A Lecture

ON

THE PROGNOSIS AND TREATMENT OF SYPHILITIC DISEASE OF THE NERVOUS SYSTEM.

Delivered at the Medical Graduates' College and Polyclinic.

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GENTLEMEN,—I have been asked to lecture to you at short notice, but fortunately a subject has been assigned to me—syphilitic disease of the nervous system. I have not, however, been told what to say. The subject far transcends the limit of a single lecture. All I can do is to present for your consideration some general principles concerning the most important practical branch of the subject, those which should guide us in the prognosis and treatment of these diseases.

I fear I can only give you that which is old. But the old is not, as such, to be despised. It has been well said by Ribot, as to senile failure of memory, that "the new perishes, the old endures." The saying is true in a much wider application, although it is only a partial truth. We may also remember another aspect of the relation. To present old knowledge to new minds involves a constant renewal of its youth. The seed that is old produces a new plant. It may be true that "there is nothing new under the sun," but there is a sense in which it is also true that there is nothing which is not new. The rising sun is old enough, but each sunrise is a new event.

Even in my restricted topic I must confine myself to the principles which seem to me of most importance. First, however, we must have a clear perception of what we are dealing with when we speak of "syphilitic disease" of the "nervous system." What do we understand by "nervous system"? If we only mean the actual nerve cells and fibres, the functional elements, I might paraphrase that chapter in a book on Iceland which Dr. Johnson said he could repeat from memory, the chapter on Icelandic snakes. Doubtless you know your Boswell, and remember that this feat of memory turned out to be the repetition of the sentence—"Throughout the whole of Iceland there are no snakes." So I might say, "there is no syphilitic disease of the nerve structures." But the term "nervous system" includes also the neuroglia, which supports and separates the nerve elements, the blood vessels, which penetrate and permeate the centres, and the membranes which enclose and protect them. These structures are among the most frequent seats of the morbid processes of constitutional syphilis. The nerve elements proper do indeed undergo degeneration after syphilis, but this is a different condition. I will refer to it presently, but it is not within our special subject.

I have not made this comparison with the snakes of Iceland merely to enunciate a paradox. Behind it lies an important fact. Syphilitic disease of the nerve centres, developing in what may be termed the "adventitial" elements, produces symptoms for the most part through the changes it causes in the nerve elements themselves. But these are simple, not specific. They are secondary to the syphilitic disease, but they are the same as would be caused by any other disease of the same character, whatever its nature. The significance of this fact is far reaching. Specific treatment acts only on the specific process. It has no direct influence on the secondary changes by which the symptoms are produced. This fact should be kept in view in all your practical conclusions, and to impress it upon you is one of my chief objects to day.

Let me give you some illustrations. You may not need them, but, believe me, the art of getting the knowledge you have not is to welcome that which you think you have.

To take first a salient example of the simple nature of the process by which syphilitic disease causes symptoms—consider syphilitic disease of a cerebral artery. The disease narrows the vessel, or narrows the orifice of a branch which arises at the affected spot, but causes hardly any symptom until a clot suddenly forms. The narrowing makes the flow so sluggish in the "backwater" just beyond the diseased spot, that clot forms on the altered wall and quickly closes the vessel. It extends on, up to a branch from which a collateral supply can maintain the circulation; if there is none it spreads to the distal twigs. The region of the brain from

which the blood supply is thus suddenly cut off at once loses its function. Unless a collateral flow can be established in an hour or two, it perishes, undergoing necrosis, "necrotic softening," of necessity enduring, with persistent loss of function. But the thrombus which forms is simple not specific, and so is the resulting softening. The only syphilitic process is that in the wall of the artery.

Reduce the disease of the artery to a cicatricial state as quickly as you can by treatment you cannot change its effects. You can exert no more influence on the thrombosis or on the softening than in a case in which the softening is due to embolism. Nor can you influence the characteristic symptoms which are due to these simple effects of the disease. This must be clear to you, but it is not so many years since I heard a man of professional distinction say of such a case of sudden syphilitic hemiplegia, "Oh, he has a node within the skull; give him mercury and he will get all right."

Sometimes the course of the case seems to verify such a favourable prognosis. Under the treatment the symptoms lessen and may pass away. They do so in the same manner and degree in many cases of embolism from heart disease, and do so whether medicine is given or not. The initial effects of any vascular lesion are much wider than those that are permanent, because the area of brain disturbed is greater than the area destroyed, and the permanent symptoms depend on the functional importance of the latter.

Take, again, the case of a syphilitic gumma growing from the membranes of the spinal cord. It slowly compresses the cord and this causes paraplegia. The effects on the cord are precisely the same as would be produced by any other kind of tumour. If pressure is slowly exerted, the fibres lose all power of conduction long before they suffer total destruction. Secondary degeneration may follow with all its symptoms, and yet certain elements of the fibres may retain such continuity as permits their ready renewal when the pressure is removed. Conduction, if it has not been lost too long, may be restored when treatment causes the compressing growth to shrink, just as when a sarcoma of the membranes is removed by a surgical operation. But the treatment does good, not by its influence on the changes in the spinal cord, on which the symptoms depend, but by acting on the specific cause of those changes. These pass away if there has not been actual destruction.

