THE MODERN TREATMENT OF ANURIA AND OLIGURIA

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There are few conditions which offer a greater challenge to the medical and nursing staff than that of acute renal failure. There are also few conditions where the application of modern techniques and careful clinical biochemical assessment are more essential to the achievement of success.

True or complete anuria rarely occurs except where there is mechanical obstruction and, as early recognition of oliguria is essential in acute renal failure, it is important to define it in a recognizable form.

The normal output of urine varies between one and two litres per day. On a mixed diet it is obligatory to pass a minimum volume of approximately 500 ml. in 24 hours (Gamble, 1947). This entails good renal function and the ability to concentrate fully to a maximum specific gravity of 1.035 (1,155 m. osm./l.).

Oliguria has been defined as less than 700 ml. in 24 hours. Where good renal function is present such urine will concentrate sufficiently to produce a specific gravity of 1.018 (595 m. osm./l.) or more. Where renal damage is present, a low specific gravity of 1.008 (265 m. osm./l.) to 1.014 (460 m. osm./l.) is to be expected (Joeke, 1957). Severe oliguria may be defined as a urine output of 500 ml. or less in 24 hours.

Where there is a urine output of 300 ml. or less, such will be the inability of the kidneys to keep pace with the production of metabolites, the condition might well be called metabolic anuria.

The object of therapy in oliguria and anuria is to tide the patient over until the kidneys have time to recover their function.

At this time, it is probably true to say that suppression of urine due to malignant hypertension, chronic nephritis and polycystic kidneys developing into oliguria, and the rare condition of bilateral cortical necrosis, is, in the main, not reversible.

The reversible causes of acute renal suppression may be listed as:

(a) Mechanical—obstruction of the ureters, by:

operative procedures; bilateral renal calculi; carcinoma of the prostate and cervix; prostatic hypertrophy, etc.

(b) Dehydration and electrolyte depletion, e.g. low salt syndrome.

(c) Tubular necrosis such as follows: gross dehydration; prolonged hypertension; separation of placenta; abortion; crush syndrome; mismatched blood transfusion; nephrotoxins, e.g. mercuric chlorides, bismuth, sulphonamides.

(d) Acute nephritis.

The history of a successfully treated case of acute suppression of urine normally falls into four phases:

(a) The precipitating condition or cause.

(b) The anuric phase.

(c) The diuretic or pre-recovery phase.

(d) The recovery phase.

The Precipitating Condition or Cause

Careful clinical assessment to elucidate the causation of anuria is important because of the undesirability of prolonging an irreversible condition, and the need of remedying quickly, and to the maximum, any condition that is immediately treatable.

Dehydration, electrolyte imbalance, low blood pressure are all easily treatable. Sulphonamide anuria usually responds to alkalis and increased fluids.

The onset of renal failure, following poisoning with bismuth or mercuric chloride, may be avoided by the early use of British anti-lewisite or calcium disodium versenate. These substances may be toxic, however, once anuria is established (Stock, 1952; Merrill, 1955).

Care must be observed in the treatment of dehydration and electrolyte imbalance in case renal damage has already occurred.

The Anuric Phase

Three factors emerge as a consequence of the acute suppression of urine:

(a) The retention of water.

(b) The accumulation of the products of metabolism, urea, uric acid, creatinine, phosphate, sulphate, etc.

(c) The metabolic upsets arising from the above, as yet little understood, but involving the shift of electrolytes from the cells to the extra-cellular fluid compartments, and for want of a better term may be called the poisoned-cell phenomenon.

The consequences of fluid retention rapidly become apparent when unrestricted fluid intake is allowed, or worse, when fluids are forced in the misguided attempt to invoke a diuresis. In either case, cardiac failure, oedema, pulmonary congestion, hypertension, cerebral oedema and the symptoms of water intoxication will result.

The most common cause of death within 14 days of the onset of oliguria due to renal disease is overhydration (Bull, Joeke and Lowe, 1949). Even when overhydration is not a factor, the retained products of metabolism produce the gradual onset of lethargy, coma, vomiting, pericarditis and lowered resistance to infection. The rising concentration of potassium in the body is reflected in high plasma-potassium levels and is associated with cardiac failure and muscle weakness.

