reservation for the view approaching the Canadian Fall on the return journey.

In conclusion I must express my regret to have skimmed over so many scenes of interest and left out others completely. My only excuse is that the region we have passed through is so replete with all that is grand in nature that it would require an abler hand than mine to give it one-tenth part of what is really its due, and I will feel that this humble attempt will have attained all I could wish for it if it draws the attention of my professional brethren to what I am sure they will agree with me is an ideal holiday.

ART. V.—*Remarks on the Present-day Diagnosis, Treatment, and Prognosis of Syphilis.*^a By J. JOHNSTON ABRAHAM, M.D. (Dubl.); Resident Medical Officer, London Lock Hospital, Harrow-road, W.

THE question as to how soon a presumed primary syphilitic lesion should be treated after it had made its appearance was a somewhat debatable point until quite recently, on account of the frequent difficulty of exact diagnosis before the appearance of definite secondary manifestations. When Ricord published his classical researches and differentiated for the first time between the soft, or non-infecting, sore and the contagium of primary syphilis, the distinguishing points given were:—that the “chancroid” was soft in consistence, often multiple, painful, appeared a few days after infection, and was liable to be followed by suppurating bubos in the nearest lymphatic glands; on the other hand, the “hard chancre,” as its name would imply, was firm, single, appeared often as late as four to six weeks after infection, and was followed by hard, indolent bubos in the nearest lymphatic glands.

Clinical experience, however, demonstrated that sores

^a A Thesis read for the Degree of Doctor of Medicine in the University of Dublin on December 19, 1908.

which at first appeared soft, afterwards often took on a firm consistence, and the subsequent appearance of secondary symptoms proved them to be syphilitic.

Again, reliance on the supposed length, or shortness, of the incubation period, based on the patient's statements, has been found practically useless as a differentiating point in many cases, because the patient either has been liable frequently, from his habits, to infection, and so cannot definitely fix the date of inoculation, or gives for some cause or other a wilfully inaccurate history.

Finally; the dictum that the hard chancre is single, though true in the vast majority of cases, has been shown not to be always so in man, whilst in women the appearance of contiguous chancres, one on either labium majus or minus, is a matter of quite common occurrence (Shillitoe).

The discovery of the specific organism of soft chancre by Ducrey did not help as much as might have been expected, as the organism is difficult to find, grows badly on most media, and even when found is not contra-indicative of syphilis, as the syphilitic virus has often been implanted on a chancroid basis.

For these reasons, therefore, most physicians declined to urge active anti-syphilitic treatment in doubtful cases, preferring to wait till secondary symptoms clinched the diagnosis.

Recent advances, however, notably the researches of Schaudinn and the serum reaction of Wassermann, have put a new and apparently satisfactory weapon in the hands of the clinician, and now the discovery of the *Spirochæte pallida* (*Spirochaeta pallidum*) in a scraping of the chancre, or a positive Wassermann, may be considered sufficient justification for immediate specific treatment.

Wassermann's Reaction.—In practice the details of Wassermann's reaction are cumbersome and constantly being altered with the idea of simplification by its author and his pupils. The principle, however, is simple, and it alone need concern us here. It is as follows:—

A suitable animal (Wassermann originally used a

sheep) is inoculated with alcoholic extracts of a syphilitic fœtus, and from it a serum is prepared. This serum is a hæmolysin—that is, it has the power of disintegrating red blood corpuscles. It is, moreover, a specific hæmolysin: it will disintegrate the red blood corpuscles of a normal individual, but has no effect whatever on those of a patient suffering from syphilis. If, then, blood drawn from a suspected case has its corpuscles destroyed by the serum that case is free from syphilis.

A caution is necessary, however. The patient must not have had any mercurial treatment before trying the reaction, as mercury seems to inhibit the hæmolysin. Experience has yet to discover, however, whether the reaction will prove as useful as the Widal test in typhoid.

