PLASMAPHAERESIS IN THE TREATMENT OF CHRONIC NEPHRITIS AND UREMIA *

JAMES P. O'HARE, M.D., HAROLD H. BRITTINGHAM, A.B.,

AND

CECIL K. DRINKER, M.D.

BOSTON

In 1914 Abel, Rowntree and Turner¹ reported on the physiologic effects in dogs of bleeding, removing the plasma and returning the corpuscles after washing with Locke's solution. Such a process was appropriately designated "plasmapheresis," and it was shown by these authors and by Turner, Marshall and Lamson² that it could be carried to a very considerable extent with entire recovery of the experimental animal. The technic presented in these articles required the use of herudin for prevention of blood coagulation, and positive evidence was secured that the German preparation of herudin then on the market had toxic properties of high order.³ While the authors in question have offered a number of suggestions as to the possible practical use of plasmapheresis, the difficulty of the maneuver, coupled with the impossibility of using herudin, seems to have prevented its clinical employment. In the course of experiments designed to disclose the toxic elements in citrated blood transfusions it became expedient to obtain data on removal and return of corpuscles from the same individual. In consequence of this need the ordinary venesections in uremia patients, which would have been carried through without return of corpuscles, were made instances of plasmapheresis, and data were obtained on the possible beneficial effects of this measure. This material is deemed worthy of a brief report.

Technic.—The blood was drawn into sodium citrate, centrifugalized and prepared for return, as indicated in a previous article,⁴ except that in no case was sodium citrate added before reinjection, nor was Ringer's solution employed. Cases of chronic nephritis with hypertension are particularly favorable subjects for the necessary technic. It was our practice to withdraw 700 or 800 c.c.

*From the Medical Clinic of the Peter Bent Brigham Hospital and the Laboratory of Physiology of the Harvard Medical School.

*This study was made, in part, under a grant from the Proctor Fund of Harvard University for the Study of Chronic Disease.

1. Abel, John J.; Rowntree, L. G., and Turner, B. B.: Jour. Pharmacol. and Exper. Therap. **5**:625, 1914.

2. Turner, B. B.; Marshall, E. K., and Lamson, P. D.: Jour. Pharmacol. and Exper. Therap. **7**:129, 1915.

3. Marshall, E. K.: Jour. Pharmacol. and Exper. Therap. **7**:157, 1915.

4. Drinker, C. K., and Brittingham, H. H.: Archives Int. Med. **28**:133 (February) 1919.

of blood, centrifugalize, wash twice with freshly made sterile 0.85 per cent. sodium chlorid solution and to return the corpuscles made up to the original volume with salt solution. On completing this return, and without inserting another needle, 700 or 800 c.c. of blood were again withdrawn. The corpuscles thus removed were washed twice and reinjected. The patient never experiences a hemorrhage of more than 800 c.c., and he is subjected to no operation except venepuncture, as it should never be necessary to cut down on a vein in such cases.

The removal of toxic products from 1,500 to 1,700 c.c. of blood cannot result in very large alteration in the patient's plasma. On several occasions we observed rather striking but brief subjective improvement in our patient, but are inclined to attribute it to the psychic effect of the formidable therapeutic maneuver to which the patient was subjected, rather than to any true benefit. The operation has been done eighteen times on eight patients, and the history of one case is presented. Other cases have been so similar as to merit no comment.

REPORT OF CASE

History.—Patient, D. J. McD., man, aged 49, Sept. 17, 1917.

Diagnosis.—Chronic nephritis, chronic uremia, hypertension.

Complaint.—General weakness, dyspnea and cough.

Family and Marital History.—Unimportant.

Habits.—Alcohol in excess.

Occupation.—Steamfitter.

Previous Medical History.—Measles and mumps in infancy. Good recovery and no complications. Weight 210 pounds, four years ago; has lost 53 pounds in the past four years.

Present Illness.—In 1912 the patient first noticed swelling about the ankles, particularly at night, but was not troubled by other symptoms until 1913, when he gradually began to have dyspnea, polyuria, especially nocturia, intense thirst and constant fatigue. Dizziness and violent headaches were soon added, and on one occasion he had an extremely severe nose bleed. By resting frequently the patient has kept at work, but has never felt really well. Vision has grown very bad. For the past twelve days he has been "all in," very dyspneic and drowsy, but unable to sleep. He is entirely unable to lie down on account of a "choking feeling."

