

**A COMPARISON OF SOME OF
THE IMPORTANT PHENOMENA
IN SYPHILIS AND
TUBERCULOSIS**

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INASMUCH as syphilis and tuberculosis are our two best known and most widely distributed chronic infections, it seemed to me that a general comparison and contrast of some of the more important phenomena in the course of the two diseases might be made the subject of a profitable study.

These two diseases have many points of similarity, yet they are widely different in other particulars. They are both chronic inflammatory infections, which, after gaining access to the body tissues, may persist within the body of the host during the remainder of his life, either with or without causing recognizable symptoms. Both diseases are accompanied by toxemia during the period when the specific causative organisms are multiplying; both possess the characteristics of infecting practically all tissues of the body; yet each one has its own peculiarities and each has certain tissues for which it shows predilection.

The greatest similarity in the two diseases comes from the fact that they are both chronic infections, and as such produce changes in the tissues where the specific microorganisms become implanted, from which toxins are given out during periods of activity and from which further spreading of the disease may occur at any time during the life of the host when the biochemical conditions of the tissues become favorable to the infectious microorganisms; and further from the fact that being chronic infectious inflammatory processes which may affect any organ or structure, similar symptoms appear no matter which disease is present. These points will be made clear as our analysis proceeds.

INFECTIOUS AGENT

The infectious agent in tuberculosis is a rod-shaped bacillus, protected by a heavy coating of wax which makes its destruction in the tissues very difficult. The treponema pallidum, on the other hand,

seems to belong to the protozoa and, while tenacious of life when imbedded in the tissues of its host, is very susceptible to the action of certain chemicals, particularly arsenic, a fact which offers hope for the ultimate specific eradication of syphilis from the body. The difficulties surrounding the destruction of both treponemata and tubercle bacilli are greatly increased by the protective cellular wall which surrounds them.

The Treponema.—The portal of entry in case of the treponema is nearly always evident, while that of the tubercle bacillus is concealed. The treponema is conveyed through contact, and it is believed that an abrasion in the surface is usually an important factor in infection. Multiplication of the microorganisms takes place at the point of inoculation, forming the chancre and giving what might be termed a primary incubation stage which lasts, on an average, three or four weeks. At the end of this period the infection has extended to the regional lymphatic glands and the second incubation period begins, during which time the treponemata again multiply and prepare for the general attack upon the host. This second incubation period is about twice as long as the first, averaging six to seven weeks. At the end of this time sufficient treponemata have developed to produce a general invasion of the body. They gain general access to the blood stream and are deposited in the tissues throughout the body. They now become implanted in the skin, producing the well-known cutaneous lesions; in the mucous membranes of the mouth and throat, causing mucous patches; and settle more or less generally throughout the tissues of the body.

It seems that, by this time, a considerable degree of specific resistance has been developed by the host, and the treponemata which have heretofore developed freely now grow sparingly and multiply with difficulty. This is evident from the fact that treponemata may be recovered from the various lesions but that the lesions remain more or less abortive in character. A long time may now elapse before the microorganisms are again found multiplying and the inflammatory processes active.

During this period of quiescence, the treponemata are embedded in the tissues living under conditions which they are able to make consistent with life but which are not favorable to multiplication and rapid growth. Renewed activity depends upon the development of conditions more favorable to the invader.

The Tubercle Bacillus.—The tubercle bacillus enters the tissues in such a mysterious way, that years of observation have not yet settled the portal of entry. Students are divided in their opinion as to the relative importance of infection through the air passages and the digestive tract; and no matter what theory one supports, he must admit his argument is not conclusive.

The tubercle bacillus does not require an abraded surface for its entrance; in fact, the undenuded mucous surface is accepted as being the most common portal of entrance. When the bacillus passes through the mucous surface, it does not leave a nodule at the point of entrance unless we accept the work of Ghon¹ as conclusive on this point. Ghon shows by postmortem evidence that the lungs of children who have enlarged mediastinal glands always have a primary nodule, often so small as to be overlooked except on most careful search, in that portion of the lung which drains into that particular infected gland. This might be considered as the primary focus conformable to the chancre; except to my mind, as I shall attempt to show, it does not necessarily mark the portal of entry. This splendid work of Ghon is set forth by the adherents of the theory that tuberculosis is an air-borne disease, to show conclusively that the primary nodule must have been formed by bacilli which have entered directly through the air passages.

