

PROGNOSIS IN TUBERCULOSIS *

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INTRODUCTORY

WHEN one considers the prognosis of tuberculosis in its widest implications he is obliged to extend his discussion to every phase of the tuberculosis problem and consider every factor which influences bacillary growth and activity or modifies individual resistance. The outcome of the disease is influenced by the virulence and numbers of infecting bacilli; the type of the disease and its severity; the constitutional peculiarities of the patient; his general reacting powers; his condition at the time when infection occurs; the character of the tissues which are involved; the nature of the lesion; the time when the diagnosis is made; the character of treatment and when it is instituted; the age, economic and social status and intelligence of the patient; the character of the climate and weather to which the patient is exposed; the psychology of the patient and of the friends who advise him; the physician who carries out the treatment, his psychology as well as medical knowledge and experience in meeting the problems of the tuberculous patient; the place where the treatment is to be carried out whether at home, in a sanatorium or in a dispensary; and many other factors of greater or lesser import.

It is not always the big thing that determines the outcome in tuberculosis. We at times see the prognosis changed from favorable to unfavorable and the reverse as a result of some very small factor which might, under ordinary conditions, seem of minor importance.

In the time allotted to this paper I shall confine myself largely to the influence which a competent physiologic reaction and a competent compensating mechanism on the part of the patient has upon the prognosis of tuberculosis; and further point out the difference in a prognosis from the standpoint of healing and from the standpoint of physical efficiency.

TWO BASIC FACTORS ON WHICH PROGNOSIS DEPENDS

The healing of tuberculosis is a physiologic process; and, when the physiologic balance of the patient is good, tuberculosis shows a strong tendency to heal. That the prognosis is favorable, provided the disease is treated intelligently in its early stages, is now generally acknowledged, because the patient's resisting power is good and the ability of the lung tissue and thoracic cage to compensate for the loss which results from infiltration cavity or fibrosis is excellent. When these early cases fail to heal it is usually due to the fact that conditions necessary to the healing process were

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not established. That the prognosis is less favorable in the far advanced stages and when improperly treated in all stages is equally well established.

With the well established forms of treatment everywhere recognized today, there are few places in civilized countries where a patient suffering from tuberculosis can not be given a fair chance of recovery if aid is sought at a time when the disease is curable. This is very different from what it was a quarter of a century ago; for even so recently as that, well trained specialists were few, the general opinion of physicians was that the disease was hopeless, and the aid necessary to cure was rarely to be had.

The two most potent factors in changing the prognosis of tuberculosis in recent years from the status of an all time hopeless disease to that of one that is curable have been the large group of medical men who have made tuberculosis their special study, and the systematic spread of knowledge concerning the nature of the disease by interested workers. It is almost an unbelievable fact that this change in prognosis has come within a single generation.

NEXT STEP IN IMPROVING PROGNOSIS

Probably the next greatest advance in prognosis will be brought about by the medical profession considering tuberculosis in the same category as other diseases. General medical men should understand tuberculosis and show the same interest in it that they show toward diseases of the heart, kidney and gastrointestinal tract, or diabetes or blood diseases. When they do this we may hope not only for an earlier recognition than today, but also for the application of treatment when it will be more effective. In no disease can a physician render a greater service to a patient or to his family than in making an early diagnosis of tuberculosis and directing him so that he at once receives adequate treatment and at once minimizes the danger of infecting others. It not only means saving the patient's life and restoring him to usefulness, but saving others who associate with him from infection. The importance of instituting immediate treatment is particularly emphasized by the fact that the disease so often affects the bread-winner and is so often found in the years of early adult life when the domestic, economic, social and cultural interests of the family depend upon the patient's ability to carry on with as little loss of time and efficiency as possible.

PROGNOSIS AS IT RELATES TO IMMUNOLOGIC REACTION

In order to make an intelligent prognosis we must understand something of the intimate reactions which make up the defense mechanism of the patient, for these are basic in prognosis. They vary greatly in different individuals. Tuberculosis is a chronic inflammatory disease. The accompanying inflammation is due to the reaction between bacilli and their products on the one hand, and the tissues of the patient on the other. The reaction, being inflammatory, carries with it local irritation of cells, dilata-

tion of blood vessels, and an exudation in the tissue spaces with an increased serum and cellular content at the site of the injury; all of which belongs to the defense reaction.