Once a diagnosis has been arrived at the question of treatment immediately forces itself upon one; and here two drugs, mercury and iodine, or one of the iodides, have stood the test of time, whilst a third, arsenic, has lately come into much prominence. It is, therefore, on the various methods of using these, their indications, and contra-indications, I wish briefly to dwell.

Preparations for Treatment by Mercury.—Before a course of mercury is begun the patient's weight should be taken, as on it largely depends the dosage, short of salivation. Similarly, it should also be taken week by week whilst under treatment—a rise indicating that all is well and the drug can be pushed with safety, a fall, especially if continuous week by week, pointing to protoplasmic poisoning, and indicating reduction, temporary cessation, or complete stoppage of the drug according to the severity of the case. Undoubtedly one of the main causes which threw this invaluable remedy into temporary disrepute, and incidentally stimulated the use of potassium iodide; in the middle of last century, was the enormous over-dosage of mercury practised—many of the specimens preserved in museums of the supposed ravages of the disease being excellent examples of mercurial necrosis produced by the

physician and not by the supposed virulence of the contagium.

Incidentally it may be noted that fat patients, especially women, stand mercury remarkably well, whilst thin patients, otherwise healthy, very quickly, even with small doses of mercury, show poisonous symptoms.

For practical purposes, therefore, women under eight stone and men under ten should be treated with especial care, and the minimal dosage capable of suppressing symptoms should be used.

Condition of the Patient's Teeth.—A second point which must be carefully attended to is the condition of the patient's teeth. It is remarkable how free from stomatitis patients with good, sound, teeth remain under treatment. On the other hand, the presence of one or more carious stumps causes endless trouble when any systematic effort to keep up continuous treatment—including even the much-lauded injection methods—is attempted. As a consequence of this knowledge all patients admitted into the London Lock Hospital have their teeth examined on admission, all carious stumps are carefully noted on a special dental chart, and treatment is not pushed till they have been through the dentist's hands.

Since adopting this as a routine we have practically got rid of the endless troubles from salivation, gingivitis, stomatitis, neuralgia, dental ulcers, &c., formerly so common in the underfed patients, often with an alcoholic history, with whom we have to deal, and so have not the disappointment of stopping treatment for indefinite periods, and watching our patients' systems becoming gradually undermined by the continuous ingestion of septic fluids from the mouth.

As a further prophylactic, following the "Aix" custom, each patient is required to gargle his mouth, morning and evening, with a solution of alum, 15 grs. to the oz. This hardens the gums, allows of the frequent use of the tooth-brush, and prevents incipient gingivitis.

A common place for gingivitis to start is the base of the

two lower central incisors. When this appears it may be readily checked by painting the inflamed area daily with copper sulphate, 10 grs. to the oz.

A third condition—namely, the presence of albuminuria—is stated to be a contra-indication to the use of mercury. On this point one can speak only with caution. Personally we have never seen any bad effects from its use in the condition.

On the other hand, one must always bear in mind that the albuminuria may be a symptom of syphilitic nephritis, a condition not so rare as is generally supposed; and when this condition occurs, as in a case recently under the care of Mr. Arthur Shillitoe, the exhibition of mercury has an almost miraculous effect in clearing up symptoms.

Coming now to the methods of administering mercury, it may be given in six ways:—

- (1) By inunction.
- (2) By fumigation.
- (3) By baths.
- (4) By the mouth.
- (5) By intramuscular injection.
- (6) By intravenous injection.

Treatment by Inunction.—This method is one of the most valuable at our disposal, and is largely employed by us, as undoubtedly patients can be very rapidly brought under the influence of the drug by its use, though it is still uncertain whether the mercury is absorbed by the skin or by inhalation. It is the method *par excellence* in the treatment of congenital syphilis in infants, and so satisfied are we with it that no other treatment is adopted in our children's wards. Unguentum hydrargyri, B.P., is used; the amount is a mass of the size of a hazel nut; it is spread on a binder, and applied daily. For adults we apply it as a collar, armlet, binder, or spica, and, as the patients are not confined to bed, the constant friction of movement, clothes, &c., rubs it in quite as well as massage.

