Progress in Tuberculosis Control in the United States*

FRANCIS J. WEBER, M.D., F.C.C.P.*

Washington, D. C.

At last year's Annual Meeting, it was my pleasure to discuss in general terms the tuberculosis control program of the United States Public Health Service. I described the fundamental objectives and major techniques of the Tuberculosis Control Division, organized as an official agency to integrate and guide activities in tuberculosis control throughout the country. I spoke of the success of the Division in cooperative work with voluntary and official State and local agencies engaged in the national control movement, and mentioned cooperative arrangements with prominent research groups. That introduction to the activities of the Division was in itself a promise to speak later of further developments.

Today, with the Division in its fourth year of operation, it is possible to discuss, in some detail, significant projects and results. The most interesting work, I should say, has been in the fields of case-finding and medical research. It would seem appropriate to discuss case-finding first, inasmuch as it provides a measure of the general problem of tuberculosis.

For those who may not be familiar with the Federal case-finding program, I should explain that the Public Health Service operates a number of photofluorographic units for demonstration purposes. At present the Tuberculosis Control Division maintains more than 40 of these units and keeps at least 35 in operation at all times. While demonstrating the value of miniature chest films in detecting early tuberculosis, the units provide direct service to the community, and every effort is made to place them where most needed throughout the States.

The Division frequently conducts chest x-ray surveys among special population groups, such as industrial workers or patients in mental hospitals. These investigations afford valuable information about the tuberculosis problem. For the most part, however, we emphasize the community-wide survey, since it covers the general population as well as special groups, and in this way offers the most to the people in terms of service. In demonstra-

**Medical Director, Chief, Tuberculosis Control Division, U. S. Public Health Service.
tions of this type, we attempt to obtain a chest film of every community member 15 years of age or older. The Division has participated in several case-finding surveys in which entire counties were covered—an approach so successful that we hope to further a national program of tuberculosis case-finding by communities.

One of the primary considerations in a large community-wide survey is the time element. We must discover and isolate as soon as possible a sufficient number of open cases to provide a marked reduction of disease hazard for the remaining population. Moreover, the Public Health Service, in the interest of the nation as a whole, must avoid a prolonged concentration of x-ray units in one area. Then again, the problem of waning community interest in the program enforces the time restriction. For these reasons, careful planning and strong community organization are essential.

Basic to any case-finding program is the question of support for the survey. In community-wide demonstrations, the Division furnishes standard, fully automatic units employing 70-mm. roll film. Along with these, we assign medical officers for the organization of the survey and interpretation of results, as well as x-ray technicians, nurses, health educators, and reporting methods analysts. In short, the Public Health Service supplies most of the technical personnel and equipment.

The community usually requires outside help to complete the survey within the time limits. In most surveys to date, the State and local health departments have provided funds and personnel necessary for publicity, clerical work, and follow-up. And for cases discovered during the survey, these departments have also provided clinic facilities, nurses, and other workers.

Many groups must take an active part in the planning and organization: the State and local health departments and other official agencies; the voluntary associations, State, local, and others; and working closely with these groups, the private physicians in the area.

At the present time (June, 1947 - Ed.), the Division is engaged in a tuberculosis case-finding survey of Minneapolis. Although the results of film readings are not yet available, I should like to discuss this program in some detail, for the planning and organization are exemplary. There is every indication that this survey will be one of the most successful ever undertaken.

The survey was initiated by the Hennepin County Medical Society, and is being sponsored by the Medical Society, the County Tuberculosis Association, the State Cancer Society, and the City Health Department. Many local groups are active participants, such as the Chamber of Commerce, the PTA, hospitals, labor
unions, the YMCA, and churches. The program is directed by the Minneapolis City Health Department in cooperation with the United States Public Health Service.

The purpose of the survey is to discover pulmonary tuberculosis, cancer in the chest cavity, heart abnormalities, and other pathologic chest conditions among all adults in a total population of more than 400,000. About four months were spent in preparing for the actual x-ray work, which was started May 5, 1947 and was to continue until December.

One of the initial preparatory steps was the organization of a committee to reach into every factory, place of business, school and home, for the purpose of explaining why everyone should have an x-ray and how it would be provided. The activities of the press and radio, and the organization of resources for the printing and distribution of pamphlets, banners, posters, and so forth, are directed by a committee on public relations. The immediate expenses of the survey are met by a contribution from the Hennepin County Tuberculosis Association, and a special finance committee has been delegated to raise additional funds.