Such syphilomata may form on the sheaths of the cranial nerves and produce the same effects—arrest of function, with palsy in the part supplied, recovering when the compressing agent is removed. It is so, also, with the similar processes in the membranes of the brain. But here, as in the nerves and the membranes of spinal cord, the processes of growth pass by degrees into another process—that of inflammation.

The subject of syphilitic inflammation brings before us some pathological conceptions which it is important to discern. The characteristic specific process is neoplastic, the formation of tissue which, when recent, is semigelatinous in aspect ("gummatous"), and resembles, histologically, granulation tissue. After a time it becomes firmer, and two changes occur. Its elements become transformed to fibres, which contract in a cicatricial change, or they undergo fatty degeneration and caseation. This caseation occurs in several discrete spots, perhaps because the vessels of the neoplasm become thickened and closed. These areas may coalesce, but do not constitute the general uniform caseation so characteristic of a tuberculous mass. This caseation in several foci, combined with the gummatous aspect of the recent parts, is the most characteristic feature of these specific growths.

Every process of tissue formation, whatever its nature, involves vascular disturbance proportioned to its acuteness. Syphilomatous tissue always forms rapidly, and the attendant vascular disturbance constitutes a state of active congestion, and even of inflammation.

Thus we can trace the two elements, the inflammatory and the neoplastic, in all syphilitic processes. In proportion as they are acute the inflammatory element preponderates. We meet with foci in the meninges, which we should call inflammation, but for the amount of gummy tissue produced, which may be such that in places the characteristic spots of caseation are seen. We may be then in doubt whether to call it a gumma with adjacent inflammation or inflammation of a gummatous character, and it is really a choice of terms. But it is doubtful how far the inflammation itself is specific or is simple. Inflammation is a curious process. You know how it spreads in some structures when once lighted up. We sometimes see this in the peritoneum in a terrible degree.

In the cerebral membranes an inflammation once excited, by whatever cause, tends to spread swiftly in proportion to its acuteness. In proportion to this the inflammatory element predominates in syphilitic meningitis, and in that proportion it has the features of simple inflammation. It speedily becomes extensive, general, and even may be bilateral. It seems as though some form of morbid agent had the power of exciting inflammation which at once attains a degree far in excess of its cause. It seems also to be less amenable to treatment in proportion to its acuteness, in proportion to the degree in which the simple inflammation runs away, as it were, from the specific cause. We meet with instances of this, happily not often, in the cerebral membranes. We meet with the same, more frequently, in the spinal cord.

Acute myelitis, focal or transverse, is met with so often in the early stage of constitutional syphilis that it is impossible to doubt a causal relation. Yet the inflammation presents similar features, and runs a course quite the same, as in patients in whom syphilis can be excluded. Remember that in all acute inflammations of organs the proper functional structures undergo rapid destructive changes which are regarded as a participation in the inflammation. But these are simple in aspect, similar in every form of inflammation equally acute. They are intense in proportion to the inflammation, and may speedily attain a degree from which recovery is slow, imperfect, or impossible. This is conspicuous in these cases of acute myelitis, and they justify the inference that in these cases also the symptoms depend on the simple effects of the specific process. It is alike true whether the inflammation is purely such or whether the damage to the nerve elements is brought about by disease of the arterial walls at the spot affected. In the more chronic forms of local inflammation in which the process passes into that which may be termed sclerosis the same fact is apparent. The morbid process is interstitial, and the nerve elements suffer secondarily.

Local chronic inflammation of the cerebral cortex has other effects which are also due to the simple damage to the nerve element in the cortical substance. Even if the effects of inflammation pass away, no structure is ever quite the same as before, and in the grey matter of the brain a slight residual alteration may entail a grave change in function. Instead of stimulated, proportioned liberation of nerve energy there is spontaneous discharge which gives rise to local convulsion. This may occur from the irritation of the active inflammation, but also as a residual effect, such as might be due to the inflammation caused by a blow. It also is a manifestation of simple changes on which specific treatment can have and does have no influence.

The points I have mentioned are not matters of theoretical pathology; they are of the utmost practical importance. On your perception of the mode in which the symptoms are produced depends the correctness of the forecast you can form, of the prognosis you can give. The essential point is that the specific process can be influenced by treatment, but this can produce no effect on the simple changes on which the symptoms directly depend. The forecast is favourable in proportion as the latter can pass away when their cause ceases to act. Hence it is important that you should cultivate the habit of picturing to yourselves what is the exact morbid state, and strive to discern the nature of the changes which give rise to the symptoms. Endeavour to acquire the habit of forming such a mental picture. Obtain all the data you can, and then strive to see with your mind's eye, and trust your vision. It may seem difficult at first, but will become easier with practice. It will often serve you in good stead in many forms of disease, in many parts.

PROGNOSIS.

