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Treatment of Hepatic Coma by Exchange Transfusion
A Report of Three Cases*

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The results of conservative treatment of coma due to acute viral hepatitis is poor[1-3]. During a period of 12 months, ending October 1966, this condition has been fatal in almost all of our patients (Table 1). Within this period we have had 26 cases of coma in a series of 175 patients admitted because of viral hepatitis.

Little is known about the basic disturbances that underlie hepatic coma. An increase of blood ammonia has been implicated in its pathogenesis, but most investigators regard hepatic coma as a metabolic encephalopathy which is not due to any single agent.

As it is seen in Fig. 1, the food protein is a source of blood nitrogenous substances. In massive hepatic necrosis hemorrhage and the presence of blood proteins in the gastrointestinal tract adds to this. The inability of liver cells to metabolize nitrogenous and other injurious substances, which are called "lethal substances", results in metabolic encephalopathy and death.

Considering the above facts and capacity of the liver for regeneration after acute necrosis, the routine management of hepatic coma includs the administration of intestinal nonabsorbable antibiotics, special amino acids

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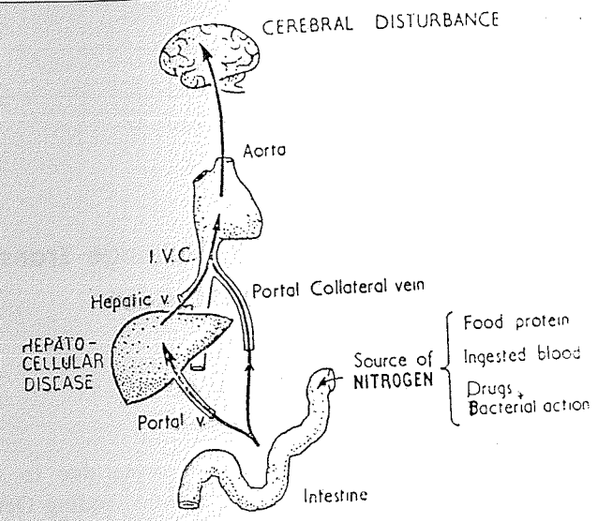

Fig. 1

(such as árginine), and massive doses of glucocorticosteroids. To date there is no evidence confirming the efficiency of the latter.

Recently, other forms of management, such as human cross circulation[4], heterologous liver perfusion[5], and hemodialysis[6], have been used, but the results have been disappointing. An interesting point is that hemodialysis, despite the lowering of blood ammonia levels, has no therapeutic effect. It appears that the injurious susbtances are at least in part protein-bound, and can not be withdrawn by hemodialysis.

Because of the above mentioned reasons, efforts have been made to lower temporarily the level of lethal substances by means of the exchange transfusion[7-10], providing an opportunity for liver cells to regenerate.

METHODS

Homologous citrated blood was administered through a polyethylen catheter introduced into the femoral vein through a cutdown. In the first case, the blood was withdrawn from the same vein, but in the other 2 cases it was withdrawn by arterial puncture from the femoral artery. Two ml. of 10 per cent calcium gluconate solution was infused after the administration of each 100 ml. of citrated blood to neutralize the effect of the citrate. In some cases hypotension and shock occured during the procedure. This was treated with glucocorticosteroids, mephentheramine,

and antihistamics. Puls rate, blood pressure, breath rate, and body temperature were recorded throughout the exchange transfusion, and 2-4 million units of penicillin was administered intravenously. Whenever the patient developed irritability and agitation, calcium gluconate and promethazine were used. After each exchange transfusion, the patients received intravenous perfusion of 5% dextrose solution toghether with penicillin, and were kept warm. During the next few days water and electrolyte balance, body temperature, and mental state were recorded. The 2nd exchange transfusion of the 3rd case was started with heparinized blood, but coagulative difficulties arose during the procedure. These difficulties, which appeared to be due to an insufficient amount of heparin, forced us to continue the procedure with citrated blood.

