Summary

A series of cases of occlusive vascular disease is described in the management of which intra-arterial injections of vasodilator substances have been used and their relative values discussed.

Improvement in a large percentage of our patients has encouraged us in the use of this method on an increasing scale. It is well within the scope of out-patient procedures, and offers a beneficial and convenient aid in the treatment of peripheral vascular disease.

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BLOOD TRANSFUSIONS IN PARAPLEGIC PATIENTS WITH TOXAEMIA

BY

J. J. WALSH, M.B., B.Ch.

Senior Hospital Medical Officer at the Ministry of Pensions
 Spinal Injuries Centre, Stoke Mandeville
 Hospital, Aylesbury

Malnutrition is a common finding in spinal paraplegic patients. It occurs as a result of the depletion of the body's protein reserve, due to infection of the urinary tract and pressure sores, combined with poor appetite and consequent low food intake. The loss of protein oozing from the sores and urinary tract may vary from 5 to 50 g. daily (Poer, 1946), and this can result in extreme degrees of malnutrition, as exemplified in numerous paraplegics on admission to this centre. The assessment of plasma proteins was not found to be a reliable guide to degrees of malnutrition in these patients, for persons with an extreme degree of emaciation comparable to that found in inmates of concentration camps may show a normal or only slightly diminished total value, although the albumin/globulin ratio is invariably altered and as a rule reversed.

If oozing of protein from sores and the urinary tract were the only factor in the development of malnutrition one would expect that its replacement by transfusion of plasma or synthetic preparations, such as "casydrol," would be effective in treating the malnutrition in these cases. However, experience gained in this centre has repeatedly shown that this is not so, as another and more important factor has to be considered—namely, the profound effect of sepsis on the haemopoietic system. These patients invariably show signs of anaemia, although the exact degree may be clouded by haemoconcentration following frequent vomiting. In most cases admitted with multiple bedsores, which are nearly always accom-

panied by heavy urinary infection, the haemoglobin estimation shows a reading below 75% and often as low as 50%. In such cases osteomyelitis of the underlying bone is the rule rather than the exception, and, as shown by x-ray examination, the amount of bone involvement is often far greater than would be expected from the size and appearance of the sores. Numerous paraplegics admitted from their homes or from other hospitals showed infiltration of the infection into the joints, leading to septic arthritis, and in some cases even resulting in complete disintegration of the head of the femur. It is our experience that such sepsis depresses haemopoiesis, and the resultant anaemia in turn renders the patient less able to overcome the infection, thus establishing a vicious circle.

Attention has previously been drawn to the profound effect which frequent blood transfusions have in combating the nutritional deficiency in paraplegics with toxæmia (Guttmann, 1945, 1946, 1949), and during recent years blood transfusions have become in this centre the most important routine method of restoring nutritional deficiency and promoting the healing of pressure sores in paraplegic patients. In this connexion it may be noted that the local treatment of sores and urinary infection alone, or even if combined with systemic chemotherapy and antibiotics, is infinitely less effective in these toxic cases than when preceded and accompanied by blood transfusions. Furthermore, in many cases of paraplegia the stage is reached when pressure sores are clean, urinary infection appears to be well controlled, and haemoglobin estimations are apparently satisfactory (80–90%), yet the rate of healing of the sore is very slow or the condition may even become quite static. In such cases a blood transfusion is usually effective in promoting a quicker healing rate.

The number and frequency of transfusions and the amount of blood given at each transfusion depend, as would be expected, on the individual case, but, in general, the greater the area of ulceration and the more toxic the patient the more frequently are blood transfusions required. In the routine treatment of a new admission with extensive bedsores 3 to 4 pints (1.7 to 2.3 litres) of blood are given in the first few days, followed by a weekly transfusion of 1 to 2 pints (0.6 to 1.1 litres) until such time as the patient's clinical condition shows that he has overcome the toxæmia, and until his blood count remains high. In many such patients 20 to 30 pints (11.4 to 17 litres) of blood were required in the course of 8 to 10 weeks, and in one particularly serious case of profound sepsis with 14 sores, including two open joints, 76 transfusions were given over a period of seven months before his condition was satisfactory and his blood picture stabilized.

