

## SPECIFIC THERAPY IN TUBERCULOSIS<sup>1</sup>

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Specific therapy is gradually gaining adherents to its cause and is not looked upon quite as useless and as dangerous as formerly. Some physicians who are still practicing will recall that it required quite a bit of courage to advocate its use. Rest has been modified and used in different ways, but little or no further improvement may be expected from any further modification. The investigators and clinicians are now turning to specific therapy in the hope of improving clinical results. The chaff of the old tuberculin era—the era of bitterness and controversy—is being winnowed again for the kernels of truth that the immortal Koch unfolded and that his pupils have extended to build a helpful therapy, a therapy that gives greater promise of becoming more useful as the antigen is improved.

To understand what is meant by specific treatment in tuberculosis, a brief review of Koch's work will aid much. It also will be necessary to understand something about the tuberculin reaction and how Koch was led to apply it in the treatment of tuberculosis; to consider briefly the tuberculin test, its accuracy, its safety and its aid in helping to find the initial dose in specific therapy.

In 1887, Koch introduced tuberculin to the scientific world and announced that he believed that he had found a cure for tuberculosis. The announcement was heralded with acclaim in all lands, and hope ran high, the discovery presaged an augury of the dawn of a new day. Smallpox had been conquered, and now tuberculosis would soon be overcome and numbered as another scientific conquest.

The toiling investigator in his laboratory left his test tubes and retorts and rushed to Koch's laboratory there to join physicians representing all branches of medicine. At the moment Koch's announcement and the promise it carried with it placed him head of the phalanx of noble scientists throughout the world. His laboratory was the Mecca of the scientific world. The high hopes and zeal of the great Koch, as well as all the scientific world and the hundreds of thousands stricken with tuberculosis, who believed that he had discovered a cure for tuberculosis, were doomed to disappointment. Even though the world did not realize its hopes, certain scientific facts were gleaned from the debacle. It was learned how to select the cases that were suitable for specific treatment, that tuberculin was not a cure for tuberculosis but only an adjunct, and that it was a diagnostic aid in some obscure and difficult cases. Koch also taught about the tuberculin reaction and fully established the fact that the reaction was specific, that is, only the tuberculous subject reacted. His first observations were made upon the guinea pig and later upon man. He ob-

<sup>1</sup>Read before the Tennessee Academy of Science at the Reelfoot Lake meeting, April 29, 1933.

served, when he vaccinated a healthy guinea pig with live virulent tubercle bacilli, the wound usually healed in a few days. But in 10 to 14 days a nodule appeared which broke down and remained an open ulcer until the death of the animal. Now, when an animal previously vaccinated was revaccinated, quite a different sequence of events were noted. No nodule formed and the wound promptly healed, but the skin turned dark and broke down, leaving a clean ulcer which healed up completely without involving the adjacent lymph nodes. These observations led Koch to use tuberculin therapeutically; thus the rationale of the present day conception of specific therapy was laid. It was learned from Koch that the tuberculin reaction is specific and that small doses of tubercle bacillus products stimulate tuberculous tissue and aid in its healing.

The tuberculin reaction has become widely used, and, in the hands of experienced clinicians, is a valuable diagnostic aid. It finds its greatest field of usefulness in children and in obscure cases in the adult; for example, mediastinal lesions, tuberculous adenitis, etc.

In the child the two methods that are usually employed are the von Pirquet and the intradermal. The intradermal is preferred as it is more accurate and there is no chance of losing the tuberculin and the dosage is more accurate. In the von Pirquet the drop method is used and drops vary in size and one never knows whether the entire drop is absorbed. In the child, when the skin is definitely reddened—hyperaemia, 1, 2, 3, 4, plus—it is known that tubercles are present and the child, even though no symptoms of the disease are present, should be kept under observation and given special attention as to diet, sun baths, and specific treatment.

