Jewish tailor, aged 35. It is true that the arteries of both legs and feet were easily palpable in this case, but the disease may be more marked on the venous side of the capillaries in the earlier stages and limited, like many cases of post-operative thrombosis, to the deep veins of the calf. Pain is often more marked in the calf than in the foot, and is a phenomenon of veins as well as of arteries.

Wheeler's¹ two cases, and the two cases simultaneously published by Smith and Patterson,² along with the fact that Telford and Stopford³ saw four cases in one year in non-Jewish patients, suggest that great care is necessary for the accurate differential diagnosis of the various types of vascular disease of the extremities. It is not sufficient to say "threatened gangrene"—nor, for that matter, is "erythromelalgia" more than a symptom.

Stopford has mentioned that the clinical characters of thrombo-angiitis obliterans were first described by von Winiwarter in 1879, long before Buerger³⁹ published the standard description in 1924. It may be added that Cornil and Ranvier,⁴⁰ in 1860, described "Oblitération des artères par endarteritis et thrombose," and pointed out that a coagulum may precede arteritis as well as arteritis precede a coagulum. Mention must be made of Rabinowitz,⁴¹ who recently claimed to have isolated a Gram-negative, rod-shaped, and beaded organism from a case of thrombo-angiitis obliterans, and to have produced by the bacillus the same lesion in the vessels of the ears and feet of rabbits as that which was present in the leg of the human. Parkes Weber's⁴² description of thrombo-angiitis obliterans as non-syphilitic arteritis obliterans of Hebrews no longer holds good. The disease attacks non-Jewish people. It belongs to the group of new diseases such as trench fever, hog cholera, and encephalitis lethargica.

In surveying the field we see that histology, in the work of Smee, Beale, Stricker, and Rouget, has made its precocious contributions. Gross anatomy and clinical surgery have opened a new line of advance determined by the investigation of the trophic lesions of cervical rib and their sympathetic origin. Leriche, Hunter, and Royle have given direction to the newer purposive surgery of the sympathetic system. Dale, Krogh, and Lewis are pioneers of a physiological and clinical line of attack. The protagonists of physico-chemical mechanisms are forging ahead. The whole of the experimental field, particularly as regards the comparative morphology of the sympathetic system, the comparative pharmacology, and the minute and laborious histology, calls for investigators. The histological work of the late Professor Kulchitsky at University College, London, was one of the mainsprings of the work of the late John Irvine Hunter. The recent surgical work in

America and Australia is promising. The Russian physiologists are extending our conception of the trophic nerves. The morbid anatomy of the blood vessels, as shown by the divers systems of classification of vascular disease in textbooks, is still chaotic. The clinical observations on the vascular diseases of the limb are limited to a few enthusiastic workers. Now, if ever, is the time to write in each hospital ward the following quotation: "Laboratory guides are mostly artificial, are reliable only in some instances, and are the handiwork of man; clinical symptoms are the natural, infallible, unalterable expressions of definite states, and are the ways of God." In each laboratory and dissecting room the text should be: "When the interest flags, strive to become the hero in the oldest of all tragedies—a deduction destroyed by a fact."

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INTRAVENOUS THERAPY.*

BY

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THIS method of treatment has a great many advocates—more, perhaps, on the Continent and in America than in this country—and a great many adverse critics. There are points for and against it, but I think it has now so far justified itself as to deserve a legitimate place in modern therapeutics. It seems better to put remedies intended to act on the blood stream itself, or on some distant organ only reached through the blood stream, directly into the veins, rather than into the stomach, where they must mix with the food and take their chance of being modified by the digestive juices, and finally be subject to the whim of the absorptive mechanism of the alimentary canal. On the other hand, remedies intended to act primarily upon the stomach or intestines are best put there through the mouth. The ease and apparent safety with which intravenous salvarsan injections can be administered has given a great impetus to the use of the intravenous route for purposes of treatment.

