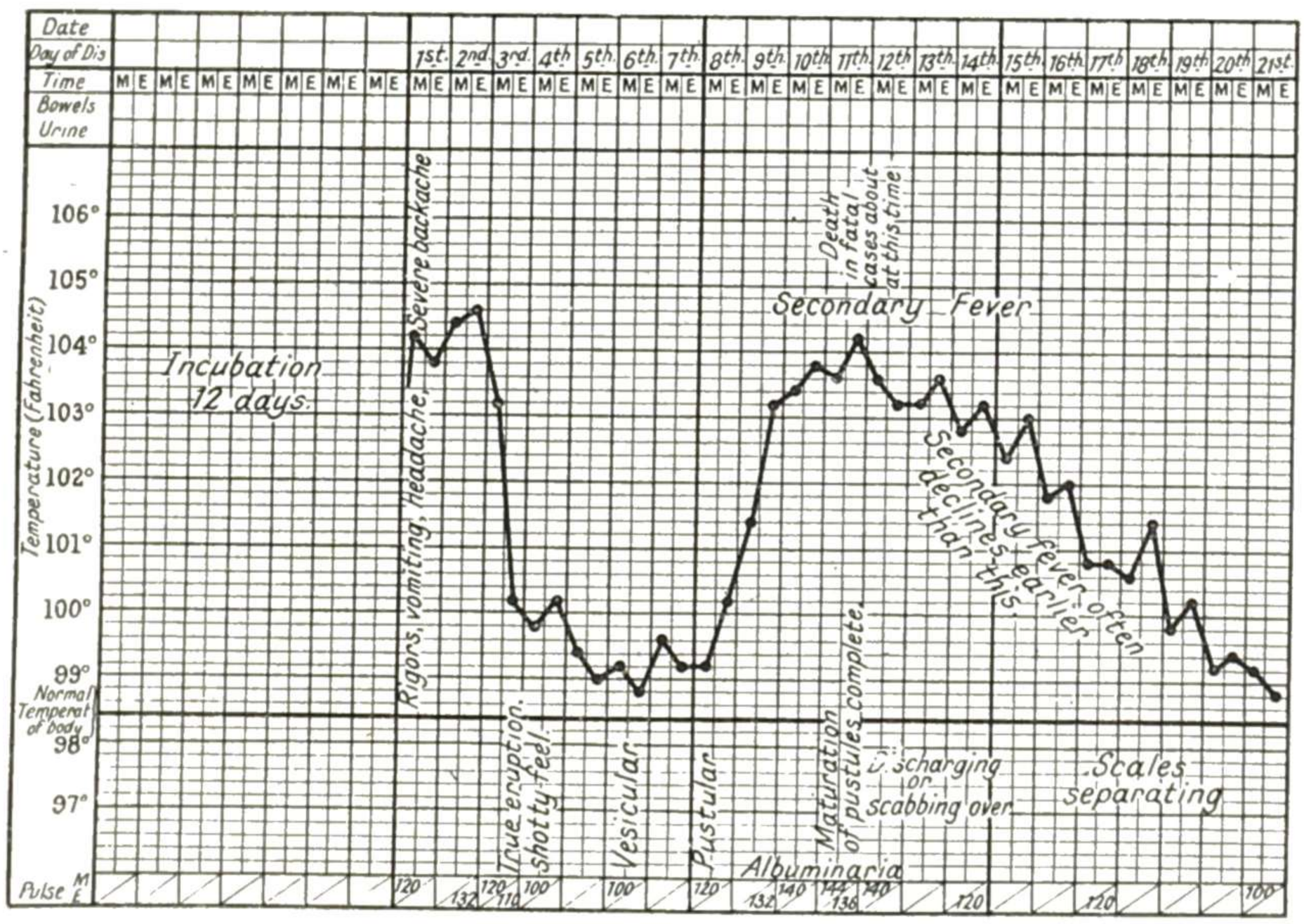


FIG. 113.—UNMODIFIED SMALL-POX.—Severe confluent case, unvaccinated, terminating in recovery. The various incidents are shown in the chart.

of the wrists, and then the eruption travels over the whole body, the chest, abdomen, groins and legs being least affected : this papular stage is complete in forty-eight hours, and the papules then more or less simultaneously become vesicular (on the fifth or sixth days). The eruption *comes out in one crop* and is never multiform in any given area of skin as in varicella. Some of the papules, however, may abort and not proceed to vesiculation. Each vesicle enlarges, and by the seventh or eighth day has become pustular : with this a secondary suppurative fever develops, which may last six to eight days and be attended by rigors (Fig. 113). In typical cases, unmodified by vaccination, each vesicle presents a depressed centre which is held down by a bridle (umbilication). The next day (eighth day) the bridle ruptures, and each pustule becomes hemispherical, about as large as a split pea, with an inflamed and indurated

base, and at this time considerable œdema of the skin is present. These pustules gradually dry into scabs, which separate about the fifteenth to the twentieth day, though in some situations, such as the scalp, forehead, and sides of the nose, considerably later, leaving patches of congested skin, and in severe cases a pitted cicatrix. The extent of the eruption and the amount of inflammatory induration varies considerably. Sometimes only the face and wrists present a few spots; sometimes the whole body is covered. The eruption is always most profuse where the skin has been irritated by any cause. The eruption on the legs always presents a proportionate retardation of development, since it appears last in this situation. Consequently, before certifying a patient as free from infection, the soles of the feet should be carefully examined, and should the thick epidermis be found to harbour any dried-up remnants of obsolescent pocks, these should be carefully dug out and removed before the case can be regarded as free from possible infection.

Varieties.—It is sufficient to describe four varieties according to the severity of the disease, the severity of the symptoms corresponding very closely with the character and extent of the eruption on the face: (1) *Mild or Discrete*, (2) *Confluent*, and (3) *Malignant or Hæmorrhagic*. During the eruptive stage, a hæmorrhagic prodromal rash may be associated with hæmorrhages within and beneath the skin, and from most, if not all, of the mucous membranes. Death ensues early, even before the vesicles appear (Fig. 115). In a second variety, which is less fatal, hæmorrhages occur into and between the pustules. (4) A *non-eruptive form* (variola sine variolis) may occur as in the other acute exanthemata, and may be mistaken for influenza. It occurs among contacts recently vaccinated.

(B) Variola Minor (synonym: Alastrim) is the term applied to true small-pox occurring in an unvaccinated person in which the severity of the disease has been considerably lessened (as compared with *V. major*) due to diminished toxicity of the organisms: the typical lesions tend to abort and the secondary fever is relatively slight. It is the type which has been most prevalent in Great Britain in the last twenty-five years.

Symptoms.—(1) The incubation period is often prolonged beyond the characteristic fourteen-day period of *V. major*: fifteen to seventeen days to the appearance of the rash is quite common. (2) The prodromal symptoms are usually slight. (3) The distribution of the typical lesions is the same as in *V. major*. (4) The papules appear more slowly, but the lesions mature more quickly. This may give a deceptive appearance of crops of lesions such as are met in chicken-pox. (5) A considerable number of papules and vesicles abort, and so secondary infection and its associated fever is slight.

Etiology.—The identity of *V. minor* with ordinary small-pox is shown by (1) vaccination is equally protective against both: (2) the distribution of the eruption is the same: (3) the serum agglutinations of *V. minor* and *V. major* are equally effective against the Paschen bodies derived from the lesions of *V minor* and *V. major*.

(C) Modified Small-pox (synonym: Varioloid) is the disease which arises when a previously vaccinated person developes *V. major*: immunity is only partial, and may be the result either of unsatisfactory vaccination, or of vaccination many years previously.

Symptoms.—(1) The primary fever and early symptoms are often indistinguishable from *V. major*, and the eruption appears on the fourteenth day. (2) Certain portions of the eruption abort and do not pass through all stages. (3) As a consequence several stages of the eruption may occasionally be seen on the same portion of skin. (4) The general eruption may be very scanty, and may consist of not more than a dozen papules, which may not even undergo vesiculation. (5) There is little, if any, secondary (suppurative) fever (Fig. 114).

Table XXV.—Differentiation between

	Chicken-Pox	Small-Pox
Age	Especially children.	Any age.
Degree of illness	Slight.	More severe, often with prostration.
Prodromal symptoms	Usually slight.	Severe for 2–3 days: high temp., headache, backache, vomiting.
Prodromal rash	Uncommon: most on chest and arms.	More common: especially groins.
Main Eruption :—	On *First day.*	On *third or fourth* days.
Temperature of eruption	Rises as rash appears.	Settles as rash appears.
Typical rash	Evolves quickly: successive crops for 4 days: several stages on one portion of skin.	Evolves slowly: one crop only.
Earliest and most profuse skin lesions	Chest and abdomen.	Forehead, wrists and forearms.
On limbs	Flexor surfaces especially.	Extensor surfaces especially.
Early stage	Superficial papules becoming vesicular in a few hours.	Deep shotty papules becoming vesicular in 2 days.
Umbilication of vesicles	Absent.	Present.
Shape of vesicles	May be oval.	Circular.
Pustulation of vesicles	Within four days.	Seventh or eighth day of illness.
Scars	Absent or slight.	Marked.
Secondary Fever	Absent or slight.	Marked.
Vaccination against small-pox	Ineffective.	Successful vaccination prevents the disease.

Diagnosis of Smallpox.—There are three important diagnostic features: (i.) Sudden advent of high fever, often with a rigor; (ii.) headache, *backache*, and vomiting at onset of the disease, of which there should always be a history, even in the mildest cases; and (iii.) the character and distribution of the papules and vesicles. The main diagnostic points and the differentiation from *varicella* are set out in Table XXV. *Measles* is the disease which is most often mistaken for variola in the early stages of the case, and therefore two plates of these diseases are presented side by side (Plates I and II). Measles is distinguished by the redness of and the running from the eyes, with other signs of catarrh, and the presence of Koplik's spots (§ 481) on the buccal mucous membrane. The rash, too, is macular rather than papular, and the individual spots as they increase in size spread out in patchy coalescence. In febrile *roseola* or lichen, the fever lasts only twenty-four hours, the efflorescence appears all over the

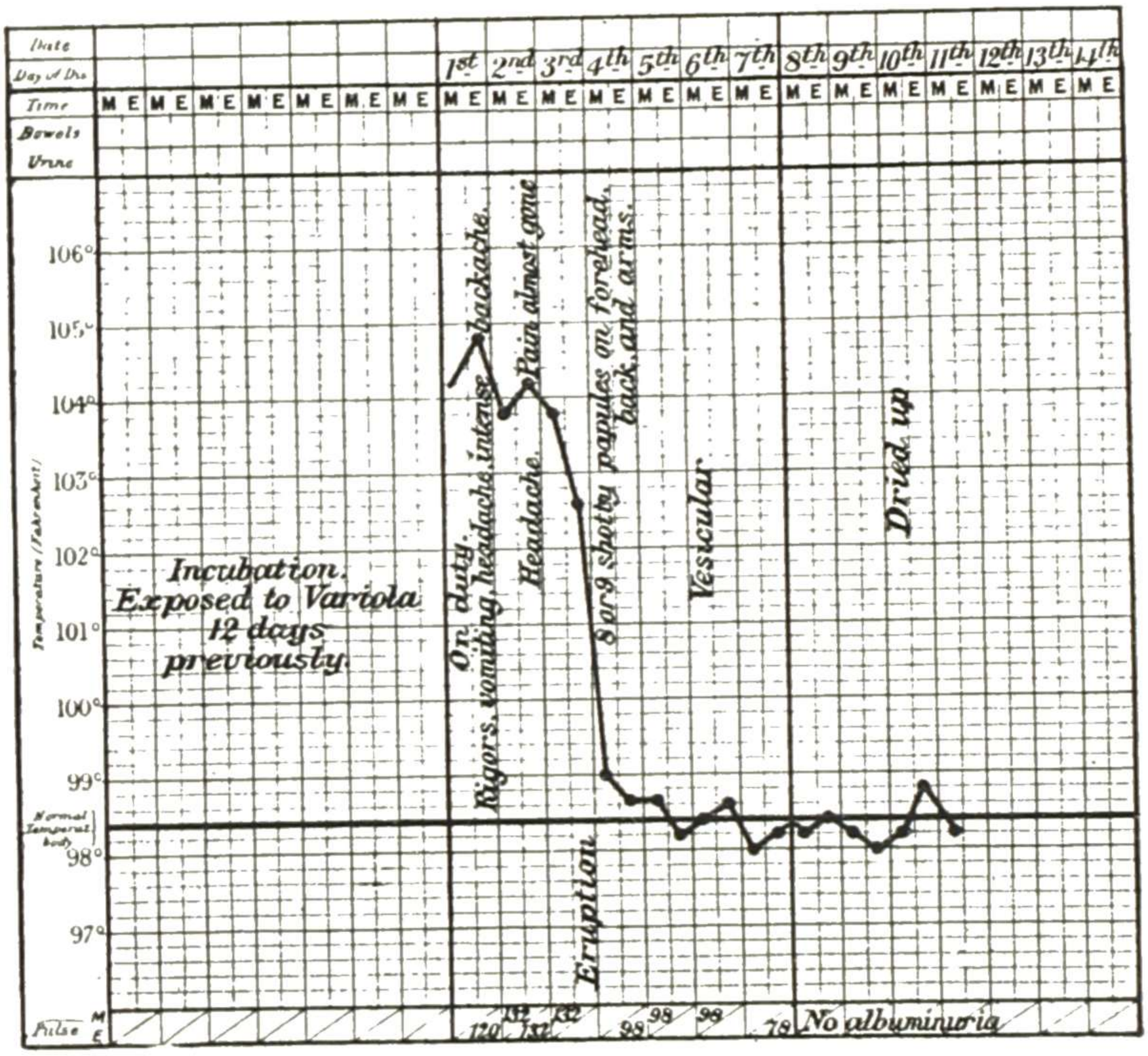


FIG. 114.—A mild case of MODIFIED VARIOLA occurring in a young woman, æt. 22, who had been vaccinated two years previously and who presented three visible cicatrices of the primary vaccination. Initial symptoms severe. **No secondary fever.**

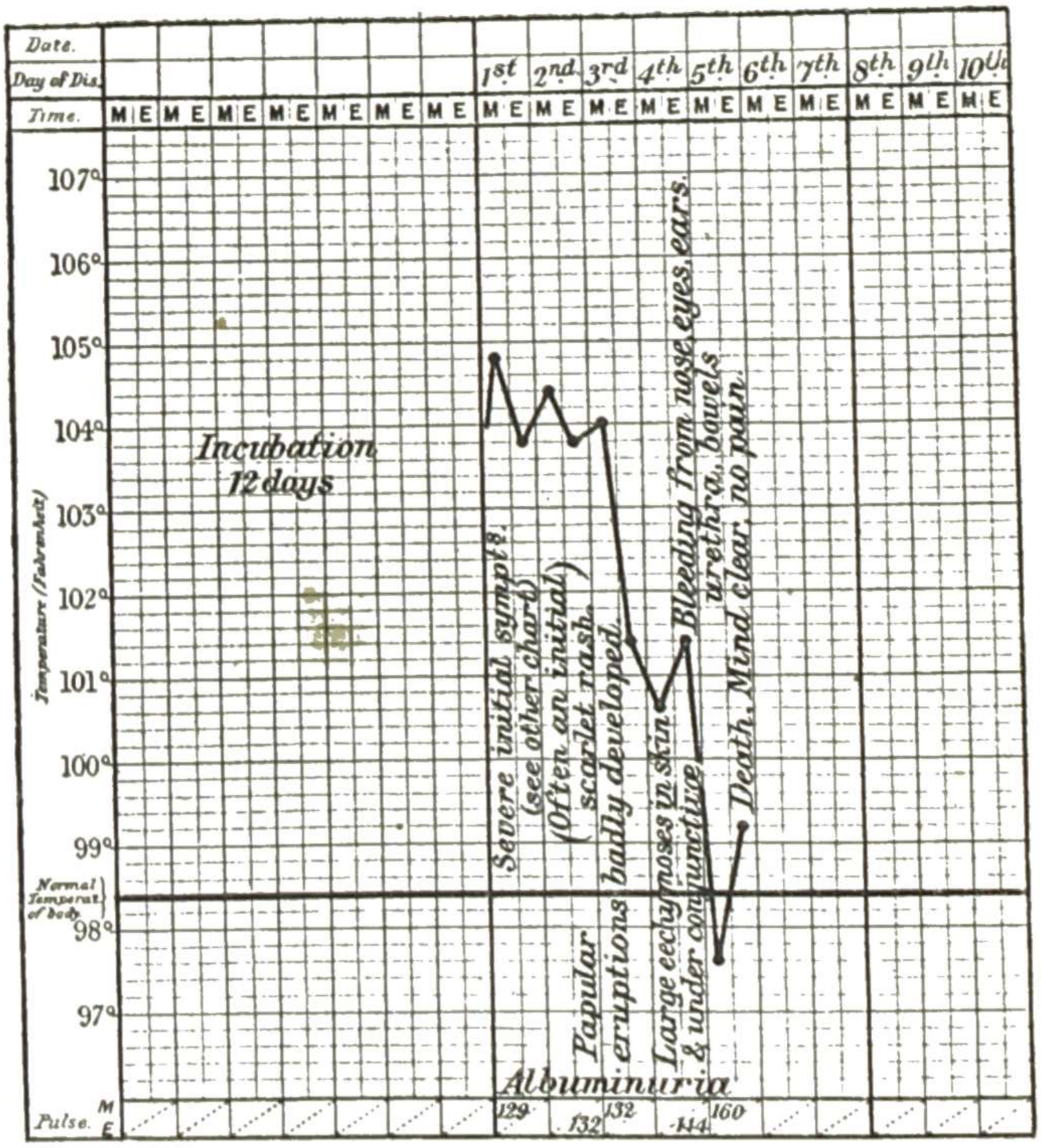


FIG. 115.—A case of MALIGNANT HÆMORRHAGIC SMALL-POX (as distinct from those cases of confluent small-pox with hæmorrhages in the pustules).—Patient unvaccinated. Death occurred on the 5th day. The various incidents are shown on the chart.

body at once, and it does not go to any further stage. *Syphilitic papules* and *pustules* are not accompanied by marked pyrexia: they remain unchanged, while in small-pox the lesions soon become vesicles and pustules (and see § 645). *Lichen urticatus* (papular urticaria) in children may be mistaken for small-pox, but is distinguished by the (1) rash being profuse on the limbs and absent or sparse on the face, (2) generally superficial situation of the lesions, (3) absence of inflammatory reaction, and (4) presence of severe itching.

van Rooyen and Illingworth have described a method of identifying microscopically the causal virus from the papules and vesicles: this method of confirmation has, in their hands, given positive confirmation in 96 per cent. of cases.

