state to meet. It would be absurd to condemn as unfit for consumption the meat of cattle which show only a caseous lymph node as evidence of the disease. In Massachusetts an attempt was made to exterminate the disease by destroying all cattle which gave the tuberculin test, but it was soon abandoned. The attempt at extermination of the disease in the present state of our knowledge regarding infection should be undertaken rather as an economic than as a hygienic measure. It might possibly be done by the general Government, but not by the States. At present in Massachusetts State control is limited to inspection of herds and destruction of cattle with evident extensive tuberculosis or with involvement of the mammary gland.

Tuberculosis of the horse is rare; the disease is often confounded with glanders, especially the chronic form of this. It is usually localized in the lungs and abdominal cavity, and resembles the bovine disease. The affected lymph nodes may form enormous tumors. Histologically the disease is characterized by the fibrous character of the tubercles, the less tendency to calcification as compared with cattle, the number of bacilli in the lesions, and their almost constant presence in the giant cells. The symptoms are not characteristic, and are not seen until a late stage of the disease. After cattle swine are most frequently affected. The disease is most often seen in young animals, and is due to infection by the digestive tract caused by feeding them with tuberculous milk or with the refuse of abbatoirs. A peculiar form of intestinal tuberculosis is sometimes seen in very young pigs, consisting in general diffuse necrosis and caseation of the mucous membrane. The lesions closely resemble those of diphtheritic dysentery. The disease often becomes generalized with great rapidity and takes an acute course. The bacilli are usually present in very small numbers. Sheep and goats are rarely affected, although the disease can be conveyed by inoculation. It takes the same form as in cattle. In Prussia in 1894 abbatoir inspection showed only 0.06 per cent. of tuberculosis in sheep. The dog, though relatively immune, may contract the disease. Villemin produced the disease in the dog by subcutaneous inoculation. Both the human and the bovine disease may be inoculated. Strauss has injected pure cultures of the human bacillus into a vein, producing miliary tuberculosis of the organs. Several cases of spontaneous infection of the dog have been reported, infection being due to the animal eating the sputum of a tuberculous master. The bacilli in the lesions are in very small numbers. Shortly after the discovery of the tubercle bacillus I had occasion to examine the tubercles in the liver of a dog for bacilli. The case was an important one at the time because it was regarded as proving the presence of tubercles without bacilli. Forty sections were examined before a bacillus was found. Tuberculosis can be easily transmitted to the cat, but the spontaneous disease is rare. The lesions have nothing characteristic. In one case of spontaneous tuberculosis the liver contained very acute lesions full of bacilli, and in many places there was an actual injection of the capillaries with masses of tubercle bacilli. It has been known for a long time that tuberculosis is frequent in monkeys living in captivity. In this animal, as in man, the pulmonary form is most common, and the lesions are very similar to those in man, though the tubercles have a greater tendency to softening and may resemble abscesses. The bacilli are present in about the same numbers as in man. The guinea-pig and the rabbit, although so susceptible to experimental tuberculosis, are rarely spontaneously affected even when in captivity. It is very rare in the laboratory, even when animals are kept in close relation with those infected experimentally, that an animal killed for any other purpose will show tuberculous lesions. Mice and rats are less susceptible than guinea-pigs and rabbits.

The tuberculosis of fowls has a special interest because it is due to a strain of the tubercle bacillus which is different from both the bovine and the human form. Infection takes place from the alimentary canal, though the mucous membrane shows no ulceration. The lesions take the form of small firm tumor-like masses seated principally on the peritoneal surface of the intestine and in the liver. The tumors are surrounded by a capsule of connective tissue and are easily enucleated. The tubercle bacilli are more abundant than in the lesions in any other animal. Section of a large nodule shows a necrotic centre which is full of bacilli. Around this is a layer of tissue containing epithelioid and giant cells in which the bacilli are less numerous. The bacilli are generally longer than the human bacilli, and the cultures can be distinguished from both this and the bovine. All experimental evidence is opposed to the idea that the human bacillus can produce tuberculosis in fowls. Strauss fed eight chickens with sputum rich in bacilli, and also gave them a chopped-up tuberculous lung. The autopsy showed no trace of tuberculosis, although masses of the tuberculous material were ingested. Martin has inoculated chickens and pigeons in the peritoneal cavity without producing any lesions. Subcutaneous inoculation of the human bacilli may produce an abscess at the point of inoculation. The results of the inoculation of the guinea-pig with the avian bacilli are distinctly different from those produced by either the human or the bovine varieties. An abscess follows subcutaneous inoculation but it does not open and produce an ulcer. The animal usually dies after some months, and at the autopsy abscesses are found at the seat of inoculation, enlargement of the lymph nodes, and a few tubercles elsewhere. The rabbit has an abscess at the point where it was inoculated, and the bacilli are not usually found elsewhere. The injection of the bacilli into the blood produces emaciation and death in the course of some weeks. The liver and spleen are enlarged and the vessels contain numbers of bacilli, but there are no tubercles.