Physical Examination.—A well-developed man, sitting upright in bed and showing occasional periods of dyspnea. He appears very ill. Face: Thin, very pale, pasty and expressionless. Eyes: There is external strabismus of the eye with ptosis of the left lid. No photophobia, lachrimation, diplopia, nystagmus, lid-lag or exophthalmos. Conjunctivae pale. The vision of the left eye is partially gone save for light, while that of the right is quite defective and blurred. Ophthalmoscopic examination: Left eye, pupil fixed, media clear, whole fundus pale and dotted with small hemorrhages. Disk covered with exudate and slightly elevated. Right eye, fundus pale. Above the disk there is a small patch of exudate and several hemorrhages. Vessels here, as in the left eye, are tortuous and pulsate slightly.

Thorax: Symmetrical; respirations 28, deep and regular. Heart: Apex impulse forcible in fifth space 12 cm. from midsternal line. No murmurs and no irregularities. Aortic second sound increased. Vessels: Marked sclerosis of radial and temporal arteries.

Blood pressure: Systolic, 225; diastolic, 185.

Lungs: Numerous râles are heard at both bases.

Edema: Moderate in both ankles. No fluid in abdomen or chest.

Further physical findings are unimportant. On admission the patient presented a typical instance of advanced chronic nephritis and hypertension with uremia.

September 17.

Laboratory Report.—Blood: Hemoglobin, 57 per cent. Red blood count, 2,040,000. White blood count, 12,200. Smear: Polymorphonuclears, 80 per cent.; lymphocytes, 15 per cent.; large mononuclears, 3 per cent.; eosinophils, 1 per cent.; mast cells, 1 per cent. Anisocytosis, macrocytosis and moderate achromia were noticed in red cells.

September 18.

Urine: Amber, pale, turbid, acid. Specific gravity, 1.013; large trace of albumin, no sugar. Sediment: occasional white blood corpuscles; large number hyaline, granular and epithelial casts. Phenolsulphonephthalein test, 20 per cent. in two hours (urine volume 175 c.c.).

September 19: The patient is sleepless and often incoherent. His dyspnea has not improved. Owing to the pronounced secondary anemia venesection does not seem advisable and plasmapheresis will be employed.

8:33 a. m., 700 c.c. of blood were withdrawn in the usual way into 25 c.c. of 8 per cent. sodium citrate, centrifugalized and red cells washed twice in freshly made sterile 0.85 per cent. sodium chlorid solution, care being taken to discard all buffy material.

12 noon, 500 c.c. saline suspension of these red cells were injected. On finishing this infusion 750 c.c. of blood were withdrawn through the same needle into 25 c.c. of 8 per cent. sodium citrate solution. This blood was treated as in the first case.

2:10 p. m., 550 c.c. saline suspension of washed cells from second removal were injected.

Total amount of discarded plasma, 1,000 c.c.

Blood urea nitrogen, before plasmapheresis, 34.5 mg. in 100 c.c.; after plasmapheresis, 36.5 mg. in 100 c.c.

Plasma chlorids, before plasmapheresis, 5.62 gm. per liter; after plasmapheresis, 5.81 gm. per liter.

September 20: The patient feels much better, has slept well and is anxious to carry through the projected treatment. Plasmapheresis will be repeated today.

9:55 a. m., 700 c.c. of blood withdrawn into 25 c.c. 8 per cent. sodium citrate.

12:55 p. m., 500 c.c. saline suspension of these red cells injected. On finishing this infusion 650 c.c. of blood were withdrawn through the same needle and treated as in the first instance.

4 p. m., 650 c.c. saline suspension of washed cells from second removal were injected.

Total amount of discarded plasma, 900 c.c.

Blood urea nitrogen, before plasmapheresis, 34.7 mg. in 100 c.c.; after plasmapheresis, 35.6 mg. in 100 c.c.

Plasma chlorids, before plasmapheresis, 5.81 gm. per liter; after plasmapheresis, 6.03 gm. per liter.

September 21: Patient much improved and encouraged. He has had no unfavorable reaction of any sort from his two experiences with plasmapheresis.

September 24: Blood urea nitrogen, 30.9 mg. in 100 c.c.

Blood: Hemoglobin, 53 per cent.; red blood count, 2,848,000; white blood count, 13,300. Smear: polymorphonuclears, 86 per cent.; lymphocytes, 10 per cent.; large mononuclears, 4 per cent. Anisocytosis and achromia present as formerly.

September 25: The patient has been out of bed in a wheel chair. He now sleeps without orthopnea. Plasmapheresis will be repeated.