One serious drawback was that numerous patients, after a variable number of whole-blood transfusions, developed undesirable reactions to subsequent transfusions, despite the fact that no incompatibility was demonstrable *in vitro*. Investigations were carried out with a view to overcoming the difficulty, and the purpose of this paper is to draw particular attention to the encouraging results achieved with transfusions of red-cell suspensions in such cases.

Method and Material

In all cases stored blood of homologous group, one to ten days old, was used, and it has been our experience that the fresher the blood the more efficacious was the transfusion. The blood was supplied by the regional transfusion service.

The anticoagulant mixture used was 2.5% disodium citrate with 2% glucose. The blood was prepared by removing the supernatant plasma from a well-settled bottle of blood and replacing it with an equal quantity of pyrogen-free sterile normal saline. The leucocyte gel layer lying between the red cells and the plasma was not removed. With one exception, the cell suspension was transfused within eight hours of preparation. The rate at which the blood was given varied, the average time for 1 pint being one and three-quarter hours; in some cases, owing to prolonged venospasm or because small veins had to be used, a transfusion of 2 pints took up to six hours.

All the 22 patients transfused were suffering from paraplegia due to spinal lesions at various levels (7 cauda equina and 15 cord lesions), and the majority were in a septic condition at the time of transfusion. Of these 22 patients 19 had previously received 65 transfusions, totalling 92 pints (52 litres) of whole blood. On 40 occasions there were undesirable reactions, and each patient exhibited one or more of the following: repeated rigors; pyrexial rise of more than 2° F. within three hours of transfusion; generalized urticaria; and chest and back pains with dyspnoea.

Results

The 22 patients under review in this paper received 62 transfusions of cell suspension, and altogether 91 pints (51.5 litres) of this type of blood transfusion were administered. The cases can be conveniently divided into the following groups (see Table I).

TABLE I

Case No.	No. of Transfusions of Whole Blood	No. of Pints of Whole Blood	No. of Reactions	No. of Transfusions of Cells in Saline	No. of Pints of Cells in Saline	No. of Reactions
1	12	15	7	3	6	0
2	3	4	3	4	6	0
3	3	3	2	4	6	0
4	5	7	4	2	3	0
5	1	2	1	1	2	0
6	6	8	5	3	3	0
7	2	2	1	2	3	0
8	4	8	2	11	14	0
9	1	2	1	2	3	0
10	2	2	1	7	15	0
11	4	7	1	2	3	0
12	1	2	0	2	3	0
13	2	2	0	1	2	0
14	1	2	0	2	3	0
15	6	9	0	1	1	0
16				2	2	0
17				2	2	0
18				1	1	0
19	6	10	6	4	6	1
20	4	5	4	2	3	1
21	1	1	1	2	2	1
22	1	1	1	2	3	1
Total	65	92	40	62	92	4

1 pint=0.57 litre approx.

Group 1 (11 Cases).—Most of these had no reaction with the early (1–3) whole-blood transfusions, but subsequent whole-blood transfusions invariably produced reactions. On the other hand, in none of these cases were any reactions encountered after transfusions with cell suspension. This was, of course, especially important in those cases (for example, 8 and 10) in which repeated transfusions, some of them at short intervals, were vitally necessary. Case 4 significantly demonstrates the value of the cell-suspension transfusions in a patient with a cauda equina lesion, suffering from a grossly infected ischial pressure sore with osteomyelitis of the underlying bone. Three of the four whole-blood transfusions produced very marked generalized urticaria, with severe irritation. Next, 1 pint (0.6 litre) of cells in saline was given without any reaction whatsoever. This was followed by 1 pint of whole blood, which again produced a marked urticarial reaction (10 minutes after the start of the transfusion). A subsequent transfusion of 2 pints (1.1 litres) of cells in saline was uneventful.

Group 2 (7 Cases).—The very poor general condition of the patient, or some other special circumstance, made it advisable to take all possible steps to avoid even a minor upset, and for these reasons transfusions of cells in saline were given, although there had not been reactions with previous whole-blood transfusions. In none of the cases of this group were there any undesirable reactions after the transfusions with cell suspension.

