REFRESHER COURSE FOR GENERAL PRACTITIONERS**MODERN VIEWS ON URAEMIA AND DEHYDRATION**

BY

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Uraemia and dehydration are not pathological entities but are syndromes with many possible causes. The presence of either is a sign that the mechanisms which conserve the composition and amount of body fluids have broken down. This may happen because the homoeostatic processes have failed, as in renal disease; or because a severe strain has been put on the regulating mechanism, as by intractable vomiting and diarrhoea. The two syndromes commonly occur together. The separation of uraemia and dehydration in the ensuing discussion is therefore to some extent an artificial one, but it can be justified by the fact that the symptomatic treatment of uraemia and dehydration is different, even though the pathological process underlying the two conditions may at times be the same.

Uraemia

Uraemia is a convenient term for the clinical and biochemical syndrome which arises when the kidneys are unable to excrete the end-products of nitrogen metabolism as rapidly as these are formed in the body. Although it is the retention of urea which gives the syndrome its name, it has been shown that urea is not itself a toxic substance, nor does its experimental administration reproduce the symptoms associated with the syndrome of "uraemia." The pathogenesis of the symptoms of uraemia remains obscure; retention of potassium, a low serum calcium, the alkalosis of vomiting or the acidosis of fixed acid retention, and changes in the osmotic pressure of body fluids—all these may play a part in different patients.

Particular confusion has arisen from the use of the term "acute uraemia" to denote the convulsive attacks which may complicate the course of acute nephritis. Here the essential lesion seems to be a spasm of cerebral vessels related to the rise in blood pressure, and nitrogen retention in this phase of nephritis is trivial and unrelated to the symptoms. Excluding this syndrome of "acute uraemia" as being quite different in nature from the other forms, we can still distinguish three types of uraemia, the aetiology and practical management of which are different: (1) the uraemia of acute renal failure, (2) the uraemia of chronic renal failure, and (3) so-called "extrarenal uraemia."

Acute Renal Failure

Suppression of urine may arise in many ways; in acute nephritis, in cortical necrosis, in calculous anuria, and as a sequel to the crush syndrome, mismatched transfusion, heavy-metal poisoning, or the administration of sulphonamides. It may be absolute, producing complete anuria, or relative in that appreciable amounts of urine are formed but nitrogen is still retained. Except as a rough approximation, it is impossible to give a volume of urine which is "adequate." Although healthy kidneys can excrete the body's metabolites in 500 ml. of urine a day, or even half that amount if the diet is low in salt and protein, this depends on their ability to produce a highly concentrated urine. Such a performance is impossible to the damaged

kidney, and nitrogen retention may increase even though a litre or more of dilute urine is being formed daily. The renal failure of alkalosis is a good example of inadequate renal function in the presence of a "satisfactory" urine volume. Anuria or severe oliguria is therefore a certain sign of renal insufficiency if extrarenal causes can be excluded, but the absence of oliguria, when a possible cause of acute renal failure is operative, does not exclude failure.

In contrast to chronic uraemia, there are few symptoms of acute renal failure, apart from those of the causal disease. Progressive drowsiness does occur and cardiac arrest may cause sudden death, but convulsions and tetany are uncommon. Diagnosis therefore depends more on a knowledge of the causes of acute renal failure than on any characteristic clinical picture, apart from anuria. If the diagnosis is suspected on clinical grounds it can be confirmed or disproved by determining either the blood urea or the non-protein nitrogen, whichever estimation is the more convenient.

The treatment of the uraemia of acute renal failure is very important, since the renal damage is often transient and reversible. Tradition associates acute renal failure with a high death rate—50% or more—but recent work indicates that untreated suppression of urine carries a good prognosis, and that many of the recorded deaths have stemmed from injudicious efforts to force a diuresis by a high intake of fluid and electrolytes. When the kidneys fail, the body loses its main defence against overloading with salt and water, and pulmonary oedema or water intoxication may cause death even when nitrogen retention is quite moderate.

