RENAL INSUFFICIENCY IN TERMINAL RESPIRATORY FAILURE

BY

D. A. K. BLACK, M.D., F.R.C.P.

AND

S. W. STANBURY, M.B., M.R.C.P.

Department of Medicine, University of Manchester

Patients dying of pulmonary failure have shown evidence of a functional renal failure with elevated blood urea (Simpson, 1957). This is not a matter which we have particularly studied, and indeed the general condition of these patients precludes extensive metabolic investigation; but in an experience of 24 patients admitted to this unit with cor pulmonale we have come across two whose terminal illness was accompanied by significant suppression of urinary output. Diminished renal plasma flow and glomerular filtration rate are of course well recognized in patients with cor pulmonale, even when the cardiac output is high (Davies and Kilpatrick, 1951; Lewis *et al.*, 1952); but we have not found any reports or recognition that anuria is likely. Acute renal failure complicating cor pulmonale may be one of those conditions which escape notice by lurking between the accepted territories of two specialties; at any rate, it is mentioned neither in the cardiological textbooks of Friedberg (1956) and Wood (1956) nor in the equally excellent monograph of Merrill (1955) on renal failure.*

Case 1

A woman aged 20 had had cough, with copious purulent sputum, from infancy; she had had spasmodic dyspnoea from the age of 4, and her activity had always been restricted. Dyspnoea on exertion had been prominent at the age of 18, and cyanosis and finger-clubbing were first noticed then. At the age of 19 she had been admitted to hospital with pyrexia and congestive heart failure, which improved with antibiotics, salt restriction, and mercurial diuretics; she remained cyanosed, breathless, and tired until her final admission to hospital on November 2, 1952, under the care of Dr. H. T. Howat. Since August, 1952, she had been confined to bed with dyspnoea and oedema, and had been on a low-salt diet, with injections of organic mercurials, to which there had been a good diuretic response until November 1, when she was given a mercurial injection, but passed no urine until admission the next day. She was treated conservatively by intragastric drip of glucose and arachis oil, the total daily intake of fluid being one litre (Bull, Joekes, and Lowe, 1949). She passed only a few ounces of urine each day until November 10, when a moderate diuresis began, and continued until her death from respiratory failure, on November 22, in spite of treatment with antispasmodics, antibiotics, and oxygen.

During the oliguric period her blood urea rose to 158 mg./100 ml. on November 10, and had fallen to 76 mg./100 ml. on the 13th. Her plasma sodium was 139 mEq/l. on November 6, and 141 on the 10th; but on the 13th, after diuresis had begun, it rose to 151 mEq/l. Her urine at this stage was of low specific gravity (1002) and contained albumin; the electrolyte content was low (Na, 5 mEq/l.; Cl, 9 mEq/l.; and K, 17 mEq/l.), although she was probably water-depleted from inability to drink sufficient fluid. Her plasma CO₂ was not increased (25 and 27.5 mEq/l. on November 6 and 10); her chloride was somewhat low (95 and 94 mEq/l.). Phosphate and organic acids were

not determined. Her plasma potassium was 6.5 mEq/l. on November 9, but had fallen to 3.6 mEq/l. the next day. On November 19, when she had been passing urine for over a week but was terminally ill, the plasma sodium was 130 mEq/l.; and the plasma potassium 7 mEq/l.

At necropsy (Dr. B. L. Williams) she was found to have very extensive bronchiectasis involving the whole of the right lung, and the left lower lobe, with a terminal bronchopneumonia. The right ventricle was grossly dilated and hypertrophied, and there was hepatic congestion, and some free fluid in the abdomen. The kidneys were not enlarged, and showed no macroscopic changes. The microscopical appearances in the kidney were as follows: Small foci of slight round-cell infiltration of boundary zone; occasional tubules show dilatation and irregular thinning of epithelium and a very few contained desquamated necrotic cells and polymorphs; no sign of epithelial regeneration; this picture is that of acute tubular necrosis of minimal degree (many nephrons show widespread fine vacuolation of tubular cytoplasm, ? fatty, ? hydropic, without any sign of necrosis).

