Round Table Discussion

EARLY DIAGNOSIS AND TREATMENT OF TUBERCULOSIS IN CHILDREN

EDITH M. LINCOLN, M.D., New York City, Chairman
J. B. SCRIVER, M.D., Montreal, and A. D. BIGGS, M.D., Chicago, Secretaries

Chairman Lincoln: We will try to stay as close to the subject matter as possible and then if we have time and you want to go off into other subjects connected with tuberculosis, we can. I think there is plenty of material for discussion in early diagnosis and the treatment of the early phases of tuberculosis, that is, primary and postprimary tuberculosis. This will take up our time without going into the discussion of chronic pulmonary tuberculosis, since that is not a form of tuberculosis which is common in children.

Specific therapy has changed the attitude of pediatricians to tuberculosis. Formerly a pediatrician took the attitude that the great majority of children who had primary infection, evidenced by positive tuberculin tests without or with positive x-rays, would get better without ever having any symptoms; that a few of them might develop complications such as tuberculoses of the cervical nodes, or of the bones or joints, which could be turned over to a specialist and not be seen again by the pediatrician. A few cases would develop fatal complications such as meningitis or miliary and promptly die. Therefore, there was little of interest to the clinician in the story of tuberculosis in the child. As recently as 5 years ago, just before chemotherapy, I talked to pediatricians in many teaching centers and I was repeatedly told that the diagnosis and the care of tuberculous children was a minor problem and that tuberculosis was practically never seen in their services.

Since chemotherapy there has been a new interest in tuberculosis and I think this is shown partly by this round table discussion. It is also shown by the increasing reports in the literature as you will note if you look over the pediatric journals of the last few years and see the unprecedented number of papers about tuberculosis. Great interest has been shown by phthisiologists as well as by pediatricians in the treatment of tuberculosis in children.

If we are going to treat tuberculosis and to control it intelligently in any community we ought to know what the extent of the problem is. In the early days of the tuberculin test we had many surveys: we know that 95% of the children were infected in Vienna; then surveys were made in St. Louis, Philadelphia and other cities and everywhere we found a high percentage of children infected with tubercle bacilli.

We know that today fewer children are infected but there are very few surveys that tell us exactly how many children have positive tuberculin tests. There are a few reports from hospital groups; we reported on our group in 1938 and showed that while there had been relatively little change in the total number of positive tuberculin tests seen at Bellevue there was a change in distribution and many fewer infants showed positive tuberculin reactions. Dr. Beaven has recently reported on a tuberculin survey of Rochester, N.Y., and has emphasized the reduction in the number of children with positive tests. In most communities, however, we have very little information about the extent of this problem; it is really up to us as pediatricians to find out how much tuberculous infection exists in the children of any community. We know that tuberculosis is a contagious disease and we know that the amount of tuberculosis in the adult population is bound to be reflected in the number of infected children. In rural areas and in moderate sized cities with relatively good housing where conditions of employment are good and where there is a low rate of tuberculosis in adults we expect and find a low rate of tuberculosis in the children and a low death rate. On the other hand, children who live in crowded sections of large cities where the rate of tuberculosis is high have more tuberculosis and a much higher death rate.

I would like to review briefly what has happened over the course of years as far as tuberculosis is concerned. Back in 1900 tuberculosis was a grave problem, although we didn’t do much about...
it; there was very little that we could do. In the years since 1900 there has been a steady fall in the number of cases of tuberculosis in the various age groups and again this decline was much more marked in the infants than in the older age groups. The last year for which I have full census figures is 1948 and I picked Minneapolis, in contrast to New York, because we all know there is an excellent tuberculosis service in Minneapolis and they are rightly proud of the low tuberculosis death rate in children. The death rate per 100,000 for all ages is much smaller in Minneapolis than it is in New York City and the difference is even greater at the beginning of 1948 than it was in 1940. This is reflected in the number of deaths from tuberculous meningitis. From 1934 to 1944 there are very few deaths from tuberculous meningitis in Minneapolis and even more in New York City than would be expected from the difference in size of population. As I have said before, the real extent of the problem as far as your own communities are concerned is something that you have to find out for yourselves, but there is always a definite relation as we see here between the amount of tuberculosis reported in any community, the number of tuberculosis deaths and the incidence of infection in children. Of course, there are tremendous variations due to differences in economic level and degree of infection. Nevertheless, the pattern of the disease remains exactly the same. That individual child who died of tuberculous meningitis in Minneapolis had exactly the same disease with the same prognosis as the children who died in New York. The difference between Minneapolis and New York is in the number of cases and in the degree of infection leading to variations in course and prognosis. Once fatal complications have developed the pattern is exactly the same.