Dubard and Terre discovered in 1897 a form of tuberculosis in carp; it was due to a bacillus, the bacillus tuberculosis piscium, which has the same staining reaction as other varieties of the bacillus, but which will not produce the disease in birds or mammals and grows at ordinary air temperatures. The cultures much resemble the human and avian forms. Frogs are susceptible to inoculation with the bacilli; the lesions are much the same as in other forms of tuberculosis, but caseation is not so evident. This bacillus contains a toxin with properties analogous to those of the tuberculin of Koch. Ledoux prepared these two toxins, making them as much alike as possible. Both the fish and human tuberculin produced a reaction in guinea-pigs inoculated with human bacilli, but the fish tuberculin was not so strong as the human. One cubic centimetre of Koch's tuberculin killed a guinea-pig which had been inoculated twenty-eight days previously. The same dose of fish tuberculin produced the same elevation of temperature, but was not fatal.

Tuberculosis in Man.—Mortality statistics from all civilized countries show that about one-seventh of all deaths are due to tuberculosis. This must be based to a large extent on the deaths in which the form of the disease is obvious. Every pathologist is aware of the frequency of cases in which death from tuberculosis was attributed to some other cause; and if all forms of the disease were accurately diagnosed, the mortality would probably exceed the figures given. There is no immunity in the human race. Certain individuals may appear to be more or less susceptible than others, but the question of greater or less exposure to infection cannot be ruled out. Differences in susceptibility could be determined only by inoculation with the same amount of the same culture. There are of course great differences in the race susceptibility in animals, but the general result of experiments has been to show that susceptibility of individuals of a species of the same age and under the same conditions is about the same. No human race is exempt, and the susceptibility in all is about the same, the relative frequency of the disease being governed mainly by the greater or less chance of infection given by the conditions of life. There may be a difference in the susceptibility

of the tissues of the body due to local conditions, which may favor the reception of the organisms. There may also be conditions brought about in various ways which may favor the multiplication of the bacilli when once established. It seems to be a general rule that the young of all species are more susceptible than adults. It is evident from the usual localization of the disease in man and the opportunities which the bacilli have for leaving the body that every individual with tuberculosis is a focus of infection, more or less dangerous according to the locality of the tissues affected and the extent of the lesions. This being so, density of the population and the greater opportunities which this gives for disseminating the bacilli, are the principal factors influencing the frequency of the disease. The disease exists independently of conditions of climate or soil. Wherever the population is dense the disease is frequent; wherever there is a scarce rural population the disease is more rare, and this whether the locality is in the east or west, north or south, whether the altitude be high or low, whether the climate be dry or moist, hot or cold. The disease is rare in high altitudes, but if one compares the tuberculosis curve with the curve representing density of population it is seen that the infrequency is due not to altitude, but to scarcity of population. The increase in tuberculosis in civilized life corresponds with the irresistible movement of the population to the cities, and the substitution of sedentary indoor professions for agricultural occupations in the open air. Paris gives a general mortality from tuberculosis of nearly 5 per 1,000, and from this there is a gradual decline according to density of population to 1.81 per 1,000 in some of the country districts. Density of population means indoor life and factories. These undoubtedly increase the danger of infection because the bacilli in the sputum and discharged in the expiration spray are not exposed to the killing influence of sunlight. Whether crowded conditions and indoor occupations apart from increasing opportunity for infection have any influence on morbidity is uncertain. They probably have an influence on mortality. The frequency of the disease is influenced by the different professions, and this to some extent independently of density of population. Tailors give a high mortality, which may be due in part to the fact that this pursuit is not undertaken by the more robust. The disease is particularly common among those exposed to the dust coming from vegetable and mineral substances. The mortality in Switzerland from stone-cutters is 10.47 per 1,000. It is also high in those subjected to metallic dust, as in the grinders. The cause of this is probably due to opportunities for infection combined with the creation of local conditions in the lungs favoring the lodgment of the bacilli. An exception to this is given in the coal miners in England, who have a low mortality from the disease, notwithstanding the fact that their life in the mines is not under conditions which we ordinarily regard as hygienic. Cornet explains this by the fact that in the mines there is no opportunity for infection, the sputum not becoming dried into dust. In Switzerland the mortality in agricultural laborers is 2.10 per 1,000, railroad employees 1.84, foresters 1.75, locksmiths 7.2, printers and lithographers 5.55, watchmakers 5.19, coopers 5.8, bakers 5.6, tailors 4.90. In Italy there is the high mortality of 4.59 in students and seminarists. Pastors in mountain villages seem to have the lowest death rate from the disease.

