Remarks ON RECENT PROGRESS IN CONNEXION WITH SYPHILIS.

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OUR knowledge of syphilis has made such strides during the last decade that we are almost justified in saying much of what we were taught as students was wrong. A quarter of a century ago our masters were only beginning to free themselves from the great error into which John Hunter had fallen when he wrote in the least illuminating of his scientific contributions:

The matter of gonorrhoea will produce either a gonorrhoea, a chancre, or the lues venerea; and the matter of a chancre will produce either a gonorrhoea, a chancre, or the lues venerea.

This statement, coming with all the force of Hunter's great authority, rendered the whole question of venereal disease chaotic where formerly there had been some glimmering of light. To the great loss of science, Hunter paid for the mistake with his life, since there is little doubt that he died of syphilitic disease of the arterial system, a result of the experiment upon which he based his inaccurate conclusion. In accordance with his teaching, mercury was given for a time in every case of venereal disease without method and merely for the relief of symptoms. It soon came to be recognized that gonorrhoea, at least, was a separate disease from syphilis, but it was not until bacteriology was well established that syphilis and soft sores were clearly distinguished from each other, and the oft-debated question of a single or dual poison was finally settled. It then became known that the gonococcus caused gonorrhoea, that Ducrey's bacillus, amongst other organisms, caused soft sores, and that syphilis was the result of some other poison. This poison still remained unknown, and was called "a virus," though curiously enough the disease itself was called by the euphemism of "specific." Most thoughtful persons had arrived at the conclusion that it was infective, and looked forward to the time when the actual organism should be discovered. Other points, too, had emerged from the darkness—that the three diseases were not mutually incompatible, that they had different incubation periods, and that they might exist in any combination in the same patient.

When we were students, only the more salient features in connexion with syphilis were recognized, and vast fields of the disease remained to be explored. Nothing was known—or at any rate was taught us—about its effects on the internal organs. Visceral syphilis was hardly recognized, and cerebral syphilis was denied. The conditions which are now grouped under the heading of parasyphilis were not even suspected; indeed, parasyphilis is so recent a term that it has hardly yet come into general use. It is a convenient expression for those conditions produced by long-standing syphilitic inflammations the consequence of, but not actually caused by, the direct action of the spirochaete itself.

Clinically I think that we were taught about syphilis as well when I was a student as we teach our dressers at present, but scientifically our masters had as much to learn about the disease as their pupils.

HISTORY OF TREATMENT BY MERCURY.

The first real advance was made when it became known that there was as much or even greater danger in a mild attack of syphilis than in one which was marked by more severe signs and symptoms, because the milder attack was apt to be imperfectly treated whilst the more severe one naturally led to more adequate treatment. The second great advance was made when it was recognized that mercury would cure syphilis, and that it was necessary therefore to give it systematically and not for

the short periods when the signs of the disease were manifest. Both these advances in knowledge were perhaps beyond the reach of our masters. The first certainly was. Histology had first to show the existence of visceral syphilis where such a condition had been doubted or categorically denied. Pathological histology in its more difficult aspects, especially in connexion with the nervous system, is a thing of our own time, and has been brought to fruition by the work of our own colleagues and pupils. The training of a first-rate histologist was in some respects superior to that of a first-rate morbid anatomist of the type of Hunter, Baillie, or Paget. It led to the observation and correlation of more minute differences. The later school, therefore, when attention was turned to the problems of medicine, often produced splendid clinical physicians by whose labours the relationship of the parasyphilitic lesions to syphilis has been mainly proved. Clinical observation and pathological histology had reached their limits in syphilis just about the time that experimental medicine and bacteriology gave a new start to the study of the disease, and during the last ten years our knowledge of syphilis has been revolutionized by the focussing of these four lights of medicine upon it.