Both bacilli and tissue cells may be destroyed as a result of the conflict which goes on for mastery. As a result of the irritation and destruction of tissue cells, enzymes are set free which produce bacteriolysis. Destruction of bacilli is further carried on by cells which possess phagocytic qualities. Resulting both from the growth and the destruction of bacilli, substances are set free into the tissues which gain access to the circulation and stimulate the defensive function of cells throughout the body. Thereafter, when bacilli or bacillary substances gain entrance to the tissues they are anchored and destroyed with increased avidity.

Local defense takes upon itself two forms, one that of bacteriolysis, the other that of tubercle formation; the one primarily destructive of bacilli, the other primarily fixative in that it tends to hold them in situ.

General defense, on the other hand, consists in establishing an increased power on the part of the tissues generally for opposing both bacilli and bacillary products. While certain cells normally have greater defensive powers than others, it seems that every cell of the body is endowed with the function of defense and that it is stimulated to unusual proportions as a result of infection. We call this increased defense immunity. This increased physiologic reaction is the factor which makes it possible for the organism to oppose successfully millions of bacilli in advanced extensive tuberculosis, although first infection may have been brought about by a very few.

While the defense strategy of the body, in case of an attack of microorganisms, consists in concentrating its most effective forces at the point of invasion it carries out the principle of universal conscription and arms all cells so as to guard every area of the body from attack while continuously sending up new forces to the front so as always to have fresh troops guarding the most exposed areas.

In order to understand how prognosis may be modified by the general condition of the patient it is necessary to understand that specific defense is a quickened and heightened response of a physiologic function normally possessed by the body cells; and, that this function is just as normal as that which produces secretions having special properties or that which produces muscular action. So, warding off infection, destruction of invading microorganisms, and the repair of the injury which has been caused are all physiologic processes, the competency of which depends much upon the condition of the patient.

The body's defense is sufficient as a rule to either wholly destroy the few bacilli which enter the tissues at the time of first invasion; or, to hold them largely fixed at the point of entry and in the lymph glands which drain the infected area. But the fact that infection is established is evidence that the numbers of bacilli are greater than the local cells, with their normal

protective function, are able to cope with; and, furthermore, it is evidence that unless this protective power can be increased the infection cannot be successfully opposed. The general principle in physiology of increased response to unusual stimulation now quickly comes into play, and within a few days after bacilli have become implanted in the tissues all cells of the body are able to put up an augmented defense. If tuberculosis extends thereafter, it does so against increased opposition which tends to restrict the extent and severity of the metastases. The prognosis in the more simple lesions which succeed the primary complex is determined very largely by the degree of competency of this protective mechanism.

Tuberculous infection, opposed by increased cellular defense, results in the so-called "adult type of infection." In the adult type, on account of this increased cellular defense, the lymphatic route of spread which was open and free to bacilli at the time of first infection is now largely closed, shutting off the easiest route for bacilli to follow in spreading throughout the body. Bacilli which enter the tissues by way of the blood and canalicular routes such as the bronchi now also meet with increased opposition to implantation and are often destroyed without producing infection; or, if infection is established, it often becomes abortive. This protection in the previously infected individual is so efficient that, unless the numbers of infecting bacilli be great, there is little danger of permanent metastases forming in the early stages of the disease provided, of course, the patient is put at bed rest and so treated as to maintain a normal physiologic response. The increased local and general physiologic responses of the body, if only the patient is maintained in a state of high physical fitness, make the prognosis in early clinical tuberculosis almost invariably favorable.

PROGNOSTIC SIGNIFICANCE OF CASEATION

While the major pathologic processes may be described as predominantly exudative and predominantly proliferative, the most serious phenomenon which is met in the pathology of tuberculosis, the one which carries with it the possibility of affecting prognosis most unfavorably, is caseation and softening, because this process is responsible for cavity formation and furnishes the source of bacilli which produce metastases by spreading through such natural channels as the bronchi.

A patient may be incapacitated by the gradual encroachment which a preponderantly proliferative lesion makes upon his reserve pulmonary tissue; but sooner or later caseation with destruction of tissue and cavity formation will usually accompany and increase such incapacity. It is caused by a violent protective reaction of immunized tissues against an unusual number of infecting bacilli or large quantities of their protein products. Multiple cavity can be largely prevented by the immediate application of adequate treatment while the disease is early.

