THE LETTSOMIAN LECTURES ON SYPHILIS AND THE NERVOUS SYSTEM.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—Permit me first to tender to you, Sir, and the Council my thanks for selection to the post of Lettsomian Lecturer to this Society, a post around which cluster so many honourable associations. The duty which that selection lays upon me, and which I have now to attempt to discharge, has difficulties of its own. This Society constitutes an audience with the widest professional interests, but, above all, with an interest in the practical aspects of medical science. This characteristic has been handed down through successive generations of its Fellows, from the time when theory bore a much smaller proportion to practice than it does now. It is not one that should be lightly esteemed or hastily discarded, especially in these days, when the "scientific imagination" is apt to wander far and free. The subject to which I propose to ask your attention is the only one within the range of my own work which seemed to be of practical importance and likely to interest both the medical and surgical Fellows of the Society. It is one in which, more perhaps than in any other, the two great branches of the profession join hands in mutual supplement of work. This co-operation is the more important because the disease we are to consider turns to each a different face. To the surgeon the processes of syphilis are for the most part open and manifest; to the physician its processes are secret, its ways obscure, its language seldom unequivocal.

This subject has, indeed, once already been made that of the Lettsomian Lectures. Those of my distinguished predecessor, Dr. Broadbent, together with the almost simultaneous work of Dr. Buzzard, were the means of first diffusing widely in this country a knowledge of the extensive influence of syphilis on the nervous system. But the fifteen years that have since passed have been prolific in additions to our knowledge, and the time seems ripe for a fresh review of at least some aspects of the subject. Not only are there many new facts that deserve notice, but there are many doubtful points that need consideration. If it is desirable to review our positive knowledge, it is not less important clearly to discern its limits. There is perhaps no subject on which there is so much of what may be termed, if the convenient contradiction is permitted, uncertain knowledge; in which there are so many opinions that rest on no secure foundation and yet are accepted as true, so many mere hypotheses that are put forward and received as more than hypothetical, so much that is possibly true and yet is still unsupported by any real evidence. Hence it seems especially desirable to consider the kind of evidence that has been or may be obtained as to the relation to syphilis of many of the diseases of the nervous system. There are, moreover, some practical questions in diagnosis and prognosis that need consideration. Lastly, there are questions in treatment on which current opinion is divided, and a discussion of these, even if partial, may at least be of service by drawing to them the attention from many which they at present receive only from a few. These, then, are the topics to which I propose to ask your attention.

I dare not depart from the time-honoured custom of a preliminary apology, especially as I feel that an apology is not unneeded. Indeed, that I may be quite on the safe side alike of custom and of conscience, I will be bold in my humility and offer you two apologies. First, you have a right to expect from a Lettsomian Lecturer something new, some definite addition to our knowledge. This reasonable expectation I fear I must disappoint; it is scarcely compatible with the chief object that I desire to attempt. My second apology arises from the fact that we cannot separate one part of a disease from the rest. In considering syphilis as it affects the nervous system, and especially

the question of evidence, I cannot avoid alluding to points in its history that I am not competent to discuss. In this also I must ask your indulgence, and it may save time and words if once for all I beg you to impute to me all due diffidence and hesitation wherever they are seemly, even though, in the exigence of the moment, they may not be manifest.

Among the visceral effects of syphilis, those that are to occupy our attention stand first in extent, variety, frequency, and gravity. Considering this fact, it may seem strange that our knowledge of these lesions should have been of especially slow growth and late development, and that so vast a range of syphilitic influence was scarcely suspected thirty years ago. But we must not forget that, thirty years hence, some future Lettsomian Lecturer, now playing with his toys, may make the same remark of the knowledge of the present day. The cause that has hindered our acquaintance with these diseases is not far to seek. It is a cause that we cannot and must not hope to be lessened in the future—the old and inevitable antagonism between pathology and therapeutics. Each flourishes at the expense of the other. The ends for which we gain our knowledge are the chief obstacle to its acquisition. In proportion as we are successful in treatment, we are dependent on the "chapter of accidents" for information as to the real nature of the disease. This influence has affected syphilis more than most other maladies.

The ultimate pathology of syphilis, even in its special relations, is beyond the limits I have set to the subject of these lectures. That the cause of the disease is a micro-organism can scarcely be doubted by anyone who has followed, even from afar, the discoveries which have transformed so much of our pathology, although it may reasonably be doubted whether the organism has yet been detected. That the organism is the immediate cause of most lesions seems also in the highest degree probable, from what has already been ascertained regarding leprosy; but beyond this I must not go. It was part of my original intention to endeavour to confer some semblance of vitality on the dry bones I have to offer you, by indicating the form in which some of the pathological problems of syphilis present themselves at the present day, and the kind of answer we may reasonably expect from the knowledge that we hope the near future has in store. But for a profitable discussion of such questions, even for a tentative discussion, the time is not yet ripe. At present we have no guide but analogy, certainly not close, and possibly misleading, and I desire to avoid as far as possible the purely speculative.

Permit me at the outset to remind you of certain general considerations regarding the effects of syphilis. They are considerations that are not speculative, but merely abstract, and are familiar to you—certainly in fact, and probably in form. If we compare the various syphilitic lesions, not limiting our view to any single organ, we seem to discern in them two elements—a process of inflammation, and a process of tissue-formation. It might seem more accurate to call the former the "congestive" element, since tissue-formation is so often a part of the process of inflammation, but the term "congestion" involves a limitation, and is scarcely wide enough for the purpose. We can mentally distinguish these two elements, and the distinction is aided by the fact that they are combined in various degrees in the different lesions. The process of tissue-formation is seen in almost a pure form in gummata, in which no more of the congestive element is to be discerned than in most other tumours. On the other hand, the inflammatory or congestive element is almost or quite pure in many of the early skin eruptions, in some cases of iritis, and in many other lesions. Generally the two elements are combined, and the most common condition is that often termed "hyperplastic inflammation." Sometimes the combination is such that it is not easy to decide in which class a lesion should be placed, whether it should be regarded as a hyperplastic inflammation or as a diffuse gumma.

If we survey the course of syphilis, there seems to be a tendency for the congestive or inflammatory element to preponderate in the early lesions and the tissue-formation in the later, although to this the earliest lesions, the primary induration and the enlargement of the nearer glands, are apparent exceptions—exceptions that will have to be considered whenever wider and deeper knowledge brings with it the possibility of framing an adequate hypothesis as to the real pathology of the disease, and the relation of the virus to the several lesions.

It has, indeed, been suggested that there is no real difference between these two elements. The tissue formed in syphilitic processes differs but little from that formed in ordinary inflam-

mation, and on this ground, and also because it is combined in various quantity with the signs of inflammation, it is urged that even the gumma has closer affinities with inflammatory products than with the true new growths. But a full admission of this opinion, if its admission is justified, does not preclude the distinction of the two, for it is often well to distinguish when we have no right to divide. The distinction seems to be justified if each may exist so far alone that we cannot clearly discern the other.