Now, we shall go on to a discussion of early diagnosis which is an important subject for pediatricians. Diagnosis of any form of primary tuberculosis, as we know, is usually made by case finding methods. It is made by a history of contact with a case of tuberculosis or by a tuberculin test. The test is done as part of a routine examination, in school, in hospitals or in the physician’s office. When tuberculosis is diagnosed by signs or symptoms, the disease is already established and you are not making an early diagnosis. The early recognition of tuberculosis in any child is important because the most serious complications, miliary and meningitis, are most likely to occur in the first 3 months of the infection. Early diagnosis of these infections will obviously be made most often if you already know that the child has a tuberculous infection and are alerted to the possibility of tuberculous complications. The pediatrician, therefore, is the one who can help most in the early diagnosis of tuberculosis by doing tuberculin tests as part of his regular yearly examinations, and more frequently when he has knowledge of a possible contact with a patient who has tuberculosis. By doing tuberculin tests the pediatrician will not only learn the prevalence of infection in his own group of patients but he will train himself to think of tuberculosis in differential diagnosis.

Diagnosis is obviously the first step toward treatment. In our own clinic we have always felt that every child with primary tuberculosis, or every child with a recent conversion of a tuberculin test, should be treated by increased rest, by a diet high in fat and protein and by extra vitamins even if he is asymptomatic. The contact history and the economic condition of the family also have to be taken into consideration in deciding whether you are going to treat the child in this conservative manner in his own home or whether he has to be sent to a hospital. The degree and duration of conservative treatment depends on an estimate of prognosis. This, in turn, is based on 3 factors: the apparent duration of the disease, the age of the child and the extent of the lesion on x-ray. The duration of the tuberculous lesion is an important factor in prognosis. We base this opinion on a study that we did between 1930 and 1940. We followed all consecutive cases of primary pulmonary tuberculosis that we saw during this 10 year period. During this period we had 622 cases of primary pulmonary tuberculosis. We found that 90% of the deaths occurred within a year of the first diagnosis; about 75% of the deaths occurred in the first 6 months after the original diagnosis and almost 60% within the first 3 months. That is why we think it is so important to follow and treat conservatively every child who has a recent primary infection whether or not you see it on x-ray. The age of the child is also important in estimating prognosis. In this same group of children the death rate was highest in the group under the age of 6 months and lowest during the so-called safe period between 4 and 9 years of age. The influence of the size of the primary complex on prognosis is harder to determine. However, an attempt was made in our series of cases to measure the primary on x-rays and we found that the mortality rate in the children with the largest lesions was more than double the rate in children with small primaries.
We think we ought to treat conservatively all cases of primary tuberculosis. How are we going to pick the children who need chemotherapy in addition to conservative therapy? The selection of cases always has to be on an individual basis, but by and large you have to depend again on a knowledge of the course and prognosis of the form of tuberculosis under consideration. In order to know what to treat we studied our statistics regarding prognosis. We knew that before chemotherapy 95% of the deaths in our group of tuberculous children were due either to tuberculous meningitis, to various forms of hematogenous tuberculosis or to local progression of the primary with cavitation and bronchogenic spread. Therefore, we decided that chemotherapy would be mandatory in these complications of tuberculosis which constitute about 20% of our ward population. Aside from these forms every case should be considered individually and streptomycin should not be used except for forms of tuberculosis in which it has been proved to be superior to conservative methods of treatment. This rule would restrict the use of streptomycin, in addition to its use for the complications already covered, to forms of tuberculosis which have been shown to yield rapidly to short courses of treatment, for example, tuberculous laryngitis and draining cutaneous sinuses; streptomycin would also be used to "cover" surgical procedures which would be dangerous or impossible without it.

Treatment may also be tried as an elective measure in other forms of tuberculosis such as endobronchial disease and tuberculosis of the bones or nodes. Criteria for treatment in this group will change as results of therapy are evaluated. For instance, after treating 30 children with endobronchial disease with streptomycin, we could find no evidence of definite response to therapy and therefore discontinued routine chemotherapy of tuberculous endobronchitis. Follow-up of months or years will sometimes be required before final judgment can be passed on the value of chemotherapy in some complications such as tuberculosis of the cervical nodes.