Etiology.—Guarnieri described what were first regarded as protozoa in the epithelial cells of the small-pox vesicle, but were subsequently proved by Paschen to be the elementary bodies or virus of the disease. The disease is highly infectious and is conveyed mainly from the upper respiratory passages. Infection may also be conveyed by feeding utensils, clothing and infected fingers, and via crusts from the skin of patients.

Prognosis.—Children, and especially infants, are particularly prone to the disease, and before the discovery of vaccination in 1796 (§ 480), it was a cause of considerably more than half the infant mortality in Great Britain and other countries.[1] One attack usually confers complete immunity: authenticated second attacks are extremely rare. In *V. major* the prognosis depends (1) mainly on whether there has been prophylactic vaccination. Until recently, the case mortality was about 37 per cent. among the *unvaccinated*; about 5 or 6 per cent. among all classes of the *vaccinated* taken together; and about $\frac{1}{2}$ per cent. among the *properly vaccinated*. The severity of the disease seemed to depend almost entirely upon whether the patient had been recently and efficiently *vaccinated*.[2] In the healthy and recently vaccinated it was a comparatively trivial disorder, but in the unvaccinated, especially in infancy, it was one of the gravest diseases. Even so, it must be realised that vaccination is not an absolute safeguard against even virulent small-pox. (2) The second factor is the question of *age*: the official records of the outbreak in Warrington in 1773 showed that of 211 fatal cases, 166 were under three years of age. (3) Alcohol and plethora add to the gravity of the disease. As regards the *varieties*, the confluent, in which the rash may come out

[1] Warrington had an epidemic of smallpox in 1773, with a death-rate of 26·5 per 1000, all the deaths occurring in persons under nine years of age. In 1892–1893 Warrington was again visited by an epidemic, with a death-rate of 1·1 per 1000 of the inhabitants, who then had only about 1 per cent. unvaccinated persons among them.

[2] The figures from the Warrington epidemic, 1892–1893, are very striking. In the *infected* houses there were 2535 persons, and 2223 of these persons had been vaccinated in infancy. Among these latter the case-mortality was **5·2** per cent. The figures also showed that in proportion as the vaccination had been more efficient, the severity of the disease was less. Finally, among all the 667 cases which occurred in this epidemic, not one had been vaccinated or revaccinated within seven years of the attack. —Appendix to the Report of the Roy. Com. on Vaccination, 1894.

on the second day and is very abundant, is much more dangerous than the discrete form. In the former the fever does not subside on the third day, and there is a great tendency to hyperpyrexia and complications. Speaking generally, the more copious the rash, the greater the danger. True hæmorrhagic smallpox is invariably fatal, but if hæmorrhage occurs *into* the vesicular or pustular rash, there is a good chance of recovery. As regards *untoward symptoms*, the more severe the primary fever in the unvaccinated, the more severe will be the disease, but this is not necessarily so in the vaccinated; profuse salivation is a bad symptom; the case is grave if there be no swelling of the skin at about the ninth day, and still graver if the swelling goes suddenly away. The case fatality of variola minor in recent epidemics is about 0·2 per cent.

Complications.—(1) Bronchitis is common in the more severe cases. Pneumonia, empyema, and rarely œdema glottidis are often fatal. (2) A toxic myocarditis occurs in the toxic and hæmorrhagic cases, and with a severe secondary fever. Endocarditis and pericarditis are rare. (3) Nervous complications include encephalitis, with delirium and convulsions, hemiplegia or acute ataxia: post-febrile psychosis may occur. (4) Some degree of conjunctivitis is not unusual: painless corneal ulcers may produce a panophthalmia and destruction of the eye. (5) Erysipelas and cutaneous abscesses are common during the secondary fever.

Treatment.—Prophylaxis. It should be remembered that vaccination is capable of modifying the disease even after exposure to infection, because the incubation period of variola is twelve days and that of vaccinia only eight days. Vaccination may, therefore, be performed with efficacy during the first three or four days after exposure; and every member of an infected household should be vaccinated immediately the disease breaks out therein. For its efficiency in the prevention and modification of small-pox, see pp. 583 and 586. Treatment *of an attack* demands immediate notification and transfer to a special small-pox hospital. The patient should be nursed on a special mattress and kept as quiet as possible; the heart muscle should be carefully guarded by skilful nursing. Headache and pains in the neck and limbs in the earlier stages require aspirin and even the use of morphia or heroin: restlessness and delirium in the secondary toxic stage need full doses of sedatives and narcotics. The eyes should be examined in a good light each day. To protect the skin, the whole body may be painted daily with potassium permanganate solution (5 per cent.) from the early papular stage: a weak dettol solution is comforting and acts as a deodorant. Finsen reported that the exclusion of all except red rays from the sickroom was beneficial, but this has not proved very helpful in this country. In the control of the secondary infection and secondary fever, sulphonamides have, on the whole, been disappointing; but the use of penicillin three-hourly from the start of vesiculation may prove more efficacious. *Hygienic Treatment* is given in §§ 523 *et seq.*

§ 480. Vaccinia.—VACCINATION is the production in a person of the

disease called vaccinia, by inoculating him with the lymph taken from the udder of a cow or calf suffering from that disease. It was noticed in 1769 by a German that people engaged in the milking of cows were exempt from small-pox. Jenner, in 1796, placed the subject on a scientific basis, and ascertained that the inoculation of a human being with the lymph taken from the unbroken vesicles on the udder of a calf suffering from vaccinia protected that person from small-pox. He was also the first to inoculate this disease (vaccinia) from person to person by taking the lymph from the vesicle on the arm which had matured on the eighth day after inoculation. Vaccination was made compulsory in 1853. In 1897 this law was repealed in response to an outcry among the public that syphilis and (?) other diseases could be conveyed from person to person in this way. Syphilis certainly has, in rare instances, been conveyed by arm to arm vaccination; but by using calf-lymph this is entirely obviated. Compulsory vaccination has been abolished by the National Health Act (1946). All public vaccinators now use lymph from the calf which has been diluted 1 in 5 with glycerol-saline, together with a preservative. Goodpasteur has perfected a method by which the virus is grown on the chorio-allantoic membrane of chick embryos.

Rules for vaccination.—The older method of four areas of vaccination has now been superseded. The area of skin to be vaccinated may be over the deltoid, on the abdomen, or over the outer side of the calf: this is washed with soap and water and allowed to dry thoroughly. Two methods of insertion may be used: (1) Three parallel lines ($\frac{1}{6}$ inch long and $\frac{1}{4}$ inch apart) are drawn by a sterile round-pointed needle, which should not draw blood: the lymph is ejected from the capillary tube over this prepared area, or alternatively the parallel strokes may be made through the lymph. (2) The multiple-pressure method is used mainly in America. A drop of lymph is placed on the skin, and pressure is applied by the side of the point of a Hagedorn needle so as to indent the skin but not to draw blood. For primary vaccination in an adult, ten pressures are made (*i.e.*, the skin is indented ten times): for primary vaccination in an infant, and for secondary vaccination, thirty pressures are made. In either case, a sterile dressing is then applied. *Primary vaccination* is safest and best performed in the third-sixth month of life. *Re-vaccination* is necessary each five to seven years, if immunity is to be maintained. An extensive skin rash, a poor general state of health, and recent exposure to other acute specific fevers, are the only indications to postpone vaccination.

The Phenomena of Vaccination.—There are no symptoms for the first two days. On the second or third day a slight pimple, on the fourth day a definite papule and on the fifth day a bluish-white cupped vesicle appears. On the eighth day (the same day of the week as that on which the operation was performed) the vesicle *becomes pustular* and the areola increases during the next two days: at the same time the axillary or groin glands draining the area become swollen and painful. After the tenth day the pustule dries up; the scab falls on the fourteenth or fifteenth day, leaving a pitted

cicatrix. In re-vaccination the reaction usually appears earlier and the vesicle becomes mature sooner than in primary vaccination. No infant should be considered insusceptible to vaccination unless the operation has been repeated several times with different varieties of lymph.

The inquiries which the author made on behalf of the Royal Commission on Vaccination into the Warrington Epidemic (*loc. cit.*) went to prove (1) that efficient primary vaccination offers absolute protection against *infection* for the ensuing five or six years, and relative protection (gradually diminishing) for a considerable time; (2) that primary vaccination lessens the *severity of the attack* of small-pox if contracted during the ensuing twenty or thirty years; (3) that re-vaccination affords absolute *immunity from attack* during the ensuing five or six years, and relative protection for the rest of life; and (4) that if everybody were vaccinated in infancy and again at twelve and twenty-one, small-pox would be exterminated.

Complications of Vaccination.—Generalised vaccinia is a rare condition almost exclusively found in children following the first vaccination. It generally occurs between the ninth and fourteenth days after vaccination and may be later still. It usually appears as a single crop of papules which mature into vesicles and pustules and later crust: occasionally there are separate crops for five to six weeks. The distribution of the lesions is not that of small-pox and there is greater variation in size of the lesions. Toxæmia is likely to be severe, but is only likely to be serious and even fatal when it supervenes on a pre-existing skin disease, especially eczema, seborrhœic dermatitis or impetigo. *Accidental vaccinia.* Persons in charge of recently vaccinated children have frequently been inoculated by lymph from the child's arm, in various parts of the body, especially on the face, lips and eyes, and occasionally on the mouth, throat and genitals.

Various transient *rashes* of a scarlatiniform or morbilliform type, urticaria, erythema multiforme, and hæmorrhagic eruptions occur. *Secondary infections* such as impetigo, furunculosis, erysipelas, cellulitis and gangrene have become rare since the introduction of calf lymph.

Post-vaccinal encephalitis, and less frequently other nervous manifestations such as meningitis, myelitis or polyneuritis develop nine to fifteen days after vaccination. *Symptoms.* There is a sudden onset with pyrexia, headache, and vomiting, which may be followed by delirium, convulsions or coma. Residual damage is rare, for cases usually end in coma and death, or in complete recovery. These sequelæ occur practically only in connection with primary vaccination, and the great majority have been found in children of school age; only 7·2 per cent. of 509 cases of post-vaccinal encephalitis occurred in the first year of life (McNair Scott). The best *treatment* of these nervous sequelæ is by intravenous or intrathecal injection of 5–10 c.c. of the serum of a person recently successfully vaccinated with the same lymph (and see § 740).

§ **481. V. Measles** (synonym: Morbilli) may be defined as an infectious febrile disease attended by catarrh of the ocular, nasal, and respiratory mucous membranes, and by an eruption of minute elevated papules which, as they enlarge, become aggregated into irregular and often crescentic groups.

Symptoms commence after an incubation period of seven to fourteen days, usually ten or eleven. At the commencement of the incubation period and a few hours after infection, there may be a transient febrile catarrh and a fleeting rash; this may occur in 10 per cent. of cases and is

known as the " illness of infection." Then the typical attack commences at the end of the incubation period. (1) *Prodromal symptoms* occur in the first four days until the typical rash appears: (i.) Pyrexia comes on abruptly, though not as suddenly as in scarlet fever, rising to 102°–103° F. on the evening of the first day. During the next two days it usually declines a little (Fig. 116). (ii.) Catarrhal symptoms arise, often with some sneezing and redness of the conjunctivæ. During the next three days these increase, with profuse lacrymation, redness and œdema of the conjunctivæ, a running nose, faucial injection, and a short dry cough with catarrh of the larynx and bronchi—indeed, if the tem-