When we consider the actual frequency of the disease, as shown by the presence of anatomical lesions which could have been produced only by the action of the bacilli, the figures are colossal. Every pathologist is aware of the frequency of caseous foci in lymph nodes, of cicatrices, nodules or indurations in the lungs, of adhesions between the pleuræ, etc., the greater part of which certainly must be attributed to tuberculosis. In the Boston City Hospital, to which patients with advanced tuberculosis are not admitted, such lesions are found in the ordinary conduct of the autopsy in about one-third of all cases. Where the determining of tuberculous lesions is especially held in view in making the autopsy, and where microscopic examination of organs and animal inoculation are resorted to for diagnosis of obscure lesions, the proportion of cases is much greater. The inoculation of animals with bronchial nodes coming from subjects presenting no macroscopic evidences of the disease has shown that the bacilli may be present without any or certainly without easily recognized lesions. I have shortly had the opportunity to examine the lymph nodes from a cow which seemed both on macroscopic and on cursory microscopic examination to be intact, but a more careful examination showed a few giant cells containing bacilli with scattered epithelioid cells around them and without any caseation. The most carefully carried out investigations on the frequency of anatomical lesions in tuberculosis are those of Naegeli made on 500 autopsies

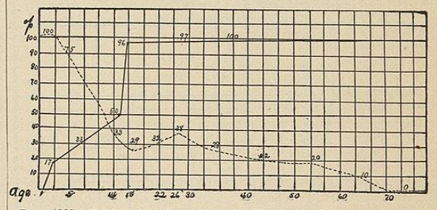

FIG. 4808.—Table taken from Naegeli, *Virch. Arch.*, vol. clx. The black line shows the frequency of anatomical evidences of tuberculosis at different ages; the dotted line, the cases in which the disease proved fatal.

(Fig. 4804). The curve shows the frequency of tuberculous lesions at different ages, reaching at eighteen the astonishing number of 97 per cent. Naegeli regards it as probable that every individual over forty has or has had at some time in his life an infection with tuberculosis. He shows that the infection increases irregularly up to 50 per cent. at fifteen years, and from that there is a rapid rise to 96 per cent. at eighteen. The dotted curve gives the percentage of fatal tuberculosis at the different ages, showing that all cases were fatal up to two and a half years, and from that a gradual decline to 29 per cent. of fatal cases at twenty in spite of 97 per cent. of infection. He argues from this that there is a special disposition in children to the extension of the disease, so that cases of infection are usually followed by generalization and death. This disposition decreases until the age of seventy, when there is practically no mortality in spite of universal infection. The figures with regard to children are misleading, and show that his autopsy material of children did not embrace the acute infectious diseases of children, and are not representative of average autopsies on children. Autopsies on diphtheria cases show a very high percentage of latent tuberculosis in children, and many of the old lesions met with in adults can be referred to infection in childhood. The percentage of lesions must, however, increase with age, for the reason that the longer a soldier remains in battle, the greater the danger of a wound. Tuberculosis was found in 35 out of 220 autopsies on diphtheria at the Boston City Hospital, or in 16 per cent. All but 21 of the 220 cases were under ten years of age. The examinations were not made with special reference to tuberculosis, and it is probable that many slight lesions which could be referred to this were overlooked. In 3 cases miliary tubercles were found only on the routine microscopic examination of the organ, there being no macroscopic evidence of the disease. In 3 cases there was healed tuberculosis of the lungs without lesions elsewhere. Contrary to general statistics which show the greatest frequency of the infection in the bronchial lymph nodes, the mesenteric lymph nodes in our cases were most frequently affected. In 7 cases the only lesions of the disease were found in these. In only 6 out of the 18 cases in which the nodes were affected was there intestinal ulceration. In but few of the cases were there

any clinical manifestations of the disease, and in most cases the character of the lesions was not such as would have given rise to symptoms. Other statistics derived from diphtheria autopsies show about the same percentage of tuberculosis. Berliner in Freiburg found 19 cases in 107 autopsies on diphtheria, or 17 per cent. The tuberculous lesions were usually old, and as a rule were

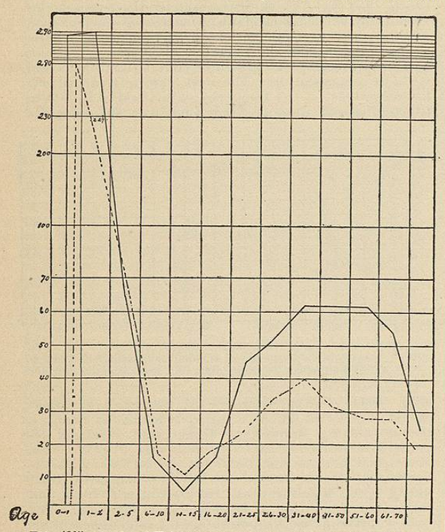

FIG. 4805.—Table of Holste, showing the Death Rate from Tuberculosis in Helsingfors for 1882-1889 for 10,000 inhabitants. The black line represents males, the dotted line females. During this period the death rate from tuberculosis was, for males 5.7 per thousand; for females, 3.8 per thousand.

not influenced by the diphtheria. Cohaus in an analysis of 45 cases in Kiel found 95 cases, or 20 per cent. Nearly one-half of his cases could be regarded as definitely healed. The smallest percentage (13.3) was found by Crenemeyer in 459 cases of diphtheria. It is probable that these figures give a fair estimate of the frequency of tuberculosis in children. It is, if anything, too low, because in none of these statistics was any special examination made to determine the presence of tuberculosis; and children who were actually ill of the disease would not be so liable from their surrounding conditions to infection from diphtheria. No fault can be found with Naegeli's methods of estimating the tuberculous character of old lesions. They show in man a high disposition for infection, and a relatively slight disposition for the infection to extend and lead to death (Fig. 4805).