Whatever be the real pathological position of the tissue formed, it presents certain characters not found in the same degree in ordinary inflammatory products, and it is very important to keep these in mind. First, the peculiarity of aspect when of recent formation—the gluey appearance to which the name “gumma” is due; secondly, the tendency to undergo certain changes—for the tissue-elements to perish in caseation, or to undergo a change into a dense contracting fibrous tissue. The gluey aspect and the caseation constitute the most important characters by which this tissue can be identified. The tendency to degeneration is so widely although unequally diffused through a mass that the cheesy change usually begins at many places. This tendency to multiple caseation, and the irregular areas thus produced, constitute the most important later criterion of the nature of the tissue. Lastly, the tendency to change to a contracting fibrous tissue is of extreme importance in relation to the symptoms produced, by which the lesion is manifested. This fibrous change often takes place in the tissue at the surface of a gumma, as part of its degenerative or cicatricial changes, and it is probably this that has given rise to the erroneous statement sometimes made that a capsule is characteristic of these growths.

We may divide syphilitic lesions into certain classes, according to our knowledge of their pathological characters, and we may expect to find these classes represented in the nervous system. First, there are morbid processes with characters that are peculiar, processes due to no other cause. Secondly, there are processes that are not peculiar; so far as we can see, they resemble those that are due to other causes, although they are produced by syphilis. Some of this second class, however, although not peculiar in pathological characters, are yet, when due to syphilis, equal in their seat and distribution. Others have not even this peculiarity, but may be described as lesions due to many causes, one of which is syphilis. I do not say they are not really special and peculiar; I only say that we cannot discern the peculiarity. Outside the nervous system we see many examples of these varieties; they are conspicuous, for instance, in the skin. A gumma, ulcerating in a serpiginous manner, is an example of a truly special lesion. Many other cutaneous syphilides, such as roseola and psoriasis, however, have no pathological peculiarity, although most of them, when syphilitic, are peculiar in distribution. Many cases of syphilitic iritis are special in aspect, but others present no peculiarity to distinguish them from inflammation of the iris due to other causes. Thus simple iritis, simple so far as we can see, has several causes, of which syphilis is one. Speaking generally, the more the congestive or inflammatory element preponderates in a lesion, the less special are its pathological features. These depend chiefly on the element of tissue-formation. Necessarily, also, as the latter needs time for its production, the more acute a syphilitic inflammation is, the less are its features distinctive. This is, I think, a very important consideration.

It is desirable to keep this classification in mind in considering the lesions of the nervous system, because the evidence as to the syphilitic nature of the lesion necessarily differs in the various classes, and it will be desirable to adopt this classification in reviewing the several lesions and the evidence regarding their nature. I must pass unnoticed those that are produced through the agency of bone disease.

We begin, then, with the lesions of which syphilis is the only cause. They possess distinctive characters, and it is found that syphilis is their invariable antecedent. It can be traced in a large proportion of the cases, and the more thorough our knowledge of the individuals, the smaller is the proportion in which the evidence of syphilis is not clear. On the other hand, these lesions are never met in cases in which syphilis can be excluded with certainty. From their special characters they may be termed “specific” lesions. We need this term for them, and it is a misfortune that the word has come to be used in a wider sense, as a euphemism for “syphilitic.” For this, moreover, there is a word that might with advantage become as current here as it is in Germany—

“luetic.” I propose, therefore, to use the term “specific” in the sense of a lesion that is special, not only in its causation, but also in its characters.

These truly “specific” lesions I must pass over with merely a brief mention, because they are the best known of the effects of syphilis, regarding which there is least room for question. It will be remembered that I am now dealing only with pathology; we shall have again to consider these lesions in regard to practical diagnosis, in which they furnish many important problems.

First there are the syphilitic growths, gummata, circumscribed masses of new tissue having the characteristics I just mentioned. They grow commonly from the pia mater, and both compress and invade the substance of the brain or spinal cord. They are rare within the substance of the brain, and rare also, although sometimes symmetrical, on the cranial nerves. Occasionally there is a more diffuse formation of similar tissue in connection with the dura mater, cerebral or spinal.

Secondly, there are the growths in the walls of the arteries which constitute one of the most important of these specific lesions; but they also are well known, and need not detain us. I would ask you to note, however, in passing, the remarkable correspondence in seat with atheroma. Except in the arteries of the brain and in the aorta, syphilitic disease is scarcely known save in association with other adjacent lesions. We ascribe the proclivity of those arteries to atheroma to the influence of strain; is this also the cause that determines their affection in syphilis? I can think of no other, but the fact must be borne in mind in connection with certain theories of the origin of the lesions.

Many points regarding this arterial disease will have to be considered in connection with the diagnostic problems connected with it, but certain of its pathological consequences must not be passed over. The first is the necrotic softening that follows occlusion of the diseased artery, or more often that of a branch coming off from the diseased spot. It is by this necrotic softening that the disease most frequently causes symptoms. It should be noted, however, that the occlusion does not always lead to softening. Induration may result especially in the cortex, and more often in children than in adults. It is no doubt due to the arterial anastomoses being sufficient to prevent actual necrosis, although insufficient to maintain the integrity of the tissue.

A second effect is the production of aneurysm of the larger arteries, those that are the special seats of the disease. We know two other causes of such intracranial aneurysms: one, very rare, is traumatic arteritis; the other is embolism, which is probably the cause of three-quarters of these aneurysms before the degenerative period of life. In the remainder, in which there is no history of injury and no evidence of embolism, there is a history of syphilis in so many cases as to justify the opinion that most of them are due to it. Often the history is imperfect, because the aneurysm has been unsuspected until the final rupture. Indeed, when we consider how great is the amount of new growth in the wall of the vessel, and how prone the new elements are to change into simple fibroid tissue, the wonder is that the aneurysm is not a more frequent consequence. Probably the explanation is to be found in the common persistence of the elastic layers, which afford the chief safeguard against permanent dilatation. I am only able to offer one additional instance of an aneurysm due to syphilis. A girl, aged about 25, who had suffered from syphilis, was admitted to University College Hospital with the symptoms of a small tumour near the crus. Soon after admission she died with symptoms of a sudden cerebral hæmorrhage. A large amount of blood was found at the base of the brain; it had come from a small aneurysm, the size of a large pea, on the posterior cerebral near its origin. No source or evidence of embolism could be found.

A third and very rare effect of syphilitic vascular disease is hæmorrhage within the substance of the brain. Doubtless the reason why it is so seldom met with is because the arteries within the substance of the brain are so seldom the seat of syphilitic disease. A few cases have been met with, and I have seen one remarkable instance of it in the inherited malady. The patient was a boy, aged 12, with clear evidence of constitutional syphilis. He had suffered from some transient cerebral symptoms at the age of 8. The hæmorrhage was a large one; it had destroyed the greater part of one cerebral hemisphere, and had burst into the ventricles. Although the source was not discovered, there was such disease as to leave no doubt of its cause. There was extensive and characteristic syphilitic thickening of the right vertebral artery, and there were some smaller spots on the posterior cerebrals. Moreover, the aorta presented some patches of similar

disease; other spots could be seen on each coronary artery (both at its origin and along its course), and several raised yellowish patches existed on the flaps of the mitral valve. There were no vegetations, and it should be added that the boy had not had rheumatic fever. The case is thus remarkable for more than one reason, and not least so on account of the comparatively late age at which the disease occurred.