Against accepting this argument as conclusive, I would call attention to two well-established facts: First, bacilli which are fed to dogs pass through the intestinal mucous membrane, are taken up by the lacteals, carried by the thoracic duct, poured into the blood stream and taken directly to the lung;² second, primary nodules are not found in the nasal, or oral mucous membranes, and but rarely in the intestinal walls to mark the point of entrance. The first opportunity for bacilli, entering via the intestines, to become enmeshed in tissues would be in the small blood vessels of the lung. So these primary nodules of Ghon may be due as well to intestinal as to respiratory infection.

In this primary nodule in the body tissues (accepting it as primary, whether the bacilli pass directly by way of the air passages, or indirectly by way of the intestine, thoracic duct, and blood stream), the bacilli multiply in the same manner but probably with less rapidity than the treponemata do in the chancre, and pass on freely as they do into the regional lymph glands where they are held

captive in most instances for a time. From the time the bacilli are first enmeshed in the body tissues, specific cellular defense begins to develop and further inoculation, whether from without or within takes place with greater difficulty.

One of the very evident differences which characterize these two diseases undoubtedly comes from the fact that treponemata develop fairly rapidly after entering the body, while tubercle bacilli develop more slowly.

Within two or three months from the time that the virus of syphilis has entered the body, general dissemination takes place and the treponemata may be found well scattered through the body tissues. Such is not the case generally in tuberculosis. This occurs commonly only in the rapidly disseminating types of the disease as found in very young children. On the contrary, the bacilli which pass from the primary nodule to the regional lymphatic glands are held captive. It is not the rule for them to emerge from the glands and infect new tissues at this time. We may assume that their growth and multiplication in the lymphatic structures is slower than that of the treponemata, also that the cellular wall which they throw about themselves in the formation of the tubercle is more perfect and prevents their ready escape; consequently, a greater specific defense has been developed by the time they are ready to become disseminated.

Within two or three months from the time that the treponemata become implanted in their host, generalized syphilitic infection is usually present; while years after the tubercle bacillus gains entrance into the tissues, tuberculosis is usually still a localized infection.

CLINICAL DISEASE

Facts concerning immunity in tuberculosis and syphilis are more or less confusing unless one bears in mind that immunity in these diseases means nothing more than an increased resistance to the causative microorganisms. Such a change in the body cells as is noted after measles, whooping cough, and smallpox, which usually makes them uninhabitable for the causative factors, does not exist. Any patient who has once been infected by either the treponema pallidum or the tubercle bacillus may be again infected if the number of organisms gaining access to the tissues be sufficiently large. This is

true both as regards inoculations from without and metastases from some focus within the body.

Syphilis.—The clinical course of syphilis shows plainly that a marked defense has developed by the time the treponemata spread from the lymphatic foci. In spite of the fact that they scatter through the body, many of the new foci which result from these fresh inoculations fail to go on to rapidly forming and spreading syphilitic lesions. On the other hand, after the virus scatters and implantation is effected in the various body tissues, there seems to be such a rapid development of specific defense that the treponemata are either destroyed or reduced in virulence and prevented from further activity. If they are to continue surviving the action of the body cells, it is necessary for them to surround themselves with a wall of defense. In this they do much the same as the tubercle bacilli. The wall of cells is more or less avascular and the organisms remain in a condition which is fairly safe from the germicidal action of the body juices. If conditions in a focus ever become favorable to the treponema, a localized active syphilitic process becomes manifest. It is probable that the difference between this late manifestation of syphilis and the early lesions is due largely to the difference in the reaction between the treponemata and body cells which are endowed with specific defense on the one hand and those which are not so endowed on the other. The fact that the activity in tertiary lues is usually in foci in which the treponemata have been a long time embedded is also a factor to be reckoned with.

Tuberculosis.—The clinical disease, tuberculosis, if we exclude the acute infection in early life, is a disease which comes on only as a result of repeated metastatic infections. There is, as a rule, no clinical disease evident when the first metastases from the lymphatic glands take place. This occurs at a time which is usually unrecognized because of a failure to produce symptoms. It is probable that bacilli pass into the blood stream at infrequent intervals and usually in small numbers and that only after many repetitions of such occurrences do sufficient bacilli survive to produce a metastatic focus; and the disturbances in body function are so slight that they are usually unrecognized. The term "clinical tuberculosis" is not even attached to the disease at this time. *Only after repeated metastases have formed and recognizable symptoms are present do we consider the infection as a clinical entity.*

SYMPTOMATOLOGY

In symptomatology these diseases have many points in common. Both are chronic infectious inflammations, which may affect almost any tissue or organ of the body. Being caused by infectious agents and being accompanied by the breaking down of tissue, both are accompanied by the same toxic group of symptoms which are due to not only an increased formation of heat but a decreased elimination caused by the action of the toxins upon the nerve centers. These symptoms are the same whichever disease is present, and no matter in what tissue the disease process is localized; differing, however, in degree, according to the amount of toxin liberated. They are such symptoms as the following:

