Postgraduate Medical Journal (August 1975) **51**, 583–587.

Ascites reinfusion using the Rhodiascit apparatus—clinical experience and coagulation abnormalities

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Summary

The results of twenty-four ascitic reinfusions in twenty patients, using the Rhodiascit procedure, are reported. The procedure was of no value in the management of patients with spontaneous functional renal failure, but was of considerable value in accelerating hospital discharge of patients with tense ascites but good renal function. Complications of the procedure were few, but tests of blood coagulation became abnormal, the most likely cause of which was deposition of fibrin on to the filtration membrane.

THE Rhodiascit ascites reinfusion technique has been used in the management of ascites on twenty-four occasions in twenty patients. The indications for use of the procedure were diuretic-resistant ascites with spontaneous functional renal failure (five patients), diuretic-induced uraemia (two), Budd-Chiari syndrome (two), in order to accelerate discharge from hospital for socio-economic reasons (ten), and one patient with cirrhosis and non-functioning kidneys (due to chronic glomerulonephritis) on maintenance haemodialysis who had recently developed ascites (Table 1).

Diuretic-resistant ascites with spontaneous functional renal failure (Cases 1–5)

The diagnosis of functional renal failure was based on the findings of uraemia, a 24 hr urine volume < 500 ml, a urine sodium concentration < 10 mEq/l and a urine : plasma osmolality ratio of $> 1{\cdot}1$. As is usually found with functional renal failure, these patients were resistant to diuretic therapy.

The procedure did not appear to be of any real value to these patients. Although ascites was at least partly relieved, all patients died within two weeks of the recirculation. Renal function was not improved by the reinfusion (Fig. 1) and since no diuresis occurred it was discontinued within 6 hr in all five cases (Table 1).

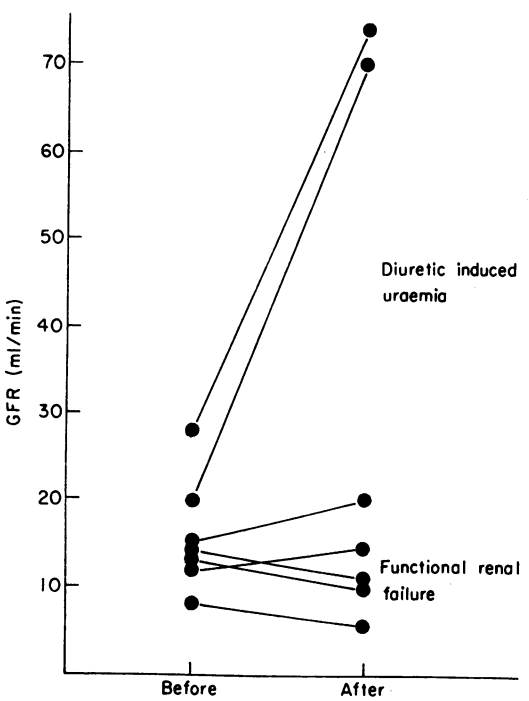

FIG. 1. The effect of ascitic reinfusion on the glomerular filtration rate (GFR).

Diuretic-induced uraemia (Cases 6 and 7)

This diagnosis was made when uraemia was accompanied by a 24 hr urine volume > 1000 ml, a urine sodium concentration > 25 mEq/l, and a urine : plasma osmolality ratio $> 1{\cdot}1$. Both patients had moderate ascites with mild encephalopathy

