Treatment and Random Thoughts
on Tuberculosis Today

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The average physician today, regardless of his specialty, has been lulled into a false sense of security concerning tuberculosis. This has been brought about mainly by the fall in the tuberculous death rate. However, the average physician fails to appreciate the fact that the number of new cases each year and the extent of disease present in patients admitted for treatment are the same as they were at least ten years ago. This includes all types of tuberculosis — primary, reinfec- tion, pulmonary and extra pulmonary — and all age groups. In addition, in recent years, tuberculous — like disease caused by chromogenic acid-fast bacilli has been reported with increased frequency. These atypical (chromogenic) acid-fast organisms have been associated with a wide variety of clinical syndromes, which have a disease spectrum similar to that of human tuberculosis. Certainly the actual clinical course of infections due to photochromogens and other atypical acid-fast organisms has not been well defined because of the relative paucity of cases and lack of controlled study. However, I trust that these opening remarks indicate the need for continued respect for the genus of microorganisms, mycobacteria, known for its single definitive feature: Acid fastness.

It is treacherous to attempt to speak about such a broad subject as “Tuberculosis”. The evolution of tuberculous pathology, factors in the general management of the tuberculous patient, etc., are subjects in themselves worthy of lengthy discussion and debate. The treatment of pulmonary tuberculosis remains a challenge both to the internist as will as the chest surgeon despite the apparently phenomenal success of present day medical therapy. Therefore, it would also be unwise for me to attempt here today to discuss treatment except in its broadest aspects. Thus, I have chosen as a title for this presentation one which allows me a lot of leeway and as stated — random thoughts.

Although tuberculosis may affect all body tissues it is the various aspects of lung tuberculosis which comes most frequently to our attention. And, it is there, in the lung, that we see most vividly the evolution of the tuberculous pathology. Let's consider this pathology for a moment.

Pulmonary tuberculosis is a changeable and unpredictable disease. Although its onset is often acute, there generally follows along, smoldering period of evolution characterized by intermittent recrudescence and quiescence.

As in other varieties of bronchopneumonic infections, reaction to invasion by the tubercle bacillus is manifested by an alveolar-filling process characterized by exudation, necrosis, and cellular proliferation. After the acute phase has subsided, this cell proliferation leads to the characteristic formation of epithelioid cells, giant cells, and tubercles.

One of the most distinctive features of tuberculous pneumonia is that tissue reactions of exudation, necrosis, and proliferation do not take place in any specific sequence. From the very beginning, local cell proliferation may occur and progress to the exclusion of all other reactions.

The factors which determine the nature of the primary reaction include the type, number, and virulence of the invading bacilli. In addition, the reaction is modified by the variable susceptibility of invaded organs and tissues. In man, for example, muscle tissue, including the heart, is rarely involved; whereas in cattle, tuberculosis of muscle is rather common. As yet, there has been no valid explanation for this well-known observation. The elucidation of this phenomenon of natural resistance could easily bring the tuberculosis problem one step nearer to
The late tissue reactions to tuberculous invasion include caseation (coagulation necrosis), liquefaction, fibrosis, calcification, and ossification. Liquefaction, which is the result of fluid imbibition by the caseous tissue, promotes rapid growth of the tubercle bacilli. Expulsion of this liquefied caseous coagulum from a lung focus results in the wellknown tuberculous cavity. It is this bacilli-laden cavity which is responsible for the bronchogenic dissemination of the tuberculous infection to other parts of the lung and to the laryngeal tissues. In addition, the repeated swallowing of the infected sputum may initiate a progressive tuberculous enterocolitis.

Anatomical healing processes are those leading either to the elimination of destroyed tissue and subsequent fibrous repair or to its waling off and stabilization.

The mechanism involved in the healing of pulmonary cavities has always stimulated much discussion. In certain instances, the cavity boundary, or "wall", may heal by elimination of the tuberculous tissue, followed by its replacement with clean granulation tissue. The remaining "hole" in the lung may then gradually shrink and actually disappear as the result of approximation and fusion of the granulating walls. More frequently, this cavity collapse and obliteration is brought about by the occlusion of the segmental-draining bronchus, leading ultimately to a segmental atelectasis and fibrosis. These are the forces of natural healing which result in the physiological exclusion of a destroyed broncho-pulmonary segment or subsegment. It should be stressed that this natural healing, when it does occur, can never be improved upon even by the most skillful surgery.

Another method of cavity healing which was considered an extreme rarity until recently, is that in which the cavity becomes free of tubercle bacilli, but remains open. However, modern antituberculous therapy has yielded both clinical and pathological evidence that this so-called "open healing" now occurs more frequently. These residual "sterile holes," which often resemble localized cystic disease of the lung, constitute one of the most difficult problems facing the chest clinician today. Whether or not all such residual, cyst-like cavities should be treated surgically is a question which cannot be answered at the present time.