CASE REPORTS

Gase 1. Fever, anorexia, abdominal pain and vomiting developed abruptly in a 16-year-old boy who had no history of any previous injections. After 6 days, the symptoms abated but jaundice appeared and increased gradually. The patient's general condition worsened and prostration forced him to go to bed. By the 20th day after the onset of symptoms, mental cofusion, vomiting and tremor occured. On the same day (October 12, 1966) the patient was admitted to the Pahlavi Hospital delirious and disoriented. He was deeply jaundiced and had some hyperreflexia. There was no neck stiffness. The liver edge was not palpable. The temperature was normal. Biochemical findings included the following: thymol test 18 units, cephalin-cholestrol flocculation test 4+, SGOT 580 units, SGPT 620 units, direct serum bilirubin 19.5 mg. per 100 ml., indirect serum bilirubin 2.5 mg. per 100 ml. and serum ammonia 566 μg. per 100 ml.

Treatment with intravenus infusion of glucose and parenterally administered glucocorticosteroid and tetracycline was started a few hours after admission.

During the next few days the patient's clinical condition deteriorated. On the 4th hospital day direct serum bilirubin rose 22 mg. per 100 ml. and indirect serum bilirubin rose to 3 mg. per 100 ml.

The 1st exchange transfusion of citrated blood (not possible to obtain fresh heparinized blood readily) was preformed that evening. Forty minutes aftes the begining of the procedure, and after 540 ml. of blood was exchanged, the patients blood pressure fell to 50 mm. Hg., the ex-

termities became cold and exterme moisture was noted on the face and neck. The blood pressure rose to normal after the injection of 15 mg. of mephentheramine and infusion of 350 ml. of additional blood. The exchange transfusion was then continued and there was a significant lightening of coma after approximately 4000 ml. of blood had been exchanged. All total 5970 ml. of blood was infused and 5380 ml. was drained in a period of four and half hours.

Next morning the general codndition was improved, the tendon reflexes were normal, and the patient was oriented and thirsty. Biochemical findings were : direct serum bilirubin of 14.0 mg. per 100 ml., indirect serum bilirubin of 2.0 mg. per 100 ml., SGOT of 80 units, SGPT of 120 units, serum Potassium of 7 m Eq. per l. and serum Sodium of 126 m Eq. per l.

On the next day, the patient was mentally clear and looked a little tiered. During the next night the 2nd exchange transfusion was carried out with 3 liters of citrated blood. The direct serum bilirubin fell to 13.0 mg. per 100 ml.; the thymol test was 12 units and the cephalin - cholestrol flocculation test 2+.

During the succeeding days the patient remained mentally alert and the jaundice gradually disappeared.

On the 21st hospital day some infection appeared at the site of the femoral vein cutdown, which was used during the 1st exchnge transfusion. There was also some leg swelling. This was treated successfully with penicillin.

The patient was discharged from the hospital on November 23, 1966 with direct serum bilirubin of 0.7 mg. per 100 ml., indirect serum bilirubin of 0.7 mg per 100 ml., SGOT of 44 units, SGPT of 25 units blood fibrin of 3 gr. per l.

Case 2. A - 5 - year old girl was admitted to the Pahlavi Hospital on November 10, 1966, with a history of fluctuating jaundice over the previous 20 days. There was a history of previous injections. Growth and development had been normal.

Physical examination showed jaundice, swelling of both feet, purpuric rashes, tachycardia, and irritability. The liver edge was not palpable. The blood hemoglobin was 65%, the red cell count 4,100,000, and the total white count 18,000. Biochemical findings included the following : thymol test 10 units, cephalin - cholestrol flocculation test 3+; SGOT

250 units, SGPT 220 units, direct serum bilirubin 5.0 mg, indirect serum bilirubin 2.6 mg. and serum ammonia 35 g. per 100 ml. Therapy included intravenously infused fluids, and orally administered neomycin, tetracyclin and glucocorticosteroids.

