Late Local Effects.—These consist principally of ecchymoses and gangrene of the vein, and ulcer; of these, the most common by far is the "injection ulcer," which is due in most cases to the deposition of the solution in the tissues round the vein. It is serious and painful, and four to six months elapse before a cure is effected. No case of injection ulcer should ever occur; it is in all cases due to carelessness in the administration of the injection. In most cases the operator has entered the vein successfully, but in the course of injection, through a momentary unsteadiness or movement of the patient, the vein has been penetrated and the solution deposited in the surrounding tissues. This should never happen if the precaution of withdrawing the plunger of the syringe in moments of doubt has been observed. The last late local effect is the complete thrombosis and gradual elimination of the vein. This takes some three to twelve months to occur, the vein gradually becoming hard and cord-like to the touch. Over the bony surfaces the process is slow, but in the thigh it is much quicker, and as a general rule it may be stated that the vein should be practically obliterated in twelve months' time.

There is only one important late general effect—pulmonary embolism. This is a very rare occurrence; in some ten thousand cases treated at the Waterloo Hospital there has so far been no record of such a sequel. Yet there is a chance that this may occur, since there are records in the medical literature of many cases.

In those cases which I have indicated above where no change takes place after injection there is one infallible method of treatment, which is known as the "twin injection." It is generally necessary to make use of this when the veins are very large with extensive varicosity. The selected vein receives simultaneous injections of 4 c.cm. of lithium and 2 c.cm. of quinine urethane solution, the sites of injection being 3 to 5 inches apart. It is possible to do this single-handed by injecting the lithium first and the quinine immediately afterwards, but in actual practice it is much more satisfactory to have assistance for one of the injections. The quinine must never be injected first, because, if this is done, when the lithium is being injected and the barrel of the syringe is being pulled out, there is a great likelihood of withdrawing some of the quinine from the vein, and this immediately causes clotting in the syringe. This "twin injection" invariably causes clotting, but it must be emphasized again that it should not be employed unless the veins are very large.

Other solutions have been tried by us, but have been abandoned for various reasons. Pure carbolic (98 per cent.) is a sticky solution; it spoils the syringe, the dose of 1-3 m is difficult to assess owing to the stickiness, and it causes perivitis, and, occasionally, haematuria. Alcohol (50-100 per cent.) in a dose of 1-5 m is too painful. Sodium citrate (20-50 per cent.) has been given in doses of 0.5 to 4 c.cm., but the results proved unreliable. Sodium salicylate (20-50 per cent.) in a dose of 1-4 m was also unreliable; about 60 per cent. of results are good if this solution is used exclusively.

In a number of hospital cases there is severe varicose vein ulceration. If the ulcer is very large the limb should always be x-rayed in order to determine whether or not there is any periostitis. Should the bone be involved the ulcer will naturally take longer to heal under treatment. In all cases a Wassermann test should be performed.

Treatment of Varicose Ulcer.

If no veins are visible Unna's paste bandage should be applied once a week. Where veins are present they should be injected weekly in addition to the use of the bandage. In severe cases the base of the ulcer should be injected with quinine urethane. Two sites are selected, and into each 2-5 m of quinine is injected at an oblique angle, the one from above the other from below. In this way a small "island" of the ulcer is cut off and heals; our method is to attack and heal a series of "islands" until the entire surface of the ulcer is healed. In very small ulcers 2½ per cent. tannic acid solution on lint is applied to the part every four hours. This forms a crust over the surface of the ulcer and stimulates healing under the crust.

The treatment of an "injection ulcer" is as follows. For the first few days hot fomentations are applied. They are followed by pure hydrogen peroxide, and then by the application of calamine lotion. These ulcers are very painful, and the patient should be warned that a cure will not occur in less than three to six months.

The contraindications to treatment are five in number.

(1) Pregnancy; the veins will probably disappear after confinement, and treatment should never be given during pregnancy. (2) Deep thrombosis. (3) Acute septic thrombo-phlebitis; at least three months must be allowed to elapse from the time that all inflammation has disappeared before treatment is attempted. (4) Advanced heart, lung, or kidney disease; diabetes; and high blood pressure. (5) If the varicose vein ulcer is very septic it is advisable to clean it up first before injection treatment is attempted.

We have found from experience that the following rules are highly important, if a satisfactory result is to be obtained in the treatment of varicose veins by this method.

Rules for Injection.

