The diagnosis of first infection tuberculosis is rarely made by the clinical picture. In most cases it is first discovered by a history of contact with a patient with tuberculosis, by a positive reaction to a tuberculin test or by roentgenogram. Unfortunately the diagnosis is often made and the child is treated solely on the basis of the roentgenologic classification. It is certainly not my purpose to belittle the use of roentgenograms for diagnosis. However, even if the initial diagnosis often has to be made by roentgen ray study, there is a real clinical picture of tuberculosis in the child.

Tuberculosis is an infectious disease showing in many respects the same basic pattern which is associated with many other infectious diseases, such as typhoid fever and meningococcic meningitis. There are for all a known portal of entry, known symptoms of invasion and a period in which the causative organism circulates by way of the blood stream, possibly reaching all parts of the body. This period is usually short, but it may be prolonged or extensive. Usually the attack is then concentrated in one place, and the disease goes on to exhibit the characteristics by which it is known. This is true of pneumonococcic pneumonia, of typhoid fever and of meningococcic meningitis. It is equally true of tuberculosis. Complications may develop by local spread of the disease or by metastasis from the original focus. Again, this evolution of the disease may apply equally to most infectious diseases. But tuberculosis does differ from these other infections. The others run their courses in a relatively short time, whereas the original lesions of tuberculosis may remain active for years. Moreover, in most infectious diseases there is a tendency for metastases to develop within a short time or not at all. Metastatic foci of tuberculosis may speedily develop into a tuberculous disease, such as tuberculous dactylitis in infants. Often, however, there is a long quiescent period, and after the primary focus has become stabilized or has even healed, active tuberculous disease may develop from a metastasis.
In order to interpret the clinical picture it is necessary to keep clearly in mind an outline of the pathogenesis of tuberculosis. The usual portal of entry is the upper part of the respiratory tract. In New York extrapulmonary primary infections are uncommon, occurring in less than 1 per cent of the patients at Bellevue Hospital. When tubercle bacilli are first inhaled they usually settle just under the pleura in the best ventilated parts of the lungs. A tuberculous lesion results at this point, and soon after the initial tubercle is formed the bacilli find their way into the lymphatics and are carried to the regional nodes usually at the hilus. This combination of the primary focus and a corresponding lesion in the regional lymph nodes together with the interfocal zone connecting the two poles is known as the primary complex. With the establishment of the primary complex there occurs a change in the reaction of the body to the tubercle bacillus and its metabolic products. Allergy is established. As one of its significant manifestations the interfocal infiltration around the primary tuberculous lesion may become more intense. The size of this area and its fate depend largely on the number of tubercle bacilli and the amount of tuberculotoxins present and also in part on individual reactions, about which relatively little is known. The exudative interfocal reaction may ultimately be entirely resorbed. The primary focus may heal by fibrous encapsulation and calcification, or it may caseate and progress by contiguity and bronchogenic spread.

The bacilli travel from the primary focus along the lymphatics to the regional nodes. Usually there is no traffic problem; the bacilli are not so numerous nor are the roads so congested that unusual halts occur, and the bacilli next settle down in the nodes and form a secondary area of caseous tuberculosis, which may be small if there are few bacilli or which may reduce an entire node or group of nodes to a mass of caseous tuberculosis. Even when there is little local progression of the tuberculous in the nodes, the tendency toward complete healing is not as great as in the primary focus, and it is not uncommon for caseation and living tubercle bacilli to persist in the nodes for long periods even though calcification is present.

