number of cases occur, however, which do not so readily respond, and these are not always patients previously neurotic, though this is the general rule. Many cases arise in those not previously overtly neurotic but of a nervous or highly strung disposition. A few cases are seen in which no trace of predisposition can be found, but it is ridiculous to regard these as the only true psychiatric casualties of the air raids.

No claim is made for originality in the methods of treatment employed. All were used in the last war, and it was from those who introduced them that I have learnt them.

Summary

The conditions under which cases of neurosis have occurred in recent weeks in London are briefly considered and contrasted with those of September, 1939.

The question of attributability to war stress is discussed.

Six typical cases are reported.

Therapeutic measures are briefly described.

TREATMENT OF ANAEMIA BY TRANSFUSION OF CONCENTRATED SUSPENSIONS OF RED CELLS

BY

D. H. G. MacQUAIDE, M.D., M.R.C.P.

AND

P. L. MOLLISON, M.B., M.R.C.P.

(From the S.W. London Blood Supply Depot)

Transfusion with a suspension of red cells in saline is no new method of therapy. In 1918 Oswald Robertson published a description of a method of preparing suspensions of preserved red cells in gelatin saline for the transfusion of patients with anaemia. His work was based on the experiments of Peyton Rous and Turner (1916). In Robertson's series the cells were diluted to 50% of their original concentration before transfusion. In 1937 Castellanos called attention to the advantages of a concentrated cell suspension and reported successful results. No other workers appear to have concerned themselves with this study until recently, when, with the setting up of blood banks in various countries, pathologists have presumably been stimulated by the sight of bottles containing separate layers of plasma and red cells. In America at least one institution (the Cook County Hospital) now provides a suspension of red cells in normal saline for use in anaemic states. This suspension, however, is more dilute than normal blood.

Lately it has become evident that plasma is much more easily stored than blood, and since it appears to be an adequate substitute for whole blood, in the treatment of shock at least, much of it is being prepared in the London depots. The plasma is pipetted off from bottles of blood that have been allowed to stand for six days. Thus large numbers of bottles containing only red cells remain, and until now no definite use has been suggested for them.

About six months ago we started using a red cell concentrate in the treatment of certain cases of anaemia. Over fifty transfusions have now been given, and the results enable us to put forward some tentative conclusions as to the uses and advantages of this method of therapy.

The Cell Concentrate

Originally the concentrate was prepared from stored blood from ten to fourteen days old. The plasma was

pipetted off, and with it the gel which lies between the red cells and the plasma. This gel is formed mainly from the breakdown of leucocytes, and is probably identical with the "clots" which may hamper the administration of stored blood. The highly concentrated red cell suspension that remained was fluid enough to be poured, and the contents of one bottle were added to another. To this mixture 50 c.cm. of 1.1% saline solution with 1% glucose was added; thus one bottle containing approximately 430 c.cm. of a highly concentrated red cell suspension was obtained, and this was the unit employed in most of our transfusions.

Hypertonic saline was used as a diluent because it was found to produce less haemolysis of the red cells than normal saline. We have since found that haemolysis can be further reduced by adding 8% instead of 1% glucose; this ensures a concentration of glucose of at least 1% in the final mixture. Hypertonic saline is necessary presumably because the citrate saline into which the blood is originally taken is hypertonic (Maizels and Whittaker, 1939), and cells stored with this fluid become hypertonic to normal saline.

Lately, as we have stated, many bottles containing only red cells have become available as a by-product from the preparation of plasma. Actually these bottles contain about 50 c.cm. of plasma above the red cell layer. The preparation of a concentrated cell suspension for transfusion is thus greatly facilitated, since it is only necessary to add the contents of one bottle to another to obtain approximately 480 c.cm. of fluid that contains the haemoglobin equivalent of two bottles of stored blood.

This second method of preparation, though simpler, has the disadvantage of leaving the leucocyte gel in the bottle. We have the impression that suspensions prepared in this way give rise to more reactions than do the saline suspensions. It seems possible that the leucocyte gel may therefore be at least partly responsible for the rather high reaction rate found in our series of transfusions with whole stored blood. This supposition receives further support from the fact that plasma transfusions seem practically reaction-free even when the plasma is prepared from stored blood. If the transfusion of suspensions of red cells is also associated with very few reactions suspicion must fall upon the leucocyte gel.

In preparing the concentrated suspension by either method particular care must of course be taken to avoid infection. It is advisable to use the suspension as soon as possible after it has been prepared.

Administration

The cell suspension may be given through an ordinary administering apparatus. If the leucocytes are not removed it is advisable to use a gas-mantle filter (as recommended by Maizels) or some other type with a large filtering surface. The red cell suspension was not warmed before administration because we desired to compare the reaction rate with that in a series in which we had used unwarmed whole stored blood. In many cases the blood was below room temperature on reaching the patient. The rate of administration and the amount given varied with the clinical condition of the patient.

One bottle of the cell suspension usually raises the haemoglobin approximately 10 to 15%. For instance, in one case, following a transfusion of six bottles of the cell concentrate, the haemoglobin rose from 26 to 90% and the red cells from 1,200,000 to 5,050,000 per c.mm.

The use of concentrated red cell suspensions is contra-indicated in cases of shock, where the immediate need is to restore blood volume rather than to increase the number of erythrocytes.

Reactions

In the table the reactions obtained are compared with those seen in a previous series using stored citrated whole

Reactions

	Age of Blood (in Days)	No. of Cases	No Reaction	Reactions	
				Grade II	Rigors
Whole stored blood ..	3-9 10-14	9 36	6 21	2 6	1 9
Total ..		45	60%	18%	22%
Cell suspensions ..	3-9 10-14 15-30	14 32 15	13 26 14	1 2 1	0 4 0
Total ..		61	87%	6.5%	6.5%

blood. As previously mentioned, the blood was never warmed before transfusion. All the cases were observed personally, and the temperature was taken every half-hour during the transfusion and for the next two hours.