A further example of nature's defense against the tuberculous cavity is the one in which the open cavity is converted into a solid focus. This occurs by blockage of the draining bronchus and, depending upon its stage of progression, such a lesion may be termed a temporarily blocked cavity, an encapsulated caseous focus, or a tuberculoma. In the tuberculoma stage, evidence of calcification or even ossification may be present. Thus deprived of oxygen, the activities of the strictly aerobic tubercle bacilli come to a standstill.

There are two possible outcomes to this tuberculous lesion. One is its complete stabilization as proved by X-Ray and clinical observation. The other is its reactivation via the re-opening of its bronchial communication or by a break through the wall of the solid focus. Bacilli, which had remained dormant for months or years, may, with renewed oxygenation, regain their ability to grow and to show clinical evidence of activity.

This latter possibility is undoubtedly the strongest argument in favor of surgical excision of these solid-appearing foci. Collapse therapy has absolutely no place in their management, since they are in no way susceptible to collapse procedures.

Before leaving the subject of the tuberculosis cavity, it may be advisable to describe a distinctive type of lung cavity which represents a phase in the evolution of chronic hematogenous tuberculosis as it affects the lungs. These cavities are most often thin-walled, have a punched-out appearance, and tend to remain unchanged for a long period. On the other hand, in the much more common type of lung tuberculosis, the early thin-walled cavity is soon transformed into the familiar thick-walled fibrotic cavity system.

This difference in pathogenesis of the thin-walled cavity is mentioned because, in my opinion, the chronic hematogenous type of lung pathology should rarely be subjected to surgical intervention. Rather, it is felt that intensive medical antituberculous therapy on an ambulatory basis should be provided for a period of three years or longer. If such hematogenous lung pathology is subjected to surgery, one should be prepared to find, with disturbing frequency, the appearance of new thin-walled cavities in
other parts of the same or contralateral lung.

Another factor, which should serve as a deterrent to aggressive surgical tactics in these cases, is the frequent presence of active disease in the regional lymph node component of the hematogenous parenchymal lesion. It is this hilar-mediastinal lymph node focus which is most often responsible for the further lymphohematogenous spread of the tuberculous process. That such a fact is not generally appreciated, is evidenced by the complete disregard of this more dangerous regional node by those who attack any and all demonstrable lung foci. It should never be forgotten that a tuberculous meningitis may lie somewhere along the path of these smoldering caseous lymph nodes and that this path may be shortened by some ill-advised surgery directed simply to the hematogenous parenchymal focus.

To summarize briefly, the surgery of pulmonary tuberculosis should be limited to the control or removal of the open or blocked cavity representing the pathology of the commonly observed type of lung tuberculosis. Surgery should rarely, if ever, be applied to known or suspected hematogenous pulmonary lesions.

Although it is not possible within the limits of this discussion to delve into the many details of clinical management of the tuberculous patient, it may be helpful to draw attention to a few of the more important factors which have contributed to successful therapy. These include:

1) The recognition and correction of the commonly associated metabolic deficiencies, hypoproteinemia and impaired hemodynamics. With regard to the latter, it has been estimated that more than two-thirds of chronically ill patients suffer from a depleted total circulating blood volume. Whole blood transfusions have not only proved very helpful in accelerating the response to therapy, but have served to eliminate many of the formerly common operative and postoperative complications.

2) The correction of a definite, though frequently unsuspected, subclinical degree of adrenal insufficiency. In several instances, adrenocortical therapy has proved life saving.

3) The improvement of bronchial drainage. One can scarcely over-emphasize the necessity for maintaining an adequate cough mechanism. The cough reflex, which is nature's sole weapon against the accumulation of bronchial secretions, must be preserved. The so-called antitussant drugs have no place in therapy of chronic cough with expectoration. Instead, patients should be taught to practice postural bronchial drainage at frequent intervals during the day. Furthermore, during bed rest periods, they should be encouraged to assume the face-down (prone) position in order to secure better drainage of the otherwise poorly draining posterior lung cavities.

4) The control of any associated secondary bronchopulmonary infection through combined parenchymal and inhalational antibiotic therapy. Intermittent courses of such therapy should be routinely employed whenever the measured 24-hour sputum totals more than one ounce. Elective surgery should always be deferred, whenever feasible, until the daily sputum is reduced to one-half ounce or less. This measure alone will greatly decrease the incidence of post-operative bronchopulmonary complications and/or tuberculous spread.

5) The securement of maximal clinical control of the tuberculous infection. This objective is best achieved, at present by combined antibiotic therapy. The ultimate goal of intensive supportive and antibiotic programs of treatment is the achievement of complete or, at least, maximal natural healing. Surgical intervention should not; as a rule, be considered unless a standstill is reached in this natural healing process.

6) The more precise evaluation of cardiorespiratory function. Before proceeding with any form of tuberculosis surgery, it is essential that the patient possess an adequate cardiorespiratory reserve. The variable extent of fibrosis and emphysema which follows lung destruction and secondary repair, may seriously hamper this function. If, in addition, pleural pathology is present, this vital function is further impaired. Because of these complications and sequelae, which encroach upon the pulmonary reserve, it frequently becomes necessary to evaluate the remaining lung function. This is accomplished by the use of fairly well standardized spirometric measurements. Occasionally, it may be necessary to measure the function of each lung separately by the more specialized bronchiospirometric method.