Progression of the disease may occur by the bronchogenic route directly from the primary focus or more commonly from the rupture of a tuberculous node into a bronchus. The possibility of progression of the tuberculosis by the hematogenous route is always present, since in most cases at least a few bacilli will progress through the lymph channels to the blood stream. Whether this seeding of tubercle bacilli will result in tuberculous disease in the metastatic area involved depends largely on how many bacilli are implanted in any one area and whether the seeding is single or repeated. The anatomic structure and the position of the area involved also play a part. The spleen and the apexes of the lungs are regions most commonly seeded. Some organs are more resistant to tuberculous invasion than others, the thyroid and pancreas for
example, but this is only a relative immunity, as heavy seeding of these organs can occur leading to tuberculous disease. Any metastatic focus may progress and become an active tuberculous lesion, or it may regress and heal completely; living tubercle bacilli and caseation may exist for years in a quiescent focus of tuberculosis.

Generalized hematogenous tuberculosis usually results from invasion of a blood vessel by a caseating focus of tuberculosis or by dissemination from a tubercle within the lumen of the circulatory system. If a generalized seeding occurs the resulting lesion will depend largely on variations in three factors: the topographic location of the disseminating focus, the dosage and the frequency of seeding of tubercle bacilli. On the variations in these factors depend all the pictures of acute and chronic generalized hematogenous tuberculosis.

On the basis of this pathogenesis of tuberculosis the clinical picture seen in the child can be recognized and interpreted. The incubation period is the time between the first inhalation of tubercle bacilli and the development of a change in the reaction of the tissue to the tubercle bacillus and its metabolic products. It can be measured by the development of the tuberculin reaction, which usually becomes positive in three to five weeks after exposure. There is some evidence that the dosage of inhaled bacilli may affect the length of the incubation period and that with small dosage the tuberculin reaction may not become positive for four months. Sometimes the development of the tuberculin reaction is delayed and the lesion appears on a roentgenogram before the reaction is positive.2

The only way in which one is privileged to see the clinical picture of the beginnings of tuberculosis in the human body is by watching the onset of the disease in children who have previously had negative tuberculin reactions (figs. 1 and 2). A child usually with a history of contact with a case of tuberculosis and with a previous negative reaction to a tuberculin test may have a fever with a temperature rarely over 102 F., lasting approximately three to ten days, with no other symptoms or signs, aside from the anorexia or languor which may accompany the fever and the first appearance of a positive reaction to tuberculin. Frequently the onset of fever coincides with a mild infection of the upper part of the respiratory tract. The roentgenograms may reveal a pulmonary lesion. Because of this insidious onset many of the cases are overlooked. Occasionally there is a stormy onset, with the signs and symptoms of pneumonia, including leukocytosis. The positive reaction to tuberculin, the persistence of the shadow on the roentgenogram after the crisis, when signs and symptoms have disappeared, and the character

of the roentgenographic shadow, with enlarged mediastinal nodes as well as a parenchymal lesion, usually make clear the diagnosis of tuberculosis. It is possible that the type of onset is determined by the degree of tissue change or allergy. There seems to be no relation between the severity of symptoms at onset and the prognosis as regards length of activity of the disease or ultimate recovery.

After the onset it is often impossible to recognize early tuberculosis by signs and symptoms. It is usually suspected by a history of exposure to a patient with tuberculosis or by a positive reaction to a tuberculin test done as a routine procedure. A roentgenogram may then localize

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**Fig. 1 (case 1).**—Chart showing the onset of tuberculosis in an infant of 4 months who was exposed to a mother whose sputum was found to contain tubercle bacilli just before the baby's admission to the hospital. The incubation period was apparently about five weeks.

The lesion. By these three means most of the cases of tuberculosis in its early stages are found. Of 542 cases of first infection tuberculosis studied at Bellevue Hospital less than 10 per cent were discovered by physical examination because tuberculosis was suspected, and many of the cases recognized by clinical means were cases of tuberculous meningitis. More than 85 per cent of this group of cases were originally discovered by case-finding methods.