The following advantages have been claimed in favour of

the intravenous route: that the dose is more precise; that irritation of the gastro-intestinal tract is avoided; that the drug is not altered or destroyed in the alimentary tract; and that drugs act more promptly when given intravenously. I propose to criticize these in detail.

Precision of Dosage.—A medical man prescribes a remedy with the idea of producing a given effect; he desires to give the exact dose which will produce that effect—no more and no less. The appropriate amount is arrived at by giving repeated fractional doses by the mouth, each being well below the full therapeutic dose; it is assumed to be the dose required by the patient in the circumstances which obtain at that moment. The fractional dose can be increased until the desired effect is obtained. It is not practical to give repeated fractional intravenous doses of a drug; therefore the intravenous dose is more liable to err. For example, strophanthin acts powerfully when given intravenously, and a number of deaths from its use in this way have been recorded. It must be admitted that it is more difficult to arrive at the right therapeutic dose by the intravenous method than by giving a drug orally.

Absence of Gastro-Intestinal Irritation.—A drug which directly irritates the gastro-intestinal mucosa might be expected to irritate also the intima of the veins. The word "irritation" is used somewhat loosely in this respect; what is really meant is that the drug causes disturbance during the process of excretion. This applies more particularly to

* Abstract of Presidential Address delivered before the West London Medico-Chirurgical Society.

the heavy metals. One of the worst cases of intestinal irritation I can remember was after the intravenous injection of a mercury preparation.

Stability of Drug.—Many drugs are readily absorbed, unchanged, through the alimentary tract—the iodides, for example. On the other hand, salts of iron and arsenic are only partially absorbed, for some of the dose given is recoverable from the faeces. Many of the gland extracts are destroyed in the alimentary canal—adrenaline is rendered inert when given by the mouth.

Prompt Action.—There can be no question that drugs act more speedily when given intravenously in acute cases, where rapid action is a matter of urgency. In the treatment of more chronic conditions a therapeutic effect is obtained more slowly whichever route is used.

Technique of Intravenous Injection.

The injection must be given as far as possible painlessly; if pain is caused it becomes increasingly difficult to get the patient to submit to further treatment. The vein should be entered at the first attempt, and the injection must never be commenced until the vein is entered with certainty. There is some excuse for not being able to get into the vein, but none for putting the injection into the surrounding tissues, thus giving rise to an area of infiltration, causing pain and local thrombosis, and incidentally failing to achieve the object desired. The needle should have a flat bevel with no shoulder, and a sharp point; it should enter skin and vein with one smooth movement. Needles, as supplied commercially, always have a shoulder and a long thin point. The shoulder is a source of difficulty in getting through the skin, and with a drawn-out point it is difficult to avoid puncturing the further side of the vein. Moreover, with such a needle part of the lumen is apt to remain outside the lumen of the vein, causing leakage into the surrounding tissue.

If the site at the bend of the elbow is chosen, the arm should lie comfortably on, and partly buried in, a pillow with the elbow-joint fully extended. A tourniquet should never be used. With the hand an assistant should compress the upper arm sufficiently firmly to obstruct the venous return, the arterial pulse still being felt at the wrist. The vein can be brought into greater prominence by stroking the forearm upwards. It is not necessary that a vein should be seen, but it must be felt. The vein should be "fixed" by stretching the skin over it between the thumb and forefinger of the left hand. This stretching renders the skin that is stretched partially anaesthetic. The vein on the central side of the fixing point becomes bulbous, and if the needle is now inserted through the upper edge of this stretched area at an angle, it should accurately enter the vein above. On entering the vein the piston of the syringe is slightly withdrawn and on the first appearance of blood the compression is at once released, and the injection proceeded with. In a nicely adjusted injection a thrill can be felt by lightly palpating the vein just above the site of injection while the fluid is running.

The injection must be given slowly, the rate depending upon the degree of concentration of the fluid and its bulk. It should be remembered that remedies introduced by the intravenous route are rapidly brought into contact with vital organs, such as the heart and the central nervous system. Time should therefore be allowed for the blood stream to distribute them.

