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.

REFERENCES

- Jewesbury, E. C. O. (1941). *British Medical Journal*, **1**, 663.
Kordenat, R. P., and Smithies, F. (1925). *J. Amer. med. Ass.*, **85**, 1193.
Lewisohn, R., and Rosenthal, M. (1933). *Ibid.*, **100**, 466.
Maycock, W. d'A., and Whitby, L. E. H. (1941). *J. R. Army med. Cps*, **77**, 173.
Riddell, V. H. (1939). *Blood Transfusion*, London.
Sharpey-Schafer, E. P., and Wallace, J. (1942a). *Lancet*, **1**, 699.
— (1942b). *British Medical Journal*, **2**, 304.
Stead, E. A. (1940). *J. clin. Invest.*, **19**, 776.
Wallace, J., and Sharpey-Schafer, E. P. (1941). *Lancet*, **2**, 393.
Whitby, L. E. H. (1942). *Ibid.*, **1**, 581.

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.

Comment

The question arises whether we are entitled to impute the death of the first two children to the action of the N antibodies detected in the mother's plasma. Of course we cannot be sure. Against this suggestion is the fact that the agglutinin was active only at room or colder temperatures, but inactive at 37° C. On the other hand the possibility cannot be absolutely excluded that under such circumstances as those present *in vivo* these cold agglutinins are able to damage the erythrocytes at body temperature. In connexion with this we recall the observations of Weiner, who, by using his conglutination technique in a case of acquired haemolytic anaemia, succeeded in demonstrating auto-agglutination *in vitro* at body temperature as well as in the refrigerator. It is clear that the circumstances *in vivo* show a greater resemblance to those of the conglutination reaction than to those of the agglutination reaction. Moreover, we do not know how high the anti-N titre had been during the first two pregnancies, and we do not know if the anti-N agglutinins then present *in vitro* were active only at lower temperatures.

Summary

In the serum of a pregnant woman anti-N agglutinins have been detected. These agglutinins are considered to be immune iso-antibodies.

The possibility of these anti-N antibodies being responsible for a stillbirth as well as for the death of a child some hours after birth is discussed.

We wish to thank Dr. R. R. Race for his kindness in confirming our serological findings and for his interest in our work.

REFERENCES

- Allott, E. N., and Holman, C. A. (1947). *Lancet*, 2, 130.
Callender, Sheila T., and Race, R. R. (1946). *Ann. Eugen. Camb.*, 13, Part 2, 102.
Singer, E. (1943). *Med. J. Aust.*, 2, 29.

Medical Memoranda

Rupture of the Stomach in an African Child

Rupture of the stomach in the following case was, we believe, caused by gross gastric distension due to the action of gas-forming fermentative organisms, and we consider this unusual case may be of some interest.

CASE REPORT

A 5-year-old Acholi boy was brought to Mulago Hospital at 4 p.m. on April 26, 1946, for the fifth injection (N.A.B. and bismuth) in a course of treatment for yaws. The child was examined by an assistant medical officer, who, finding a solid mobile tumour in the hypogastrium, admitted him to hospital for investigation. Food was brought by the mother and given to the child at 6 p.m. At 11 p.m. the patient complained of abdominal pain, and there was vomiting of mucus. The condition progressed during the night, and when he was seen by one of us (R. G. L.) at 8 o'clock the next morning there was considerable distension confined to the epigastric and right hypochondriac regions.

The general condition was very poor, the patient being only semi-conscious. Continuous intravenous saline was given, and laparotomy was performed at 11 a.m. The abdominal distension by that time had increased and had become generalized.

At operation the mobile abdominal tumour was found to be a spleen with a very long mesentery; there was nothing to suggest that recent displacement had occurred. The peritoneal cavity was grossly distended with gas and fluid, but there was no evidence of peritonitis. The stomach was spherical in shape and about 7 in. (17.5 cm.) in diameter. There was a tear about 3 in. (7.5 cm.) long in the posterior wall of the stomach beginning at the cardiac sphincter. From this tear large amounts of fluid and gas poured out as soon as the stomach was handled. The peritoneal and gastric contents had a very penetrating smell which, though clearly alcoholic, did not

resemble any form of native beer. Closure of the tear was attempted, but the child died.

