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CONNECTICUT STATE DEPARTMENT OF HEALTH John T. Black, M. D., Commissioner HARTFORD

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In the present day of widespread attention to the problems of tuberculosis any casual or intensive consideration of the subject of tuberculosis in various forms in children, might possibly be responsible for the development of several interesting queries.

And if these questions could be answered exhaustively by any of us who are giving so much attention to the subject, and if certain questions concerning the laboratory investigations of human, bovine and avian tubercle bacilli were answered as fully, it is entirely possible that two and two would equal four, no more truly than would the sum of these knowledges equal that age-old will-o'-the-wisp, the method for curing or preventing tuberculosis.

Such an assertion may sound somewhat far fetched—may appear without due thought to be overdrawn. But people who are not constantly facing the problem of tuberculosis and people who are not familiar with the limitations of our information on the subject, occasionally by very reason of their detachment are liable to frame such questions as these:

- 1. Why a description of the various forms of tuberculosis in children especially? Are the forms of tuberculosis in children so different from those seen in adults as to require separate consideration? If so, in what way do they differ and why?
- 2. Are not both children and adults infected with the same types of tubercle bacilli, and do they not both respond to this infection in the same manner, by giving exactly similar reactions or by developing the same disease?
- 3. Are the bacterial findings in the effluvia from tuberculosis lesions in children at variance with those obtained from similar foci in adults? If so in what way do they differ and why do they differ?

4. If pulmonary tuberculosis occurs most often in people over fifteen, and if bone and glandular tuberculosis is observed most frequently in children under 12, what is the explanation? Are not both conditions caused by the same bacteria and do not these bacteria gain entrance into the bodies of both children and adults through the same route?

Briefly these are some of the questions that might be asked by an audience unfamiliar with the work-a-day aspects of the problem. Tuberculosis workers do not usually ask each other such questions, or if they do they rather perfunctorily reply in most instances with a sentence which begins with the phrase, "Most authorities are agreed to the theory, etc." To but few of the queries do they ordinarily give answers which begin with "It is a proven and positive fact, etc."

It is for this reason, probably, that it is occasionally well to pause for a few moments from the discussion of the onward and progressive events in the other branches of the work, and to consider in the usual manner the question of childhood tuberculosis. This is done with the hope that perhaps by conning over and deliberating once again upon the subject so familiar in title we may arrive at something approaching definite answers for the questions propounded, and perhaps in this way reach somewhat nearer to the arithmetical will-o'-the-wisp already mentioned.

At any rate I shall endeavor to conform with that idea and shall present the generally accepted beliefs concerning various forms of childhood tuberculosis in much the same manner that they have been discussed before. In doing this I thoroughly realize that I shall risk the possibilities of being banal and may perhaps bore you before I shall have finished.

However, it is my hope that those things will be avoided and that by naming over our theories once again in much the same manner that the ancient Greeks named over their previously vanquished enemies before going into battle, such repetition will result in a stimulation of our arithmetic, insofar as it relates to a correct solution of the vast problems of tuberculosis

Let us approach the specific subject under consideration somewhat left-handedly by contemplating briefly some of the theoretical changes and advances made in the field of tuberculosis within the last few decades.

I shall endeavor to remain true to form by stating that most authorities are agreed that the following statements are closely allied to facts if not entirely true: FIRST:—The disease, tuberculosis, is always preceded by infection with the tubercle bacillus, but infection with the tubercle bacillus is not always followed by the development of the disease.

SECOND:—The new-born infant is invariably free from tuberculosis, thus indicating that infection if it occurs always occurs after birth.

THIRD:—Compiled statistics from many sources lead us to believe that during the first year of life 15% of all people living in civilized communities are infected with tubercle bacilli. During the first five years of life 50%; and before the age of 14 is reached the organisms are said to be implanted in 80% of the people.

