ing this infection and to seek medical care whenever he has a cough that hangs on more than two to three weeks after a cold, fatigue, loss of weight, or fever of unknown origin.

At the urging of the Public Health Service three years ago, a program was undertaken in a rural Arkansas county to identify all persons at risk of developing tuberculosis by instituting a county-wide voluntary tuberculin testing program followed by x-ray examination of all positive reactors. It was found that one could easily test the school children, nursing-home inmates, etc; but it proved almost totally impossible and certainly impractical to get the adult male population to come in voluntarily for the skin test for tuberculosis. Their wives would often come, but neither we nor the wives were successful in getting the men to come.

In summary, I have tried to give the goals for screening of tuberculosis infection and disease and to indicate some of the areas in which screening may be productive. I have mentioned some of the ways that I think are wasteful of time and effort. In looking for disease, it is most productive to look among sick people, such as those going into physicians' offices and hospitals. For new infections, it is most productive to look at the intimate and household contacts of recently discovered infectious cases and in hospital employees and prison inmates. Beyond this, there is an important control job to be done, but it no longer should include screening healthy populations.

While the indications for prophylactic isoniazid therapy have been grossly contracted in recent years, I think that when it is indicated, it is important for us to give it with as much enthusiasm as we use in treating patients with active disease. Screening for tuberculosis is still important in some circumstances, and it should be done in a productive way, as I have outlined.

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Tuberculosis Screening and Chest X-ray Films

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Up until recently, nothing was more familiar than the x-ray bus which took hundreds and thousands of x-ray films, seeking out the active cases of tuberculosis in order to “eradicate the disease.” Radio and television spots implored the populous to get chest x-ray examinations yearly and even more often when symptoms occurred. As late as 1970, the city of New York took almost 300,000 chest roentgenograms in a year.

SCREENING WITH CHEST X-RAY FILMS

As you know, a procedure done when it is the initial contact with the health care system is called screening. Screening x-ray films will reveal, if properly read, only obvious cardiac or pulmonary pathologic findings. Anybody who is impressed by the diagnostic ability of the 70-mm miniature film should try reading a roll on Monday and repeat them again on Friday, then compare your readings over the week, and compare them with the radiologist and chest physician. One will almost certainly find lack of agreement with himself, reading to reading, as well as with the so-called experts. The experts’ agreement among themselves will not be near 100 percent either. In other words, there is a great degree of interindividual and intraindividual variation among readings of roentgenograms. Routine x-ray films have a tendency to be misread. Recently in a large New York City hospital a misread x-ray film led to missing a case of sputum-positive tuberculosis in a delivery-room nurses’ aide and led to a recall of 726 infants for skin testing and follow-up.

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It has been well shown that the productivity of x-ray screening is the number of abnormal x-ray films it produces. In 1970 in New York City, 283,000 chest roentgenograms were taken. These, in turn, led to 44 cases not previously registered. Only 37 of these were classified as adult pulmonary (in whom the diagnosis would be expected to be made on the roentgenogram). This gives a rate of 15 new cases per 100,000 x-ray films done.

Finding 44 cases of tuberculosis is a laudable aim and seems quite productive in the absence of a denominator, but in public health practice one must think twice about what is being done and if perhaps it might be done more productively. The first thing to be looked at is the radiation dosage involved. The 70-mm x-ray films are photographs of a fluoroscopic image. They expose an individual to a radiation level generally ten times that encountered in standard 14-in to 17-in exposures. For this, they give poorly diagnostic films. If there is tuberculosis disease, the patient very likely already has symptoms; if cancer is present, it is generally beyond cure.

In February 1972, the US Department of Health, Education, and Welfare issued a statement which was endorsed by the American College of Radiology, the American College of Chest Physicians, and the Public Health Service. This stated that community chest x-ray surveys among the general population are not productive as a screening procedure for the detection of tuberculosis and should not be done. It also stated that community chest x-ray surveys among the general population for detection of pulmonary or heart diseases other than tuberculosis have not proven sufficiently rewarding and likewise should not be done. Simply stated, in addition to radiation hazard, the chest x-ray film has an inherent deficiency as a tuberculosis control tool in that it will only identify manifest disease. Thus, the individual who has been infected with the tubercle bacillus and is at risk of developing manifest disease remains undetected by x-ray examination.