In addition to the group of cases where chemotherapy is always indicated and the cases for whom chemotherapy is an elective procedure, there is a third group consisting of cases of primary tuberculosis in which we believe the use of chemotherapy is contraindicated regardless of the size of the lesion or the age of the child. At Bellevue this group represents 70% of our ward population. There is no evidence, to my knowledge, that streptomycin hastens the healing of a pulmonary primary. We have all treated children with miliary tuberculosis and tuberculous meningitis. We have seen the miliary melt away under the effect of streptomycin and the meningitis cured and yet the primary pulmonary tuberculosis takes its own course and is still present after the other complications are arrested. There is also no evidence to show that streptomycin will prevent complications. A third reason for withholding the use of streptomycin in uncomplicated cases of primary tuberculosis is the possibility of the emergence of tubercle bacilli, resistant to streptomycin. The occurrence of resistance is diminished with combined therapy, but occasionally resistance develops even when combined therapy is used. Since streptomycin is the only drug we have which will cure meningitis it does not seem fair to use it in nonfatal complications except for short terms of treatment; and certainly not in the very early stage of the disease when meningitis is most likely to develop. Except in short courses streptomycin should be used in combination with another drug. It has been shown definitely that combined therapy enhances the value of the streptomycin, that it delays the emergence of resistance and permits the continuation of bacteriostatic therapy for years. We use promizole® in meningitis, miliary, and more protracted forms of hematogenous tuberculosis. We use PAS in predominantly pulmonary forms such as progressive primaries and of course in chronic pulmonary tuberculosis.

I said before that early diagnosis is important because it leads to the early diagnosis of complications. We are quite sure there is a definite relationship between early diagnosis of complications, which in turn leads to early treatment, and good results of therapy. All over the world the best results are in those groups of patients which have been treated early in the course of their disease. The British have contrasted the good results of treatment of early cases of meningitis with the poor results obtained after late diagnosis. Similar statements have been made by writers from other countries. All the evidence shows that early diagnosis and early treatment leads to the highest percentage of cures.

It is obvious then that the diagnosis of tuberculous meningitis should be made by the pediatrician because he is the one who should be following the child with primary infection who is most likely to develop meningitis. Treatment of meningitis also belongs in the field of pediatrics.

A study of symptoms of onset of meningitis was made in a group of 167 cases that we saw at
ROUND TABLE: TUBERCULOSIS IN CHILDREN

Bellevue before chemotherapy and of course all of them died. The common symptoms, vomiting, apathy, fever, anorexia, irritability are all those that we associate with almost any acute infection. That is one reason why I think this is a disease for the pediatrician to diagnose. Of course he is going to be more suspicious of the diagnosis if he already knows that his patient has a positive tuberculin test. Some of the symptoms vary with the age of the child. You rarely see a child who complains of headaches under the age of 5. Convulsions are a common early symptom in infants but a rare symptom of onset in the older child.

We treat all our meningitis and miliary cases with combined therapy. This is an outline of what we use and, of course, no scheme is adhered to rigidly. We give children with miliary 1 gm. streptomycin daily for 4 months; we give the meningitis cases 1 gm. daily for 6 months. If the child with miliary develops meningitis we start treating by the intrathecal method at once. We usually begin with 100 mg. daily regardless of the age or the size of the child and we maintain that dose as long as we can. Sometimes we keep it up for a week, sometimes we keep it up for the full course of 40 treatments. If we can't maintain this dosage we reduce to 50 mg. or we give 100 mg. every other day. Even if the character of the spinal fluid improves rapidly we continue intrathecal therapy for a minimum of 40 treatments. If at the conclusion of the usual course the spinal fluid has not returned to normal we continue therapy by the intrathecal route.

I know there is a great deal of argument about the use of intrathecal therapy and I hope you will tell us some of your experiences treating cases with and without intrathecal treatment. I am perfectly sure that one can treat and cure some cases of tuberculous meningitis with intramuscular therapy alone. But I don't know how to pick out the cases that will be cured with intramuscular therapy. The percentage of cures in series of cases treated with both intramuscular and intrathecal therapy is far greater than in series treated with only intramuscular therapy.