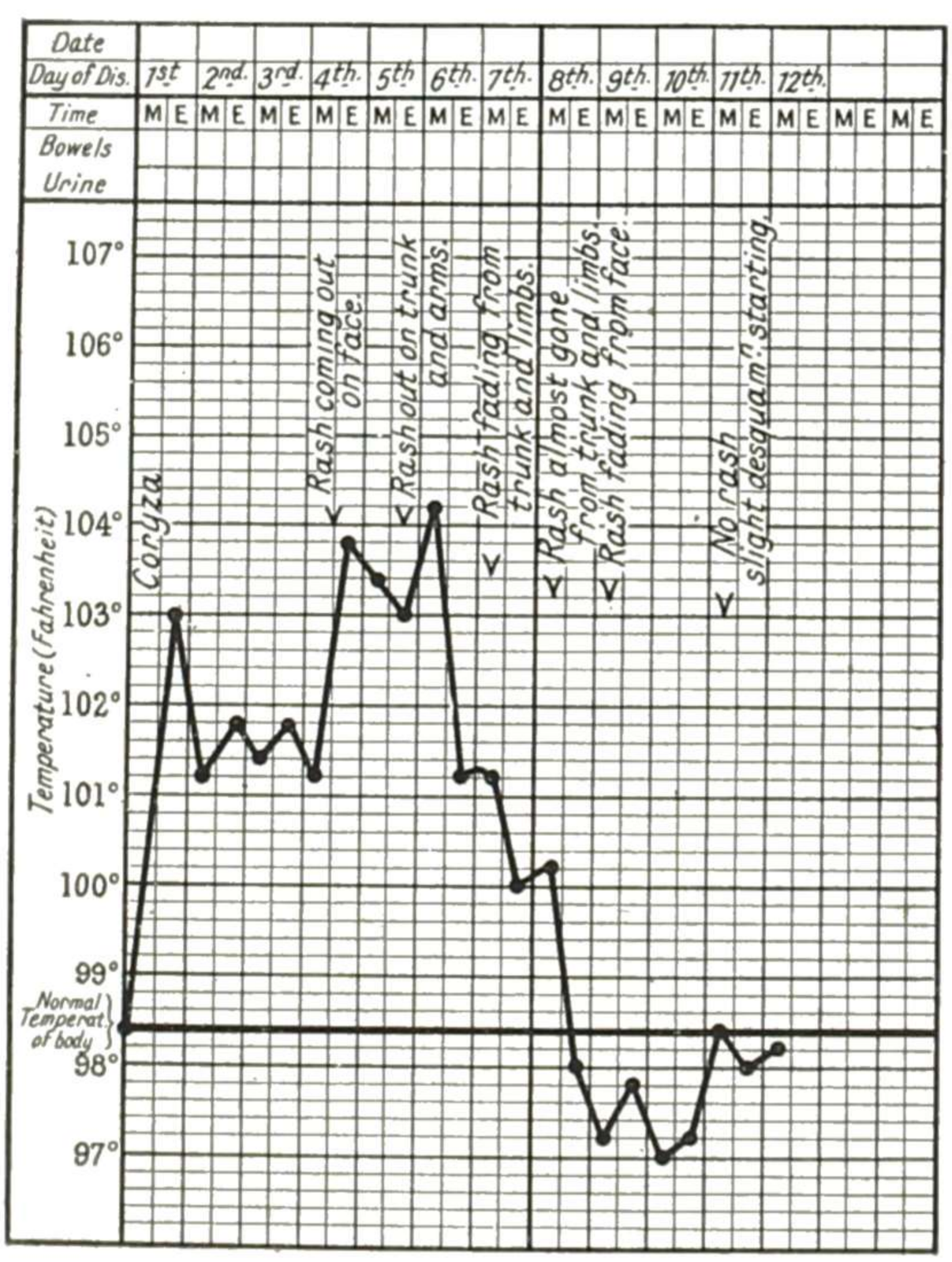


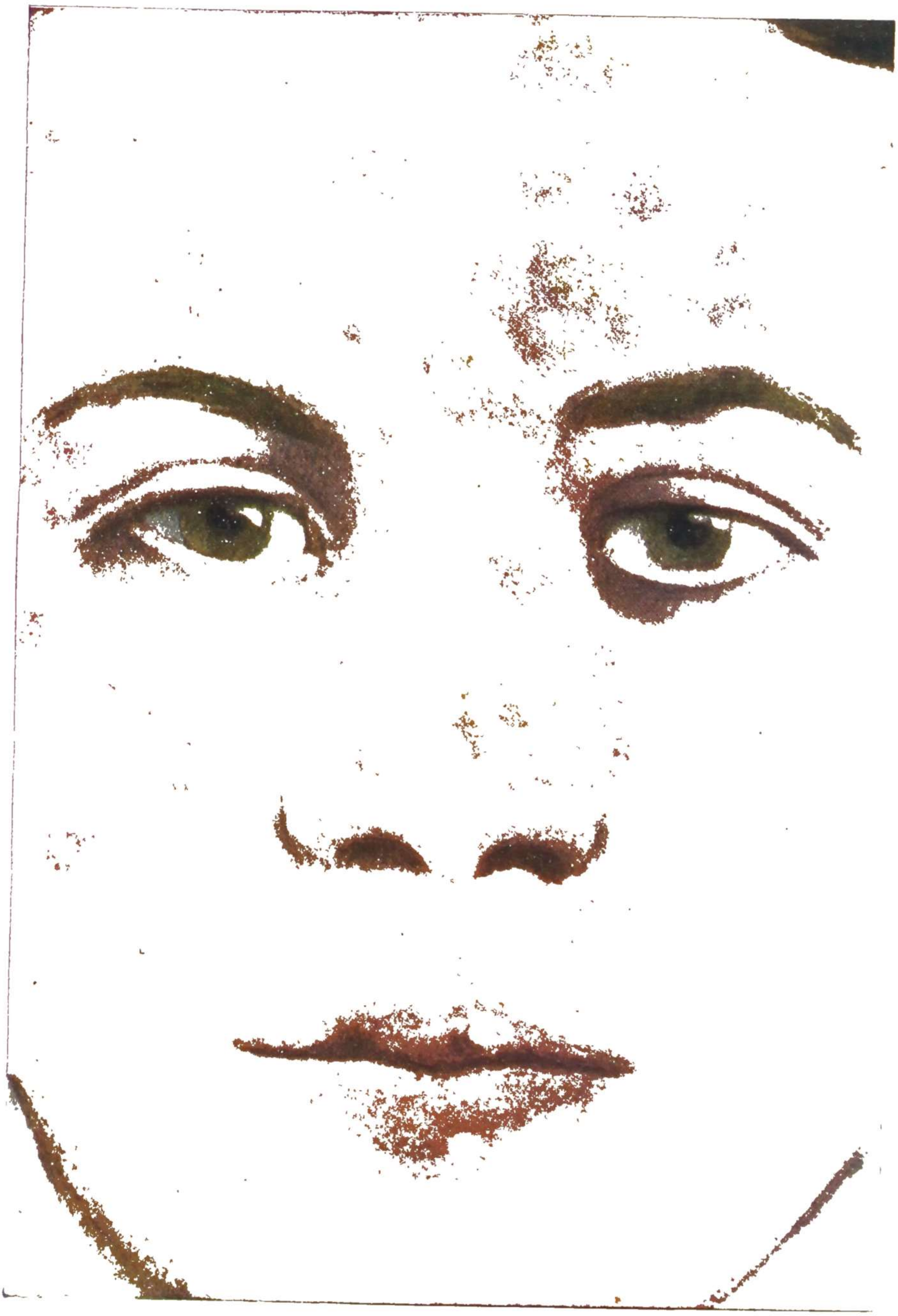
FIG. 116.—MEASLES.—Ethel H——, æt. 5 (under the author's care). Typical chart. The various incidents are shown upon the chart.

perature is not very high the case may be mistaken for coryza. The tonsils are inflamed and may present an exudation. (iii.) Koplik has described spots, which appear on the second or third day of the prodromal period, on the buccal mucous membrane opposite the bicuspid or molar teeth, and especially around and in front of the parotid duct. They are better seen in daylight than in artificial light and are often more numerous on one cheek than on the other: the typical lesions are *minute* white spots of pin-point dimensions surrounded by a red flush (§ 200). At times discrete and few in number, they may on occasion be very numerous, when they give an appearance of a white stippling on a slightly raised reddened base. They may be confused with the much larger patches of

thrush, but Koplik's spots are rubbed away only with difficulty. As they occur in at least 90 per cent. of all cases, their diagnostic significance, before the typical rash appears, cannot be over-estimated. (iv.) The tongue is at first furred, but gradually clears, so that as the rash appears the tongue may come to resemble the strawberry tongue of scarlet fever. (v.) Transient prodromal rashes of macular or scarlatiniform type are rare. (vi.) During the whole of this first phase the child looks and is "a picture of misery." Photophobia is usual. *Stage of Eruption.* (i.) The typical rash appears on the third or more usually on the fourth day (Coloured Plate II). It commences behind the ears and along the hair margin of the forehead, temples and neck. Within a few hours the whole face is involved (including the circum-oral region) and then the whole body is affected: even so the rash is always more marked on the face and trunk than on the more distant areas of the body. At first there is a reddish-brown erythema, which develops into a *macular rash* the colour of which may darken even to a maroon colour. Initially the individual lesions are discrete, but as they become more numerous they tend in the course of the next two days to coalesce into irregularly shaped blotchy patches. These are soft and velvety to the touch and the colour fades on pressure, thus differing from the early stage of small-pox papules. Soon the lesions begin to recede, and at the end of forty-eight hours to fade: within four to five days of its appearance (the ninth day of the disease) the rash has completely disappeared, except that a brownish mottling of the skin ("measles staining") remains for some time. (ii.) Occasionally the macules become petechial. (iii.) The temperature rises somewhat as the rash appears, remains up for the two days of its development (until the sixth day), and then falls by crisis (Fig. 116). (iv.) The constitutional symptoms (malaise, headache, insomnia, etc.), and the catarrhal symptoms (especially the cough) go on increasing during the development of the rash, and they all subside together about the sixth to the eighth day of the illness, as convalescence begins. (v.) Slight desquamation of minute bran-like scales sometimes occurs over the whole body, including the hands and feet. (vi.) The blood shows a leucopenia which is replaced by leucocytosis when a complication occurs.

Varieties.—Modified, Attenuated or Abortive Measles indicates a very mild attack, either as a result of a natural immunity or of the use of prophylactic measures. Before the third month of life, measles is rare, and between the fourth and seventh months attacks are usually modified by immune bodies transmitted through the placenta. In later life, the prophylactic injection of immune bodies (*vide infra*) may result in a very mild attack: catarrhal symptoms are slight, the temperature may not be raised for more than twenty-four hours, Koplik's spots may be absent and the rash is sparse and pale coloured: complications do not arise. Occasionally the initial temperature and Koplik's spots are not followed by a rash (morbilli sine morbillis). The *hæmorrhagic* or malignant variety (toxic), fortunately now rare, is very severe, and is attended by hæmor-

PLATE I.



VARIOLA.

Right side of face (left of observer) represents the second day of the eruption. The other, pustular, side represents the sixth day of the eruption ; a few of the pustules, showing commencing umbilication.

Drawn from nature by Miss Mabel Green.

PLATE II.

MEASLES.

The eruption, which is very plentiful, is eighteen hours old (second day of rash). Note the evidence of coryza in the eyes and nose.

Drawn from nature by Miss Mabel Green.

rhages from many different areas of the body: it is usually fatal. Occasionally bullous lesions are seen in severe attacks (Morbilli bullosa). In the *pulmonary* variety, broncho-pneumonia commences at the beginning of an attack.

The *Diagnosis* from a severe common cold in the absence of Koplik's spots, is very difficult until the eruption appears. *Rubella* tends to occur at a later age than measles. The catarrhal symptoms and the temperature are much less marked although in adults and even in adolescents, rubella can produce severe catarrhal and constitutional symptoms. Enlarged sub-occipital glands are characteristic of rubella, while Koplik's spots are conclusive proof of measles. *Variola* often presents a difficulty; bronchial catarrh is common to both, but watering of the eyes and nose favours measles, while the presence of pain in the back and vomiting aid us considerably in diagnosing variola. The differences between the rashes are referred to on p. 581. *Erythema Multiforme* is somewhat like measles, but is recognised by the absence of catarrh, pyrexia, and of Koplik's spots. The rash due to *sulphonamide drugs* is often morbilliform. That set up by the *injection of an anti-serum* is especially suggestive, and may lead to temporary confusion. The paramount importance of recognising Koplik's spots in the early diagnosis of measles can hardly be exaggerated.

Etiology.—Measles is especially a disease of childhood, and few escape. It is endemic in England, and two-yearly epidemics occur, especially in the spring and winter. The essential cause is a filter-passing virus which has been identified in the nasal secretions, the blood and in the brain when encephalitis occurs: the organism can be cultured on the chorio-allantoic membrane of hen's eggs. It is spread by droplet infection from the nasal and bronchial secretions. Measles is as contagious before as after the eruption has appeared, and its infectivity disappears rapidly so that most cases are not infectious a week after the rash has appeared. Secondary infections by hæmolytic streptococci and by pneumococci are responsible for many of the complications. One attack confers relative immunity: the majority of so-called second attacks are probably rubella.

Prognosis.—Measles is not a serious disease in itself, except in infancy. It has become much milder in type in the last thirty to forty years, and the death-rate in England and Wales is now 1·5 to 2·5 per thousand cases. The most important determining factors are poverty and overcrowding, and the proportion of very young children. Children up to the age of 5 months are often immune and those up to the age of 9 months relatively immune (*vide supra*): after this age, and especially in the poorer classes, secondary infections are very prone to cause pneumonia, but even then much of the terror of this complication has been removed by modern chemotherapy. In middle-class children, the maximum incidence of measles is during the school age, when *complications* are fewer. (1) The most important and most common complication is broncho-pneumonia: even when recovery occurs, some residual pulmonary fibrosis, and even

bronchiectasis may ensue. (2) Catarrhal laryngitis, laryngismus or laryngeal diphtheria also occur. (3) In all cases of measles with sudden aggravation of fever for no apparent cause, acute otitis media should be suspected: this is usually caused by a hæmolytic streptococcal infection, especially before the age of 3 years, and often results in residual damage and even total deafness with deaf-mutism. (4) Conjunctivitis is a normal phenomena, but corneal ulceration which may proceed to perforation and panophthalmitis is dangerous. (5) Cancrum oris is rare nowadays; it is usually due to infection by Vincent's organisms, and begins as an ulcer on the inner surface of the cheek, surrounded by intense inflammation: soon a black slough appears, perhaps followed by perforation. (6) Acute enteritis in children before the age of 2 years may occur alone or with broncho-pneumonia. (7) Encephalitis occurs more frequently with measles than in any other acute exanthem: about the eighth day when the temperature has returned to normal, it is ushered in by drowsiness or convulsions: it tends to a rapidly fatal issue or to complete recovery. A recognised *sequela* is tuberculosis, especially of the bronchial glands: it follows measles and whooping-cough more frequently than any other febrile disease, though measles does not rouse dormant tuberculosis into activity nor aggravate active disease so frequently as was formerly supposed.

Prophylaxis.—The serum of convalescents is collected about the fourteenth day after the commencement of an attack: if injected intramuscularly in suitable doses (Table XXVI) within the first five days after exposure to infection, it will in nearly all cases either prevent an attack or render it very mild. After the fifth day, prevention is impossible, but attenuation still occurs if given before the ninth day: when an attack

TABLE XXVI.—MEASLES PROPHYLAXIS—for Children under 3 years of Age (Intramuscular Route)

Nature of Product	*Dose for*		*Days after Exposure to be given*	*Dose for Attenuation*	*Days after Exposure to be given*
	Complete Protection	*Attenuation*			
Convalescent serum .	5 c.c.	2½ c.c.	1st–5th	5 c.c.	5th–9th
Normal adult serum .	10 c.c.	5 c.c.	1st–3rd	10 c.c.	3rd–9th
Whole blood . . .	—	10 c.c.	1st–3rd	10–15 c.c.	3rd–9th
Placental extract . .	3 c.c.	—	1st–3rd	3 c.c.	3rd–9th
For children above the age of 3 years, the above doses should be doubled.					
Immune globulin . .	0·10 c.c./lb. body-weight	0·025 c.c./lb. body-weight	1st–5th		

supervenes, it is usually very mild and results in permanent immunity. Placental extract ("immune globulin") is less effective than convalescent serum, but more so than adult serum. The gamma-globulin fraction of human serum contains most of the antibodies, and this is highly concentrated and devoid of the agent which causes homologous serum jaundice (§ 332).

Treatment.—The patient is put into a shaded room, with plenty of fresh air. Admission to a fever hospital is better avoided if adequate isolation and nursing can be given at home, for cross-infection with hæmolytic streptococci and other organisms is thus avoided. Bronchitis is treated by a mixture containing ipecacuanha and liq. ammoniæ acetatis. (General treatment, see §§ 522 *et seq.*) For broncho-pneumonia and other complications, penicillin and/or the sulphonamides (§ 123) are of great value: the oxygen tent may be invaluable in small children. Particular attention must be paid to the eyes and ears.

§ **482.** VI. **Rubella,** or German Measles (synonym: Röteln), may be defined as an acute contagious disease, characterised by a polymorphous eruption, frequent enlargement of the lymphatic glands, little or no constitutional disturbance and almost invariably mild course.

The *Symptoms* vary somewhat in different epidemics. (1) After a period of incubation varying between fourteen and nineteen days, and more often seventeen or eighteen days, the temperature rises to 99°–101°. This is accompanied in adults by headache, pains in the limbs, and soon after by *slight* conjunctivitis and catarrhal symptoms. Usually the glands are swollen, the most characteristic being the upper cervical and occipital groups. Tender swelling of the posterior cervical glands is sometimes present several days before the rash appears, the patient often complaining of "stiff neck", which he usually ascribes to having sat in a draught, or some such reasonable explanation. Occasionally the glands in other areas enlarge. Especially in children, the rash may be the first symptom of the disease, and the constitutional symptoms and primary fever are slight or absent. (2) The rash usually occurs within twenty-four hours of the first symptoms: rarely it is delayed until the third or fourth day. It consists of minute round or oval rose-red spots, varying in size from a pin's head to a pea, very slightly raised, never papular. The rash at the outset appears behind the ears and on the forehead and face, and is like that of early measles. In a day or two it becomes confluent, or nearly so, on the trunk, but on the limbs the rash is always discrete and sparse. In adults, itching may be troublesome. The rash usually lasts two to three days, and the severity of the attack is in direct relation to the severity and duration of the eruption. It is sometimes followed by slight desquamation and transient brownish staining. The blood shows a characteristic excess of Türk cells and often of plasma cells.

Diagnosis.—The characteristic features of rubella are the relative absence of catarrhal symptoms, the early appearance of the rash, and the cervical adenitis. In *measles*, the incubation period is longer, the temperature is usually higher and remains up for about six days: the child is miserable, catarrhal symptoms are marked and Koplik's spots can be identified. *Scarlet fever* shows an abrupt onset, with high fever and a high pulse-rate: the sore throat is marked with possibly a tonsillar exudate: headache and vomiting are usual. The rash appears on the *neck* and spreads downwards and is punctate in type, sparing the circum-

oral region : petechiæ occur in the flexures (Pastia's sign) and the Schultz-Charlton test is positive. *Glandular fever* is identified by the more widespread enlargement of the glands and the blood picture : rashes are rare in this disease, but sore throat with an exudation on the tonsils is common. In *secondary Syphilis*, the rash is not irritable and the roseola spares the face (§ 645). Some *drug* and *serum rashes* may have to be considered.

Etiology.—It is mainly a disease of late childhood, or of young adults. It is not so contagious as either measles or scarlet fever. One attack confers immunity. It is almost certainly caused by a virus.

Prognosis.—It is a much more trivial disease than measles. *Complications* are rare : polyarthritis and severe rheumatic manifestations, purpura hæmorrhagica and encephalitis have been recorded. The chief *sequelæ* are congenital defects in children whose mothers have had rubella during early pregnancy : cataract, deaf-mutism, mental changes and congenital heart disease have resulted.

Treatment is purely symptomatic. Isolation is necessary for five to six days.

VI*a*. The term "**fourth disease**" was suggested by Clement Dukes in 1900 as a provisional name for an acute exanthem which he regarded as distinct from scarlet fever, measles and rubella. The great majority of experts, however, do not recognise its autonomy, and are of opinion that most of the cases so described were examples of mild scarlet fever or rubella.

VI*b*. Erythema infectiosum, or "**fifth disease,**" is an acute exanthem appearing in epidemic or sporadic form and characterised by its typical localisation on the cheeks and extremities, and almost complete absence of constitutional disturbance, complications and sequelæ. On the face, where it first appears as rose-red macules it assumes the form of a butterfly's wings on both cheeks, which are hot and swollen ; a few patches are also found on the forehead and chin. The rash next involves the extremities, especially the extensor surfaces where it develops a circinate appearance. On the trunk, which often escapes, the rash is usually morbilliform. The contagiousness is very slight ; it is uncommon to find several cases in a family or institution. The *prognosis* is excellent. No *treatment* is required.