8:15 a. m., 800 c.c. of blood withdrawn into 25 c.c. 8 per cent. sodium citrate.

11:35 a. m., 575 c.c. saline suspension of these red cells injected. On finishing this infusion 700 c.c. of blood were withdrawn through the same needle and treated as in the first instance.

2:15 p. m., 575 c.c. saline suspension of washed cells from second removal injected.

Total amount of plasma discarded, 1,000 c.c.

Blood urea nitrogen, before plasmapheresis, 33.2 mg. in 100 c.c.; after plasmapheresis, 33.5 mg. in 100 c.c.

Plasma chlorids, before plasmapheresis, 5.26 gm. per liter; after plasmapheresis, 5.32 gm. per liter.

Urine: Amber, pale, slightly turbid, acid. Specific gravity, 1.006; large trace of albumin; no sugar. Sediment: occasional epithelial cell, rare red blood corpuscles; occasional granular cast.

September 28: The patient's anemia has not changed since entrance, and transfusion will be done as soon as a donor can be found. He has been up and about the ward for the last four days and has not felt any symptoms except fatigue. Systolic blood pressure remains constantly at 220 mm. Hg.

October 1: Patient received a transfusion of the washed red cells from 600 c.c. of blood from a properly matched donor. These cells were suspended in plasma from the same donor which had been cleared of formed elements by one hour of high speed centrifugalization. He had a very slight chill and temperature reaction following this transfusion.

Blood urea nitrogen, before transfusion, 40.7 mg. in 100 c.c.; after transfusion, 40.7 mg. in 100 c.c.

Plasma chlorids, before transfusion, 5.69 gm. per liter; after transfusion, 6.06 gm. per liter.

October 6: Blood urea nitrogen, 42.8 mg. in 100 c.c. Plasma chlorids, 5.53 gm. per liter.

October 13: The patient has remained constantly in bed since October 7 and has been failing steadily. Plasmapheresis again carried out.

9:30 a. m., 500 c.c. of blood withdrawn into 25 c.c. 8 per cent. sodium citrate.

12:30 p. m., 500 c.c. saline suspension of these red cells injected. On finishing this infusion 500 c.c. of blood were withdrawn through the same needle and treated as in the first instance.

3:30 p. m., 500 c.c. saline suspension of red cells from second removal injected; 600 c.c. of blood were withdrawn through the same needle and treated as usual.

6:15 p. m., 600 c.c. saline suspension of red cells from third removal were injected.

Total plasma discarded, 1,000 c.c.

Blood urea nitrogen, before plasmapheresis, 92.3 mg. in 100 c.c.; after first red cell return, 92.3 mg. in 10 c.c.; after second red cell return, 95.7 mg. in 100 c.c.

Blood chlorids, before plasmapheresis, 4.84 gm. per liter; after first red cell return, 4.66 gm. per liter; after second red cell return, 5.19 gm. per liter.

October 14: Blood urea nitrogen, 109.4 mg. in 100 c.c. Blood chlorids, 5.31 gm. per liter.

October 15: Yesterday and today the patient has been much more drowsy than previously and today he has taken little nourishment. His systolic blood pressure, previously from 200 to 220 mm. Hg, is now 270. There is no edema or ascites.

October 16: Patient has been comatose for the last twenty-four hours. Systolic blood pressure this afternoon, 290. Died at 12:15 a. m., October 17.

DISCUSSION

Plasmapheresis, in so far as it was carried in this case, has not arrested the march of uremia in any degree. The encouraging betterment which is noted early in the patient's stay in the hospital is no more than one often sees from rest and proper diet. Whether plasmapheresis can be carried to greater extent remains to be seen, but it seems improbable that real good can come from it in chronic cases with impending uremia. The other patients on whom we have used the maneuver have been of similar type and have received no benefit from it or from blood transfusion. It is possible that a case of acute nephritis with suppression of urine might be tided through a critical period of impending uremia by repeated plasma removals, but our series does not contain any such case.

It is of some interest to note that the urea nitrogen of the plasma increases slightly during the process of blood dilution. This finding corroborates that of Turner, Marshall and Lamson,² and cannot be explained without more complete studies on nitrogenous metabolism than we at present possess.

CONCLUSIONS

1. A method is described which permits repeated withdrawals of blood and return of washed cells without the use of herudin.
2. Plasmapheresis of this type has been carried out eighteen times in eight different cases of chronic nephritis and uremia without definite benefit to the patients.
3. It is suggested that the maneuver can have clinical value in no cases save those of acute suppression of urine where it is a question of tiding over a brief period.