As part of the community organization, a chest x-ray attitude poll was taken by a Chicago public relations firm. The object was to determine the attitude of employers and members of the general population toward a complete city-wide program, and to estimate the number that would turn out. One hundred and fifteen employers and 413 other people were interviewed personally by experienced field representatives.

The attitudes revealed by the poll were very encouraging. None of the 115 employers interviewed objected to the survey; only one was uncertain. When asked why they thought it a good idea, 41 employers, or 36 per cent, replied that it would aid the general health of everyone in the city. Twenty-nine, or about a quarter of the group interviewed, said that it would help prevent and control disease. Primarily, the employers wanted the assurance that their employees were free from tuberculosis, and more than 90 per cent agreed to grant their employees time for an x-ray.

The response to the general population poll was further indication of a successful educational campaign. Of the 413 men and women interviewed, 403 said they believed the x-ray survey was a good idea. Four did not think so, and 6 were uncertain. The principal reasons given for thinking it a good idea were that the survey could catch tuberculosis, cancer, and heart trouble in early stages; that it would aid in the general health and protection of the city; and that it would find unsuspected cases and help prevent the spread of disease.

As a further step in the organization of the community, a
technical committee of physicians and nurses was established, with the Tuberculosis Control Officer of the City Health Department as secretary. This committee was responsible for planning the follow-up program, and is actively engaged in making clearances with the medical and nursing professions. The city was divided into five large zones, and these into a total of 30 neighborhood operational districts, according to geographic lines and community group interests. Publicity and subsequent x-ray work are concentrated in certain areas, beginning on the outskirts of the city and progressing toward the center. In many communities, this procedure proved highly effective in war bond and community chest drives.

Three mobile and seven portable photofluorographic units, all employing 70-mm. film, are used in the survey work, and several other units are held in reserve. Radiologists of the Public Health Service are reading the films.

For the follow-up, a confidential report is mailed to each person whose screening film shows evidence of chest pathology. The report directs the person to the Public Health Center, where he is x-rayed again with 14" x 17" film. If further examination is necessary, he is referred to his private physician, who is informed of the x-ray findings; and persons found to have active tuberculosis are reported to the City Commissioner of Health. After the report is sent to the physician, the follow-up is on the normal patient-doctor basis. This phase of the program has been carefully planned, and assumes all possible assistance from professional groups responsible for diagnosis, treatment, and rehabilitation.

But I must turn, now, from the subject of case-finding to say a few words on basic research. The first project I should like to discuss is the study of minimal tuberculous lesions among student nurses, begun in 1943. The Division in cooperation with the National Tuberculosis Association has gradually expanded the Nurses Study to include research in almost all geographic regions of the United States. Approximately 12,000 student nurses in 76 widely distributed schools are systematically x-rayed and skin-tested, to determine the predisposing factors and earliest manifestations of tuberculosis.

A preliminary analysis of material from the study is in progress, with a view to obtaining a measure of the accomplishments made over the past four years. Films from two of the ten cities in the study, Columbus, Ohio, and Detroit, Michigan, were selected for the analysis; and the hospitals in those cities were regarded as though the study had been completed. All chest films were re-read. A correlation of film and skin-test readings will make possible
the first comprehensive interpretation of minimal lesions as revealed by chest x-ray, and will permit evaluation of the whole minimal lesion study.

One of the most interesting phases of the project is the investigation of nontuberculous pulmonary calcification, which has led to a study of certain fungus diseases, such as histoplasmosis. The first results were announced by Dr. Carroll Palmer of the Division on May 11, 1945. It was demonstrated that a mild sub-clinical condition, associated with sensitivity to histoplasmin, is responsible for much of the pulmonary calcification observed in negative reactors to tuberculin.

In Kansas City, where nontuberculous calcification is prevalent, the Division established a field station to further the epidemiology of histoplasmosis and to study its relation to other diseases. Approximately 15,000 school children and 5,000 adults in the Kansas City area have been x-rayed and tested with tuberculin and fungus antigens. During the past year, a number of reports on the work of the field station have been published, such as "Histoplasmin Sensitivity among Siblings" by Ferebee and Furcolow, and "Studies of Fungus Antigens" by Arden Howell.