Although this last statement would indicate that as many as 80 out of every hundred people living in civilized communities are infected with the germ of tuberculosis and that this infection takes place in childhood, yet the actual development of the disease before puberty has never until recent years attracted, in comparison with adult tuberculosis, a great deal of attention. Indeed, it is now believed that in many instances tuberculous disease, as shown by autopsies, has existed in children and has become latent or spontaneously cured without ever exhibiting any external signs. Opie who has done an immense amount of autopsy work on the tuberculous says that lesions have been found at all ages after the second year of life, but in more than half these individuals these lesions were acquired between the ages of two and sixteen years. As the result of findings such as those we began to attach much significance to the fact that tuberculosis in children produces a different clinical picture from that seen in adults.

It is perhaps well to discuss separately at this point the occurrence of tuberculosis in infants and in children, defining the first class as individuals below the age of two years, and the second or childhood class as having an age range of from two to fourteen years.

Infant Forms.

Only rarely is there seen in an infant, the localized disease of the lungs peculiar to consumption in adult patients. Tuberculosis in infants is usually an acute general infection, and when the bacilli become localized by metastasis in any part, they produce lesions somewhat resembling pyemia. And partly because of this general nature of the disease, and for other reasons, some of them unexplained, tuberculosis at this stage of life renders almost vain, any hope of recovery. There are exceptions of course, but a noted authority states that during the first three months of life hardly any survive infection; the vast majority of those infected during the second three months of life succumb to the disease or to some intercurrent disease, and the outlook for infants between six and eighteen months is very unfavorable when infected with tuberculosis. The most fatal forms of tuberculosis in children especially in early infancy are the abdominal and meningeal types. Together they are responsible we are told for about 90% of the summed mortality in children under one year and for about 75% in children between one and five years.

The abdominal variety in infants is most often of the miliary type while the ascitic and plastic types are said to occur most frequently between the ages of two and eight, and mesenteric adenitis is observed more frequently in older children. It is the opinion of a large number of observers that infection with the tubercle bacillus is most frequently followed in children by involvement of the lymph glands. Abdominal infections apparently are no exception to this rule for the literature informs us that the glands of the ileocecal angle and terminal ileum almost invariably show the greatest involvement. The process, it has been further observed, may be limited at this point as a tuberculous mesenteric adenitis, or it may become disseminated by breaking through its limiting capsule and develop as a tuberculous peritonitis.

While abdominal tuberculosis in infants is probably more prone to recovery than is tuberculous meningitis yet the outlook in infants below the age of two years is depressing to the extreme. In older children since the manner of involvement is somewhat less general, recoveries are more often noted.

Libby, Metzner and Van der Bogert after extensive study of tuberculous meningitis in infants all assert that the disease practically never terminates in recovery. However such cases are occasionally reported but these do not minimize materially the generally accepted belief that in infants, at least, the disease has a definite tendency toward producing fatality.

Pulmonary tuberculosis occurs in infants as an acute morbid process, with general involvement as do the abdominal and meningeal types. In autopsies performed upon infants who have died of this acute process the lungs show no tendency to limitation of the disease. The attack is therefore made on a wide front so that but little expectancy can be maintained for recovery.

The condition not infrequently develops following measles or whooping cough. The mortality from this type of the disease among infants under one year of age has been estimated at about 80% and in those from one to two years of age at about 60%.

Of the three manifestations of massive tuberculosis infection in infants the abdominal is probably the most frequent, and is probably followed by the greatest number of recoveries. The acute pulmonary form while followed by over 80% of deaths in young children is second in importance to meningitis in producing mortality among this class of patients. Yet since the abdominal variety occurs more frequently than does the pulmonary, it is responsible for more deaths than is the latter form.

Childhood Forms.

The most frequent form of tuberculosis observed in children of three years or over is the glandular, and in this type the cervical and tracheo-bronchial lymph nodes are the sites most usually involved.

Our experience in various clinics and sanatoria in the state has convinced us that about 75% of children have palpable cervical glands. In many children having enlarged glands however, the symptoms are negligible, or there may be no clinical manifestations at all. It is not unusual to discover enlarged glands on the neck or in the thorax of children who are apparently in excellent health. From a clinical point of view cervical glands are considered to be pathologically enlarged only when they can be easily felt or seen, and they are considered in most instances tuberculous when the patient is obviously below par in strength, endurance, and size, and is showing such constitutional signs and symptoms as anemia, malnutrition, fever, rapid pulse, loss of weight and night sweats. A positive reaction to tuberculin aids in establishing diagnosis.