Caseation often takes place early in exudative infections because the tis-

sues are in a state of hyperergy. The anchoring ability of the cells is so great that the protein is fixed in such large quantities that it obstructs the capillaries, cuts off the blood supply to the tissues, and causes them to caseate and undergo destruction; but as the tissues become more accustomed to the infection it seems that the degree of protection becomes greater while the cellular reaction becomes less violent. This is of great prognostic significance, for either a degree of desensitization of the cells takes place or the protein is prevented in some other manner from producing severe localized reactions. While cavity often accompanies an early exudative lesion, a second one rarely follows immediately thereafter, even though the infection continues to spread; and furthermore, few relatively large cavities appear during the course of chronic proliferative lesions except as a result of the fusion of smaller ones. This highly protective mechanism can be relied upon as being the greatest factor in the healing of tuberculosis. Even the extent of destruction may be kept to a minimum by taking advantage of it by the modern methods of treatment which limit the danger of metastases forming by keeping the patient in a state of high physiologic balance. This may be accomplished by the application of rest and other proper physiologic therapeutic measures immediately on the infection assuming clinical importance.

Even a large cavity, today, is far from being the hopeless phenomenon that we formerly thought. The early freshly formed cavity, unless it be situated unfavorably, will usually heal spontaneously, if the patient's reacting powers are quickly brought to a state of efficient action, for the pulmonary tissues are able at this time to take on emphysematous change, and the bony thorax is able to reduce in size and lessen its movement, and these together bring about the conditions required for healing. However, unless cavity is treated properly, it reacts very unfavorably upon prognosis, for it reduces the chances of healing and furnishes an open focus from which bacilli can readily spread and form other metastases.

PROGNOSIS IMPROVED BY ARTIFICIAL COMPENSATORY MEASURES

Up to the present time most patients who have been treated for tuberculosis have been treated after the disease has become advanced. In these cases both the physiologic balance of the patient is severely disturbed and the mechanism by which compensation takes place between the lung volume and thoracic cage has already been utilized to its limit. So physicians have spent their energy attempting to overcome the many discouraging conditions which this chronic infection presents. However, they have been unwilling to accept defeat and by their ingenuity have devised measures with which to cope with many of the mechanical conditions which adversely influence the prognosis in these cases. The physiologic factor, too, is gradually becoming better understood, but there still is no way of restoring the function of exhausted cells. In healing tuberculosis, nature lessens respiratory move-

ment and reduces the size of the thoracic cage to adjust to the volume of pulmonary tissues as it is reduced by the disease. The tissues adjoining infiltrations in the lung also adjust by becoming emphysematous and enlarging, thus relaxing and compressing the infiltrated and excavated tissues.

Experience has shown that these results may be attained artificially by utilizing relaxing and compressing measures, such as weights upon the chest wall, pneumothorax, pneumoperitoneum, paralysis of the diaphragm and thoracoplasty. These measures promote healing mechanically by reducing respiratory movement, relieving diseased pulmonary tissues of tension, and compressing them. In many cases of advanced tuberculosis these measures bring about favorable mechanical conditions without which a physiologic balance, no matter how stable, would be unable to produce healing. However, no matter how frequently healing follows, it must be understood that the protective and reparative processes depend upon the patient's physiologic response.

PROGNOSIS FOR HEALING AND EFFICIENCY DIFFERS

Through relaxing and compressing measures the prognosis in many cases of severe and serious tuberculosis has now become fairly favorable from the standpoint of bringing the disease to a state of quiescence or arrest. This is truly a great accomplishment, but it is still unsatisfactory in that it too often restores a mechanism, which has been injured by neglect, to a limited capacity when our knowledge and understanding of the problems involved warrant a restoration to full capacity. Any measure that carries with it an avoidable reduction in the patient's future efficiency, no matter if the tuberculous process is healed, has in it elements of defeat which medicine must overcome.