Group 3 (4 Cases).—In these patients undesirable reactions were observed after transfusions with cell suspension. In analysing these cases it seems to be very doubtful whether the reactions observed in Case 19 represent genuine allergic reactions to the cell suspension at all. In this case each whole-blood transfusion produced a severe urticarial reaction. Next, three transfusions of cells in saline, totalling 4 pints (2.3 litres), produced no reaction whatsoever. At a fourth transfusion 1 pint of cells in saline was given without reaction, then a second pint produced a severe rigor, with a rapid rise of temperature to 103° F. (39.4° C.) and general malaise. A pyrexial illness with repeated rigors followed, and with intensive chemotherapy subsided after three days. Investigation showed that the second bottle of cells in saline had been prepared for a different patient nine days earlier, and through a mistake was given, after this long interval, to Case 19. In Case 20 whole-blood transfusions had always produced protracted shivering, sometimes with pyrexia of 1 to 2° F., sometimes with no rise in temperature. Reaction occurred within a few moments of beginning transfusion and continued for one to two hours afterwards. When 1 pint of cells in saline was given, practically the same reaction was produced with no rise of temperature, and again continued for about an hour after transfusion had ceased. A second transfusion of cells in saline, consisting of 2 pints, caused no obvious reaction. In Cases 21 and 22 one out of two transfusions with cells in saline produced rigors with rise of temperature of 1 and 2° F. respectively. In each case 1 pint of whole blood had produced similar reactions.

Comparative investigations of haemoglobin and red cells, following both whole-blood and cell-suspension transfusions, have been carried out; examples are presented in Table II.

TABLE II

Case No.	Whole Blood			Cells in Saline		
	Amount (pints)	Hb	R.B.C.	Amount (pints)	Hb	R.B.C.
2	1	Before, 71% After, 75%	4.2 m.	1	Before, 73% After, 88%	3.6 m. 4.6 m.
4	1	Before, 55% After, 56%	Not avail. 3.2 m.	1	Before, 76% After, 88%	3.9 m. 4.6 m.
2	3	Before, 50% After, 85%	Not avail.	2	Before, 59% After, 95%	3.3 m. Not avail.
3	3	Before, 46% After, 82%	2.8 m. 4.1 m.	2	Before, 69% After, 90%	2.7 m. Not avail.

Comments

A number of workers have reported on the use of both concentrated red cells and red-cell suspensions. As early as 1918 Oswald Robertson published a description of a method of preparing suspensions of preserved red cells in gelatin saline. More recently, McQuaide and Mollison (1940) and Williams and Davie (1941), reporting on the use of concentrated red cells, noted that reactions were fewer than when using whole blood. Watson (1943), Alt (1943), and Cooksey and Horwitz (1944), using red-cell suspension, all noted that the percentage of reactions was as low as or lower than when using whole blood. No data have been available so far on this problem in spinal paraplegics suffering from septic conditions. Our results clearly show that in these cases the percentage of reactions following transfusions with cell suspension is negligible and far below that found after transfusions with full blood. This suggests that the factors mainly responsible for the undesirable reactions following transfusions in these cases were present in the supernatant serum. One point which

may be worth stressing is that in our cases the leucocyte gel layer lying between the red cells and the plasma was not removed during preparation of the suspension. Leaving this gel did not seem to play any part in the incidence of reactions. This contrasts with the impression of McQuaide and Mollison, who thought it possible that the leucocyte gel might have been at least partly responsible for the rather high reaction rate found in their series of transfusions with stored whole blood.

It is generally agreed that some of the aetiological factors responsible for the allergic reactions following blood transfusions are most common in individuals with a past history of allergic disease. Of the patients treated in our present series only two gave such a history. Case 16 had hay-fever and asthma for some years, and actually had a number of severe attacks over the period during which he was being transfused. However, there were no reactions in connexion with the transfusions with cell suspension. Case 10, who produced a marked generalized urticaria after 1 pint of whole blood, and in whom no reaction was induced by cells in saline, never had any allergic phenomena himself, but his child suffered from severe hay-fever. Skin tests for sensitivity to plasma, however, were not carried out in any of these patients.