The objections to its use are:—

- (1) Inability to regulate the dosage. In warm weather,

as during the past summer, with patients perspiring freely, we had to give it up owing to the rapidity with which salivation was produced even by small doses.

(2) A second objection is its uncleanness. To avoid this we at one time tried Unguentum Hydrargyri Ammoniati, but this ointment proved of insufficient strength except during hot weather.

(3) A third objection is that when massage is used the masseuse is liable to develop sore gums. This is obviated by using the binder as above.

But in spite of these drawbacks in cases where a well-marked papular or tubercular eruption is present this treatment is always deserving of trial owing to the rapidity of its action.

Treatment by Fumigation.—In this method calomel is used. Its usefulness is most marked in the treatment of

vulvar or peri-anal condylomata, in extensive secondary ulceration of the fauces, in vaginal chancre, or chancre of the os. Large cauliflower masses of condylomata will yield to a daily fumigation of five minutes in from ten to fifteen days. It is best applied as follows:—

A thick glass tube, eighteen inches long, is drawn out to a blunt point at one end; there is a bulb in the centre of the tube for the calomel powder, and an inflating apparatus, like that of a Junker's inhaler, is attached at the other end.

The calomel receptacle is heated with a spirit lamp and the sublimed vapour is puffed directly on to the sores.

In practice this method is usually combined with one

of the other constitutional methods—*e.g.*, pills. It is quite painless.

It is stated, however, by Mr. Arthur Shillitoe that in some cases where iodides have been given during the course of fumigations much pain has been experienced. This pain disappeared when iodides were stopped.

Baths.—This method combines the effects of calomel fumes with a vapour bath.

The patient is enveloped in a waterproof sheeting, and 30 grains of calomel are sublimed over a water bath underneath the patient's chair. Treatment lasts half an hour, and is continued daily. After a bath the patient is confined to bed for two hours.

This treatment is especially indicated in cases of ecthymatous ulceration of the lower limbs and arms. When these have cleared up the baths are stopped and treatment by the mouth adopted.

Treatment by the Mouth.—This is by far the most usual method, especially in private practice, on account of its great convenience. Of pills the most powerful is the Pil. Hydrargyri, B.P. It contains 30 per cent. of mercury. As manufactured, however, it is often so insolubly coated that it is passed unchanged per rectum. It should, therefore, be prescribed fresh, uncoated, in a soft pill mass easily flattened by pressure between finger and thumb. We use two grains per diem for patients under eight stone, and three to four grains for those over, according to weight, &c.

Another much used pill is the basic salicylate of mercury. It contains 60 per cent. of mercury, and is given in doses of one-fifth of a grain *bis terve in die*.

Its advantages over the official pill are that it never causes diarrhoea or griping, salivation and gingivitis are uncommon, it is rapidly absorbed without disturbance of the gastric mucous membrane, and it relieves the vague osteocopic pains of secondary syphilis very rapidly.

Its disadvantages are that it is not a very powerful pill, and in our experience condylomata and mucous plaques not infrequently develop while under its influence.

Tannate of Mercury, in doses of one to two grains twice daily, has the advantage of being insoluble in the stomach and soluble in the jejunum. It is useful, then, when the Pil. Hydrarg. cannot be taken. Hutchinson's pil—Hyd. c. Cretâ—as prescribed by Hutchinson, in quarter-grain doses every hour or two hours, is not much used by us except in cases of diarrhœa, where, combined with opium or Dover's powder, it often proves extremely useful. Diarrhœa, however, from the use of the usual mercurial pills is in our experience uncommon.

Owing to the convenience of pills, mixtures are not much used. But in cases of secondary iritis it has been our experience that the Liquor Hydrargyri Perchloridi, usually combined with iodides, has a more rapid effect than the insoluble preparations; and the same is true in cases where one wishes to get rid of a rash on the face as quickly as possible.

