

the circulation without difficulty or bad after-effects. In this case time was taken to dissect out the vein after the blood had been drawn into the tube.

Through the kindness of Dr. James S. Stone, surgeon to the Children's Hospital, Boston, and of Dr. W. E. Ladd, Assistant Surgeon, in whose service this case arose, an opportunity was given to put the method to a practical test.

REPORT OF CASE

Patient.—A boy, 10 years old, admitted April 25, 1913. Diagnosis, strangulated hernia. In the preceding October this child had had pneumonia and, by the mother's statement, at that time vomited a large amount of fresh blood, also passed black stools for about three weeks. From this time he had never regained his full strength. On admission, a large strangulated hernia was discovered and at operation was found to contain a large bunch of gangrenous omentum. There was also considerable free pus in the sac. The gangrenous omentum was removed and, because of evidence of peritonitis, the abdomen was opened and found to contain a large amount of pus. The abdomen was drained through the abdominal incision and also through the inguinal incision. There had been a considerable hemorrhage from the stump of the omentum. The child's condition was very poor. On May 8, 1913, it was necessary to operate again for an abscess. On removal of the wick and introduction of a finger into the wound, a very smart hemorrhage took place, partly from granulations and partly from the omentum. A piece of omentum was tied off and removed and further hemorrhage controlled by packing. No abscess was found. The child's condition was very unsatisfactory and there was marked suppression of urine, the twenty-four-hour amount being about 10 ounces; pulse and temperature high and irregular. The kidneys were excreting less than one-half of the fluids taken.

Transfusion.—On May 29, 1913, a transfusion was done, blood being taken from the mother. The technic was as follows: Under cocaine, 0.5 per cent. for the child and 1 per cent. for the mother, the median basilic vein of the boy and the radial artery of the mother were exposed in the usual way. The vein was tied off distally and a Crile clamp applied proximally. The artery of the donor was treated in a like manner. The artery was then transfixed with a cataract knife and a slit made, into which the cannula of the tube was inserted and the clamp opened. A tie around the cannula is not necessary. The tube was held vertically and in forty seconds contained a little over 85 c.c., practically 3 ounces, of blood, all that was desired in this case. The cannula was withdrawn, an assistant closing the clamp at once. The tube was then placed in the position shown in Figure 2, to prevent the blood from running out from the cannula while it was being inserted into the vein. The peculiar bend in the cannula prevents it from emptying itself of blood and avoids the injection of air. As the cannula was entering the vein it was again raised to a vertical or oblique position. After insertion into the vein and removal of the clamp an ordinary actual cautery bulb-pump was attached to the side tube. With very slight air-pressure the flow of the blood was constant. The cannula was removed before it had emptied itself so that no air should enter. The time between the withdrawal of the tube from the artery and insertion into the vein was fifty seconds. The time from insertion into the vein until the three ounces had passed into the child's circulation was fifty seconds. The entire time from insertion into the artery of the donor until withdrawal from the vein of the recipient was two minutes and twenty seconds. The child promptly appeared of better color and the veins on the backs of his hands filled out. There was no change in the donor's condition. The child's pulse increased from 96 to 120, probably because of excitement. He complained of hunger at once. Hemoglobin tests were not made. Next morning the patient was better; pulse was down and temperature also. He felt stronger, felt better and had passed double the quantity of urine he had been passing. He has improved steadily since and has been transferred to the Convalescent Home.

In using this method one should be very careful not to injure the vessels, picking the tissues away from them rather than handling the vessels themselves. We consider the use of a cataract knife, instead of fine scissors, to open the vessels extremely important, as it is very necessary not to injure the vessels or leukocytes. The knife makes a beautiful, sharply outlined opening. It is also important to pass the end of the cannula beyond the site of the Crile clamp. The slit is held open by small hooks such as are used in doing transfusion by other methods. Gentleness is the essential factor, as in all blood-vessel surgery.

It is very easily seen how simple and easy the performance of transfusion becomes by this method. The manner in which the blood is obtained is a great factor in its not clotting. With sufficient care not to injure the vessels and to have the entire tube thoroughly lined with paraffin we believe that no difficulty from the formation of fibrin ferment will be experienced if the operation consumes no more than a reasonable amount of time.

POINTS ACCOMPLISHED

The advantages gained are: (1) the elimination of the uncertainties and usual technical difficulties of direct transfusion; (2) the ability to measure the amount of blood transfused, and (3) the ability to regulate the rate of flow.

