etiology of human tuberculosis, as usually the flesh is thoroughly cooked before eating. The possibility, however, must be borne in mind, and it would certainly be safer in the interests of a community to confiscate the carcasses of all tuberculous animals. Experiments in Bollinger's laboratory show that the flesh of tuberculous subjects is very infective to guinea-pigs.

6. **Conditions influencing Infection.**—(*a*) *Constitutional Peculiarities.*—It was formerly thought that individuals of a certain habit of body, and of a certain physiognomy, the *habitus phthisicus*, were specially prone to tuberculous disease; but few now regard the so-called tuberculous or scrofulous diathesis as more than an indication of a certain type of conformation, in which the tissues are more vulnerable and less capable of resisting infection. In many instances Cohnheim is unquestionably correct in stating that the so-called phthisical *habit* is not an indication of a tendency to, but actually of the existence of, tuberculosis. The belief in a special phthisical frame has existed in the profession from the days of Hippocrates, who says, "The form of body peculiar to subjects of phthisical complaints was the smooth, the whitish, that resembling the lentil; the reddish, the blue-eyed, the leuco-phlegmatic, and that with the scapulæ having the appearance of wings." Galen also wrote upon this type of chest as specially characteristic of the disease. Certainly the long, narrow, flat chest with depressed sternum is most commonly seen in tuberculous persons, but how common it is also to meet with patients who have well-formed, well-built chests, with wide costal angle and good pulmonary expansion! The investigations of Beneke with reference to the formation of the viscera in the subjects of phthisis are very interesting. His measurements indicate that the heart is relatively small, the arteries are proportionately narrow, and the pulmonary artery is relatively wider than the aorta. This point, he suggests, would lead to increase in the blood-pressure in the lungs and favor catarrh. The lung volume he found to be relatively greater in those affected with phthisis.

Galton and Mahomed made observations upon the composite portraiture of phthisis. In 442 patients they separated two types of face; one ovoid and narrow, the other broad and coarse featured. This corresponds in an interesting way to the diathetic states formerly recognized—namely, the tuberculous, with thin skin, bright eyes, oval face, and long, thin bones; and the scrofulous, with thick lips and nose, opaque skin, large thick bones, and heavy figure. These conditions, on which so much stress was formerly laid, indicate, as Fagge states, nothing more than delicacy of constitution, incomplete growth, and imperfect development.

(*b*) *Influence of Age.*—Tuberculosis occurs at all periods of life, in the suckling as well as in the octogenarian. The distribution of the lesions varies greatly at different ages. In the first decade the lymphatic glands, bones, and meninges are much more frequently affected than at subsequent periods. Meningeal tuberculosis is most common between the third and eighth years.

The mesenteric glands are specially prone to be involved in young children, as before mentioned. Of 127 cases of tuberculosis in children, Woodhead found these bodies affected in 100 instances, in 14 of which there were no tubercles in other parts of the body. The majority of these cases occur between the first and fifth years. The bronchial glands are still more frequently involved, and of 125 cases at the New York Foundling Hospital in every one were these structures the seat of more or less extensive tuberculosis.

In adults the lungs usually contain tubercle when it is present in the body (Louis' law).

(*c*) *Soil and locality* are held by many to have an important influence in tuberculosis. The observations of H. I. Bowditch in this country, and of Buchanan in England, show that pulmonary tuberculosis is more prevalent in damp, ill-drained districts; but this increased incidence is most probably associated with a heightened vulnerability due to an increased liability to catarrhal affections of all kinds.

(*d*) *Local Conditions influencing Infection.*—These are doubtless of the highest importance, and second only to the constitutional vulnerability. Among the more important may be mentioned:

Catarrhal Inflammation.—This probably acts by lowering the resistance, or, in modern parlance, reducing the activity of the phagocytes and allowing the bacilli to pass the portals. The liability of infection in the cervical and bronchial glands in children is probably associated with the common occurrence of catarrhal processes in the throat and bronchi.