Of the several reports, Dr. Howell's has perhaps the widest significance, since it offers a solution to the singular problem of cross-reactions to the fungus skin-tests. The study demonstrates that the percentage and size of cross-reactions between histoplasmin and blastomycin in animals experimentally infected with Histoplasma capsulatum and Blastomyces dermatitidis are dependent upon the dosage of the antigens employed. If the critical titers are determined and these concentrations are used in the testing, the degree of cross-reaction is small. Dr. Howell concludes that histoplasmin and blastomycin are relatively specific for guinea pigs experimentally infected with the homologous fungi.

Another interesting phase of the field station work is a cooperative investigation with Childrens Mercy Hospital in Kansas City. As part of a program to examine all admissions, nearly 400 children have been skin-tested with histoplasmin and tuberculin; and plans have been made to examine pathological autopsy material from patients whose ante-mortem skin reactions are known. Most of the hospital admissions are x-rayed, and the readings are recorded on a card that carries the skin-test data. When autopsy is performed on histoplasmin-positive subjects, the lungs are x-rayed post-mortem, and any lesions found are studied histologically and cultured for tubercle bacilli and fungi. Similar cooperative arrangements have been established with St. Luke's Hospital, General Hospital, and the University of Kansas Hospital.
During 1946 one radiologist of the Division read more than 100,000 x-ray films of the chest, in connection with the Nurses Study and Kansas City field station activities. Clinical follow-up work is progressing among children, industrial workers, student nurses, and others tested who show evidence of pulmonary disease.

The Division has also participated actively in the search for an antibiotic effective against tuberculosis. In cooperative studies with the Rockefeller Institute for Medical Research, Dr. Alfred Marshak of the Division isolated a harmless plant substance that appears to retard the development of tuberculosis in guinea pigs. The first results of his work appeared early this year (1947 - Ed.) in Public Health Reports, under the title "A Crystalline Antibacterial Substance from the Lichen Ramalina Reticulata."

It would take a great deal of time to describe Dr. Marshak's experiments in detail; but I believe you would be interested in hearing of his principal findings, and of his reasons for investigating this particular plant. He observed that Ramalina reticulata, commonly known as California Spanish moss, has no integument and contains a very moisture-absorbing carbohydrate. From this, the invasion and growth of bacteria would seem possible; and when Dr. Marshak isolated the carbohydrate material, he found it an excellent culture medium. But the relative absence of bacterial growth in the normal plant suggested the presence of an antibiotic substance, which Dr. Marshak isolated in crystalline form.

Before the guinea pig trials, in vitro tests had shown that the growth of human tubercle bacilli was completely inhibited by the crystals in concentrations of 1 to 50 thousand, and that inhibition was noticeable in concentrations as low as 1 to 2 million. The growth of avian strains in vitro was partly inhibited, and the growth of a bovine strain, completely inhibited. In experiments on guinea pigs infected with human tubercle bacilli, there were twice as many deaths among the controls as among the treated group. The crystals can be administered subcutaneously in oil, daily for three weeks, at a rate of 10 to 20 milligrams per guinea pig, without obvious toxic effect.

In association with interested agencies, the Division has planned to secure a sufficient amount of the crystalline material to permit thorough testing.

A comprehensive discussion of antibiotics against tuberculosis must of course include mention of streptomycin. Since 1944, when Waksman isolated crude concentrates of the substance from the soil micro-organisms Actinomycetes griseus, streptomycin has been the current drug of promise. We are all awaiting the decisive results of streptomycin treatment of tuberculosis in human beings.
As you know, extensive controlled experiments have yet to be undertaken; but results to date not only give hope of suppressive action, even in meningitis and miliary tuberculosis, but also point the way to further investigation.

In April of this year (1947), the Public Health Service issued a memorandum to all medical officers in charge of Marine Hospitals, authorizing the cautious use of streptomycin for certain tuberculous diseases. Those listed were tuberculosis of the larynx, trachea, and bronchi; tuberculosis of the skin; draining tuberculous sinuses; tuberculous meningitis; miliary tuberculosis; and clinically active pulmonary tuberculosis, when not too far advanced and when not responsive to bed rest or collapse therapy. Medical officers were further requested to limit the use of streptomycin in pulmonary tuberculosis to progressive cases and to those that do not have extensive involvement of the lungs.

The memorandum continued with these statements:

If you use streptomycin in pulmonary tuberculosis, you should be prepared to examine cultures of tubercle bacilli for streptomycin sensitivity at regular intervals. There is no point in continuing treatment when tubercle bacilli have developed resistance to streptomycin.