We give promizole® orally starting with a half gram divided into 4 doses every 6 hours until we get a blood level of 1 to 3 mg./100 cc. The range of the dosage is very great as I will show you in a minute and promizole® cannot be given successfully and certainly not without toxicity unless it is controlled by a blood level. We continued promizole® in our first 25 cases for 3 years and we are continuing it in our next 25 cases for 2 years. That period is purely arbitrary of course; we wanted to obtain bacteriostatic action for a long period of time in the hope of preventing later relapse. We had shown that we could cure patients with miliary tuberculosis with promizole® and that they would stay cured. Our original group of 5 patients with miliary that were treated in 1944 are still alive and well and none has ever developed meningitis. So we knew that you could give promizole® safely over a long period of time. Other people use PAS in combination with streptomycin; it has been proved that PAS delays the emergence of resistance and this has not been proved with promizole®. However, clinically we have had no resistance develop in the spinal fluids of cases except as a terminal event. Moreover, those of you who use PAS know that it is often a difficult drug to administer. To give it to a child for 2 or 3 years would be a problem whereas promizole® is an easy drug to administer. Deafness is unfortunately something that occurs in a certain percentage of the children and why it selects some children we don't know. In the last year we have been having an increasing number of cases of deafness. However, we have never had any mutism in children who have been treated with intramuscular streptomycin for other forms of tuberculosis. All the deafness has been in patients treated for meningitis and, therefore, with intrathecal streptomycin. We have always known that patients with pneumococcic meningitis had a certain percentage of deafness but previously patients with tuberculous meningitis didn't recover so we don't know whether the deafness is due in part to meningitis or mainly to the streptomycin. The reactions to intrathecal streptomycin are much more striking than to intramuscular streptomycin. With increased ataxia and vomiting, we keep right on with intrathecal therapy because we think it is important to treat the child regularly in the first weeks of the disease. However, if the child has a high fever, as they sometimes do—40.5° or 41.0°C.—or if he has a convulsion we do reduce the dose or increase the interval between the doses. Sometimes a streptomycin reaction is seen which is more striking than the convulsions and the fever; a reaction in which the child loses all his superficial reflexes, becomes lethargic and may have marked slowing of respirations. After this type of reaction we always reduce the amount of streptomycin given intrathecally. With promizole® we almost always get a slight cyanosis of the lips and finger nails, in the early stages of the administration; a slight enlargement of the thyroid and an elevation of cholesterol usually appears after about 2 or 3 months. We have a few children in whom there has been a question of liver damage which has
been reversible after the drug was stopped. This occurred mainly in the few children who ran high blood levels on small doses of promizole. Occasionally one sees stimulation of secondary sex characteristics in girls and this is the only toxic reaction which is not reversible when the drug is withdrawn.

Reactions to PAS are ataxia, nausea, vomiting and abdominal pain. They don’t always occur, but when they do they are disagreeable, and it is difficult to have older children continue with the treatment once reactions have occurred.

In treating children with tuberculous meningitis, we have learned not to expect too much in the first week. Before therapy it was an acute disease and patients died within an average of 19½ days. The response to therapy is slow and even in the child who is going to do well we often see little change in the first weeks; under therapy neurologic signs may develop and a child may pass progressively from the first to the second and then to the third stage of meningitis and ultimately recover. The good signs such as weight gain, increased appetite and falling temperature are not usually seen until the second month of illness.

If the spinal fluid has not returned to normal at the end of the usual period of therapy treatment may be continued. We keep up intrathecal therapy until the spinal fluid has come to normal by which we mean that the sugar is normal, that the protein is stabilized at or below 100 and that the cells do not show marked variation in numbers.

Once we stop streptomycin therapy we watch the child and continue to do lumbar punctures twice a week at first and then every week for a period of at least 2 months. During this time the child is allowed out of bed for short periods. It is important to keep children quiet and keep them under close observation for at least 1 year after the diagnosis of meningitis.

The sugar returned to normal in about ¾ of our cases while they were still on intrathecal therapy. In the remaining 25%, intrathecal therapy was prolonged beyond the usual period. The protein rarely becomes normal during intrathecal therapy and is still somewhat elevated in about half the cases at the end of intramuscular treatment.

In forms of tuberculosis other than meningitis and miliary we do not give as much streptomycin; we have tried to gauge the amount of streptomycin so that we relatively give more to the small baby than we do to the older child because the prognosis is much worse in the young baby.

Dr. Milton I. Levine, New York City: I tried treating a few cases with streptomycin and with the first case I was quite thrilled in that it seemed to subside considerably quicker; however, that was my first case! After that we found no change at all and again, as Dr. Lincoln has pointed out, in cases where there was a primary which had blown up into miliary tuberculosis under treatment with streptomycin the miliary would disappear but the primary would stay. In a case with cervical adenitis a child came in with a large cervical node and then developed miliary tuberculosis. The child received streptomycin and promizole®. I think all of us who treat children with tuberculosis are impregnated with the fact and are using promizole® with streptomycin. The child recovered from the miliary so he was sent home with promizole 3 gm. a day and after about 2 years the thing blew up again. Apparently the promizole® was inadequate in preventing the growth of the organism in the cervical node.