Inflammation that is specific in its pathological features is chiefly meningeal. The special feature is its hyperplastic character, in this resembling most other specific inflammations. Much new tissue is produced, and this may undergo either the caseous or the fibroid change. Either of the two membranes may be inflamed. In the dura mater the inflammation is usually diffuse, and the tissue formed undergoes chiefly the fibroid change. This "pachymeningitis" is more common in the inherited than in the acquired disease. In the pia mater the inflammation is usually local and the new tissue abundant. It may undergo the characteristic caseation, or fibroid change may result in a layer of dense cicatricial tissue, in which any nerve roots at the part are inseparably involved.

In the spinal cord the most frequent chronic inflammation is that of the dura mater, the important and well-known "spinal pachymeningitis." This may damage greatly, not only the spinal and bulbar nerve-roots, but the cord itself. Inflammation of the pia mater is seldom local, and is usually combined with the affection of the dura mater.

Inflammation of the substance of the brain or cord, that can be regarded as pathologically specific, is very rare. Inflammatory softening and induration have been described, but some of the cases are open to the question whether the lesion was not due to arterial disease. If such lesions occur they do not seem to be specific in character. A case of chronic disseminated inflammation has been described by Charcot and Gombault, which may, however, be regarded as typically specific in character. Foci of chronic inflammation existed in the brain, pons, and optic nerves, in which there was an abundant production of new tissue, presenting, in some foci, multiple points of caseation, although in others the tissue had undergone only the fibroid sclerotic change.

Very little is definitely known of inflammation of the cranial nerves that is pathologically specific. These nerves are often damaged by gummata, and especially by chronic meningitis at the base of the brain, but there is also reason to believe that they are often the seat of syphilitic inflammation, involving the sheath and interstitial tissue. From the meagre facts that are available, it is probable that this inflammation is usually hyperplastic in such a degree as to be recognisably specific, but we must wait for more data before we can affirm the fact with confidence. It is remarkable that the peripheral parts of the spinal nerves very seldom suffer. The discovery of the susceptibility of these nerves to various toxic influences has revealed no liability for them to be influenced by syphilis.

It will be observed that, in speaking of specific pathological characters, I have alluded only to those that can be recognised by the naked eye. I do not think that, at present, any confidence can be placed on histological characters only. Even the structure of the gumma is not distinctive; all that the microscope enables us to say is that the tumour *may* be syphilitic. In the case of inflammations it is very doubtful whether the histological characters have anything like the significance sometimes ascribed to them.

Are there any lesions of the nervous system that can be said to belong to the second class, lesions that present no pathological peculiarity, lesions that are due to other causes besides syphilitic, and yet, when syphilitic in origin, have peculiarities of distribution not present when they are due to other causes? The facts hitherto ascertained are scarcely sufficient to prove the existence of such lesions; there are a few, however, that may possibly be of this character. One is a form of disseminated subacute myelitis, in which defined islets of inflammation occupy the white substance of the cord, chiefly near the surface, and are perhaps sometimes met with in the brain. This form has been described, as related to syphilis, by Julliard and Pierret, and I have met with one instance. Although syphilis seems to have been its antecedent in the cases hitherto published, more observations are needed before it can be regarded as a specific lesion, even when its peculiar insular character is taken into consideration, and the facts at present do not prove specificity apart from its distribution. The same may be said of a form of multiple inflammation of the spinal roots, regarded as specific by Kahler, and

of certain forms of sclerosis of the cortex of the brain (without arterial disease) met with by Barlow in infantile syphilis.

It is not likely that this completes the series of obviously specific lesions. Many other morbid processes may yet be added, by reason of their characters or seat, when our knowledge of them is rendered adequate by a sufficient number of observations. For the present, however, they must be placed in the class we have now to consider—the lesions of which syphilis is one of several causes, lesions analogous to the apparently simple iritis. The chief morbid processes which seem to fall into this class are, first, certain acute and subacute inflammations, and, secondly, certain forms of chronic inflammation or focal sclerosis of the nerve-centres. In the same category, moreover, we must also place the important class of primary nerve degenerations. These we shall notice later, but the methods we are about to consider are applicable to them also.

The question of evidence is of the greater importance in regard to this class, because we have to proceed to some extent without the aid of pathological observation. We can make the diagnosis during life with considerable confidence in some of these cases, especially in the acute inflammations. In these, opportunities for pathological observation come seldom, and it is very doubtful whether, when they do come, they afford any real help. We have already seen that it is the new tissue which gives to the specific lesions their distinctive peculiarity. For the formation of this tissue time is essential. In proportion as syphilitic inflammations are acute, the inflammatory or congestive element preponderates, and the lesion assumes an apparently simple character. Obviously, therefore, if an acute inflammation is produced by syphilis, we cannot expect it to present such specific features as would declare the nature. We cannot expect, therefore, that a *post-mortem* examination would decide the question; and yet we need—and urgently need—to know whether such lesions are or are not among the results of syphilis—to know it by sure conclusion, and not merely by guess-work.

In the case of these apparently simple lesions only two kinds of evidence seem at present within our reach. The first is such sequence as proves causation. The second is the evidence of therapeutics. It is desirable to examine these two kinds of evidence, to inquire how they can be obtained, and to what limitations they are subject. This inquiry is important, because current ideas on the subject are for the most part vague—at least, if we may judge by their applications—and also because, with one exception, I do not see where we are to look for other evidence.

This exception is the prospect that the progress of bacteriology may supply us with a conclusive criterion—the presence of specific micro-organisms in a lesion. Such a criterion would be available also for the specific lesions; but for them it would be merely confirmatory; for those now under consideration it would be essential. Unfortunately, such a criterion is still in the dim, if not in the distant, future. We cannot assume that it will certainly follow the discovery of the specific organism, or that its application would be unlimited. It is not likely that the test would be of negative as well as positive value—that its absence would be as conclusive as its presence. Thus, even, this criterion may not relieve us from the need for such proof as we are now to consider.

Regarding the evidence of sequence, the first important consideration is that the isolated instances of sequence are no proof of causation. Let me again remind you that I am now speaking of scientific proof, not of diagnosis. Individual sequence would be proof if we could exclude all other causes of a disease; but this is, as a rule, beyond our power. The diseases in question have many causes, and those causes are imperfectly known, so that their exclusion, in a given case, is impossible. The fact that we cannot trace them does not prove that they do not exist. We are often unable to trace the cause when there is no question of syphilis, although some adequate cause there must be. Hence, when there is syphilis, the fact that we cannot trace any other cause does not justify us in concluding that the disease in question is due to syphilis. To do so is to treat the unknown as the non-existent, and to base our induction not on our knowledge, but on our ignorance. Consider how many diseases coincide with, or succeed, constitutional syphilis, which no one dreams of attributing to it. We do not ascribe acute rheumatism, or acute sthenic pneumonia to preceding syphilis, and yet, because a morbid process occurs in an organ, as the spinal cord, which is sometimes the seat of syphilitic processes, it is assumed that the process is due to syphilis, merely because the patient is, or has been, syphi-

litic. It is perfectly certain that such a combination must often occur when there is no causation. It is certain from the mere law of chance, but such a coincidence, without direct causation, may well be more frequent than mere chance will explain. A general disease like syphilis may so influence the general health as to predispose to many diseases for which other causes may exist. Therefore, while individual instances of sequence may justly direct attention to the possibility of causation, while they may suggest a search for other evidence, they do not prove causation. Indeed, I should not venture to call your attention thus specially to a rule that is so obvious, were it not that medical literature abounds with cases in which the general causation by syphilis is assumed to be proved by a single sequence, and the possibility of mere coincidence seems never to have been thought of.