The application of these facts to prognosis should be self-evident. The prospect of improvement and recovery depends on the extent to which, after the removal of the specific disease, the simple processes on which the symptoms depend can pass away. In all tissues the tendency to recovery is great, if the change has not proceeded to actual destruction. Thus you will perceive that in arterial obstruction there is a speedy, permanent destruction of tissue, and function can only be regained in so far as it is capable of compensation by the other hemisphere, or in the degree in which initial damage exceeds actual destruction. But in the case of slow compression the possibility of recovery depends partly on its degree, but still more on its duration. Pressure always involves secondary inflammatory changes in the compressed tissues. These go on to cicatricial processes if the pressure has been long continued; in time they constitute a grave hindrance,

sometimes an insuperable obstacle, to the restoration of continuous structure and conducting function. Paraplegia from such pressure may be complete for a month, and recovery will probably, in time, be perfect. If complete for three months, recovery may possibly be perfect, but is more likely to fall short of the normal state; but if complete paraplegia from compression has endured for six months only partial recovery can be expected after even the complete removal of the cause, and after a year the return of function may be very slight, and at best will not be great. Of course, these are but rough assertions; they are, I believe, approximately true, but they are given chiefly to fix on your minds the importance of considering duration in the attempt to forecast the future of a case. You have doubtless long since learned by experience, that may have been painful and certainly must have often been trying, the urgency with which a patient, and still more the friends, desire to know the future course of the malady. They expect from us a prescience more than human. It seems reasonable to them that we should be able to see into the future with the same certainty as into the past, and the same confidence as into the present. We are fortunate when the conditions are such that we can give them that which they ask for; but you will only discredit yourselves in the long run by holding out confident hope when it is unjustified. Strive, then, to perceive the morbid state, and if you cannot anticipate much improvement it is seldom that you cannot hold out hope of some, but take care that you are clearly understood, and that your "may" is not construed as "will."

It may seem strange to some of you that any cases of this character should lose their chance of complete recovery by reason of their long duration before appropriate treatment is employed. But it seems to be a law of Nature that everything that never should be, sometimes is. One cause is because some patients suffer long before they seek advice. It is not so with paralyzing maladies, but it is sometimes with those that damage nerves, and even with arterial disease so placed as to cause only slight symptoms for a long time before arrest of the circulation is produced, and when the parts affected are those to which no motor functions are related. It is not often, now, that such disease is undetected in consequence of the ignorance of the doctor who is consulted, but it happens sometimes because he does not make a sufficiently careful search to discover slight but conclusive symptoms of organic disease. Among these optic neuritis is one of the most important and most frequently overlooked. Indeed, I may say in passing that no defect in medical education seems so persistent as ophthalmoscopic training. It will be so until the inspection of the normal disc is part of practical physiology, or at least is taught with the stethoscope at the beginning of practical medicine. Clinical work abounds with unused opportunities, because the eye is never looked into until the end of the student's course.

Another frequent reason for the prolonged unchecked development of the disease is a belief that it cannot be. One of the great lessons of life—sometimes only learned late—is hesitation in pronouncing anything impossible. Certainly, this disease is sometimes met with under conditions which suggest that it is impossible, especially to those who know the patient best. One fact, at any rate, you should always remember. It can be excluded only when there has never been exposure to possible infection in the common way. If there has been, if it has been escaped by "luck"—its denial should have very little influence on your opinion. You know also how constantly its occurrence in married women has no symptoms to make it suspected, and it is important to remember that the evidence afforded by children may be absent. Indeed, the subject is one in which it is important never to forget the rule—a rule of almost universal application—that the absence of evidence is of very little value compared with that of its presence. Nature is unvarnished as well as man, or rather seems so because our ears are tuned only to its affirmations. Its "no" is often altogether untrustworthy, but this is because we interpret its silence as negative without the least justification for doing so. Almost every common symptom of a morbid state is sometimes absent; every indication of a common cause is sometimes absent. Hence assurance is possible only when the common cause can be absolutely excluded.

Thus the practical lesson which follows from the perception of these facts is that the cause of the symptoms of the various syphilitic diseases which damage the nervous system is a secondary result of the specific process. Remove the latter by treatment, remove it as completely as possible; the secondary

effects may pass away, or may only lessen, or may persist with only slight diminution. A cicatrix from a gumma in the liver may be unimportant; in the nerve centres it may cause enduring symptoms. In the cortex of the brain organic epilepsy may be its result. Even a gumma pressing on the cord may be removed by treatment too late to prevent a degree of mischief which cannot recover, and some palsy may be enduring.

Remember also that the actual result of treatment on the specific process depends on its duration. The new formation rapidly diminishes in size under treatment. Apparently the tissue elements that are of recent formation, chiefly cellular, undergo granular disintegration, the results of which are quickly removed; but the older cells undergo a change into fibres which may perhaps also be formed between them, and the diminution in size is partly due to the progressive cicatricial contraction of this fibrous tissue, which proceeds to such an extreme degree. Treatment seems to promote this cicatricial process in the tissue elements which have attained too mature a stage to undergo disintegration and total removal. But this process has its own consequences; that which it entirely surrounds suffers inevitable constriction, which may perpetuate or even augment the effects of the active disease. This is another reason why your prognosis in cases that have proceeded unchecked for some time should be very cautious.

A year ago I had occasion to point out that this change, going on all round the wall of an artery, seemed to have induced its occlusion, and that this effect had apparently been promoted by the influence of the treatment which arrested the disease and helped the cicatricial change. Happily such annular disease is rare, whether in a nerve or in an artery, and the conducting function of a nerve may be slowly restored in spite of considerable enduring constriction. Yet the impairment may continue long after cicatrization of function is established. This fact seems to be incomprehensible to many. As long as symptoms continue, as long as the normal state is not regained, it is believed that there must be specific disease unconquered; treatment must be made more energetic, must be repeated. Iodide is continued and increased; course after course of mercurial inunction is employed. Sometimes all is to no purpose; sometimes there is the slow natural recovery we know so well when causal disease has ceased, a recovery then inevitably assigned to the persistent treatment employed, although it may be, I believe, in spite of it. You may ask, Is not this reasonable? Are we not justified in our inference, since we cannot see what is going on?