The influence of bronchial catarrh in pulmonary tuberculosis is all-important. How often is it said that the disease has started in a neglected cold, which means, in other words, that the bronchial catarrh has enfeebled the power of tissue resistance, or produced conditions favorable to the growth and development of the bacilli!

An important part in the etiology of tuberculous processes is played by *trauma*. Surgeons have for years laid great stress upon this association, but the relation, though universally recognized, is by no means easy of explanation. Bacteriological experiments, however, indicate that in tissues which have been injured organisms, which would in health have been readily and rapidly destroyed by the action of the normal juices or cells, under these altered circumstances grow rapidly and develop. Probably in the case of tuberculosis following trauma the injured part is for a time a *locus minoris resistentiæ*, and if bacilli are present they may by it receive a stimulus to growth, or under the altered conditions be capable of multiplying. Not only in arthritis but in pulmonary tuberculosis traumatism may play a part. The question has been thoroughly studied by Mendelsohn,* who reports nine cases in which, without fracture of the

* Zeitschrift f. klin. Medicin, Bd. 10.

rib or laceration of the lung, tuberculosis developed shortly after contusion of the chest.

The production of general tuberculosis is sometimes favored by *operation* upon tuberculous lesions. Surgeons have long known that resection of a strumous joint is occasionally followed by acute tuberculosis. The question has been carefully studied by Wartmann,* who gives statistics of 837 resections. Of these, 225 ended fatally, 26 with acute tuberculosis, the outbreak of which was directly associated with operation.

The acute miliary tuberculosis which, as Litten has shown, occasionally follows the aspiration of the effusion in tuberculous pleurisy, may come under this division.

The constant inhalation of *impure air* in occupations associated with a very dusty atmosphere renders the lungs less capable of resisting infection. The pulmonary affection of stone-cutters and coal-miners, though non-tuberculous at the outset and often a simple chronic interstitial pneumonia, is ultimately in a large proportion of the cases tuberculous. In manufactories metallic seems more hurtful than mineral dust. Peterson† quotes the incidence of pulmonary tuberculosis among the trades as follows: Glass-workers, 80 per cent; needle-sharpeners, 70; file-cutters, 62; and stone-cutters, 60. And, lastly, circumstances which temporarily lower the nutrition, as the *specific fevers* render the tissues more susceptible. In this way alone can we explain the frequent onset of tuberculosis after an exhausting illness. Fevers, such as measles and whooping-cough, which are associated with bronchial catarrh, are more prone than others to be followed by tuberculosis. This is often only the blazing of a smouldering fire.

General Morbid Anatomy and Histology of Tuberculous Lesions.

(1) **Distribution of the Tubercles in the Body.**—The organs of the body are variously affected by tuberculosis. In adults, the lungs may be regarded as the seat of election; in children, the lymph-glands, bones, and joints. In 1,000 autopsies there were 275 cases with tuberculous lesions. With but two or three exceptions the lungs were affected. The distribution in the other organs was as follows: Pericardium, 7; peritonæum, 36; brain, 31; spleen, 23; liver, 12; kidneys, 32; intestines, 65; heart, 4; and generative organs, 8.

The tuberculosis which comes under the care of the surgeon has a different distribution, as shown by the following figures from the Wurzburg clinic: Among 8,873 patients there were 1,287 tuberculous, with the following distribution of lesions: Bones and joints, 1,037; lymph-glands, 196; skin and connective tissues, 77; mucous membranes, 10; genito-urinary organs, 20.

* Deutsche Zeitschrift f. Chirurgie, Bd. 24.
† Medical News, 1885.

(2) **The Changes produced by the Tubercle Bacilli.**

(*a*) *The Nodular Tubercle.*—The body which we term a "tubercle" *presents in its early formation nothing distinctive or peculiar, either in its components or in their arrangement.* Identical structures are produced by other parasites, such as the actinomyces, and by the strongylus in the lungs of sheep.

The researches of Baumgarten have enabled us to follow in detail all the steps in the development of a tubercle.