VI*c*. **Exanthema subitum** or "**sixth disease,**" is the name given in 1921 to an acute exanthem which occurs in children under 2 years of age. It usually runs a mild course without any symptoms beyond a three-day fever and a morbilliform rash, which appears on the fourth day, simultaneously with the fall of the temperature. It fades without leaving pigmentation or desquamation. Cases have been reported mainly in the United States, in Europe and Japan, but only a few in Great Britain.

VII. Typhoid and some rare fevers with a rash after the fourth day are described in Group II.

§ **483.** VIII. **Dengue** (Break-bone fever : Dandy fever).—This is a specific fever lasting not more than 7 days and mainly confined to tropical climates. After an incubation period of 3 to 7 days there is sudden onset, with chilly feelings or a rigor, followed by headache, aching eyeballs and rapid rise of temperature (100° to 105° F.). Excruciating backache and joint pains follow ; the joints are involved with periarticular swelling and redness. The tongue is furred and the conjunctivæ injected. Often within 1 to 2 days the skin over the face, neck and chest becomes flushed and reddened (primary rash). Anorexia, vomiting, restlessness and insomnia may ensue. The pulse, which is at first rapid, now slows, and by the 3rd or 4th day the temperature falls to 100° F. or lower, with sweating and perhaps diarrhœa. The

patient temporarily feels better, but after a few hours to 3 days the temperature again rises, the fever lasting 2 to 3 days, and a typical saddle-back chart results. The pain returns and a measly or scarlatiniform eruption (secondary rash) appears, which implicates the limbs and perhaps the trunk and lasts a few hours to 3 days. Desquamation and itching follow. A leucopenia with relative lymphocytosis is characteristic.

Etiology.—The disease, which may occur in big epidemics, is due to a filterable virus, transmitted by aëdine mosquitoes. All ages and both sexes are susceptible and the virus is demonstrable in the blood for the first 3 days. One attack does not invariably confer immunity. The mortality rate is 0·1 to 0·5 per cent.

The *Diagnosis* is easy during an epidemic, but sporadic cases have to be differentiated from typhus, yellow fever and sand-fly fever.

Treatment.—Prevention depends on anti-mosquito measures. Medicinal therapy is similar to that outlined for sand-fly fever.

THE TYPHUS GROUP OF FEVERS consists of several related infections due to various species of rickettsias (Table XXVII). CLASSICAL or EXANTHEMATIC TYPHUS is transmitted from man to man by lice, and occurs in *epidemic* form. MURINE TYPHUS is serologically closely related, and is fundamentally a disease of rodents: it is transmitted from animal to animal and to man by fleas: in man the disease resembles classical typhus but is milder and occurs in *endemic* form. ROCKY MOUNTAIN SPOTTED FEVER and certain other forms of tick typhus form a very closely interrelated group of infections which are transmitted between the animal reservoirs of infection and man by various ticks. SCRUB TYPHUS is an epizootic (*i.e.*, endemic) disease of rodents which is transmitted from animal to animal and to man by the bites of the larvæ of various species of mites. Q FEVER is also a rickettsial disease of man, transmitted from animal reservoirs by ticks, but it differs serologically and clinically from the other tick typhuses. TRENCH FEVER is a rickettsial disease of man transmitted by lice.

The Weil-Felix reaction is of value in recognising certain of these fevers, since in some of the infections the sera of patients will agglutinate special strains of *B. proteus*. Two strains are used—*B. proteus* OX19 and *B. proteus* OXK. Strain OX19 is agglutinated by sera from patients with classical or with murine typhus, and strain OXK by sera from cases of scrub typhus. Agglutinins appear early in the second week of disease and may rise as high as 1 in 30,000 during convalescence. In the field a slide technique may be used as a rough guide. Sera from cases of tick typhus or other rickettsial diseases give negative or only weak and variable reactions with either strain. More recently specific suspensions of rickettsias have been introduced for diagnostic agglutination reactions.

§ 484. IX. **Classical** or **Louse Typhus** (Synonyms: *Typhus exanthematicus*, Hospital and Gaol Fever) is no longer found in England; its disappearance is a triumph of hygiene. As lice do not survive excessive heat, typhus appears in epidemics and may occur at any time of the year in Europe, but only during the cool weather in countries like Egypt and Palestine. Lice become infected some 5 to 10 days after feeding on infected human blood and remain infective for life. The causative agent, *Rickettsia prowazeki*, is found in the epithelial cells lining the gut of the louse and in its excreta; man acquires the disease by infected excreta entering through abrasions and not by the actual bite of the louse. Typhus is associated with overcrowding and personal squalor and is common in times of war, siege and famine. Both sexes are equally susceptible.

Symptoms.—(i.) The period of incubation varies from five to twenty days, but is usually about a fortnight. (ii.) There may be prodromal symptoms in the form of malaise, but the onset is usually abrupt, with shivering, rise of temperature to 103° or 104° F., and sometimes vomiting. The face and eyes are congested, the tongue coated, the breath foul, and there is persistent headache, bronchitis, and a characteristic drunken or stuporose appearance. In rare fulminating cases there may be fits and delirium. After a week of great prostration delirium develops, sometimes drowsiness

and coma. The temperature remains high for twelve to fourteen days, with slight morning remissions; then falls by rapid lysis as a rule, less frequently by crisis. (iii.) The spleen may be palpable, but the abdomen is not distended. (iv.) The rash appears on the fourth or fifth day, first on the abdomen and axillæ, and spreads to the chest, back and trunk: the face is rarely involved. It has two elements: a dusky subcuticular mottling, and purple roseolar macules, which may become petechial. (v.) There is no definite blood picture, but a leucocytosis of 12,000 to 15,000 is common.

TABLE XXVII.—THE TYPHUS GROUP OF FEVERS

Disease	*Vector*	*Rickettsia Organism*	*Reservoir*	*Weil-Felix Reaction*	*Remarks*
CLASSICAL or EPIDEMIC TYPHUS—usually severe BRILL'S DISEASE (mild late manifestation)	Lice	*R. prowazeki*	Man	OX19 +++ OX2 ++ OXK −	May be differentiated by using specific suspensions of rickettsias in agglutination and complement fixation reactions.
MURINE or ENDEMIC TYPHUS — widespread and usually benign. Ship typhus (Toulon), Urban Shop typhus (Malaya, etc.)	Rat fleas	*R. mooseri*	Rats and mice	OX19 +++ OX2 ++ OXK −	
ROCKY MOUNTAIN SPOTTED FEVER	Ticks	*R. rickettsii*	Wild rodents and ticks	OX19 + OX2 + OXK + (Variable low titres)	
With local lesions :— FIÈVRE BOUTONNEUSE (Mediterranean), TICK TYPHUS	,,	*R. conori* (*R. pijperi*)	Dog, rodents and ticks		
SCRUB TYPHUS (Tsutsugamushi fever)	Larval Trombiculid mites	*R. orientalis* (*R. tsutsugamushi*)	Field rodents and mites	OX19 − OX2 − OXK +++	
Q FEVER	? Ticks ? Dust borne	*R. burneti* (*R. diaporica*)	? Bandicoot		
TRENCH FEVER . . .	Lice	*R. quintana*	Man		
RICKETTSIAL POX . .	Mouse mites	*R. akari*	House mice		Indications of serological relationship with Rocky Mountain Spotted Fever.

Diagnosis —The Weil-Felix reaction (*i.e.*, agglutination of *B. proteus* OX19 by the serum of typhus cases in dilutions of 1–100 to 1–2000 or higher) is a very valuable reaction, but is not obtained until the end of the first week. (1) *Typhoid fever* was originally confused with typhus, but differs in its insidious onset, type of temperature, leucopenia, rash, bacteriology and serology. (2) In *measles* the eruption resembles the typhus spots, and appears at the same date, but in typhus it does not involve the face, it is never preceded by catarrh, is never papular, and becomes petechial. (3) Some *malarial* fevers occasionally present difficulty, but they have no eruption. (4) *Uræmia* and other causes of coma may be mistaken for it. (5) Apical *pneumonia*, *meningitis*, and other causes of the *typhoid state* may be confused with typhus. The cerebrospinal fluid may be increased in pressure and contain an excess of lymphocytes in typhus. The bubonic swellings in *plague* occur earlier, during the first week.

Prognosis.—Case-mortality, 20–40 per cent.: between the age of fifteen and twenty-five, 4 per cent.; over fifty, 50 per cent or more. Thus the mortality is greatly influenced by the age of the patient, and by previous preventive inoculation. One attack usually confers immunity. Typhus is always a serious disease, especially in the plethoric and alcoholic. It terminates fatally in three ways: (i.) Degeneration of the cardiac muscle, a very common accompaniment; (ii.) coma from toxæmia; or (iii.) pneumonia. Untoward symptoms are (i.) weak, irregular, or intermittent pulse, or other indications of cardiac weakness; (ii.) an abundant rash, with high fever; (iii.) early and protracted cerebral signs or protracted hiccough; (iv.) all complications, especially pulmonary. Of the *complications* and *sequelæ*, (i.) the pulmonary are the worst, especially broncho-pneumonia and hypostatic congestion of the lungs; œdema glottidis and pleurisy are less common. Other complications are (ii.) hyperpyrexia and meningitis; (iii.) femoral and other thromboses; (iv.) gangrene of the extremities from embolism, bed-sores and pyæmic abscesses; (v.) cardiac weakness, which may remain for a long time, on account of the granular degeneration of the muscle; (vi.) post-febrile mania; and (vii.) paralysis of various parts.

Brill's disease is a mild form of typhus found in the United States of America. It occurs sporadically among immigrants from eastern Europe and is now considered to be due to exacerbations of latent louse-borne infections. *Symptoms.*—The onset is generally rapid; the fever, which is of continuous type, terminates by crisis about the fourteenth day. Frontal headache, mental apathy and profound prostration are notable features. The eruption which is maculo-papular and rarely petechial in type, appears about the fifth day. The mortality is low and does not exceed 2 per cent.

Murine Typhus is world-wide, but occurs especially in Mexico, U.S.A., Palestine, N. Africa, Egypt and Abyssinia. It is similar to but milder than louse-borne typhus; it is transmitted by fleas from infected rats. Unlike the virus of louse-borne typhus, the murine virus produces a characteristic reaction in the tunica vaginalis of male guinea-pigs. Protective measures include anti-rat campaigns, destroying fleas by dusting rat runs and floors with 5–10 per cent. D.D.T., and protective vaccination of individuals.

§ **485. X. Rocky Mountain Spotted Fever.**—*Symptoms:* During the incubation period of four to twelve days irritation and pain may be experienced in the tick-bites. The fever often commences with a slight rigor, and the temperature rapidly rises to 103°, and later to 105° or even 107° F.; the maximum is reached by the fifth to the twelfth day. About the third day the eruption appears in the form of macules on the wrists and ankles; these rapidly spread all over the body, including the face, and may become hæmorrhagic. The spleen is palpable and tender. There may be slight bronchitis and sore throat. Epistaxis and jaundice are not infrequent. Pneumonia is a common complication. Gangrene of the fingers, genitals, etc., may occur. The temperature in favourable cases falls by lysis; if it remains high the patient lapses into a typhoid state and does not recover. Early albuminuria and a leucocytosis with an increase in monocytes are found.

Etiology.—It is due to *Rickettsia rickettsii*, spread by ticks of the genus *Dermacentor* which live on certain domesticated animals and rodents harbouring the infective agent. It occurs not only in the Western States of the United States of America but also in certain Eastern States and in Columbia.

Diagnosis.—The disease resembles typhoid and louse typhus. From the former it is differentiated by the eruption, but it cannot always be distinguished from typhus. Exposure to infection by residence in an infected region may be taken into account.

The *prognosis* varies in different localities. The Western form has a mortality as high as 90 per cent.: but the Eastern form is milder and the mortality is only 5–10 per cent.

Prophylaxis consists in the avoidance of the places which are tick-infested and by destroying the ticks by the application of ammonia, turpentine, etc. The bite may be cauterised with pure phenol. Vaccination by injection of formolised suspensions of triturated infected ticks gives good protection.

Other forms of Tick Typhus occur in the Mediterranean basin (fièvre boutonneuse, transmitted from dogs by the dog tick); also in S. Africa, India, S. America and elsewhere.

§ 486 XI. Scrub Typhus (Synonyms: Japanese River Fever, Tsutsugamushi Fever, tropical typhus, mite typhus—Sumatra, Australia, India, Burma etc., rural scrub typhus—Malaya).—A typhus-like disease occurring in scattered areas throughout the Far East, Africa, Australia and elsewhere.

Symptoms.—Some five to fourteen days after being bitten by mites the patient develops a shiver, headache, giddiness and fever lasting two to three weeks. This is at first continuous and later remittent in type. Locally there is a small ulcer or ulcers associated with a dark areola and redness, with lymphangitis and enlargement of the regional lymph glands. On the fifth to seventh day a papular and red macular eruption appears involving the face and trunk, limbs, hands and feet. The spleen may be enlarged. When the scab separates it may leave a punched-out ulcer in the second week which may take weeks to heal. The Weil-Felix reaction is strongly positive to *B. Proteus* OXK, and there is a leucopenia associated with a decrease in the neutrophils.

Etiology.—The disease is due to *R. orientalis*, transmitted by the bites of various species of larval *Trombicula* mite, the animal reservoirs of infection being various field rodents. The larva bores into the skin and causes local necrosis and ulceration followed by lymphangitis and adenitis.

Prognosis.—The mortality varies from 5 to 60 per cent.: it is better in the young and in a subsequent than in the first attack.

Prophylaxis.—Vaccination with killed suspensions of cultured rickettsias is a promising experiment. Excellent protection against mites is given by impregnating clothing and bedding with dibutylphthalate.

§ 487. XII. **Q Fever** occurs in Australia, N. and Central America, India and the Mediterranean countries, but is becoming more universally recognised.

Symptoms.—It has a sudden onset and manifestations of an atypical pneumonia with fever, lasting 1–2 weeks.

Etiology.—In Australia and America the virus, *R. burneti*, has been found in various ticks and animal reservoirs: in the European outbreaks the method of transmission and source of infection have not been determined.

§ 488. XIII. **Trench Fever** (Syn., Weigl's disease and similar fevers of Russia, Poland, Japan and Africa) is characterised by fever of a relapsing type and frequently but by no means invariably, by pains in the shins.

Symptoms.—In the acute type there is high fever for five to eight days, and after an afebrile period there are relapses recurring at five-day intervals. A macular rash, chiefly affecting the thorax and abdomen, is found in about 80 per cent. at the onset or during a relapse. Slight and transient nephritis is frequent which responds well to treatment. In the chronic type the onset shows only a lengthy period of increasing incapacity. In both types the febrile wave is accompanied by severe headache, tenderness of the loin and calf muscles and pains in the shins with nocturnal exacerbations. The spleen is enlarged in about one-third of the cases. *Etiology.*—The cause is probably *Rickettsia quintana*, transmitted in the excreta of lice. *Prognosis.*—Trench fever may run a protracted course, and the patient develop a neurasthenic condition. Disordered action of the heart is a frequent complication. *Treatment* is symptomatic.

§ 489. XIV. **Rickettsial Pox** has recently been described in New York as being carried by a blood-sucking mouse mite, which transmits *R. akari*.

Symptoms.—Initially there is a deep-seated single papule which enlarges to form a vesicle: in 1–2 weeks a scab forms which leaves a small scar. A week after the initial lesion there is sudden fever to 103°–104°, gradually declining over the next 7 days. Frontal headache, photophobia and backache may be associated with nausea, vomiting and transient splenic enlargement. Within the first four days of fever a maculo-papular rash appears which vesiculates and gives black crusts.

The *Prognosis* is excellent.

Treatment of the Typhus Fevers.—Fluids in plenty should be administered, and special care directed to the hygiene of the mouth and the avoidance of bed sores. A fluid diet, including glucose, fruit juices, broths and milk should be given. Intravenous dextrose (5 per cent.) and plasma transfusions are often helpful and cool sponging to lower the temperature is indicated. Lumbar puncture may benefit comatose patients. Hyper-immune rabbit serum or immune horse serum has been advocated: convalescent serum may also be tried. Recently promising results have been reported from administration of *p*-aminobenzoic acid, 4–8 G. initially followed by 2 G. 2-hourly by mouth: vomiting or nausea, induced by the acidity of the drug, is prevented by concurrent oral administration of sodium bicarbonate in dosage sufficient to render the urine alkaline. The new antibiotics chloromycetin and aureomycin are of the greatest value in all forms of typhus. *Prophylaxis*, especially important for doctors and nurses, depends on measures against lice and their excreta and on protective inoculation against the disease. Dichlor-diphenyl-trichlorethane (D.D.T.), 5 per cent. in an inert powder base, dusted on skin and clothes remains lethal to lice for several weeks. Overalls fitting tightly round the neck wrists and ankles may also be used. Masks and goggles may be worn to protect against infection from dried louse fæces in dust of clothes of patients. Protective vaccines are now widely used: they consist of killed suspensions of rickettsias grown in the yolk sacs of developing eggs, 2 or 3 injections each of 1 c.c. being given at intervals of a week or so followed by a maintenance dose of 1 c.c. every six months.