Well, I would ask you to consider what you do in other conditions that are beyond the direct range of observation. You infer from that which you can directly discern the character of the process you cannot actually perceive. If a patient comes to you with a recent node on the tibia you know that under iodide or mercury it will have disappeared in six weeks. If the node has existed for six months, at the end of six weeks it will have become much less, but periosteal thickening will still be felt, and this will be very slow in disappearing. It will lessen in time, just the same whether or not you continue specific treatment. The residual thickening is due to cicatricial tissue, which must persist after all the specific element is removed. So with a syphilitic ulcer of the skin. At the end of six or eight weeks' treatment—if this is adequate—all the peculiar specific thickening is gone; the ulcer may not be healed, but all that remains is a simple ulcer undergoing simple cicatrization, which will go on just as well if you do not continue specific treatment as if you do.

When the ulcer is healed, what remains? A scar, first livid, afterwards brownish, in which the skin is thinner and smoother than elsewhere—a scar which remains to the end of life. In every tissue it is the same. Every morbid process leaves its changes in proportion to its degree and character. A destructive process leaves cicatricial tissue in place of normal structure, and this may even surround a cavity if there has been a massive destruction. Simple inflammation may leave a slighter change, but usually such as to be discerned, at least by the microscope, and this degree is colossal compared to the changes in finer nutrition which must always ensue. The effect on function even of the slightest residual change is enduring, and important in proportion to the delicacy and differentiation of function of the structures affected. Hence, whenever the nerve structures are damaged by specific processes, we should be prepared for imperfect recovery, however successful our treatment of the primary process may be. It is indeed remarkable how great is the restoration of function in many cases, in the course of time.

But the fact I wish to impress upon you is that the "time" is not occupied by the removal of the specific disease, but by the recovery of the damaged structures when this has been removed.

You will perceive from what I have said that the pathology, prognosis, and treatment of these maladies are closely connected, or rather they are the same viewed from different sides. You can only frame a forecast by discerning whether the causal disease can be removed completely, and how far the nerve elements can recover. For this purpose it is essential to form a mental conception of the process as precisely as you can, and trust to your inference from it. When you cannot see with the eye you must strive instead to see with the mind. The great difference between various processes will then rise clearly into view, and all that the difference entails.

For the most part the symptoms of these processes are hardly ever really *slow* in their production. They are subchronic, subacute, acute, or sudden, reaching a considerable degree in less than three months, and often in much less. Of all it is true that the more rapid the development of the symptoms, the less is their course affected by specific treatment. Those which are most deliberate are chiefly the result of a gumma, compressing, or irritating, or of gummatous inflammation of the membranes. Over these treatment exerts its greatest influence, and in them the prognosis is the best, subject to the limitations I have mentioned—long duration and irritative influence. The acute symptoms, acute as distinguished from sudden, are for the most part the result of inflammation. This, although excited by a specific cause, varies in the relative amount of inflammation proper, which is greater the more acute the process. The nerve structures suffer chiefly from this, and the more rapidly the symptoms develop the greater is the destructive implication of the nerve elements, the less is the room for the influence of specific treatment. We see this strikingly in the cases of acute transverse myelitis, so frequent in syphilitic subjects, in whom, as I have said, it runs a course differing in no respect from that which it pursues in other patients. The cases of actually sudden onset present a course over which specific treatment can have and does have no influence. I need not repeat what I have said regarding this point.

TREATMENT.

It may seem strange that the therapeutic progress of the last half century has left us without any new remedy for syphilis. But we need not be ashamed of the nineteenth century since it has produced the second of our two certain remedies, iodide. Its value was discovered in the thirties, and in England. Like the majority of our most useful drugs, its service was found by empirical observation, indeed, it may be said, almost by accident. The real or supposed influence on goitre of burnt sponge led to the discovery that it contained iodine, and to the use of combinations of iodine for other swellings, among them for nodes. From this the step was small to the discernment of its power over other syphilitic processes, a power as certain as it is mysterious.

The older remedy, mercury, has come down to us from the dim distance of a thousand years. Its use by the Arabians is said to have been anticipated in India, but the Orient shrouds in impenetrable mist the beginnings of all things. Its service in syphilis is believed to have been one of the Eastern lessons the Crusaders brought back to Europe, unless it had been conveyed by the Moors to Spain with skill in other arts, such as the Alhambra retains for us.

The two agents stand on a different level. We have other facts regarding the power of mercury which make its influence on syphilis less strange. It is possible that it has a capacity of arresting many diseases that depend on an organismal virus, although it is only in a slow disease that we can avail ourselves of this effect. The fact was ascertained in the early days of the Brown Institution that an animal under the influence of mercury was unaffected by a dose of anthrax virus which would certainly be fatal to a similar animal not so protected. It is believed to have an influence on all processes of inflammation. Those of our profession who have occasion to watch the only internal inflammations which can be directly observed, those within the eye, are firm in their belief in the influence of mercury upon them, irrespective of their specific nature. I may add that it has been employed in most of the cases of cerebral meningitis, including some apparently tuberculous, in which recovery has been known. This is, at least, true of my own experience. Mercury is a poison, but a considerable quantity may be contained in the blood, if gradually introduced, and we can understand that this may be sufficient

to be fatal to the organisms of disease long before it is fatal to the living elements of the body. But to permit this effect the disease must be one of slow development.