The main object of treatment is to prevent overloading with fluid, and to this end the fluid intake should be restricted to a litre or less a day, and salt should not be given. It is also desirable to diminish nitrogen breakdown and so retard the increase in the blood-urea level, even though there is no direct evidence that retained urea is harmful. Protein breakdown is at a minimum on a diet which is protein-free but adequate in calories. Bull and his colleagues (1949) have devised a practicable regime which seems to meet the indications in anuric uraemia. A plastic stomach tube is passed, and in each 24 hours the following mixture is dripped in steadily:

Glucose	...	...	...	...	400 g.
Peanut oil	...	...	...	...	100 g.
Acacia	...	...	...	...	q.s. to emulsify
Water	...	...	...	...	to 1 litre

No salt is given, but any vomit is collected, filtered through lint, and dripped back into the stomach, so that no actual loss of electrolytes occurs by vomiting. This regime is continued until diuresis starts. A good deal of fluid and salt are then lost in the urine, and the intake of water and salt must be correspondingly increased.

I believe that this regime, or some close analogue of it, will become the accepted treatment in anuria, and that

FIG. 1.—Body fluid compartments (man of 70 kg.).

in the ordinary case it will obviate any of the ingenious methods which have been devised to perform artificially the excretory part of renal function. These methods have the disadvantage of needing detailed supervision, and carry a constant risk of water and salt imbalance. In special cases in which the rate of nitrogen formation in the body is increased (as by infection or trauma) it may be necessary to lower the blood-urea level. Also, when oedema is already present as a result of overloading with fluid, there may be an indication for controlled dehydration. For these purposes intestinal intubation with a Miller-Abbott tube and perfusion with hypertonic solutions have been used by various workers. Black and Stanbury (1948) used sodium sulphate, but some sodium is probably absorbed, and Brun (1949—personal communication), of Copenhagen, has successfully used 5% lactose for intestinal perfusion. For most cases of urinary suppression, however, there seems no point in going beyond the practical and successful regime advocated by Bull *et al.* (1949).

Chronic Renal Failure

This may arise in the terminal phase of nephritis, in chronic pyelo-nephritis, polycystic kidney, the urinary obstruction of prostatic enlargement or congenital malformation, and in diabetic or hypertensive nephrosclerosis. These are a few of the common causes. As expected of a chronic state, the symptoms are more prominent and varied than in the uraemia of acute renal failure; the presenting symptoms may have little apparent connexion with the kidneys, to which fact uraemia owes its reputation for evading diagnosis. It encroaches on the terrain of almost every medical specialty, and therefore is a valuable reminder that a knowledge of general medicine can never safely be allowed to atrophy.

The main clinical features include wasting, pallor due to a refractory normocytic anaemia, respiratory distress and hyperpnoea, nausea, vomiting, and diarrhoea, general lethargy, and, in some cases, convulsions or tetany, distur-

bance of vision with retinopathy, and a liability to such complications as pericarditis or dehydration. Some of these symptoms are of course related to the hypertension which so commonly accompanies renal failure, and others are related to changes in water and electrolyte metabolism rather than to nitrogen retention. The suspicion of uraemia should prompt close inquiry into the past history for evidence of acute nephritis, recurrent urinary infection, or difficulty in passing urine. Increasing frequency of micturition, especially at night, is a valuable sign of progressive renal failure.

Examination of the urine may show albumin or a deposit of red cells or casts, but these signs may be masked by the polyuria of renal failure, especially when progressive fibrosis of glomeruli has lessened the amount of albumin and the number of red cells entering the urine. Addis has stressed the importance of broad "renal-failure" casts as signs of advanced kidney disease. Blood-urea estimation confirms the diagnosis of uraemia. Estimation of the serum calcium, sodium, and alkali reserve may be of some use in symptomatic treatment.

