TRAUMATIC URAEMIA

A COLLECTIVE REVIEW

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Traumatic uraemia has been considered largely in association with crushing injuries, but more recent evidence indicates that renal failure with characteristic biochemical changes and clinical features may be due also to trauma of non-specific type [53, 54, 100, 125], and to many other conditions of apparently different etiology [71, 111]. The pathological changes are now well established [37, 100].

HISTORICAL REVIEW

Early references to traumatic uraemia were all associated with injury of a crushing type. Colmers [45], who was sent to the relief of victims of the Messina earthquake, noted that crushing of limbs by falling masonry was almost universally fatal. The condition was largely overlooked during the First World War, despite the crushing injuries of trench warfare [32, 72, 84, 94]. Minami [119] suggested that renal failure was due to the toxicity of myohaemoglobin released from damaged muscles. He based his conclusions on three factors: 1) that the crushed muscles were pale and oedematous, thus suggesting loss of pigment; 2) that there were haemoglobin casts in the damaged kidney tubules; 3) that there was similarity between this form of uraemia and equine paralytic myohaemoglobinuria, a comparison which was confirmed by Gilmour [75]. Bywaters [33] and others described the classical sequence of events which they termed "crush anuria" [14]. This syndrome became well known during the years 1941-43 and most observers accepted the view that release of myohaemoglobin from damaged muscles was the principal cause of the renal failure [21, 36, 39, 68, 101, 112, 115, 117], this view being strengthened by identification of the pigment in the kidney tubules and in the urine [34, 35]. The histological findings were, however, indistinguishable from those of incompatible blood transfusion (the use of stored blood being at that time in its infancy). Nevertheless a case reported by Mayon White and Solandt [116] proved that blood transfusion was not necessarily an etiological factor. Moreover doubt was expressed as to whether muscle damage was the essential cause; and when Glen [76] recorded a fatal case of uraemia after damage to the iliac artery, but without crushing injury, the problem assumed new complexity. Shortly afterwards other writers reported cases with the same histological pattern due to different etiological factors [31, 155, 156], and Foy [71] made the first real attempt to correlate the many conditions which might be responsible.

In 1944 clinicians who studied cases of blackwater fever [109] and gun-shot wounds [53, 125] found difficulty in accepting the view that haemoglobin and its derivatives were nephrotoxic and suggested the theory, supported by experimental evidence [46, 48, 98, 118], that the mechanism of renal failure might be lack of blood supply due to shock, hypotension, or renal vaso-constriction. Maegraith, Havard, and Parsons [111] suggested that the essential etiological factor was "renal anoxia." Nevertheless traumatic uraemia seemed to be associated particularly with crushing injury, and Lucké [100], after examining 538 fatal cases and excluding those due to sulphanilamide poisoning or incompatible blood transfusion, came to the conclusion that in 57 per cent. of cases severe trauma was the important cause.

Despite this clear association of uraemia with injury there has been increasing evidence of similar biochemical and histological changes in the kidneys from many different causes,

TABLE I

Group 1 Shock	Group 2 Electrolyte water balance	Group 3 Pigment	Group 4 Allergy	Group 5 Chemical nephrotoxin
Gun-shot wounds [53, 54, 67, 125]	Haematemesis [18, 15]	Crush anuria [122, 14, 21, 33, 36, 37, 41, 66, 88, 99, 119]	Favism [71]	Mushroom poisoning [100]
Shock [121]	Pyloric stenosis [108], with vomiting [105]	Incompatible blood trans- fusion [6, 151]	Sulphanilamide (some forms) [16, 22, 134, 132, 154]	Oxalate [63]
Head injury [51, 52]	Acidosis [85, 90, 101]	Burns [9, 114]	Serum sickness [131]	Mercuric chloride [128]
Severe injury [93, 81]	Alkalosis [104, 107, 123]	Yellow fever [111]	Incompatible blood trans- fusion (some form) [89, 115]	Alloxan
Post-operational azotaemia [15]	Cholera [44, 142]	Hepato-renal syndrome [30, 111]	Pitressin [146]	Phosphorus [128]
Post-partum haemorrhage [155]	Addison disease [43]	Blackwater fever [71, 109, 111, 138, 149]	Epinephrine hydrochloride [146]	The bite of the lactro dictus mactaus (Black Widow) [128]
Concealed accidental hae- morrhage [156]	Hypochloroemia [20, 24, 25, 113, 26, 27, 102, 103, 104]	Equine paralytic Myohaemoglobinuria [75]	Staphylococcal toxin [146]	Cresol poisoning [128]
Septic abortion [31]	Dehydration [133, 71]	Weil's disease [111]	Meningococcal toxin [23]	Carbon tetrachloride [152]
Reflex anuria [50]	Diabetic coma [101, 15]	Heat stroke [100]	Typhus fever [3]	Phosphate [61, 107]
Hysterical anuria [146]	Intestinal obstruction [15]	Icterus neonatorum [120]		Uranium [92]
Vascular injury [76]	Repeated haemorrhage [118]			Uric acid [64]
Anoxia [49]	Pernicious anaemia [139, 140]			
CO poisoning [60]	Decreased fluid intake [15, 29]			
	Pneumonia [15]			
	Potassium excess [70]			
	Sodium lack [73, 96]			