How, then, can sequence prove causation? How can the fact that a disease follows syphilis be evidence that it is due to syphilis? Only by the strength of numbers. The sequence that is without significance when isolated, is all important when traceable in a series of cases. This method is so well-known, and has been so largely employed in the case of tabes and other maladies of the same class, that it may seem needless to consider it in detail. But its use must be widely extended if we are to ascertain whether or not many other diseases are related to syphilis, and its value depends largely on the manner in which it is employed. The number of cases necessary will vary according to the field of observation, the frequency of the disease, its incidence on age and sex, and the nature of the proof required. A small number of coincidences, in a fair field of observation, may be sufficient to prove the mere fact of causation, although a much larger number will be necessary to enable its extent to be estimated.

It is only practicable to approach the question from the side of the disease to be tested, because even those diseases that are certainly consequences of syphilis are rare consequences, so that from the side of syphilis it is not easy to get an adequate view of them. It will also be convenient, in the case of many diseases, to restrict the inquiry to the age at which syphilis is common, and the sex in which it is most readily ascertained. If the restriction is the same in each series compared, the validity of the result is not affected. In inquiring into the influence of syphilis in causing disease, therefore, it is wise to let the cases compared be those of males only, and over 25 years of age. In some cases it may be well to narrow the limit to cases between 25 and 50.

The first task is to ascertain the average frequency of past or present syphilis in males over 25. This term of comparison, which we may call "the standard," will be the same for all diseases. It is of great importance that it should be ascertained, once for all, from a field sufficiently extensive to place the conclusion beyond the reach of doubt. Although one standard will be sufficient for all diseases, it will probably not be sufficient for all classes or for all places, for it is probable that in both class and place the frequency of syphilis varies. It is probably greater in the lower than in the middle and upper classes; greater in urban than in rural districts; greater in seaports than in inland towns. Attempts have been made abroad, on a small scale, to ascertain the facts, but not, I think, in this country. I regret that I am not able to offer a contribution to the question of more than a very small extent. I venture, however, to hope that the need, once pointed out, may not be long unsupplied. Messrs. Raymond Johnson and Marriot have kindly collected the venereal history, positive and negative, of 120 patients at University College Hospital, not under treatment for syphilitic diseases, and Mr. Littlewood that of 200 patients at the Leeds Infirmary. The result is that in London there is a history of syphilis (including a few of certainly hard chancre only) in 10.5 per cent., and of a chancre of uncertain nature in another 10 per cent. At Leeds the percentage of syphilis or hard chancre is only 6.4, and of a chancre of uncertain nature only 6 per cent. This shows clearly the need for more than one standard. But such standards ought to be obtainable without much difficulty. A few months' observation by the registrars of all the London hospitals would supply us with a London standard drawn from at least 5,000 cases, which would be available for all similar inquiries for many years to come.

But the figures I have given place before us at once one of the difficulties of the process of comparison. It is certain that some of the patients who give a history only of a chancre have had an

infecting sore; but how many? What proportion of the chance percentage should we add to the syphilis percentage to obtain the nearest approximation of the truth? Mr. Berkeley Hill, and others, in this country and abroad, have published analyses which show that at least two-thirds of all venereal sores are infecting. We have, however, already taken account of the cases of certain syphilis, and of the remaining sores probably the majority are not infecting. If we add to the percentage of syphilis one quarter of the cases of chancre, it will give us 13 per cent. of syphilis in London, and about 8 per cent. at Leeds. In London, therefore, among the lower classes, syphilis may be assumed in at least one-seventh of males over 25. The proportion among the middle and upper classes is probably less than among the poor, and I doubt whether it reaches a tenth, even in London; but definite facts will be less easy to ascertain.

In the other terms of the comparison we ascertain, in a similar manner, the percentage of syphilis among the sufferers from the disease in question, who are of age and sex corresponding to the cases compared in the standard. If the proportion exceeds that of the standard, the excess must be due either to the one disease being a cause of the other, or to the fact that both are due to a common cause. Obviously, however, the only conceivable relation is that syphilis is in some way the cause of the disease in question. If the excess is slight, and if the interval is short, indirect causation is possible; that is, syphilis may have predisposed merely as any other depressing disease may predispose. If the excess is considerable, we must assume direct causation. But the comparison itself is not quite a simple matter; the significant fact is the *excess* of the syphilitics among those who suffer from the disease, and we have to ascertain this excess. It may seem sufficient to deduct the percentage in the standard from the percentage in the disease, and to consider the difference as the percentage of causation; but this would be erroneous, at any rate in many cases, as an example will show. Let us assume, taking simple numbers for convenience, that the percentage of syphilis in the standard is ten, and in the disease fifty. It is not right simply to deduct ten from fifty, and assume 40 per cent. causation. We start with 100 cases, and if we thus deduct forty as the proportion of causation, we have left ten cases of accidental coincidence and fifty without syphilis, making sixty in all. Thus we assume that in ten cases out of sixty there is mere coincidence, whereas our assumed standard shows that in sixty persons the proportion of syphilitics will be only six. The true method, I take it, may be expressed in the following rule: deduct from the syphilitics the number that bears the same proportion to the non-syphilitics as is found in the standard; the residue will represent causation. Thus, in our example we must deduct from the fifty syphilitics not ten, but five and a half, because five and a half bears nearly the same relation to fifty as ten does to ninety (10 in 100), and the proportion in which there is causation will not be forty, but forty-four and a half.

It is certain that such a deduction for mere coincidence is absolutely necessary in the case of diseases that are often due to other causes, although it is open to consideration whether this deduction is justified in the case of diseases of which syphilis is the chief cause. But its amount lessens in inverse ratio to the proportion in which syphilis can be traced, and, when this proportion is high, the deduction becomes so small as to be unimportant. If, for instance, syphilis can be traced in 80 per cent. of the cases, the deduction for coincidence would be less than 3 per cent. The error from neglecting it will then be scarcely appreciable, especially in the face of the graver source of uncertainty we have next to consider.