When the kidney begins to recover it secretes a dilute urine of low concentration, which, on reaching a volume of a litre or more, begins to reduce the blood urea.

The kidney at this stage still has an impaired tubular function, unable to concentrate and to differentiate between electrolytes. Thus, the passing of a profuse dilute urine may soon lead to dehydration, and electrolyte imbalance and depletion.

Within a variable period of time, usually six to eight weeks, full return of kidney function is to be expected, sometimes with no detectable abnormality (Lowe, 1952; Oliver, 1953).

The Regulation of Water

The fluid requirements in the anuric patient need to be assessed accurately each 24 hours so that the building up of a positive or negative imbalance is avoided as time progresses. These requirements amount to the fluid loss through the skin, lungs, urine, vomit and faeces.

Although various formulae are available for the assessment of insensible loss through the skin and lungs, none can be applied with confidence to every patient.

The simplest and most accurate method is to record the daily change in weight, the weighing being performed at the same time each day and on the same scales, with the bladder empty. Ideally this is done on a bed weighing machine, but mobilization of the patient for weighing, where

this is clinically possible, is by no means contra-indicated.

An accurate record of all additions to the patient in the form of fluids, such as medicines, ion-exchange resin, etc., and all losses in the form of vomit, urine and faeces must be kept, in order for this assessment to be made.

The measured insensible loss of the average adult is now accepted to be less than one litre in 24 hours and generally falls as the time from the onset of anuria progresses, probably because of endogenous production of water from fat metabolism (Swan and Merrill, 1953).

With this in view, and the probability that some degree of overhydration may have occurred by the time the oliguric state has been recognized, as little as 400 ml. in 24 hours can be recommended in the early stages of treatment, and a gradual loss of weight, as food stores are used up, is to be desired (Merrill, 1955).

The accurate measurement of urine output is of paramount importance, not only for the assessment of fluid replacement, but for the determination of the progress of the patient, and the amount of urea and electrolytes excreted.

If necessary, therefore, a self-retaining catheter should be inserted into the bladder and, after emptying, a measured quantity of fluid, containing an antibiotic, passed back into the bladder through the catheter: 30 ml. of fluid containing 100 mg. of chloramphenicol has been used successfully. This volume is deducted from the volume of urine obtained on releasing the catheter.

In order to avoid the oral complications associated with oliguria and its treatment, i.e. parotitis, thrush and ulceration, part of the fluid intake should be taken by mouth. This regime should be reinforced by the sucking of pure glucose sweets, followed by bland antiseptic mouth washes.

The Suppression of Harmful Metabolites

The main metabolic consequences the anuric patient has to face arise from the metabolism of protein, producing a rising blood non-protein nitrogen, cardiotoxic levels of plasma potassium, and release of unexcretable fixed acid.

Therapy is therefore directed towards a completely protein-free intake and the reduction of endogenous protein metabolism. Advantage is therefore taken of the protein-sparing effect of glucose and, owing to the necessity of restricting fluid intake, this entails the use of hypertonic solutions. Up to 50 per cent. glucose can be safely injected into a large vein by means of a polythene catheter (Bull, 1952). Although the procedure of passing the catheter is simple, in the condition of anuria, where it may by necessity stay *in situ* for three weeks, maximum precautions for sterility

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should be enforced and complete sterility maintained at the changing of each bottle.

To each 500 ml. of glucose solution are added 2,500 units of heparin, and one unit of insulin is added for every 3 g. of glucose. The slow infusion of not less than 200 g. of glucose which should be aimed at, can be achieved in only 400 ml. of water.

The advantages of this regime over the tube feeding of fat and glucose, such as has been advocated (Bull, Joekes and Lowe, 1949; Borst, 1948), are seen in the complete control obtained over fluid and calorie intake, the absence of any stimulation to vomiting, and the possible greater protein-sparing effect of glucose over that of fat (Engle, 1952). In addition, the urea and electrolyte content of vomit is such that it is often valuable as an excretory mechanism, and its return down the stomach tube in an attempt to maintain balance is contra-indicated.