and observers have been struck by the similarity between these conditions and both traumatic uraemia and crush anuria. The list of possible etiological factors has now become so vast that they cannot be given in full. They are, however, summarised in five groups in Table I. Despite some overlap, each group is distinguished by an outstanding etiological feature—for example in group 1 the common factor is shock, in group 2 disturbance of the electrolyte water balance, in group 3 presence of pigment in the circulation, in group 4 an allergic basis, and in group 5 factors of chemical nephrotoxins.

Shock and renal function—Ever since the original work in 1937 of Husfeldt and Bjerling [93] on renal failure due to injury it has been clear that shock, whether or not accompanied by blood loss, is characterised by failure of renal secretion. Van Slyke and his team [59, 129, 147] showed that when shock was due to bleeding or injury there was progressive decrease in the flow of blood through the kidneys, and that when fluid loss amounted to 40 to 50 millilitres of blood per kilogramme renal blood flow and secretion of water fell almost to zero level. These authors drew analogy between the renal function of dog and man, and stated that in human beings with anuria due to severe and prolonged shock it was possible to restore the kidney circulation by blood transfusion without gaining sufficient renal function to prevent death from uraemia some days later. Other observers noted that after blood transfusion, oxygen extraction of the kidney was not increased proportionately to the increase in other parts of the body, which was even more remarkable in view of the fact that the decreased blood in the kidneys was due to constriction of the renal arterioles. This important observation suggested a possible shunt mechanism whereby certain areas of the renal bed were by-passed. Such a theory is supported by studies in the renal circulation, published in 1947, by Trueta *et al.* [146]. It has been confirmed by other workers who showed that experimental tourniquet shock was accompanied by considerable alteration in the blood flow of the kidneys [95]. Unfortunately it has not been possible to reproduce the conditions of crush anuria in animals [38, 62, 69] because they are unable to withstand the shock of the procedure, and moreover myohaemoglobin in these animals is not in labile form [147].

No less important in determining the essential factor of traumatic uraemia was the work of Cournand [48] and Lauson *et al.* [98] who carried out precise clearance tests in conditions of shock. They demonstrated that there was reduced blood flow to the kidney which might be due in part to renal vaso-constriction but might also be due to changes in renal haemodynamics. This work answered effectively the theory that reduced renal blood flow in shock was due to hypotension (Maitland [112], Tombs [143], and Moon [121], who went so far as to say that the syndrome was a direct sequel of shock). Recently it has been shown that there is neurogenic control of the renal circulation. Trueta [145] observed that over-stimulation of the peripheral nerves in shock might cause persistent spasm of the renal and other arteries. Trueta and Barnes proved that trauma applied to one limb cause widespread arterial spasm extending to vessels of the other limb and to those of the viscera [11]. Trueta and others also showed that renal ischaemia could be produced by stimulation of the splanchnic nerves, and that similar changes could be produced by shock, bleeding, and crush injury. They drew attention to the fact that anuria could be induced reflexly and by emotional disturbance [146].