Remember also that the usual period of treatment recommended is three to four months, the dosage one to three grams per day. Do not start treatment on a case unless you have adequate amounts of streptomycin for the entire treatment period.

In renal tuberculosis, streptomycin has shown no evidence of permanent benefit, although some investigators report some symptomatic relief. Accordingly, its use in renal tuberculosis is not recommended at this time.

The memorandum concluded with a warning:

Bear in mind that streptomycin treatment is not without complications. Deafness, vestibular disturbance, dermatitis, fever, nausea, and vomiting are not uncommon.

These statements reflect the present policy of the Public Health Service with regard to the streptomycin treatment of tuberculosis.

One important research project remains to be discussed: the study of BCG vaccination. On September 7, 1946, a conference was held in the offices of the Public Health Service, with representatives of seven States, Denmark, and China. Guided by recommendations from this conference, the Tuberculosis Control Division will extend its research program to include studies on the effectiveness of BCG vaccine in preventing tuberculosis. I should like, now, to review briefly the history of BCG, and to present the recommendations in general terms. This will serve to introduce a description of the present BCG studies of the Division, including the vaccination program now in progress in Columbus, Georgia.
You may recall that the literature on BCG usually mentions Dixon as the first to attempt immunization with living tubercle bacilli. In 1889 Dixon inoculated experimental animals with an old culture containing club-shaped and branching forms of the organism. A few years later, Trudeau found that the resistance of rabbits to infection was increased by subcutaneous injections of tubercle bacilli of the avian type; and still later, Von Behring immunized calves with human tubercle bacilli, or “bovo-vaccine.” Von Behring’s method was abandoned when the organisms were later found in the milk. In 1911 Webb and Williams showed that the resistance of guinea pigs could be augmented with minute doses of living tubercle bacilli, beginning with one organism and gradually increasing the dosage; and a few children were vaccinated in this way with apparent success.

Then, in 1924, the French bacteriologist Calmette advocated inoculation with bovine bacilli attenuated by cultivation on bile-potato medium for 15 years. The vaccine, Bacillus Calmette-Guérin, was acclaimed in countries of eastern Europe and South America, where French influence was strong. In Great Britain and the United States, however, it was either ignored or opposed, for the most part, until impartial investigations were undertaken about eight years ago; and only today can it be said that we fully appreciate the possibilities of BCG.

The United States Public Health Service and the Office of Indian Affairs, Department of the Interior, began an investigation of BCG in December 1935. The vaccine was to be used in an attempt to reduce the high incidence of tuberculosis among North American Indians. Since there was uncertainty at that time as to the validity of many reports on the subject, it was decided to conduct a controlled study, rather than an uncontrolled broad-scale program of vaccination. The study group comprised 3,007 persons, aged 1 to 20 years, who were selected on the basis of a negative tuberculin reaction. BCG was given intracutaneously to 1,550, with 1,457 serving as controls; and the group was followed for six years with annual tuberculin tests and chest x-ray examination.

During the six-year period, 60 deaths from all causes occurred among the 1,457 children in the control group, and 34 among the 1,550 vaccinated. There were 28 deaths from tuberculosis among the controls, and only four such deaths among the vaccinated group. In short, the results indicated that a high degree of protection was afforded by the vaccine.

The success of the study among Indians urged that the possibilities of BCG vaccination be thoroughly explored, especially among population groups highly exposed to tuberculosis. Accord-
ingly, the conference was held last fall by the Tuberculosis Control Division to consider the use of BCG among such groups, and to make recommendations for further investigation. It was strongly advocated that the vaccine should not be produced commercially as yet, since information is incomplete as to the amount or duration of conferred resistance. But on the basis of all published reports and the experience of members of the conference who had actually performed vaccination, it was agreed that no proved cases of progressive disease among human beings can be attributed to the vaccine. Further research should be undertaken, however, in an effort to reduce the number of severe local reactions.

It was recommended that a single laboratory be established by the Tuberculosis Control Division to produce the vaccine for use in research programs, and that extensive investigations be conducted in cooperation with recognized research groups throughout the country. Research was strongly recommended to measure the efficiency of BCG; to develop a vaccine composed of dead bacilli; and to simplify the vaccination technique. It was suggested that the Public Health Service undertake a controlled study in a community with a population of 100,000 or more, to determine immediate and long-range results. Another objective must be the development of standardized methods for preparing a potent and stable vaccine for use in the United States and, if possible, throughout the world.

