SYPHILIS AND TUBERCULOSIS.

THE WORK OF EMILE SERGENT.

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THE association of syphilis with tuberculosis, denied by Hunter, has long been a matter of established fact. The names of Morton, Morgagni, J. Frank, Graves, Bazin, Ricord, and more recently those of Fournier, Landouzy and Gaucher, mark the stages of our knowledge of this subject and strengthen the idea of reciprocal action which is evinced, in the realm of pathology, by these two great infections.

Before Sergent's time general reports only were considered, and research had never striven to investigate more than the susceptibility of an organism weakened by one infection to the attacks of another, or the way in which the development of one was influenced by the presence of the other. But Sergent in a series of experiments¹ based principally upon clinical methods has approximated to a much greater extent the study of these two diseases, and it will be seen that the ideas of this authority are of much more than mere doctrinal interest, for they put the matter in an altogether new light, pregnant with results in the triple field of diagnosis, prognosis and therapeutics.

A summary of the whole question, following the order adopted by Sergent, will occupy three chapters. The first chapter will be concerned with the general etiological relationships of syphilis and tuberculosis, the question of the influence of "soil." The second will deal with the interaction of the two diseases developing in the same organism, i.e., the study of the nature of their pathological interdependence. The third will summarise the deductions drawn for diagnosis, prognosis and treatment from the clinical discussion of the two preceding chapters.

I.—THE SYPHILITIC SOIL.

The etiological relations between syphilis and tuberculosis include the influence which may be exercised by one of the two diseases in inducing the advent of the other upon the site of the first. As a matter of fact there is not much evidence bearing on the predisposition produced by tuberculosis for the appearance of syphilis, and the question goes no farther than the establishment of the possibility of inoculation of a tubercular ulcer by a syphilitic agent. All the interest of this etiological chapter is, on the other hand, found in the predisposition induced by syphilis for the subsequent development of tuberculosis in the organism. The growth of tuberculosis may follow a direct or an indirect course.

¹ See Bibliography at end of article.

Direct Inoculation.

The definite inoculation of a syphilitic ulcer by the bacillus of Koch is rare, but that it has occurred has been proved.

Inoculation does not take place in the stage of secondary ulceration when the phagocytic activity seems to check the development of tubercle bacilli; but it takes advantage of atonic ulcers of slow growth, gummatous tissues and centres of necrosis.

In these cases if the bacilli of Koch multiply in the region of inoculation, it is a singular fact that the tuberculosis remains localised, even in pulmonary lesions, and shows no tendency to become general.

If, on the other hand, the syphilitic ulcer serves merely as an entry into the system, and if the bacillus is not associated with the trypanosomes in the formation of lesions, the growth is altogether different, and as a rule infection spreads to the viscera. This is what is observed in the case of laryngo-tracheal syphilis or in that of chronic and persistent lesions of the tracheo-bronchial area at the end of the secondary period and the beginning of the tertiary. In this connection Sergent has emphasised the frequent occurrence of syphilis of the larynx among the conditions preceding laryngeal phthisis; "So much so," he writes "that I am inclined to take laryngeal phthisis to be an indication of syphilis, whether it has developed solely on a syphilitic laryngopathy, or whether this has served merely as a port of entry for a pulmonary tuberculosis which then spread to the larynx."

Indirect Infection.

But much more often tubercular inoculation takes an indirect course; predisposition towards tuberculosis is created by the existence of syphilitic soil. Here Sergent, taking up the ideas entertained by Bazin, Ricord and Fournier, and formalised by Landouzy and his students, delivers his own verdict. "Syphilis prepares the soil for the seed of tuberculosis," and the soil is made ready for the reception of the seed in two ways.