Electrolyte water balance and kidney function—Disturbance of the electrolyte water balance has been the subject of much research, and it is now established that water deficiency [71, 133], hypochloraemia [20, 103, 113], alkalosis [104, 108, 123], acidosis [85, 90, 101, 96, 73], and loss of available base, are accompanied by rise in blood urea and non-protein nitrogen [15, 29, 113]. These conditions have been ascribed to extra-renal azotaemia for the reason that post-mortem studies have shown no gross histological changes in the kidneys. But evidence in human cases and animal experiments has suggested that there is not only oliguria but also fall in the glomerular filtration rate. Similar changes are found in dehydration due to insufficient fluid intake, intestinal obstruction [15, 29], diarrhoea [44], and

gastro-intestinal haemorrhage [13, 19]. Recent opinions suggest that hypochloraemia is of greater importance than was formerly believed [113] but it is not always possible to determine clinically which of these factors is most essential for the maintenance of renal function because there is a constant effort in the body to maintain and adjust the electrolyte water balance [4]. Kidney function is often restored by correction of the missing factors, but it must be recognised that when renal failure has already supervened, maintenance of the electrolyte water balance requires much judgment and care [5, 54, 110].

Although azotaemia has been thought to result from excessive breakdown of protein it is now suggested that histological changes in the kidney are worthy of more study [15]. There may be degeneration of renal tubules and even cast formation [108]. More recently Verney's work [148] has shown that liberation of an anti-diuretic hormone from the posterior pituitary is dependent upon osmotic pressure in the arterial plasma. It is known that in cases of water depletion, intestinal obstruction, and cholera, there is considerable alteration in the plasma osmotic pressure which may lead to renal failure and azotaemia [113].

Haemoglobin and kidney function—Hitherto most observations have been made in attempting to determine the cause of renal failure in blackwater fever and incompatible blood transfusion. Much of this work is hypothetical, many authors being insufficiently aware of the difficulties of producing a sterile, stroma-free haemoglobin, and often failing to state the amount of haemoglobin used in various experiments. The experiments of Barratt and Yorke [12], Yorke and Naus [153], and Baker and Dodds [10] are misleading. They produced haemoglobinuria in rabbits and found that anuria developed when the animals were acidotic. They concluded that precipitation of haemoglobin in acid urine caused death by obstruction of the tubules and that the remedy was to maintain an alkaline urine. Later investigators, while confirming the significance of acidity of the urine, gave conflicting evidence as to the particular haemoglobin derivative which was responsible [17, 40, 55, 56]. This work has been criticised on the grounds that acidotic rabbits are dehydrated and for this reason are liable to develop uraemia in any case [71]. Gersh [74] injected the haemoglobin of pigs into rabbits and found that cast formation was greater if the animal was dehydrated. Govan and Parkes [80] found that acidosis in the rabbit caused degeneration of the renal epithelium. Convincing proof was also put forward by many workers [8, 13, 28, 57] that haemoglobin and its derivatives were not toxic provided only that they were sterile and stroma-free. This was confirmed by clinical reports, for it was found that haemoglobin is excreted freely in blackwater fever [138], and that uraemia may develop equally in the presence of acidosis, alkalosis, or a normal alkali reserve [109, 149]. These findings are supported by our own observations which showed that severely wounded men often excreted myohaemoglobin without developing uraemia.

Light has been shed on the subject by Yuile *et al.* [158] who showed that when the kidney was damaged by sub-lethal doses of sodium tartate, or by incomplete occlusion of the renal artery, the addition of stroma-free haemoglobin caused fatal uraemia of the type seen in blackwater fever and in traumatic uraemia. Nevertheless the explanation of the initial injury to the kidney is still wanting. Ingenious theories have been postulated. Bayliss [13] suggested that although stroma-free haematin of the blood is non-toxic, globin produces an anaphylactoid reaction which is most marked in the kidney. Later workers suggested that a similar mechanism may be responsible for renal vaso-spasm [89, 115, 127, 150].

Allergy and kidney function—Although it appears that excretion of haemoglobin is not itself the cause of renal failure, it is nevertheless true that fatal uraemia is a common sequel to many forms of incompatible blood transfusion. It is possible that, as a result of haemolysis of blood, an antigen is liberated which not only causes general circulatory failure but has specific vaso-constrictor action upon the renal arterioles, which is then followed by irreversible renal damage [6, 89, 115, 127]. Similarly it has been suggested that sulphanilamide anuria may be due to hypersensitivity of the kidney to combined protein

sulphanilamide, a combination which may occur as the result of intolerance to this group of drugs [16]. In support of this theory, Foy *et al.* [71] believed that the perplexing form of anuria which may follow the eating of broad beans, and is known as "favism," could be explained by protein sensitivity. More recently Black-Schaffer *et al.* [23], studying the Schwartzman phenomenon, produced experimental cortical necrosis of the kidneys in rabbits, presumably the result of an antigen-antibody response to injections of specially prepared cultures of meningococci. Similar results have been secured with staphylococcus toxin [146]. This mechanism may account for the renal changes which are produced by pitressin and epinephrin hydrochloride. The hypothesis is also supported by the finding of azotaemia in serum sickness by Rackemann *et al.* [131].