While the morbidity of tuberculous adenitis is high, the age period in which the condition occurs is remarkably free from mortality and though the symptoms may be severe, death only infrequently occurs as a direct result.

Perhaps the most troublesome and certainly the most noticeable forms of tuberculosis in children are the osseous and articular variety.

Tuberculosis of bone is dependent upon infection of the marrow of bone by the tubercle bacillus. The tubercle bacillus gains access to the bone marrow and causes the formation of miliary tubercles which arise from proliferation of the connective tissue of the marrow around the primary tubercle.

In the majority of instances the process begins in the epiphysis in the long bones. It is only in very rare cases that primary tuberculous involvement of the shaft of a long bone can be definitely authenticated.

Tuberculosis of the spine or Pott's disease is an infection of the spongy tissue of one or more vertebral bodies, generally at the anterior portion, and more often near the articular cartilage than elsewhere. The laminae, spinous and transverse processes are less often attacked though such involvement is occasionally demonstrated.

Arthritic tuberculosis or tuberculosis of the joints is most often explained, though the explanation is not satisfactory to all, by the fact that since the tuberculous process arises in the epiphysis and extends peripherally, the tendency of the condition in long bones is to extend to and infect and involve adjacent joints.

With one exception bone tuberculosis is essentially a disease of middle childhood, that is it develops usually during or after the third year. This exception is the involvement of the phalanges, or tuberculous dactylitis and is very nearly always seen in young children or infants.

Bone and arthritic tuberculosis are probably second in frequency of incidence, in childhood, but death occurs in very probably less than four per cent of these cases. The terrible deformities which are seen as a result of these forms of tuberculosis, such as various degrees and types of spinal curvature, ankylosed joints and contracted limbs however serve all too constantly as an index to the frequent occurrence of these manifestations of tuberculous disease.

Tuberculous involvement of the lungs of children over two years is unlike that seen in infants in many respects, but the greatest difference is in the course. That is in older children the lung tuberculosis shows greater tendency to localize and is more chronic in the development than in infants.

Most textbooks until recently have refrained from discussing at any great length the subject of pulmonary tuberculosis in children as differing from that observed in adults. And it was formerly rather generally conceded that the number of children who had definitely localized tuberculosis of the lungs was small. However, in late years the great variety of attention given to the subject of juvenile infection has brought to light the fact that this condition exists rather more often than was formerly supposed. Indeed very lately at the Meriden Sanatorium which is exclusively for children suffering with tuberculosis, we have been able to show that children between the ages of three and fourteen are afflicted with a form of lung tuberculosis identical with the consumption of adults much more frequently than has usually been granted. In 197 individuals presenting various forms of tuberculosis the lungs showed signs of localized tuberculous disease of the parenchyma in 34 cases. Following the method established by others we have further classified among these children a condition known as pulmonary tuberculosis, juvenile type, in which the tracheo-bronchial glands or hilus of the lungs were responsible for physical signs, and in which there were observed symptoms such as cough, fever, night sweats, anorexia and loss of weight.

While these are authenticated facts it still must be granted that the bone and glandular types occur more often than do the pulmonary varieties and of these last the juvenile is much more common than the adult type. And it must be further stated that although the morbidity of pulmonary tuberculosis is higher among children than is commonly estimated yet the mortality therefrom is probably only about one-half as great as that caused by tuberculous meningitis, and the greater majority of children who succumb to tuberculous lung disease are under the age of two years. Pulmonary tuberculosis therefore, between the ages of three and fourteen can not be said to induce a high death rate.

But since children have been shown to suffer with pulmonary tuberculosis in such a mild form it is perhaps not too much to believe that this is the type of tuberculous involvement which causes the focal scars in the lungs of individuals who come to autopsy after having died of some other disease.

The skin is not rarely the seat of the ravages of tuberculosis, and when it is extensively involved the results are in the highest degree disfiguring and repulsive. The consequences of tuberculous invasion of the skin are usually declared early in life, more particularly just prior to and during puberty, because it is in those periods that the skin is most easily involved, and it is probable also that at these ages the habits and environments of the individual are conducive to the occurrences.