These are: ( ) The multiplication of the fixed cells, especially those of connective tissue and the endothelium of the capillaries, and the gradual production from them of rounded, cuboidal, or polygonal bodies with vesicular nuclei—the *epithelioid cells*—inside some of which the bacilli are soon seen.

(β) From the vessels of the infected focus, leucocytes migrate in numbers and form the lymphoid cells which were thought to be so characteristic of tubercle. They do not, however, undergo division.

(γ) A reticulum of fibres is formed by the fibrillation and rarefaction of the connective-tissue matrix. This is most apparent, as a rule, at the margins of the growth.

(δ) In some, but not all, tubercles *giant cells* are formed by an increase in the protoplasm and in the nuclei of an individual cell, or possibly by the fusion of several cells. The giant cells seem to be in inverse ratio to the number and virulence of the bacilli. In lupus, joint tuberculosis, and scrofulous glands, in which the bacilli are scanty, the giant cells are numerous; while in miliary tubercles and all lesions in which the bacilli are abundant the giant cells are few in number.

The bacilli then cause, in the first place, a proliferation of the fixed elements, with the production of epithelioid and giant cells; and, secondly, an inflammatory reaction, associated with exudation of leucocytes. How far the leucocytes attack and destroy the bacilli has not been definitely settled—Metschnikoff claiming, Baumgarten denying, an active phagocytosis.

Once formed, a tubercle undergoes caseation and sclerosis.

Caseation.—At the central part of the growth, owing to the direct action of the bacilli, a process of coagulation necrosis goes on in the cells, which lose their outline, become irregular, no longer take stains, and are finally converted into a homogeneous, structureless substance. Proceeding from the centre outward, the tubercle may be gradually converted into a yellowish-gray body, in which, however, the bacilli are still abundant. No blood-vessels are found in them. Aggregated together these form the cheesy masses so common in tuberculosis, which may undergo (*a*) softening; (*b*) fibroid limitation (encapsulation); (*c*) calcification.

Sclerosis.—With the necrosis of the cell elements at the centre of the tubercle, hyaline transformation proceeds, together with great increase in the fibroid elements; so that the tubercle is converted into a firm, hard

structure. Often the change is rather of a fibro-caseous nature; but the sclerosis predominates. In some situations, as the peritonæum, this seems to be the natural transformation of tubercle, and it is by no means rare in the lungs.

In all tubercles two processes go on: the one—caseation—destructive and dangerous; and the other—sclerosis—conservative and healing. The ultimate result in a given case depends upon the capabilities of the body to restrict and limit the growth of the bacilli. There are tissue-soils in which the bacilli are, in all probability, killed at once—*the seed has fallen by the wayside.* There are others in which a lodgment is gained and more or less damage done, but finally the day is with the conservative, protecting forces—*the seed has fallen upon stony ground.* Thirdly, there are tissue-soils in which the bacilli grow luxuriantly, caseation and softening, not limitation and sclerosis, prevail, and the day is with the invaders—*the seed has fallen upon good ground.*

The action of the bacilli injected directly into the blood-vessels illustrates many points in the histology and pathology of tuberculosis. If into the vein of a rabbit a pure culture of the bacilli is injected, the microbes accumulate chiefly in the liver and spleen. The animal dies usually within two weeks, and the organs apparently show no trace of tubercles. Microscopically, in both spleen and liver the young tubercles in process of formation are very numerous, and the process of karyokinesis is seen in the liver-cells. After an injection of a more dilute culture, or one whose virulence has been mitigated by age, instead of dying within a fortnight the animal survives for five or six weeks, by which time the tubercles are apparent in the spleen and liver, and often in the other organs.

(*b*) *The Diffuse Infiltrated Tubercle.*—This is most frequently seen in the lungs. Only a great master like Virchow could have won the profession from a belief in the *unity of phthisis*, which the genius of Laennec had, on anatomical ground, announced. Here and there a teacher, as Wilson Fox, protested, but the heresy prevailed, and we repeated the striking aphorism of Niemeyer, "The greatest evil which can happen to a consumptive is that he should become tuberculous." It was thought that the products of any simple inflammation might become caseous and that ordinary catarrhal pneumonia terminated in phthisis. It was peculiarly fitting that from Germany, in which the dualistic heresy arose, the truth of Laennec's views should receive incontestable proof, in the demonstration by Koch of the etiological unity of all the various processes known as tuberculous and scrofulous.