The use of testosterone propionate to inhibit protein catabolism has not proved very successful, but the newer synthetic non-virilising compounds may be of value (McSwiney and Prunty, 1947).

Electrolyte Imbalance

Lowered plasma sodium, calcium, bicarbonate,

and pH, and raised phosphate and sulphate, are all found in the uraemic state.

Lowered serum sodium may be due either to sodium depletion or more probably to dilution by overhydration. The therapy for the latter is intense water restriction. The shift of sodium from the plasma into the cells, due to the poisoned cell phenomenon, is also a possible factor. The administration of the sodium ion is to be avoided. If, however, sodium depletion is considered to have occurred, small quantities of sodium in the form of lactate, bicarbonate, or chloride can be administered. If clinical improvement results, further quantities can be given until the deficit, as calculated from the plasma deficiency and total body water, has been made good. This quantity should never be exceeded.

e.g. weight of patient = 70 kilo.

Total body water estimated at 60 per cent.
of body weight = 42 l.

Plasma sodium = 120 mEq./l.

$42 \times 20 = 840$ mEq. of sodium are required to correct the observed deficit and bring the plasma sodium level to 140 mEq./l.

No marked clinical improvement is to be ex-

pected from attempts to modify the acidosis resulting from the accumulation of fixed acids, phosphate, sulphate, etc., by administration of alkali in the form of bicarbonate or lactate (Grollman, 1954; Merrill, 1955). Also tetany, due to a further lowering of the already decreased level of plasma ionized calcium, may occur on the administration of alkali.

Treatment of Hyperkalaemia

A complete potassium-free intake should be instituted and maintained throughout the period of anuria. Milk, fruit, etc., are banned. Tea without milk may relieve the monotony of glucose drinks.

A raised plasma potassium occurs mostly due to its release from protein catabolism and probably partly as an inherent metabolic consequence of anuria. When toxic levels are reached, muscular weakness, cardiac irregularities, absence of tendon reflexes can be demonstrated. The E.C.G., when plasma levels of 7 or 8 mEq./l. are reached, shows high-peaked T waves, absent P waves, slurred widened Q.R.S. complexes. Cardiotoxic levels of potassium vary with each individual, age and duration of the disease. Rapid onset of potassium intoxication is to be expected following major operative procedures and where gross tissue damage has occurred (Bywaters, 1944).

Treatment for the control of potassium intoxication should be instituted early, before pathological levels appear. Intravenous glucose tends to alleviate the condition by the uptake of potassium in its metabolism (Bull, 1952). Ion exchange resins which exchange ammonia or sodium for potassium may be used (Elkington *et al.*, 1950; Knowles, 1953; Milne and Yellow Lees, 1953). Fifteen g. of resin given in 30 ml. of 5 or 10 per cent. glucose water is well tolerated orally when given early in the disease, and can be given, if necessary, three times a day: 30 to 60 g. of ion exchange resin can be given rectally in 200 ml. of water or 1 per cent. methyl cellulose. It may be necessary to administer a glycerine enema in order to obtain return of the resin, as retained resin is of only limited value. The rectal route can be combined with oral administration or used alone when the patient is vomiting or unable to swallow.

Attempts to make use of the low potassium content of stored packed cells have proved disappointing, but there is some recent evidence that exchange transfusion may be of some benefit in this respect (Hughes, 1958).

It must be borne in mind, however, that transfusions of blood or plasma are associated with increased protein metabolism. Attempts to correct anaemia should be avoided for this reason unless found to be essential, i.e. an haematocrit of less

than 25 per cent. The infusion of 100 ml. of 10 per cent. calcium gluconate every 24 hours will do no harm and on physiological grounds may help to mitigate the effects of hyperkalaemia (Meroney and Herndon, 1954). It may be added to hypertonic glucose solutions. Hyperkalaemia is an indication for dialysis. The rapid infusion of hypertonic saline or of sodium bicarbonate will temporarily, for one or two hours, reverse the cardio-toxic effect of potassium (Merrill, 1955) and may be used, for example, prior to dialysis.