Whatever is the ascertained proportion of syphilis, this will assuredly fall short of the truth. This is due to the fact that persons may suffer from syphilis and not know it, or know it only with a knowledge which soon passes from their memory. Many persons who present unequivocal signs of old syphilis can give a history only of a chancre, and others not even of this. We meet with persons who know of no sore, who give no history or any evidence of syphilis, and yet have had the disease. This fact of imperfect knowledge is well known, but it is so important that I venture to emphasise it with an instance. A gentleman had once, and only once, a slight sore. He showed it to a doctor, who said it was of no importance, and touched it with caustic; in a few days it was well. It was soon almost forgotten, for no after-symptoms occurred to keep it in mind. In a year or so he married a lady in his own station of life. She bore him two dead children, and then a living one; the latter soon showed signs of

syphilis, and became paralysed and imbecile. Then the wife died from the effects of the same disease. Similar cases—we may hope less tragic—must have been met with by all practitioners, cases in which the transmission of the disease to others first proves its existence. A striking instance is the first case of progressive ophthalmoplegia in which the nature of the lesion was proved. I suppose that there is no one more skilled in tracing syphilis than Mr. Jonathan Hutchinson, and yet in this case the search, many times renewed, failed to reveal any indication of the disease. There was not even a known sore to suggest it; and yet, after the man's death, a child of his was brought to Mr. Hutchinson with interstitial keratitis and notched teeth. I have met with many patients who had signs of the past disease—some unequivocal cicatrix in eye, tongue, throat, or skin—who could give no history of a chancre. But I am able to offer you more definite facts, for which I am indebted to my friend Dr. Radcliffe Crocker. He has been kind enough to ascertain from his case records at University College Hospital the proportion of cases of tertiary syphilitic skin eruptions in which there was no history of a chancre. He has found 56 cases of such eruptions, cases that are consecutive and unselected, and in no less than eleven of these the occurrence of any chancre was unknown. This is a proportion of 20 per cent. It cannot be doubted, moreover, that, besides such cases, there must be many more who have no late symptoms whatever to reveal the disease.

These facts suggest a question most important in regard to the problem we are considering—the frequency of what may be termed “latent” syphilis, in which the manifestations of the disease are either absent or quite insignificant, and receive no attention or no treatment, so that years afterwards the memory of them is reduced to a vanishing point in the vista of the past. May not such cases be far more frequent than is generally thought; more frequent, indeed, than we can ascertain? Besides the facts I have mentioned, there are others which, if they do not suggest this frequency, at least harmonise with it and are explained by it. Many observers have noticed how often severe late lesions have followed an early stage that was slight or unnoticed. It has indeed been more than once suggested that there is an actual alternation in severity between the early and the late effects. Such an alternation would explain the facts, but cases are frequent enough in which both stages are alike severe or slight. May not the frequent apparent alternation be simply due to the great frequency of mild or latent syphilis? Take, again, the fact epitomised in what is termed (abroad more often than in England) Colles's law: the fact that a woman who bears a syphilitic child, although apparently free, is proof against infection and must therefore have suffered. It is supposed that pregnancy is in some way antagonistic to the activity of the disease, but this assumption also is opposed by many facts, and the apparent anomaly may be explained by the frequency of latent syphilis.

It is, therefore, certain that the facts we can ascertain will fall short of the real facts, and will fall short of them by a quantity which, because it is unknown, must not, therefore, be neglected. Whatever the actual amount of the discrepancy, its influence will be the greater the larger the number of cases in which syphilis can be traced. For instance, to take what may be an extreme proportion (but may possibly be less than the truth), let us suppose that syphilis cannot be ascertained in one-quarter of the patients who have suffered from it—that besides the cases in which there is clear evidence of the disease, there are one-third as many more, on an average, in whom we cannot ascertain it after the lapse of years. This would raise the proportion of syphilis among adult males to about 15 per cent., but it would raise a proportion of 50 per cent. to 70 per cent., and of 60 per cent. to 80. To ascertain the mere fact of causation, we may indeed neglect the discrepancy, but we must recognise at least the fact of its existence when we endeavour to estimate the extent of causation.

One last general remark. For the comparisons to be significant the facts must, as a rule, be specially observed. It is one of the many lessons of scientific history, in no part more conspicuous than medicine, that facts observed without special reference to the question at issue are of very little value for its decision.

On the second kind of evidence, that of therapeutics—the influence of drugs on a disease—I must and can be more brief. The considerations are not less important, but they are familiar, at least in the abstract, and we shall have occasion to return to them in discussing the problems of diagnosis. Unfortunately, the

limitations to the use of this method are such as to reduce very much its scientific value. The chief conditions that must be secured may be thus enumerated: 1. The effect of the drug must be decided and unequivocal. 2. Its influence must not be obscured by any other change in the measures employed that might cause the improvement observed. 3. The lesion must not be one of which the symptoms tend to subside spontaneously. 4. The lesion must not be one that can be influenced by the drug when it is not due to syphilis. 5. Before a negative result can be admitted as evidence that the lesion is not due to syphilis, we must be satisfied that the damage produced is not so great that its manifestations *cannot* speedily subside. These conditions render the process almost useless for our present object. The method is applicable chiefly to chronic lesions in which the influence of treatment can be clear and decided. Acute lesions, if they are slight, have too great tendency to subside, if they are severe, have effects of prolonged duration.

We may briefly glance at the lesions to which these methods of proof apply. First, there are two important acute inflammations, those of the membranes of the brain, and of the substance of the spinal cord. Are these ever due to syphilis? Unfortunately I can only ask the question, and try to show how to obtain the answer, which I am not able to give. That syphilis causes chronic cerebral meningitis is one of the surest facts of medicine. It seems, however, to be still uncertain whether the disease also causes acute meningitis, such as reaches a considerable degree of intensity in a few days. Analogy suggests that an acute meningitis, like an acute iritis, may be due to syphilis, but this is enough only to make us search for evidence. Morbid anatomy, as we have seen, is not likely to supply an answer. The therapeutic test is of little value on account of its essential limitations, for we dare not secure the absence of other influence, and there is reason to believe that mercury may determine the subsidence of an inflammation that is not syphilitic. I have once known the symptoms of a general meningitis to develop most acutely in a man who had suffered from syphilis, and those slowly passed away under the influence of mercury, but such a case can alone do no more than raise or strengthen a suspicion. It cannot supply the needed proof. Acute meningitis is very rare in adult men, but it does occur when we can exclude syphilis; and hence the question of causation can be decided only by a series of cases. The readiness with which acute meningitis is ascribed to syphilis by some writers is astonishing, or would be astonishing were not the capacity for wonder often already diminished by the process of the diagnosis of the disease. To give one instance; a patient suffered, for a few days only, from pain in one temple, an elevation of temperature of half a degree Fahrenheit, and diminished frequency of the pulse. This was considered to justify the diagnosis, not indeed of meningitis, but of a lesion safe in the region of hypothesis—local congestion of the membranes. This assumed lesion was further ascribed to syphilis, because the symptoms occurred twenty-five days after—not definite constitutional symptoms, not even after enlargement of the glands, not even after the primary induration was discovered—but twenty-five days after the exposure to infection! After this, we scarcely marvel to find that this case is regarded as affording strong support, indeed as part of the proof of a theory that the early symptoms of syphilis frequently include congestive lesions of internal organs, especially of the nerve centres, which are analogous to the early eruptions on the skin. I think our time may be better occupied than by discussing this theory in detail.