Chemical nephrotoxin and kidney function—It is well known that certain chemicals have specific nephrotoxic action and that necrosis of the tubular epithelium is caused by such substances as mercuric-chloride, oxalates, phosphates, etc. These substances appear to be precipitated in the loops of Henle as the result of a fall of the pH of the glomerular filtrate [66]*. Such toxic materials may cause necrosis of renal epithelium by direct action, but equally they may give rise to vaso-constriction of the renal arterioles as a reflex defence mechanism, thus explaining reflex anuria [50] and the anuria of incompatible blood transfusion [89, 115, 127].

Such histological findings suggest that in each of the five groups there is sufficient alteration of blood supply to cause necrosis of renal epithelium, but before discussing this statement it is well to examine the evidence from post-mortem and histological findings.

AUTOPSY FINDINGS

Macroscopic findings are few. When death occurs in consequence of crushing injury, incision of the injured muscles shows oedema, swelling, and pallor, with obvious loss of pigment. It is important to note that the skin overlying the injured region may show little or no change. Not infrequently there is also fat embolism with a characteristic petechial rash and changes in the brain, lung, and other organs. There is often oedema of the lung with cardiac dilatation. This appears to result mainly from difficulty in controlling intravenous therapy rather than from the uraemia itself, but it may be due to peripheral vascular failure. Probably the only characteristic change of the syndrome of traumatic uraemia is in the kidney itself which is increased in weight. The capsule is under tension. On section, the cut surface is everted and the cortex is pale; it has a yellow, granular sheen. The pyramids and medulla stand out in contrast and are brick red in colour. When uraemia is due to sulphanilamide therapy, crystals may be seen pouting from the pyramids or in the terminal parts of the tubules.

Histological findings—In tracing the nephron through its course it is found that the glomeruli usually show little or no change, although there is noticeable lack of blood in the tufts themselves. In some areas the glomerular spaces are filled with an albuminous deposit which is most marked round the periphery and is adherent to Bowman's capsule. The epithelium of the first convoluted tubule shows early degenerative change and the cytoplasm stains irregularly; the nuclei are pyknotic and there is usually an eosinophilic catarrh of the lumen. These changes are observed both in traumatic uraemia and in death from intestinal obstruction [15]. The most marked damage occurs, however, in the loops of Henle, for which reason it has been named by Lucké "lower nephron nephrosis" [100]. Degeneration of epithelium in this area is frequently patchy and the tubule is sometimes so distorted as to make it impossible to tell whether it is of the ascending or descending type. The importance of this widespread degeneration is often overlooked because there is a wide

* Since writing this article Harrison *et al.* have shown that this can no longer be accepted, since they have found that the casts removed by micro-dissection are freely soluble in pH of 6.6 or lower, and insoluble in an alkaline medium. (Journal of Experimental Medicine, 1947, 86, 339.)

variety of casts, mainly of two types, some composed of protein and others of pigment origin. The structure of the casts is of interest; they tend to form round particulate matter such as degenerated epithelial cells or crystals such as sulphanimide. In many cases the epithelium is stripped and adherent to the outer surfaces of the cast. Another curious cast, which stains red with Mallory and may contain pigment, is granular in appearance and consists of many distinct minute fragments. The ascending convoluted tubule also shows complete destruction with desquamation of epithelium which is stripped in a plicated concertina manner [37]. All types of cast formations are seen. Occasionally the cast is arranged peripherally in the form of a hollow cylinder [42]. The collecting tubules show degenerative changes, often with casts showing evidence of regeneration and polymorphic infiltration. When sulphanimide has been a factor, the lumen of the collecting tubules may be encrusted with crystals. The intermedullary and interstitial tissue is congested.

FIG. 1

Section at the level of the loops of Henle showing the wide variety of casts which tends to obscure the tubular degeneration.

