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REFERENCES

- Bruce-Chwatt, L. J. (1952). *Ann. trop. Med. Parasit.*, 46, 173.
 Chinard, F. P. (1951). *Methods in Medical Research*, 4, 38. Year Book Publishers, Chicago.
 Dacie, J. V. (1954). *The Haemolytic Anaemias*. Churchill, London.
 — and White, J. C. (1949). *J. clin. Path.*, 2, 1.
 Dähne, G. (1943). *Disch. tropenmed. Z.*, 47, 129. Abstracted by B. G. Macgrath, *Trop. Dis. Bull.*, 1950, 47, 202.
 Davidson, L. S. P. (1954). *The Principles and Practice of Medicine*, 2nd ed. Livingstone, Edinburgh and London.
 Edozien, J. C. (1957). *J. clin. Path.*, 10, 276.
 Fairley, H. (1934). *Brit. med. J.*, 1, 451.
 Holt, L. E., and McIntosh, R. (1953). *Holt Pediatrics*, 12th ed. Appleton-Century-Crofts, New York.
 Lawson, J. B., and Lister, U. G. (1956). *Clinical Report of the Department of Obstetrics, University College Hospital, Ibadan*. Vail, London.
 Nelson, W. E. (1945). *Mitchell-Nelson Textbook of Pediatrics*, 4th ed. Saunders, Philadelphia and London.
 Pontoni, L. (1936). *Haematologica*, 17, 833.
 Rubinstein, M. A. (1950). *Ann. intern. Med.*, 32, 1095.
 Strong, R. P. (1945). In *Silt's Diagnosis, Prevention and Treatment of Tropical Diseases*, 7th ed., vol. 1. Lewis, London.
 Trowell, H. C. (1949). *Trans. roy. Soc. trop. Med. Hyg.*, 42, 417.
 — (1956). *Trop. Dis. Bull.*, 53, 121.
 Walters, J. (1956). "The Health of a Yoruba Village in Western Nigeria." From an address delivered to the Clinical Society, University College Hospital, Ibadan. To be published.
 Whitby, L. E. H., and Britton, C. J. C. (1953). *Disorders of the Blood*, 7th ed. Churchill, London.
 Wiseman, B. K., and Doan, C. A. (1939). *J. clin. Invest.*, 18, 473.
 Woodruff, A. W. (1951). *Brit. med. J.*, 2, 1415.
 — (1955). *Ibid.*, 1, 1297.

PROLONGED ANURIA COMPLICATED BY EPILEPTIFORM FITS

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The dietary and fluid restrictions imposed on patients with anuria has been fully described (Bull *et al.*, 1949; Merrill, 1955). The occurrence of severe convulsions late in the course of treatment is not a generally recognized complication.

The patient whose case is described below had very severe epileptiform fits on her 17th day of anuria, and recovered. The management and aetiology of the fits, as well as the nature of the residual renal lesion and its effect on child-bearing, are discussed.

Case History

A primigravida aged 26 was first seen on March 25, 1955, at the 25th week of pregnancy. Her blood pressure was 130/80 mm. Hg; there was no proteinuria or past history of renal disease. During the 29th week of gestation she was admitted to hospital complaining of abdominal pain, vomiting, absence of foetal movement, and anuria for some hours. She was pale and anxious, and her blood pressure was 140/90. There had been no vaginal bleeding. A small quantity of urine was obtained from the bladder by catheter, and there was no proteinuria.

On examination the uterus was hard and tender, and foetal parts could not be palpated nor the foetal heart heard.

Two pints (1,100 ml.) of blood was given, and three hours after admission uterine contractions were felt, so the forewaters were ruptured. Eight hours later a stillborn foetus was expelled, with 5 pints (2,840 ml.) of blood clot and the placenta. A further 2 pints (1,100 ml.) of blood was trans-

fused. No fall in blood pressure had occurred since she was admitted to hospital.

