Direct Exchange Blood Transfusion in Treatment of Hepatic Coma

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The first recorded case of recovery from hepatic coma after an exchange blood transfusion was that of Lee and Tink (1958). They gave two exchange transfusions of fresh blood to a boy aged 13 who was deeply jaundiced and comatose. After the first transfusion of 3,260 ml. his condition was unchanged, but when a second exchange of 3,140 ml. was given he improved and recovered completely.

Trey *et al.* (1965) reported seven cases treated by exchange transfusion. Approximately twice the patient's blood volume was exchanged. Freshly donated heparinized blood was administered under pressure on the venous side while blood was simultaneously removed from an artery. Five of the seven cases recovered completely. They were fully reported by Trey *et al.* (1966). Berger *et al.* (1966) put on record another recovery from fulminating hepatitis after exchange transfusion.

In the above cases fresh heparinized blood was used, and it is the purpose of this paper to describe a technique for directly giving large quantities of unmodified blood.

Materials and Method

Rotary pumps designed by Julian Smith (1941) for direct transfusion were used. Rubber tubing was replaced by polyvinyl tubing (Portex size 12E), which gives a better flow rate and is translucent. A disadvantage of polyvinyl tubing is that at low temperatures it is inelastic, so sterilization is carried out in boiling water immediately before the transfusion to ensure that the tubing is warm and elastic when used. Julian Smith transfusion needles with an inside diameter of 1.6 mm. and highly polished internal surface are used to withdraw blood from the donors.

Plastic catheters for the recipient are prepared from Teflon tubing with an internal diameter of 1.5 mm. Percutaneous catheterization of veins is performed with the Seldinger (1953) technique.

The rotary pumps are mounted on two bridges—one on each side of the patient. On the donor side a clamp for holding a flask of sterile normal saline is attached to the bridge.

Exchange transfusions are performed under local anaesthesia. Usually from 8 to 11 donors were used, and they were examined and tested for compatibility immediately before the transfusion was begun.

The patient lies on his back with one pillow under the head and a small pad under the sacrum. The thighs are slightly abducted and local anaesthesia is injected in the skin and subcutaneous tissue just medial to the femoral artery. A small incision is made in the skin and a Seldinger needle is inserted into the femoral vein. With the usual technique the Teflon catheter is guided into the femoral vein by the flexible wire, which is then removed. The catheter is connected to polyvinyl tubing fitted in the pump, while the other end of the tubing passes into a transparent measuring cylinder into which the blood flows.

A second Teflon catheter is inserted into a vein on the other side of the patient. If there is no suitable vein at the elbow the catheter may be inserted in the other femoral vein so that it passes into the inferior vena cava proximal to the first catheter.

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In the meantime polyvinyl tubing has been fitted into the second rotary pump and the tubing filled with normal saline. One end of the tubing is then taken out of the saline and connected to the Teflon catheter, which will transfuse blood into the patient.

The first donor is brought in and lies on a trolley adjacent to the patient. The transfusion needle is usually inserted in a distal direction and is not connected to the polyvinyl tubing until it is well placed in the vein (see illustration). With this technique a small amount of blood is spilt.

Blood transfusion rotary pump with polyvinyl tubing and insertion of transfusion needle in donor.

The transfusion is started by rotating both pumps simultaneously so that blood is removed from the patient at the same rate at which it is transfused. The usual rate of a direct blood transfusion is 500 ml. in four minutes. The needle is removed from the arm of the donor, who is immediately taken to a rest-room. The flask of saline is replaced and a fresh vinyl tube is fitted into the pump. The second donor comes in to give blood, and the procedure is repeated with each donor in turn until the operation is finished. Throughout the transfusion the volumes of blood infused and removed are checked and the clinical condition of the patient is assessed. The volume of saline must also be noted, and can be kept to a minimum by not connecting the vinyl tubing from the donor until the saline has been pumped out.

After completion of the transfusion the two catheters are removed and the sites of entry compressed for a few minutes.

Results

We have given direct exchange transfusions to four patients in hepatic coma. The first suffered from cirrhosis of the liver with oesophageal varices, and coma occurred after massive haemorrhages. In the other three patients coma was due to fulminating hepatitis. The clinical reports are briefly as follows.

Case 1

A man aged 53 was admitted to the Alfred Hospital on 1 July 1962. Recent investigation had shown oesophageal varices, and laboratory tests gave the following results: bilirubin 3.0 mg./100 ml.; cephalin flocculation positive (+++); S.G.O.T. 132 units; S.G.P.T. 70 units; prothrombin 60%. On the day of admission he passed three melaena stools. Haemoglobin was 7 g./100 ml. An intravenous drip was set up and he was given 4 units of acid citrate dextrose blood, 1 litre of 5% dextrose, and 0.5 litre of 0.9% saline. His condition deteriorated; he became mentally confused and had further melaenas. A second transfusion of 2 units of acid citrate dextrose blood, 1 litre of 5% dextrose, 1 litre of 0.9% saline, and 1 litre of Hartmann's solution was given, but there was no improvement. He was then given a direct blood transfusion from one donor (500 ml.), and his condition improved—he was more alert and able to answer questions intelligently. Three days later there was further haemorrhage and he became deeply jaundiced and comatose. On the eighth day after admission he was given a direct exchange transfusion from seven donors (volume 3.5 l.), but there was no improvement in his coma. He began to have convulsions, and died eight hours after the transfusion. A complete necropsy was not performed, but the abdomen was opened and the stomach and upper bowel were examined. There had been no recent haemorrhage. Histological section of the liver showed portal cirrhosis and nodular hyperplasia.