The other important problem, apart from the question of reactions, is whether or not the cell-suspension transfusion is as effective in counteracting malnutrition and septic conditions and improving haematopoiesis and the general condition of the paraplegic patient as the whole-blood transfusion. Judging from the haemoglobin and red-blood-cell estimations (Table II), and the clinical condition of our patients before and after transfusion, it can be concluded that the cell-suspension transfusions were found to be at least as beneficial as the whole blood.

Summary

The immense value of repeated blood transfusions—the most effective method in the treatment of spinal paraplegics suffering from malnutrition and septic conditions due to infection of pressure sores and the urinary tract—is stressed.

In a series of 22 patients the occurrence of undesirable reactions following blood transfusions is discussed.

Transfusions with cell suspensions in saline were found to be more effective in decreasing the incidence of undesirable reactions than whole-blood transfusions.

Certain factors responsible for allergic reactions following blood transfusions are discussed.

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According to Dr. Niels Sjørlev, medical director of the Fight Against Tuberculosis in Denmark, his country's tuberculosis sanatoria cannot be kept full. There are not enough cases in Denmark requiring sanatorium treatment. Dr. Sjørlev was speaking in London before a joint meeting of the Anglo-Danish Society and the National Association for the Prevention of Tuberculosis called to hear about a scheme for sending British children with tuberculosis to the Vordingborg Sanatorium in Denmark.

USE OF A FUCHSONIUM COMPOUND FOR NON-SPECIFIC CERVICITIS AND VAGINAL THRUSH

BY

D. MCKAY HART, M.B., Ch.B., F.R.F.P.S.
F.R.C.O.G.

AND

C. HUTTON BROWN, M.B., Ch.B., M.R.C.O.G.

(From the Western Infirmary, Glasgow, and the Royal Maternity and Women's Hospital, Glasgow)

The treatment of vaginal discharge has always been a troublesome problem. This is obvious from a scrutiny of the literature, in which a multitude of remedies are recommended with varying claims of success. In those cases in which the discharge is related to an organic lesion or to a specific infection the question resolves itself into the relatively simple one of treating the cause. There remain, however, a very large number of patients in whom no gross organic lesion is present and from whom no definite pathogen can be isolated. It is these patients who prove most difficult to treat, especially as the remedies must of necessity be largely empirical. In current medical literature the condition has been referred to loosely as "non-specific cervicitis."

Various treatments for this condition have been tried and recommended. For some time it was thought that the reaction of the vaginal fluid was most important, and local treatment with lactic acid in some form was very popular. Occasionally other acids were employed; for instance, acetic acid as a vinegar douche. In more recent times claims have been made on behalf of sulphonamides and antibiotics, but it is remarkable that gentian violet still finds a place in the treatment of this condition, and it is the only remedy which seems to have maintained its place as a vaginal therapeutic agent over a long period. We have made use of these various remedies, and have found gentian violet the most effective. It has, however, certain disadvantages. It stains hands, clothing, and bed-linen, and sometimes causes severe irritation and even "burning" of the tissues. With this in mind we have been searching for a substance similar to gentian violet but without its disadvantages. Recently we have made a clinical trial of a new preparation containing a sulphonated derivative of fuchsonium and sodium baborate. Altogether we have treated 80 cases of "non-specific cervicitis" and 60 cases of vaginal thrush.

It is convenient to consider the cases in two groups, Group I being the 80 cases of "non-specific cervicitis" and Group II the 60 cases of thrush.

Group I

The patients in this series were drawn from the gynaecological clinics of two hospitals in the City of Glasgow, and were under the personal care of either D. M. H. or C. H. B. Most of them were in the child-bearing age group, the average age being 32.3 years, with extremes of 19 and 66 years. Seventy-one were parous, the average parity being 2.1. The main complaint was of vaginal discharge accompanied by a varying degree of vulvar and vaginal irritation and discomfort. The average duration of these symptoms was 2.3 years, with extremes of 6 weeks and 11 years.

The discharges varied very much in character, but could be divided roughly into three types according to the colour—