We fully appreciate that the method has not been sufficiently tried out, but it was so successful in the case described above that we feel that it merits all that is claimed for it. We hope that it will be tried by others and will gladly assist by giving whatever information we can. The tubes used in our experiments, designed and made by Mr. Brown, varied in capacity from 25 to 100 c.c., but can be made of any desired size by a competent glass-blower.

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WHEN AND HOW TO USE NITROGLYCERIN *

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There appear to be three general indications for the use of nitroglycerin in medicine, namely, to relieve distressing or dangerous symptoms due to local arteriosclerosis or arterial spasm; to lower the general blood-pressure when its continuance at the existing height threatens accidents to the cardiovascular apparatus, and to clear the diagnosis.

The power of nitroglycerin is perhaps best shown when it is used to free the circulation in vitally important regions of the body where the supplying arteries are unduly contracted. The two most important vital regions are the heart itself and the brain; and arterial disease in these regions is usually attended with high blood-pressure. Sclerosis of the coronary arteries, when the lesion is pronounced, may be attended by some or all of the following symptoms: soreness, oppression or pain in the precordium, especially behind the sternum; pain in the neck, shoulders and arms, particularly the inside of the left arm; attacks of tachycardia; attacks of dyspnea, which are often intense, and often attended with palpitation; and the symptoms of myocarditis. Precordial distress, which may be of all degrees from a

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slight sense of oppression to angina pectoris, and dyspnea, are the most common symptoms, and they, as well as the other symptoms, are apt to be brought on by slight or moderate exertion or excitement, and to come on after eating and in the night. Truly marvelous relief of these symptoms, in cases with high blood-pressure, often follows the administration of nitroglycerin, combined, it may be, with small doses of strychnin, and, if there is much myocardial insufficiency, with strophanthus also, and always with a suitable diet. I have seen patients who were rendered very miserable by such attacks of cardiac pain and dyspnea, occurring both during the day and at night, recover for considerable periods comfort and apparent cardiac balance when so treated.

Part of the benefit derived from nitroglycerin in these cases of localized arteriosclerosis may be due to the lowering of the blood-pressure which it produces, and the consequent relief of the strain on the diseased arteries; and that is particularly probable in sclerosis of the aorta near the heart, which is often associated with coronary sclerosis, and which, by itself, especially if there is also dilatation of the diseased aorta, can give symptoms similar to those mentioned above. Aortic sclerosis is frequently associated with very high blood-pressure.

Cerebral arteriosclerosis can exist without giving subjective symptoms, and its first local manifestation may be apoplexy; but it may produce abnormal sensations of a vague character in particular regions of the brain, head noises, vertigo, especially when the head is placed in certain positions, and severe headaches. These symptoms are frequently relieved, and sometimes for long periods, by nitroglycerin, but only in cases in which the blood-pressure is high. Abnormal sensations in the head are frequently associated with low or relatively low blood-pressure; and in such cases nitroglycerin is contra-indicated.

Arteriosclerotic pains in the legs, occurring mostly at night, are particularly amenable to nitroglycerin. The pains due to splanchnic arteriosclerosis seem to be less so, though they may be relieved by it.

Nitroglycerin can be used to lower general high blood-pressure which threatens accidents to the cardiovascular apparatus, but it has not the superlative value in this class of cases that it has in those in which the symptoms are due to localized arteriosclerosis, or arterial spasm. Aconite and veratrum often serve better in these cases, especially if the myocardium is in fairly good condition. The quickest and most effective means of lowering the blood-pressure when it threatens injury to the cardiovascular apparatus is venesection; and the one which keeps the blood-pressure down for the longest periods is regulation of the diet.

The use of nitroglycerin for diagnostic purposes has been mentioned and described by me in former articles.¹

This drug can be employed to show whether certain symptoms are due to contracted arteries or to some other cause. The symptoms which invite this test are chiefly pains and abnormal sensations in various parts of the body associated with elevation of blood-pressure. If the administration of nitroglycerin produces marked relief of these symptoms, they are probably due to arteriosclerosis or arterial spasm. It is my custom, if a patient with high blood-pressure complains of head-

ache or other symptoms which might be due to localized arteriosclerosis, to put a hypodermic tablet of one one-hundredth of a grain of nitroglycerin under his tongue and watch results. In three or four minutes, if the headache or other symptom is due chiefly to arterial contraction, relief is experienced. If relief does not come, or if aggravation ensues, the cause is probably not arteriosclerosis; and in the case of a headache, it is apt to be toxemia or a neoplasm. In conditions of low blood-pressure this test is of no value.