Case 2

A man of 44 had a 20-year history of cough and breathlessness, with an episode of "pneumonia" 15 years before his death and a transient haemoptysis four years before death. He was admitted to hospital on November 11, 1952, after collapsing in the street. He had noted increasing breathlessness and swelling of the ankles for two months.

On admission he was apathetic, cyanosed, and breathless, with sacral and ankle oedema. There were scattered crepitations in both lungs, but no dullness was found. He was given penicillin and treated in an oxygen tent. On November 12 he passed urine after a test dose of 0.5 ml. of a mercurial diuretic; but after a dose of 2 ml., the next day he became anuric and remained anuric, until his death on the evening of November 14. On that day his blood urea was 78 mg./100 ml.; plasma sodium 138 mEq/l.; and potassium 7 mEq/l. He had a leucocytosis of 44,200/c.mm., with 94% polymorphs.

Necropsy (Dr. B. L. Williams) showed a chronic bilateral tuberculous bronchopneumonia with caseation, many acid-fast bacilli, and scattered foci of polymorphonuclear infiltration indicating a secondary pyogenic infection. The right ventricle was dilated and hypertrophied, and the liver showed centrilobular congestion and necrosis. The bladder was empty. The kidneys were slightly enlarged (right 200 g., left 210 g.), but the capsule stripped easily, and the cortex and medulla were moderately differentiated. The right kidney had a small demarcated caseous focus in one of the pyramids. On microscopical examination no abnormality was seen (apart from some fine vacuolation of tubular epithelium—? fatty, ? hydropic).

Discussion

The main cause of death in these two patients was advanced pulmonary disease, with cardiac failure. The first patient died at an unusually early age, from very extensive bronchiectasis; she had passed through an anuric episode, from which she was recovering. The second patient, with an infected tuberculous bronchopneumonia, was terminally anuric. The most likely mechanism to account for acute renal failure in association with cor pulmonale is a further substantial reduction in an already low renal blood flow. Each of these patients was specifically noted to have cold extremities, a weak radial pulse, and a systolic blood pressure of 100 mm. Hg. It can be inferred that they had passed into the low-output advanced stage of cor pulmonale (Wood, 1956). In Case 1 the clinical course and necropsy findings are consistent with the hypothesis that the patient had an episode of ischaemic acute tubular necrosis; the second patient died before the full course of this disorder could be clinically manifest. Both patients had been given mercurial diuretics, but in the second the amount given was only 0.5 and 2 ml.; and neither patient showed the renal lesion of a mercurial nephropathy.

*Since writing the above, we have found the possibility of anuria referred to by Stuart-Harris and Hanley (1957) in these terms: "A severe oliguria or anuria with resulting uraemia may be seen terminally."

Although mercury salts in large amounts can cause a full-blown tubular necrosis, the effect of small amounts of mercurials, such as are in question here, is to produce an epithelial necrosis limited to the proximal tubule and not involving the basement membrane (Oliver *et al.*, 1951). The first patient had had a full course of mercurials while on a low-salt diet, so that iatrogenic sodium depletion is a possible additional cause of lowered renal blood flow; against this possibility is the absence of hyponatraemia in the early anuric stage, and the restoration of urine flow spontaneously, while on a sodium-free intake. Arterial desaturation may well aggravate the effects of renal ischaemia; but hypercapnia is probably not a critical factor, as it was absent in the first patient. We have not observed anuria in other forms of cardiac failure.

In the last few days of illness both patients had hyperkalaemia (7 mEq/l.); one had a definitely low plasma sodium (130 mEq/l.) and the other a low-normal value (138 mEq/l.). We have recently seen another patient with terminal cor pulmonale, but without anuria, whose plasma sodium was 130 mEq/l. and potassium 7.6 mEq/l. Anoxia and acidosis are recognized causes of a shift of potassium from cells to extracellular fluid; so that the obvious explanation of hyperkalaemia in terms of diminished renal output of potassium may be less important than internal shifts of potassium, and possibly also of sodium. This is a question which could only be settled by full balance-studies, which are not likely to be made. It is relevant, however, to mention that Moore *et al.* (1954), studying other types of acute renal failure, found that patients whose total exchangeable potassium was low quite often had a high plasma potassium; and one of us (D. A. K. B.) has seen a patient with corrosive sublimate poisoning whose plasma potassium fell from 8 to 3.5 mEq/l. in 24 hours, during which time metabolic acidosis had been corrected by infusion of 200 ml. of molar sodium lactate.