The former is very obvious—it is the depression exercised by an initial severe syphilitic attack in weakening the organism and increasing its susceptibility to the bacillus. The second is of much greater interest, and consists in the particular predisposition which is characteristic of the soil of tertiary or congenital syphilis. Syphilis produces a state of receptivity especially favourable to tuberculosis, but this predisposition is not limited to acquired syphilis or confirmed congenital syphilis, but concerns also the apparently healthy descendants of syphilitic subjects. Sergent further develops his thesis by maintaining that acquired syphilis produces a soil which makes the subject resistant to another infection; this soil is transmissible (with the exception of its immunity) as is the syphilis itself. The result is that the inheritance of syphilis takes two forms, complete inheritance (virus and soil) and incomplete (soil only).

The child of a syphilitic subject is, we have said, predisposed towards pulmonary tuberculosis. Five cases are recorded by Sergent of tuberculosis in children whose parents were under his medical supervision, and in all of these he found syphilis amongst the parental ancestors. The child

of syphilitic parents is predisposed in the same way to local tubercular lesions, i.e., to scrofula.

But before proceeding any farther with the study of the connection between syphilis and scrofula, I shall attempt to investigate a channel which will enable us better to follow the exposition of the particular line of thought which I have set myself to analyse.

The History of Scrofulosis.

A century ago, in the time of Albert, Stoll and Astruc, scrofula strayed into the domain of syphilis—Laennec and Lebert distinguished from it tubercular adenitis. In 1861, Bazin isolated it as a morbid entity due to defects in the lymphatic circulation characterized by successive appearances on the ganglions and skin, the mucous surfaces and connective tissue, finally the bones, articulations and viscera; it is the “*pessimus colli morbus*” of Hippocrates.

Then under the influence of histological and bacteriological progress, the bacillary theory was accepted and scrofula was considered to be identical with tuberculosis: this is the opinion of Thaon, Friedländer, Charcot, Cohnheim, Cornil and Babes.

Professor Fournier took a different view. He distinguished from tuberculosis the adenopathies of late hereditary syphilis and tertiary adenopathies.

Quite recently Professor Gaucher, according to Meyer and Gallois, finally laid down the bases of the general theory which connected scrofula and syphilis.

The inflammation of the adenoid tissue of the rhino-pharynx is the cause of adenitis and scrofular suppurations such as otorrhea and impetigo. The toxins of these chronic infections impregnate the organism and scrofula is summed up as a chronic toxic infection of exogenous origin. But the adenoid inflammation which is responsible is in most cases due to congenital syphilis. That was the state of affairs when Sergent took the matter up. He separates at once two groups of facts.

Sergent brings Order out of Chaos.

In the first group, evidenced in the case of hereditary syphilitic subjects with open lesions, the subsequent tuberculosis invades the ganglions, and is seen either accompanying syphilitic lesions or else in a sort of hybrid connection with syphilis: these are the “*scrofulates de vérole*” of Ricord. It is probable that in these cases hereditary syphilis has directly opened the way for tuberculosis—and this applies also to the facts comprehended by the theory of Gaucher and Gallois which we have just considered.

A second group is observed amongst the apparently healthy descendants of syphilitics, the inheritors of prepared soil. This soil has aided the introduction of the bacillus of Koch in the course of an adenitis, bronchitis, or common enteritis; it invades the ganglions, the skin, the mucous surfaces, the connective tissue and later the bones and articulations. The scrofula has become established. This process is of common occurrence: “I consider scrofula to be derived from syphilis, and I am

convinced that if we could search for syphilis among the ancestors of all those scrofulous subjects which come under our notice we should find evidence of it very often, if not always.”¹

It is interesting to examine in the light of these ideas the conception of scrofula at which Sergent arrived. He first of all understands scrofula to signify tuberculosis with a tendency towards ganglionic, cutaneous, mucous, and osteo-articulatory localizations recorded before by Bazin. Adenoid infection of the cavum is simple to begin with and may remain so; if it progresses it becomes polymicrobial, and leads finally in the normal way to invasion by the bacillus of Koch—but the primordial condition which leads to the primary infection is inherited syphilis.

It is possible to summarise the conclusions which are derived from the preceding line of investigation in the following manner:—

A Summary of Chapter I.