The Extra Renal Removal of Metabolites

When conservative treatment, as described above, is inadequate to control or maintain the patient until the pre-recovery stage develops, the extra renal removal of metabolites becomes essential.

This requires strict biochemical and physiological control and a well-trained team. The indications for this procedure, which should be regarded as part of general therapy and not as a substitute for the regime described above, may be summarized as follows:

(a) General clinical deterioration—'the uraemic state.' No hard and fast rules can be laid down, as individual tolerance to raised-plasma non protein nitrogen levels appears to vary so much, and are not necessarily in themselves indications for dialysis. A careful clinical assessment of the rate of progress as manifested by drowsiness, pericarditis, vomiting, muscular irritability, etc., must be made.

(b) Hyperkalaemia—cardiotoxic plasma potassium levels of 7 mEq./l. or more as shown by E.C.G. recordings.

(c) Acidosis—a plasma bicarbonate of less than 15 m. mo./l.

(d) Gross overhydration.

The therapeutic methods available are intestinal irrigation, peritoneal lavage and dialysis.

Intestinal Irrigation. The perfusing of hypertonic fluids of varying composition through the gut at a constant rate is difficult to perform and may be associated with complications of intestinal haemorrhage, perforation, ileus and pulmonary oedema.

It has not gained much popularity except on the Continent.

Peritoneal Lavage. The use of the large peritoneal surface for dialysing is, on physiological principles, sound and of value clinically (Grollman, 1954).

Slightly hypertonic sterile solutions, varied according to the biochemical needs of the patient, are perfused through the abdominal cavity.

In hyperkalaemia, for example, no potassium is added to the perfusing fluid and solution A would

be found suitable. Where hyperkalaemia is not a factor, then a solution such as B would be indicated.

Solution A

	mEq./l.		g./l.
Na ..	134	NaCl ..	6.26
Ca ..	4	NaHCO ₃ ..	2.27
Mg ..	1.1	MgCl ₂ ..	0.05
HCO ₃ ..	27	CaCl ₂ ..	0.22
Cl ..	112	Glucose ..	22

Solution B

	mEq./l.		g./l.
Na ..	132	NaCl ..	6.20
Ca ..	3	NaHCO ₃ ..	2.18
Mg ..	1.1	MgCl ₂ ..	0.05
K ..	4	CaCl ₂ ..	0.17
HCO ₃ ..	26	KCl ..	0.3
Cl ..	114	Glucose ..	21.6

Total osmolarity 400 m. osm./l.

In each case it is essential that the fluid be hypertonic compared with the patient's plasma and it can be kept so by the addition of glucose.

The sterile fluid, to which streptomycin may be added, is perfused at the rate of 2 to 3 litres per hour for 10 to 16 hours though canulae passed through the abdominal wall under local anaesthesia. The canulae may be replaced by plastic catheters. A catheter is passed through the lumen of each canula, and the canula withdrawn.

Sedation is necessary, and the procedure best performed on a weighing bed. Abdominal pain, meteorism, intestinal haemorrhage, perforation of bowel, peritonitis are some of the obvious complications of this procedure.

The Artificial Kidney. Whenever possible extra renal removal of metabolites should be performed by the more effective and safer procedure of dialysis through an artificial kidney. Various models for dialysis are in existence but the principles involved are the same (Kolff, 1947; Skeggs and Leonards, 1948).

Blood is pumped from an artery or vein through one or more tubes of cellophane and back into the patient through a large vein. The cellophane tubes are bathed in a circulating fluid of composition suitably adjusted to the needs of the patient.

A well-trained team, a weighing bed to detect changes in circulating blood volume, facilities for quick electrolyte determination, are essential for the successful outcome. Blood pressure and E.C.G. recordings must be taken at short intervals.

The patient may be dialysed for 8 to 10 hours using frequent changes of fluid.

The Diuretic or Pre-Recovery Phase

With the production of urine volumes of 1 l. or more, clinical improvement is to be expected and is reflected in falling N.P.N. plasma levels.

