The Tuberculin Test as a New Approach to the New Era of Tuberculosis Control*

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In the past two decades great progress has been made in the treatment of tuberculosis. The discovery of potent antituberculosis drugs and the advances in thoracic surgery have brought about a dramatic decline in the death rate from tuberculosis. Such accomplishment certainly can be viewed with pride and satisfaction. However, while much has been achieved in preventing death due to tuberculosis, not nearly as much has been accomplished in preventing sickness. Even in the United States today, new cases of tuberculosis are being reported at the rate of 100,000 per year and this figure does not include those patients who are not being reported to the health authorities. This disheartening fact stands out in spite of the tremendous progress against tuberculosis that has been made in recent years.

A survey of the cases reported reveals that the majority of them were diagnosed in the advanced stages of the disease. This fact is worthy of our attention, because failure of early diagnosis is an important cause of treatment failure today. The potent antituberculosis drugs now available have made the cure of early cases easy. On the other hand, once the disease is allowed to advance to late stages such factors as drug resistance, persistent cavities and necrotic residuals become great hindrances to the success of treatment. From the public health standpoint the advanced cases are responsible for the spread of tuberculosis to healthy individuals. As will be shown later, child after child and family after family are infected by unrecognized or uncontrolled cases of pulmonary tuberculosis. Therefore, from the clinical standpoint, the present method of tuberculosis control is inadequate since too often it fails to find tuberculosis in its early stage. From the public health standpoint, the present method of tuberculosis control is also inadequate because too often it fails to prevent the spread of the infection to healthy individuals. In this paper two aspects of tuberculosis control will be discussed; first, what can be done to prevent the infected from getting sick and second, the early diagnosis of tuberculosis and prevention of infection by an improved case finding technique.

What Can Be Done to Prevent the Infected from Getting Sick?

To answer this question it is essential to know how tuberculosis begins in the human body, what course it takes and where along this course the

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infection can be checked to prevent it from evolving into manifest disease. The formation of the primary complex following the initial penetration of tubercle bacilli is well known. However, the story of primary tuberculosis does not end at this point, for soon after the infection begins there follows a generalized dissemination of the bacilli, with seeding in various tissues of the body. It should be emphasized that this initial dissemination of tubercle bacilli occurs before the tuberculin reaction becomes positive.\(^1\) Recent studies with \(^{32}P\) labelled tubercle bacilli have shown that the dissemination occurs within a few hours following the inoculation of tubercle bacilli into the human body.\(^2\) Therefore, by the time the tuberculin reaction becomes positive all these changes have already taken place in the body. Knowing this, we should appreciate the great clinical significance of a positive tuberculin reaction. Curiously enough, despite such widespread infection, children seldom appear sick with primary tuberculosis; however, this outward appearance of well being should not lull us into the illusion that primary tuberculosis is an innocent disease, because all too frequently more trouble is to come.\(^{3,4}\) The risk of primary tuberculosis is shown in Figure 1.

Until very recently no effective therapy was known for the treatment
of primary tuberculosis. Whether the infection would remain dormant or develop into manifest disease was entirely unpredictable. The discovery of isoniazid has opened a new era. Extensive clinical experience has proved that isoniazid is the most potent and the least toxic of the antituberculosis drugs. Since its general introduction into medicine five years ago, there has been a sharp decline in the incidence of tuberculous meningitis and miliary tuberculosis in children.\textsuperscript{7} Figure 2 gives the rationale of isoniazid treatment of primary tuberculosis.\textsuperscript{8,10}

This does not mean that every child with primary tuberculosis, as evidenced by a positive tuberculin reaction, should be given isoniazid. Only those with primary tuberculosis in its active stage and whose bodies harbor active tuberculous lesions are likely to profit from the treatment. The detection of active primary tuberculosis requires a careful clinical examination, which has been discussed in another paper.\textsuperscript{11} The patients who are considered to have active primary tuberculosis and in whom isoniazid therapy is recommended at the Houston Children's Tuberculosis Clinic are described in Figure 3. With the development of effective agents for the

![Diagram](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21303/)
SELECTION OF CASES FOR PROPHYLACTIC ISONIAZID THERAPY OF PRIMARY TUBERCULOSIS

1. Children under 3 years of age with positive tuberculin reactions.

2. Older children whose tuberculin reactions converted from negative to positive within 6 months.

3. The demonstration of tubercle bacilli in cultures taken from gastric content, urine, biopsy material or other specimens.

4. Radiographic manifestations, if present.

FIGURE 3

TUBERCULIN TESTING AND REFERRAL OF POSITIVE REACTORS

FIGURE 4
treatment of tuberculosis, a diligent search for primary tuberculosis becomes mandatory. Tuberculin testing is the most reliable method of detecting primary tuberculosis. It must be made a routine procedure in well baby clinics, nurseries, schools and children's clinics. In particular, special efforts for tuberculin testing should be directed to infants and adolescents, because primary tuberculosis acquired during these periods of life is liable to develop into progressive disease. The scheme of tuberculosis case finding in children by tuberculin testing in Houston and Harris County is shown in Figure 4.