We can thus at least seem to understand the influence of mercury in syphilitic processes, and also the trust, placed in it in the early stage, when the organisms must be in their first flush of growth in a fresh soil. But iodide has no such toxic property. It is a salt not far removed in nature from common salt, yet its influence on the processes of syphilis is certain. This must be due to the iodine, and it is said to be possessed in equal degree by the combination of iodine with a vegetable oil, "iodipin," or "iodinol." Iodide, in itself, seems almost inert on the normal processes of the body, and yet it has a profound influence on this morbid process. But we must remember that all these elementary bodies seem able to enter into combination with albuminous substances, modifying their influence, sometimes profoundly. A slight change in constitution will transform a food into a poison. The mystery of the certain influence of iodide is made more salient by our uncertainty as to its effect in other morbid states. It has been, and is, thought to do good in many; but, if we search for stringent proof, we shall find ourselves in agreement with Nothnagel, who, in his great book on *Materia Medica*,¹ says: "The therapeutic influence of iodide is undoubted only in one condition, tertiary syphilis, and it is possible in hyperplastic affections of the lymphatic glands and thyroid. In all other conditions its influence is doubtful and uncertain. We have employed it much, very much, but in other maladies we have never obtained definite and incontestable certainty that the improvement and recovery occasionally observed were due to it."

Of course, its administration in many maladies must often coincide with spontaneous improvement, so very easily ascribed to coincident treatment. But when due allowance is made for this, and when the cases in which it has failed are given their weight, does the lesson of the residue differ much from the experience of Nothnagel? The contrast presented by its power over syphilitic new formations is most strange. Not less so is its innocuous character compared with the toxic power of mercury. It is difficult not to believe that the future has some revelation in store for us, which may not only explain what is now mysterious, but in doing so may augment our resources alike in means and method.

It is not through diseases of the nervous system that any new means of combating syphilis are likely to be discovered. Duty precludes us from the attempt. The effects of such disease are so grave, and are rendered graver by every day's delay, that we dare not pause to search for a new agent. We must employ at once the means we know and trust, and leave the task of discovery to those whose province is less profound. As a fact, moreover, nothing is such a hindrance to the discovery of new remedies, truly such, as the efficiency of those we have. If we know what will cure, we seldom dare search for another remedy.

The difference between the two agents is familiar and important. Iodide can be thrown into the system in any quantity; mercury can only be introduced gradually. For the chief lesions of constitutional syphilis they seem equally useful. But when the process is inflammation, we should expect mercury to have the more certain influence, and observation affords some confirmation of this. It is not for a physician to express an opinion on the treatment of the early stage of the disease, but in this there is a consensus of opinion of the need for mercury on the part of those who can speak with authority. Regarding the later processes, there seems to be a general feeling, rather than opinion, that mercury can do a little more, and can do it more thoroughly, than iodide, but that the latter does its work more speedily. The feeling deserves respect, even practical respect, but I do not think it rests on strong evidence—at least so far as the nervous system is concerned. The opinion is largely due to the use of mercury after iodide has lessened the symptoms, and probably after the syphilitic process has been entirely removed. The damaged nerve structures have slowly regained function during the subsequent mercurial treatment, to which the later improvement has been assigned. No delicate therapeutical inferences ought ever to be drawn from these diseases. We are right to apply to them all we can know or suspect, but the pitfalls of fallacy are, as we have already seen, many and treacherous. Real knowledge can only be increased from that which is within the range of vision, from the surface of the body. It rests with the dermatologists to augment our certainty, and increase our power. They can see and we cannot. The risks that delay involves are to them trifling. They

should endeavour to eliminate every source of fallacy, to distinguish between the specific and the simple elements in the processes they treat, and to make their therapeutic observations precise, multiple, and widely known. Then we should feel sure of much we now only suspect, and perhaps we should doubt some things we now believe.

Of one thing I am quite sure, that the symptoms of a syphilitic growth may diminish and pass away as rapidly if iodide only is given, as we can conceive possible. I do not affirm that is always so, but I remember many cases in which 10 gr. three times a day produced in a week cessation of headache and distinct diminution of early optic neuritis, which had vanished at the end of a fortnight. In one such case slight hemiplegia had disappeared at the end of a month, and hemianopia which had been complete was reduced to part of one lower quadrant. But this remained permanent.

It is said that much larger doses of iodide are sometimes necessary, but I have not myself met with evidence of this, except in patients who have long been taking moderate doses. The use of large doses—30 gr. or 40 gr.—has been called the new American system. I have already referred to the saying that "there is nothing new under the sun." Many years ago I had occasion to go through some of the old casebooks of University College Hospital, and I found one case in which Dr. John Taylor gave 40 gr. three times a day for constitutional syphilis, somewhere about 1847. The same physician, by the way, at the same time, made constant use of the thermometer to ascertain the presence and degree of fever, long before it came into general use.