Chairman Lincoln: Whenever you have an area that is inaccessible to the drugs, and it has been shown that streptomycin is not absorbed well in caseous areas, you will have a progression of the lesion.

Question: Dr. Lincoln, would you say a word about the contagiousness of the primary tuberculosis? In most hospitals they are put under strict precaution.

Chairman Lincoln: Dr. Wallgren, as you know, has shown pretty conclusively that primary tuberculosis is probably not contagious. Nevertheless, the presence of tuberculous children on a pediatric ward creates a compensation problem. After all primary tuberculosis is caused by the same tubercle bacillus which is responsible for tuberculosis in adults. On the other hand, those of you who try to obtain tubercle bacilli out of gastric washings know how difficult it is to obtain positive cultures; and the only reasonable method of transmission of these bacilli would be by cough. I don't really think that in the absence of a cough that you have any right to call primary tuberculosis a contagious disease. However, I feel strongly that one should not send a child with a fresh primary to a home where there is a newborn infant without warning the mother of the possible risk of contact, because I think in this very young age group it may take only one cough or sneeze to infect the baby.
Among our best results with tuberculous cervical nodes are cases where we have permitted the nodes to suppurate. The fluid was then aspirated and streptomycin 1.0 gm. reinseted. If in a week the node was again fluctuant, a similar treatment was performed. Usually the size of the node diminished considerably in several weeks and there was no further evidence of activity.

I am in complete agreement with Dr. Lincoln's concept concerning the treatment of complicated tuberculosis. However, I believe I am somewhat more optimistic as regards the child with uncomplicated primary tuberculosis between the ages of 2½ years to 12 years. In our observations during this age period we have found no harm whatever in permitting these children to be ambulatory without restriction as long as they remained afebrile. There was no increase in the number of complications and there was no decrease in the speed of recovery. This is in contrast to the opinion of Dr. Arvid Wallgren who advises bedrest until the sedimentation time has returned to normal, reporting that he finds an increase in complications when children with primary lesions of tuberculosis were ambulatory.

However, I can't help but feel that there is something different about the response to primary tuberculosis in European children as compared to American children. This opinion is shared by a number of other workers who have made numerous observations in Europe and the United States.

For instance, we see very little erythema nodosum accompanying primary tuberculosis in this country, whereas its occurrence is very frequent in Europe. In my own experience of 22 years I have seen no more than a half dozen cases.

Furthermore, in Europe pleural effusions are not uncommon during the course of the primary complex. In this country they are comparatively rare.

It is difficult to determine the cause of these differences in geographic sections of the world, but it probably accounts for necessity of a much more rigid regimen of treatment as advised by Dr. Wallgren in Sweden.

New Speaker: I have been interested in the primary in St. Luke's hospital in the outpatient department and about 10 years ago decided to conduct a little clinical experiment on primary tuberculosis. We gave a tuberculin test to every child who came into the outpatient section. In the first 2 years we had 460 children whom we tested; exactly ¼ of them had a reaction. Each one of those children, 115, have been studied by me since then: I have kept close track of them and the results are remarkable. Any child who reacts we call a primary. It is our opinion that if you analyze x-rays carefully (and we have one of the best x-ray men in the field in our hospital) you can see some kind of a shadow in almost every primary. Not as soon as you get the reaction—but if you follow it you see a shadow eventually. Perhaps you can't distinguish it from a respiratory infection, whooping cough, etc. We took an x-ray every 3 to 6 months, then every year and then the patients were followed for 10 years. At the same time, we took blood counts, urinalyses, sedimentation rates: we weighed and measured the patients every time they came in. They had to come back every 2 months and then once a year. We compiled our data; those children did not have any significant gains in their blood count, there was no change in their urine analysis and that group as compared with the total group gained at the same rate. They gained in height at the same rate and those that we classified as an ordinary primary had no physical findings. Now the pediatricians have a little different viewpoint. Twenty-five per cent of our children who came to the dispensary had ordinary primary and we wouldn't have known it if we hadn't done the tuberculin test and followed up with x-ray. According to what we think, those children don't need anything but there are a few in that group who have an extraordinary primary or a massive shadow. Those that have massive shadows are the ones who go to the tuberculosis people and when our tuberculosis people are talking about primaries they are talking about the unusual primary that get to them. The ordinary primary is a child who plays and runs about actively with unsuspected tuberculosis; these children don't have to be treated. This is entirely different from the patient Dr. Lincoln is discussing; I would call her type of patient an extraordinary primary. The ordinary primary according to our work and the one which the pediatrician usually sees is entirely an asymptomatic disease and you wouldn't know the child had it if you didn't take the tuberculin test. I hope this doesn't confuse the issue.