Fifty years ago the main concern of tuberculosis control was the care of the sick and dying, because the disease could not be diagnosed until a person developed symptoms of consumption. Later, with the introduction of roentgenographic examination it was found that pulmonary tuberculosis could be detected long before a person felt sick. In the past three decades, therefore, much effort has been directed to the finding of tuberculosis by roentgenographic chest surveys. Now we are entering a new era of finding tuberculosis and treating it before roentgenographically demonstrable changes appear. Tuberculin testing has become of paramount importance today, because it is the only reliable test for tuberculosis before the roentgenographic shadow appears. As Dr. Meyers stated in one of his recent articles, "In the past, little effort has been made to attack the vast army of tubercle bacilli to prevent their destructiveness. Most work has consisted of following far behind these armies and trying to repair the damage they have done. The time has arrived when the major attack must be made upon the tubercle bacillus itself rather than waiting until infected persons have developed complications which have resulted in symptoms and liberating tubercle bacilli or casting visible roentgenographic shadows."12

**Early Diagnosis of Tuberculosis and Prevention of Infection by an Improved Case Finding Technique**

Finding tuberculosis is the most important part of tuberculosis control, because unless the cases are found, all the great progress made in treatment will be of no benefit to the patients. Where can tuberculosis be found? Today, in the United States, tuberculosis exists in small nests. Because of the spotty distribution of cases and the lowering of incidence of tuberculosis in the general population, mass x-ray survey has become less and less efficient for tuberculosis case finding. A new method of case finding is in demand if the present epidemiologic situation is to be effectively met. Being a pediatrician, I see the problem from the child's side. Children are sensitive "Geiger counters" of tuberculosis. A positive tuberculin reaction in an infant invariably points to a contagious case of tuberculosis in its immediate environment. In older children recently acquired tuberculin sensitivity has the same significance. Since tuberculosis is transmitted by close contact, examination of the adult and children contacts of these infected children will uncover the nest from which tuberculosis is being spread. We feel this is the most direct approach to the problem of tuberculosis case finding today.
During the past three years a technique of case finding by family contact investigation has been developed in our clinic, the effectiveness of which is illustrated in Figures 6 and 7. Figure 5 is a key to the status of patients shown in all the family contact studies (Figures 6-13). These examples emphasize certain important points concerning family contact investigation:

1. Examination should include not only the immediate family, but also related families which are in frequent contact. A patient with contagious tuberculosis will infect not only his immediate family, but also friends and relatives who have been in close contact with him. It is often necessary to search beyond the immediate household for the source of infection. Once the source is found all contacts must be examined. This should include both adults and children, because in such family groups more cases of active tuberculosis are found in children than in adults.

2. Contacts should be examined not once, but periodically. Individuals who have been exposed to tuberculosis may not show signs of tuberculosis on the initial examination; however, if they are observed over
CASE FINDING BEGINNING WITH ONE TUBERCULOSIS CHILD

JAN 1956
ONE CHILD DIAGNOSED TB.

FEB-MAR 1956
PARENT'S HOME

AUG. 1956
SOURCE OF INFECTION TRACED TO GRANDFATHER

CASES FOUND BY FAMILY INVESTIGATION

AUG. 1956
ONE CHILD DIAGNOSED TB.

FIGURE 6

CASE FINDING BEGINNING WITH ONE TUBERCULOSIS ADULT

AUG. 1954
ONE ADULT DIAGNOSED TB + SPUTUM

MAY 1956
FAMILY FOUND

CASES FOUND BY FAMILY INVESTIGATION

FIGURE 7

7 NEW CASES OF TUBERCULOSIS FOUND WITHIN 2 YEARS
a period of time one may see tuberculosis sprout and bloom among them. Children with negative tuberculin reactions may become tuberculin positive in a few weeks or a few months (Figure 7). Adults with initial “negative” chest roentgenographs may develop active tuberculosis on follow up examinations (Figure 7). Watch for sprouts where the seeds have fallen. This is the most fruitful way of finding tuberculosis and finding it early.

3. Injudicious use of tuberculin testing and x-ray examination should be avoided. Children, as well as adults, should be tuberculin tested. There is little reason for substituting roentgenographic examination for tuberculin testing as has been so widely practiced. Today in the United States with children and young adults 70 and 90 per cent tuberculin negative, tuberculin testing has become the most important guide for tuberculosis case finding. Negative tuberculin reactors do not have tuberculosis. What they need is not a chest roentgenograph, but periodic tuberculin skin testing to detect the onset of tubercu-

[Graph showing primary tuberculous infection in children and contact with tuberculosis]
lous infection. Positive tuberculin reactors already have the tuberculous infection in their bodies. For this particular group of individuals all facilities and efforts of roentgenographic follow up should be concentrated, because it is from the positive tuberculin reactors that all cases of active tuberculosis evolve.