Clinical medicine had already shown that mercury was the most reliable and potent drug for the cure of syphilis. It had, indeed, been employed as a remedy for syphilis ever since the introduction of the disease into Europe at the end of the fifteenth century, but it had fallen somewhat into disrepute, owing to the reckless manner in which it was given. It was too often replaced by potassium iodide, guaiacum, arsenic, and other drugs which are now recognized as valuable adjuvants in the treatment, although they are wholly ineffective in the cure of syphilis. As a result of the abuse of mercury it was detested by the laity, for it was believed that every patient was salivated, and that it was never eliminated by those who took it. It was an everyday remark in the out-patient room when I was a student that "I won't take mercury," or "Please don't give me mercury." This fear seems wholly to have vanished, and the present generation has lost its inherited dread of the drug. Many medical men are still practising who hold that syphilis is not cured by mercury "unless the gums are touched," but such an assumption is wholly unwarranted. It shows that the remedy has been given with insufficient precautions, and on a system governed rather by routine than by that study of the individual case which should alone be followed in the treatment of every disease. Mercury was originally given by the mouth or by inunction, and wholly for the relief of symptoms. Blue pill in the earlier times and grey powder at a later period were the standard preparations. For those who could afford the expense and the time a visit to Aix for one, two, or three seasons of six weeks each enabled the inunction method to be employed with a minimum of inconvenience. Attempts were made from time to time to administer mercury by other channels than by the mouth and skin, but they were not extensively adopted until intramuscular injections had been made comparatively painless, and surgery had advanced sufficiently to ensure that their administration should be aseptic.

Professor Fournier in Paris, Professor Lang in Vienna, and Sir Jonathan Hutchinson in England must have the credit of administering mercury to cure syphilis, and not to cure the signs of syphilis. The success of their method of treating the disease by small doses of mercury, continued for long periods of time, is well seen in the general condition of the population in our large towns. Syphilis formerly left ineradicable traces upon multitudes of people. It is as rare now to see the signs which were formerly so familiar as it is to see a face badly marked with small-pox. Even in congenital syphilis it is constantly necessary to warn students not to place too much reliance upon the facial aspect or upon the absence of Hutchinson's triad—teeth, eyes, and ears—as an indication that syphilis is absent when other indications point to it as a factor in any given case. The advance of knowledge has fortunately given us more trustworthy tests than the clinical ones upon which reliance had formerly to be placed.

We cannot, however, take the whole credit to ourselves for this improvement. Mercury is, indeed, given earlier and more systematically than it used to be, and the patients are neither salivated nor insufficiently treated, as happened when they were only treated for the signs of

sypilis. But the general standard of health and hygiene has improved markedly during the last quarter of a century. Drunkenness is less common, and the resisting power of the individual therefore is greater. We must consequently refuse the whole credit for the improvement and give a share of it to the community at large. It is clear, at any rate, that the disease is not becoming more frequent, and it is equally clear that the outward stigmata of sypilis are not diminishing because as a nation we are becoming immune to the disease owing to a general sypilization.

SCHAUDINN'S DISCOVERY.

The advances I have mentioned hitherto all date antecedently to the year 1905—a year which must be for ever memorable in the annals of sypilis, because Schaudinn discovered the *Spirochaeta pallida*, and thus allowed of the possibility of a rational line of treatment. Schaudinn's discovery was not accidental. It was the end of a long series of researches undertaken to determine the cause of sypilis. The advance of bacteriology and the discovery of micro-organisms which produce the diseases now called 'infective'—for example, tubercle, osteomyelitis, septicaemia, and others—led every scientific surgeon to the belief that sypilis belonged to the same group, although it presented certain peculiarities which did not bring it quite into line with the rest. Many observers brought forward many organisms, each of which was confidently affirmed to be the sypilis germ. Each in turn failed to prove his claim, and even as late as 1908 the more cautious pathologists preferred to speak of the virus of sypilis rather than of its micro-organism which had already been discovered for three years.

At last the German Academy of Science, at the instigation of Franz Schulze, the Professor of Zoology in Berlin, determined to devote serious attention to the subject. A commission of experts was appointed. Fritz Schaudinn, a young protozoologist who had already made his name in connexion with spirillar infection in birds and in the relapsing fever of man, was entrusted with the actual work of investigation. Erich Hoffmann, a recognized authority on sypilis, was associated with Schaudinn in the research that he might act from the clinical side. By good luck the very first case examined showed a number of motile spirilla which were at once obvious to the trained eye of Schaudinn. The patient was seen on March 3rd, 1905. She was found to have a primary chancre on the left labium majus, with several slightly ulcerated papules on the vulva. Subsequent examination of other cases of sypilis showed the existence of similar spirilla in varying numbers, both in the primary and secondary stages. Schaudinn's familiarity with protozoa soon enabled him to group these organisms into two classes—the *Spirochaeta refringens*, the larger organisms with few spirals and deeply staining, and the *Spirochaeta pallida*, smaller, more slender, with numerous spirals and staining with difficulty. He further determined that the *Spirochaeta refringens* is found in non-sypilic affections as well as in some ulcerated sypilic lesions, and that *Spirochaeta pallida* is found only in sypilis.