Case 2

A man aged 61 was admitted to Fairfield Hospital on 9 April 1966 suffering from infectious hepatitis. After admission his condition deteriorated—jaundice became deep, and foetor hepaticus, ascites, and flapping tremor occurred. He became increasingly drowsy, proceeding to a precomatose state. Melaena stools were passed and he vomited blood. He was given a direct exchange blood transfusion from eight donors (volume of blood 4 l.). Results of laboratory tests before and after the transfusion were as follows. Prothrombin increased from 27 to 51%. The platelets rose from 44,000 to 116,000/cu. mm. Bilirubin fell from 46.8 to 29.4 mg./100 ml. Serum protein increased from 3.7 to 4.9 g./100 ml. Clinical improvement was shown by less drowsiness, disappearance of foetor hepaticus, and no further bleeding. Two days later deterioration occurred. He developed signs of a chest infection and candida were grown from sputum and blood culture. He became anuric and died on 18 May. At necropsy the liver was shrivelled with surface abscesses. The lungs were congested, with consolidation in the upper lobes.

Case 3

A woman aged 38 was admitted into the Royal Melbourne Hospital on 4 August 1966. On admission she was drowsy and deeply jaundiced. She had foetor hepaticus and liver flap. Two days later her condition deteriorated; she became mentally confused and developed ascites. Peritoneal dialysis was begun, but without any improvement, and eight days after admission she was deeply comatose. At this stage, when extremely ill, she was given a direct exchange transfusion from eight donors (volume transfused 4 l.). Blood values showed an improvement; the bilirubin fell from 33 to 17 mg./100 ml. and platelets rose from 90,000 to 125,000/cu. mm. There was no clinical improvement, however, and she died seven hours later. At necropsy the liver was small with a wrinkled capsule (weight 730 g.). Nodules of regenerating tissue could be seen among areas of necrotic liver substance.

Case 4

A woman aged 31 was admitted to Fairfield Hospital on 15 July 1966. Eighteen days previously she had noticed jaundice, which progressively deepened. On admission she was mentally confused, with foetor hepaticus and a flapping tremor. The following day she was stuporous, jaundice was deeper, and the liver had become impalpable. On the third day after admission she became comatose and was given a direct exchange blood transfusion from 11 donors (volume transfused 5.5 l.). Laboratory tests showed an improvement—the bilirubin fell from 32 to 15 mg./100 ml., the prothrombin increased from 15 to 56%, and the platelet count rose from 180,000 to 260,000/cu. mm. Two days later, while comatose,

she was given an exchange transfusion of heparinized blood (5.5 l. was exchanged). There was no improvement in her mental state, while the platelet count fell from 169,000 to 125,000/cu. mm. and prothrombin was 34% before the transfusion and 34% at the end. Two days later another exchange transfusion of 5.5 l. of heparinized blood was given. The platelet count fell from 101,000 to 83,000/cu. mm., while prothrombin increased from 24 to 37%. There was no immediate clinical improvement, but 36 hours later she was mentally alert and rational and made a complete recovery. A further gastrointestinal haemorrhage occurred, and was controlled by a direct transfusion from two donors.

Discussion

The first and third patients were given direct exchange transfusions when in a terminal state, but in both there was no further bleeding after the infusion of unmodified blood. The main advantage of direct transfusion over heparinized blood is its better effect as a haemostatic. This was indicated by the blood tests before and after transfusion in Case 4. Both platelet count and prothrombin increased after the direct exchange transfusion, while the platelets were less numerous after heparinized blood and the prothrombin remained the same. It has been said that serious liver disease is a contraindication to heparin therapy and heparin should not be given to patients with potential or actual gastrointestinal bleeding (Griffith and Boggs, 1966).

In hepatic coma the use of citrated blood is contraindicated because of the danger of citrate intoxication and the possibility of enhanced bleeding from massive transfusion. The terminal liver failure in the first patient may have been contributed to by massive haemorrhages and replacement by citrated blood. If direct blood transfusion had been given initially bleeding could have been controlled.

Platelets and coagulation factors transfused by the direct method have a limited survival period and if bleeding is persistent repeated transfusions are necessary. In the treatment of hepatic coma repeated exchange transfusions have been advocated. In the second case, where only one exchange transfusion was given, death occurred subsequently from infection; whereas in the fourth patient a direct exchange transfusion was followed by two heparinized blood transfusions and a further small direct transfusion. This patient probably recovered because she was kept alive long enough for regeneration of a sufficient number of liver cells.