I do not think it matters where the injection is made. The veins at the bend of the elbow are usually chosen because here they are more accessible and less covered by fat, but the following may be taken: the internal saphenous vein, where it crosses the internal malleolus; the posterior ulnar vein; the radial vein; the femoral vein; the external jugular vein; and, in young infants, the superior longitudinal sinus, though the anterior fontanelle is usually taken; this is a simple and safe procedure if the middle line is strictly adhered to, and the needle inserted into the posterior angle of the fontanelle, for here the superior longitudinal sinus is nearest the skin.

BLOOD TRANSFUSION.

Blood transfusion is now recognized as a therapeutic measure of the first importance. The donor's blood can be used in the form of whole blood, defibrinated blood, or citrated blood. The one I favour most is the citrated blood method; the transfusion can be given more deliberately, and there is time for the blood to be carried from a distance, if for any reason the donor cannot come to the recipient. The objection to this method is that toxic effects follow the introduction of sodium citrate into the blood stream, and that when transfusion is given as a pre-operative measure oozing is more likely to take place. I argue that, if the right amount of citrate be used and no more, no toxic effects will follow, and the oozing will not be greater than with any other method. The strength I use is 10 c.cm. of a 2 per cent. solution of sodium citrate for every 100 c.cm. of blood. It should be arranged to add the citrate solution by fractions, each fraction being sufficient to prevent clotting of 100 c.cm. of blood. At the commencement of the second 100 c.cm. the requisite amount of citrate solution is added.

The defibrinated method has much to recommend it, but it is, I think, easier to introduce clots into the circulation by this than by the citrate method, for it is not always possible to be quite sure that the blood used is all defibrinated, even after filtering.

Technique.

The simpler the apparatus the better. I have now abandoned the various complicated forms in favour of the simple one on the lines of the ordinary tube and funnel with a glass window near the needle. The blood is allowed to run in by gravity, this force being quite sufficient. A fairly long tube should be used, a few coils being allowed to rest in a vessel of water kept a few degrees above blood heat. The injection should proceed slowly—about twenty minutes being taken to inject 500 c.cm. If the patient is restless and apprehensive the injection may be made easier by first giving 1/6 grain of morphine or heroin. The blood should be filtered through several layers of gauze after citration. Grouping should be carefully performed, and in choosing a donor it is important to take one of the homologous group and not the so-called "universal donor"—Group IV. Many members of this group are not quite negative to the other three groups, and I feel sure it is owing to this that many unpleasant symptoms arise—such as restlessness, dyspnoea, obscurations of vision, noises in the ears, difficulty of speech, fever, shivering, pain in the chest.

I am much in favour of repeated small transfusions—say, 200 to 500 c.cm.—rather than one big one; they are especially useful in the chronic anaemias, and in arresting internal haemorrhages such as from a leaking gastric or duodenal ulcer.

Blood transfusion should never be undertaken lightly. The conditions in which it is indicated are many, and each case must be judged on its merits. It is especially valuable (1) in industrial surgery, where accidents have been accompanied by great loss of blood; (2) in sudden loss of blood from any other cause, such as a bleeding gastric or duodenal ulcer; (3) in any conditions of chronic anaemia where the blood state cannot be improved by other forms of treatment, especially in people around and past middle life—this group would include the toxæmic states, the anaemia here being secondary to the chronic intoxication; (4) as a pre-operative measure, where the red-cell count and haemoglobin estimation are definitely below normal. I deprecate giving a blood transfusion until a full and careful blood examination has been made. It is often indicated for operations on malignant growths where there is a secondary anaemia. In splenic anaemia, where the spleen is being removed, it is advisable to transfuse at the time of operation. I believe the main value of transfusion is due to the stimulus it gives to the blood-forming mechanism.

SALINE INFUSION.