I think it is not wise to give iodide and mercury together in full doses, except for a short time in a very urgent case, when every means and measure are needed to stem life-threatening disease. There is reason to think that iodide promotes the elimination of mercury, as it does of most metallic substances, and thus hinders the retention in the system of enough to act upon the processes of the disease. We cannot be sure that an adequate quantity is present in the blood unless we have such evidence as is afforded by slight inflammation of the gums. The difference in the readiness with which this is produced is probably due to differences in individual power of elimination, which seem to be effected chiefly by the liver.

This explanation is, at any rate, plausible, and I think useful. It suggests that, if there is not the sign in the gums of enough mercury in the blood to act on the tissue processes, we should increase the dose—double it, treble it—until we obtain the evidence. But it is wiser not to give at the same time an agent which has the power of promoting its elimination, except there be the urgency I have referred to. All experience shows that the affection of the gums is evidence that enough is present in the system. It may then be stopped for a day or two, and continued in smaller quantity to maintain the effect for three or four weeks; then the iodide may wisely be resumed. It will have its own effect, and may also at first maintain the influence of the mercury by bringing into the blood that which has entered the tissues.

We cannot improve on the physicians of long ago in the method of administering mercury. The object is to get enough in the system, and this can only be slowly achieved, or inconvenient toxic symptoms result. One of these is gastro-intestinal irritation, which is always greatest when the administration is by the mouth. The old method was to rub it into the skin, and it is, I am sure, the wisest. One modern method is to inject it under the skin. Whether or not this is equally effectual, it is certainly much more uncomfortable than inunction. By the latter the gums can be affected in five or six days, which is as speedily as the result can safely be obtained by any system.

Inunction is much facilitated by the use of the oleate, which is not only cleaner in aspect, but, I think, surer in result. Order a drachm of the 10 per cent. oleate to be rubbed in twice a day for three or four days, and then continue once a day until the end of a week. If the gums then show no sign, resume the two daily rubbings until they do. But remember one small precaution, which I should be ashamed to mention to you did I not know how much depends upon the trifles of our work. See that the same small piece of flannel is always used, and let the first inunction be 2 drachms. Otherwise the nurse will think it so much cleaner and nicer to take a fresh piece of flannel each time, which will retain more than half the dose, and you will wonder why your patient's gums show no sign.

I do not think it matters into what part the mercury is rubbed. It is often convenient to have it rubbed in as near

as you can to the affected part—close to the scalp if it is the brain, down the back if it is the spinal cord. This has a certain reason, that the oleate makes the skin rather sore, and thus effects slight counter-irritation. It has another reason, of a kind not to be despised. There is nowadays too much knowledge, public and popular, regarding the use of drugs and their purpose. Many of the laity, not alone of the male sex, draw an immediate inference from the use of mercury, an inference which is undesired by the patient. It is prevented when the site of inunction is near the seat of the disease, and when the unmeaning oleate is employed, instead of the blue ointment with its suggestive colour. Such a device for the avoidance of distress does not merit any deprecation on the ground of high morality. If it is true that "things are not what they seem," it is equally true that they sometimes should not seem to be what they are, when the seeming can do no good and may do harm.

One element in treatment I have yet to mention. I have left it to the last because it runs counter to the cherished practice of many of those who have had experience in the treatment of this disease. It concerns the duration of treatment. Regarding the processes of the constitutional disease, definitely such, my conviction is that specific treatment should be energetic, brief, renewed, but not continuous. By "brief" I mean that it should stop at the end of eight weeks or so, and be renewed after two, four, or six months, and that the patient should have three or four weeks' treatment with iodide every four months during the first year after any true specific symptoms, and every six months for the next three or four years.

Let me tell you the reason for my conviction. I have said it before, but a teacher who hesitates to repeat, shrinks from his most important duty, and a learner who dislikes to hear the same thing twice over lacks his most essential acquisition. Many years ago a patient came under my care with symptoms of a cerebral syphiloma. Under 10 gr. of potassium iodide three times a day the symptoms rapidly passed away, and the patient seemed well. He continued, however, to attend this hospital and to take the medicine. At the end of three or four months he presented symptoms of disease of the upper dorsal region of the spinal cord. They progressed rapidly, and caused his death. It seemed impossible that the disease could be syphilitic, since he was still taking the medicine which had so speedily removed all indications of such disease in the brain. But the necropsy shook our confidence in the seemingly impossible. In the brain there was the shrunken relic of the gumma; in the spinal cord, invading it from the membranes on one side, was a similar growth, in the active stage, typical under the microscope, and typical also in the naked-eye feature of disseminated caseation, a character of conclusive significance.