Syphilis and tuberculosis are two different infections and can develop separately in the same organism. Syphilis produces a soil for the tuberculation of the infected subject—but especially does the syphilis of the father prepare for the tuberculous infection of his son. Many forms of tuberculosis and in particular scrofula tuberculosis develop most often in favourable syphilitic soil.

II.—METHODS OF ASSOCIATION OF TUBERCULOSIS WITH SYPHILIS.

The association of syphilis with tuberculosis or at any rate with scrofula in the same organism has been the subject of much work: Bazin recognised the connection between the two soils, Ricord has characterised his view by his “scrofulates de vérole,” Devergie refers with the same meaning to “scrofulosyphilides” and Fournier gets as far as “hybridité syphilostrumense.”

Sergent recognised the existence of mixed lesions—hybrid lesions, either in the same tissue or in neighbouring tissues or organs, but the hybrid nature of this phenomenon is in nowise a combination of specific lesions of two different germs leading to a new histological formula, it may more correctly be called an approximation, the intricate juxtaposition of two pathological entities modified by the reciprocal action which they exercise upon their common soil. There is thus a hybrid soil, a syphilo-tuberculosis soil, but there are no hybrid lesions—and this holds good even for the most markedly hybrid example, the hybrid of syphilis and lupus with which we shall shortly be concerned.

The associated lesions should be studied in those cases where they are peripheral, then in those cases where they are visceral.

Associated Peripheral Lesions.

(1) The peripheral or local examples comprise all those cases of syphilo-scrofula with which we are acquainted. The established facts of association can be arranged in three groups on which Sergent furnishes us with

¹ The two forms, syphilo-scrofula and scrofulo-tuberculosis, must not be confused with that arising from acquired or congenital syphilis alone, which etiology distinctly separates, although clinical methods alone are often incapable of distinguishing them; these Sergent calls the “formes scrofuloïdes de la syphilis.”

interesting observations. Scrofula grafted onto a case of long established or hereditary syphilis—scrofula grafted onto a recent syphilis case—and syphilis grafted onto a previously scrofulo-tubercular case.

It is not possible for us here to consider these groups in detail, and we shall be limited to the following general observations.

Throughout the course of these observations Sergeant relies upon the only diagnostic tests: the presence of the bacillus of Koch on the one hand and the results of mercurial treatment on the other.

From the point of view of morbid anatomy the three groups above defined develop along the general, definite, persistent lines characteristic of syphiloscrofula. This peculiarity is particularly striking in the last type—syphilis grafted onto scrofulo-tuberculosis. At the primary period: pustules with a tendency to suppurate; at the secondary period: large adenoid suppurations and ulcers (*écrouelles secondaires*) and tertiary affinity for tissues attacked by scrofula: periostitis, osseous abscesses, cold arthritis, iritis, keratitis, otitis, rhinitis.

Finally, from a therapeutic standpoint, it must be remembered that mercurial treatment has a good effect upon this association, even in the absence of any syphilitic influence, by its action on the soil.

In addition to the syphilo-scrofula, Sergeant has also described the hybrid—syphilis and lupus, which has been thoroughly studied by Leloir; but even in this case, where the histological lesions of the two diseases develop intimately mixed, he is most concerned with the hybrid nature of the soil and explains thus the beneficial effect of mercurial treatment on the part produced by tuberculosis.

Associated Visceral Lesions.

The visceral association between syphilis and tuberculosis is only known in the lungs. The combination behaves here in exactly the same way as in the other tissues, either when the lesions develop promiscuously, or when the two infections are modified by mutual interaction. This is the more frequent case and one of arresting interest. It would be possible to describe a pulmonary syphilis in a tuberculous subject, but in reality, when the syphilis which has been attracted to the lung by the tuberculosis creates there a specific pathological condition, it loses its own character and passes into the second state which we are just about to describe—that of pulmonary tuberculosis in a syphilitic.