To make my meaning clear it is only necessary to contrast the health and full efficiency which a patient suffering from an early limited lesion usually secures through treatment, with the handicap of limited efficiency and insecurity which he usually obtains through the most effective treatment possible when the lesion is far advanced. When we see the interference with the mechanics of respiration, the reduction in lung volume, and the resultant inability to compensate and measure up to the calls for extra physical exertion which is a common occurrence following the best result that can be attained in many far advanced cases of tuberculosis, we should be led to bend every energy towards securing treatment at a stage when such handicaps would rarely follow.

DISCUSSION

From the preceding discussion it may be established that in combating tuberculous infection and in promoting healing we are dealing with functions with which the patient is normally endowed. If cure is accomplished, the patient accomplishes it through these normal functions. If we, as physi-

cians, improve the prognosis, we do it by increasing the patient's own powers and facilities, not by adding something new and extraneous. If only we bear in mind that the phenomena which we meet in the tuberculous process; the proliferation, the exudation and the necrosis, are intimately connected with the immunologic and healing processes, which in turn depend upon the physiologic mechanism of the patient, we will be able to make a more accurate prognosis.

In regard to prognosis it can be said that with stable physiologic equilibrium and favorable conditions for compensatory adjustment on the part of an individual, a limited infection produced by a relatively large number of bacilli, or a smaller number of relatively virulent bacilli, may readily heal; and an infection which may occur at a time when the host's physiologic equilibrium is temporarily lowered may be healed by restoring his physiologic processes to normal; but, should an infection be large or the bacilli be extra virulent, or should the host's physiologic processes remain in a condition of instability for too long a time, then healing of the process may not only fail to take place but metastases may form creating other foci of infection, and from these further metastases may take place, repeating the cycle until healing may become impossible.

While mildly reacting limited lesions are comparatively easy to overcome, multiple or extensive lesions produce a proportionately greater disturbance in the host's physiologic and compensatory processes and bring about a relatively greater tax on his defensive and healing powers. So an advanced and advancing process reduces the favorableness of prognosis by presenting greater difficulties to be overcome before healing may be accomplished, and by causing the host's protective and healing mechanism to be rendered less effective for its task. It is self-evident, then, that the favorableness of prognosis steadily decreases as the tuberculous infection extends quantitatively and as the pathologic changes advance in severity. It is likewise self-evident that a rapid restoration of the patient's physiologic functions, among which is that of defense against infection, greatly improves the prognosis in any case.

Theoretically, one should have little fear but that a normal physiologic function on the part of an individual with a limited tuberculous infection would be able to bring about healing provided it is maintained long enough; and this has been proved by many years of experience. Theoretically, one should expect that the more advanced the process quantitatively and qualitatively the greater the difficulty in securing a healing and the less efficient the patient would be thereafter; and, the experience of many years has shown this to be true. Theoretically, advanced tuberculosis with destructive lesions should be difficult and often impossible to heal by any possible restoration of physiologic balance, and many years of experience have also shown this to be true.

The prognosis in tuberculosis is modified by the character of the lesion,

which depends very much upon the individual patient and his particular physiologic reaction. It furthermore is plain that these two factors are largely in the hands of the physician, to be modified through the application of therapeutic measures. Whether the disease will spread or the patient will be able to defend himself successfully against it depends very much upon the treatment which is carried out. Since healing is primarily physiologic this places the burden of prognosis largely upon the physician, for he determines whether or not a proper physiologic balance is established and maintained.

Before the necessity of maintaining an equilibrium between the size of the thoracic space and the lung volume was understood as being a prime factor in prognosis, pneumothorax and other measures of relaxing and compressing the pulmonary tissues were established, and it was thought that their main purpose was compression or enforced rest to the lung. While this is often true in far advanced cases, it is hardly so in those early cases which will heal spontaneously under hygienic measures alone. Compensation in these cases is necessary rather than active compression.

It is generally accepted that pneumothorax has improved prognosis more than any other measure used in treatment. There is no doubt that it reduces the danger of spreading; that it improves the chances of certain advanced cases that were found to be incurable by older methods, and that it gives the physician a control over the patient. It will not only produce favorable results in a very large group of comparatively early cases, but also in another group that rarely heals without some form of artificial aid. This, particularly, is what has made it so popular, for most cases under treatment belong to this class. However, let us not deceive ourselves, for the best prognosis, with or without compression, is found in early cases.