The lesson this case taught me I have since seen confirmed by other cases, not my own, however. It is that treatment may lose its power if continuously maintained. It is not altogether unintelligible that this should be. We cannot doubt that syphilis is an organismal disease, that it depends on bacilli as yet unidentified. We have yet no definite objective acquaintance with these microbes, but the symptoms of the disease harmonize best with the theory that their life is continued by germs which persist in various parts of the body when the organisms die. The course of the malady suggests that these germs may long lie low and latent, but develop from time to time under influences we cannot discern. A consideration of the course of the disease and its relation to treatment compels the conclusion that this has no influence whatever on the latent germs. It seems to destroy the developed and developing organisms, and thus dissipates the morbid processes they excite. But the most thorough treatment may fail to prevent future development of the disease, at whatever stage it is adopted, however early. I do not say that it has no such preventive effect; but instances have been met with by every one who has had much experience, in which there was recurrence after recurrence, in spite of most thorough treatment. The only reasonable explanation of this seems to be that the germs are indestructible. They cause no symptoms until some influence induces and permits their development. After a given outbreak there may be none left, and treatment then seems to have cured the disease. In another case there may be many, and then recurrence occurs after the same treatment. Hence, whether syphilis is or is not incurable as a constitutional malady, it is certainly one of the cure of which we can never be sure.

Hence my belief that the essential principle of treatment is that it should be energetic but not continuous. Energetic mer-

curial treatment is, of course, such as to affect the gums, and this cannot well be continued for more than six or eight weeks, nor need it be. Iodide can be given persistently in large doses for many months with no grave constitutional inconvenience, and I know that such long continuance is thought by some to be an essential element of thorough treatment. But the organisms seem sometimes to become acclimatized to the presence of the iodide and to develop in spite of it. The fact is not unintelligible. Dallinger found that a temperature which surely killed certain organisms failed to hinder their vigorous development if successive broods were gradually inured to heat which was increased by slow degrees. So we can conceive that the syphilitic germs may gradually become accustomed to the presence of iodide. Even then, it is true, a great increase in the dose may arrest their development. But the increase cannot proceed indefinitely, and the question is, Is this long-continued treatment needed? My own conviction is that after eight weeks of adequate treatment the specific disease is at an end. All that remains is the non-specific element in the process, or, especially in the case of the nervous system, the secondary simple effects in the nerve elements, which can only slowly pass away, and sometimes cannot pass away completely.

These diseases present striking illustrations of the sources of error which beset our therapeutic reasoning. Let me repeat what I have already suggested. A gumma of the spinal cord, after six weeks' treatment, may have lost all its specific element, and be in process of rapid cicatrization, but it may be six months, or necessity, before the spinal cord can recover from its compression, and can regain its normal structure and its normal function. If iodide is given through this time, the inference is natural that this has caused the slow improvement, with which really it had nothing to do. Even more obvious, perhaps, is the frequent fallacy regarding the effect of treatment in the arterial disease. If a patient has an attack of incomplete hemiplegia from obstruction of an artery, whether due to this or embolism, great improvement is certain to occur, and can be confidently looked for—the imperfect degree shows that there is not total destruction of the motor path or centres. If iodide or mercury is given the improvement will assuredly be ascribed to it. Of course, such treatment should be adopted promptly and with energy, because other vessels may be near occlusion, which may be thus prevented. But we are not justified in ascribing to it any apparent effect on the symptoms. Here again we may see the value of the pathological imagination, in enabling us to discern clearly that which is, and hence to infer that which can be, and cannot be.

Thus the nerve elements suffer simple changes in consequence of the specific process adjacent to them, changes which are not directly influenced by the treatment of the latter. In the same way some of them may suffer simple degenerative processes, not as the direct effect of adjacent specific disease, but as a mysterious sequel to constitutional syphilis. These also are not influenced by specific treatment. They are the post-syphilitic or para-syphilitic degenerative diseases, of which locomotor ataxy and general paralysis of the insane are the most frequent forms. They are primary degenerations such as we know to be caused by chemical poisons, organic and inorganic, and they are probably due to a toxin, the result of the previous presence of the organisms of syphilis. Similar effects have been traced to a more acute organismal disease—diphtheria. We cannot doubt that the relation of these diseases to syphilis is similar, that the constitutional malady induces a perversion of some part of the chemistry of the body and a poison results, perhaps, with the help of other morbid influences—a poison that endures long afterwards. The evidence is purely that of sequence. It is neither pathological nor therapeutical. Most tabetic patients have iodide given, and hope is held out of benefit, but the cases are very few in which even slight improvement can be traced. A large majority are sure they derived no benefit, and not a few are certain that it did harm. The same is true of mercury, except that energetic treatment seems more often to be productive of distinct deterioration.

But you should know that these toxic degenerative diseases sometimes develop before the true constitutional disease is at an end, while gummata and gummatous inflammation still occur, for which specific treatment is needed. The important fact is the combination of symptoms produced and the difficulty of discerning their causes. In early distinct tabes, paralysis of ocular muscles may occur, which may be of the nature so common in tabes, or may be due to a syphiloma of the nerve or specific neuritis. Still

more perplexing are the cases to which Erb's attention has lately been specially directed, in which specific spinal pachymeningitis has coincided with true tabetic degeneration. If the nature of the disease is such as I have suggested—if germs are deposited in the system which develop from time to time under influences of which we know nothing—it is easy to understand that the organismal processes, truly syphilitic, due to later germs, should coincide with degenerations which are the effect of toxins, the result of earlier broods.

Let me remind you, however, of one useful criterion of the existence of post-syphilitic degeneration which is often of service when you are puzzled by symptoms which may be due to either process. This is the isolated light-inaction of the iris—"isolated" because it still acts readily on accommodation. You are familiar with this, which is known by the name, as just as it is cumbersome, of the "Argyll-Robertson symptom." You know its association with tabes and general paralysis as degenerative sequelae of syphilis, but you may not know that it is met with in association with other conditions, and also as an isolated symptom. Even then it is of great significance as an indication of old syphilis, and I have many times had reason to appreciate the guidance it has afforded.