The discovery aroused great interest and much controversy, and I well remember the pride with which Metchnikoff demonstrated the spirochaete to us at the Institut Pasteur in Paris on May 13th, 1905. Schaudinn's contention that the *Spirochaeta pallida* was the cause of sypilis was further strengthened by the discovery of the organism in the liver and spleen of an infant with congenital sypilis, and it is now generally admitted that sypilis is a chronic spirillosis. The disease, therefore, has established its claim to be considered infective, and its peculiarities are explained by the fact that the infecting agent is a protozoon and not a protophyte like the bacteria and micrococci causing the other diseases in allied groups. Schaudinn, having completed his life's work, died at Hamburg of an obscure pelvic suppuration on June 22nd, 1906, at the age of 34. A man of modest and retiring disposition, whose friendship it was a pleasure to have, and who could well have been spared to make further advances in the science of protozoology, which he had already made his own.

Metchnikoff, in the meantime, had been doing equally good work in Paris on the etiology of sypilis. He showed that the disease was inoculable not only upon the higher primates, but also upon monkeys, and his experiments

proved that sypilis was not a purely human disease, as was generally stated, and that the infection was in the earliest stages as purely local as tetanus or hydrophobia. He showed that it took an appreciable time for the infection of sypilis to become generalized, and he was so sure of the truth of this important fact that he allowed one of his pupils to be inoculated from two patients who had sypilis, to wait an hour after the inoculation, and then to have the virus destroyed by the inunction of a mercurial ointment which was rubbed in for five minutes. A monkey inoculated at the same time and from the same cases developed a chancre. It was not treated by inunction of the mercurial ointment. The inoculations were performed on February 1st, 1906.

THE WASSERMANN REACTION.

Various observers had worked from time to time at the serum reaction of sypilis, hoping to obtain by this means a test for the disease. In 1906, Wassermann, Neisser, and Bruck drew attention to the sypilic reaction which is now commonly known as Wassermann's test. It is based upon the reaction, first published in 1901 by Bordet-Gengou, that haemolysis is prevented when the complement has first been incubated in the presence of cholera vibrios together with cholera immune serum. What was true of cholera proved to be true of typhoid, and hence came Widal's test. What was true of enteric was also shown to be true for sypilis, and thus Wassermann's test came into use. The reaction was developed by experiments upon apes, and as it proved to be reliable in their case it was soon employed for the recognition of sypilis clinically.

The general outcome of the work of Wassermann, Neisser, and Bruck has been to show that a positive reaction is given by sypilic patients from five to eight weeks after infection—that is to say, from the tenth to the thirtieth day after the appearance of the primary sore, although the reaction has occasionally been positive as early as the eighth day. The reaction is not the earliest sign of the disease, therefore, nor is it the first proof that the sypilis has become generalized, because excision of the sore as soon as the test has become positive has still been followed by sypilic manifestations in the ordinary way. The blood is usually employed for Wassermann's test, but the cerebro-spinal fluid has also been used with great success, more especially in cases of parasyphilis. Major Harrison states that in 489 cases where the test was applied it was positive in 71.8 per cent. of cases of primary sypilis, in 90 per cent. of cases of secondary sypilis, and in 83.5 per cent. of tertiary sypilis. It was only positive in 50 per cent. of patients who were tested during the latent periods—that is to say, when there were no active sypilic manifestations; but it was positive in 80–90 per cent. of cases of general paralysis of the insane, and in 50–75 per cent. of cases of tabes.

Major Harrison is justified in stating:

The value of the Wassermann test lies in the fact that it enables a diagnosis of sypilis to be made in many cases from the fifteenth day after the appearance of the sore, and from three weeks to a month earlier than any assistance could be derived from clinical methods. Its value in this respect may not be as great during the secondary stage, because the clinical signs are then sufficiently clear, but in stages later than the secondary, where the malady frequently manifests itself in a manner which does not display the true character of the underlying disease, the test must be of the greatest assistance in affording evidence that the patient is, at any rate, suffering from sypilis in a more or less active form. Wassermann's reaction is also said to occur in sleeping sickness, which is also a trypanosomiasis, and in some cases of malaria, but for all practical purposes a patient in England who gives a positive Wassermann reaction is infected with *Spirochaeta pallida*, and is therefore sypilic. (*A System of Syphilis*, vol. vi, p. 175.)