- Malaise,
- Feeling of being run down,
- Lack of endurance,
- Loss of strength,
- Nervous instability,
- Digestive disturbances of the type of lessened secretion and lessened motility,
- Loss of weight,
- Increased pulse rate,
- Night sweats,
- Rise in temperature,
- Blood changes,

In syphilis these symptoms may manifest themselves very shortly after infection occurs. They are often quite marked during the secondary stage and may occur whenever evidence of increased activity is present. In tuberculosis they do not occur as a rule until metastases with repeated extension have taken place and a focus of considerable size is the seat of active disease. This is usually years after the bacillus has gained entrance to the body.

Every important organ that is involved in an inflammatory process causes reflex symptoms in other organs. These reflexes depend on the fact that the nerves which supply the organ are irritated by the inflammation. For the principal internal organs, such as the lungs, heart, intestines, liver, pancreas and kidney, in each case both the *greater vagus* (Eppinger and Hess)³ and sympathetic nerves are irritated, and reflex symptoms may appear in many other organs

through the former, and in the skeletal structures, muscles, subcutaneous tissue and skin, which are innervated by the segments of the cord which receives afferent impulses from the inflamed organ through the latter.

GENERAL CLINICAL CHARACTERISTICS

Syphilis and tuberculosis are each able to infect any tissue of the body but each shows predilection for certain structures. The lymph glands receive the virus early; and it is in these structures that the treponemata and bacilli multiply before making a massive attack upon the host. Owing to this fact, both of these diseases are spoken of as being primarily lymphatic infections. These lymphatic infections result from the fact that the virus drains into the lymph glands from the primary portal of entry, they having the purpose of receiving and the power of destroying microorganisms which attempt to invade the tissues. Their infection is evidence of the fact that the amount of virus was greater than they were able to cope with. We must assume that microorganisms gain access to the lymph glands more or less frequently during life but are destroyed by defensive forces which are stationed there.

Both treponemata and bacilli gain access to the blood stream now and then during the course of the disease. Treponemata are found in the blood under a great variety of conditions; and far more commonly than tubercle bacilli.

The blood vessels are attacked commonly in syphilis, the treponema penetrating and infecting the walls. This is not common in tuberculosis; the vessels are penetrated, but rarely infected except as they take part in the process about an inflamed tubercle.

Syphilis is then, as a rule, a more generalized infection throughout its course, than tuberculosis. *Infection of many body structures at one time rarely occurs in tuberculosis, except as one of the manifestations of the later stages of the disease, while it is the rule in syphilis from the time of the first escape of the treponemata from the lymphatic glands.* When bacilli escape from the lymphatic glands it is usually to form only a single metastasis.

It seems that two factors stand out plainly as markedly influencing the character of these two diseases, making the one a generalized infection from the time it leaves the lymphatics, and the other a localized metastasis until late in the disease. For some reason the treponemata are not acted upon so adversely by the lymph elements as the bacilli

are. Infection being more direct the number of infecting organisms is probably greater. They develop more quickly, escape sooner, and infect the tissues of the host generally before the tissues have developed a specific defense. Retardation of growth and a tendency to localize the infection does not show itself until many tissues have been infected. In tuberculosis, on the other hand, a marked defense develops before the bacilli leave the lymph glands; in fact, this is usually so potent that it is able to prevent metastases from taking place until a long time, often years, after the lymph glands develop their infection. Another factor which seems to alter the two pictures is the behavior of the two infectious agents toward the blood vessels. In syphilis the treponemata, gaining access to the blood stream before a strong immunity has been developed, enter the coats of the vessels and surround themselves with conditions favorable to their existence; and while they may not go on at once to multiplication and the production of active disease, they do so at the first opportunity whether it be months or years later. Tubercle bacilli, on the other hand, do not escape in large numbers until the body cells and body fluids are endowed with specific protective properties; consequently most of the escaping bacilli are destroyed, and it is only now and then that conditions are exactly right for an infection to occur; and then the metastasis is usually single and not multiple.

The effects of the two diseases upon the central nervous system are very different. Syphilis invades the central nervous system as a chronic, slowly developing, progressive infection, producing organic changes which lead to loss of function. The meninges, and brain and cord substance, and the nerves themselves may be involved. This infection often starts in the blood vessel walls. Tuberculosis, on the other hand, rarely affects these structures except secondarily, and then only if a blocking of the bacilli in the vessels takes place or if some condition favorable to their penetration of the vessel walls exists. When it does occur, it usually produces an acute process, which goes on to a rapidly advancing clinical disease, although now and then quiescent and healed tubercles are found in the meninges and brain.