And now I should like to say a few words on the controlled program of BCG vaccination among school children, begun recently by the Tuberculosis Control Division in Columbus and Muscogee County, Georgia. As a first step, the parents were asked to sign "consent" cards, which set forth the general procedure and purpose of the inoculations. The children whose parents approved were then tested with tuberculin, and only those whose tests showed no tuberculous infection were vaccinated. Three Public Health Service teams, each composed of a doctor, nurse, and clerk, administered the tests and then the vaccine. To reduce the number of severe local reactions, Rosenthal's multiple-puncture method was used, and with a high degree of success—though I should mention that the time required to vaccinate and the objections of the children to the 30 successive punctures occasioned some difficulty. The problem of sterilization precluded the use of devices for simultaneous inoculation. Dr. Johannes Holm of Denmark provided the PPD, and Dr. Rosenthal, who was present in Columbus as a consultant, furnished the BCG.

It will be several years, of course, before the effectiveness of the vaccinations can be accurately determined; but we can say now that the study to date has been very successful. We attribute
this success, mainly, to the earnest cooperation of the city and county school boards, PTA's, the county medical society, and the State and local health departments. The work in Columbus is the first step in a program of research that will be extended to other cities.

These are a few of the activities and achievements of the Tuberculosis Control Division of the Public Health Service. They appear to reflect the progress of the entire control movement in the United States. All agencies engaged in that movement must have as their primary function the planning of a decisive and concentrated attack to attain four objectives: First, the discovery of every person in the country infected with tuberculosis. Second, isolation and medical care for every patient needing treatment. Third, after-care and rehabilitation. And fourth, protection of the afflicted family against economic distress. The objectives of the Division, and to some extent the methods for their attainment, are in reality common to all who seek the eradication of this disease.

In State and local tuberculosis control work, guidance is the principal role of the Division. It is our practice to withdraw from active participation in a State program as soon as adequate control measures are established, and to serve mainly through financial aid and research. Today, I have tried to show, by a few examples, how the Division provides direct service, and I believe I have covered our most significant research projects.

Although reported figures show that tuberculosis mortality is on the decline, we are all aware that many grave problems confront us in the fight against the disease. The Tuberculosis Control Division is dedicated to assist all interested persons and agencies in solving those problems. It will continue to conduct research, and to provide aid to States through financial grants, training, and direct service to communities. As the States develop smoothly operating programs, the target of the Federal attack will change, until every State and community is prepared to war effectively against tuberculosis.

SUMMARY

During the past year material progress has been made in the several phases of tuberculosis control. Case-finding through mass radiography has been substantially extended. Controlled research on the efficacy of B.C.G. vaccine as a preventive measure has been initiated. The Tuberculosis Control Division has continued the study of histoplasmin sensitivity among nurses. The search for an antibiotic which will be effective against the tubercle bacilli continues with great promise for the future. Results of the use of
streptomycin in miliary tuberculosis, cutaneous fistulae, and tuberculous meningitis are encouraging, with preliminary studies indicating promising results in pulmonary tuberculosis. A crystalline substance has been isolated from California Spanish Moss which appears to retard the progress of tuberculosis in guinea pigs.

By direct services rendered through demonstrations and the loan of personnel, the Division has continued its policy of aid to States and local communities.

RESUMEN

Durante el año pasado se han llevado a cabo adelantos importantes en las varias fases del control de la tuberculosis. Se han extendido substancialmente el descubrimiento de casos mediante la radiografía colectiva. Se ha iniciado la investigación comprobada sobre la eficacia de la vacuna con B.C.G. como medida profiláctica. La División para el Control de la Tuberculosis ha continuado el estudio de la sensibilidad a la histoplasmina entre las enfermeras. La búsqueda para encontrar un antibiótico que sea eficaz contra los bacilos tuberculosos continua con un futuro prometedor. Son alentadores los resultados del uso de la estreptomicina en la tuberculosis miliar, las fistulas cutáneas y la meningitis tuberculosa, y los estudios preliminares indican resultados prometedores en la tuberculosis pulmonar. Se ha extraído una substancia cristalina del Musgo Español Californiano, la que parece retardar el avance de la tuberculosis en los cobayos.

Mediante servicios directos, que han incluido demostraciones y préstamos de personal, ha continuado la División en su plan de ayudar a los Estados y a las colectividades locales.