TABLE 1. Clinical and reinfusion data

Case	Age	Hepatic disease	Indication for reinfusion	Plasma		Duration of reinfusion (hr)	Volume of ultra-filtrate (l)	Diuresis during reinfusion (ml)	Complications of reinfusion
				Urea (mg/100 ml)	Creatinine (mg/100 ml)				
1	45	Alcoholic cirrhosis	Functional renal failure	221	4·5	4·5	4·5	200	Hyponatraemia
2	42	HBAg + cirrhosis	Functional renal failure	145	3·9	1	0·5	0	Pyrexia 39·5°C, rigor
3	38	Cryptogenic cirrhosis	Functional renal failure	121	3·3	6	4·0	150	Hyponatraemia
4	63	Alcoholic cirrhosis	Functional renal failure	203	3·9	6	8·5	200	Hyponatraemia
5	42	Cryptogenic cirrhosis	Functional renal failure	191	2·8	6	4·5	100	None
6	65	Alcoholic cirrhosis	Diuretic-induced uraemia	51	2·8	9	8·0	1800	None
7	50	HBAg + cirrhosis	Diuretic-induced uraemia	98	3·1	10	5·0	1600	None
8	27	Budd-Chiari	Diuretic-resistant	71	2·0	6	5·0	800	None
			Diuretic-resistant	145	4·8	3	3·0	200	None
9	23	Budd-Chiari	Diuretic-resistant	56	2·3	6	6·0	900	None
			Diuretic-resistant	160	5·2	6	4·0	0	None
10	48	Alcoholic cirrhosis	Accelerate Discharge	45	1·2	9	7·0	1000	Pyrexia 38·5°C
			Accelerate Discharge	46	1·3	3	2·5	400	None
11	59	Alcoholic cirrhosis	Accelerate Discharge	34	1·2	5	5·0	600	None
12	60	Alcoholic cirrhosis	Accelerate Discharge	26	1·1	6	5·0	450	None
13	50	Alcoholic cirrhosis	Accelerate Discharge	20	1·0	26	18	5000	None
14	49	Alcoholic cirrhosis	Accelerate Discharge	18	1·0	22	14	4500	Pyrexia 38·0°C
15	60	Crypto. cirrhosis	Accelerate Discharge	21	1·1	12	8·0	1800	None
16	62	Crypto. cirrhosis	Accelerate Discharge	20	0·9	14	10	2400	Pyrexia 38·3°C
17	56	HBAg + cirrhosis	Accelerate Discharge	21	1·0	8	5·0	2200	None
18	42	HBAg + cirrhosis	Accelerate Discharge	28	1·1	10	10	1600	None
19	57	Primary biliary cirrhosis	Accelerate Discharge	45	1·1	12	10	2900	Pyrexia 38·0°C Hyponatraemia
20	54	Post-hepatitic cirrhosis	Chronic renal failure	33	3·8	10	8·0	0	Pyrexia 38·2°C
			Chronic renal failure	62	4·9	16	10	0	None

(drowsiness and confusion). A rapid improvement in renal function resulted from the reinfusion (Fig. 1) and encephalopathy also improved. Ascites was thereafter controlled by lower doses of diuretics than the patient had received previously, and both patients were discharged from hospital free of ascites.

Budd-Chiari syndrome (Cases 8 and 9)

These two patients were particularly interesting. Case 8, a 27-year-old female with Budd-Chiari syndrome possibly induced by the contraceptive pill, had a packed red cell volume (PCV) of 63% at the time of presentation with gross ascites. However, measurement of red cell mass showed this to be normal whereas the plasma volume was markedly reduced (1·1 litre) which accounted for the high PCV. The low plasma volume was attributed to a redistribution of the extracellular fluid into the ascites compartment. She was give diuretics on admission but failed to respond. Following a 6-hr reinfusion the PCV fell to 49%, associated with a marked clinical improvement, and response to diuretics. A similar sequence of events was observed in the other patient (Case 9). Both of these patients were discharged from hospital, but unfortunately readmitted later with reaccumulation of ascites and a deterioration in liver function. A second reinfusion was carried out in each case but both patients died of hepatic failure within a week of the procedure.

For socio-economic reasons (Cases 10–19)

These patients all had good renal function (normal plasma urea and creatinine concentrations, Table 1), but marked ascites. Conventional diuretic therapy would have taken 2–3 months to relieve the ascites, accepting a daily weight loss of 0·5 kg, whereas each

patient was discharged within 2 weeks of the reinfusion. The procedure was continued either until all ascites had gone or until the filtration membrane clogged. In one case (No. 13) 26 hr of continuous recirculation were performed. All patients had a good diuresis during reinfusion and the ultrafiltrate volume ranged from 2·5 to 18 l (Table 1).