§ **490.** XV. **Anthrax** (Synonym: Malignant Pustule) is due to infection with the *Bacillus anthracis*. The lesion is almost always situated on exposed parts, the dorsum of the hand, arm or face; 82 per cent. of the cases show the pustule on the head or neck. It affects woolsorters, furriers, feltmakers, ragsorters, and others who come in contact with animals or their hides or fur; 40 per cent. of the cases in British leather-workers are due to handling Chinese or East Indian goods. No case has been traced to wet salted hides.

Symptoms.—The incubation period is 24 to 72 hours. First a papule forms at the seat of inoculation, which rapidly enlarges, and becomes on the second day a vesicle, with serous or hæmorrhagic contents and with considerable local œdema. On the third day this bursts, leaving a raw exuding surface, which, on the fourth day, turns to a dry black slough, surrounded by a zone of intense inflammation slightly raised above the surface. Upon this inflammatory zone there appears, also on the fourth day, a characteristic ring of small red vesicles. The œdema extends around, and the lymphatics and the glands inflame. The pain is usually very slight, and no pus forms until about the tenth day, when the slough begins to separate. The constitutional symptoms bear no proportion to the local mischief. The pyrexia may be so slight as not to interfere with the patient's ordinary avocation, and it may not come on until some days after the local signs. Usually, however, it is severe, comes on early, soon assumes a typhoid character, and there is a positive blood culture. *Intestinal* and *Pulmonary* types are also described, according to the method of infection. In the former intense vomiting and diarrhœa occur, with great prostration and cramps, with, in some cases, cyanosis and dyspnœa, and towards the end convulsions and spasms. The spleen is enlarged. In the pulmonary type, due to inhalation of diseased wool or hair (*woolsorters' disease*), there are urgent dyspnœa, and pain in the chest of sudden onset. The temperature rises to 102° to 103° F., and death may occur with profound collapse in twenty-four hours. Sometimes delirium and convulsions, or diarrhœa and vomiting, occur.

Diagnosis.—It may have to be diagnosed in the first place from the sting of an insect, from various conditions which lead to solitary vesicles or bullæ on the second day, from erysipelas (if on the face), lymphangitis, and other causes of œdema. The occupation of the patient assists, but a diagnosis may be made by examining the serum or secretion of the sore, stained by Gram's method (§ 921), under the microscope; the *Bacillus anthracis* is thus readily discovered.

Prognosis.—The mortality varies with the position of the primary lesion, being 40 per cent. when this is on the neck or face, and 12 per cent. when situated elsewhere.

Treatment.—This includes local and general rest combined with the administration of penicillin, 50,000 units 3-hourly subcutaneously, or large doses of sulphathiazole: if œdema is not controlled within two to three days, anti-anthrax serum should be given, 200–500 c.c., repeated every 12 to 24 hours until œdema is checked. If penicillin or sulphonamides are not available, neoarsphenamine may be tried. Mild antiseptics, such as a dilute solution of formalin, should be applied to the lesion.

§ 491. XVI. **Glanders** (Synonym: Equinia) may be defined as a contagious febrile disease attended by a discharge from the nostrils, and sometimes an eruption on the skin, due to the inoculation of the *Bacillus mallei*, in a person attending to HORSES affected with the disease. The eruption, which only occurs in ACUTE GLANDERS, consists of a general erythema, on which a crop of pustules of hemispherical shape appear in the course of a few days or hours. They vary in size between a lentil and a florin. There are also nodules of granulomatous material in the subcutaneous tissue and muscles, which usually suppurate, leaving large foul ulcers. The other symptoms are (i.) a copious discharge of viscid, semipurulent matter from the nostrils; (ii.) pains in the limbs and joints; and (iii.) high fever, with rigors and prostration, passing on to the typhoid state.

In CHRONIC GLANDERS (Farcy) the pyrexia and constitutional symptoms are absent, also the cutaneous eruptions (erythema, pustules, and nodules which leave ulcers and sinuses). The discharge from the nose may be the only sign.

Diagnosis.—The pustules of acute glanders resemble those of variola, but they are larger, are not umbilicated, and the temperature in glanders does not fall with the rash in those cases which present a generalised pustular eruption.[1] The pain and swelling of the joints and limbs bear some resemblance to acute rheumatism, and still more to pyæmia. The reaction to mallein may assist.

Treatment.—At present the disease is extremely fatal. Specific serum and vaccine treatment, as well as drugs, have hitherto been unsuccessful. In FARCY or CHRONIC GLANDERS the death-rate is 40 or 50 per cent. Good results have accrued from inunction by unguentum cinereum, and the use of X-rays or Finsen light.

GROUP II. CONTINUED PYREXIA

§ 492. In this group the pyrexia tends to assume a CONTINUED TYPE —*i.e.*, it runs a continuous course except for the slight normal diurnal variation (§ 471). This group is distinguished from Group I by the absence of an eruption during the first four days of the illness. It is distinguished from Group III mainly by the course of the pyrexia, though aberrant types of one group are found in the other.

Some of the fevers rare in this country have an eruption which develops usually after the fourth day. (See next page.)

TYPHOID FEVER, which may be taken as a type, may in exceptional cases present no other symptoms than *the characteristic pyrexia.* The rash, when present, may be ill-marked, and does not appear till the second week of the disease. In DIPHTHERIA there is the characteristic *throat lesion;* in INFLUENZA there are *pains in the limbs* and a more sudden advent; in PERTUSSIS the *characteristic cough;* and in MUMPS the

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[1] The author once notified a case of this kind as small-pox, and the case passed as such through the hands of two of the most experienced medical officers of the Metropolitan Asylums Board, the mistake not being cleared up until after death, and a full investigation had been made of the *circumstances under which the disease arose.* It was then ascertained that the patient was a stableman, who attended glandrous horses.

parotitis. Various PATHOLOGICAL TESTS may aid us in the diagnosis. CHOLERA (§ 309) and DYSENTERY (§ 308) might also be included in this group, but the pyrexial disturbance is quite a subordinate feature compared with the intestinal manifestations. Dr. Cabot (*loc. cit.*) analysed 784 cases of fever lasting two weeks or longer without dropping to normal, and found that 90 per cent. were cases of typhoid fever (586), sepsis (70), or tuberculosis (54). Under "sepsis" he included all forms of septic contamination of the blood-stream, as by wounds, abscesses originating from the appendix, gall-bladder, genito-urinary tract, or alimentary canal or empyema (§§ 496 and 516).

Common.		*Rare in Britain.*	
I. The Enteric Fevers (Typhoid and Paratyphoid) ..	§ 493	VII. Glandular fever	§ 499
II. Diphtheria	§ 494	VIII. Plague	§ 500
III. Influenza	§ 495	IX. Undulant fever	§ 501
IV. Rheumatic fever, pneumonia, and various other inflammatory disorders, usually attended by local signs	§ 496	X. Yellow fever	§ 502
		XI. Cerebro-spinal fever ..	§ 503
		XII. Relapsing fever	§ 504
		XIII. Other fevers, rare or unknown in this country transmitted by ticks, sandflies, etc.: Tularæmia, Kala-azar, Phlebotomus fever, Rat-bite fever	§ 505
V. Whooping cough	§ 497	XIV. Psittacosis	§ 506
VI. Mumps	§ 498	XV. Bornholm Disease ..	§ 507
		XVI. Heat stroke	§ 508

The ENTERIC FEVERS include Typhoid and the Paratyphoid Fevers. In young children the clinical picture differs from that in adults, and commonly manifests itself as gastro-enteritis or broncho-pneumonia.

§ **493.** I. **Typhoid Fever** is an acute specific fever of about four or five weeks' duration, and is due to the ingestion of typhoid bacilli. In contrast to the fevers in Group I, the onset is insidious but profound toxæmia develops, often attended by successive crops of rose-coloured spots and characteristic ulceration of the Peyer's patches of the small intestine.

Symptoms.—The period of incubation is ten to fourteen days, but may be shorter or longer. There is a stage of increasing illness and bacteriæmia (first week), followed by a continued high temperature and profound prostration (second and third weeks): in cases that recover there follows a slow decline in fever (fourth and fifth weeks) before convalescence is established.

First week.—(i.) The most important early symptom is severe frontal headache: otherwise there are simple malaise and lassitude, some degree of bronchial cough, epistaxis, and disturbed nights. (ii.) Anorexia and nausea are associated with abdominal discomfort, flatulence, and indefinite pain in the right iliac fossa. The bowels are irregular with constipation or temporary looseness of action. (iii.) The tongue is always heavily coated with a white fur. (iv.) The temperature is characteristic (Fig. 117), tending to rise in step-ladder fashion, being higher in the evening than in the morning. Yet the pulse rate is often slowed in proportion to the temperature, and rather soft. (v.) The bacteriæmic

nature of the symptoms in this first week is demonstrated by the frequency with which a positive blood culture can be obtained. A polymorph leucopenia is almost invariable.

During the *second and third weeks* the condition of the patient deteriorates. The *three characteristic features* in this stage are: (i.) The temperature remains up (continued pyrexia) at 103° to 105° F., the diurnal remissions often being no more than are met with in health (Fig. 117). The pulse is slow in proportion to the temperature, is soft and often dicrotic in character and the blood pressure lowered. (ii.) The rash generally comes out about the seventh to twelfth day (average, tenth) in successive crops [1] of small rose-coloured lenticular spots, slightly elevated, soft, and disappearing on pressure. Each spot lasts about three or four days. They are never petechial. They are chiefly met with on the abdomen, sometimes on the rest of the trunk, very rarely on the face or limbs. The number of these spots varies considerably, but they are seldom abundant. They may be very small, and thus be overlooked or mistaken for flea-bites. (iii.) The spleen is generally enlarged during this period. It is seldom large, it may be tender and the lower edge is rather soft, which makes it more difficult to feel. Otherwise, (iv.) Lethargy becomes very marked and gives rise to an aspect which is fairly characteristic (*facies typhosa*): the drowsiness deepens to semi-coma and in severe cases the typhoid state eventually supervenes. (v.) Some diarrhœa is usually present after the first week—at least in cases of moderate severity—and the stools are of a characteristic pea-soup or yellow ochre colour—this feature is of less value as a means of diagnosis if the patient is wholly on a milk diet. The number of stools passed in twenty-four hours is very variable, but tends to decrease in the third week. In more than half the cases there is no diarrhœa throughout, but these include the large proportion of mild attacks: complete absence of diarrhœa is exceptional in cases of any severity. (vi.) Tympanitic distension of the abdomen (meteorism) is common (especially if the patient be injudiciously fed), and there is pain and gurgling in the right iliac fossa, though great care should be used to elicit this symptom, as the intestinal wall is thinned by disease. (vii.) The mouth becomes dry and sordes collect on the teeth and lips. The tongue at first develops a brown fur, but in the second week this clears, and the tongue becomes glazed and dry or red and smooth: shallow transverse fissures are often seen on it. (viii.) A toxic albuminuria is usual.

The *fourth and fifth weeks* are characterised by a gradual improvement in the patient's condition. (i.) The temperature gradually falls in a step-ladder fashion, the reverse of the initial rise (Fig. 117). (ii.) The extreme mental and physical apathy give place to a slowly renewed interest. With increasing appetite weight is gradually regained. (iii.) The stools become more formed and constipation often follows. Prolonged *convalescence* is necessary, for energy is slow in returning. After an apyrexial

[1] This fact may be revealed by enclosing each of the spots which appear on one day by a circle, next day by a triangle, and so on, by a skin pencil or aniline ink.

period, relapse may occur, with a recrudescence of the symptomatology, although such is rarely as severe as the original attack. It is particularly during the third and fourth weeks that the dreaded complications of perforation or hæmorrhage of the ulcerated Peyer's patches are most liable to occur.

The *varieties* of typhoid fever are legion. It is a safe rule to remember that continued fever of any kind may be due to typhoid, whatever symptoms are presented. The predominant symptoms may be those of broncho-pneumonia or of meningitis. In the *septicæmic variety*, the disease commences suddenly with a rapid rise of temperature, vomiting and rigors: intestinal symptoms are usually absent. In the *ambulatory form* the patient keeps about, and perforative peritonitis or intestinal hæmorrhage may be the first manifestation.

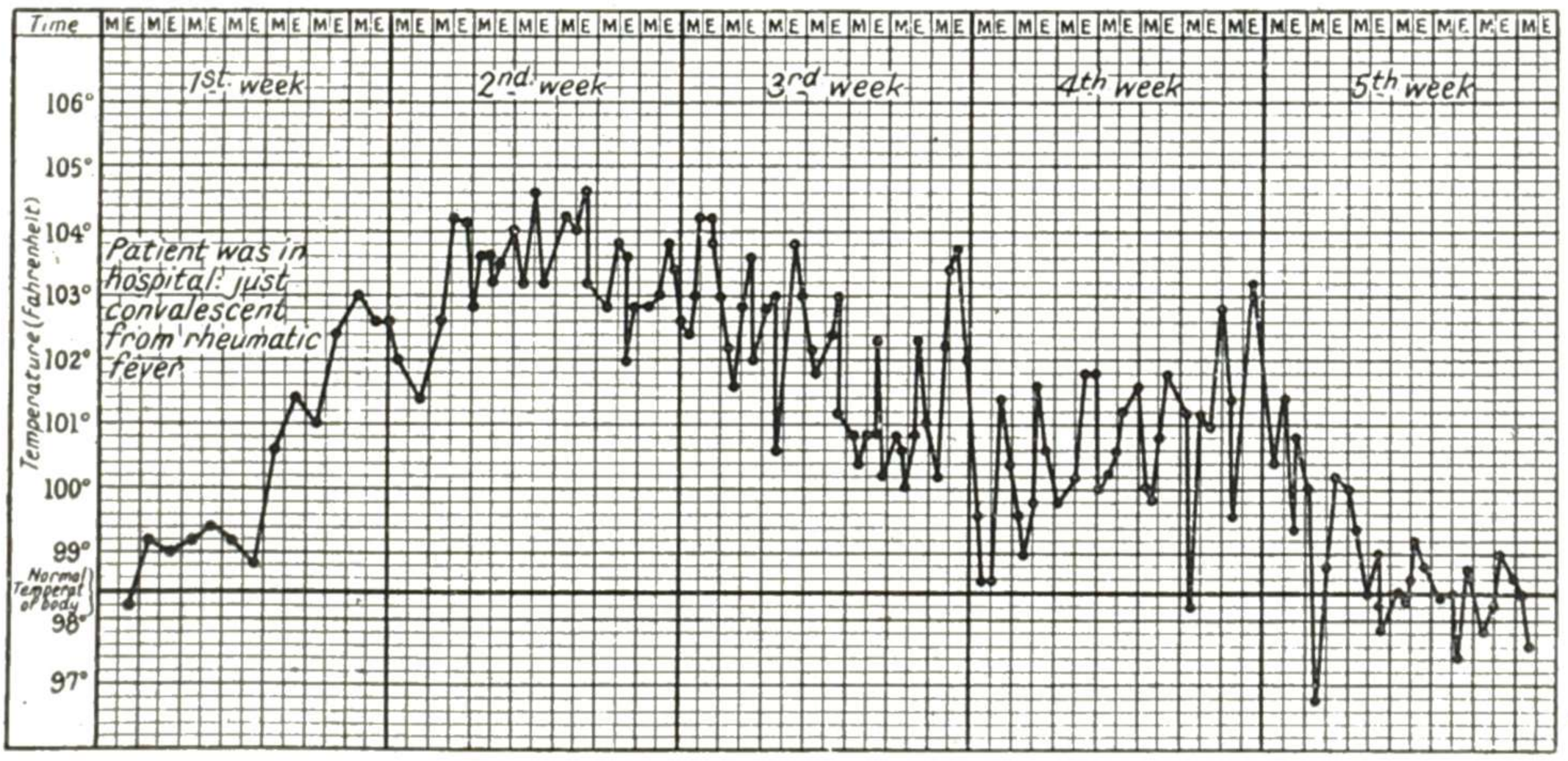

FIG. 117.—TYPHOID FEVER (typical chart), Henry H——, æt. 22, was in hospital when he developed typhoid fever. There was an apathetic mental condition, feeling of profound illness and headache, watery pea-soup stools, and bronchial catarrh. The chart shows the continued character of the pyrexia in the second and third weeks, with gradually increasing remissions in the fourth and fifth weeks.

Diagnosis.—The chief clinical features are the insidious onset and prolonged course of the illness, the profound prostration, the temperature chart and slowed pulse rate, the rash and the enlarged spleen. By cultural methods the organism may be found in the blood (especially in the first week), in the stools (first to third weeks) or in the urine (third week). A blood count which shows a polymorph leucopenia in the presence of a high temperature is highly suggestive of uncomplicated typhoid. The diazo reaction is positive between the fifth and tenth days and in all but severe attacks becomes negative in the second or third week: by itself it is not diagnostic. The Widal reaction is rarely positive before the tenth to fourteenth days, and may be negative throughout: however, a positive reaction is diagnostic. Difficulty may arise in previously inoculated persons: even so in the acute stage the "O" (somatic) antigen titre rises, while the "H" (flagellar) antigen titre remains low throughout.