The possible relation of acute myelitis to syphilis is one of the most difficult problems connected with this subject, and it is one on which definite evidence is much needed. The term, even in its narrower sense, includes diseases widely different in their nature and pathological relations, and these relations are still imperfectly known. We can, however, distinguish acute transverse myelitis, subacute disseminated myelitis, and acute poliomyelitis, as fairly well defined forms, which have distinctly different causal relations, and the relation of each to syphilis must be separately ascertained. In each of these the investigation has still to be made. The fact that special observations are necessary renders it difficult for the evidence to be obtained by any one person. It is certain that not one of these forms is exclusively related to syphilis, and it is not probable that the relation is, in any one of them, so preponderant that the fact could be decided by a small number of observations; for we must depend almost entirely on the evidence of sequence. The limitations to the method of therapeutics are here prohibitory

The course of the symptoms is no more guide to that of the inflammatory process than is the course of a cardiac murmur evidence of the course of the endocarditis to which it was due. If the inflammation of the spinal cord is trifling, the tendency to spontaneous improvement deprives the subsidence of the symptoms of any significance. Moreover, there is some evidence to suggest that the less acute forms may be due to syphilis and yet may not yield to its treatment. In the case of an inflammation such a statement seems self-contradictory, but in dealing with facts we must lay aside all our preconceptions. I mentioned just now a form of insular myelitis, possibly always syphilitic in origin and specific in its distribution. (To avoid confusion, I may point out that in this form the inflammation is in small islets; in the common form of disseminated inflammation, larger scattered tracts or areas are affected.) If this insular myelitis is syphilitic, it does not seem distinctly amenable to treatment. In the cases hitherto observed the patients have died. In some of them, and certainly in my own, anti-syphilitic treatment had no influence on the disease. I have seen several other cases of subacute and subchronic myelitis in syphilitic subjects, in which neither iodide in large doses, nor mercury pushed to salivation, had any appreciable influence on the lesion, either on its extension in the cord or its intensification in the parts before affected. This seems also to have been true of the remarkable case of caseating inflammation, described by Charcot and Gombault, to which I have already alluded as a lesion pathologically specific. Here, then, we are driven back on sequence for our evidence of causation, and the needful observations, serial and unselected, have yet to be made. The same statement must be made regarding acute transverse myelitis, the most common variety, recognisable during life without much difficulty. My own experience is suggestive only. I have seen several cases in which the disease followed syphilis—more, I think, than mere coincidence will explain. On the other hand, I have met with no cases of acute poliomyelitis suggesting a syphilitic causation, and the significance of a few cases that have been published as evidence of such causation seems to me open to doubt. We must remember that the subacute form has only lately been distinguishable from peripheral neuritis; and the most common cause of peripheral neuritis, alcoholism, is sometimes associated with syphilis as a consequence of mode of life.

Another acute affection of the spinal cord, the mysterious acute ascending paralysis, has also been supposed to be a result of syphilis, partly on the ground of sequence, partly on that of recovery under the influence of mercury. The proportion of published cases in syphilitic subjects is certainly large, and justifies careful investigation. In considering the influence of mercury, we must remember that there is some evidence that other acute toxic states besides that of syphilis are modified by mercury. In the course of some investigations made in 1885 at the Brown Institution, Dr. Cash discovered that animals brought under the influence of mercury resist otherwise fatal inoculation with the anthrax bacilli—a remarkable fact, which does not seem to have attracted the attention it deserves.

Regarding the focal sclerosis of the nerve centres, or what may be termed "chronic sclerotic inflammation," I have little to say. The evidence seems to be against any relation to syphilis of true insular sclerosis. Only future observations, for which we may have long to wait, can determine the question as regards certain other extremely rare forms of diffuse sclerosis. A remarkable case of miliary degeneration of the grey matter of the brain, which was published by me some years ago, occurred in a syphilitic subject. Many years ago I examined, for Dr. Hughlings Jackson, a brain of an old syphilitic, which presented a remarkable induration of a large part of the white substance of one hemisphere, without change in tint. (The history of this case, unfortunately, we have been unable to trace.) Lastly, sclerosis of the cortex in infantile syphilis, as we have already seen, may possibly be sometimes primary, although generally it is the result of inflammation in infarcted areas.

The processes that we have hitherto considered originate either outside the nerve centres themselves, or when within the nerve tissue are essentially interstitial. Of all, therefore, it seems to be true that the primary morbid process is independent of the nerve elements themselves. These elements suffer just as they would from any similar process, not syphilitic in nature. It is on these simple processes in the nerve elements, and on these only, that most of the symptoms depend—a fact of the utmost practical importance.

Until lately, it was believed that the influence of syphilis was limited to the production of such lesions as we have hitherto considered. But modern observations, led by those of Fournier, have resulted in a considerable amount of evidence that the effects of syphilis are not thus limited, that the disease is followed by lesions of a totally different nature, and is followed by them in a way that admits of no other explanation than that it causes them. These lesions are degenerations of the nerve-structures, with such a distribution according to function as can be explained only by assuming that the process begins in the nerve elements themselves. The relation of these "system degenerations" to syphilis was first asserted in the case of tabes, locomotor ataxy, and this disease is still the most conspicuous example, around which most of the controversies have turned. The assertion that syphilis causes lesions so totally unlike the known effects of the disease, was sufficiently startling to be received with surprise and suspicion, a suspicion not lessened by the fact that the only evidence of the relation was, and still is, that which depends on numbers for its weight. Various objections were urged. It was said that syphilis could not cause such disease; that cases of true syphilitic lesions had been mistaken for degenerations, and that if tabes were due to syphilis, the lesion must be primarily interstitial, and not a primary nerve-degeneration. The common absence of benefit from anti-luetic treatment was urged in support of the objection, and the statistical evidence was met by other figures of different significance, obtained from existing records. Some of these arguments, however, were manifestly untenable when they were clearly stated. The assertion that syphilis could not cause a lesion different in nature from the effects previously known was too obviously a transfer to medicine of the method employed by Canute upon the seashore. The absence of evidence of one kind, that of therapeutics, was manifestly no refutation of a totally different species of proof. The comparison of statistics, moreover, resulted in a curious and instructive episode in the history of medicine. When these observers, who had gathered their cases from old records, came to make fresh observations on the subject, they found that the two sets did not correspond. They found that the proportion of syphilis yielded by the special observation was much higher, and in more than one instance the special inquiry transformed an opponent into a supporter of the new opinion. It was one more instance of the uselessness of figures based on observations not made with the special question in view.

The proportion of cases of tabes in which syphilis has been traced by different investigators has varied much, from 90 per cent. down to a proportion that has been held to be not far above the range of accidental association.

Instead of detailing to you the various statements that have been made, it may be more instructive to give the figures supplied by a consecutive and unselected series of cases which have come under my own observation. Of 70 cases of characteristic tabes in males, there was evidence of syphilis (in a few confined to a chancre certainly hard) in 55 per cent. In another 14 per cent. there was a history of a sore only, of unknown nature. In only 31 per cent. could neither be ascertained. Of the 170, 92 were seen in private, and 78 were hospital patients. The percentage of syphilis in the private cases was 57, in the hospital patients 52. Probably the difference is due to the more accurate information to be obtained from those who are more likely to notice and remember such diseases. It is remarkable, however, that the proportion between the cases of syphilis and the cases without even a chancre is exactly the same in the two sets—as 11 to 6. The difference in the percentage arises from the fact that the history of a sore of unknown nature was almost twice as frequent among the hospital as among the private patients. In either series, the addition to the syphilitics of one quarter of the cases of chancre will give about 60 per cent., and a deduction for mere accidental coincidence would leave at least 55 per cent. of unquestionable causation. But it is certain that to this a large addition must be made for untraceable syphilis. These figures are obtained by placing all doubtful cases on the negative side, including many with a strong presumption of syphilis. If it is true that latent syphilis is common, and if the disease can be proved to be a cause of tabes in more than half the cases, is it not almost certain that a large proportion of the remainder are really due to it? In most of them no other cause could be traced. In not more than 5 per cent. of the whole had there been no exposure to the risk of infection. Although the method of those who have found syphilis in an ex-

ceedingly large proportion of the cases may be open to question. I cannot but think that the observers who describe it in 75 or 80 per cent. are not far from the real truth.