Pulmonary tuberculosis in a syphilitic affords the greatest interest of these pathological associations and should be studied under two conditions, the first when the syphilis attacks a tuberculous subject, and the second when a syphilitic contracts tuberculosis.

Syphilis in a Tuberculous Subject.

To begin with, tuberculosis does not predispose to syphilis, but on the contrary may help to preserve its victims from it in some degree by the continence which it enforces.

When the spirochæte attacks a tuberculous subject, its action depends on two things, the condition of the tubercular soil and the virulence of the newly-arrived infection. If it attacks a medium deeply intoxicated or in

a state of advanced tuberculosis it will undoubtedly excite the tubercle bacillus; this is the view expressed by the well known idea that syphilis aggravates tuberculosis. The case, however, is different in early lesions, when the general health is good and the phthisis "*torpide*"; then if the victim can survive the critical period when association occurs with secondary reactions, the tubercle bacillus may act as though the presence of the spirochæte had no effect, in fact it is even stated that syphilis appears to favour recovery from tuberculosis by inducing sclerosis and calcification. Sargent gives some arresting examples of this, and in some cases has noted the expectoration of mulberry-shaped masses having the appearance of tuberculous sputum, and in which the presence of Koch's bacillus has been demonstrated.

The other factor—the virulence of the new infection—acts in a similar way. Virulent as it is, both through its intensity and by its persistence, it adversely affects the prognosis until the time when the subject has turned the danger point and presents a condition similar to those indicated above.

Tuberculous Infection of the Syphilitic.

The tubercle bacillus finds in the syphilitic a medium well prepared for its reception. How does the invasion progress? The clinical form it takes varies according as it arrives at the commencement of the syphilis or during the course of an established syphilitic infection.

At the beginning of syphilis the arrival of tuberculosis may be very dangerous for the patient, especially when it attacks at the beginning of the second period a subject weakened by the rapid growth of the trypanosome—then it is capable of assuming its very worst forms: the galloping or generalised conditions. But after the end of the secondary stage the character of the reaction changes. The organism has got over the bad effects of the invasion, and the bacillus of Koch insinuates itself through the aperture, which is opened to it by laryngitis, bronchitis, or by one of the tenacious subacute tracheo-bronchial inflammations which are often the first stage of tertiary stenosis, or by a secondary pleurisy, of which it has been said that "if they are of syphilitic support they are of tubercular origin." Sometimes, and more often, the bacillus takes advantage only of the predisposition created by an overtaxed system. In these cases the tuberculosis, although serious, does not assume a critical form; after the first attack, if it has been controlled, it may weaken and take on one of the favourable sclerotic forms.

During the course of established syphilis, tuberculosis makes an appearance in two very different ways; it either grafts itself onto a syphilitic pulmonary lesion, or else settles down in a system prepared by the syphilis.

Tuberculisation of a syphilitic pneumopathy may occur in the region of the larynx, and tertiary laryngitis may be either the means of entry or the focus of attraction for the laryngeal phthisis; it may settle down in the region of the trachea and the bronchi upon a tracheo-bronchial lesion, or even upon a tertiary stenosis; finally, it may help to aggravate a true pulmonary lesion.

The existence of cases of tuberculosis grafted onto pulmonary syphilis,

admitted by William Porter and exaggerated by Hiller who considered that all pulmonary lesions with a tendency to break down in syphilitic subjects were tuberculous, has been demonstrated by Fournier (in gummatous tissues), by Potain (in the sclerotic form) and by Gongenheim (in the sclerogummatous form). Sergent has asked whether, given the difficulty of differential diagnosis, all so-called syphilitic pulmonary complaints cured by treatment are free from tuberculosis. He is inclined to think that hybrid association in the case of the lung is of more common occurrence than can be proved, and makes use of this suggestion to explain the action of mercurial treatment on the tuberculosis of a syphilitic.