Undoubtedly many slight cases of typhoid are overlooked and regarded as *Febricula*. Slight cases may also be mistaken for *influenza*, which except for the more sudden advent and brief duration, much resembles mild typhoid. The other *specific fevers* in this group may also have to be excluded. In most cases of typhoid a mild *bronchitis* and *hypostatic congestion* of the lungs occurs, and nothing is commoner than to confuse this with the early stages of typhoid fever. Early headache and delirium may suggest *meningitis*, but the latter is recognised (apart from examination of the cerebro-spinal fluid) by (i.) the retracted abdomen: (ii.) the headache persists longer, and may concur instead of alternating with delirium: (iii.) signs of increased intracranial pressure and local cranial palsies supervene. (It must be remembered that true meningitis and also pneumonia occur due to typhoid bacilli.) *Typhus Fever* has a sudden onset with high fever, a greater tendency to delirium in the early stages, conjunctival injection, a rash on the fourth day which is dark red in colour and does not invade the face, and the Weil-Felix reaction is positive. *Acute Pulmonary* or *Miliary Tuberculosis* sometimes closely resembles typhoid. The positive signs of typhoid are wanting, and the presence of tuberculosis is suggested by (i.) the intermittent character of the temperature and its prolonged course; (ii.) the lung symptoms are much more marked; (iii.) the rapidity of breathing is out of proportion to the other signs of illness: and (iv.) the result of a chest X-ray. *Malignant endocarditis* is recognised by (i.) the intermittent character of the temperature (usually), often with rigors, (ii.) the cardiac signs, and (iii.) the positive blood culture. Pyæmia is differentiated by the wide range and irregularity of the pyrexia.

Undulant fever (§ 501) resembles typhoid in its insidious onset, high fever and enlargement of the spleen, but is distinguished by the patient's serum agglutinating *Brucella abortus* and having no effect on the organisms of the typhoid group. Tularæmia, which, like undulant fever, may attack laboratory workers and cause a prolonged fever, is also distinguished by an agglutination test.

Etiology.—Typhoid fever is due to the typhoid bacillus (the Eberth-Gaffky bacillus). Most epidemics are due to contamination of the water supply by sewage: especially in rural areas this is more common after a dry summer when leakage from cesspools and drains permits contamination of shallow wells. Infection has also been traced from sewage-contaminated waters to oysters and other shell-fish, to ice-creams and to the milk supply. In a patient, *all discharges from the stomach, bowels, bladder and lungs* are infective: thus nurses, and friends of patients contract the disease by handling bed-pans, sheets, and other articles contaminated by these excreta: the discharges become more virulent after standing for twelve to twenty-four hours. The urine and fæces may contain typhoid bacilli long after restoration to health: "typhoid carriers"[1] are persons whose stools have been shown to carry bacilli many years after an attack—the

[1] The best example was "Typhoid Mary," who during her employment as cook in different households and institutions initiated 10 outbreaks with 51 cases.

original nature may not have been recognised. The gall-bladder harbours the organisms which are periodically discharged into the bowel and thus the stools are periodically rendered infective. Second attacks are rare but an attack of typhoid does not protect against a subsequent attack of paratyphoid fever. The greatly diminished incidence of typhoid fever in recent years has been attributed partly to the immunisation of a large proportion of the susceptible population during the two Great Wars, partly to the more careful supervision of water and milk supplies, and to chlorination of any water which may be suspect. The toxins of typhoid seem particularly prone to produce weakness of muscular action: hence the extreme asthenia of voluntary muscle, the myocardial weakness, and the hypotonia of involuntary muscle.

Prognosis.—The case mortality varies in different epidemics from 5 to 20 per cent. It is always a serious disease on account of the numerous complications, prolonged course, and its exhausting nature. The usual duration is four or five weeks, though it can vary from ten days to six weeks even without relapses which are by no means infrequent. Many fatal issues would be avoided if it were remembered that slight attacks require just as much care as severe ones, being liable to hæmorrhage or perforation if the patient does not remain at rest. The prognosis is more favourable between 5 and 10 years of age. It is more serious (i.) in children under 3 and persons over 60: (ii.) when the fever is severe and continued, especially when it remains above 104° F. throughout the second week and especially if the diurnal remissions do not increase, as they should do, in the third week: (iii.) when there are vomiting (except at an early stage), urgent diarrhœa at any time, severe tympanites or hæmorrhage, or marked delirium. A sudden fall in temperature suggests hæmorrhage, or perforation with peritonitis. The most common *complications* are: (1) Pneumonia and pleurisy. Especially towards the end of the third week (2) Hæmorrhage due to the separation of the sloughs from Peyer's patches, occurs in 8–10 per cent. of cases, and for the same reason (3) Perforation with local or general peritonitis is a still more serious complication. Peritonitis arising in typhoid fever is often unattended by the pain so characteristic of that disorder. Its occurrence can then only be recognised by (i.) vomiting; (ii.) great aggravation of the already existing prostration; (iii.) a small rapid pulse (120 to 140); (iv.) immobility followed by distension of the abdominal wall; (v.) sudden frequency of micturition; (vi.) a sudden fall, usually followed by a rise, of the temperature; (vii.) a rising leucocytosis; (viii.) the *facies Hippocratica.* (4) Myocarditis is present to some extent in every case: it can be severe and associated with a general circulatory failure of toxæmic origin, which may prove fatal. (5) Other complications are thrombosis of the femoral or popliteal vein, local suppurations and inflammations, such as parotitis, periostitis, cholecystitis, cancrum oris, and laryngeal ulceration; and, rarely, arthritis leading to dislocation, typhoid spine due to spondylitis (§ 457, 15) and rupture of the rectus abdominis, simulating intestinal perforation. As

sequelæ multiple abscesses, various psychoses, polyneuritis, phthisis, and miliary tuberculosis may occur.

The temperature may rise again after convalescence has begun. Such *recrudescence* may be due to too liberal a diet, excitement, or constipation; or it may be due to a *relapse*, which occurs in about 10 to 15 per cent. of all cases. There is usually an apyrexial interval of about five to ten days, but sometimes the temperature has never dropped satisfactorily. The second attack is usually less severe and shorter than the first, but there may be fatal relapses. As many as five relapses may occur, though more than two are rare in this country.

Treatment.—There are five indications: (*a*) to conserve the energy of the patient, and in the third and fourth weeks to take every care to prevent hæmorrhage or perforation by skilled nursing; (*b*) to give a suitable diet, and avoid meteorism; (*c*) to use such drugs as will support the strength of the patient and reduce diarrhœa and flatulence; (*d*) the use of serum-therapy; and (*e*) to use barrier nursing in its strictest sense. (*a*) *Bed rest* is of the highest importance, and as the patient will probably be in bed for at least six weeks, a sorbo type of mattress is most comfortable. During the third and fourth weeks when the dangers of hæmorrhage and perforation are greatest, the patient should not be allowed to turn himself in bed: perforation may occur if a patient is allowed to raise himself as in changing a draw-sheet. It is a great mistake, however, to keep the patient continually on the flat of his back, as this tends to induce congestion of the lung bases and also the formation of bed sores—he should be carefully turned every two hours by day. Especial attention should be paid to the care of the skin and of the mouth. (*b*) The *diet* now given is of higher nutritive value than used to be the custom, and this undoubtedly supports the patient's strength. Milk in quantities of 2–3 pints a day is the staple diet: it should be sufficiently diluted and barley water, lime-water or sodium citrate (gr. 2 to 1 fl. oz.) added to prevent the formation of curds. Custards, junkets, jellies, eggs, chicken broths, clear soup, beef tea, chocolate and cocoa are nutritious and non-putrefactive: toast, cereals, plain biscuits, and boiled or steamed pounded fish are added if the patient can digest them. Predigested foods such as Benger's are an aid to promote assimilation, especially if the tongue is heavily furred, and pepsin is said to be of service. (*c*) Chemotherapy with chloromycetin may prove effective—give G. 4 initially, then G. 3 daily and when the patient is afebrile follow with decreasing doses. Cardio-vascular weakness is dealt with by injections of nikethamide, and prostration with a very feeble pulse is aided by cortin (10 c.c. twice daily intramuscularly), with an initial intravenous dose of ascorbic acid 1 G. If profuse, the diarrhœa must be checked by enemata of starch and opium (℥ 30 of tinct. opii to fl. oz. 3 of mucilage of starch); or liq. morphinæ ℥ 20, with dilute sulphuric acid ℥ 10, every three or four hours. If these fail, give acetate of lead, bismuth carbonate, or bismuth salicylate. Constipation should never be treated by purgatives, but by glycerin suppositories, liquid paraffin

by mouth, aided by cautious small enemata. If the abdomen is tympanitic, reduce the amount of food and of milk and give it peptonised or more diluted: a flatus tube or a small turpentine enema may help. Hæmorrhage should be checked by the administration of opium, absolute rest must be enjoined, and the amount of the diet temporarily reduced. For perforation, immediate laparotomy and suture of the bowel is usually necessary. (*d*) Felix has recently introduced a serum which has given good results; for adults the dose is at least 50 c.c., followed by two doses of 25 c.c. intramuscularly, daily. (*e*) Typhoid patients may be treated in a general hospital ward, but great care taken by everyone to prevent spreading the infection: the doctors and the nurses must wear gowns, and when handling bedpans and urinals, rubber gloves. The stools must be immersed in and stirred with liq. cresol sap. (lysol) 10 per cent., which is left in contact for 12 hours: the urine and all other excreta, all utensils, bed linen, and the separate thermometer must be disinfected for several hours with 5 per cent. phenol.

Typhoid carriers arise in those persons who harbour the bacilli and excrete them at regular or at irregular intervals. There may previously have been a recognised attack of typhoid, or such may not have occurred, the disease having been mistaken for influenza, etc. Such persons are most dangerous when they handle food, milk or water supplies. The carrier state may be temporary or permanent: for its detection bacteriological testing of the stools and urine is necessary. If the Vi- (Virulence) agglutinins are present, and particularly if with tests at three-monthly intervals the titre is rising, a carrier state must be strongly suspected, and a considerable number of specimens of stool and urine examined. Urinary carriers respond well to sulphonamides, but fæcal carriers may be incurable; cholecystectomy cures 75 per cent. of cases.

Prophylactic Treatment is based on a knowledge of the origin of the disease and its mode of introduction into the system via the mouth. The incidence of typhoid in a community is a fair index of the purity of its water supply: when any doubt arises, and especially in rural areas, the water should be boiled or chlorinated. The carrier state must be carefully searched for, and preventive measures taken to ensure that such persons do not handle food, water or milk. Preventive vaccination, originally introduced by the late Sir Almoth Wright, has proved an established success, as was well exemplified in the fighting forces during the last two Great Wars (for the method, see § 521). The vaccine is usually given hypodermically, but several observers have claimed that oral administration is equally effective. Felix has prepared a particularly efficacious vaccine containing Vi and O antigens. In any case vaccine therapy is not effective in the treatment of typhoid fever.

Paratyphoid Fever is due to infection by B. paratyphosus A, B or C. Paratyphoid A is almost unknown in England and Holland, and is uncommon in Germany, but is common in France, Italy, the Balkan countries, Soviet Russia and the tropics. Paratyphoid B is now commoner than

typhoid fever in this country. Paratyphoid C, which is much less frequent, is prevalent in the Middle East and Mediterranean. Paratyphoid has assumed such prominence that inoculation against the A and B paratyphoid fevers has to be carried out as carefully as against typhoid fever. A mixed vaccine (T.A.B.) is now usually employed (§ 521). It is best distinguished from typhoid fever by cultural examinations and the Widal test. On clinical grounds, differentiation in any individual case is at the best uncertain. However, in paratyphoid infection, the disease tends to be rather less severe, and to run a shorter course : in fact, the temperature may return to normal within 2–3 weeks. It has often been remarked that paratyphoid infection tends to give a much greater profusion of the eruption on the trunk, and that the spots tend to be more obvious as they are darker in colour : but often no rash is visible at any stage of an attack. Intestinal symptoms and complications are not so frequent, in consequence of which the mortality rate in some epidemics is only 1–2 per cent. Even so, it is most unwise to presume on this, and treatment to guard against intestinal hæmorrhage and perforation must be just as strict as in typhoid fever. Mixed infections of two or more of the varieties of enteric fever are not uncommon. *Treatment* is as for typhoid fever.

Enteric Fever in Infants and Young Children usually does not conform to the clinical picture presented above. Whether the cases occur sporadically or in epidemics, it is often necessary at first to make a tentative diagnosis of " pyrexia of uncertain origin." The onset is often sudden, and in infants the presenting symptom is that of gastro-enteritis : in slightly older children, the symptoms and signs are those of broncho-pneumonia, of meningitis, or of appendicitis, the origin of which is only established by careful bacteriological study. Even in children dying of the disease, intestinal hæmorrhage and perforation are rare. Relapses are more frequent than in adults.

§ **494.** II. **Diphtheria** is a contagious fever due to the Klebs-Loeffler, or diphtheria bacillus (§ 921). It most commonly involves the throat, but may start on or spread to the nose or larynx, and more rarely the ear, the conjunctiva, the vagina, or a wound of the skin. The organisms rarely penetrate the surface, but multiply and cause the formation of a surface coagulum (" the membrane "). Dangers arise chiefly from the absorbed exotoxins which attack especially the myocardium and the peripheral nerves : in the narrow laryngeal passages of children, obstruction to respiration is serious.

Symptoms of Faucial Diphtheria.—The incubation period is variable, but it is often two to four days. (1) The onset is usually gradual (extending over a day or two), but in some cases is more sudden. (2) There is general listlessness, *pallor*, and often headache and vomiting. A trace of albumen in the urine is common. (3) The temperature is low in proportion to the appearance of illness, and temperatures above 100° F. are unusual : in many of the worst cases the patient is apyrexial. The pulse is soft and rapid. (4) Sore throat and dysphagia, though usual,

are not always complained of by young children. For the first few hours the throat may only be congested. Within twenty-four hours one or both tonsils shows a characteristic patch of creamy-white, wash-leather-like membrane situated on an obviously congested surface, and if forcibly removed this leaves bleeding-points. The patches tend to run together, and to spread beyond the tonsils on to the fauces, soft palate, uvula and pharyngeal wall. The presence of membrane on these parts is a diagnostic feature of great value from simple tonsillitis. The size and rapidity of spread of the membrane, and the amount of œdema present, are an index of the severity of the case. (5) The membrane spreads to

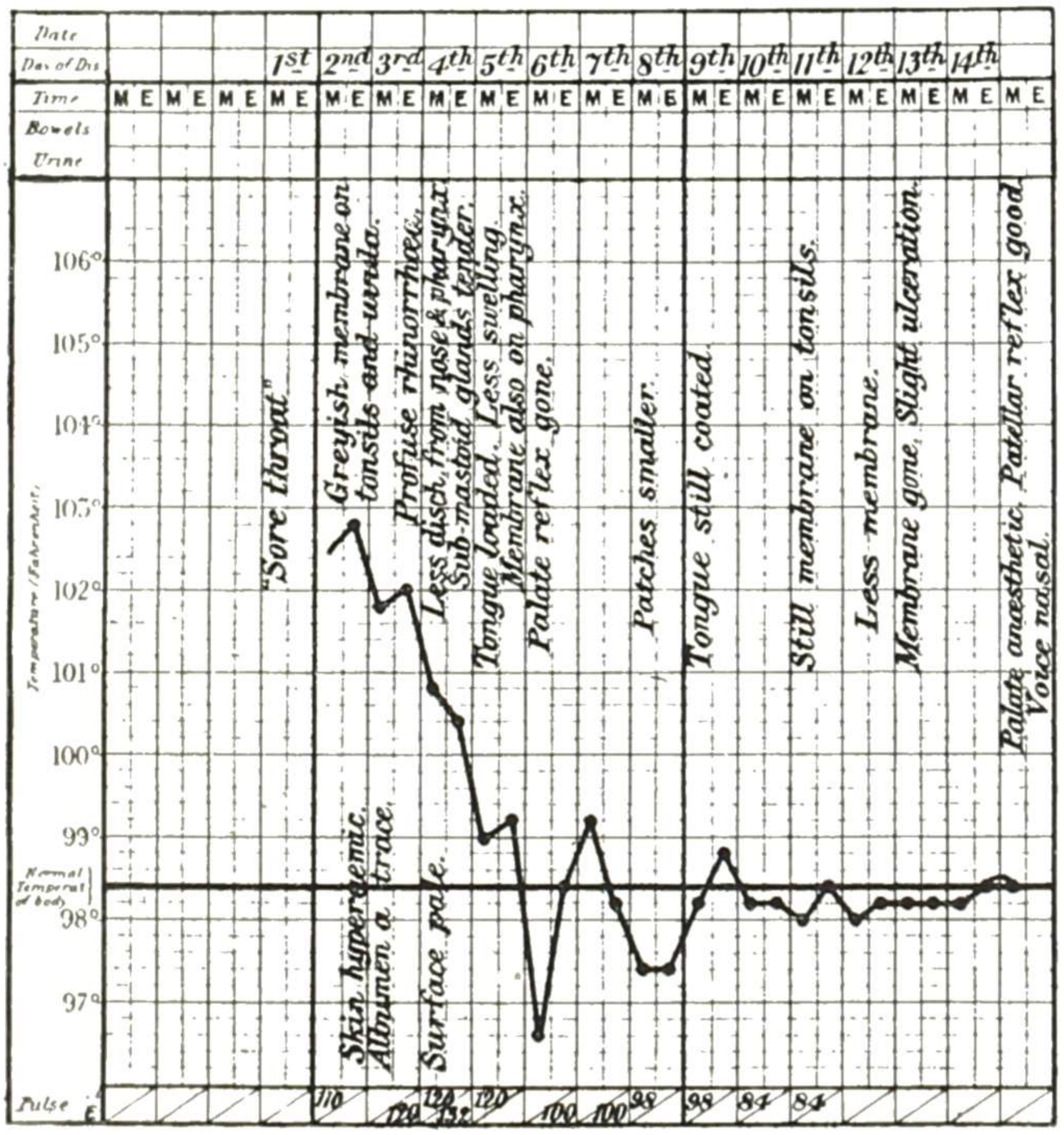

FIG. 118.—DIPHTHERIA.—Male, æt. 9. An ordinary case of faucial diphtheria without implication of larynx. The palate was still anæsthetic one month later. Not followed by paralysis. The different events are indicated on the chart.