Romer who suspects that the skin may play some part in receiving or dismissing primary infection believes as do many others that there are many forms of tuberculous skin lesions not generally recognized.

Tuberculosis of the eye occasionally exists in children and is evidenced most frequently by grayish red nodules or as a solitary tubercle in the iris. Other forms are described in the literature not infrequently such as tuberculosis of the conjunctivae, of the choroid, of the cornea and of the optic nerve. Phlyctenular disease is at the present time receiving much attention.

Various other organs and localities are occasionally reported as being the seat of manifest tuberculous disease in children but from the present evidence in the matter we may sum up somewhat as follows:

Tuberculosis in infants under two years generally occurs in one of the following forms:

- 1. Abdominal.
- 2. Meningeal.
- 3. Pulmonary in a general and acute form in contradistinction to the chronic slowly progressive consumption seen in adults.

In children two years of age and over the disease usually manifests itself by involvement of

- 1. The glands, most often cervical and intrathoracic,
- 2. The bones and joints,
- 3. The cortex of the lungs, and less frequently the parenchymal lung tissue,
- · 4. The skin, eye and other organs.

In discussing each form we mentioned its mortality as compared with other forms. A survey of the subject reveals the following interesting facts:—

Deaths of children from tuberculosis occur in by far the greatest majority in those under two years of age. We are justified therefore in considering abdominal, meningeal and pulmonary tuberculosis in infants as disease of an exceedingly malignant type.

The death rate from tuberculosis during the years from three to ten is the lowest at any time during life until senility is reached.

It appears from this therefore that we may be entitled to classify as the mild forms of the disease those types occurring most frequently during this age period such as glandular, bone, arthritic, pulmonary and skin tuberculosis.

With these comparatively well authenticated facts in mind it is perhaps malapropos to consider somewhat briefly a few of the theoretical conceptions which have been formed as a result thereof concerning the infection and course of tuberculosis in the human body.

One of the most interesting of these is that of Hamburger who having given considerable attention to the question likens the course of tuberculosis to that of syphilis, with periods of health and quiescence or latency, interrupted or followed by periods of acute or subacute exacerbations. The primary lesion is inoculated in childhood before the individual reaches the tenth year of life. During infancy this primary focus, if massive infection has taken place, or if the resistance is low, may cause acute fatal tuberculosis or hematogenic metastasis, but in the vast majority of people it heals or remains dormant.

In those in whom metastastic deposits of tubercle bacilli are distributed in various parts of the body secondary tuberculous manifestations make their appearance consisting in tuberculosis of the glands, bones, joints, meninges, etc. After the tenth year the advanced manifestations make their appearance in various forms such as the several varieties of chronic pulmonary phthisis, tuberculosis of the larynx, certain types of joint disease, of the kidney, of the pleura, etc.

Others simply state their belief that consumption is an exacerbation of tuberculosis which has been acquired during early childhood, in doses not sufficiently massive as to cause death, and has remained latent for years until some exciting cause or a reduction of the powers of resistance has brought about conditions favorable to its development.

Still others believe that the occurrence of tuberculosis in one of its mild forms during childhood, which we have just described confers a certain amount of immunity against the development of phthisis or consumption in later life. This contention is borne out somewhat by observers in various clinics and sanatoria who report that comparatively few adult consumptives are seen who present scars on the neck as the result of old glandular disease, or who have ankylosed tuberculous joints or who show inactive bone tuberculosis. In a comparatively recent Medical Journal one observer reported that in a survey of thirty-five hundred cases of adult phthisis but twenty-four could be found who had old cervical scars due to tuberculous disease which had occurred in childhood.

Taking the other side of the subject there are others who have raised the question as to whether every child infected at an early age is destined to become a consumptive. Fishberg ably contends against this by saying that if this were the case tuberculosis among adults would not kill one out of seven or ten individuals as is found, but that over 90% of humanity would succumb to phthisis.