This latent tuberculosis, to which the term healed is often erroneously applied, is of great importance. We can regard a lesion as healed only when the cause which produced it is also destroyed and the lesion is no longer a source of danger for the body. The bacilli in these lesions are not destroyed; they can often be detected on microscopical examination, or, still better, by animal inoculation. They remain a fertile source of future, and often fatal, outbreaks of the disease. Even those which macroscopically appear to be healed may show the contrary on microscopic examination. I once examined a small caseous nodule in the apex of the lung of a young man who died from an accident, and who was apparently in a condition of perfect health. The caseous nodule contained bacilli, and around it were a number of miliary nodules in the cicatricial tissue, each with bacilli. Nothing shows the important part which latent tuberculosis plays more strikingly than the statistics of prison tuberculosis. All who have studied the question have been struck with the high mortality from tuberculosis, reaching in some cases up to seventy-five per cent. of all deaths. It is rare that it comes below fifty per cent. At first this was attributed to greater opportunities for infection in prison life. But this cannot be shown to be the case. The prisoners are generally under better hygienic relations, certainly as regards air and cleanliness, than they would be outside. Investigations of prison dust have not shown bacilli at all, or not in numbers sufficient to explain prison mortality by infection. Moreover, the mortality is greater during the first three years of prison life, and this is too short a time for death to have followed a primary infection in the prison. The study of mortality in cellular prisons, where each prisoner is separately confined and has no opportunity for infection from his fellows, shows about the same mortality as when they live in common. The attempt has also been made to explain it, in part, by the assumption that prisoners as a class are apt to be tuberculous. But the examination of those entering has not shown a percentage of tuberculosis much exceeding the average. The mortality can be explained only by the supposition that prisoners in common with other individuals of a like age have the disease in a latent form, and that the conditions of prison life favor the extension of the primary focus. It is a striking instance of the well-known fact of the influence of conditions of both body and mind on disease. Laënnec gives a striking example of the influence of external conditions on the mortality from the disease. In Paris he attended for six years the house of a religious order which had not the recognition of the religious authorities and was only tolerated. The inmates were depressed in spirits, their thoughts were always on the gloomy side of religion, and they were subjected to a rigorous discipline. The effect was the same on almost all. At the end of one or two months' sojourn the menses stopped and phthisis shortly appeared. In six years he saw two or three times almost complete destruction of the sisterhood, the exceptions being a small number composed of the superior, the door attendant, the sisters who had charge of the garden, and the cook. These were all persons who had more distractions than others, and whose work took them into the open air.

Infection.—The tubercle bacilli are the only source. The bacilli are obligate parasites. They probably never find natural external conditions favorable for their multiplication. They are not spore-producing organisms, and though more resistant than most vegetative forms of organisms, they can easily be destroyed by rational methods of disinfection. Exposure to sunlight destroys them. Individuals with the disease are the source of infection, and infection is in most cases at least confined to the immediate neighborhood of such individuals. The situation of the lesions of the disease particularly favors the extension of the infection. The lungs are chiefly attacked, and the sputum is the chief vehicle by which the bacilli are discharged. In advanced phthisis they are contained in the sputum in immense numbers. They may also be discharged from the body in the fæces in cases of intestinal tuberculosis, and by the bladder in genito-urinary tuberculosis. Tuberculosis of the skin rarely takes a form in which the bacilli are discharged to any extent. In the question of infection only the sputum need be considered. Individuals with the disease, except in the last stages, are not usually confined to rooms, but they mix with their fellows and carry the danger of infection with them. Infection can take place from the respiratory passage, from the alimentary canal, and from the skin. Infection from the respiratory passages is by far the most common. This is shown by the localization of the disease in the lungs and in the bronchial glands, in by far the majority of cases, and by other evidence.