Chairman Lincoln: I would like to say that in our own group of children with primary tuberculosis we realize we are dealing with a heavily infected group. Before chemotherapy about 20% of our patients died and we have fortunately been able to continue to follow most of the survivors.
Probably many of our survivors fall into the group of simple primaries to which the last speaker referred but on first observation it is not possible to determine which children are going to do well. Eighty-five per cent of the patients we have on our ward were originally sent in because they were contact cases or were found on our own pediatric wards through the routine use of the tuberculin test.

Dr. John T. Kometani, Honolulu: Of those who recovered from meningitis, what about their mental status?

Chairman Lincoln: The best way to answer that is to say that we never had a child survive whom we regretted treating. We have no so-called 'vegetables.' We have had children who had behavior difficulties when they recovered but children who have been in bed for 6 or 8 months would very likely have difficulties if they had some other disease. The deaf child is particularly apt to have behavior problems. I am sure, however, that with continued follow-up of our cases that we will find evidence in some children of cerebral damage.

Dr. Cochrane, Toronto: Would you mention the place of (a) intraventricular therapy and (b) old tuberculin in meningitis according to any results you have had?

Chairman Lincoln: Most of the early cases that are treated recover; most of the cases that are diagnosed late and a few of the cases that are diagnosed early don't do well. After a month or more of therapy they are still drowsy or even comatose and they may develop signs of block. Since severe reactions occur in the course of PPD therapy it is essential that burr holes be made before beginning treatment in order to be able to relieve pressure promptly.

Dr. Henry B. Strenge, Oklahoma City: What would you think of the administration of PAS to each child with primary tuberculosis in an effort to avert complications?

Chairman Lincoln: The experience of people who have treated meningitis with streptomycin and PAS is that the combination has as little effect on the primary as streptomycin has, so that I don't think there is any reason to think that it would cure the primary when administered without streptomycin. The same answer holds for prevention of complications.

Dr. Ralph D. Swaiman, Burlington, Vt.: What is your opinion as to the value of the patch test?

Chairman Lincoln: I think the patch test is a valuable screening test, but I don't think it should be used as a final answer if you suspect tuberculosis. If any child has been shown to be tuberculin negative to 1 mg. it is sufficient to do a patch test at intervals thereafter to discover tuberculosis. It is extremely important that the doctor know how to read the patch test. The directions state that you must have vesiculation but about twice a year I see a child who has had a patch test interpreted as positive on the basis of swelling and redness without vesiculation, which proves to be negative when tested with a Mantoux through 1 mg. in strength.

Dr. Alfred D. Biggi, Chicago: Should the streptomycin dose be divided?

Chairman Lincoln: We give streptomycin only once a day unless the child is very small and very thin in which case we divide the dose. In many of our cases, exclusive of the miliary and meningitis cases, we are giving streptomycin only twice a week with PAS every day, as this method has been shown to be as effective in adults as daily administration of streptomycin and markedly delays the emergence of organisms resistant to streptomycin.

Dr. Biggs, Chicago: Do you not have occasional cases where it is difficult to tell whether it is a primary or reinfection?

Chairman Lincoln: I presume that you refer to cases in older children or adolescents. Dr. Amber-son always says that it doesn't make any difference in this age group whether you have reinfection or primary tuberculosis because you should treat it as reinfection in either case.

Dr. Biggs, Chicago: So they get streptomycin anyway?

Chairman Lincoln: They get conservative therapy for minimal disease and streptomycin for moderately or far advanced tuberculosis.

Dr. Henry C. Thatcher, Auburn, Me.: What is the present consensus of opinion in regard to the treatment of nonsuppurative lymphadenitis with x-ray?

Chairman Lincoln: We believe it is primarily a surgical condition. With x-ray treatment there is the danger of increased fibrosis making ultimate surgery more difficult. It may have a place in therapy but we have not used it for many years.

Dr. Morley P. Welles, Columbia, S.C.: How long do you continue the use of streptomycin in cases other than meningitis?
Chairman Lincoln: It varies with each case. We usually treat with daily streptomycin for 2 to 4 months. In children with progressive primaries the bronchogenic spread usually regresses during this time but the cavity may be persistent. Often in these cases we use prolonged therapy for months or even years with biweekly streptomycin and daily PAS until resection of the persistent cavity can be done with relative safety.