After delivery no further obstetrical complication arose, but complete anuria persisted for the first 11 days, and oliguria for another six (see Table and Chart). The anuria

Fluid Intake and Output

Day	Input (ml.)				Output (ml.)		
	Mouth	Intra-gastric Drip	Intravenous Drip	Total	Urine	Vomit	Total
1	780	—	1,000 (blood)	1,780	—	—	—
2	120	600	1,000 (blood)	1,720	1	—	1
3	—	1,000	—	1,000	28	—	578*
4	—	800	—	800	—	—	—
5	800	—	—	800	10	150	160
6	800	—	1,000 (blood)	1,800	—	—	—
7	800	—	—	800	—	30	—
8	840	—	—	840	100	803	903
9	—	800	—	800	—	510	510
10	—	500	—	500	—	350	350
11	—	400	500 (blood)	900	—	240	240
12	—	500	—	500	510	360	870
13	495	—	700	1,195	150	105	255
14	480	—	1,000	1,480	270	—	270
15	180	—	1,025	1,605†	330	—	330
16	—	—	1,000	1,600‡	360	30	390
17	—	—	1,940	1,940	690	—	690
18	—	—	1,600	1,600	1,080	—	1,080
19	—	—	2,300	2,300	1,875	135	2,010
20	—	—	3,000	3,000	2,130	150	2,280
21	—	—	3,000	3,000	2,475	30	2,505
22	—	—	3,500	3,500	3,540	255	3,795
23	30	—	4,500	4,530	3,600	30	3,630
24	210	—	4,500	4,710	4,860	150	5,010
25	600	—	6,000	6,600	5,100	30	5,130
26	450	—	6,000	6,450	6,960	—	6,960
27	1,040	—	5,000	6,040	5,490	90	5,580
28	2,500	—	4,000	6,500	6,120	—	6,120
29	2,625	—	4,000	6,625	6,480	—	6,480
30	4,130	—	2,500	6,630	5,295	—	5,295
31	4,230	—	900	5,130	4,065	—	4,065

* 550 ml. in faeces. † 400 ml. by enema. ‡ 600 ml. by enema.

was treated on conventional lines at first, with 400 g. of glucose, 100 g. of peanut oil, emulsified to 1 litre of water (Bull *et al.*, 1949). As the anuria persisted the quantity of fluid was reduced to 800 ml. a day, given by mouth as 50% glucose with adequate vitamins. Excessive vomiting occurred on the eighth day, and the fluid was then given by intragastric drip: further attacks of vomiting necessitated changing to 40% glucose, given by caval drip (de Keyser *et al.*, 1949; Bull, 1952; Russell *et al.*, 1954). The electrolyte balance of the patient was followed at frequent intervals, and on the 12th day the serum potassium had risen to 7.6 mEq/l. This was reduced to 4.2 mEq/l. by giving 100 g. of "zeo-carb. 225/Na," suspended in 1 litre of water, administered in five divided doses over two days. The anaemia was twice treated by transfusion of concentrated red blood cells, 2 pints (1,100 ml.) on the sixth day and 1 pint (550 ml.) on the eleventh day.

Epileptiform Fits.—On the 17th day, just as renal function was returning, a series of epileptiform fits occurred, and at the first fit a blood pressure of 220/90 was recorded (a blood pressure of 170/100 had been recorded earlier in the day, a slight rise over the 160/80 of the day before) (see Chart). These fits were not controlled by the prompt administration of 4½ gr. (0.3 g.) of phenobarbitone sodium intramuscularly, nor by 3 g. of NaCl intravenously. The fits started to come at ever-increasing frequency and violence, 10 occurring in about two and a half hours. Thio-pentone sodium, 0.5 g. intravenously, brought immediate respite, and a further 0.25 g. was given when muscular twitching became apparent 15 minutes later. Bromethol ("avertin"), 6 ml. in 8 oz. (230 ml.) of water, was given, and this was followed by a fall in the blood pressure to 140/90. A further 4 ml. of bromethol was given three hours later, when the blood pressure had risen to 195/110. The blood pressure then fell to 165/90, and did not rise again, nor did fits recur. Sodium amylobarbitone, 3 gr. (0.2 g.), was given intravenously for the next six nights, which kept her in a very drowsy state. She was discharged from hospital on the 43rd day after the onset of the concealed accidental haemorrhage.

Fluid and Electrolyte Balance During Recovery Period.—The urine output returned in ever-increasing quantities following the occurrence of the epileptiform fits. During the period of semi-coma the fluid balance had to be maintained with intravenous therapy, and this was reinforced by the addition of sodium, potassium, chloride and bicarbonate. On the 23rd day, when the patient had regained consciousness, she was still nauseated, and the fluid requirement had to be maintained intravenously. This nausea

haemorrhage, although there is no reason to suspect pre-existing renal damage on the findings at her first antenatal visit.