If we were to discuss the manner in which prognosis is influenced by various procedures, we should divide the patients into those in whom artificial compression measures are necessary and those in whom they are not. As it is now, credit is given to compression measures in many instances in which the lesions would have probably healed under hygienic measures alone. Those early cases in which the patient is able to make his own compensation, if collapsed, add to the prestige of pneumothorax, when in reality a similar result could have been obtained without it.

Pneumothorax has become exceedingly popular in instances in which adequate medical supervision cannot be had. The great majority of tuberculous patients are treated in public institutions in which the number of beds is inadequate and the medical service is undermanned. Therefore, it has become necessary to meet the problems with the facilities which are at hand. To do this compression therapy has been used, not so much because it is necessary for healing, but as a matter of expediency in order to make the facilities meet the needs of the community. Early cases in which the question of healing under hygienic measures is hardly questioned are submitted to

compression therapy, the purpose of which is to render patients bacillus-free as quickly as possible and send them back to their homes, leaving the beds in the institution for others.

All of the early cases that are collapsed in this way add to the prestige of collapse therapy. The effect is to brand the prognosis in most cases of tuberculosis as unfavorable unless collapse therapy is used. That such an attitude is wrong may be shown by the statistics of institutions which treated tuberculosis before artificial compression was generally used. How wrong it is cannot be determined until statistics covering many cases treated with and without pneumothorax are analyzed in an unbiased manner. Recent studies from English sanatoria show better results without operative measures while those from Detroit show best results with.

Admitting that artificial compression, particularly pneumothorax, will enable us to secure a healing in many patients in whom we would fail otherwise, let us not forget that rest with spontaneous compensation or spontaneous compensation supplemented by temporary phrenic interruption will bring about healing in a very large percentage of the early cases and restore the patient to health with a minimum degree of physical inefficiency, produced either by the disease or as a result of the therapy. Pneumothorax produces injury to the respiratory mechanism of the patient in quite a number of instances, and in discussing prognosis all such injuries must be considered. Thoracoplasty, which is a boon to the patient who faces the alternative of healing with incapacity of one lung or of remaining ill, cannot be defended as a desirable treatment. It is the treatment that all would like to escape if possible; but the years of life and comfort it adds are a blessing to the one who cannot do better. We hope, however, that its necessity will become less and less as the truths about tuberculosis become more generally disseminated.

Tuberculosis specialists should urge early diagnosis and immediate restoration of physiologic balance as one of the most important factors in improving the prognosis of this disease. No one would take from far advanced cases the opportunity of healing, even though they are seriously handicapped during the rest of their lives, but the fact that these patients with advanced disease can be handled successfully from the standpoint of cure must not blind one to the unnecessary loss of efficiency that is brought about by treating cases which are far advanced instead of early.

The improvement in prognosis which has been brought about by scientific ingenuity should be accepted for what has been accomplished, but it should not satisfy medical men if better results are possible. On the contrary, it should stimulate humanitarian sentiments so that every tuberculosis worker would proclaim long and loud, in season and out of season, that lives and efficiency are needlessly sacrificed by allowing clinical tuberculosis to extend beyond the time when its cure can be brought about in most instances through the stimulation of normal physiologic functions and through na-

ture's own compensatory mechanism, or at most by the use of the simpler operative measures.

SUMMARY

The cure of tuberculosis is accomplished through normal physiologic processes. The lung may be reduced in volume by infiltration, cavity and fibrosis; and the adjustment of lung volume to the size of the thoracic cage is important in healing. In advanced cases healing may be prevented unless such compensation can be made. The prognosis, then, depends upon physiologic competency and compensatory adjustment.

The prognosis for healing and for efficiency differs. The prognosis in tuberculosis in its early stages is favorable for healing, and also for the future efficiency of the patient. The prognosis in far advanced cases, with the newer methods of treatment, is quite favorable for healing, but the prognosis for efficiency is lowered.

The profession should not be satisfied with the present status of therapy. Too many patients come under treatment only when the lesions are of such severity that the measures required to produce healing are so radical as to entail a lamentable reduction in the patients' future respiratory efficiency.

In order that patients may be treated during the favorable stage of the disease, the medical profession should take the same interest in tuberculosis as it does in other diseases; prepare itself for making early diagnoses and understand the principles of therapy, so that proper treatment may be immediately applied.