should be carried out in order to determine the dosage of the drug required and the length of its administration in the treatment of the abscess. Minor toxic symptoms were observed. The drug can be safely used as a therapeutic test if diagnosis is doubtful.

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“DANGEROUS RECIPIENTS” OF TRANSFUSION

INCOMPATIBLE REACTIONS AFTER TRANSFUSION OF GROUP O Rh-NEGATIVE BLOOD

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The following case reports are placed on record to re-emphasize that Group O Rh-negative blood is not free of potentially dangerous blood-group factors, and that inexperienced medical staff are not suitable persons to undertake the matching of blood for transfusion.

Case 1

A multiparous woman aged 26, known to be Group O Rh-positive, was delivered of her third baby by elective caesarean section. Because of haemorrhage during the operation a transfusion of 2 pints (1,140 ml.) of blood became necessary, and the house-surgeon “matched” two bottles of Group O Rh-positive blood against the patient's serum by a saline slide technique. No incompatibility was detected, but on the day after the transfusion the patient was noticed to be “slightly jaundiced.” The baby also had developed a definite jaundice within a few hours of birth, but since the mother was Rh-positive and the baby's haemoglobin was 140% (20.7 g. per 100 ml.) the possibility that the mother's serum contained irregular blood-group antibodies was not considered.

Seven days later the mother's general condition was unsatisfactory and her haemoglobin 35% (5.2 g. per 100 ml.). Transfusion of a further 2 pints (1,140 ml.) of blood was therefore prescribed, and on this occasion the house-surgeon selected and matched 2 pints (1,140 ml.) of Group O Rh-negative blood, presumably as a safeguard against a haemolytic transfusion reaction. No incompatibility was detected, but the transfusion was discontinued after 1½ pints (850 ml.)

had been transfused because the patient had developed a severe rigor. During the next 48 hours she had jaundice and oliguria. Although her haemoglobin remained at 35% (5.2 g. per 100 ml.) she refused any further transfusion and made a gradual recovery to normal health during the next six to eight weeks.

Laboratory investigations showed the patient's blood to be Group O Rh-positive, Rh genotype cDE/cDE, and that the transfused Rh-negative cells had undergone haemolysis. Immune antibodies, type anti-e + anti-C, were demonstrable in the patient's serum to a titre of 256 with homozygous e-positive red cells (Rh-negative cells, cde/cde) suspended in saline and in albumin. The titre against heterozygous cells (R₁R₂CDe/cDE) was 64.

Inquiry into the patient's previous history revealed that she had been transfused with 4 pints (2,270 ml.) of blood (Rh group unknown) at her first pregnancy seven years before, because of a severe accidental haemorrhage, and was subsequently delivered of a stillborn macerated foetus. Her second pregnancy, three years later, had resulted in the delivery of a healthy female child who had shown “a slight jaundice” shortly after birth, but whose subsequent progress was uneventful. The third baby, the outcome of the pregnancy under discussion, was subsequently found to be Group A, R₁R₂ (CDe/cDE); a direct antiglobulin (Coombs) test on its red cells was positive, and by the twenty-ninth day of life its haemoglobin had dropped to 42% (6.2 g. per 100 ml.). After a transfusion of Group O blood of genotype cDE/cDE it made a satisfactory recovery.

Case 2

A woman who had had two normal children received an emergency blood transfusion (group unknown) during an air raid in 1941. Later she had one normal full-term child and then two miscarriages, each being a six-months foetus. At the age of 42 she was admitted to hospital because of menorrhagia. After a few days in hospital she had a sudden haemorrhage at night, and a resident house-surgeon transfused a pint (570 ml.) of Group O Rh-negative blood in emergency and without previous direct matching. At the same time another member of the resident medical staff “matched” a further bottle of Group O Rh-negative blood for her by a slide technique, but transfusion of this blood was found not to be necessary. Nine days later it was decided to transfuse this “matched” blood so that the patient might be made fit for curettage. She developed a rigor at the conclusion of this transfusion, followed by jaundice, haemoglobinuria, and oliguria for the next seven days.

Serological investigations demonstrated the patient to be Group O Rh-positive, Rh genotype CDe/CDe. Immune antibodies of the type anti-c + anti-E were demonstrable in the post-transfusion sample of her blood to a titre of 32 in saline and 256 in albumin against homozygous c-positive cells (Rh-negative cells, cde/cde), and 2-4 in saline and 16-32 in albumin against heterozygous c-positive cells (R₁R₂, CDe/cde). The patient's post-transfusion sample contained no Rh-negative cells, thus confirming that the blood transfused was incompatible.

Comments

Both these patients nearly lost their lives, and both suffered severe renal damage, because of the transfusion of Group O Rh-negative blood. Fortunately, although Rh-negative corpuscles contain the Rh antigens c, d, and e, and may contain other antigens such as Kell, Fya, and S, which are known to have been the cause of similar haemolytic transfusion reactions, few patients requiring transfusion possess the corresponding antibodies, anti-c, anti-e, anti-Kell, etc., in their plasma. In consequence incompatible transfusions from this cause remain a rarity. The fact, however, that immune antibodies of this type may be present in the circulation of certain patients, even on rare occasions, constitutes a challenge, and, by a more thorough applica-

tion of knowledge already well established regarding the hazards of transfusion therapy, accidents from this cause need not arise.