Not only is the relation of tabes to syphilis beyond reasonable doubt, but we are beginning to discern that there are other diseases that stand in a similar although unequal relation to the disease. One other group of degenerations we can, indeed, connect with syphilis as surely and as extensively as tabes—the degenerative ocular palsies, which, often associated with tabes, occur also alone. There is strong evidence of a similar relation in simple atrophy of the optic nerve. Among the motor palsies, one of the most important to the physician, although the least important to the patient, is the isolated loss of the light-reflex of the iris with which the name of Argyll-Robertson is connected. I have notes of only twenty-two cases in which this symptom existed apart from other degenerative affections of the nervous system, but I believe that it is much less rare than this number might suggest. It is seldom looked for unless other symptoms suggest degenerative disease. Of these twenty-two cases, syphilis was certain in twelve, and highly probable in three others, while two more had a history of a venereal sore. In six cases there was no history or evidence of either syphilis or a chancre; nevertheless, two of them had had an attack of sudden hemiplegia in early adult life, without any indication of a cause of embolism, an event that always affords ground for suspecting syphilis. From these facts we may feel confident that syphilis existed in two-thirds of the cases, and we may suspect that it existed in three-quarters. I may add that one of the cases was a young girl, the subject of inherited syphilis, and another case was this girl's mother. The relation of this symptom to syphilis makes it one of great practical value. It proves that a degenerative process is at work in the nervous system, and it raises a strong presumption that this process is the result of syphilis. It is true the dependence of the symptom on central degeneration has not been proved by observation, but the evidence of this dependence is as strong as it can be short of actual observation.

The more extensive palsies, external and internal, to which the term "ophthalmoplegia" has been applied, are much more rare. They occur in syphilitic subjects in association with tabes and also alone, as was clearly proved by Mr. Jonathan Hutchinson. In the case of external ophthalmoplegia in which I made an examination of the nerve-centres, preceding syphilis was certain, and the lesion was as pure a nerve-degeneration as can be conceived. But these diseases, like tabes, are not exclusively related to syphilis; they certainly occur now and then in persons in whom syphilis can be excluded.

This evidence seems to leave no room for doubt. It receives, moreover, a strong emphasis from the remarkable fact that nerve-degenerations, such as succeed acquired syphilis in the adult, are met with also in young persons who are the subjects of the inherited disease. Such cases, it is true, are rare, but the rarity may be due less to any difference in the influence of the disease than to the greater vital stability possessed by younger tissues. I have myself met with two or three examples, and their interest may justify a brief mention of them. One case was a lad who in infancy and early childhood suffered much from various manifestations of syphilis, including slight hemiplegia and choroiditis. At the age of 17 the symptoms of locomotor ataxy were distinct. There was unsteadiness in standing and walking, there had been lightning pains, and no trace of the knee-jerk could be obtained. It was difficult to ascertain when the symptoms commenced; the unsteadiness had only attracted attention during a year or so. A second case was that of a girl aged 15 (seen through the courtesy of Mr. Nettleship). She had typical teeth, and traces of characteristic inflammation in cornea and choroid. The left knee-jerk was absolutely lost, and only a very slight movement could be obtained on the right side. There was no ataxy or anaesthesia. In each iris the light reflex was quite absent, although there was full action to accommodation, and vision in one eye was normal.

Another malady of great importance in regard to which this question has arisen is general paralysis of the insane. The disease is probably to be classed with primary nerve-degenerations, but in many cases, it would seem, the secondary changes attain a very considerable independence of degree. Its close alliance with tabes is shown by the conditions of age and sex in which it occurs, by the degenerative ocular palsies common to the two, and by their actual combination in many instances. This would lead us to expect a similar relation to syphilis. The scientific proof, however, is beset with many difficulties, and the statistics ob-

tained have varied greatly; no less than 75 per cent. of certain syphilis is described by Mendel in 146 cases. One serious difficulty arises from the great variations presented by the disease. Typical cases form a minority of those that may be classed under the name, and both the typical and untypical forms certainly also occur independently of syphilis. I believe, however, that syphilis can be traced in a large proportion of each indistinguishable variety, although I am not able to offer you any definite figures. Fournier has pointed out how often symptoms resembling more or less closely those of general paralysis seem to result from organic syphilitic lesions of the brain, and I believe that the explanation of this fact is to be found less in the fact that the organic diseases cause these symptoms than in the profound degenerative tendency which so often results from syphilis. This tendency may accompany the organic lesion, and is perhaps sometimes actually excited by it, for I have occasionally observed that degenerative symptoms, mental and articulatory, may distinctly come on soon after a sudden organic syphilitic lesion, and may subsequently lessen and even pass away.

Another central degeneration that is perhaps an occasional consequence of syphilis is the chronic muscular atrophy due to degeneration of the motor cells, with or without the signs of lateral sclerosis. Great care is necessary to avoid the error of mistaking for this the atrophy that results from syphilitic pachymeningitis. In several cases that I have seen, the true degenerative affection has been an early sequel of syphilis and no other cause could be traced. Similar cases have been published by others, but these cases do no more than suggest the relation, although they suggest it strongly, and my own notes do not enable me to offer any statistical evidence on the question. The difficulty of the investigation is increased by the large number of cases of senile character. The exclusion of these would simplify without hindering the search for evidence. The investigation should thus be restricted to cases commencing between 25 and 50, the standard being limited to the same age.

The other common forms of degenerative diseases of the spinal cord are associated with syphilis only in a proportion so small as to raise a doubt whether there is any causal relation between the two. Nevertheless they occasionally follow syphilis when no other cause can be traced. This is especially true of the primary lateral sclerosis that probably often underlies spastic paralysis. Ataxic paraplegia, combined lateral and posterior sclerosis, seems to be very seldom preceded by syphilis.

It must be admitted that the relation of these degenerative diseases to syphilis is a startling extension of our knowledge of its influence. And yet, perhaps our surprise is not altogether justified. Other facts exist which, if they do not lessen the marvel, at least may prepare us for it. We are familiar with the influence of chemical poisons on certain parts of the nervous system, with the way in which atropine, curare, digitalis, strychnine pick out for isolated derangement certain nerve elements, leaving unaffected adjacent structures. This must be the result, not only of the nature of the poison, but also of the nature of the nerve elements influenced, through which they, and they only, have a responsive susceptibility. That an organised virus may exert a similar elective influence the symptoms of hydrophobia clearly show, and those of whooping-cough at least suggest. The phenomena and pathology of diphtheritic paralysis demonstrate that an acute degeneration of certain nerve elements may also be the effect of an organic virus. We may note also that the effects of the poison of diphtheria sometimes so closely resemble those of the poison of syphilis, that cases of diphtheritic paralysis have been repeatedly mistaken for tabes, and we have seen that syphilis has, like diphtheria, a special tendency to derange an intra-ocular muscle. Further, in the fact that the palsy is a sequel rather than a concomitant of diphtheria, we have a fact not without relation to those we have considered, a fact whose significance is not destroyed by the difference of interval in the cases, since the difference of interval is not proportionately greater than is the difference in duration of the primary maladies. Diphtheria runs its course in a few days, and its effects on the nervous system are developed in weeks or months. Syphilis lasts, in the stage of a blood disease, at least for months, and perhaps for much longer, and its effects on the nervous system are developed only in the course of years. But there is possibly even more than an analogy between the effects of the two diseases. I have seen a few cases in which there was evidence of a persistent, and even a progressive lesion of the spinal cord after diphtheria, and I lately saw a woman in whom true primary

atrophy of the optic nerves, with partial external ophthalmoplegia was a distinct sequel to a true diphtheritic paralysis. Hence we may hope that the discovery of the mechanism by which diphtheria affects the nervous system, will take us a step nearer to the elucidation of these mysterious sequelæ of syphilis.

