severe bronchitis, and was treated conservatively till the chest was better. Unfortunately he had a relapse about 12 days after operation, and finally died on the 63rd day. Case 3 was admitted with cardiac failure and auricular fibrillation. I therefore attempted to tide him over with catheterization, but when this had failed to relieve him and the cardiac condition had improved operation was undertaken. Possibly these patients might have survived had they been treated with simple suprapubic drainage. In neither instance was there evidence of much renal damage, and therefore not such strong contraindication to tube drainage and its associated sepsis.

Among the cases of overflow retention there were three deaths out of 27 operations. Case 5 had a bad setback with post-operative clot retention, and this was a material factor contributing towards his death. Case 6 had been kept in bed for five weeks before I saw him, and this fact probably contributed to the onset of the chest condition to which he succumbed. Case 7 was a bitter disappointment: in spite of an initial blood urea of 266 mg., he made good but slow progress till the 19th day. At this stage it was decided to expedite his recovery with a blood transfusion. While this was in progress he had a rigor followed by left-sided facial paralysis, and died shortly afterwards. Necropsy showed a poor myocardium, and Dr. H. R. Mavor, the pathologist, considered death was due to transfusion reaction.

Of the group classified as "prostatic syndrome," Case 8, a fit man of 61, developed mild wound sepsis, but unfortunately at that time there was an outbreak of streptococcal infection in the ward, and he died on the 21st day from cross-infection: blood culture showed a haemolytic streptococcus. Cases 9 and 10 both insisted on having something further done as they were so miserable with their suprapubic tubes: in each instance they were advised against further operation. Case 9 had refused to have his tube put back when it was taken out by his doctor for routine replacement, and was in a miserable condition owing to a suprapubic fistula. Case 10 always had a low-grade infection around his tube, and this resulted in an unpleasant eczematous condition of the genitalia.

Commentary

Admittedly it is difficult to draw conclusions from a small series of cases, and owing to the advent of new sulphonamides and penicillin the three series quoted here are not strictly comparable. However, it is submitted that the figures shown give strong support to the theories put forward by Wilson Hey (1945), who maintains that "post-operative uraemia is due to infection and is encouraged by any method of slow decompression, open drainage, or instrumentation." Certainly it has been my experience that cases catheterized before admission were far more apt to give trouble during their convalescence.

If only selected cases are submitted to radical operation a low mortality rate can be obtained, but emphasis is laid on the fact that *all* my cases are included in this report, and some were extremely sick patients and really deplorable operative risks.

The benefits of immediate prostatectomy for the patient with retention of urine are very great, for he is spared prolonged and sometimes painful pre-operative treatment and a long illness. Some notice must also be taken of the economic factors involved, as the rapid recovery of patients is most necessary at the present time, when there is such a shortage of hospital beds.

Attention to details in treatment is of paramount importance, for even a comparatively trivial setback, such as a blocked catheter, may have serious consequences in

elderly and decrepit patients. All cases get out of bed the day after operation, and to this may be attributed the low incidence of chest complications. The majority go home in good condition about the 12th to 16th day.

Summary

A consecutive series of 141 cases of benign prostatic hypertrophy is recorded; 138 were submitted to radical operation.

Except on very rare occasions, drainage before operation, whether by catheter or suprapubic tube, is not considered necessary or desirable.

There were 97 cases of retention of urine which, wherever feasible, were treated by immediate prostatectomy: 7 (7.2%) died; 70 were operated on for acute retention, with 4 (5.7%) deaths.

As many cases were admitted in very poor condition, the results shown are considered satisfactory. It seems that the method of immediate prostatectomy is well worthy of an extended trial.

I am indebted to Dr. J. Clutton Brock, who was responsible for most of the anaesthetics, and to my house-surgeon, Mr. P. F. Philip, for his help in compiling statistics and for doing some of the emergency operations on my behalf.

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SOME SIMPLE OBSERVATIONS ON TRANSFUSION REACTIONS

BY

JOHN WALLACE, M.B., B.Sc.Edin.

*West of Scotland Blood Transfusion Service; Late Specialist in
Blood Transfusion and Resuscitation, R.A.M.C.*

AND

R. D. RICHARDS, M.B., B.Ch., B.Sc.Wales, F.R.C.S.Eng.

*Surgical Registrar, Morriston Emergency Hospital;
Late Surgical Specialist, R.A.M.C.*

During the training of several hundred transfusion orderlies it was possible to make some simple observations on transfusion reactions. It was essential that these orderlies should be able to perform venepuncture and to carry out transfusions themselves lest at any time under active service conditions the medical officer was not available. In order to give them the opportunity of acquiring the technique of inserting needles into veins, the majority of the orderlies volunteered to undergo venesection and subsequent reinfusion by their colleagues, under the supervision of one of the instructors. The volunteers were each venesected to the extent of 440 ml. of blood, and their own citrated blood was reinfused. In this way 324 collections and reinfusions of blood were performed, and in addition 56 infusions of glucose-saline, each of 540 ml., were given. The reactions observed are described.