Chronic renal failure (Case 20)

In this patient without urine output there is no other means of controlling ascites, and so far he is being treated by repeated reinfusion at approximately 3 monthly intervals. This patient's uraemia remains well controlled on haemodialysis.

Complications of reinfusion

Complications were few. On six occasions body temperature rose by $> 1°C$ (in one patient, Case 2, the procedure was discontinued because of a rigor). A fall in plasma sodium concentration by > 5 mEq/l was observed on four occasions; in one, Case 3, the plasma sodium fell from 105 mEq/l to 87 mEq/l after a 6 hr reinfusion. Additional intravenous saline, as recommended by others (Benkemmoun, 1972) was not given to any patient in this series. There were no instances of pulmonary oedema, but the procedure was always discontinued after 6 hr if there was not a diuresis of > 500 ml. Bleeding, hypotension and peritonitis were not seen as complications.

Abnormalities in coagulation

In the earlier cases in the series it was observed that the plasma prothrombin time often became prolonged following the Rhodiascit procedure. Detailed coagulation studies were therefore performed on six consecutive patients (Cases 6, 7, 8, 9, 13 and 19).

The prothrombin time and concentrations of fibrinogen, factor V (a 'common pathway' factor), factor IX (an 'intrinsic pathway' factor), and factor VII (an 'extrinsic pathway' factor) were measured on peripheral venous blood immediately before starting reinfusion and at 6 hr after commencing reinfusion. Fibrinogen, factors V, IX and VII were also measured in the ascitic fluid before and after concentration, both at the commencement of reinfusion and after 6 hr, samples being taken from the peritoneal catheter and the venous reinfusion line.

Assay methods

Prothrombin time

The 'one-stage' method was used, 0·1 ml of citrated plasma being added to 0·1 ml of a standard thromboplastin and the time taken to clot measured after addition of 0·1 ml of 0·025 M calcium chloride.

Fibrinogen (plasma)

This was measured by the weighing of the dried fibrin clot formed by addition of 0·025 M calcium chloride to citrated plasma. Fibrinogen could not be detected in ascitic fluid using this method.

Fibrinogen (ascitic fluid)

A clot is formed by addition to the sample of EACA in saline and thrombin in calcium chloride. The clot is dissolved by 1% sodium hydroxide and a reaction formed by addition of Biuret. Samples are read spectrophotometrically.

Factor V

The time for clotting of a solution containing substrate plasma, thromboplastin and test solution is noted after addition to 0·025 M calcium chloride.

Factor VII

This is similar to factor V but a factor VII deficient plasma is used.

Factor IX

The clotting time of a solution containing substrate plasma, test solution, platelet substitute and kaolin is noted after addition of 0·05 M calcium chloride.

Results

As shown in Fig. 2, the plasma prothrombin time invariably became more prolonged after 6 hr of recirculation (mean increase 6 sec, range 4–13). Plasma fibrinogen concentrations also fell (mean fall 54%, range 25–67%). Plasma levels of factors V, VII and IX fell with mean reductions of 15% (0–39%), 36% (10–65%) and 19% (11–29%) respectively (Fig. 3).

There was also evidence of loss of coagulation factors on to the filtration membrane. Concentrations in the fluid after passage across the membrane should be higher than those in the unconcentrated fluid. By measuring the total protein content of 'pre- and post-membrane' ascitic fluid, the degree of concentration of fluid was estimated, values ranging from 1·8 to 2·5. The absolute value of the coagulation factors in the 'post-membrane' fluid was therefore divided by the concentration factor to give the 'corrected' concentration. There was a marked difference between unconcentrated ascitic fluid concentrations and the corrected concentrated concentration of all factors measured. Thus, at the commencement of the procedure the following mean decreases were found: fibrinogen 61% (53–71%), factor V 68% (62–72%), factor VII 45% (10–62%) and factor IX 62% (43–71%). After 6 hr of recirculation the loss of coagulation factors continued, the following mean falls being found: fibrinogen 49% (48–50%), factor V 67%