The treatment of chronic uraemia is essentially palliative, except when urinary obstruction can be relieved surgically. Rest and a low protein diet will prolong life, and the fluid intake should be adequate, at least 2 litres a day. A high urine volume assists the elimination of urea. In the presence of oedema a salt-poor diet may be indicated, but care is needed in this, as sodium reabsorption is impaired in a minority of patients with renal failure, and such patients easily become dehydrated if the dietary salt is restricted. A few patients may even need a high salt diet when large amounts of sodium chloride are lost in the urine. The distressed breathing of a conscious patient with acidosis can be relieved by M/6 lactate infusion. Calcium gluconate, 10 ml. intravenously, will relieve tetanic spasms. Attempts to rid the body of accumulated urea by purgation or other means are not justified in chronic uraemia.

FIG. 3.—Showing the osmotic relationship between the body fluid compartments.

FIG. 2.—Composition of plasma and tissue fluid (extracellular) compared with that of intracellular fluid. The scale is graduated in milliequivalents per litre of water (= milligrammes per litre ÷ atomic weight × valency).

FIG. 4 (Modified from Marriott).—Relative amounts of fluid in the different compartments in pure water depletion and pure salt depletion. Note that in water depletion the fluid levels are low, but there is no loss of solutes from the body, so osmotic pressure is increased; also, the fluid losses are spread equally over the compartments. In salt depletion the loss of salt forces a contraction of extracellular fluid, and also a fall in osmotic pressure; there is no loss of solutes from the cells, so water passes into these to bring the osmotic pressure down to the level prevailing in extracellular fluid; the actual amount of fluid in the cells is thus increased.

"Extrarenal" Uraemia

This is a complication of severe loss of blood, vomiting, diarrhoea, traumatic shock, Addison's disease, diabetic coma, acidosis, alkalosis, and of other conditions in which there is gross diminution of plasma volume or change in the electrolyte composition of body fluids. Although increased breakdown of body protein probably plays some part in the production of this type of uraemia, the most important cause is a functional renal failure. Detailed studies have always shown a reduction in renal blood flow and in glomerular filtration rate. The symptoms and treatment of this form of uraemia are the same as those of the causal disease. It is of some importance as an indication that replacement of blood or fluid is not yet adequate.

Dehydration

It is unfortunate that this term has been used to denote two syndromes which are opposite in their cause, in their effects, and in the appropriate treatment—the syndromes of water deficiency and of salt deficiency. Advances in intravenous technique have made it possible to drown a patient or to pickle him in a very short space of time, and such events can be avoided if a few quite simple facts about body fluids are understood and applied.

The primary division of body fluids is into the fluid inside the cells and the fluid outside the cells (intracellular and extracellular fluid). The intracellular fluid contains negligible amounts of sodium chloride ("salt") but is rich in potassium and phosphate. The extracellular fluid contains sodium and chloride with some bicarbonate; it is further subdivided into plasma and tissue fluid. The relative amounts of these different fluids are as follows:

	% of Body Fluid	Salt	Protein
Intracellular fluid	40	—	++
Extracellular fluid { Tissue	20	+	—
Plasma	5	+	+

Although the plasma is small in volume compared with the tissue fluid, it is important not only because it is accessible to analysis but also because it is the fraction of body fluid which perfuses the alimentary tract, the lungs, the kidneys, and the skin, which among them regulate the amount and composition of body fluid. Water passes rather freely between the fluid compartments, but salt is effectively limited to fluid outside the cells. Since water can pass freely between the compartments, the total ionic concentration of the various body fluids is identical, if we ignore the variations caused by their different protein content; any local increase in ionic concentration would cause an influx of water until equilibrium is restored.

Experimentally, relatively pure water deficiency and salt deficiency have been produced both in man and in animals. In water deficiency both compartments share in the fluid loss and there is an increase in the ionic concentration of the body fluids generally. In salt deficiency, by contrast, the extracellular fluid compartment is selectively depleted, for salt loss does not affect the intracellular electrolyte; the intracellular fluid is actually increased in salt deficiency, for the ionic concentration of body fluid is lowered by the salt loss, and water passes into the cells to dilute their electrolyte down to the general level.