An attempt has been made by some to deny or to minimize infection by inhalation. The bacilli discharged in the

sputum when this becomes dry may enter into the dust. Those discharged in the open by the sputum may be disregarded. They are destroyed by sunlight and other conditions in the open. They are not present, or at least not present in a living condition, in the dust of the street. In close spaces (rooms) they have been found in the dust when the rooms were occupied by tuberculous patients. Sputum containing tubercle bacilli has been dried on pieces of carpet, and guinea-pigs have been caused to inspire the dust which came from beating the carpet, with positive results. Strauss has found bacilli in the nose of healthy individuals, by mopping out the nose with pledgets of cotton, washing this out in bouillon and injecting guinea-pigs. Moeller found tubercle bacilli in his own nose after two hours in the consultation room. Flügge thinks that it is not the bacilli in the dried sputum, and which may enter into the formation of dust, which convey the disease, but small particles of fluid containing the bacilli which are projected into the air in the act of coughing and even speaking, and which may remain for some time suspended in the air. Moeller suspended cover-slips in the vicinity of tuberculous patients, and found bacilli on them carried there by spray particles. He thinks the sputa containing the bacilli are with difficulty broken up into dust when dried. The infectiousness of the bacilli contained in the spray he showed by placing guinea-pigs in the rooms with tuberculous patients and having them cough into the cages. Several of the guinea-pigs became infected in this way. Flies may also convey the bacilli from the sputum either by carrying particles containing bacilli to food, or by their excreta. There would seem to be no question that the infection can be extended by inhaling either dust or spray particles, but there is little chance for this mode of infection to occur in the open except in the immediate vicinity of a case of pulmonary tuberculosis. Pigmentation of the lungs by carbon shows that solid particles can be carried into every part of the lungs. The expired breath in calm respiration is free from bacilli. It has also been shown that the bacilli retain a close connection with the sputum which comes from the lungs. The saliva has been found in most cases to be free even when the lung expectoration contains numbers of bacilli. Kitasato has also shown that a large proportion of those contained in the sputum are dead.

There has been considerable opposition to this idea of infection by inhalation. Those opposing have based their belief on the examination of healthy lungs of animals which, it has been asserted, are free from organisms; also on the seeming impossibility of causing solid particles to be carried by air currents along complicated systems of tubes representing the bronchi. The best series of investigations, however, have shown that the lungs of healthy animals may contain organisms. That none was found is by no means proof that the animal had not inhaled them, for they may be taken into the lymphatics and removed from the lung with great rapidity. After injecting the blood into the trachea of an animal it is scarcely possible to kill it quickly enough to prevent the corpuscles from passing from the lung into the bronchial glands. Neninger found that B. prodigiosus was carried into the lungs by the inhalation of spray containing the organisms; also, when the organisms were placed in the mouth and the animal caused to make forcible inspirations, they were found in the lungs.

Infection by dust and sputum particles need not take place solely by inhalation. Articles placed in the mouth or food may become contaminated and infection take place by the alimentary canal. Primary tuberculosis of the tonsils, which is not infrequent, and tuberculosis of the cervical lymph nodes are to be referred to infection from the mouth or pharynx. It is not necessary to assume that every case of primary tuberculosis of the intestine and the mesenteric nodes is due to the tubercle bacilli contained in milk. Bacilli may be taken into the digestive tract in many other ways than in milk. Infection by the intestinal canal, even secondary, is not very common in view of the possibilities. We often find no intestinal lesions in cases of advanced phthisis, notwithstanding the enormous numbers of bacilli which are swallowed with the sputum.

There have been a number of cases reported of infection by the skin. Most of these have been in connection with circumcision, the practice being to suck the wound to stop the bleeding. Other cases have come from tattooing, the saliva of an individual with pulmonary tuberculosis having been used to moisten the pigments. Infection cannot take place by the intact skin even when bacilli are rubbed on the surface.

The most common form of skin infection is that given in the post-mortem wart, the tuberculosis verrucosa. There seems to be a strong local predisposition to this, which is probably due to some anatomical condition of the skin. Some individuals become infected while others under the same circumstances of exposure are exempt.

It is in most cases extremely difficult to say when and how infection takes place. It very often does not occur under conditions which would seem to be the most favorable. In the acute infectious diseases in many cases it is possible to trace definitely the infection. Tuberculosis is a disease of slow development. The infection, when it takes place, may lead only to a latent tuberculosis, which may become the active cause of the disease many years afterward. In the study of tuberculosis in families there are cases which show that one member of a family after another may be attacked, the disease becoming a house epidemic.

The study of marital tuberculosis has shown that infection may not take place under conditions seemingly the most favorable. Leudet has investigated the frequency of infection in 74 marriages where one individual was tuberculous. In 61 cases there was no infection. Of the 13 cases in which the survivor became tuberculous, in 6 of these the ancestors were tuberculous. In 112 cases of widows or widowers, the former partner having been tuberculous, only 7 had the disease. These cases, collected by Leudet, were from the better classes, in which the chances of infection were less. Delacour investigated 54 marriages, in which one individual was tuberculous. In only 4 cases did the survivor die of tuberculosis. The general result of all these inquiries is to show that in marital tuberculosis the female is more apt to be affected than the male. It is probable that the chances of infection in marriage have been somewhat over-estimated. The parties are separated for a greater part of the time, and the chances of infection would not be probably so great as in the case of a mother or of two sisters living in the same house. There are quite a number of cases in which an individual with chronic tuberculosis had communicated the disease to successive wives.