Necropsy was performed three hours after death (J. N. P. D.). In view of the history a careful search was made for evidence of trauma, but nothing was found. Relevant findings were confined to the abdomen. An enlarged spleen was lying in the right iliac fossa, its long mesentery lying across the transverse colon but below the stomach and causing congestion in the part of the pancreas which was lying underneath. The peritoneal cavity was full of gas and of a frothy grey-white fluid, like thin gruel, in which were floating solid particles of food. A curious penetrating alcoholic odour was given off. This could not be identified by anyone present, including the head African mortuary attendant—a great expert in recognizing post-mortem alcoholic odours.

The posterior wall of the stomach showed a linear tear 3 in. long that extended about 1/2 in. (1.25 cm.) into the oesophagus. The stomach otherwise was normal. It was filled with gas and liquid similar to that in the peritoneum; the fluid continued to ferment and to produce quantities of gas and ethyl alcohol from the particles of sweet potatoes which were identified in the peritoneal fluid.

Microscopically the stomach wall was normal and showed no evidence of any condition likely to lead to rupture. The peritoneal contents on culture grew a mixture of organisms, including Gram-negative cocci and bacilli. This mixture of organisms fermented a wide range of sugars and produced large quantities of gas, but unfortunately the cultures were lost and further investigation was impossible.

DISCUSSION

Close inquiry revealed that no native medicine or beer had been given to the child, and, as stated, there was no evidence of trauma. We suggest that the fermentation of the evening meal of sweet potato produced gas under such pressure as to rupture the stomach. It may be that a very slight trauma inflicted on a greatly distended stomach might have caused the rupture. Clinically it appeared clear that at 8 a.m. the distension was of gastric origin, whereas by 11 a.m. general distension had occurred following intraperitoneal rupture, and during this time the child was lying in bed. By European standards the meals taken by African children are enormous, which probably accounts for their thinner stomach walls, with presumably a greater tendency to rupture. In this case there seemed to be no reason why the gas should not have been eructated. The dependent spleen seemed to be of no concern here.

It is perhaps of interest to point out that the overdistension of the African stomach not infrequently leads to death because of the inhaling of vomitus. This was the cause of death in six cases out of 100 necropsies performed by police request on cases of sudden death not due to violence recorded at Mulago Hospital.

A further case is on record of a young male African child whose death was due to shock from rupture of a grossly over-distended stomach, the result of an enormous meal. As in the case here recorded there was no history or sign of disease or trauma.

Our thanks are due to the Director of Medical Services, Uganda, for permission to publish.

R. G. LADKIN, B.M., B.Ch.,
Medical Officer, Colonial
Medical Service, Uganda.

J. N. P. DAVIES, M.B., Ch.B.,
Pathologist, Colonial Medical Service,
Uganda.

Advances in medical knowledge are reported in an increasingly large number of publications, and it is now more difficult than ever to discover every paper published which has some bearing on a particular topic, such as leprosy. The British Empire Leprosy Relief Association, therefore, has started publishing monographs by recognized authorities covering recent advances in knowledge on various aspects of leprosy. The first monograph is a well-produced illustrated pamphlet entitled *The Lepromin Test*, by Dr. Dharmendra, and is obtainable from B.E.L.R.A., 167, Victoria Street, London, S.W.1 (price 2s. 6d.). Dr. Dharmendra considers the active principle of lepromin to be a protein antigen of the leprosy bacillus. He discusses a method for preparing lepromin standardized by the weight of dry leprosy bacilli. He then considers the results of the test in cases of leprosy, contacts, and non-contacts, and concludes that a positive reaction is an allergic phenomenon. He regards the test as of definite prognostic value in all cases of leprosy, but of little use in diagnosis or treatment.