On the 9th hospital day the clinical state deteriorated, the jaundice increases, and coma developed. Exchange transfusion was begun. A total of 2300 ml. of blood was infused and 2170 ml. was withdrawn. Improvement in consciouness was noted after exchange of 1000 ml. of blood, and by the end of the procedure she was speaking, but was still in a delerious state. A 2 nd exchange transfusion was carried out the next day with an exchange of 1800 ml. of blood. Sever tachycardia and generalized seizures occured during the procedure, which was treated with celanid and promethazine. At the end of the exchange transfusion the patient was vomiting and developed disrrhythmic tachycardia. The SGOT fell to 55 units, SGPT to 34 units, direct serum bilirubin to 0.8 mg. per 100 ml., and indirect serum bilirubin to 1.0 mg. per 100 ml. The thymol test was 12 units and the cephalincholestrol flocculation test 3+. The next day the patient died in a state of dyspnea, cyanosis, and arrhythmia.

At autopsy, there was a shrunken nodulated liver. Diffused foci of hepatization were found at the base of the lungs. Microscopical section showed massive necrosis of the hepatocytes.

Case 3. A-25-year old male was admitted to Pahlavi Hospital on December 6, 1966, because of malaise, abdominal pain, and jaundice of 7 days' duration. He had lost consciousness on the night before admission. On examination, he was noted to be deeply stuporous, and responded sluggishly to painful stimuli. The pupils were equal and reacted to light. The level of consciousness was fluctuating and a few hours after admission there was exterme disorientation and violent behavior. The blood hemoglobin was 60%, and the total white cell count 16,800. The thymol test was 16 units, and the cephalin - cholestrol flocculation test 4+. The SGOT was 860 units and the SGPT 1200 units. The direct serum bilirubin was 12.0 mg. and the indirect serum bilirubin 2.5 mg. per 100 ml.

The 1st exchange transfusion was carried out with 5 liters of citrated blood. There was no significant improvement in general condition until the next morning, when mental clarity improved somewhat. A further exchange of 5 liters was carried out on the 2nd hospital day. At

the end of the procedure the mental state had improved so that he could answer simple question. A few houers later he was mentally alert and asking for water. The SGOT fell to 420 units, and the SGPT to 580 units. The thymol test was 25 units, the cephalin - cholestrol flocculation test 3+, the serum direct bilirubin 100 mg. per 100 ml., and the serum indirect bilirubin 2.5 mg. per 100 ml.

During the next few days the jaundice at first increased slightly, gradually decreased and disappeared. The patient was discharged from the hospital on January 4, 1967, in a good general condition.

DISCUSSION

Indications for exchange transfusion in hepatic coma are still not clear. Tery et al.8 have graded the level of consciousness of their patients according to the criteria proposed by Adams and Foley, and have cosidered a Grade 3 or Grade 4 disturbance of consiousness as an indication for exchange transfusion. As there is no direct correlation between the levels of serum glutamin oxalacetic transaminase on one hand, and the severity of the underling disorder on the other, these biochemical criteria are not reliable as an indication for exchange transfusion. Repeated measurment of cerebrospinal - fluid glutamin proves impractical, and therefor can not be used as an indication for exchange transfusion. Some investigators belive that exchange transfusion should be carried out if after 24-48 hours of standard treatment there is no improvement in the clinical condition.

The high mortality rate of hepatic coma amoung our patients, and our experience, although limicted, on the management of these patients with exchange transfustion showes that:

A. Exchange transfusion should be carried out in all patients who are admitted in coma due to viral hepatitis.

B. It should be carried out in all patients who are initially in a good mental state but begin to show signs of mental deterioration.

C. Although the use of citrate as an anticoagulant rises the ammonia content of blood, and theoretically there is a danger of aggravating the encephalopathy, exchange transfusion should not be avoided when heparinized blood is not avilable.