Febrile Reactions

Oral temperatures were recorded by leaving a thermometer *in situ* for at least three minutes, and records were taken before, and at hourly intervals for four hours after,

infusions. Out of a total of 324 infusions of blood a rise of temperature was observed on nine occasions, an incidence of 2.8%. Using the classification of Riddell (1939), seven of these reactions were Grade II (2.2%) and two were Grade III (0.6%). It was possible to state the probable cause of these reactions in all but one case.

Investigation of the first reaction showed that a new orderly had inadvertently taken a set from the non-sterile pile unknown to the supervising medical officer. This was a Grade II reaction, and that it was not more severe was probably explained by the fact that the set had been recently assembled from carefully washed components, and by the fact that the blood was fresh and therefore still retained some bacteriostatic properties.

The second febrile reaction occurred in a volunteer reinfused with his blood, which had been collected into a sample of sodium citrate free from moulds but containing numerous small particles such as are not infrequently present in bottles of crystalloid transfusion fluids. A Grade III reaction ensued, but an interesting feature of this case was that the onset of the rigor was delayed for some two hours after the end of the transfusion.

For the third observed febrile reaction no explanation could be found, but the remaining six reactions were very interesting. It was customary to use "giving" sets assembled and sterilized by the transfusion orderlies, or sets recently issued from the Army Blood Supply Depot. One day it was discovered that an orderly had collected sets sterilized eighteen months previously. Although the "cellophane" wrapping had lost its "crispness," these sets were still sealed, and it was therefore decided to use them. Out of five infusions three subjects developed Grade II reactions. The following day only three subjects were reinfused with these old sets, and all developed a febrile reaction, including one Grade III reaction.

No febrile reactions have followed the 56 infusions of glucose-saline, but it is of interest to note one false reaction. In this particular case it was found that the subject had a temperature of 102° F. (38.9° C.) four hours after the infusion. He was, however, found to be suffering from acute follicular tonsillitis.

Infusions

Duration of Blood Storage.—In most cases the reinfusion was started within one hour of collection, but in 11 cases the blood was stored for two days and in 20 cases for seven days before reinfusion. The blood was cleanly and properly collected, and immediately, accurately, and continuously refrigerated between 2 and 6° C. In none of these 31 cases did a febrile reaction follow the infusion.

Temperature of the Infusion Fluid.—In 36 infusions of glucose-saline the fluid was given at room temperature, while in the other 20 the fluid was warmed in a bucket of water at approximately 40° C. As previously noted, febrile reactions did not occur in any of these saline infusions. The infusions of blood were performed at room temperature, the refrigerated blood being warmed to that temperature. In three cases blood was taken straight from the refrigerator and immediately reinfused (as was the practice in several field transfusion units on active service) without any reaction apart from venous spasm in one case, described below.

Rate of Administration.—The saline infusions were given at a standard rate of approximately 40 ml. a minute and no reactions were observed. With blood the usual rate of administration was 20 ml. a minute, but in 24 cases a rapid infusion was given at rates varying from 80 to 110 ml. a

minute. The following observations were made during these 24 rapid infusions:

Nature of Reaction	No. of Cases in which Observed
Rise in temperature	0
Flushing	9
Venous filling	9
Fullness in head	7
Shivering and feeling of cold	3
Feeling cold without shivering	3
Tingling of lips	14

These reactions were transient, and in each case passed off a few minutes after ending the infusion.

Venous Spasm

This was observed in five cases only. In three of these the intense local spasm of the vein was enough to interfere with the administration, but on the application of local heat the spasm was relieved and the infusion given without difficulty. In all five cases it seemed to be the mechanical insertion of the needle which caused the spasm. Veins which were large, obviously visible, and easily palpable suddenly became small and almost impalpable on the insertion of the needle. In one case, however, the temperature of the fluid was an additional factor causing venous spasm, and this case is described in detail.