As a clinician, of course, one would like to be able to say that tuberculosis in its early stages can be recognized by the appearance of the child if not by his symptoms and physical signs. But it is usually

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D.H. BH15505 Admitted March 24, 1939
FH: Mother Diagnosed TBC March 1939
RH: Always Well Breast Fed Until Admission
PI: Cough and Fever Three Days

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impossible to diagnose primary tuberculosis by looking at the child or by using the ordinary methods of physical diagnosis. There is no characteristic facies (fig. 3). How often has the clinical observation been verified that an infant doomed by tuberculous meningitis may be fat and rosy when the diagnosis is first made? Later in the course of tuberculosis, and especially when there is extensive bronchogenic spread or intestinal involvement, one may observe the listlessness and pallor, the long eyelashes and the general increase in body hair. When this picture of a chronically ill child is found, one also can usually detect symptoms and physical signs which obviously lead to a diagnosis of tuberculosis.
The usual case of primary tuberculosis gives no clinical clues to help in the diagnosis. Even with extensive parenchymal exudate the child rarely coughs; there is no expectoration, and when tubercle bacilli are demonstrated, it is by gastric lavage. Fever may be absent after the initial rise or there may be an occasional rise to 101 F. once or twice weekly, an irregular low grade fever. With extensive caseation in the mediastinum sometimes a daily rise in temperature to a high level is seen, but it is amazing how infrequently this type of fever is found even with marked disease. With intelligent parents one can often elicit a

Fig. 3 (case 2).—Photograph of a 3 year old girl showing excellent nutrition. She had a normal temperature and no abnormal physical signs. Tuberculosis was discovered by a routine Mantoux test. The mother was found to have tuberculosis.

history that the child seems to fatigue more easily than usual, but aside from this symptoms are usually lacking.

The paucity of abnormal physical signs in the early lesions of tuberculosis is also striking. There may be a large area of parenchymal involvement with normal physical signs or at most slight dullness or diminished breath sounds. Rarely bronchial breath sounds can be demonstrated, but moist rales are absent.

With the progression of the parenchymal lesion, signs of destruction of lung tissue are ultimately heard, and the resonant rale is the most characteristic sign. Constant rales, even if few, should always lead one to suspect bronchogenic spread.
Symptoms and signs due to encroachment of the enlarged nodes on bronchi and trachea present characteristic clinical pictures, the tuberculous nature of which is often overlooked. The mildest form, usually seen in children over 2 years of age, may be only unilateral bronchitis, which should always arouse suspicion of endobronchitis due to irritation by a mass of tuberculous nodes. With this syndrome there may be fever, and almost always there is a loose frequent cough. In infants the cough is spasmodic with a suggestive whoop and often leads to an erroneous diagnosis of pertussis. Sometimes there is only a harsh, frequently repeated expiratory cough, and often the diagnosis of large

Fig. 5 (case 3).—Illustrations of change in nutritional state with progressive tuberculous disease. A, photograph of a 3 year old girl in the postprimary stage of first infection tuberculosis. Phlyctenular conjunctivitis is present, but no fever or abnormal signs in the chest. B, photograph taken five months later showing marked loss of weight and prominent abdomen. The roentgenogram of the chest was essentially unchanged, but many consonating rales were heard over the lower lobe of the right lung. Tuberculous peritonitis was present. Death occurred three weeks after the photograph was taken.

Fig. 6 (case 3).—Roentgenogram taken at the time of photograph A in figure 5, showing a large area of parenchymal tuberculosis in the lower lobe of the right lung with marked involvement of nodes.
mediastinal nodes is suggested by this symptom. Usually in infants rhonchi are heard throughout the chest. The diagnosis of asthma is not infrequently made. Sometimes the wheezing respirations suggest a foreign body. There may be complete obstruction of a bronchus causing a collapsed lobe, or with incomplete obstruction emphysema is often present. The diagnosis of compression of the bronchi may often be confirmed by the bronchoscope, which may reveal not only narrowing of the lumen but ulceration of the bronchial wall. If the enlargement of the nodes is due largely to perifocal reaction, the symptoms of bronchial obstruction may clear within a few days. More often the nodes are caseous, and it is weeks or months before the obstruction is relieved.