Infiltrated tubercle results from the fusion of many small foci of infection—so small indeed that they may not be visible to the naked eye, but which histologically are seen to be composed of scattered centres, surrounded by areas in which the air-cells are filled with the products of exudation and of the proliferation of the alveolar epithelium. Under the influence of the bacilli, caseation takes place, usually in small groups of

lobules, occasionally in an entire lobe, or even the greater part of a lung. In the early stage of the process, the tissue has a gray gelatinous appearance, the *gray infiltration* of Laennec. The alveoli contain a sero-fibrinous fluid with cells, and the septa are also infiltrated. These cells accumulate and undergo coagulation necrosis, forming areas of caseation, the *infiltration tuberculeuse jaune* of Laennec, the scrofulous or cheesy pneumonia of later writers. There may also be a diffuse infiltration and caseation without any special foci, a wide-spread tuberculous pneumonia induced by the bacilli.

After all, the two processes are identical. As Baumgarten states: "there is no well-marked difference between miliary tubercle and chronic caseous pneumonia. Speaking histologically, miliary tuberculosis is nothing else than a chronic caseous miliary pneumonia, and chronic caseous pneumonia is nothing but a tuberculosis of the lungs."

(*c*) *Secondary Inflammatory Processes.*—(1) The irritation of the bacilli invariably produces an inflammation which may, as has been described, be limited to exudation of leucocytes and serum, but may also be much more extensive, and varies with varying conditions. We find, for example, about the smaller tubercles in the lungs, pneumonia—either catarrhal or fibrinous, proliferation of the connective-tissue elements in the septa (which also become infiltrated with round cells), and changes in the blood and lymph vessels.

(2) In processes of minor intensity the inflammation is of the slow reactive nature, which results in the production of a cicatricial connective tissue which limits and restricts the development of the tubercles and is the essential conservative element in the disease. It is to be remembered that in chronic pulmonary tuberculosis much of the fibroid tissue which is present is not in any way associated with the action of the bacilli.

(3) Suppuration. Do the bacilli themselves induce suppuration? In so-called cold tuberculous abscess the material is not histologically pus, but a *débris* consisting of broken-down cells and cheesy material. It is moreover sterile—that is, does not contain the usual pus organisms. The products of the tubercle bacilli are probably able to induce suppuration, as in joint and bone tuberculosis pus is frequently produced, although this may be due to a mixed infection. Koch, it will be remembered, states that the "tuberculin" is one of the best agents for the production of experimental suppuration. In tuberculosis of the lungs the suppuration is largely the result of an infection with pus organisms.

II. Acute Tuberculosis.

The truly infective nature of tubercle is best shown in this affection, which is characterized by an eruption of miliary tubercles in various parts of the body. The clinical picture varies with the general or localized distribution of the growths. The tubercles are found upon the pleura and

peritonæum; in the lungs, liver, kidneys, lymph-glands, and spleen; upon the membranes of the brain, occasionally in the choroid coat of the eye, and in the bone-marrow. They may be abundant in some organs and scanty in others. Thus, in the meninges of the brain they may be thickly set, while there are few or none in the abdominal viscera or in the lungs. On the other hand, the lungs may be stuffed with granulations while the meninges of the brain are free. In other cases, again, the distribution is uniform in all the viscera.