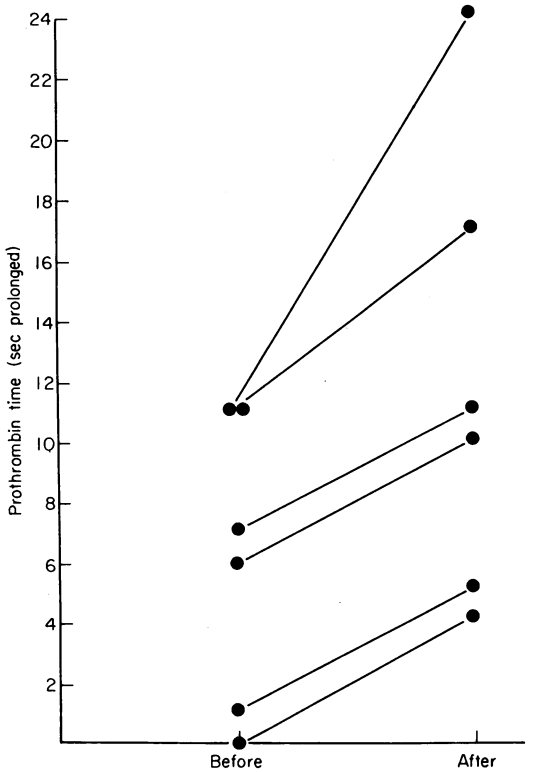

FIG. 2. The effect of ascitic reinfusion on plasma prothrombin time.

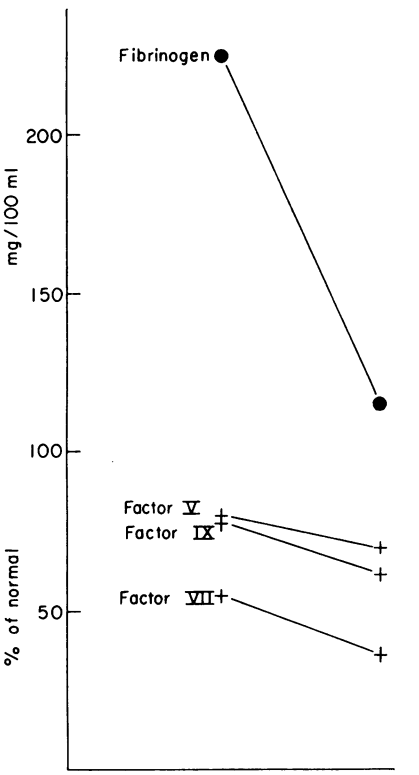

FIG. 3. The effect of ascitic reinfusion on plasma levels of clotting factors (fibrinogen expressed as mg/100 ml and factors V, VII and IX as percents of normal plasma value).

(60–83%), factor VII 49% (20–60%) and factor IX 56% (37–73%) (Fig. 4).

In view of the pore size of the filtration membrane (mol. wt 45,000) it is unlikely that the loss of coagulation factors across it was due to filtration. It is well established that fibrin and other clotting factors may adhere to haemodialysis membranes (Lindsay *et al.*, 1972), and so after completion of the Rhodiascit procedure the membrane was taken apart and examined for fibrin by both histochemical and immunofluorescent techniques. Dense deposits of fibrin were found on the membrane (Fig. 5a and b).

Thus adherence of coagulation factors to the filtration membrane might be an important factor in the pathogenesis of the changes in coagulation factor levels in the peripheral blood described above. Disseminated intravascular coagulation with thrombocytopenia, and a widespread haemorrhagic diathesis has also been reported as a rare consequence of the Rhodiascit procedure (Lévy, Buffet and Conard, 1973). No patient in the present series had any evidence of bleeding, but the findings suggest that the procedure should not be used in any patient with a recent history of bleeding or in patients with markedly abnormal tests of coagulation.