Management of the Anuria

No new principles were involved here. The original recipe of glucose, peanut oil, and water (Bull *et al.*, 1949) is no longer advocated (Bull *et al.*, 1955; Parsons and McCracken, 1957). In particular, the peanut oil has been found unnecessary because, in the first place, the average reserves of fat in a patient developing acute anuria are sufficient to tide the individual through the anuric phase (Merrill, 1955), and, secondly, because of the incidence of nausea and the occasional occurrence of fat pneumonia. The amount of glucose to be administered should be pushed to the maximum dose of toleration for the purpose of reducing endogenous protein breakdown. A glucose-water mixture, adequately supplemented by vitamins, can often be taken by mouth without having to resort to an intragastric drip, but in this patient nausea occurred early, and the intragastric drip had to be used after the eighth day. Then, because of incessant vomiting, 40% glucose was delivered into the inferior vena cava by a "polythene" catheter from the 13th day onwards. Intravenous therapy had to be maintained in this patient even after the anuric phase had given place to the recovery phase, as vomiting and nausea prevented adequate oral intake to keep pace with the urinary output.

The quantity of fluid required during the anuric phase could not be ascertained with certainty in this patient, as no weighing scales were available. The total fluid balance for the first 16 days' treatment is given in the Table: input exceeded output by 8.7 litres, an average of 550 ml. per 24 hours, which probably is the amount of fluid required to satisfy the insensible loss when the water of oxidation and the water released in the cells when protein is

decreased and more fluid could be given by mouth, but not until the 31st day of her illness was it possible to stop the intravenous supplement, the caval drip having operated for 19 days. Thereafter the patient returned to a full diet, taking all fluid and medication orally. On the 41st day—that is, two days before her discharge—the output of urine was 1,500 ml.

Subsequent Course.—One year after leaving hospital the patient was reinvestigated. Protein was still present in the urine in considerable quantity, as were a few pus cells and an occasional red blood cell. No casts were found. An intravenous pyelogram showed no abnormality other than a slight distortion of the calices of the left kidney. The plasma levels of sodium, potassium, chloride, calcium, phosphorus, and protein, and the carbon dioxide combining power were within normal limits, but the blood urea was 66 mg./100 ml. The haematocrit reading was 47%. The inulin clearance was 49 ml. a minute, and the P.A.H. clearance 224 ml. a minute. It was apparent, therefore, that considerable impairment of renal function existed. The nature of the residual lesion was obscure, particularly as no values were available prior to the onset of the accidental

mobilized are taken into consideration. These calculations would suggest that perhaps no overhydration had taken place in the course of treatment. It is, however, emphasized that the fluid-balance chart can be notoriously inaccurate in these situations, and the only satisfactory investigation that can be performed to guard against overhydration is to weigh the patient daily (Merrill, 1955).

The degree of metabolic breakdown that was occurring during the period of anuria was not high in this patient, for the average daily rise in the blood urea nitrogen during the period of anuria was only 11.4 mg./100 ml.

The dangerous rise in the serum potassium level that occurred on the 12th day was treated by giving ion-exchange resin zeo carb 225/Na. As this could not be administered orally it was given by slow rectal drip, the resin being suspended in water. It will be seen from the Chart that this dose of resin successfully reduced the serum potassium level from 7.6 to 4.2 mEq/l.

Epileptiform Fits

The aetiology of the fits can only be a matter for conjecture. It seems unreasonable to postulate the occurrence

of eclampsia as long as 17 days after delivery, unless the renal failure had delayed the excretion of a substance responsible for eclamptic fits. These were associated with a marked rise in the blood pressure, and, although the treatment used in this patient caused a marked drop in the blood pressure with the cessation of the fits, it is no explanation simply to attribute the fits to the raised blood pressure, for this only leaves unsolved the aetiology of the sudden hypertension.

It is well known that overhydration with water can cause convulsions of an epileptiform type, but the fluid-balance investigations did not indicate an excessive intake of water, and certainly no clinical evidence of overhydration occurred. These findings were supported by the fact that rapid intravenous injection of 3 g. of sodium chloride failed to control the fits. Indeed, prior to the onset of the fits sodium had already been administered in the form of the ion-exchange resin.

From the evidence available it can only be assumed that the fits were associated in some way with the anuria and progressive uraemia, for after restoration of renal function the fits ceased and did not recur.

The treatment of the convulsions was entirely empirical, and was based on the management of eclampsia. Thiopentone was used as an emergency, followed by a full dose of bromethol. This was effective in controlling the fits initially, and a further small dose of bromethol was given three hours later, when the blood pressure began to rise again. Fortunately no harm came from the use of these drugs despite poor renal function.