A way in which these two chronic infectious inflammations affect the nervous system similarly is through their toxins. The unstable, inefficient nervous system possessed by patients suffering from syphilis and tuberculosis (neurasthenia) is well known. The toxins act

centrally and produce an unstable nervous equilibrium. The threshold of response of the nerve cell is lowered and a general instability of action results.

The expression of toxins is most marked through the sympathetic nervous system⁴ and results in a general inhibition of action throughout the digestive and respiratory tracts, and the secretory glands in general. Those glands which are normally stimulated by the sympathetics respond, however, with increased activity. This is shown by an increase in adrenalin, a forcing of glycogen from the liver, and an increased activity on the part of the thyroid. The heart beat is increased. General vasoconstriction results which interferes with the elimination of heat and a rise of temperature sometimes results. The symptoms produced by toxins are tabulated above.

DIFFERENTIAL DIAGNOSIS

Inasmuch as the two diseases are both **chronic infectious inflammations**, it can readily be understood that there might be considerable difficulty in differentiating between them when they involve a given organ. This may be illustrated by the processes as they affect the lung. Both syphilis and tuberculosis of the lung during activity produce exactly the same group of toxic symptoms. These have been mentioned above. Since both affect the same nerve endings, they produce the same reflex symptoms in other organs through the pulmonary vagus and in the skeletal tissues through the sympathetics:

Hoarseness,
Tickling in larynx,
Cough.

Digestive disturbances: hypersecretion and hypertonus in the muscular coat often resulting in spastic constipation and intestinal stasis,

Loss of weight,
Circulatory disturbances,
Chest and shoulder pains,
Flushing of face,
Apparent anemia.

Being inflammatory processes in the pulmonary tissue, the same symptoms may result from the disease processes themselves:

Frequent and protracted colds (tuberculous or syphilitic bronchitis),
Spitting of blood,
Pleurisy,
Sputum.

We are aided in diagnosing tuberculosis by finding tubercle bacilli in the sputum if the disease has reached the open stage. The fact that a person having a pulmonary lesion reacts to tuberculin in one case and gives a positive Wassermann reaction in the other, does not prove that in the one case the pulmonary lesion is tuberculous and in the other syphilitic. Data of this kind must be utilized with great care in forming an opinion. When conditions are found, however, which simulate pulmonary tuberculosis, the predilection which the tubercle bacillus shows for pulmonary tissue and the comparative infrequency of syphilitic infection of the lung should cause one to assume that the process is tuberculous unless definitely proved otherwise.

The same general statement may be made with regard to other organs. A laryngeal involvement suspicious of either syphilis or tuberculosis, if secondary to open pulmonary tuberculosis, should be considered as being tuberculous; otherwise syphilitic, although it may be a double infection. Intestinal involvements secondary to open pulmonary tuberculosis, should be considered as being tuberculous. Lesions of other viscera, when open pulmonary tuberculosis is not present, are usually more apt to be syphilitic in character. It is common for syphilis to affect organs other than the lung, while it is comparatively uncommon in adults for tuberculosis to do so except after an open pulmonary lesion has existed for a long time. Differentiation here is aided by the Wassermann reaction. *Syphilis affects the arteries commonly while tuberculosis affects them rarely. In fact, syphilis shows as marked a predilection for the arteries as tuberculosis does for the lungs.*

TREATMENT

In comparing the treatment of syphilis and tuberculosis, we find the key to the difference in the attitude of the members of the profession toward these two diseases. The profession as a whole is interested in syphilis, while comparatively few show a vital interest in tuberculosis. *In syphilis measures for treating the disease predom-*

inate, while in tuberculosis reliance is almost exclusively placed on measures directed toward the patient. In syphilis reliance is placed mainly in remedies to destroy the treponema pallidum, such as mercury and arsenic, which may be used with a fair degree of success by physicians generally. In tuberculosis there is no known remedy which has a marked antibacillary action and the best known and most widely utilized measures are those which build up the patients' general resisting power, such as open air, light, rest, exercise, food, cheerful and optimistic environment, and remedies which relieve distressing symptoms and complications, which are more difficult to apply successfully because they presuppose an intimate and effective control of the patient. In syphilis much more attention should be given to the treatment of the patient who has the disease; while in tuberculosis, search for remedies, with antibacillary action should continue, so that these two diseases may be approached from the standpoint of both the disease and the patient, and thus make their future treatment far more successful than it is today.

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