In neither of these instances was the transfusion of whole blood so pressing that advantage could not have been taken of existing laboratory facilities for blood-matching by trained laboratory staff. These cases serve as a reminder that this must be done whenever circumstances permit if the best service is to be given to the patient. As soon as plasma prepared during the war years was found to carry a risk approaching 10% of inducing hepatitis in the recipient, preliminary plasma transfusion whilst the matching of blood was being undertaken, or as the sole emergency transfusion for cases of moderate haemorrhage, wisely fell into disrepute. Now that the transfusion of "small-pool" plasma carries little greater risk of transferring the hepatitis virus than does a transfusion of whole blood, and, alternatively, satisfactory plasma substitutes, dextran and polyvinylpyrrolidone, are available, we believe with Discombe (1952) that greater use should be made of such fluids for the avoidance of incompatible transfusions.

Immune antibodies active against transfused corpuscles of the patient's own ABO group are particularly likely to be present in the circulation of recipients who have had jaundiced or stillborn babies, or who have reacted adversely with a rigor, jaundice, or haemoglobinuria to a previous blood transfusion. Even in a dire emergency, therefore, such as a domiciliary "flying-squad" emergency, where the transfusion of unmatched whole blood may seem entirely warranted, strenuous efforts should be made to have blood specially matched against the patient's serum when there is a history suggesting the presence of immune antibodies. It is such patients that one of us (Tovey, 1950) has proposed should be termed "dangerous recipients," and in each of the above cases the patient's history would have placed her in this category.

Dangerous recipients run a particular risk in that if they are Rh-positive the immune antibodies they have developed may well be of the type anti-c or anti-e, and thus active against Rh-negative corpuscles (cde/cde). Or, should the recipient be Rh-negative with Rh antibodies (anti-D) in her serum, an Rh D-positive bottle of blood which has been misgrouped or mislabelled "Rh-negative" may give rise to a serious haemolytic transfusion reaction. Moreover, in some instances incompatibility from immune antibodies can be detected *in vitro* only by methods of direct matching which are too complicated to employ as a routine, such as an indirect antiglobulin technique or a titration procedure using bovine albumin. It is important, therefore, that clinicians obtain a history of the outcome of previous pregnancies or transfusions from any patient about to be transfused. Should the history indicate the patient to be a dangerous recipient, blood should not be transfused until it has been matched by the special procedures mentioned. Whenever possible, the danger in the event of an emergency transfusion should be anticipated, and as soon as it is known that a patient has given birth to a jaundiced or stillborn baby or has suffered a serious reaction to transfusion a full serological examination should be carried out to determine whether immune antibodies are present, and, if so, their exact type.

In neither of the above patients, although their histories indicated the need, had such serological investigations been made before the transfusion accidents. Although Gunz (1946) drew attention to the need for a standard history sheet to accompany every request for transfusion, and such a sheet has been employed by regional transfusion centres for the past six years, many hospitals are still not taking this precaution as a routine for their cases for transfusion.

Case 2 further illustrates that, although a patient may be transfused without serious reaction with blood of a certain ABO and Rh group, this does not mean that a later transfusion of blood of the same ABO and Rh group will be similarly unaccompanied by reaction. It is important to bear in mind that the transfusion of blood can result in

the stimulation of dangerous antibodies, and any further blood for transfusion should invariably be matched on a freshly taken sample of the recipient's serum if more than 48 hours have elapsed since a previous transfusion.

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SENSITIVITY OF AUTONOMIC GANGLIA TO HEXAMETHONIUM IN HYPERTENSION

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The introduction of hexamethonium bromide (H.M.B.) by Paton and Zaimis (1949, 1951) as a substance which blocks the transmission of nervous impulses across the synapses of autonomic ganglia presented a potentially valuable therapeutic means of controlling hypertension. The specificity of its action on autonomic ganglia makes it also a most valuable tool in the study of the autonomic nervous system, and this property is used here to study the underlying mechanisms producing hypertension. Repeated doses of hexamethonium bromide or bitartrate* are given intravenously, and the following points are observed:

- (1) the sensitivity of the blood pressure to depression by autonomic blockade;
- (2) the level to which the diastolic blood pressure may be depressed; and
- (3) the dose required to affect the pupillary light reflex.

The first indicates the state of activity of the autonomic ganglia controlling blood vessels, and incidentally the suitability of patients for treatment. The second gives the minimal diastolic pressure which is used to differentiate various types of hypertension. This term is used in the sense defined by Frew and Rosenheim (1949), as the pressure maintained by the inherent tone of the blood vessels and circulating pressor substances, and corresponds to the term blood pressure "floor" of Ferris *et al.* (1948). Both of these authors used tetraethylammonium bromide (T.E.A.B.) to block autonomic ganglia.

Material

Tests were performed on patients who had been in hospital for at least seven days, and in one-third of the cases repeated tests were performed to establish the reliability of the method. The admission of patients to hospital was made for the investigation and treatment of hypertension or renal disease, and was quite independent of the present study. Cases with heart failure, extreme renal failure, or a history of recent thromboses were excluded.

The clinical diagnosis of essential hypertension was made after exclusion of other causes. Renal hypertension was assumed to be present if evidence could be obtained of

*All doses are expressed as those of the dibromide salt. Messrs. May and Baker kindly gave supplies of the bitartrate used in this investigation.