In the adult the intradermal method is also used, but I would hesitate to make a diagnosis on the intradermal reaction alone. However, Krause says that a positive skin reaction means that there is still antigen being given off into the circulation from unhealed tubercles. The subcutaneous method will give one all the information that the intradermal will and more. In the subcutaneous three reactions occur, the local, general and focal. At the point of injection there is a hyperaemia, heat and swelling; the general reaction manifests itself by general aches and pains, fever 99-100-101, lassitude and often headache—infrequently chills; the focal reaction in the lungs by rales, cough and expectoration increased; in the larynx by hyperaemia; in joints by pains and increased tenderness. When a febrile reaction of 99 3/5-100 plus occurs there are unhealed tubercles present. It may be that the lesions are quiescent but with other clinical data and history a diagnosis of tuberculosis may be made.

As to the accuracy of the test, Frankel found in 8,000 cattle, tested and autopsied, that the findings varied only from 2% to 3%. Voges in 7,327 found only 2.7%. Von Behring's experiences are equally conclusive. After making due allowance for known sources of error they conclude that the tuberculin test in animals is just as reliable and accurate as autopsy findings. The reaction is accepted as con-

clusive of hidden tuberculosis, and, even if not found by the pathologist, the autopsy must carry the burden of proof.

Is the method safe? If the test is made with care; that is, a careful examination and care as to dosage, it is safe. Pottenger says that with care and judgment the test is safe, and my experience agrees with his. To test out the sensitiveness of the patient, the intradermal test should be used. In the sensitive patient one may get a general reaction to the intradermal test. If the intradermal test is practically negative the usual subcutaneous doses are 1, 3, 5, 7, 10 mgms.

From his experiments Koch concluded that tuberculin would be helpful in treating tuberculous disease. In fact, he believed that he had found a cure and that the tuberculosis problem had been solved. Future events, however, proved that his high hopes and enthusiasm were to be doomed to great disappointment. He had not discovered a cure but only an adjunct, as it has been established to the satisfaction of those who have given it an impartial trial.

Tuberculous lesions, wherever located, will respond favorably to specific treatment if conditions are suitable for its application.

In bone and joint tuberculosis all necessary surgery should be done before instituting specific treatment. One would not expect a focal reaction to remove necrotic material and dead bone, but focal stimulation will aid healing and should be used in connection with other post-operative measures. Many old draining sinuses, that have failed to heal after surgery, yield to specific treatment.

Results in ocular tuberculosis to specific treatment are, in the main, good; at times the end result is nothing less than brilliant. In many instances the vision is restored to almost normal.

Laryngeal tuberculosis is a serious complication of pulmonary tuberculosis. Early diagnosis and proper treatment are very useful in helping to obtain the desired end result. In lesions of the larynx one does not have to guess at the reaction or its extent, as it is easily seen. Under repeated stimulation and rest, many early lesions heal and even far advanced ones are influenced beneficially—a few heal out completely.

However, we shall not attempt to consider the entire subject of tuberculosis, but discuss briefly specified treatment in pulmonary tuberculosis.

For those who are beginning the use of specific remedies there are a few simple rules that will aid them if followed: (1) Selection of cases; (2) Preparation; (3) Dosage.

1. *Selection of cases* is very important. Early cases free from fever respond more favorably than the more advanced cases. It is the wiser plan to withhold specific remedies in the presence of high fever, 100 or more, until there is decided recession, probably in the majority of cases afebrile. It is obvious that specific treatment will exert a more favorable influence in every case before extensive fibrosis and cavitation take place. In the more advanced cases the fibrosis and walled off cavities interfere with the circulation to the lesions, and

of necessity the antigen reaches the diseased process in small amounts or not at all.

2. There is quite a difference in *preparation*. Pottenger lists all preparations under tuberculin, which I believe to be a mistake. When one uses the term "tuberculin," at once Koch's Old Tuberculin is thought of and justly so unless otherwise specified.

What is tuberculin? Koch's Old Tuberculin is a product made by concentration of a peptone, bouillon culture of tubercle bacilli to 1/10 of its normal volume and then filtered through a Berkefeldt filter. There is only a faint trace of bacillary protein, the oxogenous products of the bacillus (products given off during growth and multiplication of the tubercle bacillus), peptone and beef products constitute Koch's tuberculin. One would not expect to build up a strong immunity against the tubercle bacillus with tuberculin but rather against the oxogenous products of the bacillus.