I have mentioned earlier that the mass x-ray survey is becoming less and less efficient for tuberculosis case finding. This is true the country over and we also find it true in Houston and Harris County. In 1955 the yield of cases of active tuberculosis by mass x-ray survey was only 0.09 per cent, which means that for every 1,000 persons examined in the general population not quite 1 case of active tuberculosis was found. On the other hand, what was found by family contact investigation was quite amazing. At the Houston Children's Tuberculosis Clinic when a child is found to have active primary tuberculosis a family investigation is carried out. Recently, 50 randomly picked family charts were reviewed. It was found that the yield of cases of active tuberculosis in these tuberculous households was as high as 25 per cent of the children and adults examined. This is in sharp contrast to the 0.09 per cent by mass x-ray survey. Many children with active primary tuberculosis do not show roentgenographic shadow. To pronounce a child nontuberculous on the basis of a "negative chest film" is not justified. Indeed, by conferring a false sense of security much harm can be done.

I do not mean to minimize the importance of mass survey. Tuberculin survey and x-ray survey are like the use of radar in navigation. They spot where the dangers lie. Once a danger spot is located, whether it be a tuberculous adult or a tuberculin positive child, it calls for an intensive search for tuberculosis around that case. That is when the real task of case finding begins. Failure to follow through a mass survey by contact investigation is missing the best chance of finding tuberculosis and leaving the most important part of case finding undone. Recently, questions have often been raised as to whether mass x-ray survey is worth the effort in time and money to find so few cases of tuberculosis. I believe it is worthwhile to find these few cases provided the few cases found are taken as a clue to locate the nests from which tuberculosis is being spread.

The Importance of Periodic Tuberculin Testing

Primary tuberculosis can be detected in its very early stage by periodic tuberculin testing. Figure 8 indicates that children in contact with tuberculosis run a tremendously higher risk of acquiring tuberculosis than children in the general population. Figure 9 shows five children in one household who became infected within three months from one tuberculous adult. Figure 10 shows how three children converted their tuberculin reactions one after another because the contact with a tuberculous father could not be broken. Even after a child has been removed from a tuberculous home it is important to do retesting. Figures 11 and 12 show how children develop tuberculin sensitivity several weeks after removal from tuberculous environment. Children living with adults who have arrested
tuberculosis may become infected when the disease in the adult reactivates. Figure 13 is an example of the conversion of tuberculin reaction in two children coinciding with reactivation of tuberculosis in the father.

These cases illustrate the contagiousness of tuberculosis and the susceptibility of children to tuberculosis. In these days where there is so much talk about home care of tuberculous patients, it behooves us to think
twice before we sacrifice the health of the children in the family for the convenience of adult tuberculous patients. Personally, I feel there is no room for home care of contagious or potentially contagious cases of tuberculosis.

Recent tuberculin converters have primary tuberculosis in its active stage, which we believe will profit by isoniazid therapy. A diligent search
for fresh primary tuberculosis among the contacts will contribute much to our knowledge of primary tuberculosis and its drug therapy.

The Need for Organized Effort and Education

Tuberculosis control is a community project. It requires an organized effort of the official and voluntary health agencies as well as the active participation of the public. The easy-going way of reporting tuberculosis cases

**FIGURE 13**

**TWO CHILDREN BECAME TUBERCULIN POSITIVE**

**FIGURE 14**

**PROPOSED SCHEME FOR TUBERCULOSIS CONTACT INVESTIGATION**
by form letters and paying little or no attention to the contact examination will never control tuberculosis. The initial reporting of the case to the health authorities should include at least the patient and his immediate family. Then the contact families should be identified and examined. The scheme of approach of tuberculosis case finding in Houston and Harris County is shown in Figure 14.

It must be remembered that tuberculosis is largely a hidden infection and a hidden disease. People must be educated to see the hidden danger. Parent education is, therefore, very essential to the success of contact investigation. For without the understanding of the parents, it is impossible to get their cooperation to carry out a thorough contact investigation. At the Houston Children’s Tuberculosis Clinic before the clinic starts, a simple talk on the basic facts concerning tuberculosis is given to the parents as a group in the waiting room. After the children have seen the doctor the parents are interviewed individually by a qualified public health nurse. Pictures are used to illustrate the spread of tuberculosis in families and the importance of having every member examined. The significance of the tuberculin test and x-ray examination is explained. Active participation for family contact examination can be expected only after the families have been educated.