Acute renal failure occurring in such circumstances may well be regarded as almost the least of a patient's troubles; while it constitutes an additional therapeutic problem, the situation may sometimes be met by conservative treatment, which is more likely to succeed if the condition is promptly recognized. More important, perhaps, than the treatment of established renal failure is the recognition that it can occur in patients with lung disease, whose cor pulmonale has been complicated by a lowering of cardiac output, often associated with acute respiratory infection. These observations perhaps reinforce in some small degree the already strong case for the prompt and vigorous treatment of suspected acute respiratory infection in patients with bronchitis and emphysema; in this way, the dangerous situation of peripheral circulatory failure may be prevented or cut short.

Summary

Two patients with terminal respiratory failure had in addition acute oliguric renal failure; in one the urine flow returned before death, while the other died before this could happen. It is suggested that a terminal fall in cardiac output in patients with cor pulmonale may on occasion produce ischaemic tubular necrosis.

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MEPROBAMATE IN THE TREATMENT OF STUTTERING

BY

ROY D. H. MAXWELL, M.D., B.Sc., F.R.F.P.S.

AND

JAMES W. PATERSON, L.C.S.T.

From the Neurology Clinic and Speech Therapy Department of the Western Infirmary, Glasgow

Speech defects are common, affecting 3–10% of children. Surveys such as those analysed by McAllister (1937) and Burt (1937) have shown an incidence of approximately 1% of stuttering in schoolchildren. The aetiology of stuttering is complex. Klingbeil (1939) quotes Charles Bell (1773–1842), professor of anatomy at Edinburgh, as attributing the condition to a choreiform affection of fluency of speech. Many have considered it a conflict for dominance between the cerebral hemispheres for control of the speech mechanism. Various other theories have been propounded.

Stuttering is an expressive disorder of communication the tendency to which is probably present from the beginning of development of speech. As the child grows in age a complexity of factors adds a reactionary overlay, a major factor being the disorder of speech itself. In the adult, methods of speech therapy are inseparable from psychotherapy to relieve anxiety and tension.

In view of the handicap which stuttering presents, the application of drugs which allay states of anxiety merits consideration. We decided to apply meprobamate in support of the accepted methods of speech therapy.

Clinical Results

Eighteen patients were selected for treatment. All were severely affected by stuttering and had been treated by speech therapy previously, with little improvement, at this

Results of Treatment

No.	Sex	Age	Occupation	Drug Dosage Tablets per Day	Response to Treatment
1	M	18	Van driver	3	No improvement
2	M	19	Draughtsman	3–6–8	Slight improvement
3	M	23	Compositor	3	Good
4	M	24	Joiner	3–6	"
5	F	24	Housewife	3	"
6	M	25	Butcher	3	Very good
7	M	26	Printer	3	"
8	M	26	Railway fireman	3–6	Good
9	F	28	Catering trade	3	"
10	M	28	Architect	3–4–6	"
11	M	29	Draughtsman	3	"
12	M	29	Engineer	3	Slight improvement
13	M	31	"	3–6	Good
14	M	34	Compositor	3	Very good
15	M	37	Post Office worker	3	" "
16	M	39	Wood-working machinist	3	" "
17	M	42	Technical manager	3	" "
18	M	50	Storeman	3	No improvement

Very good = Extent of improvement such that speech difficulty appears only during exceptional emotional tension. Good = Subjective and objective improvement permitting satisfactory employment as indicated, with intermittent speech hesitancy.

and other centres. Secondary tonic or secondary tonic-clonic stuttering was present in all cases. They all had defects in social adjustment.

The patients were seen at intervals of one week during active treatment and later at intervals of one month. The period of such supervision was eight months. Meprobamate was used in tablets of 400 mg.; one tablet three times a day was employed initially, and in some cases this dosage was increased according to effect. The results of treatment are summarized in the Table.