The knowledge when to use nitroglycerin involves the knowledge when not to use it. The indications for its use have been suggested; what are the contra-indications?

Low blood-pressure is the main contra-indication. In general, it may be said that nitroglycerin should never be given when the patient's blood-pressure is lower than normal for his age and condition; that it should not be given, as a rule, in advanced nephritis with very high blood-pressure, or in toxic conditions producing high blood-pressure; that it should not be given to modify the action of the so-called vaso-constrictor heart stimulants; that it should not be given to patients who have any idiosyncrasy in regard to its action, and that it should never be given for a heart stimulant.

The administration of nitroglycerin is attended with very few difficulties. It can be given by injection under the skin, by placing a soluble tablet under the tongue, which is almost as speedy a way of getting its effect, and by the stomach, which is the least reliable method. I usually give it under the tongue, if the patient is conscious.

The dosage of nitroglycerin varies ordinarily between one two-hundredth and one fiftieth of a grain. Its effect passes off in less than half an hour, so that the dose may have to be repeated often to produce a persistent effect; though it frequently happens that the relief from a single dose or a few doses endures long after the physiologic effect, as such, has ceased. I am accustomed to put into the hands of patients suffering from symptoms of sclerosis or spasm of the coronary arteries or arteries in the head or extremities, hypodermic tablets of one one-hundredth of a grain, with directions to put one under the tongue when the symptoms appear, and to repeat the dose if necessary. In some cases one or two repetitions may be required, seldom more, unless tolerance has been established, in which case the dose must be increased and continued longer. For the purpose of lowering the general blood-pressure the drug should be given every hour or half hour. As a general rule, I may say that nitroglycerin, in the absence of contra-indications, should be given in sufficient doses to produce the desired effect.

Although nitroglycerin appears to be a comparatively harmless drug, bad consequences can follow if it is taken too freely. I have seen patients who took it excessively develop cardiac weakness and irritability, localized edema, excessive sweating, and visual disorders. A woman 80 years old, who took nitroglycerin steadily for more than a year, by my direction, to relieve arteriosclerotic pains in the thighs, and who during that period gradually increased the dose from two or three tablets of one one-hundredth of a grain during the night to eighteen tablets during the night, developed edema in one foot, profuse perspiration and a visual disturbance characterized by the appearance of fine black specks in the field of vision. The perspiration and the black specks disappeared promptly after the drug was discontinued.

1. Cornwall, E. E.: Value of an Antiputrefactive Diet in Differential Diagnosis of Conditions Producing High Blood-Pressure, *Arch. Diagnosis*, July, 1912; Some Practical Points in Interpretation and Management of High Blood-Pressure, *Med. Rec.*, New York, Nov. 16, 1912.

SUMMARY

In conclusion I wish to repeat and emphasize the following points:

1. The general indications for the use of nitroglycerin are (1) to relieve symptoms of localized arteriosclerosis or arterial spasm in vitally important regions of the body, and, when there is pain due to contracted or diseased arteries, in other regions; (2) to reduce general high blood-pressure in selected cases, if its continuance threatens accidents to the cardiovascular apparatus; and (3) to clear the diagnosis.

2. The chief contra-indications to the use of nitroglycerin are (1) low or relatively low blood-pressure; (2) advanced chronic nephritis with very high blood-pressure and toxemic conditions producing high blood-pressure, as a rule; and (3) the presence of an idiosyncrasy in regard to its action.

3. Nitroglycerin should never be used for the primary purpose of a heart stimulant.

4. Nitroglycerin given under the tongue produces almost as prompt an effect as when injected under the skin.

5. Nitroglycerin, if given too long or in too large doses, can produce injurious effects, which, however, usually pass away, at least apparently, when it is discontinued.

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POSITIVE RESULTS FOLLOWING THE INOCULATION OF THE RABBIT WITH PARETIC BRAIN SUBSTANCE

A PRELIMINARY NOTE

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In a previous article in *THE JOURNAL*¹ we stated that we had been engaged for some time in the inoculation of rabbits with spinal fluid and brain substance from cases of paresis, but so far with negative results. Recently we have had an encouraging, though not conclusive finding, which we reported, May 8, 1913, at the annual meeting of the American Association of Bacteriologists and Pathologists, and which we desire to record in a preliminary note on account of the difficulties which seem to beset this line of work.