**Screening with the Tuberculin Test**

The alternative is clearly the tuberculin skin test. It is well known that persons infected with *Mycobacterium tuberculosis* exhibit a reaction when injected with protein prepared from *M tuberculosis*. This is the Mantoux tuberculin skin test. The tuberculin test is an example of delayed-type hypersensitivity produced by a cell-mediated immune response. Persons never infected and a few persons who are anergic for various reasons do not react. The probable mechanism is that after tuberculosis infection has occurred, *M tuberculosis* antigens contact T-lymphocytes, and antibodies specific to the antigens from the mycobacteria form on the surface of the lymphocytes. An immunologic commitment to the tuberculin occurs, and when tuberculin is readministered, the lymphocytes combine with the antigens. Migratory inhibitory factor is probably released, and macrophages accumulate in the area of the reaction, causing induration.

The most important aspect of screening for tuberculosis is that all the 39,500 patients in 1971 had positive tuberculin tests, but 92 percent of them had positive tuberculin tests at the beginning of the year. In other words, the overwhelming majority of all new active tuberculosis in the United States each year comes from breakdown, for unknown reasons, of previously infected individuals. The 8 percent who were not previously infected got infected from contact with other active cases. Through the projections of Riley, we know that this occurs via dissemination of aerosol over a long period of time and close contact.

Thus, the tuberculin skin test, without exposing the surveyed population to any radiation hazard, discovers both those individuals with manifest disease and those at risk of developing manifest disease by identifying those persons infected with the tubercle bacillus.

**Preventive Therapy with Isoniazid**

Tuberculin testing, as opposed to screening x-ray examination, also raises the possibility of prevention. This is because if a positive skin test is evidence of tuberculosis infection (this is the definition of infection, as opposed to disease, which is ruled out by x-ray film in all positive reactors), then one year of isoniazid therapy will go far in eradicating the infection. If most people at risk of getting tuberculosis are infected, then preventive therapy should diminish this propensity to get disease. It has been shown that it does, and that protection is now continuing for many years.

Naturally we must consider drugs of any type carefully. All treatment, as well as any screening method, has a certain risk-benefit ratio. In the early days of preventive therapy for tuberculosis infection, many experts advocated giving isoniazid therapy to all positive reactors. With an apparently increasing incidence of hepatitis in patients receiving isoniazid therapy and with the realization that all tuberculosis-infected patients are not at the same risk of developing tuberculosis disease, greater care in treatment is necessary. The American Thoracic Society and Public Health Service criteria for preventive therapy of tuberculosis are given in the following tabulation, which shows various groups in order of priority for receiving preventive therapy:

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**Tuberculosis Screening**

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1. Household members and other close associates of persons with recently diagnosed tuberculous disease.

2. Positive tuberculin reactors with findings on the chest roentgenogram consistent with nonprogressive tuberculous disease, without positive bacteriologic findings, and without a history of adequate preventive therapy.

3. Newly infected persons.

4. Positive tuberculin reactors in the following special clinical situations:
   (a) Prolonged therapy with adrenocorticoids
   (b) Immunosuppressive therapy
   (c) Some hematologic and reticuloendothelial diseases; such as leukemia or Hodgkin's disease
   (d) Diabetes mellitus
   (e) Silicosis
   (f) After gastrectomy

5. Other positive tuberculin skin test reactors.

   It is now thought that isoniazid-associated hepatitis is clearly age related. Since persons below age 35 are rarely at risk of hepatitis, they should all be given the benefit of isoniazid preventive therapy for tuberculosis infection. Referring to Figure 3 of Edwards (see page 453), new reactors are at 4.2 percent/yr risk of getting disease. Persons with an abnormal roentgenogram with inactive disease have about a 1 percent/yr risk. Persons with a reactive tuberculin test and normal x-ray film are at a smaller, but well-defined, risk. When we consider that the risk of isoniazid-associated hepatitis is for the year of treatment only, while the protection afforded for tuberculosis may well be lifelong, in most of these cases we can opt towards isoniazid preventive therapy. Of course, anyone taking isoniazid can get hepatitis; and surveillance for this complication, as well as for compliance in drug taking, is mandatory. At best, if a patient has a 4.2 percent chance of getting active tuberculosis, he has a 95.8 percent chance of not getting it. So if he gets symptoms referable to liver disease while receiving isoniazid therapy, the drug should be discontinued. Because of the specter of isoniazid-associated hepatitis, no preventive therapy should be given unless facilities are available and committed to follow the patient. There is still some suspicion that some of the deaths ascribed to isoniazid-associated hepatitis in patients occurred because they continued to take their medication, without stopping, upon the development of symptoms.