Treatment by intramuscular injections, although practised in Italy as early as 1825, was soon discontinued, owing to the ignorance of antiseptic precautions then prevailing. It has recently been revived largely in this country and on the Continent, more especially in military practice.

The most suitable site of injection is the gluteal region, in the area above a line between the anterior and posterior superior iliac spines (Lane's line). By keeping strictly to this area the hip-joint cannot be entered, and the patient is able to sit about in comfort after the injection. Two varieties of mercurial injections we use—(1) Soluble; (2) Insoluble.

Of soluble preparations those most used have been:—

(1) Sal Alembroth, 10 minims of a 5 per cent. solution twice weekly.

(2) Hydrargyri Perchloridum, $\frac{1}{2}$ gr. in 10 minims every second day.

(3) Hydrargyri Succinimidum, $\frac{1}{4}$ gr. in 10 minims every second day.

The advantages of these preparations are the rapidity with which they are absorbed.

Their disadvantages are :—

(1) They have to be injected every day or every second day, entailing much trouble to both patient and surgeon.

(2) The difficulty of maintaining asepsis owing to the frequency of the injections.

(3) The great pain produced.

This is the really great objection to their use, and is especially so in the case of the perchloride—intense pain like sciatica being produced, and a brawny induration appearing at the puncture point without any evidence of sepsis. On account of this pain it is impossible to induce patients to submit to the treatment for any length of time, and we have entirely given up the use of soluble mercurials.

Of insoluble preparations two only need be mentioned—

(1) *Calomel cream*, prepared after the formula of Lambkin.

(2) *Oleum Cinereum* (grey oil), a preparation of metallic mercury in olive oil stiffened by various animal fats, especially palmitin.

Of these two preparations calomel cream is much the quicker in its action, and so is indicated in cases with extensive secondary ulceration. It is given in injections of 10 to 15 minims, containing $\frac{1}{2}$ to $\frac{3}{4}$ grain of calomel, once a week. It is much less liable to be followed by septic induration and inflammation around the injection point than is the case with oleum cinereum; but the great objection to its use is that in some 30 per cent. of cases it is followed by acute pain. This pain differs from that produced by the soluble mercurials in that it comes on on the third day after injection and not immediately or within twelve hours afterwards as with perchloride. On account of the pain produced Fournier condemns it root and branch, stating that 90 per cent. of his cases developed pain. We, however, are a more phlegmatic people than the French, and it has been noticed that in our cases they were Jewesses, Frenchwomen, and Italians who usually complained.

Nevertheless, on account of the undoubted pain produced, for routine treatment, we have fallen back upon grey oil (*oleum cinereum*), and find it most satisfactory. It is compounded in such strength that 10 minims contain one grain of Hg, and so the dosage is 5 to 10 minims per week. It is practically painless, but unless careful antiseptic precautions are taken is liable to be followed by painful induration going on to suppuration at the seat of puncture. These brawny areas heal, however, rapidly on incision and fomentation.

The advantages of the treatment are:—

(1) The absolute knowledge that the patient is getting the mercury. This is why the treatment is so useful amongst soldiers and hospital patients, whose mental calibre is so poor that they often throw away, or forget to use, the medicine supplied them.

(2) Salivation and gingivitis are comparatively infrequent, even in cases with septic mouths.

(3) Symptoms are rapidly got under control.

The disadvantages are:—

(1) The impossibility of calculating the rapidity of absorption. Each patient in this respect is a law unto himself.

(2) Though gingivitis is rare, when it does occur there is great difficulty in curing the condition, as the surgeon has no means of preventing the absorption of mercury already injected.

(3) It is probable that it has no effect in preventing abortion.

This is an exceedingly important point, on which more evidence is required. Our cases are too few to dogmatise. One case, however, which had been under weekly injections continuously for eight months was delivered of a still-born foetus, in which enormous numbers of spirochætes were seen in smears taken from liver, spleen, and bone marrow.