A negative Wassermann reaction does not necessarily exclude sypilis, but if it is repeatedly negative when the patient is not taking mercury, he is probably not sypilic, for no spirochaete infection exists. The reaction is by no means ideal, and will probably prove capable of improvement. At present it is useful for a variety of purposes, and it is clearly an advance towards accurate scientific knowledge. It has shown already that the earlier a course of mercurial treatment is begun in acquired sypilis the sooner does the reaction become negative. It has thus set aside, once and for all, the teaching that mercurial treatment should not be commenced until the appearance of "secondary" symptoms. The test can also be applied to

measure the utility of other forms of antisyphilitic treatment, and it has met with marked success in gauging the value of the various organic compounds of arsenic. A time limit has hitherto been employed in the treatment of syphilis, the limit being quite arbitrary and varying with each surgeon's experience and preconceived ideas. It seems probable that by using the Wassermann test we shall be able to say when the spirochaete infection has been destroyed and, consequently, when mercury and arsenic may be safely discontinued. And if we can say when syphilis is cured we shall also be able to answer the many important subordinate questions which hang upon the main issue. The test also serves to differentiate those difficult cases of aneurysm, phthisis, white swelling of joints, and tumours of the testicle, by showing which are and which are not due to spirochaete infection. It is said, too—but of this I have no experience—that in infants it will distinguish between hereditary syphilis and syphilis which has been acquired during or shortly after birth. I confess that it took me some time to appreciate the value of Wassermann's test, and that at first I was inclined to undervalue it, but a better acquaintance with its help in difficult and doubtful cases has led me to think very highly of it.

THE PRINCIPLES OF MERCURIAL TREATMENT.

The cause of syphilis being known and a test having been obtained, it has at last become possible to employ a rational treatment. Before 1905 it was indeed recognized that the disease could no longer be treated in a routine manner, but that each patient must be considered individually. It was recognized, too, perhaps on the analogy of influenza, that syphilis always picked out the weakest tissues in the body, or perhaps it would be more correct to say the tissues which had been subjected to the greatest physiological strain. In one person, therefore, the bones suffer most, in another the skin, in another the mucous membrane, in another the heart and arteries, and in yet another the central nervous system. Many tissues may be affected in a minor degree, but the brunt of the disease is generally borne by one or more structures.

Little by little, too, it had been learnt that syphilis was curable when treatment was persisted in for long periods of time, and that so long as mercury was given the particular preparation was of less importance than the duration of its administration. The adjuvant drugs, upon which too high a value had been placed when mercury was dreaded on account of the reckless manner in which it had been given, were gradually relegated to their proper position. Potassium iodide, guaiacum, sarsaparilla, arsenic, and the whole group of "blood purifiers" were made to give way to mercury by those who had the interest of their patients at heart and were not blinded by prejudice. Formerly, as I have said, our masters taught by precept and practice that it was enough to treat a patient when and so long as he had manifest signs of syphilis. Even at Aix active treatment alternated with long periods of intermission. For some years before 1905 the prognosis of syphilis had become more settled, and in place of a cheery optimism that the disease would work itself out, or the black pessimism that "once syphilitic always syphilitic," a patient would be told that a well regulated and prolonged course of mercury afforded him a fair chance of complete recovery without any of the disastrous results associated with salivation. Precautions were taken to put the patient into the best state of health to meet such a course, and the more especial sources of danger were foreseen and, as far as possible, guarded against. The mouth and teeth were put into the most favourable hygienic condition; the state of the alimentary canal was regulated, and it was understood broadly that whatever might be the cause of syphilis its virus acted most powerfully in the presence of pyogenic micro-organisms, and upon parts where there was a continuously increased blood supply.