The infusion of normal saline into the veins is a measure of very old standing, and until salvarsan injections were started, in 1909, it was the commonest form of intravenous treatment. When normal saline is injected intravenously the immediate effect is a rise in blood pressure and a fall in the specific gravity of the blood. This is followed in thirty minutes or so by a fall in pressure and a rise in specific gravity, the effect of osmosis, the excess of fluid introduced into the circulation being rapidly excreted by the kidneys and the skin. If circulatory failure is present, or the heart is acting very feebly, as in old people, this excess of fluid is apt to become lodged in the tissues, particularly in the lungs, thus rendering the patient's last condition worse than his first.

Hypertonic saline was introduced with the idea, of course, of attracting the fluid from the tissues into the vessels. The same physical laws, however, obtain with hypertonic saline as with normal saline; since the vessel wall is permeable to salts the condition which occurs with normal saline is rapidly brought about. It appears, therefore, that blood lost cannot be permanently replaced by a simple saline solution; the benefit obtained is too transient, and saline infusion, therefore, should be regarded simply as a temporary measure. It would seem that the fluid advocated by Bayliss (sodium chloride 2 grams, potassium chloride 0.05 gram, calcium chloride 0.05 gram, powdered gum acacia 5 grams, distilled water 100 c.cm.) is, when prepared exactly as he described, the best injection for loss of blood, where blood cannot readily be obtained. Blood, if it can be obtained, is, of course, better than gum saline. For gum saline to be effective there must be present a sufficient percentage of haemoglobin to carry on the process of oxygenation. Saline infusions, in

addition to their use for temporarily replacing blood lost, are of great value in treating the toxæmic states—uraemia, eclampsia, etc.—the patient being bled and then infused; though here again a better result is obtained by using blood.

INTRAVENOUS MEDICATION.

With regard to the introduction of remedies into the circulation I will confine my remarks to those of which I have personal experience.

Intravenous proteins I have used in the treatment of many disabilities—chiefly spasmodic asthma, infective arthritis, and chronic skin diseases, all conditions in which the nature of the infective agent has not been determined. I should say that about half the cases so treated have been benefited. The proteins used have been T.A.B. emulsion 100 to 500 million, *Bacillus coli* emulsion 100 million, *Staphylococcus aureus* 500 million, and Witte's peptone, 10 c.cm. of a 2 per cent. solution. The most marked reaction is ushered in by a shivering attack, followed by a rapid rise of temperature, with a corresponding increase in the pulse rate; the leucocyte count is raised; headache, malaise, and aches and pains in joints and limbs may be present. The reaction passes in the course of thirty-six hours, and is followed in a favourable case by improvement in the clinical condition. The injections should be repeated four times or so at intervals of seven to ten days. There appears to be a direct relation between the amount of reaction and the improvement obtained; for this reason T.A.B. injection proves the most efficacious. Vaccines when given intravenously act more potently than when given under the skin. I believe that too much has been made hitherto of the specific nature of a vaccine, and that careful preparation is more important than any other single factor.

With regard to intravenous injection of antitoxic serums I have had a very limited experience. Candidly I am rather afraid of this method. I tried it during the war in cases of acute sepsis. I was never sure that the benefit obtained was commensurate with the reaction and upset to which it generally gave rise, and I am still not convinced that intravenous serum has any advantages over the intramuscular and subcutaneous routes.

Of the other remedies I have used intravenously I may mention in particular mercury perchloride. So high an opinion have I formed of this drug that I think every clinician who may be called upon to treat acute cases should keep a solution of it prepared; a suitable dose—1/64, 1/32, or 1/16 grain—could then readily be chosen; the strength I suggest is 1/16 grain of mercury perchloride in 8 c.cm. of normal saline. I have used it chiefly in the following conditions: (1) pneumonia, lobar and lobular; (2) acute staphylococcal infections; (3) chorea, subacute rheumatism; (4) chronic infective arthritis of undetermined origin; (5) encephalitis lethargica.