Our seventh attempt with brain substance was as follows:

The patient, W., aged 48 on admission, Nov. 2, 1911, had syphilis in 1899 and was treated for it; symptoms of paresis appeared in March, 1911. He was alcoholic; clinically and serologically, a typical parietic. He died Feb. 8, 1913; immediate necropsy was held; histologic examination was typical of paresis according to opinion kindly given by Drs. Meyer and Ferguson of Johns Hopkins Hospital. No spirochetes were found in the brain by Levaditi's method.

Inoculations of two rabbits were made within an hour of death. One rabbit has remained entirely negative. The second rabbit, 108, was injected in each testicle with 1 to 2 c.c. of an emulsion of brain substance from the right and left frontal

areas. Weekly examinations were made and nothing was noted until March 31 (fifty-one days), when the left testicle seemed larger than usual, but with no definite nodule; a tapping was negative for spirochetes; the same finding and the same result on two following weeks; then the testicle became normal in size and we were about to discard the animal, April 28 (seventy-nine days), when it was noticed that both eyes showed a marked complete interstitial keratitis with injection of corneal margin; Wassermann reaction ++ (Captain Craig). The testicles were excised and no lesions or spirochetes were found. Both eyes were excised, and small pieces of the cornea and corneal emulsion were injected into two rabbits' testicles. The cornea showed a round-cell infiltration and a disintegration of lamellae identical with that found in proved syphilitic keratitis. No spirochetes were found in the cornea by dark-ground illumination or by Levaditi's method.

One rabbit has remained entirely negative. The second rabbit had a very small nodule in the testicle after thirteen days; no spirochetes were found. In twenty-eight days, examination of the fundus by Dr. Green and Captain Davis showed a definite disseminated chorioiditis of both eyes. Wassermann ++ (Captain Craig). On the thirty-second day the right eye was excised, the chorioid scraped off, ground up in salt solution and inoculated into the testicles of two rabbits. No spirochetes were found by dark-ground illumination or by Giemsa's stain. On the thirty-fifth day, the suspected testicle was excised and a small hard nodule was found which was typical in appearance and consistency, but no spirochetes were found. Transfers were made to two other animals.

In brief, the inoculation of the rabbit's testicle with typical parietic brain substance, in which no spirochetes were found, has resulted in a doubtful lesion of the testicle and the production of definite interstitial keratitis, identical with that which is known to be due to *Spirochaeta pallida* in experimental syphilis in the rabbit. On transfer of the cornea to a second rabbit, a definite lesion of the testicle has been followed by a typical chorioiditis. In neither rabbit have spirochetes been definitely demonstrated, but both animals have shown a strong Wassermann reaction with small amounts of serum which, in our hands, has never reacted positively in normal animals.

While we have not been able, as yet, to demonstrate *Spirochaeta pallida* in the lesions of these rabbits, we believe that the lesions are syphilitic and that in further transfers we shall be able to demonstrate their nature. Uhlenhuth and Mulzer² have called attention to the very small primary lesions which may occur in the testicle after inoculation of blood and other body fluids, and we believe that in these rabbits the testicular lesions were so minute that the organisms were not detected and that the virus has found a more favorable place to multiply in the eye. We have been particularly impressed with this view because the strain of *pallida* which we obtained from the spinal fluid in a case of nervous relapse has shown a marked affinity for the eye after testicular or intravenous injection. It regularly produces typical pannus and keratitis. Spirochetes have been found in these lesions by Levaditi's stain, but only after several attempts. Igersheimer³ has emphasized the difficulty of finding spirochetes in lesions of the eye which have not been produced by direct inoculation; and we believe that several transfers may be necessary before the spirochetes will become sufficiently habituated to the rabbit to produce a clear-cut lesion of the testicle.

1. Nichols, Henry J., and Hough, William H.: Demonstration of *Spirochaeta pallida* in the Cerebrospinal Fluid from a Patient with Nervous Relapse Following the Use of Salvarsan, *THE JOURNAL A. M. A.*, Jan. 11, 1913, p. 108

2. Uhlenhuth and Mulzer: *Centralbl. f. Bakteriol.*, orig., 1912, p. 165.

3. Igersheimer: *München. med. Wchnschr.*, 1912, p. 2089.