However, reverting to further consideration of the various forms of tuberculosis observed in children we find ourselves confronted with the necessity for indicating the type of tubercle bacillus to be observed in these several manifestations of the disease. In many instances the statistics upon the subject are unreliable but I quote the following from the accurate pen of one who is not only Connecticut's dean of tuberculosis, but who is also a striking figure in the international field of endeavor in this line,-Dr. Stephen J. Maher. He states that "a few authorities including Nathan Raw of England insist that most of the bone, glandular, meningeal and abdominal tuberculosis in children is caused by the bovine tubercle bacillus and by the drinking of the milk of tuberculous cows, but the other authorities including all American and German and French and Scotch authorities agree that most of these forms of tuberculosis are of human origin, putting the percentage due to milk at from ten to fifty per cent in all but abdominal tuberculosis where the bovine tubercle bacillus confessedly everywhere causes more than half the cases. Of tuberculous meningitis, in onefourth of the cases examined the bovine tubercle bacillus was found."

Other authorities such as Park and Krumweide believe that in children under five years of age 61 per cent of cervical tuberculous adenitis, 58 per cent of abdominal tuberculosis and 66 per cent of the generalized tuberculosis and meningitis, and of alimentary origin are caused by the bovine bacillus.

Fishberg states that in adults bovine infection if it does occur at all is so rare that it is of no significance from any standpoint, and that only in children under five years of age are bacilli of bovine origin apt to cause disease.

Others have asserted that these mild bovine infections of the cervical, mesenteric and thoracic glands while in themselves harmless, as evidenced by the low mortality therefrom, nevertheless confer immunity to the organism which may last for life and in that way adults may be made safe against infection by human tubercle bacilli.

We, in Connecticut, who have witnessed the work of Dr. Maher and Dr. Stockwell in transmutating or changing the morphological forms of tubercle bacilli are not yet ready to recognize the validity of such a claim—and there is as yet insufficient evidence that protection against phthisis conferred by early tuberculous disease is dependent upon infection with bovine tubercle bacilli as some observers have contended. A consideration of some of the statements just mentioned indicates clearly however, the variety of attention being given to the subject of childhood tuberculosis.

Being keenly cognizant of the potentialities involved in this phase of the problem, the Connecticut Tuberculosis Commission in 1919 opened the Seaside Sanatorium for the treatment of bone and glandular tuberculosis in children and in July, 1920, converted the Meriden Sanatorium which for ten years had been an institution for adults, into one devoted exclusively to the care of children suffering with pulmonary tuberculosis.

This was done for several reasons:

- 1. That the children of the state who were suffering from tuberculosis might have ready access into institutions equipped for the care of tuberculous children, yet segregated from tuberculous adults.
- 2. That these tuberculous children might receive antituberculosis and general health education which would assist them in building sufficient resistance to overcome their present disease and contribute towards a certain amount of immunity to re-infection in later life.
- 3. That intensive attention might be given by men interested in tuberculosis work to the subject of childhood infection and disease with the hope that by observation and research there might be evolved a solution of some of the knotty problems of infection and immunity such as,—

(a) What bearing has any form of tuberculosis in children upon the development of phthisis in later life?

(b) Will any form of tuberculosis in childhood grant immunity to reinfection?

(c) Why is the bacillus of tuberculosis so difficult of demonstration in the excrement of tuberculous children? Is it possible that the tubercle bacillus, which is now known to be pleomorphistic, is present in some involutional forms, not recognized as such?

(d) If it is true that so much of tuberculosis infection occurs in early life, will not intensive study of tuberculous children give some clue as to what conditions

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prevent all but ten or twelve of the population from succumbing to the disease. And will not such intensive study reveal to us a better answer than we have yet received to that intriguing question, "What is the route of infection with the tubercle bacillus, aerogenic, hematogenic, lymphogenic or otherwise?"

(e) And finally will not close attention to the various forms of tuberculosis in children yield more information concerning bovine infection in human beings and its bearing upon and relation to human infection and disease?

When the correct solutions for these problems have been attained then it is possible that we may battle with the disease tuberculosis, with reasonable assurance as to the victorious outcome.

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