As to the length of time injections should be continued opinions vary greatly. Army surgeons in India find that

gingivitis becomes troublesome if they are continued for more than six weeks.

In this country, following the lead of Lambkin, thirteen weeks is considered sufficiently long to prevent active symptoms recurring. It was even suggested that if the case was seen and treated sufficiently early this was enough to kill the spirochæte. Unfortunately, this has been found to be incorrect; and some of the most marked cases at present under treatment here are recurrences after this so-called "full-course" of treatment. Consequently, we have continued injections indefinitely provided the patient's weight does not recede, and no signs of gingivitis ensue. One patient recently discharged had had sixty-five injections of grey oil, and left the hospital two stone five pounds weightier than on admission.

Intravenous Injections have now been given up by most surgeons. Soluble mercurials were used, but difficulties in getting the patient's consent, irritant diarrhœa, the necessity of daily injections, and the constant risk of thrombosis and pyæmia, narrowed the field of usefulness so much that it seemed unjustifiable to continue.

Iodine and the Iodides.—The subject of the use of iodine and the iodides may be briefly summarised thus:—

(1) It is now generally admitted that their chief usefulness is in the third stage; combined with mercury they may be useful in the secondary; in the primary they are useless.

(2) Potassium iodide is the most useful of the salts, but on account of its depressing effect it should always be combined with ammonium carbonate, as suggested by Sir James Paget.

(3) The combination of sodium and ammonium iodide with small doses of arsenic is less liable to produce symptoms of iodism than the most powerful salt.

(4) When an iodide rash appears doubling the dose is useless. Since adopting the suggestion of Ward, iodide rashes have practically disappeared from our hospital. The patient is instructed to drink half a pint of hot water

half an hour before taking iodides, following the drug with an equal quantity of hot water fifteen minutes afterwards.

(5) In cases of mercurial stomatitis iodides should not be given, as thereby the system is flooded with a soluble mercurial. Instead magnesium sulphate in the form of the *Mist. Ferri Laxans* of most hospital pharmacopœias is given, with frequent gargles of peroxide of hydrogen.

(6) Instead of the iodides, iodine, in the form of "Iodopin" (iodine in oil of sesame), is often useful when the weight is falling, and this is especially so with regard to combinations of iodine and glycogen such as "Iodolose."

(7) In the occipital headaches so frequently complained of in the secondary period, iodides have a marvellously remedial effect.

(8) When gummata have been cleared up under the action of iodides, small doses of mercury should be continued for some months. Otherwise the tendency to relapse is great.

Arsenic in Syphilis.—This drug has recently come very much into prominence in the treatment of syphilis.

In the form of Fowler's solution it has, of course, been used for years, combined usually with the iodides. But it was the fancied resemblance between the spirochæte and the parasite of sleeping sickness (*Trypanosoma gambiense*) and the known effect of organic preparations of arsenic, particularly atoxyl, in this condition that suggested the use of arsenic as a substitute for mercury in the treatment of syphilis.

Brilliant results from the injection of atoxyl have been recorded by numerous Continental physicians, particularly Uhlenhuth and Hallopeau. But, on the other hand, fatalities, such as acute arsenical poisoning, blindness, deafness, paraplegia, &c., in certain cases showed that as regards syphilis at any rate atoxyl was certainly not deserving of its name in all cases; and accordingly English surgeons have been loth to use it.

There is a short account of four successful cases in the *British Medical Journal* of December, 1907. But it is

largely due to the initiative of Lambkin that it has recently been much before the medical public. Lambkin used atoxyl first, and later another organic aromatic preparation of arsenic of the arylarsonate group which was a close imitation of atoxyl, containing 22.8 per cent. of arsenium, said to be much less toxic than atoxyl, and to have one-fortieth of the toxicity of arsenious acid.