One of the most interesting features is the occurrence of venous thrombi in the boundary zone associated with rupture of tubules into the veins [37, 66]. When serial sections have been cut it has sometimes been found that thrombi are adherent to a local lesion of the vein without evidence of tubular rupture [54]. The interstitial tissue at this point is infiltrated with lymphocytes and histiocytes. In other cases this infiltration may be isolated, and when an allergic origin is postulated they may be largely eosinophilic. Other investigators of the renal arterial system have shown the presence of abnormal cells in the juxta-glomeruli complex. Goormaghtich [77, 78, 79] showed that such cells are more plentiful in peripheral cortical areas in the crush syndrome and may also be produced by incomplete ischaemia of the rabbit's kidney. The cells are thought to excrete renin and are said to be responsible for the hypertension which is a clinical feature.

The only other histological finding which may be of significance is necrosis of the central vein of the liver. In patients who survive for several days this is accompanied by reticular replacement and early fibrosis.

DISCUSSION

Of etiological theories which have been advanced, that of tubular blockage has now been generally discarded. Nevertheless Bywaters [41, 42] renewed interest in this theory,

and suggested that oliguria might be due to failure of reabsorption from the second convoluted tubules by reason of the deposition of pigment in the form of a hollow cast. Such a deposit would cause destruction of epithelium and renal failure. A closely allied theory was suggested by Peters [128] who claimed that renal failure was due to rise in the intrarenal pressure. He believed that the primary cause of oliguria or anuria was decrease in the effective filtration pressure caused by interstitial oedema and dilatation of the tubules due to inflammatory changes produced by nephrotoxin. This theory gains support on histological grounds because there is marked interstitial oedema, but the absence of dilatation of the tubules and of the glomerular spaces makes it unlikely.

In a previous communication the author suggested that tubular degeneration was the precursor of this syndrome [54]. It is a matter for debate whether this is caused by nephrotoxic agents or by disturbance of the renal circulation. Supporters of the nephro-

FIG. 2

Section of cortical area showing bloodless glomeruli, degeneration of convoluted tubules, and cast formation in the ascending loop.

toxic theory base their conclusions on the fact that after injury to muscles, pigment may be found in the urine and in the kidney. But the findings summarised earlier in this communication indicate that haemoglobin can no longer be considered toxic unless there is also damage to the kidney. Furthermore the condition is seen also when there is no evidence of haemolysed blood or of intravascular pigment [54, 100, 116]. On the other hand it is possible that the investigations of Green and Stoner [82, 83] may have a bearing, for they demonstrated adenosine triphosphate in increased amounts, both experimentally and clinically, in cases of injury, shock, burns, and ischaemia of muscle. It is not yet clear whether such toxin has direct action upon renal epithelium or whether it produces alteration in the renal circulation.

The possibility that this syndrome may be due to changes in renal haemodynamics has been over-shadowed for some years, for it has been shown already that renal failure is capable of demonstration by more delicate kidney tests in shock and in the majority of conditions classified in Table I.

The recent work of Trueta and others [146] has helped to solve this problem. They have shown that when rabbits are shocked by trauma or bleeding, ischaemia of the renal cortical area develops, with vaso-constriction of the renal arteries, thus suggesting that

there is considerable reduction of blood flow causing anoxia of the kidney epithelium and finally cortical necrosis of the kidney. This theory is supported by histological studies. The fact that renal epithelium is susceptible to anoxia is well known [7, 106, 136, 147]. It is important to know, therefore, the period of time during which anoxia must be maintained before such changes become irreversible. This varies from animal to animal. Allen [1, 2] found that rats were sensitive to renal ischaemia lasting no more than two hours. Van Slyke *et al.* [147] demonstrated that dogs could withstand ischaemia up to five hours and that the duration of renal ischaemia had a direct relationship to the mortality rate. When ischaemia was maintained for no more than three hours all animals were capable of recovery, although there was urea retention for several days; when the arteries were restricted for four hours there was a 50 per cent. mortality rate; and when ischaemia was continued for six hours no animal recovered. On this analogy it is thought that the length of time necessary to produce such changes in the human being may be in the region of eight hours or more. This does not, however, explain the high mortality rate when there is also intravascular deposition of pigment. Yuile *et al.* [158], working with rabbits, produced ischaemia by incomplete occlusion of the renal artery, or by sub-lethal doses of sodium tartrate, and found that when a non-toxic stroma-free haemoglobin was injected there was significant rise in the mortality rate. We confirmed this work and showed that the histological changes of traumatic uraemia could be simulated closely in rabbits by incomplete occlusion of the renal artery except that cast formation was largely of the albuminous type. We showed also that the mortality rate in rabbits after one hour of occlusion was 20 per cent., after one and a half hours 60 per cent., and after two hours 100 per cent. [7]. In subsequent experiments the procedure was repeated and stroma-free haemoglobin was injected intravenously. The mortality rate was not influenced in cases of ischaemia for not more than one hour, but there was significant increase to a mortality of 83 per cent. when ischaemia was maintained for ninety minutes [8]. These experiments suggest that when there is shock sufficient to cause irreversible degeneration of epithelium the chances of recovery are materially affected if haemoglobin is free in the circulation, but that when ischaemia is of lesser degree, and there is sufficient normal renal tissue remaining, it is possible for the animal to excrete haemoglobin without further embarrassment of the kidney.