Mercury was given in every case of venereal ulcer so long as the cause was unknown, and so long as a single poison was thought to be capable of producing either syphilis or soft sores. No question of diagnosis arose until it was recognized that there were two poisons, the one requiring mercury, the other curable without it. The typical hard sore of syphilis and the multiple soft sores were not difficult to distinguish, but as the general health of the population improved, drink became less fashionable, and cleanliness

was held in higher esteem, the hard sore began to lose the characters assigned to it classically, and the differential diagnosis between it and a chancre became less easy. The "parchment sore" was described, and later the non-indurated syphilitic sore. The dread of mercury persisted, and for fear of giving it unnecessarily the patient was left untreated until he showed unmistakable signs of syphilis. Perhaps the last thing learnt was that the poison of soft sores and the virus of syphilis were not mutually antagonistic, and that it was quite usual for a patient to become infected at the same time with chancroids and syphilis. Careful treatment would cure the soft sores before the incubation period of syphilis had expired, and the more serious disease might thus manifest itself when a favourable prognosis had already been given. From this danger we are saved by the timely use of Wassermann's test.

Blue pill, blue ointment, and grey powder served for many years as the vehicles by which mercury was introduced into the body of a patient with syphilis, but the advance of chemistry and improvements in pharmacy, with the gradual abolition of routine treatment, have led to the production of a great variety of mercurial preparations and a more varied method of administration. A great step in advance was made when the broad principle was established that mercury was the only cure for syphilis, and that it did not matter very much how it was given. Practitioners still exist who pin their faith on a single form of the drug and on one method of administration. It is abundantly clear that any method and any preparation is equally efficacious if it introduces sufficient mercury into the system and for a sufficient length of time to destroy the spirochaetes and the products of their action. We do not yet know and we have still to learn by scientific means how much mercury must be given and how long a time it requires completely to destroy the infection. Personally, I think that small doses for long periods of time are no less effectual than larger doses for the same period, and the small doses are certainly less dangerous. The time has almost arrived when we shall cease to guess, because the accumulated experience of many Wassermann tests will enable us to give a certain answer.

There is no need to employ one preparation of mercury exclusively even for the same individual. Grey powder, perchloride of mercury, and the iodides of mercury are interchangeable with good results. Neither is the administration method of the first importance. Inunction, pills, draughts, and powders held undisputed sway for many years. It is only within our own memory that these means have been displaced to any great extent. When mercury was given for a short time to cure symptoms a course was no great hardship, but as soon as it was given for prolonged periods to cure the disease a mercurial course became so irksome and distasteful to the majority of patients who had acquired syphilis that they shirked it when it was compulsory, or abandoned it altogether when it was entered upon voluntarily. It was often difficult in a long course to prevent gastric disturbance, whilst inunction could rarely be carried out satisfactorily in this country. Other methods were sought, and foremost amongst them was the use of intramuscular injections. Adopted on a large scale and with excellent results in the navy and in the army, intramuscular injections mark the division between the old and the new school in the treatment of syphilis. The old school believed in the efficacy of large doses of some particular preparation of mercury given for short periods; the new school thinks that smaller doses continued for many months are more certainly curative. It remains for modern research to show which is the better method. Intramuscular injections were run a little too hard at first. They were soon found to be unsuitable for every case, and their careless or injudicious use was sometimes followed by untoward results which detracted still further from their undoubted merit. The method is now finding its proper place as a valuable alternative to inunction and oral therapy in the treatment of syphilis. Its employment has emphasized the rule that duration and regularity of treatment are of more importance in the cure of syphilis than the quantity of mercury given or the exact method by which it is administered.

TREATMENT BY ARSENIC COMPOUNDS.

Knowledge had proceeded thus far in 1905 when the discovery of the spirochaete enabled syphilis to be classified