But these degenerative conditions are not within my present subject and I have reached the limit of time at my disposal. I have endeavoured to put before you some general principles which should be kept in mind. If you strive to apply them to cases that seem clear, you will find it easier to use them in cases that are obscure. It is necessary to accustom yourselves to analysing the symptoms in simple cases, and discerning the grounds on which the prognosis is founded and the treatment based, in order to obtain the ability to do so in cases that are complex. Even those that seem most difficult will generally yield to a deliberate effort to apply to them the principles I have given you; they will yield, if not altogether, at least in a degree sufficient for immediate need. Moreover you will, I believe, seldom fail to find that your conclusions are confirmed and your treatment justified by that to which we have all to look,

"The balance in the hand of time."

REFERENCE.

Nothnagel and Rossbach, *Arzneimittellehre*. 7te Aufl., 1894, p. 299.

CASE OF ACUTE ACROMEGALY.

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SINCE Pierre Marie in 1886 drew attention to the remarkable affection which he called acromegaly many cases of the disease have been recorded, until at the present time there exists an extensive literature on the subject. As acromegaly is a rare disease, the amount of writing on the subject of its pathology and clinical features may appear quite out of proportion to its real importance. Nevertheless, this disease is one of extreme interest, and its full investigation may tend to throw some light on the subject of "internal secretions," to which in late years the attention of many physicians has been directed.

The following case which was lately under my care is a typical one of what Sternberg calls "acute acromegaly," and in connexion with which he remarks: "In all cases with acute progress—and only in these cases—a true sarcoma of the hypophysis is present."

O. L. H., a married woman, aged 20—under the care of Dr. Roberts, of Pontypridd—came to my out-patient department at the Cardiff Infirmary on June 26th, 1902, complaining of severe headache, failure of sight, and alteration in personal appearance.

Family History.—Good.

Personal History.—Patient was a seven-months child, and her mother states that she was delicate until 12 months old, but after that time quite healthy until 14 years of age, when she commenced to suffer from occasional headaches of a mild character. Menstruation commenced when 14 years of age, and was quite regular till the onset of her illness. Patient was married two years ago, but has had no children.

History of Present Illness.—Three years ago (when 17 years of age) patient noticed that her eyesight commenced to fail and this was accompanied by very severe headaches. These symptoms becoming worse compelled her in two months time to give up her work in a post-office and they have gradually become more marked. The headaches though very severe, especially in the frontal region, have not been constant, and she has frequently been free from them for days at a time, but the failure of eyesight has shown no remissions. She has never suffered from vomiting. Men-

struation has entirely ceased since the commencement of the illness. For nearly twelve months before admission her friends had noticed that her face was becoming broader, her lips thicker and the nose enlarged and that her hands and feet were somewhat larger. During her illness she has been in good spirits and her mental powers have remained unimpaired except for occasional transitory loss of memory and confusion of ideas. On July 3rd she was admitted to the Cardiff Infirmary as an inpatient under my care.

State on Admission.—She is a woman of average height, and although only 20 years of age, looks considerably more. Her type of face approaches that of the "negress." The skin of the face is coarse and thick and the nose large, broad and bulbous. The lips are thick and everted but the gums and teeth are normal. The tongue is broad and large, and its movements free. The hair on the head is thick, black and luxuriant. The eyebrows are thick, black and well-defined. There is a marked development of hair on the arms and legs and an increase of the normal amount in the axillae and on the pubes. The bones of the skull are not enlarged. The nasal bones and cartilages, especially the latter, are thickened. The lower jaw is thick and prominent, but the lower teeth do not project beyond the upper ones. The hands and feet are broad especially the phalanges. No other bones are affected. The thyroid is not apparently enlarged.

Fig. 1.

Nervous System.—Memory is at times bad, and there is occasional confusion of ideas. When free from headache she is bright and cheerful and quite intelligent. Speech is unaffected. Sleep is good, and patient is frequently rather drowsy. Headache is very severe, and though diffused over the whole head is most marked over the frontal region, and particularly severe above the left eyebrow, where it is associated with marked local tenderness. The headache is not constant, there being intervals of freedom for some hours at a time. The reflexes are normal. Muscular power is good. The special senses are all normal except the eyesight, which is very defective, the acuity of vision being, with right eye $\frac{1}{2}$, and with the left eye, $\frac{3}{8}$. There is slight ptosis of the left lid, but the ocular movements are otherwise normal. There is well-marked bitemporal hemianopsia, and optic atrophy of both discs is present. The other organs are normal.

Progress.—The patient after admission rapidly became worse. The headaches increased in severity, and though at first slightly relieved by phenacetin and other drugs, and by the administration of thyroid extract these had no effect afterwards. The eyesight rapidly became worse until the patient was practically blind. She suffered also from occasional vomiting, which was always associated with the taking of food or medicine. Her features during the short time (four weeks) that she was under observation became much coarser, and the increased enlargement of the lips was especially noted.

On July 24th (three weeks after admission) she had a severe "convulsion,"