CLINICAL RECOGNITION

For the traumatic surgeon it is the ability to recognise, prevent, and treat this condition which is important. The earliest sign is anorexia, accompanied by hiccough, and followed within a few days by copious and effortless vomiting. The tongue is dry. The patient is drowsy and he suffers hallucinations with acute attacks of restlessness. Localised areas of oedema may develop. The two most characteristic symptoms, apart from vomiting, are oliguria and hypertension. It may be difficult to recognise the oliguria unless an intake and output chart is kept because these bear direct relationship to each other even although there may be considerable retention of fluid. Examination of the urine may give no indication as to the severity of illness because the specific gravity remains constant between 1014 and 1018. Excretion of urea is fixed between 0.9 mgm. per cent. and 1.6 mgms. per cent. and the pH is held between 5.2 and 6.4. In other cases there may be complete anuria. In the early stages, when shock is severe, the blood pressure may be very low; but as a rule hypertension develops slowly over a period of days, the systolic pressure often exceeding 200 mm. of mercury. One of the most remarkable features of the syndrome is the rapidity and height to which blood urea or non-protein nitrogen may rise. The blood urea is always greater than 100 mgms. and anaemia is common. Other associated changes are rise in the levels of serum potassium and inorganic phosphate, this being accompanied by a fall in the level of serum calcium and serum proteins. There may be reversal of the albumin-globulin ratio.

In a previous paper [5] it has been shown that there is also acidosis and hypochloraemia, but this is not necessarily part of the syndrome since it may also be found in any seriously injured patient. In cases where the limbs have been crushed, amputation does not necessarily prevent uraemia; death usually occurs between the sixth and eighth days [100].

TREATMENT

Preventive treatment—It is estimated that from 16 to 19 per cent. of deaths from gun-shot wounds are due to traumatic uraemia [100], and that when the syndrome is fully developed the mortality rate may be as high as 90 per cent. Preventive treatment is clearly of great importance. Shock must be combated with all possible speed in order to prevent irreversible kidney changes. Before major operations are undertaken the anaemia and electrolyte water balance must be corrected in order that function may be restored in the kidneys before added strain is thrown upon them. Trueta suggested that change in renal haemodynamics may be prevented by splanchnic or spinal block [144]. Porritt *et al.* [130] reported unfavourably on this treatment but success has been achieved by early splanchnic block [86, 87, 135, 137]. When there is limb injury local treatment is important. Patey and Robertson [126] advocated firm bandaging in order to prevent the development of oedema or the release of nephrotoxic substances. Emergency immobilisation is necessary to avoid neurogenic shock.

Correction of electrolyte balance—When once the syndrome is established treatment is much more difficult. Correction of the electrolyte balance may not always be successful but nevertheless it should be put in hand immediately [5, 91, 110]. In assessing the quantity of sodium chloride, sodium bicarbonate, or sodium lactate which should be given the formula of Discombe (1943) has given the most consistent results [58]. The calculation is based upon the approximate weight of the patient in kilogrammes, and the plasma level of chlorides expressed as sodium chloride. The amount of salt which is necessary to correct plasma level is estimated by the formula: $\frac{W(590-X)}{200}$ G, W being the weight of the patient in kilogrammes, X the level of chloride expressed as sodium chloride, and G grammes. The bicarbonate necessary can be calculated by the formula: $\frac{W(64-Y)}{60}$ G, W being the weight of the patient in kilogrammes, Y the level of CO₂ combining power expressed in vols. per cent., and G grammes. In practice this second calculation has not been found necessary unless the level of CO₂ combining power is below 30 vols. per cent. Further disturbance of the electrolyte balance may be shown in the fall of serum calcium and the rise in serum potassium. These changes together may cause serious cardiac complications: if the level of potassium exceeds 40 mgms. per cent. there is danger of fibrillation and death [91]. Sudden death is often observed in cases with oliguria [113]. For this reason care should be taken to avoid sudden and unnecessary movements of the patient. The use of a gastric tube with continuous suction is valuable [91] not only because it avoids the unnecessary distress of vomiting but because it reduces the level of serum potassium, potassium salts being excreted freely in the gastric juices. The calcium level is corrected by intravenous injections of calcium gluconate.

