Medical Memoranda

Use of Plasmapheresis in Blood Donors

Our studies on this subject began in May, 1950, because the demand for plasma in our blood bank far exceeded that for packed cells. It seemed a pity to throw away the red cells, which are precisely the portion of blood that requires more time and material for its regeneration. It is known that 100 ml. of blood contains some 16 g. of haemoglobin, a specialized protein whose metabolism is linked with the metabolism of iron, while the same amount of blood contains only 4 g. of plasma proteins, whose regeneration is considered to be both qualitatively and quantitatively much easier. It is also well known that in most cases haemoglobin regeneration is the deciding factor in establishing the safe interval between bleedings of blood donors. To regenerate 100 ml. of whole blood the building material for 16 g. of haemoglobin and 4 g. of plasma protein plus the corresponding amount of iron should be supplied. To regenerate the amount of plasma yielded by 100 ml. of whole blood only the building material for 4 g. of plasma protein should be supplied. There are, of course, many other considerations that make it clear that the production of plasma protein in man should be expected to be much more rapid than haemoglobin production.

METHOD

From May, 1950, to July, 1951, we performed plasmapheresis in over 320 cases. Our experience has led us to adopt the following technique.

At weekly intervals the donor is bled for plasma, using the same apparatus as for blood collection, approximately 400 ml. of blood being drawn into acid-citrate-dextrose mixture. Immediately after the bleeding the red-cell suspension taken the previous week from the same donor is injected by gravity through the same needle, using a drip counter. The whole collection-injection process is thus made with a single venepuncture, and as a rule takes some 8-10 minutes. Shortly after collection the blood is centrifuged, and is kept in this condition in the refrigerator until the following week, when the plasma is removed and the packed cells are suspended in citrate-saline, ready for injection.

As implied, donors are bled for plasma every week—actually the same day each week. We presumed that such a time interval should be more than sufficient for plasma regeneration, and we felt that the reinjected cells could hardly have been damaged by storage. Our expectations have been fulfilled. In two instances we have performed weekly plasmapheresis for about one year with scarcely any interruption. Plasma examinations do not show significant change, and subjectively these plasma donors declare that they feel quite normal throughout.

SELECTION AND EXAMINATION OF DONORS

As a routine, however, we prefer to change our donors as a safety measure after a few months of plasmapheresis. We think this precaution is worth adopting, as we are dealing with a new technique in which there is no experience beyond our own.

We have chosen as our plasma donors those who appear to be in the best physical condition and whose standard of living leads us to expect that plasma regeneration will not be hampered by poor constitution or undernourishment.

Laboratory Examinations.—Every week we perform haemoglobin and total plasma protein estimations. Every month we carry out Wassermann and Meinicke tests and determine the albumin:globulin ratio. So far no donor has had to be rejected for failure to regenerate the plasma protein completely.

Besides the advantage that with plasmapheresis there is no waste of red cells, there are other advantages—for

example, easy control of the donor's health and the practically complete exclusion of danger of transmission of jaundice. The method also reduces the number of donors as well as the clerical work, since the donors come automatically at regular intervals, usually once a week.

We have also carried out plasmapheresis in a few pathological conditions. In essential and renal hypertension we have found a striking subjective improvement, which, however, is not matched by a corresponding betterment of the objective symptoms. Thus headache and mental sluggishness disappear, while blood pressure and renal-function tests show little improvement. The use of plasmapheresis in treatment of disease will be the subject of further study.

SUMMARY AND CONCLUSIONS

The first use of plasmapheresis in blood donors is described, with details of the technique employed and of the criteria adopted for the selection and regular examination of plasma donors.

About 200 ml. of plasma may be drawn safely from a healthy person every week for short periods, and perhaps even for longer ones.

Subjective improvements are reported from a few pathological cases.

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Spontaneous Arterial Occlusion During an Epileptic Fit

The development of a spontaneous obstruction in a peripheral artery during an epileptic fit is a rare occurrence. It is therefore of interest to record a case in which the lumen of the left posterior tibial artery became occluded during a major epileptic attack, with subsequent ischaemic cramp in the leg.