as a form of infective disease, other groups of which were well known. Hitherto it had been considered a disease apart, now it fell into its proper place in the scheme of classification of disease. Dr. H. Wolferstan Thomas, of the Liverpool School of Tropical Medicine, published the results of his treatment of trypanosomiasis with atoxyl, an aniline compound of arsenic. The paper appeared in the BRITISH MEDICAL JOURNAL of May 27th, 1905 (vol. i, p. 1140). The results were so satisfactory that by parity of reasoning atoxyl was soon used in the treatment of syphilis, at first for the disease produced experimentally in animals and afterwards in human syphilis. The drug relieved the symptoms, but was found to be so uncertain and dangerous in its action that its use was abandoned. It more than justified its existence, however, because Ehrlich, with the help of Hata and Wertheim, started, from it as a basis, upon an elaborate experimental research into the action of the organic compounds of arsenic as destructive agents for pathogenic parasitic protozoa. Experimenting at first with the pentavalent arsenic molecule contained in atoxyl they were soon led to the conclusion that the trivalent molecule was a more potent germicide, whilst it had a less poisonous action upon the tissues of the host. Various organic compounds of arsenic were successively produced and were put to the test of experiment. Many were clearly unsuitable, and as Ehrlich's work was purely scientific he did not trouble to give names to the various products, but contented himself with numbering them. The task is not yet ended, but occasional halts have been made when some serviceable body was obtained. No. 418, or arseno-phenylglycin, appeared for a time to answer the expectation of the master who started in quest of a substance which should destroy all the pathogenic protozoa with the least possible injury to the infected tissues. Further work showed that No. 592 or di-oxy-diamido-arsenobenzol was more useful, and in 1909 the hydrochloride of this body was prepared as No. 606, and sold as a commercial product under the name of "salvarsan." The remedy proved very serviceable, but it required a little additional preparation before it could be injected, and it had to be given carefully. It was not, therefore, ideal, and the quest continued. Early in the present year "914" came into use under the name of "neo-salvarsan." It has the advantage of being soluble in cold water, of not requiring any special preparation before it is injected, and of being at least as efficacious as salvarsan. The dose of salvarsan was 0.6 gram, and of neo-salvarsan 0.9 gram; but salvarsan was best administered in a pint of sterilized salt solution at a temperature of 105° F., whilst neo-salvarsan only needs to be dissolved in 6 oz. of freshly distilled water at a temperature of 60° to 70° F. Both salvarsan and neo-salvarsan should only be dissolved immediately before they are used, as prolonged solution seems to alter their chemical properties. Both preparations are as interesting scientifically as they promise to be valuable curatively. They are of scientific interest because it is the first time that pharmacology has embarked deliberately upon the preparation of a highly complex body designed to destroy infective micro-organisms. The problem to be solved was wholly different from that which has provided the vaccines and serums with which we are familiar. These aim at teaching the tissues to fight their own battles. Ehrlich and his fellow workers design to poison the infecting organisms without injuring the tissues of the host, and without necessarily calling upon those tissues to take any share in the process. It is pioneer work, therefore, of the highest order, not dealing with any individual disease, but with the cause which produces a whole group of diseases, each one of which may differ widely in its symptoms and effects. Syphilis, fortunately, is amongst the group of spirillar diseases which has been first attacked, and the work has been crowned with remarkable success. Not absolute, of course, because reactions which answer admirably in the laboratory are by no means uniformly successful at the bedside, where the conditions are much more complex and are less capable of control. The results already attained bear out the contention that the spirochaetes are actually destroyed by the intravenous injection of these organic preparations of arsenic. There is not only a marked and rapid improvement in the signs of syphilis after their use, but there is also evidence that a spirochaete infection which has been in abeyance can be

roused by them into sufficient activity to cause the Wassermann reaction to become positive where before their injection it had been negative. Salvarsan and neo-salvarsan, therefore, may be used as tests for the presence or absence of spirochaetes, and it will be possible by their means to say whether or not a patient is cured of syphilis. We are not yet able to state, however, the exact destructive action of these remedies, nor how far their effects are lasting. It was hoped on their first introduction that a single injection would be sufficient to destroy all the spirochaetes. Such a result seemed unlikely, and the hope has not been borne out after a more extended experience. The general conclusion arrived at is that the earlier salvarsan or neo-salvarsan is given after infection the greater and more lasting is its therapeutic value, but in all cases the injections must be repeated at comparatively short intervals.

My house-surgeons at St. Bartholomew's Hospital have made great use of salvarsan and more recently of neo-salvarsan. Their results have been very satisfactory in causing the speedy disappearance of signs and in giving relief to the symptoms of syphilis. They find that a primary sore disappears more rapidly after an intravenous injection of salvarsan or of neo-salvarsan than when mercury is given; that gummatous ulcerations repair rapidly; that ulcerations of the tongue with leucoplakia, which are in the condition known as precancerous, clear up wholly if cancer is not actually present, but only to a modified extent if the deeper tissues have already become involved in an epitheliomatous growth. They have found, too, that the pain of periostitis and of osteitis in patients who have acquired or congenital syphilis is markedly improved. The results have not been so satisfactory, indeed they are negligible, as might have been expected, in cases of extensive syphilitic necrosis of bone where the pathological condition is due rather to the action of pyogenic organisms than to the *Spirochaeta pallida*. Neither have good results been obtained in cases of symmetrical synovitis of the knees, which we are accustomed to speak of as "Clutton's joints," possibly because there is a tuberculous as well as a syphilitic infection in the children who suffer from them.