It may, I believe, be regarded as a general law—and a law of much importance in practical diagnosis—that the isolated impairment of nerve structures that have a certain function when acute indicates a toxic influence, when chronic a degenerative process. It is instructive to note that these two mechanisms are not entirely dissociated—that the degenerative process may be a late result of a toxic agent.

The problems we have last considered have an interest which is at present, alas, purely scientific. It is a strange anomaly, this scourge of the sinister side of civilised life. Its direct effects we can control more than those of any other malady of like nature, and yet both the essential element of the disease and its remote effects seem alike beyond our reach. But the knowledge that is not power now may be power in the future. When the specific organism has been identified and isolated, when it has yielded the secret of its life history, then we may look for means, if not of destroying it, at least of modifying its processes and effects, and of modifying them not only in the experimenter's flask, but within the human body. Until this can be accomplished, the light of research does but reveal, in vaster range and more complete detail, the grim features of the malady. Still, the light is welcome. We see how far the grasp of the disease extends into regions believed to be beyond its reach; we see how long its consequences endure, living on their own life after the disease itself has ceased to be a power for evil; but we see also how much more vast than once was thought will be the saving influence of prevention or of cure.

GRASSE, ALPES-MARITIMES, AS A HEALTH-RESORT.

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MUCH impressed with a short visit I paid to Grasse last Christmas, and convinced that its value and claims as a winter resort are imperfectly known and appreciated in this country, it may not be inopportune that I should, at this season, state some of the advantages it seems to me to possess as a health-resort. And first of all, to those for whom a quiet life possesses some attractions, and who share the oft-quoted opinion of Sir G. Cornewall Lewis that "life would be tolerable were it not for its amusements," Grasse is exactly the kind of quiet retreat to suit them. A quaint old town, bright, sunny, olive-clad terraces, fields of odorous blossoms all around, a girdle of picturesque mountains, a fine sweep of undulating country stretching down to the shores of the Mediterranean, excellent carriage roads leading to drives of great beauty, promenades amongst the hills around of endless variety and interest, and the sun of Provence overhead—such is Grasse!

One reason, perhaps, why Grasse has not hitherto been frequented in the winter by visitors in numbers proportioned to its obvious merits is that it has only been within the last few years that visitors have been able to obtain there the accommodation of a really first-class hotel. The Grand Hôtel at Grasse is in an admirable sunny situation, quite out of the town, though close to it, commanding a fine view, and under the same excellent management as the noted Beau Séjour at Cannes.

The old Provençal town of Grasse is situated about ten miles to the north of Cannes, with which it is connected by rail as well as by a good carriage road. It contains over 12,000 inhabitants, and is built on the southern slope of a hill (the Rocavignon), at an elevation of about 1,000 feet above the sea. Having a screen of mountains close behind it, it is greatly protected from those winds which are the bane of the other winter resorts on the Riviera, while it gets all the advantage of the abundant sunshine of this highly-favoured region, and those who find the sea breezes and the sea air of the coast too exciting and injurious will obtain

at Grasse the same dry, sunny climate removed ten or twelve miles from these disturbing influences. This is a very important consideration also to those sensitive invalids who suffer from sleeplessness when dwelling close to the sea.

It is true that when snow falls low down on the mountains, as occasionally happens in the course of the winter (snow seems to have been a much more frequent visitor to this coast of late years than it used to be), Grasse is somewhat colder than the towns on the coast, but those who have passed the whole winter there declare that they have found these cold days bracing and health-giving, and by no means unpleasant.

For some of the following details of the climate of Grasse I am indebted to a careful and scientific observer who passed the greater part of last winter there.

The Marbrière and Rocavignon hills of limestone rock overhanging the town assist, by absorption and radiation of heat, in keeping up an equable temperature. The air is very light and dry. October and November are generally the rainy months, but, the showers being frequently almost tropical in their violence, the number of rainy days is not high. From about December 20th to January 20th is the coldest time of the year.

The following meteorological table refers to the year 1887:

Month.	Cloudless Days.	Rain Fell.	Snow Fell.	Cloudy Days.
January	16	1	3	4
February	10	3	1	4
March	11	3	—	4
April	9	3	—	2
May	7	3	—	8
June	16	—	—	3
October	13	4	—	2
November	8	13	—	3
December	13	4	2	3

"Cloudless days" are those on which at no time was the sun obscured by cloud. Under "Rain Fell," all the days are reckoned in which there was even the smallest quantity of rain. "Cloudy Days" refer to those on which the sun was obscured the whole day. The days not included in this table were those on which the sun was obscured during portions of the day.

The following is the temperature table for the same period.

Month.	Average Maximum.	Average Minimum.	Greatest Maximum.	'Lowest Minimum.
	Deg. F.	Deg. F.	Deg. F.	Deg. F.
January	46.9	34.8	55.4	32
February	48.7	36.5	57.2	32
March	57	48	66.2	33.8
April	61	48.9	68	37.4
May	64.04	50.3	73.4	44.6
June	73.2	61.3	84.6	51.8
October	58.8	46.04	71.2	39.2
November	51.08	42.08	60.8	39.2
December	48.2	36	57.2	26.6

The excellent observer to whom I am indebted for these figures says of the winds: "There is, perhaps, no prevailing wind." The north-east and east winds appear to be the wet winds. The north wind is a cold wind, and it is the wind which generally brings such snow as falls there. The mistral (from the west and north-west) is unpleasant while it lasts, but has this compensation, that it always brings fine weather, and purifies the air. It blows with much less force at Grasse than on the western side of the Esterels, as this range of mountains affords this district a considerable protection from its violence. The sirocco, from the S.S.E., generally brings cloudy weather, but not rain. The S.E. is a warm, fine weather wind.

As Grasse is situated at an elevation of nearly 1,000 feet above the sea, the air there is lighter and drier than on the coast, and many persons with chest affections, and especially asthmatics, find they can breathe more freely there, and for the same reasons they sleep better. Many people who find a difficulty in sleeping at the sea-level are able to sleep soundly at Grasse.

The mists which are occasionally observed hanging over the undulating tract that lies between Cannes and Grasse do not, as a rule, reach the latter place. Grasse is much freer from dust than some of the coast towns, such as Nice, and when, owing to a continuance of fine weather, there is a certain amount of dust