CASE REPORT

The patient, a man aged 47, had suffered from attacks of idiopathic major epilepsy for many years. These had been controlled by soluble phenytoin and phenobarbitone tablets, but on April 9, 1950, he had three fits following one after another. When he regained consciousness he found that his left leg was white and lifeless below the level of the mid-calf. There was no sign of any external injury. It was 16 hours before sensation returned to the leg, and the foot remained numb for four days. He then complained that the left foot felt cold and that cramp occurred in the calf and foot when he had walked about 200 yards (183 metres). The pain wore off after resting for a few minutes.

He was first seen at the West End Hospital for Nervous Diseases a month after the onset of the symptoms. The whole of the left foot was then colder and paler than the right. There was no pulsation in the dorsalis pedis artery or in the posterior tibial artery at the ankle. Above the knee and throughout the right leg normal pulsations were felt. The cardiovascular system was otherwise healthy; there was no evidence of peripheral arteriosclerosis, and his blood pressure was 130/85. The blood Wassermann reaction was negative, and no vascular calcification was seen in the radiographs of the legs.

He was treated with Buerger's exercises and was given tolazoline hydrochloride ("prisol"), 25 mg., and nicotinic acid, 100 mg., each three times a day by mouth. The symptoms in the left leg subsequently improved. By September he could walk 300 yards (274 metres) before experiencing cramp in the calf, and could manage to play nine holes of golf. In January, 1951, the foot was warm as far as half-way down the instep, but it was cold beyond this, without, however, any discoloration of the skin. In April he could walk without experiencing any cramp at all and play a full round of golf. The left foot was equal in warmth to the right to within an inch (2.5 cm.) of the base of the toes. There was still no pulsation in either the dorsalis pedis or the posterior tibial artery.

COMMENT

It is assumed that the symptoms referred to in the left leg were the result of a sudden arterial occlusion that occurred during the epileptic convulsions. There are two possible explanations to account for the obstruction. The first is that the convulsions led to the displacement of an atheromatous plaque somewhere in the arterial tree which passed distally and lodged in the left posterior tibial artery. The alternative explanation is that the severe and prolonged contractions of the leg muscles damaged the intimal lining of the artery, with resulting thrombosis. In spite of the absence of objective evidence of peripheral arteriosclerosis, it seems more likely that the symptoms were due to arterial obstruction by a dislodged atheromatous plaque, possibly from the aorta.

I am grateful to Dr. C. Worster-Drought for permission to publish this report and for his advice in its preparation.

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Toxic Hepatitis and P.A.S.

To date, three isolated instances of toxic hepatitis occurring during the course of treatment with *para*-aminosalicylic acid (P.A.S.) have been recorded (Cuthbert, 1950; Hurrell, 1950; Landsborough, 1951). The Medical Research Council Report (1950), which deals with the results of combined streptomycin and P.A.S. therapy, makes no reference to this complication; it therefore seems opportune to present a further case in detail.

CASE REPORT

A 2-para aged 31 was admitted to hospital on September 28, 1950, suffering from active bilateral pulmonary tuberculosis complicated by laryngitis. She had received treatment for pulmonary tuberculosis in a sanatorium in 1945, and remained well until 1950, when pregnancy supervened; she was confined in July of that year. At the time of admission to hospital active lesions involved the upper and mid-zones of both lungs, and there was advanced tuberculous infiltration with ulceration of the vocal cords and epiglottis.

Routine treatment was prescribed, and streptomycin dihydrochloride, 1 g. in divided daily doses, and sodium P.A.S., 15 g. daily, were given from October 3 until November 8. On October 31 the patient developed a rise in temperature, with rigor and sickness, and eight days later a generalized scarlatiniform erythema with gross oedema of the face was observed. Streptomycin and P.A.S. (total dosage 540 g.) were then stopped, and mepyramine hydrogen maleate ("anthisan"), 1 g. thrice daily, was administered. This was discontinued in favour of diphenhydramine hydrochloride ("benadryl"), 300 mg. a day, as from November 15.