Good as these results are, I do not think that the time has come or that it will come for several years when we should pin our faith entirely to these arsenic compounds as a cure for syphilis. They may and ought to be given in the treatment of syphilis with a view to shorten the course of the disease, but mercury should also be administered by some of the ordinary methods and for the usual length of time, lest in the end we find that we have trusted too implicitly to an incomplete scientific experiment. It is only three years since salvarsan was introduced. It has already been improved upon, and the technique of its administration has been simplified. The progress and the results are most satisfactory, but as the administration of these arsenic compounds is not incompatible with the use of mercury, every patient with syphilis should be protected from all risk of failure by the employment of both remedies. The final results to be obtained from arsenic are still unknown; we are well acquainted with the effects of mercury, and its limitations are known.

What has been said this evening will show that the knowledge and treatment of syphilis has been systematized and improved in a remarkable manner in our own lifetime. But if much has been done much still remains to be done. The discovery that a spirochaete is the cause of syphilis gives an individual and human interest to the peculiarities and behaviour of protozoa when they have learnt to become parasitic. A large amount of research has been devoted to the life-history of the protozoa, but much less attention has been given to the protozoa about which nearly everything has still to be learnt. It is certain that the tissues of the body are able to destroy them in many cases, even when they appear to have gained a secure lodgement, for the spontaneous cure of syphilis is of no infrequent occurrence. It is equally certain that they have a remarkable power of remaining latent for indefinite periods. In their normal life-history they show this proclivity, because in patients suffering from syphilis periods of seemingly perfect health are interspersed with recurrent periods in which signs of the disease are manifest. During these periods of inaction the spirochaetes may be roused by the administration of

salvarsan in many cases and by mercury less frequently, and there are few practitioners who have not seen the signs of syphilis become worse or more generalized whilst the patient was upon a mercurial course. Hardships, deviations from good health and other debilitating influences will often provoke syphilitic symptoms which might otherwise have remained in abeyance. It will be interesting to learn, as we probably shall do in the future, how and why these intermissions occur. There is already some evidence to show that the infective protozoa pass a part of their life-cycle in a resting stage, during which they are undiscoverable by any microscopical examination known to us at present. It is assumed that they become intracellular during this period, but more must be learnt about them before any definite statement is possible, and the resting stage may prove to be only one of many interesting peculiarities serving to distinguish protozoal infection from that of the vegetable microbes.

Lastly, the important question arises: What should be the treatment for a case of syphilis as it is seen in general practice? The broad answer is: Make sure of your diagnosis, and make sure of it as early as possible. This can be done soon after the initial lesion has appeared by finding spirochaetes in the chancre either by means of the ultramicroscope or by the Indian ink method. The diagnosis being thus made, it can be confirmed in a short time by employing Wassermann's test. It is not desirable to await this confirmation, because the earlier the organic arsenic compounds are given, the better are the results obtained from them. Neo-salvarsan should be given by intravenous injection, and it should be followed at once by a systematic course of mercury. The neo-salvarsan should be given on the clear understanding that a single injection will not be sufficient except in very exceptional cases, and it should not be postponed because the patient thinks it will do just as well later. The experience already gained shows that the later it is given in the course of the disease the less marked are its effects, and the more frequently must the injection be repeated. On the other hand, there is still too great a tendency to rely exclusively upon the organic compounds of arsenic, and it is necessary therefore to repeat that for the present neo-salvarsan must always be associated with a regular course of mercury controlled by repeated Wassermann tests. These tests should be made during the intervals when mercury is not being taken, for the presence of mercury may render the test negative, although the spirochaete infection still persists.

Potassium iodide should be reserved for the later stages of syphilis, and it should be given in short courses of 10 or 15 grains three times a day. I do not believe it is useful in the earlier stages, as there is no evidence that it destroys the spirochaetes, and it is wasteful to order it in 5 grain doses to be continued indefinitely, as is too often done, because the tissues quickly become habituated to its presence, and excrete it as rapidly as it is ingested. In the light of our present knowledge, a patient is cured of syphilis when he has been through a prolonged course of mercury, and repeated tests have shown that the Wassermann reaction is negative even when neo-salvarsan has been employed as a provocative, and if he has remained free from signs and symptoms for a year after cessation of all treatment.