This selective depletion of extracellular fluid is a very important aspect of salt deficiency, for it implies an early fall in plasma volume, with peripheral circulatory failure appear-

ing early. For any given total loss of fluid, salt deficiency causes much graver circulatory impairment than does a corresponding water deficiency. If salt solution is given to a patient with water deficiency even more water is sucked out of the already depleted cells. If glucose solution is given to a patient with salt deficiency some of the fluid taken is excreted, and some goes into the already dilute intracellular fluid. These are both examples of ineffective and even harmful replacement therapy.

In clinical work pure patterns of water or salt depletion are uncommon, and it is usual to find a mixed depletion in which either water or salt loss is the dominant but not the sole lesion. The problem is further complicated by the fact that clinical fluid depletion is often attended by acidosis or alkalosis, and by impairment of kidney function. These complications may obscure diagnosis and add to the difficulty of treatment. For example, a patient with diarrhoea who is given only water to drink will become deficient in salt, but he will also develop acidosis, as the intestinal secretions are alkaline in reaction. Although the urine might be expected to be free from chloride owing to the salt deficiency, in point of fact it will contain significant amounts of chloride, because of the attempt by the kidneys to counteract the acidosis by excreting fixed acid. But if renal failure is also present the urine may be chloride-free, owing to a gross fall in glomerular filtration. This example shows the sort of difficulty which individual cases may present; in this particular instance the most trustworthy guide to treatment is a knowledge of the characters of the fluid which the patient has lost. Replacement demands a salt-containing solution, possibly with sodium lactate added.

General Principles

The detailed assessment of fluid therapy requires a good and rapid biochemical service, and cannot appropriately be discussed in an article of this type. A few general principles will be stated, the study of which may help to avoid the grosser mistakes in intravenous therapy even when no biochemical facilities are available.

1. As much information as possible should be obtained, by history and by direct observation, about the amount and character of any fluid lost from the body. In spite of the difficulties, vomitus and fluid faeces should be collected and measured; an assessment of fluid loss even in pints is better than the usual ignorance on this subject.

2. Alimentary-tract secretions have a total ionic concentration about the same as plasma. They must be replaced by saline solutions. To replace vomit, 0.45% saline is suitable, but an even better method when the patient is being fed by drip is to strain the vomit and return it in the drip (Bull *et al.*, 1949). A solution containing 6 g. of salt and 3 g. of sodium bicarbonate per litre is suitable for replacing fluid lost in watery stools; this can be given by duodenal tube. Patients with diarrhoea are thirsty, but if they are given only water and non-saline drinks salt deficiency will be caused.

3. When the main cause of fluid imbalance is a defective intake of fluid, water deficiency is likely to occur, because the fluid lost from the body by skin and lungs is hypotonic, and if the urine volume is reduced the kidneys cannot get rid of an amount of salt corresponding to the fluid lost by extrarenal channels. If fluids cannot be given by mouth 5% glucose should be given intravenously. A suitable amount for a patient without fever in a temperate climate is one litre a day; with fever or thermal sweating, this amount should be increased.

4. In the absence of renal disease, oliguria is a sign of fluid depletion. A urine volume of less than one litre a day in a patient with no vomiting or diarrhoea means that the fluid intake is inadequate, and the intake of watery fluid by mouth should be increased to two litres or more.

5. A good rough test for salt deficiency is the Fantus drop test for urinary chloride, carried out as follows:

One drop of 20% potassium chromate is added to ten drops of urine. The pipette is washed in distilled water, and used to add 2.9% silver nitrate to the urine until the yellow colour changes sharply to brownish red. The number of drops used indicates the number of grammes of salt per litre of urine. The colour change may occur with the first drop of silver nitrate added, showing a salt content of less than 1 g. per litre.