Table 1. Survival in Coma Due to Acute Viral Hepatitis

Source of Data	Date	Total No. of Cases	No. of deaths	Therapy
Katz et al3	1962	23	14	Glucocor; Antibiotics
Mc Donald et al.2	1963	13	9	Protein withdrawal; antibiotics; some patients received glucocor.
Sherlock1	1963	11	8	Protein withdrawal; antibiotics.
Present report	1967	26	25	Clucocort. Antibiotics protein withdrawal.

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Summary

Three cases of hepatic coma due to acute hepatitis were treated by exchange transfusion with citrated blood. This was preformed in the first 2 cases (patients No 1 and No 2) after failing to respond to other forms of treatment, and in the last patient, who was admitted to hospital in coma, a few hours after admission. (patient No 3) Two of the 3 patients, patients 1 and 3 recovered, 1 died, (patient No 2) although 2 successive exchange transfusions alleviated coma to some degree.

Resumé

Nous avons traité 3 cas de coma hepatique (par suite d'hepatité virale aigue) par la exsanguino transfusion avec du sang citraté. Parmis ces cas 2 avaient failli de repruche aux traitements le troisieme a été apporté à l'hopital à l'etat de coma.

Le premier et le dermier malades sont gueri mais le deuxieme succomba quoique 2 exanguino transfusion successives avaient bien l'etat a certain degree.

References

1. Sherlock, S. (1963). " In Diseases of the Liver and Biliary System ", P. 85. Oxford: Blakwell scientific publications, London.
2. McDonald, R., and De La Harpe P. L. (1963). Hepatic coma in Chi-ldhood. J., Pediat., 63, 916.
3. Katz, R., Velasco, M., Klinger, J. and Alessandri, H: (1962). Cortico-steroids in treatment of acute hepatitis in coma Gastroentrology, 42, 258.
4. Burnell, J. M. et al. (1965). Observations on cross circulation in man. Am. J. Med., 38, 822
5. Eiseman. b., Liem, D. S., and Raffucci, F. (1965). Heterologous liver perfusion in treatmens of hepatic failure. Ann. Surg., 162, 329.
6. Kiley, J. E., Pender, J. C., Welch, H. F., and Welch, C. S. (1958). Ammonia intoxication treated by hemodialysis. New Eng. J. Med., 274, 473.
7. Lee, C., and Tink, A. (1958). Exchange transfusion in hepatic coma : report of case. M. J. Australia, 1, 40.
8. Trey,C., Burns, D. C., and Saunders, S. J. (1966). Treatment of hepatic coma by exchange transfusion. New Eng. J. Med., 274, 473.
9. Berger, R. L., et al. (1966). Exchange transfusion in the treatment of fulminating hepatitis, New Eng. J. Med., 274, 497.
10. Berger, R. L., and Stohlman, F. Jr. (1966). Avaluation of blood exch-ange in the treatment of hepatic coma. Amer. J. Surg., 112, 412.

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A Test For Impending Thrombo - embolism Conditions.*

Preliminary rerort.

The incidence of human intravascular thrombosis has been long att-ributed to the process of hemostasis, that is platelet aggregation, blood clotting and vasoconstriction. The present **in vrtro** study of blood drawn from normal controls and patients with acute myocardial infarction suggested the diagnostic value of this test. Samples of whole blood were obtained from control and thrombotic patients. Blood samples were trea-ted with heparin, EDTA and followed by administration of strontium chloride in different molar concentration (i, e, 0 005 - 0.50M). Blood smears were made and stained with Wright's stain routinely. Microsco-pic observation of blood smears prepared from thrombotic patients showed an affinity of platelets and leucocyte to from specific aggregates. The degree and pattern of aggregation revealed mild and/or severe thrombotic episodes. Normal control smears showed fewer aggregates of different and specific cytocomposition. Squamous epithelial and cornified cells were found in smears of patients with acute myocardial infarctions whose blood was drawn from either vena punctures and/or taken from subclavian cannulae These findings suggest that physiologic change in blood vessels may lead to certain acute thrombotic conditions eventually through the involvement of other hemostatic mechanisms.

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