Reactions may be classified as follows (Riddell, 1939). Grade I: rise of temperature to 100° F.; no other objective features. Grade II: similar or greater rise of temperature, with a feeling of cold or shiveriness but no actual rigor. Grade III: definite rigor. No jaundice or haemoglobinuria was encountered. Since Grade I reactions are symptomless it is on the whole misleading to include them in the "reaction rate," as they will only appear in a series which is being closely investigated.

As will be seen from the table the incidence of definite rigors was as high as 22% with whole stored blood, whereas only 6.5% occurred when the cell suspension was given. Furthermore, the blood given in the concentrated form was distinctly older on the average.

A striking example of this freedom from rigors was the case of a woman aged 43 who was suffering from acholuric jaundice. She had had five previous transfusions of whole blood, all followed by rigors. Following a splenectomy she was given six bottles of the cell concentrate over a period of thirty-six hours. No rise of temperature occurred and there were no symptoms referable to the transfusion.

Cases of acute haemorrhage have been excluded from both series, since it is usually believed that such cases have a particularly low reaction rate. Urticaria occurred in 7 of the 45 patients who were given stored blood. In the 61 who received cell suspensions, however, no urticaria was seen. This might have been expected from a theoretical consideration of the subject.

Summary

A method is described for the preparation and use of a concentrated red cell suspension.

It is suggested that this concentrated suspension has the following advantages over whole stored blood in the treatment of anaemia: (a) Less than half the usual volume of fluid will produce the same rise in haemoglobin. (b) The plasma of whole stored blood can be saved for a shocked patient. (c) Reactions are fewer. (d) The danger of transfusing potentially incompatible agglutinins when using Group O (IV) blood is greatly lessened.

Sixty-one cases have been treated with the cell concentrate; the incidence of rigors was 6.5%. This figure is contrasted with that found in a similar series of transfusions with whole stored blood, in which 22% of rigors occurred.

We should like to thank Dr. J. O. Oliver, former director of this depot, and Dr. O. M. Solandt, his successor, for permission to carry out this work. We should also like to thank Mr. E. J. Lucas for preparing the suspensions.

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Clinical Memoranda

Sulphaemoglobinaemia following Prolonged Administration of Phenacetin

The report of a case of chronic cyanosis from acetanilide poisoning by Drs. T. N. Morgan and A. Greig Anderson in the *Journal* of August 10 (p. 187) prompts us to record briefly a recent case of sulphaemoglobinaemia following prolonged dosage with the related drug phenacetin. The latter, by virtue of its inclusion in veganin and "A.P.C." tablets, is now being ever more widely used, so that it may well account for increasing numbers of patients presenting themselves with cyanosis.

CASE REPORT

A clerk was admitted to Guy's Hospital on January 16, 1940, for polyarthritis of fourteen months' duration. Previous to admission he had been under the care of Dr. J. P. Conway and had been taking a fair amount of aspirin and some veganin in order to mitigate pain.

On January 18 he was transferred to the sector base hospital, where the ward sister noted that he had a rather dusky complexion. From that time he continued to receive some phenacetin each day, the actual amount varying between 3 and 18 grains during the twenty-four hours. The patient is now strikingly cyanotic, and his appearance is a feature of the ward. As none of the usual causes of cyanosis seemed to be operative, and as the haematological findings revealed no abnormality beyond a slight anaemia (red cells 4,500,000 per c.mm. and haemoglobin 76%), a sample of his blood was investigated for the presence of abnormal pigments. On July 17 Dr. S. J. Hopkins carried out a spectroscopic examination and reported that the characteristic band of sulphaemoglobin was well marked.

COMMENT

Two points arising out of this case call for some comment. The first is that the patient on March 18 received an injection of solganal B, and he himself dates his colour change from that occasion. The sister who first noticed his peculiar hue in January also agrees that it became more pronounced after the injection of gold. We have been unable to trace any instance of gold salts having produced sulphaemoglobinaemia of themselves, but we have seen the suggestion made by some workers (Findlay, 1939) that the activity of aurothiosulphate may depend on the sulphur-containing part of the molecule rather than upon its gold. With this suggestion in mind it seems reasonable to conjecture that in the present case the earlier cyanosis may have been due to methaemoglobin, and the solganal may have precipitated the further formation of sulph-aemoglobin. It may be added parenthetically that this cannot be a case of "chrysiasis." The latter variety of pathological pigmentation resulting from gold therapy is only seen after the treatment has been persisted with for a matter of years, and is, of course, due to actual deposition of gold in the patient's skin (Kochs, 1938).

The other interesting point is that on July 25 the patient was given an intravenous injection of 10 c.cm. of 1% methylene blue, and was declared by several neutral observers who saw him within two hours to have become appreciably pinker. This effect is in contrast with a previous observation (Wendel, 1939), when it was found that the cyanosis due to sulphaemoglobinaemia was unaffected by methylene blue, although that due to methaemoglobinaemia was readily abolished.

The question of possible addiction to phenacetin cannot be fairly discussed in relation to the present case, since the preparation used also contained codeine, whose innocence in this respect is not unimpeachable. However, the patient has continued to take his phenacetin and is now as blue as ever, but, apart from this and some disability resulting from his joint condition, he remains well and very contented.

R. V. COXON, M.B., M.R.C.P., F.R.C.S.
J. P. CRAWFORD, L.R.C.P., M.R.C.S.

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