the larynx and bronchi in certain cases, and it may spread upwards to the nose (especially in children). An ichorous discharge from the nostrils in a child lying prostrate and fretful in bed is very characteristic of severe diphtheria. (6) The glands at the angles of the jaws are enlarged even in mild cases, and the patient may complain that the neck feels stiff. When the membrane inside the throat is extensive, the glands become much more swollen, and these and the surrounding œdema may give an appearance of "a bull-neck." (7) There is often a diagnostic odour to the breath: recognition of this is most valuable, but depends a great deal on the observer's acuity of smell. In mild cases and particularly in those energetically treated by antitoxin at a very early stage, the

disease aborts in a few days and the membrane separates. In moderate and in severe cases, and especially in those who are not given antitoxin until later, the toxin may have become fixed in the tissues, and the patient's condition then undergoes a change for the worse. Even when the case appears to be mild, and is treated early, these toxic effects may arise, and so every case must be treated by strict bed rest. The three major specific effects of the toxæmia are: (8) In the first week, and in virulent cases, general toxæmia gives rise to death by the seventh day. (9) From the end of the first week and progressively during the second week, myocardial damage and failure occur. Slight cases show a rise of pulse rate, a fall in systemic blood pressure and some enlargement of the heart to the left: in more severe cases, tachycardia is marked (up to 140 per minute), the heart sounds become feeble, the blood pressure may fall to very low levels: and the resulting failure of the cerebral circulation leads to restlessness, drowsiness and coma, while failure of the right heart causes symptoms or signs of this disease (§ 55): vomiting, progressive liver engorgement and suppression of urine occur in fatal cases. Disorders of rhythm, bradycardia, heart block and electro-cardiographic changes have all been recorded. There is a tendency to recovery in a period of weeks, and the heart muscle appears to return to normal. (10) Diphtheritic paralysis is due to polyneuritis. It comes on usually in the third or fourth week, sometimes later. In order of its appearance we find: (i.) it starts in the palate, and therefore a nasal voice or dysphagia is the earliest symptom, and fluids are returned through the nose. (ii.) Next we may get loss of accommodation, with blurred vision on attempting to read. A squint and other cranial nerve pareses are unusual. At this stage loss of the knee and ankle jerks may be seen. (iii.) About the seventh to eighth weeks polyneuritis of the limbs is seen (§ 791). The attitude and gait in children may be characteristic, the little patient walking with a shambling gait, drooping head and shoulders (from weakness of the neck and trunk muscles) and marked foot-drop. (iv.) Especially in severe cases, there may be paralysis of the diaphragm, pharynx and intercostals: the abdominal reflexes are lost only in the severest cases. Temporary involvement of the pyramidal tract, with a positive Babinski, and various forms of motor and sensory impairment occur, such as paraplegia, ataxia, numbness, formication, astereognosis and loss of vibration sense.

Other Varieties of Diphtheria occur in conjunction with faucial diphtheria or alone. The varieties are: (1) Laryngeal diphtheria (membranous croup). *Symptoms.*—The patient is usually under 5 years of age and (i.) there is a croupy cough with a hoarse cry: (ii.) there is inspiratory stridor, followed soon by (iii.) symptoms of laryngeal obstruction. These may be continuous, or intermittent, with inspiratory recession of the ribs, and of the suprasternal notch accentuated by the use of the accessory muscles of respiration, and some cyanosis. (iv.) The child is pale and ill, with a low grade temperature and other signs of diphtheritic toxæmia. (2) Nasal diphtheria, when it occurs alone, is a mild disease of young

children (§ 179. V). (3) The auditory meatus, the conjunctiva, the vagina, and wounds of the surface may harbour diphtheria bacilli. Care must be taken to prove these organisms are pathogenic, and not diphtheroids which are normal inhabitants of mucous membranes and of the skin.

The *Diagnosis* of diphtheria is made by finding the Klebs-Loeffler bacillus in swabbings from a characteristic membranous lesion. In cases of doubt a virulence test must be performed. The diagnosis of the sore throat caused by tonsillitis, scarlet fever, and diphtheria presents certain difficulties, and is given in Table X, § 156. *Follicular tonsillitis* is distinguished by the absence of the definite wash-leather-like patches on the fauces, nasal, or laryngeal passages, and usually the presence of higher fever. There may also be a history of previous attacks, though an inference based on this may be very misleading. Albuminuria, too, is much less common. *Scarlet fever* is distinguished by its abrupt onset, higher fever, rash, strawberry tongue, and generally the absence of membrane from the throat. Simple "*croup*" (catarrhal laryngitis) is distinguished by the history of previous attacks and the absence of patches in the throat, but this is often the case in true diphtheria, in which case an appeal must be made to bacteriology. *Membranous croup* is always diphtheritic. *Vincent's Angina* is distinguished by the bacteriological examination (§ 155*d*), and the fact that the patch is usually depressed instead of being raised above the surface. For differentiating *agranulocytic angina* and the anginose variety of *glandular fever*, see § 155*e*, *f*.

Etiology.—The disease is due to the diphtheria bacillus (*Corynebacterium diphtheriæ*), of which three strains are now recognised, *gravis*, *intermedius* and *mitis*: generally speaking, the gravis strains are the most virulent and produce most toxin, whereas some mitis strains are avirulent to man. The infection is spread by droplet infection and by formites—cups, spoons, etc.: occasionally it is conveyed by milk. Diphtheria carriers may be the cause of local epidemics.

Prognosis.—The case-mortality varied widely in different epidemics, and used to be 25 to 50 per cent.; since the introduction of serum therapy it has fallen to 3 or 4 per cent. Faucial cases in adults are usually mild. During the first week, the disease in little children is often fatal, by the spread of membrane to the larynx. The prognosis is greatly improved when adequate doses of serum are given in the first twenty-four hours: every few hours' delay, especially in virulent cases, increases the risk of complications and lessens the recovery rate. *Untoward Symptoms.*—The prognosis is unfavourable in severe cases, especially when (i.) fœtor of the breath is marked; (ii.) periglandular œdema forming a "bull-neck" is present; (iii.) in the presence of hæmorrhage or epistaxis, purpuric cases being almost invariably fatal; (iv.) marked albuminuria is a bad sign. Other unfavourable symptoms are (v.) a low temperature with severe local lesions; (vi.) when the membrane is extensive, thick and persistent, especially in young patients; (vii.) rapid extension of the membrane to the larynx, leading to croupy cough, dyspnœa and cyanosis. The appear-

ance of a well-marked serum rash within a week of injecting antitoxin is a favourable sign (J. D. Rolleston). *Complications.*—(1) Bronchopneumonia, formerly so frequent in laryngeal cases, now attacks only 4 per cent. since modern treatment is available. (2) Nephritis and dropsy during convalescence are very infrequent, and permanent lesions of the kidney are rare. (3) Otitis media is not uncommon. (4) Embolism secondary to cardiac thrombosis may occur and give rise to hemiplegia or gangrene of a limb from blocking of a main artery.

Treatment.—The indications are (*a*) to neutralise the toxin ; (*b*) to keep the patient at rest in order to diminish the effects of myocarditis and polyneuritis ; (*c*) to inhibit the local process and (*d*) to treat complications. (1) *Antitoxin* will neutralise diphtheria toxin only if it has not become fixed in the tissues. It is therefore vitally important to administer a sufficient dose immediately the condition is suspected or diagnosed, without waiting for bacteriological confirmation. Doses and methods are given in §§ 521 *et seq.* (2) Heart failure is liable to occur about the tenth to the fourteenth day in severe cases. From the commencement of the disease, therefore, the patient must be kept lying down and at *strict rest in bed*—one pillow at the most being allowed for comfort : during this time he must be fed and washed. This position is maintained even in mild cases for two weeks, and for longer in more severe cases, and any subsequent activity will be curtailed immediately evidence of myocarditis shows itself. In a severe case, when myocarditis is likely to be followed by polyneuritis, it is not unusual for the patient to have to remain in bed for 2–3 months. Extra activity is only allowed very gradually. Glucose should be freely given by mouth ; in severe or malignant cases, and in the presence of vomiting, 50 c.c. of 50 per cent. dextrose should be given intravenously once or twice daily. Restlessness must be combated by sedatives and even by small doses of morphia. (3) Antitoxin has rendered *local* treatment by syringing, spraying or swabbing unnecessary in the great majority of cases, especially in young children. Older patients, however, may derive comfort by having their throat syringed by some pleasant lotion such as one containing tinct. lavandulæ or tinct. myrrhæ. Disinfectants are not required. (4) When the larynx is involved steam inhalations and hot applications to the neck give much relief. Tracheotomy or intubation will have to be considered : the results are more satisfactory when *done early*, and all laryngeal cases should be closely watched for the epigastric retraction during inspiration which indicates severe inspiratory obstruction. The instruments must always be at hand and sterile for immediate use, and oxygen may be helpful. In the United States good results are reported from the use of laryngeal suction, by means of a catheter attached to a suction machine and passed through a laryngoscope. The Drinker or Paul-Bragg apparatus is of great use in replacing or augmenting the failing respiratory mechanism in diaphragmatic paralysis. *Freedom from infection* is proved by three negative cultures for C. diphtheriæ, taken from the nose and the throat at not less than two-day intervals. *Prophylaxis.*—A

carrier of virulent C. diphtheriæ may be (1) a person who has just recovered from an attack (convalescent carrier), or (2) one who is innocently harbouring the infection. Especially in the latter the virulence of the organism must be proved. When a carrier state is persistent, any local contributory cause should be treated: it will often respond to systemic penicillin, or in faucial cases to tonsillectomy.

The question of susceptibility to diphtheria is settled by the Schick test. This is described, together with the method of prophylactic immunisation, in § 521, p. 655. Although diphtheria may sometimes occur in the immunised, the attack in the great majority of such cases is mild and fatalities are very rare.

§ **495.** III. **Influenza** is an acute fever which, although endemic in the winter and spring months, is liable to break out in epidemics. It has been known for at least five centuries, and certain of the great pandemics (as in 1918–19) have been attended by a considerable mortality.

Symptoms.—(1) After an incubation period of one to three days, the patient's temperature rises in a few hours to 102°–104°. The onset is frequently attended by severe headache, pain behind the eyes, shivering, anorexia, and pains in the limbs and back which form such a characteristic feature of influenza. (2) The pulse rate is often relatively slowed in proportion to the temperature, and a true bradycardia may occur. (3) The constitutional symptoms, malaise and prostration are out of all proportion to the pyrexia and to the local signs. (4) Catarrh usually accompanies the fever—*i.e.*, there is some redness and watering of the eyes, nasal catarrh, sore throat and a dry cough. (5) The face is flushed and the tongue heavily coated. (6) *Eruptions* of erythematous or urticarial type occur. (7) Some cases present only the above symptoms and signs: but *types of the disease* occur in which different systems of the body are attacked. Some of the symptoms thus presented are of the nature of complications: (i.) The *respiratory tract* is very frequently involved, and laryngitis, tracheitis, bronchitis and pneumonia may arise. (ii.) The *heart* may be affected by myocarditis. (iii.) Involvement of the *alimentary* tract may be evidenced by gastro-enteritis, diarrhœa, vomiting, etc. ("gastric influenza"). (iv.) The *nervous system* may possibly be attacked, and encephalomyelitis occur. Cases of disseminated sclerosis and encephalitis lethargica are attributed to this disease. Influenzal meningitis is due to Pfeiffer's bacillus and not to true influenza.

Diagnosis.—The term "influenza" is often improperly applied to what is really febrile catarrh. In addition to the absence of the influenza virus in febrile catarrh, this clinical distinction is drawn by C. H. Stuart Harris: (1) Premonitory symptoms, such as coryza, sore throat or cough, are uncommon in influenza, in which the onset is sudden, whereas febrile catarrh starts insidiously with a "cold" and fever. (2) The first symptoms of influenza are constitutional rather than respiratory. (3) The cough in influenza is short and dry; in febrile catarrh it is paroxysmal, painful and often productive. (4) Sore throat is constant in febrile catarrh, but is not a feature of influenza. (5) Laryngitis is rarely severe in

influenza, but a very hoarse voice is common in febrile catarrh. (6) Bronchiolitis and pneumonia are the characteristic complications of influenza, and basal bronchitis and broncho-pneumonia of febrile catarrh. Leucopenia is usual in uncomplicated cases.

Etiology.—The agent responsible is a virus, of which two varieties, A and B, have so far been identified. Wilson-Smith, Andrewes and Laidlaw have reproduced influenza in ferrets by intranasal installation of filtrates of throat and nose washings containing the virus from influenza patients, and have found that mice are susceptible to the virus of human and swine influenza, and that this virus can be retransmitted to man. The virus can be grown on the developing chick embryo, and the serum of human convalescents contains specific virus-neutralising antibodies. Pfeiffer's bacillus is not causal, but this organism, hæmolytic streptococci or staph-aureus are responsible for many of the complications. One attack confers no immunity: old and young, rich and poor are attacked alike.

Prognosis.—The case-mortality is about 1 per cent. among the old and young together. In middle-aged and elderly people the respiratory type is very apt to end fatally with pneumonia, and undoubtedly many cases presumed to be primary pneumonia are really secondary to influenza. It is fatal only through its complications. The disease itself is usually trivial, and the patient soon recovers. Relapses are not infrequent.

Complications are chiefly respiratory, and include sinusitis, otitis media and mastoiditis, bronchitis and broncho-pneumonia. These are caused almost entirely by the associated secondary infections. Relapses are common. The *sequelæ* are often more troublesome than the disease itself: (i.) There is a neuro-vascular asthenia, causing weakness in the legs, tachycardia or bradycardia, palpitation, flushings, faintings, perspiration, dyspnœa, and the like. (ii.) Anxiety states, depression, neurasthenia, neuritis and neuralgia may be very persistent. Insomnia can be very troublesome.

Treatment.—There is no specific treatment. During the attack, and for several days after the temperature has become normal, the patient should be kept in bed in view of the sequelæ: aspirin, sodium salicylate and codein will reduce the fever and lessen the pains in the limbs. For the complicating infections, the sulphonamides and/or penicillin are most useful. *Prophylaxis.*—It is well to keep elderly people away from infection during an epidemic. A patient is not infectious to others forty-eight hours from the onset, unless pneumonia ensues, when infection can be transmitted up to 6 days. The prophylactic value of vaccines has not yet been substantiated.

§ **496.** IV. **Rheumatic Fever, Pneumonia, and other Inflammatory Disorders,** which usually present well-marked **local manifestations.**—The three groups of fevers just described are those commonly met in England, in which the pyrexia may run a continued course, and which have no eruption during the first four days. But it must not be forgotten that

certain inflammatory disorders may give rise to pyrexia of a continuous type, and that the usual local signs of these disorders may be absent, at the time when the patient is first seen. It will be well, therefore, to mention those which might be mistaken for an acute specific fever.

(*a*) OBSCURE (so-called) LOCAL [1] INFLAMMATORY DISEASES are mostly met with as complications secondary to fevers. They can usually be detected by a thorough examination of all the organs in the body (§ 473). Nevertheless, certain cases of (1) *pericarditis* or *malignant endocarditis*, or (2) *pneumonia*, *pleurisy*, or *empyema*, may be latent—*i.e.*, the usual physical signs may occasionally be wanting or overlooked. (3) Various affections in or around the *throat, nose and ear ;* (4) some *abdominal* disorders, such as cholecystitis, pyelitis, deep-seated abscesses (hepatic, subphrenic, perinephric, tubal), inflammation of the mesenteric glands or pancreas, etc. ; (5) certain rare cases of *sarcoma* and *carcinoma* ; or (6) inflammation of the *meninges*, tuberculous or epidemic, may also give rise to an elevation of temperature sometimes unattended by marked local symptoms ; (7) *parasitic infections;* trichinosis, actinomycosis. In obscure cases of long-continued fever the causes to be suspected are pulmonary tuberculosis, typhoid and undulant fever, deep-seated abdominal abscesses, endocarditis, Hodgkin's disease and syphilis (cp. §§ 516 and 517).