Direct exchange of unmodified blood has advantages but also the disadvantage of a more difficult technique. Firstly, suitable donors must be obtained, and in Melbourne the Red Cross Blood Transfusion Service has a special list of donors available for emergency. Secondly, the technique must be learnt and practised—it is not suitable for occasional use only.

With plastic materials and a rotary pump there is minimal difficulty from blood-clotting, and the only hazard is the donor, who must have good veins to ensure a rapid flow of blood. The usual practice is for the donor to wait in the rest-room with his forearm immersed in an arm bath of hot water.

In cases of hepatitis the risk of infection of donors is to be considered and special precautions are necessary. The donor is separated from the patient by a plastic screen—he is in the room for a few minutes only and does not have contact with the recipient except through the polyvinyl tube. Obviously the flow of blood must be in the one direction, but even if it was accidentally reversed it would take several turns of the pump to bring blood from the patient to the donor.

We have successfully given more than 100 direct exchange transfusions without risk to the donors.

Summary

The technique of exchange blood transfusion by the direct method is described. Two transfusion pumps are rotated

simultaneously to give blood from donors and remove blood from the patient. Polyvinyl tubing and Teflon catheters are used to lessen the risk of blood-clotting. In four patients suffering from hepatic coma this method of treatment was given. Blood values showed improvement and one patient recovered. It is postulated that unmodified blood transfusion has a place in treatment of liver failure particularly when associated with severe bleeding.

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Survey of Influenza Antibody in England by the Strain-specific Complement-fixation Test

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The susceptibility of a community to current strains of influenza virus is an important factor in the development of epidemics of influenza. Predictions of the likelihood of such epidemics and therefore recommendations for the use of vaccines against influenza should be based on what is known of the susceptibility of the population at risk and on the identity of circulating virus strains.

The influenza antibody survey described here was made to estimate the susceptibility to influenza viruses of all age groups in populations in several areas of England.

The laboratory tests previously used to determine antibody to influenza have certain drawbacks. Thus the haemagglutination inhibition test is sometimes difficult to interpret, since virus strains vary in their avidity for antibody and in their sensitivity to nonspecific inhibitors present in serum. Also the serum neutralization test in tissue culture is laborious and expensive.

By contrast the complement-fixation test is simple, and, as a microtest, economical in reagents. This test may be done by using as antigen either the type-specific S antigen or the sub-type or strain-specific V antigen (Lief and Henle, 1956). The former is excellent for the diagnosis of acute influenzal illness, but because the antibody titre declines soon after infection it cannot be used to detect residual antibody. In addition to this limitation the soluble antigen is common to all influenza A viruses and will not react solely with influenza A₂ antibody.

By the development of the V antigen, strain-specific reactions were obtained in the complement-fixation test. Henle *et al.* (1958) demonstrated the value of this test for the antigenic analysis of influenza virus and showed also that antibody detected with the V antigen would persist for several years after infection. It seemed likely that this would indicate the proportion of a population which had already experienced influenza A₂ virus infection. The strain-specific complement-fixation test was therefore employed in this investigation.

Materials and Methods

Public health laboratories in five different locations in England sent samples of serum each week to the Virus Reference Laboratory during the period October 1965 to May 1966. These samples were selected by the sending laboratory from

the number submitted for various routine tests, the majority being for the estimation of antistreptolysin O titres or for Wassermann reactions. Sera from patients with acute respiratory illness were excluded. From October 1965 to January 1966 a first series of 729 sera were examined, and from January to May 1966 a second series of 1,054 sera.

Virus Strains.—In the first series sera were tested against a single V antigen prepared with influenza A₂/England/7/65 virus. For the second series three V antigens were prepared with the influenza A₂/Singapore/1/57, A₂/England/129/66, and B/England/5/66 viruses.

Antigens.—These were prepared by the methods of Lief and Henle (1956). Allantoic fluids were harvested from eggs inoculated 48 hours previously with the strains of influenza virus. The virus harvests were adsorbed to fowl cells at 0° C., followed by elution into small volumes of phosphate-buffered saline at pH 7.2 over a period of three to four hours. This cycle was repeated two or three times. The final eluates were then tested quantitatively for specific complement fixation by the chessboard method against a homologous antiserum prepared in ferrets and against an S specific antiserum prepared in guinea-pigs. The dilution of each antigen for use was taken to be that which fixed complement with the highest dilution of homologous ferret antiserum. This varied between 1/4 and 1/32. If there was fixation of complement with the S specific antiserum, further adsorption-elution cycles were done.

Complement-fixation Test.—The method was described by Pereira *et al.* (1964). It used 0.025 ml. unit volumes of the reagents in W.H.O. plastic plates and overnight fixation at +4° C. Sera were diluted in fourfold steps and mixed with the optimal dilution of the appropriate V antigen. Titres were recorded as the reciprocal of the highest serum dilution producing 50% fixation with the antigen.

Results

There was no indication of any appreciable difference in the results of tests on the sera from the different laboratories. In the analysis all the results have therefore been combined.

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