This test is significant only when the urine specimen is reasonably concentrated, and when there is no disease of the suprarenal glands. Moreover, it may fail to show salt deficiency in the presence of acidosis. With these reservations a salt concentration of less than 5 g. per litre indicates the need for increasing the saline intake.

6. Whenever possible, fluid should be given by mouth, and parenteral therapy reserved for those patients whose vomiting or diarrhoea makes the alimentary route impracticable. If a duodenal tube can be passed and retained, it may enable the alimentary tract to be used in a patient with vomiting. Large amounts of fluid can be given safely in this way, and it is an old observation that fluid given by the bowel is better retained than parenteral fluid. Moreover, intravenous fluid carries some risk of circulatory overloading and pulmonary oedema.

In concentrating on the essentials of fluid therapy I have had to omit such important topics as the effect of alkalosis and acidosis, the dangers of potassium depletion by copious saline infusion, the special problems of infancy, and even the general clinical signs of fluid depletion. The excuse for this last omission must be that the diagnosis of fluid depletion is less difficult than a decision about appropriate treatment. The other omissions seem to me to concern matters which cannot well be dealt with apart from accurate laboratory investigation and hospital treatment. Marriott (1947) gives a fuller review of the problems of dehydration in his Croonian Lectures, which were published in the *Journal*.

Diagrams reproduced by kind permission of Professor Gamble and Dr. H. L. Marriott.

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A joint committee has been established in Glasgow to consider the best methods of combating tuberculosis in that city. Representatives have been appointed by the Scottish Western Regional Hospital Board, the Glasgow Executive Council, and the Glasgow Corporation. After the first meeting of this committee it was stated that there were two immediate problems: one concerned the shortage of beds and was the responsibility of the Hospital Board, and the other was the danger of infectious patients in the home, this being the responsibility of the local authorities. It was reported to the committee that notifications of pulmonary tuberculosis in the city increased by 62% between 1938 and 1949. The total number of beds available for tuberculous patients is now 1,300, and it is hoped that an additional 132 beds will shortly become available. At the end of December, 1949, 1,403 patients were awaiting admission to sanatoria: this figure compares with 1,423 in July, 1948, and 1,700 in the middle of 1949.

THE ROTHWELL STERILE-WATER SYSTEM AND ITS UROLOGICAL APPLICATION

BY

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To prevent furring of the water-sterilizing plants waste condensate water from the steam-heating systems has from time to time been used in hospitals in areas where the water was exceptionally hard, but so far as I can ascertain it is only during the past few years that use has been made of the fact that this sterile distilled water was ready for use in the operating theatre.

Some years ago the original experimental plant was designed by the hospital engineer, Mr. E. Rothwell, and installed at Birch Hill Hospital, Rochdale. It is no exaggeration to say that it has continued to function without interruption or difficulty until the present day. As is the case with many brilliant inventions, the basic idea was extremely simple once the principle had been grasped. The system is founded on the fact that in all steam-heating systems cooling of the pipes causes part of the steam to be condensed as sterile distilled water, and in the normal plant this condensate is collected in steam traps and is piped back to the boilers to save fuel. Such condensate is absolutely sterile, as it is usually produced from steam delivered from the high-pressure boilers in the region of 70–80 lb. per square inch (4.92–5.62 kg. per cm²).

The Rothwell system makes use of this condensate by collecting it in a suitable tank in a basement and pumping the water by a simple steam-operated float pump, which requires no attention, to tanks over the operating theatre (Fig. 1). The hot condensate can then be carried by gravity direct to the theatre, where hot sterile water is available from a wall tap for all purposes, thus eliminating all water boilers and sterilizers from the theatre. A part of the hot

FIG. 1.—Main storage tank for sterile water, installed in the basement. Its contents are automatically pumped to auxiliary tanks above the operating theatres. A = Main storage tank. B = Automatic steam float pump. C = Condensate temperature controller (calorifier).