Management of water metabolism—Control of fluid intake is often more important than correction of the electrolyte balance. In consequence of oliguria there is accumulation of fluid within the body with oedema of the lungs and overloading of the circulation. The amounts of fluid needed in twenty-four hours can be estimated by adding the volume of urine and vomit excreted the previous day to the amount of fluid presumed lost by the lungs and sweating (which may usually be taken as 1000 millilitres per day [113]). In order to ensure that the fluid is absorbed it should be given in the form of an intravenous drip. Although this may lead to difficulty in introducing sufficient sodium chloride solution, as much as 4 per cent. can be given without harm provided that the plasma level of sodium chloride does not exceed 475 milligrammes per cent.

Use of sodium sulphate—It has been suggested recently that the administration of sodium sulphate is of benefit [124] but former impressions proved disappointing. It is submitted that sodium sulphate should be used only for the initial stages of sulphanilamide poisoning before kidney tubular damage has occurred. This may cause sudden diuresis with the possible ejection of crystalline deposits of sulphanilamide or haemoglobinuric casts.

Artificial kidney—This new treatment has aroused much interest; it is designed to remove the toxic products resulting from renal failure and to give time for the kidney to regenerate. A sufficient number of cases has now been published to show that the method warrants further study [97]. At the same time it must be recognised that the dialysing fluid is of the simple electrolyte water type which allows passage of water into the circulation of the patient with consequent overloading. Furthermore the machine is bulky. In a paper shortly to be published it is hoped to show how these difficulties have been partly overcome.

Peritoneal dialysis—There are two dangers in the technique of peritoneal dialysis in which large quantities of sterile isotonic fluid are injected into the peritoneal cavity and subsequently extracted. Not only is it difficult or impossible to withdraw all the fluid, but it is difficult to avoid peritonitis due to contamination of the fluid with pathogenic organisms.

Renal decapsulation—Surgeons have advocated bilateral renal decapsulation with the object of relieving increased intrarenal pressure. The procedure is said to be performed easily and often to be followed by diuresis [128]. This was not confirmed by Styron and Leadbetter [141] who performed decapsulation of one kidney and by ureteric catheterisation demonstrated clearly that there was no difference in function of the two kidneys, either in the acute or in the convalescent stages. It would seem that much more justification is needed for the adoption of so heroic a measure in patients who are desperately ill.

SUMMARY

Traumatic uraemia is of particular significance to orthopaedic surgeons in so far as this complication is responsible for high mortality in cases of severe injury, crushing injury, traumatic shock, gun-shot wounds, incompatible blood transfusions, and the misuse of tourniquets. In this contribution the association between muscle injury and renal failure is reviewed.

The syndrome of the "crush kidney," which at first was thought to be the result of deposition of myohaemoglobin in the renal tubules, is almost certainly due to the association of many factors, all of which lead to alteration of the renal circulation and renal ischaemia.

Certainly the combination of ischaemia of the kidney with deposition of pigment and haemolysis of blood causes a high mortality in animals, and it is believed that this may account for the serious prognosis in human cases where there is both shock and haemolysis.

Disturbance of water balance, allergic phenomena, and chemical nephrotoxic action are also discussed. The pathology is considered together with significant changes in the blood chemistry.

A plea is made for early recognition of this clinical syndrome with its characteristic features. Important aspects of treatment are discussed. The dangers of excessive intravenous infusion are emphasised.

Closer investigation and further research promise to throw light on the more accurate localisation of function in the nephron, to add to our knowledge of traumatic arterial spasm, and to explain many orthopaedic problems which hitherto appeared insoluble.

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