Dr. James B. Snow, Oklahoma City: Do you advocate streptokinase as an adjunct to the treatment of the meningitis?

Chairman Lincoln: We have tried this in a few cases and I would say the answer is no. We have seen severe reactions which are not easily controlled in the older children and the young adults may develop psychoses. I think that streptokinase has its place in tuberculosis, perhaps in bronchial lesions and in secondary abscesses. I think we are never going to be able to cure a high percentage of cases of tuberculous meningitis who are first seen in a late stage. There is not any doubt that a few have been cured but in the majority of cases, if you don't get them early you lose a large per cent of the cases. Of course, we keep on trying but I think we might do better to start on a campaign of trying to teach early diagnosis and increase our percentage of cures by diagnosing more cases in the first stage of meningitis.

Dr. Samuel S. Brown, Brooklyn, N.Y.: Would you please define progressive primary tuberculosis?

Chairman Lincoln: I mean locally progressive primary tuberculosis—a primary that, instead of disappearing slowly over a period of months leaving eventually only a small calcification, enlarges during the early months, develops a highlight on x-ray and evidences of bronchogenic spread from the cavity. If you follow these cases from the beginning you can often see the whole picture.

Dr. C. Read Boles, Clayton, Mo.: Would you discuss the diagnosis of tuberculosis in children who have received BCG?

Chairman Lincoln: If you don't have a positive tuberculin after BCG then I think the diagnosis is the same as if the child had not received BCG. When BCG has been followed by a positive tuberculin which has persisted, diagnosis is often difficult. That is Dr. Myers' objection to the use of BCG. I would like to hear what Dr. Levine thinks about it.

Dr. Levine: If BCG inoculation is successful in causing a tissue sensitivity to tuberculin, as evidenced by a positive tuberculin test, then it is rarely to get primary tuberculosis pulmonary infiltration—because the primary focus has already been localized at the point of BCG inoculation, whether it is on the arm or leg.

In cases where the allergy following BCG vaccination disappears, there is again the possibility of a new primary tuberculous infection in the lungs. However, the occurrence of primary lesions of tuberculosis after a successful BCG inoculation is extremely rare.

Chairman Lincoln: Of course, Dr. Wallgren's idea is that BCG is a temporary help and should give you enough immunity so that the natural infection when it occurs will not be a progressive one.

Dr. Levine: Vaccination with BCG may be of some real importance in late adolescence and young adult life, for there is some reason to feel that during these age periods the primary pulmonary infiltration becomes progressive instead of subsiding and calcifying at the point of primary focus. Recently a study was made of soldiers in the Swedish Army which demonstrated that only a few months after having negative chest x-rays and negative tuberculin tests, a fair number had developed caseous tuberculous pulmonary lesions with cavitation.

In other words, there had developed a progressive primary rather than the usual sequence of a primary focus to calcification. If we can prevent a pulmonary primary in an adolescent or young adult by placing a primary lesion in the arm or thigh, we might possibly prevent the occurrence of such progressive primaries.

Dr. Thomas P. Saltiel, Chicago: Do you use streptomycin in early tuberculosis of the hip?

Chairman Lincoln: I think that would be one of its elective uses. We have used streptomycin when a child came in with acute tuberculosis of the spine with high fever for which no other cause could be found except tuberculosis. The child went on to eventual operation. He did not develop meningitis. We treat a good deal of bone and joint tuberculosis incidentally in our meningitis cases and most of them go on to progressive disease and surgery. There are, however, physicians who think that bone and joint tuberculosis responds to streptomycin. Cases have to be followed for a long time after treatment to be sure of permanent results.

Dr. Levine: Recently there was a paper in which it was stated that the test for bacterial resistance
to streptomycin is not comparable to the body reaction to streptomycin. In other words, by test, the organism may be quite resistant to streptomycin but it was felt that in the body streptomycin could still be effective.

Chairman Lincoln: I think there is no doubt about the fact that you can have a certain degree of resistance to streptomycin as found in the bacteriologic laboratory and still get benefits from streptomycin. We are quite sure of that in some cases. I am also sure that organisms from one portion of the body may be resistant and tubercle bacilli from another area may be sensitive to streptomycin. We had a child with endobronchial tuberculosis and meningitis and treated him with streptomycin and promizole® in the usual way. He was cured so the organisms in his spinal fluid probably weren't resistant. In a bronchoscopic examination about a year later we obtained a culture of tubercle bacilli that was completely resistant.