The subject was a healthy young man with very large veins. When he had been venesected it had been noted that his large vein suddenly became small on the insertion of the needle, but the spasm rapidly passed off. On this particular occasion the blood for reinfusion, which had been stored for two days, was administered at the temperature of the refrigerator. The venepuncture of an antecubital vein was cleanly performed, but the vein immediately went into spasm. In spite of the fluid's being cold the spasm appeared to pass off and 540 ml. was given without difficulty in half an hour. The only subjective phenomenon was that he felt his arm cold, and it was observed that the skin of the upper arm was much colder on the infusion arm, although the skin of the forearm appeared equally warm on the two sides. No difference in colour was noted between the two sides. About half an hour after the end of the infusion the subject complained of "stiffness" of the upper arm used for the infusion. There was at this time full movement at the elbow, but the skin of the upper arm was intensely cold. The subject was reassured, but two hours later he reported acute stiffness of his elbow.

On examination only a few degrees of flexion at the elbow was possible and supination was limited. There was acute tenderness over the biceps, particularly over the tendon, and this was limited to the muscle. The skin was now equally warm on both arms and the brachial pulses were equal. There was no evidence of any discoloration; the vein which had been used for the infusion was still patent and there was no tenderness over it. Otherwise the subject felt perfectly well and his pulse and temperature were normal. The diameter of the upper arm was 2 in. (5 cm.) greater on the affected side than on the other. He was given a hot bath and a sedative and sent to bed. The next day his movements at the elbow were almost normal and he had only slight stiffness. The difference in diameter persisted, but there was only slight tenderness over the biceps. No abnormality of the vein was detected. Then 48 hours after the infusion he noticed a bluish discoloration over the medial aspect of his forearm. Movement at the elbow was now normal, the difference in diameter was 1½ in. (3.75 cm.), and there was no discoloration in relation to the vein used for the infusion. The vein itself was patent and there was no pain or tenderness along it. The discoloration spread along the medial aspect of the forearm, but the whole condition cleared up in a few days, the normal difference in diameter between the two arms being 1 in. (2.5 cm.).

A similar phenomenon was observed in another of the five cases of venous spasm, although in this case the reinfused blood was at room temperature. Here also it had been noted that the vein went into spasm during the collection of the blood. The venepuncture for the infusion was cleanly performed, and 100 ml. was infused without

difficulty in three minutes in spite of the fact that the vein had gone into spasm at the insertion of the needle. Then the subject complained of intense pain over the upper arm and the infusion was stopped. The subsequent course was very similar to the previous case, with restricted movement at the elbow and swelling of and intense tenderness over the biceps muscle. The discoloration did not appear until 72 hours after the infusion.

It is suggested that these two cases were not examples of extravasation of blood from faulty venepuncture, because of the apparently clean insertion of the needle, the ease of administration, the absence of pain around the site of puncture, and the long delay in the appearance of the discoloration. Rather it is suggested that there was an intense spasm of veins draining the biceps muscle, with rupture of some tributaries within the muscle. To support this we have the swelling and tenderness confined to the biceps and the delayed appearance of discoloration as the blood slowly tracked down.

Other Reactions

Thrombosis of the vein used for reinfusion occurred in only three cases. Apart from slight pain there were no other subjective features in these cases of thrombosis. There were no cases of *infection* following the venepuncture or the use of the local analgesic. Mild *sensitivity* to the "elastoplast" dressings used was seen in only one case. Air embolism never occurred, but the danger was constantly emphasized, particularly from the emptying of the transfusion bottle when using the Army overseas pattern set with its one-way air inlet.

Careful records were kept of reactions occurring during or after venesection. There were no cases of fainting either during or after the collection of blood. Out of the 324 blood collections there were only six cases which showed mild incipient and transient features of the vasovagal syndrome. These all occurred a few minutes after the blood collection had ended. There were no cases of delayed faints among the 31 subjects in whom the blood was not immediately reinfused.

Discussion

Kordenat and Smithies (1925) and Riddell (1939) state that nearly all transfusions of fresh blood were associated with a rise of temperature even though this might be symptomless. Again, Jewesbury (1941) states that a rigor occurs in about 8% of fresh blood transfusions. These febrile reactions are caused by foreign protein, dead bacteria, stale distilled water, impure chemicals, and, above all, dirty apparatus. It was shown by Lewisohn and Rosenthal (1933) that the incidence of febrile reactions was reduced from 12% to 1.2% by the scrupulous cleaning of apparatus and by using freshly distilled water. The present observations show that with fresh blood, stored blood, and crystalloid solutions febrile reactions can be reduced to almost negligible proportions provided every care is taken in the preparation of the solutions and apparatus and in the collection and storage of the blood. Whitby (1942) emphasizes the care that is necessary in the handling of stored blood in order to avoid these hazards.