**Conclusion**

Proper screening will show tuberculosis infection and this can be kept from proceeding to disease by proper use of preventive therapy. How does this information affect a private practitioner or a jurisdiction in their desire to participate in up-to-date tuberculosis control?

First, one can reassess who is being screened and in what way. In 1972 the staff of New York City's Bureau of Tuberculosis reviewed the New York City Health Code to see who was being screened with x-ray examinations. It found that just about everybody was. Periodic x-ray films were required by law in prenatal mothers, contacts of new bacteriologically positive tuberculous patients, persons working in a maternity and newborn service and in food preparation for such a service, park department employees, and board of education employees. The health code was amended to require tuberculin tests in all of these, with x-ray films taken only as medically indicated (medically indicated referred to the presence of symptoms or a positive skin test). The city continued to offer roentgenograms to those age 50 and above who were smokers or others who had pulmonary symptoms.

This action immediately permitted us to close down a number of walk-in screening x-ray units. With the closing of these units, tuberculin testing units were substituted in their place. But the giving of skin tests by doctors or nurses was, we felt, an unproductive use of their time. So we recruited a group of community health aides who were involved in patient follow-up activities. They were trained to apply, read, and interpret the Mantoux test. A two-week intensive training course of skin test application, interpretation, and counselling was held, and a practical examination was given. Upon completion of the course, a certificate was presented by the city health commissioner. These tuberculin testing technicians were assigned to walk-in tuberculin testing units located in the five boroughs of New York City where the old x-ray screening units had been. They give and interpret each test. All persons who have a positive tuberculin test are given a chest x-ray examination. If no tuberculosis disease is found, the patient then consults with a health department physician who determines, with the patient in attendance, if preventive therapy is indicated. All patients below age 35 and others in the previously mentioned criteria of the American Thoracic Society are strongly offered preventive therapy. The patient is told that there is a slight risk of hepatic reaction to the drug and that he must be seen at no less than monthly intervals for the one year of treatment. If the patient accepts, only one month's supply of isoniazid is given at one time. The subsequent 11 visits are usually in a nurse-operated clinic where the patients are seen by a nurse or physician associate who interviews the patient with the aid of a checklist form. Unless complaints or complications arise, the patient does not see a physician after his first visit. No follow-up x-ray examination is done in patients...
who have received a complete course of preventive therapy.

The system has worked. The number of screening x-ray films fell in the first year of the program from 283,000 to 35,000. When the board of education's triennial x-ray survey, as required by the health code, came up, the amendment permitted a tuberculin testing program to be done. Over 100,000 persons were skin tested with a reactor rate of about 15 percent. The system is cheaper and more useful and has given rise to prevention directly from the basic screening method.

This experience is for a large metropolitan area with a high rate of new active tuberculosis. In many other areas, however, the chance of getting tuberculosis is so low, that except on the basis of documented exposure or unexplained symptoms, a tuberculin test need not be done. Both persons in contact with active cases and also hospital and health workers should have periodic tuberculin testing done as part of an ongoing tuberculosis control program, in order to protect patients as well as themselves.

With the reentering of tuberculosis into the mainstream, the health establishment must take over its share of meaningful screening. Programs that use screening to get to prevention with great benefit and little risk to the patient are most productive in this regard and are actually more inexpensive than previous programs.

This is one of the few situations in medicine where the modern state of the art is more economical than the old one.

## Screening for Tuberculosis*

*Phyllis Q. Edwards, M.D.*

The purpose of screening a group of persons is to sift out the ones who may have the condition or disease for which you are looking. In tuberculosis screening, we are looking for persons who have the disease, as well as those who are likely to develop the disease. Disease can be treated; and the chances of developing disease can be significantly reduced by preventive therapy. Screening is, therefore, undertaken in order to detect the particular individuals for whom some form of treatment may be indicated.

The question is: What kinds of people should be screened, and how should they be screened? Screening is most profitable in the groups of people where tuberculosis is most concentrated. This may sound self-evident in this cost-benefit-conscious society of ours, but it is worth mentioning because times have changed, and keep changing, and so does tuberculosis. Where are most of the cases today, and where will cases be developing tomorrow?

Let's look at where tuberculosis is in today's society. Figure 1 is a profile of the total US population, showing our best estimate of the age distribution of the 15 million persons infected with tubercle bacilli sometime in the past. These are the tuberculin

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