Question: How often do you have them return for spinal punctures after discharge?

Chairman Lincoln: We do punctures every week or twice a week, for at least 2 months after streptomycin is discontinued and if the child has a good home we let the child go home at the end of that period and come back every 2 weeks for a puncture; after a few months we try to secure a monthly tap for a variable time, never longer than a year.

Question: You mean you do have symptoms?

Chairman Lincoln: Yes, because while we have never had a relapse later than 43 days, we want to be sure.

Question: What tuberculin test do you think is the most suitable?

Chairman Lincoln: I think the best is a Mantoux test with PPD or Old Tuberculin. I use the patch test, too, as I have mentioned before. One important point in regard to the patch is to notice the date of the box; if it isn't too old, it is an accurate test if you are sure you know how to read a positive patch test.

Dr. Sidney R. Kaliski, San Antonio: Have you ever used patch tests quantitatively in the sense that you are using a time element of application for evaluating the degree of sensitivity?

Chairman Lincoln: No, and as you know the degree of reaction in any tuberculin test is not thought to be of value in prognosis.

Question: Do you use neomycin?

Chairman Lincoln: No, it is much too toxic.

Dr. Levine: The cases we studied were very different from those observed by Dr. Lincoln. Our observations were on children in tuberculous homes usually from the moment they were born. They received roentgenograms and tuberculin tests at approximately 3 month intervals, so we were in many cases actually able to see what is usually missed, the earliest onset of a primary tuberculous infection of the lungs, and follow through either until calcification or death.

Of the 90 children followed through the primary complex of tuberculosis, 27 acquired their infection during the first year of life, the remainder at a later period when they were able to walk. Of the 60 children who were ambulatory throughout the full course of the primary complex, except during the early febrile period, there were only 4 deaths. These children were in no way restricted—even attending school.

The tuberculosis mortality in these cases was derived almost entirely from the group of children under 2 years of age. It appeared that the age of the child at the time of infection rather than the method of treatment was the important factor in determining prognosis. There was no evidence that rest in bed influenced in any way the course of the primary complex or reduced the incidence of complications and no evidence that lack of rest in bed was in any way detrimental.

Dr. J. Arthur Myers of the Lymanhurst Clinic in Minneapolis, who has followed many thousands of tuberculous children, has stated that, in his opinion, a primary tuberculous infection will follow its own course whether a child rests in bed, has collapse therapy, whether they are as unrestricted in activity as normal children. Myers also minimizes the importance of the sedimentation rate.

We do not treat primary tuberculosis with streptomycin unless complications develop. We have not seen any real evidence that the primary pulmonary infiltration is influenced by streptomycin.

As a matter of fact, we have seen cases where a miliary tuberculosis, treated by streptomycin, clears completely on x-ray, leaving the primary infiltration exactly as it was before the hematogenous spread developed.

Question: You don’t treat them in bed then?
Dr. Levine: Not at all, we let them go to school. Dr. Wallgren actually published a paper on this. He keeps his children in bed until the sedimentation time has gone to normal. We don't pay any attention to sedimentation time. In other words, he keeps some children in bed most of a year and then for the year following puts them in bed for perhaps 3 hours a day so they get some rest in the middle of the day. I can't help but feel there is some difference among the children that he treats in Europe.

Chairman Lincoln: Dr. Levine has brought out the important part of this controversy about the treatment of primary tuberculosis. I think we all agree that primary tuberculosis is potentially a serious disease; that it varies in different localities, possibly according to the degree of infection and according to a number of other factors about which we know very little; that it is the business of the pediatrician to follow his cases and to watch for complications. Dr. Myers has done a wonderful piece of work as far as antituberculosis work has been concerned but, unfortunately, he emphasized too much the fact that in his own group the mortality was low, and concluded from that, therefore, that tuberculous children needed no treatment at all. He implied that even supervision was not necessary and I think that did a great deal of harm because it influenced pediatricians to believe that it wasn't necessary to follow children who had acquired first infection tuberculosis.
Round Table Discussion: EARLY DIAGNOSIS AND TREATMENT OF TUBERCULOSIS IN CHILDREN
EDITH M. LINCOLN, J. B. SCRIVER and A. D. BIGGS

Pediatrics 1952;9;791

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/9/6/791

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints
Round Table Discussion: EARLY DIAGNOSIS AND TREATMENT OF TUBERCULOSIS IN CHILDREN
EDITH M. LINCOLN, J. B. SCRIVER and A. D. BIGGS
Pediatrics 1952:9;791

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/9/6/791