The influence of heredity in the extension of tuberculosis must be considered under two heads. On the one hand, there is a widespread belief that the disease itself is not inherited, but that the offspring of tuberculous individuals have tissues of a peculiar character, in that they offer a better soil for the development of the tubercle bacilli and the extension of the lesions. Some even go so far as to refer such a supposed inheritance to remote ancestors, and see this disposition to the disease affect entire families. This is a widespread belief, and one which it is difficult to prove or disprove, either statistically or experimentally. Experiments on animals give no basis for the belief. The young of tuberculous animals, if they have not undergone an intra-uterine infection, and if they be removed from sources of contagion, are no more susceptible than the young of healthy animals. It cannot be denied that children of parents with tuberculosis, as the children of parents weakened by any disease, are as a class weaker and have less general resistance than children of healthy parents, and when the infection is once established the disease may spread more rapidly in such cases. The disease is so common that if we consider the remote as well as the immediate ancestors as a source of such a predisposition, it is possible to find an inherited source in almost every case of tuberculosis. It is impossible to consider this

supposed predisposition to the disease apart from the greater chances for the infection to which children, in families in which some one member is affected, are subjected. Even with the best of care as regards sputum, the surroundings of such individuals must become infected by the sputum spray. The infection of the child may not manifest itself for years; only a latent tuberculosis may develop and the disease afterward appears, giving a supposed example of inherited predisposition.

The other view is that there is an actual inheritance of the disease. True germinal inheritance due to infection of either male or female germinal cell need not be considered, and the inherited tuberculosis is really a congenital disease due to intra-uterine infection of the embryo or fœtus. This undoubtedly may take place, but all the evidence with regard to it tends to show its rarity. It has been demonstrated experimentally, the most important work being that of Gaertner. He inoculated white mice in the peritoneal cavity with tubercle bacilli and then had them fecundated. Mice are less susceptible to the disease than guinea-pigs, a slow form of tuberculosis being developed without any interference with function. The period of gestation is only three weeks, and two or three litters can be obtained before the mother dies of the disease, the later broods being obtained in an advanced stage of the disease in the parent. The skin and alimentary canal were removed from the fœtuses, the entire body was rubbed up in water and injected into the peritoneal cavity of guinea-pigs. Two or three fœtuses were used to inject a single animal. One hundred and sixteen fœtuses so obtained were injected into thirty-six guinea-pigs and two of these developed tuberculosis. This is not a large number when it is considered how favorable the conditions were for infection. He also inoculated canary birds, by way of the peritoneum. These laid nine eggs, which were used for the peritoneal inoculation of nine guinea-pigs, the result being that tuberculosis developed in two of the animals. Gaertner does not think that such experiments represent conditions analogous to those in man. Relatively enormous numbers of bacilli were placed in the peritoneal cavity, and infection of the eggs and young took place through the oviduct. He injected the bacilli into the blood of ten pregnant rabbits. These lived a variable time, and fifty-one young were obtained from them. He took from each fœtus the entire liver, the bronchial lymph nodes, the spleen, and other tissues and injected the whole into the peritoneum of guinea-pigs. Five out of the fifty-one became tuberculous. He also inoculated mice in the trachea with a single drop of culture. The inoculation produced tuberculous foci in the lungs, a large spleen, and a liver containing numbers of bacilli. Gaertner obtained from these mice seventy-four young, which were used for the inoculation of thirty-nine guinea-pigs, with positive results in seven.

A number of cases have been published in which congenital tuberculosis in both animals and man has been demonstrated. The first case was that of Johne, who found tuberculous lesions with bacilli in a new-born calf. The bacilli have also been found in the tissues without any lesions. Schmorl and Birch-Hirschfeld investigated the placenta and fœtus from a woman who died of acute miliary tuberculosis in the seventh month of pregnancy. No tubercles were found in either placenta or fœtus. Bacilli were found in the placental sinuses, and animals inoculated with the tissues of the fœtus acquired the disease. Ouche and Chamberlain found both tubercles and bacilli in the placenta of a woman who had acute miliary tuberculosis, and who died shortly after the birth of the child. The child lived for twenty-six days and died of general tuberculosis. We may be warranted in assuming congenital infection in a considerable number of children who died of the disease in the first weeks or months of life, but such cases are rare. It is probable that infection of the fœtus can take place either from the blood or by means of the genital canal, and either the father or the mother may be the source of infection. Jani was the first to show the presence of tubercle bacilli in the testicles and seminal vesicles, and even in cases in which these organs were not the seat of the disease. His work has been confirmed by other investigators. Very few bacilli have been found. Experimentally it has not been possible to transmit the disease by coitus either to the mother or to the fœtus. Friedman successfully infected embryos by injecting the bacilli into the vagina immediately after coitus.