Maycock and Whitby (1941) state that too fast a rate can cause a rigor, which ceases instantly if the rate is slowed. In the present observations no rigors occurred in the cases of rapid infusions, but some of the subjects receiving them felt cold and shivery. This shivering passed off almost immediately after the end of the infusion, and it should be noted that no rise of temperature was associated with the shivering. In our opinion these shivering attacks and rigors associated with rapid infusions are not true

febrile reactions. In our clinical experience of true febrile transfusion reactions it has been noted that slowing the rate of administration does not abolish the shivering of a true febrile reaction. The exact nature of these non-febrile shivering attacks or rigors sometimes associated with a rapid transfusion is not clear. It is of interest to note in the present series that the three cases of shivering and the three cases of feeling cold during the rapid infusion did not show any signs of vasodilatation such as fullness in the head, flushing, or distended peripheral veins; indeed, in three of these six cases the subject became pale. Conversely, none of the subjects showing signs of vasodilatation during the rapid infusions developed a feeling of cold or shivering. It is suggested that the sudden introduction of a large volume of fluid at room temperature into the circulation produces in some subjects a compensatory vasoconstriction, with a resultant feeling of cold. In a previous observation made by one of us (Sharpey-Schafer and Wallace, 1942a, 1942b) on rapid infusions in subjects who had been venesected and then infused with serum there were no rigors or shivering attacks even in those who showed no signs of vasodilatation, although the volumes of fluid infused were much larger than in the present series. In the previous series, however, the infused fluid was warmed to body temperature, whereas in the present one it was given at room temperature.

If this explanation of these shiverings and rigors associated with rapid transfusions is the correct one it raises the practical problem of the advisability of warming transfusion fluids. It is theoretically sound to warm all transfusion fluids to body temperature, but in practice in a busy resuscitation ward this has usually proved impossible. In those cases of oligæmic shock which have developed a shivering attack or a rigor during a rapid infusion of fluid at room temperature it has been our practice to continue the rapid infusion if the level of the blood pressure demanded a rapid transfusion. Our impression has been that those suffering from oligæmic shock who had developed these shivering attacks improved dramatically with the onset of the shivering just as if there had been a stimulation of the vasomotor centre. It must be emphasized, however, that this rapid infusion of blood should be continued only if it is not a hæmolytic reaction or circulatory overloading which is causing the rigor.

It was shown by Sharpey-Schafer and Wallace (1942b) that when the blood volume was reduced by a large venesection (1,000 ml.) injection of serum or saline in similar quantities at a rapid rate produced little or no change in venous pressure or other signs or symptoms of vasodilatation. In the present series, however, where the venesection was smaller and the replacement fluid was blood, some subjects did show a transient rise in venous pressure and manifestations of vasodilatation. After a large venesection in man hæmodilution is slow, but in some cases there is an immediate small dilution (Stead, 1940; Wallace and Sharpey-Schafer, 1941). In a small venesection (440 ml.) this immediate dilution may be enough to restore the blood volume to its original level, and it is probable that the cases showing vasodilatation in the present series were those which had already restored their blood volumes by this rapid initial dilution.

The complete absence of faints following blood collection and the low incidence of even mild vasovagal attacks are probably explained by the type of donor with whom we were dealing. These orderlies were intensely interested in transfusion work, and most of them had volunteered for it. The whole atmosphere was friendly and reassuring, for although most of the venepunctures were performed by orderlies there was always a medical officer in attendance.

Summary

The collection of 440 ml. of blood and the reinfusion of this citrated blood were performed on 324 individuals. An infusion of 540 ml. of glucose-saline was given to 56 individuals.

Febrile reactions occurred in nine of the 324 infusions of blood, but in none of the infusions of glucose-saline. The causes of these reactions are elucidated.

Febrile reactions are no more common with stored blood than with fresh blood, provided the blood is cleanly collected and properly stored.

The effect of the temperature and the rate of administration of the infused fluid on reactions are described.

Venous spasm, thrombosis, and mild vasovagal features were observed in a few cases.

The avoidance of pyrexial reactions and the cause of rigors associated with rapid infusions are discussed.

These observations were made during the routine training of transfusion orderlies, and we thank our commanding officer, Brigadier Sir Lionel Whitby, for his great interest and help in the training of personnel in transfusion and resuscitation.