1. Never inject more than 1 c.cm. at the first sitting.
2. Never inject more than 6 c.cm. at the one sitting in one limb.
3. Never inject more than 2 c.cm. of quinine urethane at the one sitting.
4. Never inject more than 4 c.cm. of lithium or sodium chloride.
5. Inject weekly.
6. Avoid small doses and multiple punctures.
7. Work from below upwards.
8. Never inject if the veins are painful, or if at the time of the introduction of the solution there is bulging of the veins.

Remarks.

An injection ulcer appears in about 1 per cent. of all cases. With quinine or lithium about 20 per cent. of cases will not "take." These 20 per cent. of cases will "take" with the twin injection. For a few days following the injection the limb may be painful, and patients should be warned of this; they should also be warned of the local and general effects. When injection is performed near the ankle some oedema of the feet nearly always results. The final results may be very good, but varicose veins may form in other parts of the limb, and even veins which have thrombosed as a result of the treatment may recanalize.

Provided that there are no complications or contraindications there are no cases which will not, with care and time and judgement, respond satisfactorily to treatment by the injection of suitable sclerosing solutions.

INTRAVENOUS SCLEROSING SOLUTIONS.

BY

T. HENRY TREVES BARBER, M.D., B.Sc.

It has frequently been stated that the nature of the clot, subsequent to sclerosing injections, is dependent upon the chemical used for the injection, some forming a soft friable clot, others a firm adherent one. As a matter of fact the consistency of the clot is entirely independent of the drug injected.

To elucidate this important question the following experiments have been made. They prove that: (1) the injected solution has but a very fugitive effect upon the endothelium of the injected vein; (2) no primary formation of a clot is possible from the blood itself with the solutions and doses used, since the normal clotting of the blood (*in vitro*) is retarded by its admixture with them.

Withdraw from a varicose vein 2 or 3 c.cm. of blood, and pour into a test tube, A; it is dark red. Leave the needle in place, adjust it to a syringe charged with 5 c.cm. of a 20 per cent. solution of NaCl and inject. When the injection is about half-way done, aspirate some of the blood into the syringe; it will be seen to be of a brighter colour. At the end of the injection the piston is immediately and slowly withdrawn. Brilliant scarlet blood flows into the syringe for fourteen to forty-five seconds, according to the rate of the circulation in the selected vein (rapid change of colour is found in those vessels having a sufficient circulation). In all cases, however, within a full minute of terminating the injection the blood appears to have resumed its normal colour.

Withdraw 2 c.cm. of this mixed blood and pour into another test tube, B. It is found that this blood remains a bright scarlet for many hours, and also remains liquid for some hours after the normal blood has not only coagulated but a large clot has formed.

These reactions are, of course, more marked when a considerable amount of the solution is still in the blood (large dilated ampullae) and when it is withdrawn immediately after the injection has been given. The withdrawal of this amount of medicated blood has not—in my experience in over 20 cases taken at random—prevented the veins from reacting and being cured. Further experiments might be undertaken with other drugs, so as to discover whether the desired obliteration could be accomplished by injecting followed by the immediate withdrawal of as much of the drug as possible, so that more active doses might be used and idiosyncrasy avoided.

Deductions: (1) The solution remains but for a very brief period *in loco*. (2) Addition of NaCl solutions (20 per cent.) to blood withdrawn from a varix retards its clotting *in vitro*.

Since the solution remains in the vein for something under one minute, and as we know that for about twelve hours no naked-eye or microscopical changes are discernible in the vessel walls, after which time, however, changes begin and are progressive to the formation of a blood clot, it seems only logical to deduce that this clot is the after-result of a momentary, severe, but purely local chemical reaction on the endothelium at the time of the injection. The physical properties of this clot are most likely due to the extent and degree of the reaction from the sclerosing effect of the solution, and whether or not some degree of infection was present in the vein at the time. If the vein is free from active infection and the reaction severe, the clot will be hard, adherent, and possibly extensive. Should there be any infection present the clot might soften, break down, and cause an embolism at some future date. All cases of emboli, if they are ever to be directly attributed to sclerosing solutions, as being their sole origin, must occur either during the injection itself or at least a very short time after it. A few such cases have been reported from time to time with quinine and urethane, and also with sodium salicylate; the recorded symptoms are suggestive of some embolic complication, but of a transitory nature, and the patients recover very rapidly. Other cases are on record where huge doses of drugs have been injected, doses that converted an otherwise non-productive infarct substance into an infarct-forming one, causing immediate clotting of the blood *in situ*. It is not remarkable that in such circumstances fatal cases have been recorded.

As already stated, NaCl retards coagulation; it is improbable that at any time, in normal conditions, this solution is ever capable of giving rise to an embolism. On the other hand, it has frequently been accused of always causing pain, and often very severe reactions. It sometimes causes a very intense reaction, so may quinine and sodium salicylate, but under these conditions (due entirely to the individual) there is little left to choose between them as regards the intensity of the pain and discomfort experienced by the patients; the end-results will, however, generally be excellent.