(*b*) Certain GENERAL INFLAMMATORY DISORDERS are attended by pyrexia, which may similarly give rise to difficulties in diagnosis. (1) In *rheumatic fever* and *acute gout* the pyrexia is nearly always continuous. The joint lesions are the cardinal feature in these cases ; but it must not be forgotten that acute rheumatism may commence with inflammation of the pericardium (the structure of which very much resembles that of a joint), and that the joint lesions may not be apparent for several days. (2) There are several conditions special to infancy and childhood which are attended by continued pyrexia : (i.) *Infantile paralysis* (acute anterior poliomyelitis) is attended at its outset by a considerable rise in temperature, which may last for several days, and be accompanied by restlessness, peevishness, etc. ; (ii.) *meningitis*, tuberculous or epidemic. (3) Septicæmia, and see § 515. (4) Certain blood diseases, especially acute leukæmia and pernicious anæmia, may for a time be overlooked. (5) Examination of the urine may reveal bacilluria, an unsuspected cause of pyrexia. (6) *Constipation* also may cause fever. (7) *A nervous or hysterical pyrexia* has been described, and I have seen the temperature go up in an erratic manner, at odd times, in nervous subjects. But while admitting that the nervous system plays a very important part in the production of fever it is difficult to prove that there is not a compound cause in operation in such cases. Only a thorough *post-mortem* and bacteriological examination would enable us to be certain that none of the many obscure foci of inflammation above mentioned were present.

[1] The word " local " is here used in a qualified sense. Many of these diseases with local manifestations are now known to be due to a general infection.

§ 497. V. **Whooping Cough** (Pertussis) is an acute specific infectious disease characterised by an initial catarrh, and usually followed by paroxysmal attacks of coughing, succeeded by a long noisy inspiration (or whoop) and usually vomiting. The disease is most common in those under five years of age, but adults are not exempt.

Symptoms.—Following an incubation period of 7–14 days there is (1) a preliminary *Catarrhal Stage* which is apt to be overlooked unless enquired for. Running from the nose and sometimes from the eyes is attended by malaise and a low-grade temperature. Soon a short dry cough develops and becomes more persistent, and the individual coughs become grouped together. This catarrhal state lasts up to a week or more, and is followed by (2) *Paroxysms of Coughing.* (i.) These are more noticeable at night and vary considerably in severity. In milder cases there are a series of explosive coughs in rapid succession, followed by a long-drawn inspiration. In typical cases the explosive coughs follow one another until the child has largely emptied the lungs of expired air; and this is succeeded by a loud inspiratory crow or *whoop*, through the narrowed chink of the half-closed glottis. One attack may succeed another, punctuated by a series of whoops, until the child manages to dislodge and cough up a small piece of tenacious mucus, often with *vomiting*. In the process, the face and eyes become more and more congested, and the lips cyanosed, and when the attack is over there is temporary exhaustion. (ii.) The onset of an attack is often recognised by the child who runs to his mother for comfort: attacks are made more frequent by food and by any excitement. (iii.) As a result of the straining cough, the face remains somewhat swollen between the attacks; and subconjunctival hæmorrhages, epistaxis, and a blood-streaked sputum may occur. (iv.) The number and severity of the paroxysms increases to a maximum which is maintained for a week or more, and then starts to decrease. The whoop gradually disappears, but the paroxysmal cough persists for weeks or months after the acute phase has passed. (v.) The temperature is lower than in the catarrhal phase, unless complications ensue, but usually there is some tachycardia: in milder cases the child is apparently quite well between the attacks of coughing, although a puffiness of the face may persist. (vi.) There are no characteristic physical signs in the lungs, and bronchitic signs are generally not as numerous as the severity of the cough would suggest. (vii.) The disturbed sleep and the difficulties of feeding cause considerable exhaustion even for weeks or months. (viii.) There is a tendency for the whoop to return on taking a fresh cold, for months or years, without any return of the original infection.

The clinical *varieties* are: (1) The disease passes through the catarrhal stage to that of the paroxysmal cough, but whooping never eventuates: even in the absence of whooping, repeated paroxysms of coughing succeeded by vomiting, render the diagnosis almost certain. (2) In some adults, and when broncho-pneumonia supervenes in the catarrhal stage in children, the cough may be spasmodic without being paroxysmal.

(3) In one atypical form in infants, attacks of sneezing or hiccough replace the paroxysmal cough.

The *Diagnosis* is usually simple during an epidemic, but otherwise the early catarrhal symptoms may be mistaken for *coryza*. Tuberculosis or other causes of *enlargement of the tracheo-bronchial glands* gives rise to a paroxysmal cough, but the whoop is absent. In the first stage of the disease there is a leucopenia, but during the second stage there is a leucocytosis usually ranging from 15,000 to 27,000, with 70–80 per cent. of lymphocytes. The erythrocyte sedimentation rate is slightly retarded or normal in uncomplicated cases, but rises with any complication. Isolation of *H. pertussis*, either by the cough plate method, or by inoculating a penicillin plate of Bordet-Gengou medium from a post-nasal swab, is the most certain means of diagnosis early in the disease, and is of particular value in atypical and abortive cases.

Etiology.—Bordet and Gengou found that the causal organism is a cocco-bacillus (*Hæmophilus pertussis*) which is most abundant in the respiratory mucus in the catarrhal stage.

Prognosis.—With the decrease of virulence of diphtheria, scarlet fever and measles, whooping cough has become one of the most serious of the specific diseases of childhood, and as such is now compulsorily notifiable in England and Wales. The immediate prognosis depends particularly on the age of the child, as it is more likely to be fatal under one year: otherwise on the severity of the attack, and especially on the occurrence of secondary infections with a hæmolytic streptococcus, pneumococcus or H. influenzæ: then a serious *complication* is broncho-pneumonia, the importance of which has lessened with the advent of chemotherapy. Convulsions in infancy are more liable to occur if there is a tendency to infantile tetany. Spasm of the glottis may be the cause of sudden death. Other complications include cerebral or retro-bulbar hæmorrhages, otitis media, right-sided cardiac dilatation; an ulcer under the frenum of the tongue is due to the forced protrusion against the teeth in the act of coughing. Among the *sequelæ* there is a particular tendency for broncho-pneumonia to be followed by fibroid lung and bronchiectasis; whooping cough may reactivate a dormant tuberculous infection in the chest: and herniæ or prolapse of the rectum are seen.

Treatment.—The child should be nursed in an airy room, with considerable bed spacing from other children to prevent secondary infections being spread from the one to the other. Food should be in small quantities at short intervals, and if a feed is vomited, another immediately after is less likely to set up a paroxysm of coughing. Belladonna is the most useful drug, and aureomycin (given early in an attack) is on trial: children will stand ℥ 10–15 of tinct. belladonnæ if the dose is increased gradually: it may be usefully combined with small doses of chloral and of bromide. Antipyrin, ephedrin and phenobarbitone (gr. $\frac{1}{12}$ at 3 months, gr. $\frac{1}{6}$ at one year t.i.d.) have been advocated. Broncho-pneumonia calls for the use of the sulphonamides and/or penicillin to combat secondary infections:

unfortunately these drugs have no effect on the causal organism. For convulsions, a hot mustard bath or lumbar puncture is most successful: chloroform inhalation may be needed. A period of *isolation* of four weeks from the onset of the whoop is sufficient, but infectivity does not necessarily last as long as this, and many cases can be proved to be no longer infectious after three weeks—by exposing three successive cough plates at intervals of one to two days. The value of vaccines in treatment is not proven, but 10–20 c.c. of convalescent serum is of distinct value in the initial catarrhal stages, or in *prophylaxis*. For this, a vaccine of Phase I organisms is also of value in doses of 5, 7 and 10 billion organisms at weekly intervals above the age of 10 years, the dose being one-fifth of this under one year.

§ 498. VI. **Mumps** (**Acute Epidemic Parotitis**) is an acute febrile infectious disorder characterised by inflammatory swelling of one or both parotid glands. The period of incubation is usually 17–18 days, and in exceptional cases up to 4 weeks.

The *Symptoms* usually commence with (1) moderate fever (102° F.). This usually commences insidiously, but may start with a rigor. The pulse is often slowed. (2) There are constitutional symptoms with headache, malaise, anorexia and constipation. (3) Attention may be drawn to the neck by a complaint of sore throat and stiffness in the neck. (4) When looked for, and especially in an epidemic, there is at an early stage, redness around the mouth of the parotid duct on one or both sides. *Characteristic symptoms* appear on the first to the fourth day with (5) pain and swelling of one or both parotid glands. Usually one side is first affected, followed by the other in a day or two: both may be affected together, or one side may escape altogether. The glands are acutely tender, the skin over them is stretched, and trismus may be so marked as to prevent the mouth being opened more than a quarter of an inch. (6) The secretion of saliva is usually suppressed, the mouth becomes dry and the tongue remains furred. (7) The local pain and the deficiency of saliva make swallowing a very painful and difficult process. (8) The blood shows a leucocytosis chiefly due to an increase of lymphocytes. The temperature subsides in three or four days to a week, constipation becomes less troublesome, and the glandular swellings slowly subside, unless complications ensue.

Varieties.—Particularly in epidemics, the submaxillary and even the sublingual glands are also affected. Sometimes the parotid glands escape, and one or more of the other salivary glands are alone involved.

Diagnosis.—Enlargement of a *pre-auricular lymph gland* is unilateral due to some local source of sepsis, and does not involve the deep part of the gland. *Simple and suppurative parotitis* (§ 9) are associated with oral sepsis such as occurs in typhoid and typhus fever, and in abdominal and cachectic states; mumps is almost always bilateral and very rarely suppurates. Care must always be taken to exclude "the bull-neck" of *toxic diphtheria*; *Mikulicz' Syndrome* is usually mistaken for mumps

(§ 9). In the *uveo-parotid syndrome* the parotitis is harder and less obvious, and only the pre-auricular part of the gland is involved.

Etiology.—It is almost entirely confined to children and the young between 5 and 25. It is rare in the very young and very old, but is often epidemic and runs through a school. The infective agent is a filterable virus spread by droplet-infection from the nasal secretions and saliva of patients: the disease can be reproduced from these sources in monkeys, and is most infectious at the end of the incubation period. Death is very rare. The chief *complications* are (1) orchitis, and much less often, oophoritis. Orchitis is very rare before puberty and is most frequent in young adults who are sexually active. It usually follows about 7–10 days from the commencement, when the parotitis and fever have settled. There is sudden pyrexia, with enlargement of one testicle, which becomes very tender and possibly fluctuant; the inflammation settles slowly in a week or ten days, and as usually only one testicle is involved, the incidence of subsequent sterility is low. In some epidemics there may be a swelling of a mammary gland or of a testicle, preceding or accompanying that of the parotids, and cases occur in which there is no parotitis. (2) Meningo-encephalitis is not uncommon in the presence of orchitis: most cases recover. Other complications are (3) albuminuria, most liable to occur in severe attacks and in adults; (4) pancreatitis (§ 256); (5) meningitis, usually ill-developed, but sometimes typical; (6) encephalitis; (7) neuritis; (8) otitis interna, which usually causes permanent deafness; (9) œdema of the larynx secondary to submaxillary localisation of mumps; (10) joint symptoms, usually arthralgia, but sometimes serous or suppurative arthritis. Diabetes mellitus is an occasional sequel. *Treatment.*—Rest in bed is essential until the glands have subsided and the temperature is normal: and the patient is isolated for at least a fortnight. A kaolin poultice to the neck is comforting. Feeding may of necessity be through a straw, and rarely nutrient enemata are required. Orchitis and the other complications are less likely to occur if the patient is kept in bed and the bowels freely opened: sexual stimulation of any kind should be avoided. Infectious precautions with all feeding utensils and handkerchiefs are necessary. *Prophylaxis* by injection of human convalescent serum is of doubtful advantage and has resulted in infective hepatitis.

§ **499.** VII. **Glandular Fever** (Infectious mononucleosis) is an infectious fever occurring in sporadic or epidemic form, in children and adults, probably due to a virus. After an incubation period of five to twelve days the disease shows itself in one of three fairly well-defined clinical syndromes. The GLANDULAR TYPE is the commonest, and occurs chiefly in children and young adults. *Symptoms* are: (i.) Sudden onset with fever of 101° to 103° F., often with vomiting; (ii.) transient sore throat or mild tonsillitis; (iii.) fairly severe frontal headache and limb pains; (iv.) sweating may be profuse; (v.) on the second or third day painful enlargement of the upper cervical glands, which remain discrete and tender. Sometimes they reach a considerable size, and are followed by enlargement of the axillary, inguinal, and epitrochlear glands. (vi.) Abdominal pain and tenderness, with pyrexia and vomiting indicate enlargement of abdominal glands, and may precede cervical adenitis—then appendicitis is often diagnosed. (vii.) Some enlargement of the liver

and spleen is common; (viii.) a painful cough may indicate enlarged mediastinal glands. In the ANGINOSE VARIETY a membrane is present on the tonsils and surrounding œdema is severe—simulating diphtheria. Vincent's bacilli and spirochætes are often present in the membrane. The FEBRILE FORM is most common in adults. *Symptoms.*—(i.) There is a sudden onset, with sore throat, headache and even a rigor. (ii.) Macular, papular or urticarial rashes appear particularly on the trunk, towards the end of the first week. (iii.) Glandular enlargement is relatively late—even in the third week. (iv.) Fever may be prolonged for three or even four weeks; at first remittent, it later becomes intermittent. (v.) Splenomegaly is rare. In all three clinical forms, the course of the disease may be prolonged. In the glandular variety the glands begin to decrease in 5–7 days without suppuration, but may still be palpable months afterwards: the fever often takes two to three weeks to settle and leaves considerable exhaustion. The Wassermann reaction may be completely or incompletely positive. Shortly after the commencement, the blood shows a leucocytosis between 6,000 and 20,000 per cu.mm.: the differential count reveals a large number of mature and immature mononuclear cells, which may constitute 60–75 per cent. of the total: sometimes cells of the lymphocytic variety predominate.

Diagnosis.—Owing to the difference in prognosis the diagnosis from *leukæmia* is very important. In glandular fever the onset is usually sudden, sweating is marked, the cervical glands are usually first involved, and purpura is very rare. In *acute leukæmia* there is often previous malaise, the glands in different areas enlarge simultaneously, anæmia and purpura are common, and the patient progressively deteriorates. An agglutination test (*Paul-Bunnell test*) shows the presence of heterophile agglutinins for sheep cells in the serum: it is positive in many cases of glandular fever towards the end of the first week, in a dilution of 1 in 64 (§ 924).

The *prognosis* is excellent. *Complications.*—A relapse, hæmorrhagic nephritis, or jaundice may occur.

Treatment is symptomatic and convalescence should be reasonably prolonged. The severe anginose form may respond very rapidly to sulpharsphenamine or neoarsphenamine, giving 0·30 G. to an adult on two successive days, even when Vincent's organisms have not been demonstrated: a transient acute laryngeal œdema has been reported following intravenous medication. Sulphonamides should not be used.

The remaining fevers in this group are PLAGUE, UNDULANT FEVER, YELLOW FEVER, *which are met with abroad;* CEREBRO-SPINAL FEVER, *which until recent years has for a long time been rare in this country; and* RELAPSING FEVER, *met with in epidemic form only in times of famine. In* HAY FEVER, DYSENTERY, *and* CHOLERA, *there is some disturbance of the temperature.* WEIL'S DISEASE is described in § 334.

§ 500. VIII. **Plague** (Bubonic Plague, Typhus Bubonicus, Oriental Plague, the Black Death) may be defined as a highly infectious and fatal fever, characterised by inflammatory glandular and periglandular swellings, hæmorrhages beneath the skin and from the mucous membranes. The last great epidemic in London was in 1666. Its chief epidemic centres in the present day are Northern India, China, Mongolia, and Uganda. Since 1894 there has been a pandemic over most of the civilised world, and our present knowledge of the disease has therefore greatly increased.

Symptoms.—(1) The incubation period is from two to ten days. (2) There is often a prodromal stage, with depression and pains, but usually the onset is sudden, with shivering, and fever rising to 103° or even 107° F. Mental aberration is not uncommon. Prostration is marked, and may be accompanied by vertigo, staggering gait, and lethargy, soon passing into the typhoid state. The spleen and liver may be enlarged. In some cases the speech is halting and staccato, the expression vacant, and the eyes congested; the condition is sometimes mistaken for acute alcoholism. A small vesicle, corresponding to a flea bite, is occasionally observed in the early stages of the disease; and examination of the fluid contents may reveal plague bacilli. (3) On the second or third day a tender swelling of the lymph glands (bubo) appears, the affected group, dependent on the site of the infecting flea bite, being inguinal and femoral in 70 per cent., axillary in 20 per cent. and cervical and submaxillary in