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ISO-IMMUNIZATION BY THE BLOOD FACTOR N

BY

L. DE KROMME

AND

L. A. M. VAN DER SPEK, M.D.

(From the Blood Transfusion Laboratory of the Onze Lieve Vrouwe Gasthuis, Amsterdam)

It is well known that blood factors of the ABO, MN, and Rh systems are found in the erythrocytes of every human being. In contrast with the ABO system, no naturally occurring antibodies directed against the Rh factors are found in the plasma. Immune or normal M and N antibodies are very rarely observed in human sera in spite of the fact that in giving blood transfusions no account is taken of the M and N blood types of donor and recipient. From this we may conclude that the M and N factors are very weak antigens for human beings.

Allot and Holman (1947) found several irregular antibodies, including one anti-N agglutinin. The late G. L. Taylor also found normal N antibodies in one case (Callender and Race, 1946).

So far as we know, only two cases of an N immunization are described in the literature. The first was published in 1943 by Singer. It concerned a Rh-positive patient with blood type M. This patient had received a transfusion with Rh-positive N blood. After further transfusions, again with Rh-positive N blood, the patient showed a haemolytic reaction. Anti-N agglutinins were indicated in the serum. Transfusion with M blood was endured without any reaction. The second case was described in 1946 by Callender and Race. A patient suffering from lupus

erythematosus diffusus displayed a great aptitude in forming various rare antibodies—so much so that some “new” blood factors were discovered by the authors. During the course of her illness, in which a number of large and small transfusions were given, anti-c (anti-Hr') and anti-N antibodies were found in the plasma. These two cases of iso-sensitization by the N antigen occurred in patients who were immunized in consequence of blood transfusions.

In recent years we have become conversant with another method of iso-sensitization—namely, with the immunization of mothers by Rh and A or B antigens of the foetus. It is now generally known that iso-antibodies formed during pregnancy are responsible for erythroblastosis foetalis. The question arises whether an antagonism in MN blood types of mother and child might be responsible for symptoms of the newborn. No cases of iso-sensitization by the N antigen in MN heterospecific pregnancies are mentioned in the literature so far. At the end of 1946 we came into contact with the following case.

Case History

A married woman, aged 33, had had her first pregnancy end in 1944 at term with the birth of a foetus maceratus. Her second, in 1945, ended at term after a long partus. A living child was born, which died, however, some hours later. From this infant no further clinical data could be obtained. In the seventh month of her third pregnancy a specimen of her blood was sent to us by Dr. Castelein, St. Elisabeth Hospital, Tilburg. It was Rh-positive and had the blood formula R_1R_2 (CDe/cDe)-A-M. In the combination CDe/cDe of rhesus elementary antigens only d is missing. Concerning the possibility of a sensitization within the Rh system, therefore, this mother theoretically should be able to form only anti-d antibodies, but this antibody could not be found in the serum at any time.

In the meantime we also received blood from the husband for examination. He also was Rh-positive and had the blood formula R_1r (CDe/cde)-O-MN. Contrary to our expectation the blood cells of the man were agglutinated by the serum of the woman. By testing a large number of A and O bloods with the serum of the mother we obtained some more positive reactions, without finding any connexion with the factor d.

With regard to the MN types, it was possible that the woman (M) had been immunized by the factor N inherited from the husband (MN)—a possibility overlooked before. Indeed, the serum of the mother was found to contain anti-N antibodies and to agglutinate only N or MN blood (Group A or O being used). We supposed the N antibodies originated from the iso-immunization during the preceding pregnancy(ies), and that both affected foetuses had inherited the N antigen from the father. Naturally this could not now be proved. If the N antibodies had made both children ill it would be expected that the subsequent child, if MN, would show symptoms. If the child turned out to be MM then it might be expected not to show symptoms.

Three months after our examination caesarean section was carried out. Blood from the umbilical cord was sent to us for examination. The child was Rh-positive and had the formula R_1r (cDe/cde)-O-M. It is certain that this child could not have suffered from the existing abnormal anti-N antibodies, which, moreover, could not be detected in his own serum. As we expected, the baby seemed to be completely normal at birth and it developed like a healthy child. We believe that the occurrence of the anti-N agglutinins in the mother's plasma must be due to sensitization by foetal agglutinogens during the first two pregnancies. Indeed, though it is remarkable that the first child was affected, we are fairly certain of the correctness of this assumption, since 10 months after the second pregnancy the agglutinin titre seemed to be rather low (<4), tending to decrease slowly but continuously during the following three months—the last three months of the third pregnancy. Also, anti-N agglutinins could not be detected in the child's plasma at the moment of birth.