Colt, using sodium salicylate with 10 per cent. NaCl, stated some time ago that he believed it was better to use large quantities of medium strength solutions than small concentrated ones; the theory seems to be borne out by the above experiments. Gillespie and Strobel state that they, too, use large doses of 20 per cent. NaCl—10 c.cm. for one injection, up to 20 or 30 c.cm. at one time; or with 5 or 10 c.cm. three or four injections can be made at one sitting. They claim that with this solution a more adherent and extensive thrombosis, and a better end-result, is obtained than with other sclerosing solutions.

Why are NaCl solutions the most active in this form of treatment? Probably because they have a greater destructive power upon the endothelium, and because it is possible to give such large doses that the chemical effect upon the vessel wall is proportionately of longer duration than it is with other drugs used in small but concentrated solution. The reaction on the vessel is greater, more lasting, and probably more penetrating, which may account in part for the transitory pain which is frequently, but not

invariably, encountered. These solutions of NaCl are not necessarily painful, but only so under certain conditions due to the pathological state of the veins themselves. At all events, it may be affirmed that they retard clotting of the blood, and that therefore they are incapable of giving rise in the ordinary way to any thrombosis, either at the time of injection or subsequently; they are probably the most effectual and the safest to use at present, and will remain such until the ideal solution has been discovered.

In conclusion, mention might be made of a new and very interesting sclerosing agent—namely, sodium morrhuate, as recommended by Higgins and Kittle (*Lancet*, January 11th, 1930). I have used it in a small number of cases with good results. If time and experiments should prove it to be always reliable and safe, it will probably supersede all other sclerosing solutions now in general use.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

ACUTE BRONCHITIS WITH VAGINAL BLEEDING AND ACUTE ABDOMINAL PAIN.

THE following case, in which an attack of acute bronchitis with abdominal pain and vaginal bleeding simulated a ruptured ectopic pregnancy, is perhaps of sufficient interest for publication. The occurrence of bleeding per vaginam from the uterus or adnexa, when the origin cannot clinically be determined, is a puzzling feature in questions of abdominal diagnosis. Cases of such haemorrhage depending on general or local vascular disturbance have long been recognized and cannot be rare (vide Kelly's *Gynaecology*, p. 708), and no doubt many of the elect have from time to time been deceived.

A married woman, aged 40, was admitted to the Withington Hospital on October 30th, 1929, as a case of ruptured ectopic pregnancy.

Previous Medical History.—She had had two children, the second being born fifteen months previously. There was no history of abortions, and the periods were regular. No leucorrhoea was present.

Present Illness.—This started with acute abdominal pain, which was most marked in the lower abdomen, and especially on the left side. Lower abdominal hyperaesthesia and tenderness were present. Rigidity was not great, owing to a lax and obese abdominal wall. Before admission she had lost per vaginam three-quarters of a pint of blood. The temperature was 98.6°, the pulse 90, and the respirations 28.

Bimanual Examination.—The cervix was found to be closed; the uterus and adnexa were normal. A slight boggyiness was felt on the right side, possibly due to constipation, since it disappeared later after an enema. Blood was deposited on the examining finger.

Lungs.—The acute bronchitis was not well established till later, but rales and rhonchi were heard in both lungs. The respiration was hurried; the facies was anxious and slightly cyanotic.

Progress.—Expectant treatment was adopted, but solely at the time on account of the lung condition. On an hourly pulse and respiration chart the pulse rate was never above 100, while the respiratory rate increased in a few hours to 40 per minute. The temperature never rose above normal. There was no more vaginal bleeding, and, following appropriate treatment, the chest condition quieted down within twenty-four hours. She was discharged apparently perfectly well ten days later.

This case clinically was without doubt one of acute bronchitis, as is especially evident in retrospect. No pelvic lesion could be demonstrated to account for the vaginal bleeding. With subsidence of the chest signs the patient improved rapidly, and on discharge was apparently perfectly well. I feel certain that laparotomy would have shown a normal uterus and adnexa.

The bleeding was due presumably to vascular congestion consequent upon the acute bronchitis, for on admission the patient was slightly cyanotic. The possibility of an adnexal tuberculous process could not be excluded, as the patient had been in a sanatorium for tuberculosis for three weeks seven years before, but this condition had apparently cleared up completely. The only reason why laparotomy was not performed was on account of the chest condition, as the diagnosis of ruptured ectopic pregnancy was foremost in our minds.

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