Nature of the Residual Renal Lesion

The presence of proteinuria even one year after the episode of anuria suggests that the renal lesion was of some magnitude, and this is supported by the lowered inulin and P.A.H. clearances. The presence of pus cells also requires further explanation. No organisms were found in the urine either during the period of anuria or subsequently. Cystoscopy revealed no abnormality, and a retrograde pyelogram was essentially normal in the follow-up period. Perhaps the pus cells are the result of gross renal damage undergoing repair.

Future Pregnancies

In the chronic phase of Ellis type I nephritis the chances of foetal survival are very poor, and deterioration of the maternal condition is very great when the blood urea level is raised above 40 mg./100 ml. at the beginning of pregnancy (Dodds and Browne, 1940; Hamilton, 1952). In chronic pyelonephritis of comparable severity, on the other hand, the prognosis for the infant would not be so poor, and the maternal risk would lie more in the danger of superadded acute renal infection. In any case, the possibility of a recurrent pre-eclampsia and even accidental haemorrhage has to be considered. It would seem, therefore, that there would be considerable risk to mother and foetus in a further pregnancy. If the husband and wife are still determined to try again we could only keep a close watch, and offer termination of pregnancy immediately signs of deterioration develop.

Summary

A case is described of anuria for 11 days and oliguria for a further six days following severe concealed accidental haemorrhage.

Epileptiform fits occurred on the 17th day of reduced renal output. They were associated with a sudden rise of blood pressure.

The detailed management of the anuria and of the fits is described.

The results of renal investigations one year later are given. They showed persistent proteinuria and pyuria, with considerable impairment of renal function.

The management of anuria, the possible aetiology of the fits, the nature of the residual renal lesion, and the prognosis for future child-bearing are discussed.

REFERENCES

- Bull, G. M. (1952). *Proc. roy. Soc. Med.*, **45**, 848.
 ———, Joecks, A. M., and Lowe, K. G. (1949). *Lancet*, **2**, 229.
 ——— (1955). *Ibid.*, **2**, 1152.
 Dodds, G. H., and Browne, F. J. (1940). *Proc. roy. Soc. Med.*, **33**, 737.
 Hamilton, H. F. H. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 25.
 Keyser, R. de, Beekhoutte, P., van, Kop, P. S. M., and Kolff, W. J. (1949). *Ned. T. Geneesk.*, **93**, 2386.
 Merrill, J. P. (1955). *The Treatment of Renal Failure*. Grune and Stratton, New York and London.
 Parsons, F. M., and McCracken, B. H. (1957). *Brit. J. Urol.*, **29**, 424.
 Russell, C. S., Dewhurst, C. J., and Brace, J. C. (1954). *Lancet*, **1**, 982.

CORTICOTROPHIN IN TREATMENT OF HYPERTHYROIDISM

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Harris and Woods (1956) reported that electrical stimulation of the tuber cinereum of rabbits by remote control rarely produced the expected increase in thyroid activity unless preceded by adrenalectomy. After reviewing other evidence for the possible inhibitory action of the adrenal cortex on thyroid function, they concluded that further investigation of the effects of corticotrophin administration in early and previously untreated cases of Graves's disease would be of interest. This communication records such an investigation, a preliminary report of which was given by Richardson (1957).

Methods

Eight patients with hyperthyroidism were admitted to hospital. The clinical diagnosis was confirmed by observation for at least 10 days, during which time radioiodine studies and protein-bound iodine estimations were made. Basal metabolic rate (B.M.R.) estimations were also carried out on three days towards the end of the observation period. Corticotrophin gel was then given by intramuscular injection for from two to five weeks, the initial dose of 20 units b.d. being halved in some cases after 7 to 11 days. At the end of the period of treatment the laboratory studies of thyroid function were repeated (Table I). The potency of the batch of corticotrophin which was used throughout had previously been demonstrated on a healthy subject. Confirmation of the efficiency of the adrenocortical stimulation was provided by the fluid retention which occurred and by the increases which were detected in the urinary excretions of 17-ketosteroids and 17-ketogenic steroids. Excessive retention of fluid was combated in the thyrotoxic subjects by injections of mersalyl, but such injections were not given when radioiodine or urinary steroid excretion studies were being made. However, in spite of precautions, pulmonary congestion developed at the end of the course of treatment in two patients.

A ninth patient with hyperthyroidism was treated with prednisone, 20 mg. b.d., for 14 days and studied in a similar way.

Results

A significant improvement in the hyperthyroid state was observed in only one patient, a man aged 40 with mild hyperthyroidism, a diffuse goitre, and symptoms of short duration (Case 2). Even though the improvement was only