These tests, which actually represent a refinement of the earlier-crude vital capacity studies, indicate...
the patient's ventilating efficiency or the mechanism involved in the supply of oxygen to the alveoli and the removal of carbon dioxide from the lungs. Tests, which measure the diffusing capacity or the mechanism by which the exchange of oxygen and carbon dioxide is effected between the alveoli and the pulmonary capillary blood, are not as yet sufficiently developed for routine clinical use.

In general, ventilatory function studies are indicated whenever the usual clinical investigation suggests a borderline respiratory reserve. They should be carried out routinely in all bilateral disease problems, in the older age groups, and whenever extensive lung resection or collapse is contemplated.

Attention to these factors has not only contributed greatly to the successful therapy of the tuberculous patient medically but also has extended both the scope and the safety of definitive surgery. Now, for a few more words about therapy in general.

There are five characteristics of tuberculosis which make it a particularly difficult disease to treat: first is the tendency of tubercle bacilli to become resistant to any known antibiotic when they can continue to multiply in the presence of small concentrations of the drugs; second is the tendency of blood vessels in the diseased area to become obliterated, which in turn further decreases the concentration of drugs where they are most needed; third is the tendency of the disease to produce destruction of tissue (caseation) which then has no blood supply and the drugs cannot diffuse into it in sufficient quantity to be bactericidal; fourth is the presence of visible tubercle bacilli inside macrophages so that any antibiotic such as streptomycin, which does not penetrate the cell membrane, is not effective; and fifth is the tendency to obstruct the normal drainage pathways, for example, in bronchial stenosis or ureterostenosis. Because of these difficulties a very careful evaluation of each patient is necessary if the tools we have today, in chemotherapy and resection, are to give the best results possible. It is impossible to predetermine from bronchoscopic and histologic examination which specimens will give positive cultures for tubercle bacilli. It is also impossible to distinguish between patients with negative gastric cultures and those with negative cultures of lesions resected after reactivation. It is a good policy to resect pulmonary lesions at the end of three to four months of combined therapy, before the emergence of drug-resistant organisms which increase the complications of resection. Whether or not resection is performed depends on the type of pathological change seen in routine anteroposterior tomographs taken after three months of combined chemotherapy, and, if there is a question of endobronchial disease, the results of bronchoscopy using right angle and foreoblique telescopes. All bronchial stenosis and bronchiectasis should be resected. All large caseous foci over 2 cm in diameter and all thick-walled cavities should be resected. If a patient has a resectable lesion and does not have associated disease which contraindicates surgery, he should not receive long-term drug therapy because if reactivation occurs later the response to drugs will not be as good as with the first course, and the prognosis at surgery is poor.

All patients with active tuberculosis should be hospitalized to establish the diagnosis, the extent and type of disease, and whether or not resistant organisms are present. While certain groups of patients have a higher incidence of toxic reactions to the various drugs (for example, the P.A.S. reactions in patients with emphysema streptomycin and dihydrostreptomycin reactions in patients with renal tuberculosis, and isoniazid reactions in patients with epilepsy) these reactions can and do occur in other patients, even in children. These reactions may be serious, and can be fatal if not recognized.

The purpose of the tuberculosis hospital is to isolate patients while contagious and to treat them so that there is reasonable assurance that they will not have reactivation of their disease. Since reactivation therapy is related to the type of pathological change present, it is the physician's responsibility to rule out or remove, if possible, these types of reinfecive tissue. The time spent in a hospital is not nearly as important as the treatment that is given during the hospital stay.

A great deal has been written about the drug treatment of non-hospitalized patients with tuberculosis. It is worthwhile as well as enlightening to compare the results of this type of program with the results obtained from immediate hospitalization.
the use of controlled drug therapy, the use of tomographs and bronchoscopy, and the use of early resection when indicated. A review of this kind will, I believe, convince you that drug therapy of non-hospitalized tuberculosis patients falls for short in every respect of that which can be achieved with immediate hospital care. Outpatient treatment results in a relatively low percentage of conversion of sputum cultures to negative, and if the patients deny bringing up any sputum they usually are automatically considered negative, which is definitely not so. An alarming high percentage of consistently contagious cases will remain, as patients with chronic disease. And, because of this great number of chronic cases, such a program is not economical either in restoring patients to normal productive life or in saving tuberculous funds. This type of program, in my opinion, leads to an increasing number of patients with resistant organisms as a result of contact with "open" cases. This as I have outlined is an ideal approach to the Tuberculous problem.

This approach can not always be followed. I'm sure, because conditions of finance and economy may dictate other more expedient although less effective means of dealing with the tuberculous patient.

These thoughts that I have presented are not new. They have been expressed before by others. I have chosen to re-emphasize them today since I think that as outlined, the tuberculous problem might be brought closer to control; and certainly if tuberculosis is to be eradicated as a disease, principles such as these must be adhered to.