The treatment of lobar pneumonia has hitherto chiefly been symptomatic. I have from time to time tried various serums, and also typed vaccine, but have not been struck by the results. Quite empirically I started, about eighteen months ago, systematically injecting cases of lobar pneumonia, at whatever stage they came under observation, with 1/32 grain of mercury perchloride. Most of those I have so far treated have responded favourably. Such figures as I have point to an association between the injection of the mercury perchloride and the favourable turn which these cases have taken. I have had quite marked results in bronchopneumonia also, especially in children. Infections by *Staphylococcus aureus* appear to be consistently benefited by injections of perchloride. It is of value in the more chronic infections, such as boils, and in the acute cases, such as acute infective osteomyelitis.

It is a matter of common experience that acute rheumatism under treatment usually clears up within a short time, but the subacute forms, particularly in children, with possible endocarditis and manifestations of chorea, hang fire; the treatment of these patients is unsatisfactory. I have injected a number of these cases with mercury perchloride. Some cases of chorea I have treated have shown

improvement in the movements and in the general health, but the fever has continued; in the end the fever too has disappeared. I realize that here, as with pneumonia, one is on very shifty ground, for these things may happen by treating with rest alone. It is only, however, by taking a large number of cases treated with mercury, and comparing them with a similar number treated without, that it is possible to arrive at conclusions. My impression, so far, is distinctly favourable to the mercury treatment.

Cases of chronic infective arthritis, where there is no septic focus which can be determined after careful search, have been improved by intravenous injections of mercury perchloride 1/32 grain every three days. I have also used in such cases sodium salicylate 15 grains with sodium iodide 15 grains in 20 c.cm. of distilled water.

Among many other drugs which have been used intravenously iron cacodylate in half-grain doses every other day is a very efficient way of raising the haemoglobin content. Tylcalcin (a calcium salt of salicylic acid) is a useful form of salicylate for intravenous injection in acute and subacute rheumatism. Acriflavine (40 c.cm. of 1 in 1,000 solution in normal saline) should certainly be tried in septicaemia. Magnesium sulphate (20 c.cm. of a 10 per cent. solution) is of use in controlling the convulsions in eclampsia and uraemia by virtue of its sedative action on voluntary muscle; it also promotes urinary secretion when given intravenously. Urotropine acts more powerfully when given intravenously.

How do these intravenous remedies act? On this point I must at once confess ignorance. It is inconceivable that 1/32 grain of mercury perchloride, for example, can have any antiseptic action when diluted in the blood stream. Perhaps the reaction may be simply that which is associated with putting a foreign substance in the blood stream.

The intravenous route has much to recommend it. By whatever channel drugs are given, they must ultimately reach the circulating blood. Therefore it would appear to be only logical to put them straight into the blood stream. But intravenous medication demands careful handling, and, in using it, one must err on the side of caution.

THE TREATMENT OF RODENT ULCER BY TRICHLORACETIC ACID.

BY

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BEFORE the days of radium and x rays surgeons were often compelled to treat malignant growth by means of caustics. The need of some chemical which would destroy the growth was felt when the growth occurred on the eyelids or the inner canthus of the eyes, or on the side of the nose, or in the nostril, where complete removal of the growth would entail great deformity.

Various caustics were employed, such as solid "potassa fusa," zinc chloride, acid nitrate of mercury, Vienna or arsenical paste, antimony, and pyrogallol acid. The use of these chemical agents gradually dropped into oblivion, since their use was accompanied, not only by severe pain, but not infrequently by accelerated metabolism, whereby a quiet growing tumour was converted into a growth of a more malignant type.

We know why these caustics fell into disrepute; it was because of their dangerous tendency to set up oedema, which was followed by rapid destruction of cells in the superficial parts of the tumours with absorption of toxic products and accelerated growth in the deeper parts. It may be laid down as a general rule that a caustic which increases the water contents of a malignant cell should always be avoided.

The superiority of trichloroacetic acid in the treatment of rodent ulcer lies in the fact that its action leads to complete coagulation of the cell contents. The compounds