A profuse dilute urine excretion soon leads to dehydration and electrolyte loss, so that daily weighing and plasma electrolyte recordings must be maintained.

As further recovery proceeds, intravenous therapy may be abandoned and dietary restrictions relaxed. Care should be taken, however, that each step taken towards a normal regime should be preceded by a careful biochemical assessment.

Discussion

Although a large volume of literature exists on the subject of acute renal failure the condition often goes unrecognized and many cases of uraemia still die due to the incautious administration of fluid in the early stages of oliguria and to the lack of precision in biochemical control.

Many patients still are not allowed the advantage of dialysis until their condition is such that recovery becomes improbable.

This paper is an attempt to interpret existing literature, much of which is in part controversial, in the light of modern knowledge, and experience.

It is to be hoped that no case of acute renal suppression shall be considered hopeless until the cause has been shown to be irreversible.

Summary

The modern treatment of anuria and oliguria is outlined. Stress is placed on the importance of restricting fluid intake, which should be carefully controlled by accurate daily weighing.

The early treatment of hyperkalaemia and caution in the elevation of a low plasma sodium, bicarbonate, and haemoglobin is urged.

A method for giving a protein sparing high calorie diet in small fluid volume is described.

Methods for the extra renal removal of metabolites are mentioned, dialysis by the artificial kidney being recommended and the importance of the correct timing of this procedure is emphasized.

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Summary

All the cases described had features which led to the presumptive diagnosis being made clinically, and in every case L.E. cells were demonstrated in the peripheral blood. In one case the diagnosis was confirmed at autopsy.

High fever, loss of appetite and weight, painful swollen joints and pleural involvement were common to all. Splenic enlargement and ulceration of the mucous membrane of the mouth was noted in one case and peripheral vascular phenomena and hepatic enlargement in another. The characteristic butterfly rash on the face occurred only once. Other interesting features have been discussed in the footnote to each case. Although widespread joint involvement was common, X-ray failed to demonstrate any lesions in the affected joints. Examination of the blood showed mild to moderate hypochromic anaemia and a leucocyte count ranging from 4,000 to 5,000 per c.mm. The B.S.R. was raised in all cases, ranging from 63 to 105 mm. (Westergren one-hour reading). Plasma proteins were raised (7 to 10 g./100 ml.), with the rise mainly in the globulin fraction, a finding in keeping with reported series. In those cases in which plasma proteins were repeated they were found to be uninfluenced by steroid therapy.

Since the L.E. cell phenomena was first demonstrated by Hargraves *et al.* (1948) several new techniques have been introduced. The test is now being widely used and there are a number of conditions other than systemic lupus where it is found to be positive. Positive L.E. cell tests have recently been described in rheumatoid arthritis by Friedman *et al.* (1957). One of our cases, which is not described here, had painful deformity of the small joints of the hands of six years' duration. She had a mild hypochromic anaemia, but no other visceral manifestations were noted. L.E. cells were found in the peripheral blood. She is still under observation, but is at present considered to be a case of rheumatoid arthritis.

Dubois (1956) states, on the other hand, that, despite recently introduced refinements of tests,

L.E. cells are not found in all patients with the disease. In all the cases L.E. cells were found in the peripheral blood and we felt that the test, taken in conjunction with the clinical findings, is of the greatest value.

Regarding the management of cases, the consensus of opinion at present favours the use of conservative measures in milder cases. In the acute stages bed rest is essential with the necessary symptomatic treatment. The joint manifestations may be helped by suitable splintage and salicylate therapy. Pneumonic episodes should first be treated with appropriate antibiotics. In this series all cases were acutely ill and it was felt that steroid therapy was indicated. Apart from the case which lived only a short while after admission, all responded to large doses of steroids and were able to be discharged on a reduced dosage under outpatient supervision. An exacerbation of symptoms occurring in case 5 while on maintenance therapy was controlled by increasing the steroid dosage. As symptoms abated it was found possible to once more reduce the dosage.

While steroids have undoubtedly been life-saving in the acute exacerbations, no evidence has been found of alteration in the underlying pathological processes.

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