One final possibility remains for our attention. Tuberculosis in old syphilitic soil. The temperamental condition produced by syphilis predisposes the system to the germination of the tubercle bacillus, but on the other hand it retards its development. In a confirmed syphilitic, phthisis takes a fibrous form of slow growth, giving rise to emphysema. Clinically this type is quite common; emphysema with chronic bronchitis and bronchial dilatation, with copious expectoration, a tendency to hæmoptysis, with dyspnoea also often aggravated by the presence of lesions in the circulatory system and concomitant arterio-sclerosis; it progresses slowly to an asystole of pulmonary origin.

This particular method of development is so common in syphilitics, that Sergent considers that inquiry should be made in the case of all fibro-tuberculous subjects *for a history* of syphilis. Possibly this condition may result from the arterial diseases, so frequently found in confirmed syphilis, but it seems more probable that the process of sclerosis has its origin in the humoral qualities of syphilitic soil.

In Congenital Syphilis.

A word may be said on the subject of tuberculosis in cases of congenital syphilis.

In a young congenital syphilitic, tuberculosis instead of taking on the broncho-pneumonic form general in subjects of this age, develops as an excavation, the cavity being either the product of associated action or of the bacilli only; in any case mercurial treatment should be commenced, and will help the cicatrization of pulmonary lesions, even when the bacillus of Koch may have become established. In the case of a congenital syphilitic, apparently without lesions, the phthisis becomes sclerotic, and as in the adult is accompanied by asthma and emphysema.

Finally, it should be remembered that the frequency with which syphilis is found in the children of tuberculous parents, whoever they may be, has prompted Sergent to wonder whether tuberculosis is not often the indirect result of the inheritance of syphilitic soil, and to put forward his claim that tuberculosis may be a symptom of congenital syphilis.

III.—DIAGNOSTIC, PROGNOSTIC, AND THERAPEUTIC CONSIDERATIONS.

We are now in a position to group under the three headings of diagnosis, prognosis and therapeutics, the clinical results which can be derived from the preceding study.

Diagnosis.

There is no need to analyse here the diagnostic discussions by means of which Sergent sifted the lesion analogous with the two infections before attacking the clinical problems which presented themselves, and I can only say that if he does occupy half his volume on "Syphilis and Tuberculosis" with such discussions, this does but indicate his constant anxiety to establish the dogmas which he there asserts by the most abundant symptomatic evidence. But I should like to emphasise by means of a short summary the various results which, apart from the general conclusions, became evident in the course of his clinical researches. In making a diagnosis the following points should be borne in mind:—

Laryngeal phthisis is often a symptom of syphilis. Fibrous pulmonary tuberculosis should lead to a search for syphilis. In general, tuberculosis is perhaps an indirect result of the inheritance of syphilitic soil—syphilitic pneumopathies often conceal a hybrid association with tuberculosis, and the remedial effect of mercurial treatment is not alone sufficient evidence (when its influence on the soil is known) for discarding the possibility of the presence of tuberculosis. In children many diseases of tuberculous origin—especially scrofula-tuberculosis—develop readily in syphilitic soil.

It is easy to appreciate the importance of these factors in determining both the nature of the treatment and the prognosis of the disease.

Prognosis.

The prognosis of the syphilo-tuberculous association depends upon various factors already considered: the period at which association takes place and the degree of virulence. The therapeutic considerations which follow must also be remembered.

The basis of the prognosis varies between the alternatives of priority of the two infections.

In the case of a tuberculous subject who has become syphilitic the relationship makes the prognosis serious at the beginning if the patient has but little resistance and the infection is severe. Afterwards the prognosis is lightened by the tendency to fibro-calcareous cicatrisation of the lesions. Mercury, far from being nocive, reacts favourably upon the tuberculosis which precedes syphilis, and afterwards proliferates in its soil; it may in any case remain without action at the beginning, but after the initial crisis it will cure the syphilitic part and weaken the hold of the tuberculosis, and the general health will benefit from it.