Baumgarten has been the most persistent advocate of the theory of congenital tuberculosis. He was led to advance the theory as an explanation of the rarity of spontaneous infection of laboratory animals when they are exposed to it, and from the difficulty of explaining the situation of many primary foci by the assumption of infection from without. Primary foci are undoubtedly found in bones and other situations, to which the bacilli could be carried only by the blood stream. He thinks the bacilli are transmitted to the fœtus or embryo by either parent. The bacilli enter into the blood and may be deposited in various organs or tissues. The fœtal tissues are an unfavorable soil for the growth of the bacilli and the development of the lesions. The bacilli may remain and the lesions slowly develop and remain quiescent for long periods, becoming cases of latent tuberculosis. He considers this to be the most obvious explanation for primary tuberculosis of the bones.

There is absolutely nothing in favor of Baumgarten's theory that congenital tuberculosis plays any considerable part. It undoubtedly occurs, but it leads not to a latent but to a rapidly generalized tuberculosis. There is no evidence to show that the tissues of the embryo or fœtus are an unfavorable soil for the growth of the bacilli. All statistics which have been collected on the presence of latent lesions have shown that these increase progressively up to adult life. There is no necessity for resorting to the congenital theory for the explanation of tuberculosis in bone or other places where the bacilli could be carried only by the blood current. It is comparatively rare that we find this localization of the disease without an older focus at some place in the body from which the bacilli in small number should have been carried into the blood and deposited in the bones or elsewhere. It is not even necessary to have an older focus. Bacilli may be taken into the circulation without any evidence of a local lesion where they enter the body. Most of these bacilli would be stopped in the filter of the lymph-nodes and develop lesions in these. Ribbert and others explain the frequency of pulmonary tuberculosis not as a primary disease of lungs due to inhalation, but as a secondary blood infection coming from primary lymph-node tuberculosis. Most of the bacilli would be stopped in the lymph nodes, but it is possible under certain conditions that a few of them might get through into the blood without the production of lesions, or of lesions which can be recognized macroscopically. One sees not infrequently tuberculous lesions in the lymph nodes which are apparent only on careful microscopic investigation. The relative frequency and gravity of tuberculosis up to five years of age are due to the greater opportunity of the young child for infection and the relative lack of resistance of its tissues to the bacilli.

The character of the lesions produced by the tubercle bacilli and the histogenesis of the cells entering into the lesions have been the subject of numerous investigations, and by leading men in pathology. Not only has the histology of the tubercle process been cleared up, but much light has been thrown on other infectious processes by the study of tubercles. We may divide the changes produced into two classes: in one, tissue proliferation is produced alone or predominates; and in the other, exudations, which differ only in their ultimate end from exudations produced by a variety of influences. The new formation of tissue which results from the proliferation can appear in the form of small isolated nodules, or of larger nodules composed of aggregations of the small, or as a diffuse formation of tissue of the same character as that composing the nodules. The most numerous cells, and often the only cells, are known as epithelioid

cells. These are cells which vary somewhat in form and size, and have, as their name suggests, some similarity to epithelium. The protoplasm is clear or finely granular, the nucleus is vesicular, and usually oval or slightly incurved. Among these epithelioid cells there are larger cells with numerous vesicular nuclei. These giant cells vary in size and shape and in the number and arrangement of the nuclei. They may be round or irregular, with numerous protoplasmic processes extending out among the epithelioid cells. The nuclei are generally arranged around the periphery of the cell enclosing a central space free from nuclei, or the cell is elongated and the nuclei are arranged at either end. The giant cells may be found either at the centre of the nodule or at one side. They may be found singly, without any epithelioid cells about them. Outside of the epithelioid cells, and often among them, there are numbers of lymphoid cells. Between the lymphoid cells there is a fibrous-tissue reticulum, which may extend a short distance between the epithelioid cells, but which does not anastomose with the reticulum formed by the protoplasmic processes of the giant cells. The fibrous reticulum is continuous with the surrounding connective tissue. Such a structure as this is found only in the smallest and most recently formed tubercles. The best examples are found in the tubercles developing in fibrous or granulation tissue and in certain organs, as the liver. The diffuse tuberculous tissue is formed on surfaces under conditions in which ordinarily only granulation tissue would be formed. It is found in joints, at the bottom of tuberculous ulcers, on serous surfaces, and in the lungs. In this formation the general appearance is that of granulation tissue composed of various kinds of leucocytes, formed and forming connective tissue, and young blood-vessels. In this tissue the epithelioid cells with scattered giant cells are not sufficiently circumscribed to be regarded as tubercles. Occasionally such a structure is found only on the surface.