The *etiology* has been in part considered, and the only additional statement necessary is that in a great majority of all cases it is an *auto-infection*, arising from a pre-existing tuberculous focus, which may be latent and unsuspected. The following are the most common sources of general infection: Local disease of the lungs, which may be quite limited and unproductive of symptoms; tuberculous affection of the lymph-glands, particularly in children; and tuberculosis of the bones and of the kidneys. Of these sources perhaps the most common are the tracheal and bronchial lymph-glands, which are so often the seat of local tuberculosis. Weigert has shown that in many cases the infection results from the rupture of a caseous pulmonary nodule into a vein, or of a caseous bronchial gland into one of the pulmonary veins. A general infection may, as shown by Ponfick, result from invasion of the thoracic duct by tubercles. With special care the source of infection can usually be discovered at post-mortem examination. The connection between tuberculous lymph-glands and veins has often been demonstrated. In many instances it is impossible to say what determines the sudden and violent onset of the disease. It would seem sometimes as if general rather than local conditions influenced the outbreak. After certain fevers, particularly measles and whooping-cough in children—affections, it is true, which are associated with long-continued bronchitis—miliary tuberculosis is not uncommon. The prostration and constitutional weakness which follow protracted fevers frequently seem in the adult a predisposing cause.

Clinical Forms.—For practical purposes the cases may be divided into those with the symptoms of *acute general infection* without special localization; cases with marked *pulmonary* symptoms; and cases with *cerebral* or *cerebro-spinal* symptoms.

Other forms have been recognized, but this division covers a large majority of the cases.

Taking any series of cases it will be found that the meningeal form of acute tuberculosis exceeds in numbers the cases with general or marked pulmonary symptoms.

1. **General or Typhoid Form.**—*Symptoms.*—The patient here presents the symptoms of an infectious disease with few if any local symptoms. The cases simulate and are frequently mistaken for typhoid fever. After a period of failing health, with loss of appetite, the patient becomes feverish and weak. Occasionally the disease sets in more abruptly, but in

many instances the anamnesis closely resembles that of typhoid fever. Nose-bleeding, however, is rare. The temperature increases, the pulse becomes rapid and feeble, the tongue dry; delirium becomes marked and the cheeks are flushed. The pulmonary symptoms may be very slight; usually bronchitis exists, but not more severe than is common with typhoid fever. The pulse is seldom dicrotic, but is rapid in proportion to the pyrexia. Perhaps the most striking feature of the temperature is the irregularity; and if seen from the outset there is not the steady ascent noted in typhoid fever. There is usually an evening rise to 103°, sometimes 104°, and a morning remission of from two to three degrees. Sometimes the pyrexia is intermittent, and the thermometer may register below normal during the early morning hours. The inverse type of temperature, in which the rise takes place in the morning, is held by some writers to be more frequent in general tuberculosis than in other diseases. In rare instances there may be little or no fever. On two occasions I have had a patient admitted to my wards in a condition of profound debility, with a history of illness of from three to four weeks' duration, with rapid pulse, flushed cheeks, dry tongue, and very slight elevation in temperature, in whom (post mortem) the condition proved to be general tuberculosis. In one instance there was tolerably extensive disease at the right apex. Reinhold, from Bäumler's clinic, has recently called attention to these afebrile forms of acute tuberculosis. In nine of fifty-two cases there was no fever, or only a transient rise.

In a considerable number of these cases the respirations are increased in frequency, particularly in the early stage, and there may be signs of diffuse bronchitis and slight cyanosis. Cheyne-Stokes breathing develops toward the close.

Active delirium is rare. More commonly there are torpor and dullness, gradually deepening into coma, in which the patient dies. In some cases the pulmonary symptoms become more marked; in others, meningeal or cerebral features develop.

Diagnosis.—The differential diagnosis between general miliary tuberculosis without local manifestations and typhoid fever is extremely difficult. A point of importance, to which reference has already been made, is the irregularity of the temperature curve. The greater frequency of the respirations and the tendency to slight cyanosis is much more common in tuberculosis. There are cases, however, of typhoid fever in which the initial bronchitis is severe and may lead to dyspnœa and disturbed oxygenation. The cough may be slight or absent. Diarrhœa is rare in tuberculosis; the bowels are usually constipated; but diarrhœa may occur and persist for days. In certain cases the diagnosis has been complicated still further by the occurrence of blood in the stools. Enlargement of the spleen occurs in general tuberculosis, but is neither so early nor so marked as in typhoid fever. In children, however, the enlargement may be considerable. The urine may show traces of albumen, and unfortu-