The case of fulminating phthisis furnishes one exception to the above rule; another more insistent is the case of tuberculous ulceration of the tongue, which, like a malignant cancer, may be aggravated by the application of mercury.

In the case of a syphilitic who has become tuberculous the prognosis remains favourable, unless the tuberculous infection occurs during the secondary period, as the tuberculosis develops in prepared soil and has a tendency to fibrosis.

It is evident that mercury—which affects this soil—will be particularly efficacious in its action upon the tuberculosis sown therein.

Therapeutics.

The treatment of the syphilo-tuberculous combination in all these cases is indicated by diagnosis, and consists in the administration of mercury in the usual form—or of novarsenobenzol, the application of which is suggested by its composition more especially in the case of the tuberculosis of syphilitics, but as it has so recently come to the fore, Sergent has not yet been able to investigate its effect.

I should like to point out that for mercury Sergent has recommended its application in the form of "frictions" in syphilo-scrofula, and frictions on the thorax at the base and summit alternately in pneumopathic syphilo-tuberculosis. His observations have shown him its greater general efficacy as an injection, and he recommends the soluble salts, especially the benzoate and periodide. On the other hand he rejects potassium iodide because of its tendency to produce attacks of congestion, and he uses the greatest prudence in its application in fibrous tuberculosis showing an emphysemic syndrome.

In addition to mercury and novarsenobenzol we must mention the adjuvant medicines; the treatment of recalcification according to the method of Ferrier, calcium chloride in the case of advanced stages of the malady attended by diminished gastric secretion; small doses of creosote in catarrhal and destructive forms; iodo-tannic-phosphate, in torpid and scrofulous cases, and the usual prescription of counter irritation, general hygiene and diet.

Mercury is the remedy to be used for all combined lesions; it cures the syphilis and helps to cure the tuberculosis.

The following brief statements indicate our agreement with Sergent's results:—

Syphilis and tuberculosis are very intimately connected.

Syphilis provides a soil for the tubercle bacillus. If the organism overcomes the initial effects of the association, and if treatment is commenced, the tuberculosis exhibits a tendency to assume a fibrous nature. Mercury, far from being nocive, is the remedy for syphilo-tuberculosis.

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See also—

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THE PNEUMOTHORAX TREATMENT OF PULMONARY TUBERCULOSIS.¹

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THE treatment of pulmonary tuberculosis by artificial pneumothorax has now achieved a fair hold in this country, and there can be few dealing with tuberculous cases who have not by now acquired some knowledge of its theory and practice. Since the subject is too wide to be covered in a single lecture, I shall presume at least a nodding acquaintance with it on your part, and devote my time to such points as suggest themselves to me on account of their special interest or importance. Having published a small text-book on the subject some two years since, I am, perhaps, especially desirous of laying stress on points which I then too lightly emphasised, but also of bringing forward certain matters which have forced themselves on my notice recently. I will not remind you here of the history of collapse of the lung in the treatment of tuberculosis, nor go into theories of its effects. I am anxious to stick to practical points! I will, therefore, wander over the headlines of the subject, and pick out such points as may suit my present purpose.

INDICATIONS AND CONTRA-INDICATIONS.

Artificial pneumothorax stands apart from other methods of treating pulmonary tuberculosis especially in one particular namely, in the possession of more definite and clear-cut indications and contra-indications. One of the unsatisfactory features about tuberculosis treatment in general is the very imperfect knowledge we have acquired of the applicability of individual methods and remedies to individual cases. In spite of the variety that exists among cases in type, activity, amount and location of disease, and other elements in the response of the individual's tissues, but very little is definitely known of the therapeutic indications which should be based upon them. True, the experienced physician acquires in process of time a certain intuition as to the therapeutic requirements of particular cases, but the grounds on which it rests seldom become sufficiently clear and defined to enable him to hand on the results of his experience to others. No doubt our knowledge of the disease, and of the various actions of the remedies

¹ A lecture delivered at the Royal Institute of Public Health on November 13, 1919.