A rapid cessation of signs and symptoms of obstruction, especially when accompanied by a change in the character of the cough, should always lead to the suspicion that ulceration into a bronchus has occurred. Rarely large amounts of caseous material may be coughed up. Sometimes the material can be aspirated by a bronchoscope.

If the node actually ruptures into the bronchus, the resulting clinical picture will depend on the dosage of tubercle bacilli and the amount of tuberculotoxins. Every grade of bronchogenic spread is seen, from bronchogenic miliary tuberculosis to massive caseous pneumonia. When the dosage of tubercle bacilli is low there may be no abnormal physical signs; with larger dosage physical signs of pneumonia may appear in a few days, but usually there are no constant signs for weeks.

Analogous symptoms due to pressure of tuberculous nodes may occur in the abdominal cavity when nodes encroach on the intestinal tract, causing partial obstruction and tremendous distention.

With progression of the primary tuberculous lesion by way of the blood stream there may be no symptoms or signs. But usually if a child with recent primary tuberculosis is carefully watched, within one to six weeks one can detect the clinical picture of what has been termed occult hematogenous tuberculosis, which is really just part of the postprimary stage. Fever is usually absent, or there may be one or two rises in temperature to 101 or 102 F. Attention may be drawn to the child by the appearance of one or two phlyctenules. These are often fleeting and may disappear in twenty-four hours. A few papulonecrotic tuberculids may appear. The spleen at this time is often easily palpable or distinctly enlarged, and there is frequently a general enlargement of all the superficial lymph nodes. This picture of occult hematogenous spread usually lasts only a short while. It may have no clinical sequelae. In 2 per cent of


the cases in the Bellevue Hospital series apical calcifications were later seen on roentgenographic examination, as a result of this postprimary seeding. Because of this clinical course every child with a known recent primary infection, even if the roentgenogram is normal, should be carefully observed for three to six months. During this period any part of the body may show evidence of seeding of bacilli. There may be serous sympathetic meningitis, with the clinical picture of tuberculous meningitis, but with ultimate recovery, or transient red blood cells may be found in the urine owing to the development of a few tubercles in the pelvis of the kidney. With a larger dose of tubercle bacilli a frank metastasis, such as tuberculous dactylitis or tuberculous adenitis, may develop. It is usually in this postprimary period that tuberculous meningitis develops. Of my cases of meningitis at Bellevue Hospital 85 per cent occurred within six months of the first diagnosis of tuberculosis. Usually the size of the original tuberculous lesion and especially of the node involvement bears a direct relation to the seriousness of complications. Meningitis can occur with a small primary infection or even with a normal roentgenogram, but this course of events is uncommon.

If generalized hematogenous tuberculosis occurs, the clinical picture is often easily recognized, although the differentiation between miliary and medium-sized lesions may be difficult without a roentgenogram. Protracted multiform hematogenous tuberculosis is the result of repeated seedings of varying doses of tubercle bacilli, causing widespread tuberculous lesions of varying sizes. The clinical picture is striking. There is usually involvement of all the serous surfaces and of all the superficial lymph nodes, sometimes forming enormous masses which may obstruct lymphatic drainage. Not infrequently there is involvement of bones and joints as well. The roentgenogram usually shows rounded areas of density of varying sizes scattered through both lungs, but abnormal physical signs may be entirely absent until breaking down of these lesions occurs with bronchogenic spread.

The clinical pictures produced by the late evolution of tuberculous disease from metastases are the same in children and in adults. Chronic tuberculosis of the lungs is seen as well as chronic tuberculosis of the bones, lymph nodes and intestinal or genitourinary tract (figs. 7 and 8).