A SEQUEL TO NOVOCAIN INJECTION.

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THE following case is of interest, as in the past five years novocain has come so much more into general use that it is important for those who are administering it frequently to have brought to their notice any case of true or alleged poisoning.

E. P., an unmarried girl aged 20, in domestic service, at 5 p.m. on November 6th was injected with 40 minims of a 2 per cent. solution of novocain to have three upper incisors extracted. The operation was successfully performed, the patient stating afterwards that she felt perfectly well. She went home to supper with her parents, returning later to her

mistress's house, where she carried out her usual duties, and went to bed apparently in good health at 10 p.m.—that is, five hours after the administration of the novocain.

The following morning her mistress called her as usual; she was unable to get a reply and allowed her to sleep on. The maid remained unconscious for the next twenty-four hours, and her mistress, becoming alarmed, sent for a doctor, who pronounced her to be suffering from cocaine poisoning. The girl's parents were then communicated with, and at their desire one of us (S. G.) saw her at 11 a.m. on November 8th, about forty-two hours after the extraction of the teeth.

The patient was a well-developed muscular girl who rather presented the appearance of a case of cerebral irritation. Her face was slightly flushed, but respiration, pulse, and temperature were normal. She resented any interference. The jaw was tightly clenched; she refused to attempt to swallow or to take heed of what was said to her. She kept her eyes firmly closed; on opening them the pupils were equal and dilated; they reacted to light. The deep and superficial reflexes were normal. She had passed neither urine nor motion under her. The bladder was found to be nearly empty, although according to the history she had been in an unconscious condition about thirty-eight hours. What urine there was was normal in consistence. The catamenia had just commenced.

As every effort to rouse her was useless, she was ordered 2 minims of croton oil, to be given in butter. By 6 p.m. she had considerably improved; though still drowsy she would answer questions. The bowels had acted as the result of the croton oil, and for that purpose she had been able to get out of bed. She had taken milk. Her jaw was no longer clenched, and she was now awake. Two hours later she went to sleep and slept until the morning, when again it was found to be impossible to rouse her, and at 11 a.m. on November 9th her condition was exactly the same as on the previous day. The croton oil was repeated, with the same effect; but when the patient got out for the bowels to act she was not allowed to go back to bed, but was assisted to dress, and at 6 p.m. she opened the door perfectly recovered, and has remained well since.

Novocain is believed to be four to six times less toxic than cocaine, so that $\frac{1}{4}$ grain, the dose administered, was not excessive. Liebl injected himself with 0.4 gram in 10 per cent. solution without producing any toxic symptoms; 0.75 gram, more than eight and a half times the dose given to this girl, caused temporary inconvenience for one and a half hours. Frequently $1\frac{1}{2}$ grains is safely given by lumbar puncture.

There were no symptoms of poisoning when the girl went to bed five hours after the operation, and when first seen by one of us (S. G.) it was stated that she had been unconscious thirty-eight hours and yet there was no distension of the bladder and her clothes were unsoiled; as soon, however, as the croton oil acted she was obliged to wake up because she was under observation; probably, therefore, she had seized her opportunity to urinate secretly.

The curious relapse and ultimate instantaneous and complete recovery combined with the other points in the case, all point to it being a case of feigned coma in a hysterical subject rather than one of toxæmia due to a narcotic poison.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

RUPTURE OF A DERMOID CYST DURING PARTURITION.

I VENTURE to place on record the notes of the following case, as it presents unusual features.

At 2 a.m. on October 2nd I was called to Mrs. K., aged 35, who was in labour. This was her second pregnancy, the first child being 5 years old. The pains had started nine hours previously, but were said to have been weak and infrequent, and the waters had broken when the pains started.

The presentation was occipito-anterior vertex, the head just engaged in the brim, and the os was about the size of a half-crown; the pains were very weak and infrequent, occurring about every ten minutes. The woman's condition was excellent, she was not at all distressed, her pulse-rate was only 84, and I left her, returning about 10 a.m.

Her condition was then about the same, the pains still infrequent and weak; very little progress had been made; at 1 p.m. very little difference could be noted. At 5 p.m. the pains had increased in strength and were more frequent, so the patient was put under chloroform and forceps put on. After the first pull (which made little alteration) the forceps