Results published in the *Journal of the R. A. M. C.* for April, 1908, the *British Medical Journal* of August 15th, 1908, and the *Lancet* of December 5th, 1908, would indicate that the treatment was worthy of an extended trial. Accordingly, we put some twenty cases on this new treatment, using two of these proprietary articles, *Soamin* and *Orsudan*. All the trials were carried out on women, and the amount injected was 10 grains twice a week till 100 grains were given.

The following is a summary of the results and the conclusions drawn from them:—

(1) The injections are painless and are not followed by sepsis.

(2) In no case was any symptom of arsenical poisoning noted.

(3) Contrary to what one might have expected, knowing the extensive use of arsenic amongst dermatologists, the effect on rashes was practically nil. Knowing that rashes, particularly roseolous rashes, tend spontaneously to disappear, we could not satisfy ourselves that any improvement noted was due to the drug. In not one case had the rash disappeared when the course of 100 grains was completed in five weeks.

(4) In several of the cases mucous plaques and fresh condylomata appeared while the patients were under treatment; some condylomata, present when the treatment commenced, healed; whilst others remained *in statu quo* at the end of the course.

(5) In none of the cases could we honestly say that at the end of the course all symptoms of the disease had disappeared.

(6) Knowing the effects of mercury in the same period of time, we reluctantly came to the conclusion that arsenic in these forms was undoubtedly inferior to mercury.

(7) After the completion of a course mercury was given to all the cases, and we now find Lambkin in his latest publication advocated this also (*Lancet*, December 5th, 1908).

Our results, therefore, obtained in women contrast most unfavourably with Lambkin's published results in men. This may be due to—

(1) A greater resistance to arsenic in women.

(2) To the fact that, considering the lesser body weight of women, we used 20 grains per week instead of 30 as recommended by Lambkin for men.

Accordingly, we are now trying larger and more frequent dosage. But results up to now are not sufficiently advanced for comparison (December, 1908).

Having now considered the treatment, I should like, in conclusion, to review the opinions that are held as to the length of time treatment should be continued with the idea of eradicating the disease.

Opinions on this all-important subject still differ greatly. In the treatment of congenital syphilis many consider six months ample, because as a rule no symptoms appear after that period. It is probably much safer, however, to treat each child as an adult, and continue for the two years which general opinion considers the minimum for an adult. Neisser, indeed, as a result of his experiments on monkeys in Java, puts the minimum as high as four years. He bases his opinions on the following facts:—

(1) He found that a monkey suffering from the disease was incapable of re-inoculation with the virus as long as he showed symptoms of the disease. He could not produce a fresh chancre on a subject already infected.

(2) At the end of two years' treatment he still found he was unable to produce a fresh chancre in an infected subject, and therefore concluded it still had the disease.

(3) At the end of four years' treatment he discovered he was able to produce a fresh primary chancre, and that the monkey behaved as if it had developed syphilis for the first time. He therefore concluded that under treatment it had got rid of its first infection and was in the same state as a subject that had never had the disease.

Four necessary corollaries follow from the results of this experiment:—

(1) That syphilis once acquired and cured is no preventive of a second attack.

(2) That even four years' mercurial treatment is not a prophylactic against a fresh attack.

(3) That as it was impossible to reinfect till after four years' treatment, therefore four years' treatment is necessary to cure the disease.

(4) That the reason a patient who has once had syphilis does not develop it again, when exposed to infection, is because he is still suffering from the disease and requires further treatment.

It is obviously impossible to repeat the same experiment in man. But it may be possible to apply Wassermann's reaction for the same purpose. After stopping treatment for some months, to eliminate the effects of mercury, a blood test which produced a disintegration of the red blood corpuscles of the patient would indicate that he was at last free from all taint of the virus. Should future results show that this reaction can be relied upon to distinguish absolutely between the blood of a non-syphilitic, or cured syphilitic, and that of a patient still carrying the active virus in his body, we shall have a weapon of incalculable value in diagnosis and prognosis of this most protean of diseases.

I have to thank Mr. Arthur Shillitoe and Mr. Charles Gibbs for permission to make use of their cases for the material for this article.