The histogenesis has been chiefly studied experimentally, by injecting tubercle bacilli either into the general circulation or into the vessels of single organs. The epithelioid cells have the same genesis as they have in granulation tissue, and the same marked property of phagocytosis. They are derived from the large mononuclear, homogeneous leucocytes of the blood, the macrophages of Metschnikoff, the epithelium of serous membranes and of certain organs as the lungs, from all varieties of lymphatic endothelium and from the endothelium of blood-vessels, and from connective-tissue cells. They differ from the epithelioid cells of granulation tissue in being somewhat larger and paler.

When the bacilli are injected into the circulation tubercles are formed about collections of them in capillaries. They may be primarily taken into polynuclear leucocytes at these places, but these leucocytes do not enter into the formation of the tubercle. The tubercle begins with the presence of the bacilli in the endothelial cells of the vessels, and the first cells are formed by endothelial proliferation followed by the proliferation of adjoining cells. In the tissues the close relation of the endothelium of blood-vessels cannot be so easily followed. Baumgarten from his studies of the histogenesis of the tubercle believes that all sorts of epithelium as well as the cells of mesodermic structures can form the cells of the tubercle. He supports his view by the presence of nuclear figures in the adjoining cells. The nuclear figures are found, however, around the formed, and not the forming tubercle, and represent regenerative proliferation. There are two views as to the histogenesis of the giant cells. Weigert has always defended the view that they are formed by a proliferation of nuclei of epithelioid cells, the cell being so injured by the bacilli that it stops short of complete division. Metschnikoff also believes they are formed by nuclear division in a single cell, but denies that this is a degenerative process. For him the giant cell is an active phagocyte and one of the means of defence in the struggle between the bacilli and the tissues. The other opinion regards them as formed by the union of single epithelioid cells. The formation of the tubercle and tuberculous tissue is due to the action of the tubercle bacilli themselves. Similar changes cannot be produced by the injection of chemical substances derived from the bacilli. Typical tubercles can be produced by the injection of dead tubercle bacilli. Conglomerate tubercles are formed by the diffusion of the tubercle bacilli into the tissue around a single focus. The bacilli may be carried into the tissue by lymph streams or by leucocytes or the epithelioid cells. Between the individual tubercles forming the nodule there are numbers of lymphoid cells. Around the tuberculous tissue there are changes of a non-specific character due to the presence of the tubercles.

More characteristic even than the structure of the tubercle is the degeneration of the cells composing it. The cells lose their shape, the nuclei disappear, and the centre of the tubercle becomes changed into an opaque, homogeneous mass which may contain nuclear detritus derived from the nuclei of the degenerated cells. This change (caseation) is due to the tubercle bacilli, probably to toxic substances formed by them. Prudden and Hodenpyl have shown that the injection of dead tubercle bacilli into the circulation will lead to the production of nodules similar in structure to ordinary tubercles, the only difference being that caseation does not take place in them. It has been held that the caseation of the tubercle is due to its non-vascularity, but the tubercle produced by the dead bacilli is equally devoid of vessels. The tubercle may not only undergo caseation, but other forms of degeneration. The cells may become converted into a perfectly homogeneous refractive hyaline mass, hyaline degeneration, or the connective-tissue formation may involve the entire structure, giving rise to the fibrous tubercle. Caseation is usually preceded by fatty degeneration of the cells. Fresh sections of tubercle show fine fat drops in the cells outside of the caseous centre, and even giant cells often show fat inside the row of nuclei. As the tubercle increases in size the degeneration extends until it may involve the surrounding tissue. The caseation varies in its extent and in the rapidity of its formation. It is usually more extensive in tuberculosis of lymph nodes than in any other tissue. Lymph nodes may become completely caseous, with little or no evidence of formation of tubercles or of tuberculous tissue within them. Tuberculosis of lymph nodes is usually secondary to a tuberculous focus in their territory of lymph supply. If the caseation is due to the active substances formed by the bacilli, it is evident that such substances can be brought to them from the affected territory as easily as can the bacilli. With the beginning of the caseation polynuclear leucocytes appear in numbers in the surrounding tissue and in the tubercle. The necrotic tissue of the tubercle attracts them as does other necrotic tissue. The number of bacilli in the tubercle varies greatly. They can always be found in young forming tubercles and often in considerable numbers; in the older formations, single bacilli only are found or they may not be demonstrable. They lie in the caseous centre or enclosed in the epithelioid or giant cells. They are more frequently found in the giant cells in animal than in human lesions. Occasionally they are found in the granulation tissue outside of the tubercle, lying between the lymphoid cells and without any specific reaction about them. It is not easy to explain why the tubercle once formed should not homogeneously increase in size by the continued formation of tissue in the periphery and continued central caseation. The large tubercles are never formed in this way, but increase by the coalescence of single centres. The large solitary tubercles in the brain show centres of caseation with a tissue between them which finally becomes caseous without undergoing the specific change into tuberculous tissue. The large tubercles in bovine tuberculosis show a similar conglomerate structure. Even the diffuse formation of tuberculous tissue does not lead to the formation of large masses. A possible explanation might be that the tissue which lies just outside the caseation has acquired an immunity to the