Most deaths from tuberculosis in children occur within a year of the onset of the disease and are usually due to metastases from the original


Nevertheless the child dies of tuberculosis as a direct result of the inhalation of tubercle bacilli, even though a complication is responsible for his death. If the child survives his first attack of tuberculosis and its complications, he may never have a recurrence of tuberculous disease, or after a quiescent period further tuberculous lesions may develop. Late manifestations of tuberculosis may occur at any age, but chronic tuberculous of the lungs usually first manifests itself during the adolescent years, irrespective of the date of the primary infection.

It is possible to trace the origin of many lesions of chronic tuberculosis occurring in late childhood and in adolescence. Such lesions are usually due to the progression of metastases, either from the original focus or from some secondary area of tuberculosis. If a hip joint has been previously seeded with tubercle bacilli, an injury may result in tuberculosis of the hip. A streptococcic infection of the throat may stir a few quiescent caseous foci in the cervical nodes into acute tuberculous adenitis. In an analogous way it is possible to postulate that some force about which little is known, glandular or chemical, acts in the adolescent girl to produce destructive tuberculous disease from old apical seedings.

As in other infectious diseases the prognosis of tuberculosis as regards life and complications seems to depend in large part on the severity of the attack. Just as it is better to have a mild attack of typhoid fever,
Fig. 8 (case 4).—Illustrations of late development of complications of tuberculosis.  

A, roentgenogram taken at the time of the photograph in figure 7 (1931), showing dense calcification behind the fourth right rib, with calcifications in the right bronchopulmonary nodes and calcifications in the second left interspace. Interpretation: well calcified primary tuberculosis with active disease in the axillary nodes, infected by the hematogenous route.  

B, roentgenogram taken seven years later (1938), showing, in addition to the findings in the roentgenogram of 1931, calcification of axillary nodes and a small area of density above the right clavicle containing calcium.  

C, roentgenogram taken in May 1939, showing infiltration in the second and third right interspaces, interpreted as indicating chronic pulmonary tuberculosis. The sputum contained tubercle bacilli. The patient received collapse therapy. No further contact with a patient with tuberculosis could be discovered. The condition is probably an example of endogenous chronic tuberculosis.
it is much better to have a mild attack of tuberculosis. A mild attack of typhoid has a better prognosis for life and much less danger of complications, although a hemorrhage or perforation occasionally occurs during an apparently light attack. Patients with mild tuberculosis have a better prognosis and less danger of serious metastases than those with conditions due to heavy dosage of tubercle bacilli, although occasionally a patient with a normal roentgenogram or a small lesion dies of meningitis. It is probable that this fact explains in part the great difference in statistics regarding prognosis which have been published from various parts of the United States. Brailey's \(^8\) figures from Baltimore and the figures from Bellevue Hospital agree on the high mortality rate of children with tuberculosis. Of the group of 472 children with primary tuberculosis at Bellevue Hospital whom my associates and I were able to follow, 25.4 per cent died of tuberculosis within a year, although in 85 per cent of them the condition was first discovered by case-finding methods. Myers,\(^9\) on the other hand, reported a mortality rate of 0.5 per cent in a group of 206 children with primary tuberculosis, of whom 155 were followed until the condition was healed. Possibly one explanation for the difference in mortality statistics may be the crowded living conditions in Baltimore and New York, giving the opportunity for prolonged and intimate contact with a patient with tuberculosis, which in turn may be responsible for a heavy dosage of tubercle bacilli and a progressive primary complex. Because of the great variations in statistics it is important to emphasize that data from different racial and social groups should not be applied indiscriminately. Results obtained in a midwestern city with a population of 500,000 may not apply to large urban centers, such as Baltimore and New York.

Great strides have been made in the prevention of tuberculosis in children by stressing the infectious nature of the disease. But tuberculosis in children is still a serious clinical problem. The most effective treatment in early stages, in order to reduce the immediate mortality from tuberculosis, is yet to be determined. How to prevent the later development of chronic pulmonary tuberculosis in those who survive the initial attack is not yet known. Possibly further study and analysis of the clinical pictures produced by first infection tuberculosis will help to solve these important problems.

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