An ideal product, then, would be one that would represent all constituents of the tubercle bacillus in adequate proportions. In other words, an antigen that represented a completely dissected bacillus chemically. We have not been able to find out all of the component parts of the tubercle bacillus but we have found out some things. We know that the capsule is composed of a wax-like substance; the bacillary protein of a very complex nature and carbohydrate. Von Ruck's preparation fulfills these requirements more fully than any I know, and Much's partial antigens probably come next.

3. The *dose* must be found for each patient. No set rules can be laid down, as no two respond alike. It is good practice to test each patient's sensitiveness by the intradermal test as quite a bit of information is derived by this test. If the test is strongly positive, a very small dose of the antigen selected is indicated. Should the intradermal test give a weak response a somewhat larger dose may be used. The initial dose is usually 1/10 mgm. or 1/100 c.c., gradually increasing the dose to produce the desired reaction. There is no maximal dose as the clinician determines the maximal dose by the reaction and clinical findings in each case. When there is no reaction observed to 1.5 cc. to 2 c.c. or to 100 or more mgms. of tubercle bacillus antigen and the physical findings indicate the end result desired, and, if the x-ray films confirm these findings, the patient is discharged as apparently arrested.

How does specific treatment aid in the healing of tuberculosis? The immuno-biological reaction to the tubercle bacillus antigen is very complex and is not fully known. However, we have been able to make some observations from experimental work and treatment of the patient. In addition to these observations, theories have been proposed by different workers to explain the so-called tuberculin reaction.

The clinician has observed that in patients who reacted focally, the tuberculous lesions begin to improve more rapidly than in those who failed to respond definitely to specific remedies. A well defined reaction is one that produces a hyperaemia in the tuberculous lesions

that can often be determined on auscultation and by the x-ray. The hyperaemia manifests itself by an increase of the previous physical findings, viz., roughness, rales. By repetition of the focal stimulation, hyperaemia, absorption of the tubercle and its products is hastened and more complete and fibrous connective tissue is formed and scar tissue is laid down more rapidly and more densely. Besides aiding the healing process, an increased resistance, or immunity, has been conferred on the patient. It is believed that the mechanism involved in this process, the reticulo-endothelial system, is principally responsible for the immunity conferred.

This is not all that specific treatment does, not by any means. The clinicians who have used specific remedies a sufficient length of time to acquire a sound knowledge of their use and limitations, have observed that relapses do not occur nearly so frequently. The more permanent results are explained by more completely healed lesions and by an increased resistance or immunity.

To summarize:

1. The tuberculin reaction is specific.
2. The tuberculin test is a diagnostic aid of great value under proper interpretation.
3. Specific remedies in experienced hands are a valuable adjunct in the treatment of tuberculosis.
4. Rest in the treatment of tuberculosis must be enforced just as rigidly when specific treatment is used as with rest alone.
5. Specific treatment is safe and helpful when properly used.
6. End results obtained by the addition of specific treatment to the ordinary method in vogue are more permanent and fewer relapses occur.

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## MORE CHILDREN—LESS MONEY

Seven hundred twenty-eight thousand more children were enrolled in high school in 1932 than in 1930; 115,000 fewer children were enrolled in elementary school in 1932 than in 1930. . . . Net gain, 613,000 pupils. This is more than the entire population of Montana. It is more than the combined populations of Atlanta, Des Moines, and Salt Lake City. It is more than were enrolled in all our public high schools in 1900. Today 93 of every 100 city children enroll in high school; 55 of every 100 rural children do likewise.

Abolition of child labor in industry by the NRA will, it is estimated, put another 100,000 children on the high school doorstep. In one small Southern town it added 137 pupils.

*Any industry faced with rapid increase in business would expect an increase in total operating costs. But schools, forced to carry an increased burden, are required to carry on with less funds.—School Science and Mathematic.*