On November 16 the temperature was 103° F. (39.4° C.), and she continued to be febrile for a further period of 18 days, fever being accompanied by rigor, sickness and diarrhoea, and albuminuria. Jaundice developed on November 18, became pronounced within a few days, and was accompanied by mental confusion and hallucinations.

A blood examination on November 17 showed: leucocytes, 12,500 (polymorphs 40%, lymphocytes 50%, monocytes 7.5%, basophils 2.5%). The plasma bilirubin content was 6.5 mg. per 100 ml.; blood urea, 30 mg. per 100 ml.; prothrombin time, 41 seconds (control 19 seconds); blood level of P.A.S., 0.52 mg. per 100 ml. Blood culture was sterile and W.R. negative.

Despite the evidence of hepatic dysfunction, streptomycin was restarted and was continued without further interruption until January 13, 1951 (total 94 g.), but P.A.S. was not again given, since, in the opinion of one of us (A. G. F.), it had been the probable cause of both the toxic erythema and the hepatitis. Lead acetate lotion was applied to the face and ung. oleum eucalypti to the remainder of the body.

Blood examination on November 22 showed: serum proteins, 5.75 g.% (albumin 1.6 g., globulin 4.15 g.); alkaline phosphatase, 39.5 units; bilirubin, 12.5 mg. per 100 ml.; thymol turbidity, 9 units. On November 25 jaundice was still present and the liver was moderately enlarged and palpable below the costal margin. One week later the generalized erythema had almost completely faded, and a fine branny desquamation was observed. The jaundice was subsiding, and the patient seemed to have improved, her mental attitude being much brighter. By December 8 both jaundice and erythema had cleared; the local treatment was now discontinued, and benadryl was gradually withdrawn.

Blood examination on December 6 showed: serum proteins, 6.25 g.% (albumin 3.6 g., globulin 2.65 g.); serum bilirubin, 1.8 mg. per 100 ml.; alkaline phosphatase, 16.4 units; thymol turbidity, 7 units; and on December 27 serum proteins 8 g.% (albumin 4.4 g., globulin 3.6 g.); alkaline phosphatase, 18.3 units; bilirubin, 0.6 mg. per 100 ml.; thymol turbidity, 8 units.

At the time of discharge from hospital, on June 1, the patient's general condition was satisfactory; she felt well and had gained weight. Radiological examination showed the pulmonary lesions in the upper zones to have become inactive; sputum had been tubercle-negative on three consecutive monthly examinations, and the tuberculous laryngitis was found to have healed. Over a month later she was still apyrexial and symptomless, and there had been no recurrence of rash: sputum was tubercle-negative, and the x-ray appearance of the lungs was unchanged.

DISCUSSION

The pathogenesis of this hepatic dysfunction is still obscure, and in consequence the evidence that P.A.S. caused a toxic hepatitis can only be presumptive. Nevertheless, a search for other possible causal factors, including contact infection, was unsuccessful.

Features peculiar to this patient, which differ from previous reports and are worth special mention, include:

(1) The widespread scarlatiniform character of the rash, associated with fever and collapse. Hitherto the sensitization rashes noted and described in association with P.A.S. therapy have most often been of morbilliform type, and there seems to be some evidence that untoward cutaneous reactions to P.A.S. are due to its salicyl radical (Horne, 1949; Kierland and Carr, 1949). Eruptions due to ingestion of salicylates are usually either scarlatiniform or morbilliform erythematous.

(2) Despite the gravity of her tuberculosis and the serious nature of the hepatitis she not only survived but was much improved on discharge from hospital, the tuberculous lesions having apparently healed. Of the other cases previously reported one died and two recovered.

(3) The total dosage of P.A.S. given was 540 g., dosage until the onset of symptoms being 435 g. (Cuthbertson gave 800 g., Hurrell 163 g., and Landsborough 270 g. until the onset of symptoms, total dosage 465 g.). It would appear that reaction is due to individual idiosyncrasy rather than to overdosage with P.A.S.

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