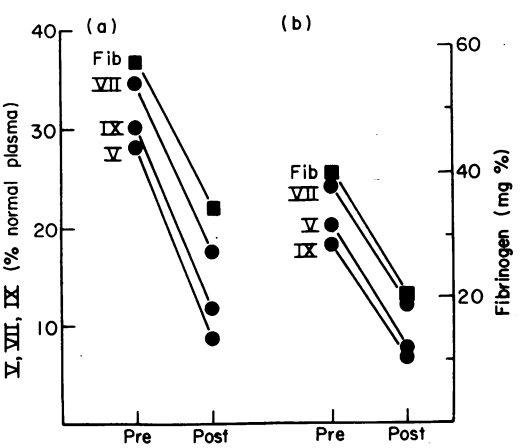

FIG. 4. Corrected concentrations of fibrinogen (Fib), factors V, VII and IX in afferent (Pre) and efferent (Post) lines of reinfusion apparatus. (a) Start; (b) after 6 hr.

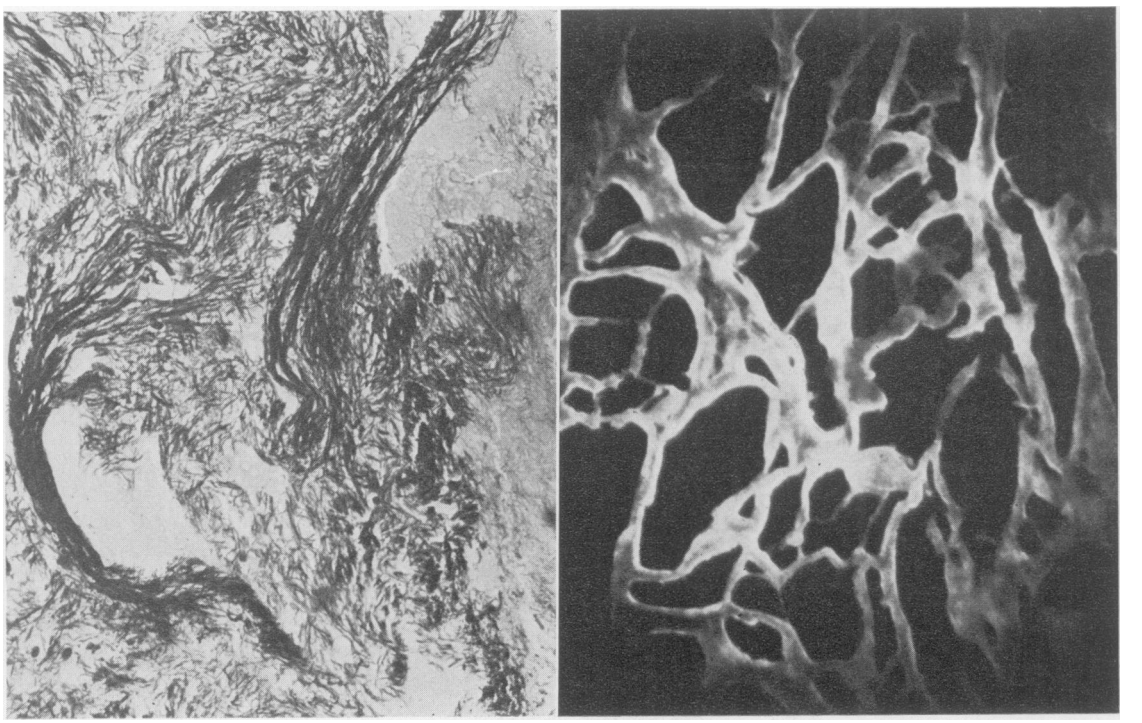

FIG. 5. (a) PTAH stain of scrapings from dialysis membrane to show dense deposits of fibrin (× 128); (b) as (a) but staining for fibrin by immunofluorescence (× 640).

References

BENKEMMOUN, R. (1972) *Traitement des hyponatrémies des cirrhotiques ascitiques par réinjection concentration.* Thèse (Paris).

LÉVY, V.G., BUFFET, C. & CONARD, J. (1973) Troubles de la coagulation au cours des réinjections continues du liquide d'ascite. Fibrinolyse ou coagulation intra-vasculaire. *Nouvelle Presse Médicale,* **2,** 446.

LINDSAY, R.M., PRENTICE, C.R.M., DAVIDSON, J.F., BURTON, J.A. & MCNICOL, G.P. (1972) Haemostatic changes during dialysis associated with thrombus formation on dialysis membranes. *British Medical Journal,* **4,** 454.