SUMMARY

1. We are in a new era of tuberculosis control, a period in which tuberculin testing is assuming a new significance. Because so few children are tuberculin positive today a positive reactor stands out as a warning signal indicating where tuberculosis is being spread and thus pinpointing the spot where intensive search for tuberculosis should be directed.

2. The advent of isoniazid has introduced a new approach to tuberculosis control; that is, prevention of tuberculous sickness by early drug therapy of primary tuberculosis. This calls for intensive tuberculin testing programs to seek out infected children in order to afford them the protection of modern drug therapy.

3. Family contact investigation is the most effective method of finding tuberculosis today. It must be carried out with every new case of tuberculosis found, whether it be a tuberculous adult or a tuberculin positive child.

4. For a thorough and systematic contact investigation the organized effort of health agencies and education of the public are essential.

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RESUMEN

1. Nos encontramos en una era nueva del control de la Tuberculosis en la que las reacciones tuberculínicas asumen una significación nueva. En virtud de que tan pocos niños son tuberculino-positivos ahora, un reactor positivo se destaca como una señal de advertencia que señala donde está desarrollándose una diseminación de la tuberculosis y apuntando así al lugar donde debe hacerse una investigación rigurosa.
2. El advenimiento de la isoniazida ha introducido una nueva manera de atacar el problema del control de la tuberculosis; tal es la prevención de la enfermedad tuberculosis por el tratamiento temprano de tuberculosis primaria. Esto requiere planes intensos de búsqueda de niños infectados por medio de la reacción tuberculínica para ofrecerles la protección de la drogoterapia moderna.

3. La investigación del contacto familiar es el método más efectivo de encontrar la tuberculosis al presente. Debe investigar se en cada caso nuevo encontrado ya se trate de un adulto o de un niño tuberculino-positivo.

4. Para la investigación sistemática de los contactos el esfuerzo organizado de las unidades de salud y de educación del público, se consideran esenciales.

RESUME

1. Nous sommes dans une nouvelle phase de l'éradication de la tuberculose, une phase dans laquelle le test à la tuberculine prend une valeur nouvelle. Parce qu'il y a maintenant peu d'enfants qui réagissent à la tuberculine, le porteur de réactions positives se dresse comme un signal d'alarme pour indiquer le foyer de la tuberculose, et les lieux où doivent être intensifiées les recherches.

2. L'apparition de l'isoniazide a introduit un nouveau moyen qui laisse espérer la disparition de la tuberculose; c'est la prophylaxie de la maladie tuberculeuse par l'administration précoce de la médication lors de la primo-infection. Ceci demande un programme intensif de tests à la tuberculine, pour découvrir les enfants infectés, afin de leur apporter la protection des médications modernes.

3. Les investigations portant sur les contaminations familiales sont le moyen le plus efficace pour découvrir la tuberculose aujourd'hui. Elles doivent être mises en œuvre pour chaque nouveau cas de tuberculose, que ce soit un adulte tuberculeux ou un enfant porteur de réactions positives.

4. Il est capital de coordonner l'effort des services de santé publics et l'éducation du public pour aboutir à un contrôle complet et systématique.

ZUSAMMENFASSUNG

1. Wir befinden uns jetzt in einer neuen Aera der Tuberkulose-bekämpfung, einer Periode, in der die Tuberkulinprüfung eine neue Bedeutung gewinnt. In Anbetracht dessen, dass heute so wenig Kinder tuberkulino-positiv reagieren, tritt eine Person mit positiver Reaktion in den Vordergrund als ein Warnungszeichen, das darauf hinweist, von wo sich die Tuberkulose auszubreiten im Begriffe steht, und das auf diese Weise den Punkt markiert, an dem intensive Tuberkulosebekämpfungsmassnahmen angesetzt werden müssen.

2. Die Einführung des INH hat einen neuen Weg für die Tuberkulosebekämpfung eröffnet; nämlich die Verhinderung der Tuberkulose als Krankheit durch frühzeitige medikamentöse Therapie der Primär tuberkulose. Dieser Umstand spricht zu Gunsten eines intensiven Tuberkulin-
prüfungsplanes zur Auffindung infizierter Kinder mit dem Ziel, diesen
einen Schutz in Form der modernen medikamentösen Therapie zu ge-
währen.

3. Untersuchungen von intrafamiliären Kontaktfällen sind die best-
warussame Methode, um heute eine Tuberkulose zu entdecken. Sie müssen
bei jedem neugefundenen Tuberkulosefall ausgeführt werden, sei es nun
ein tuberkulöser Erwachsener oder ein tuberkulinpositives Kind.

4. Um eine durchgehende und systematische Kontaktuntersuchung aus-
führen zu können, bedarf es der geplanten Bemühungen der Gesundheits-
behörden und einer Erziehung der Öffentlichkeit.

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