ACUTE RENAL INSUFFICIENCY MADE RIDICULOUSLY SIMPLE

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CHAPTER I

CONCEPT AND CLASSIFICATION

Concept

Acute renal failure (ARF) is an acute decrease in renal function (Fig. 1) that can be due to several causes and usually lasts from four to six weeks.

Figure 1 Urine output is decreased and the doctor has to deal with the problem of acute renal failure.

As we will see later, acute decreases in renal function can be divided into three main categories: prerenal (hypoperfusion of the kidneys), intrinsic renal damage and postrenal (obstruction). Once the kidney has developed intrinsic renal damage the signs, symptoms and treatment are usually independent of the etiology. We can compare it to a patient with a broken arm. You can break your arm falling down stairs or in a car accident, but the symptoms and treatment are going to be the same regardless of what caused the fracture. However, in patients with intrinsic ARF secondary to a specific cause (e.g., allergic interstitial nephritis due to methicillin) we should do everything possible to discontinue the insult to the kidney. In this example, we ought to stop the administration of methicillin as soon as possible.

Cortical necrosis is a rare form of ARF in which the renal cortex is destroyed. The outcome of this entity is usually catastrophic and patients often end up on dialysis. There are different degrees of cortical damage. In the so-called patchy cortical necrosis, enough renal function may be recovered after a few months and the patient may be able to live without the need of dialysis.

Classification

ARF can be divided into three main categories:

Prerenal (hypoperfusion of the kidneys)
Intrinsic renal damage
Postrenal (obstruction)

Prerenal Acute Renal Failure

In this situation a decrease in renal function is secondary to a decrease in renal perfusion (Fig. 2). When there is dehydration, hypotension, acute hemorrhage, severe congestive heart failure (CHF), hepatorenal syndrome, renal artery occlusion, etc.) the blood supply to the kidney diminishes (ischemic kidney) and, therefore, renal function also decreases. It is important to make a distinction between this situation, that usually resolves when renal perfusion improves (increasing fluid intake, correcting hypotension, treating CHF, etc.) (Fig. 3); and one in which the kidney has been hypoperfused for too long. In this latter

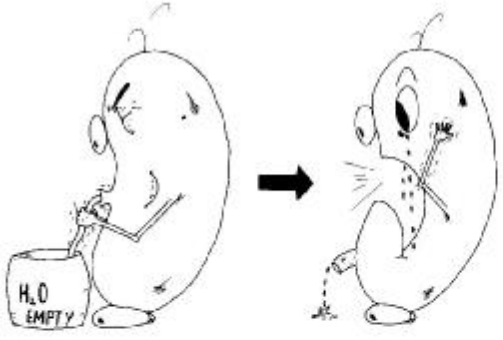

Figure 2 Prerenal acute renal failure: There is no urine output because there is no fluid intake.

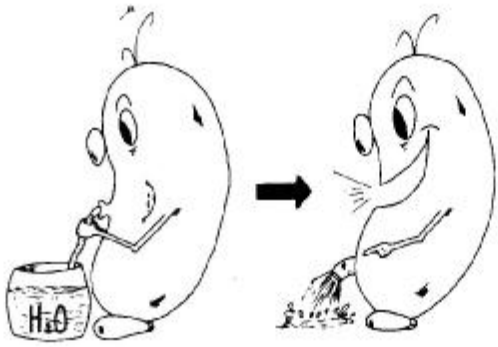

Figure 3 **When there is good fluid intake, there is good urine output (provided that tissue damage did not occur).**

situation, because of a long period of ischemic anoxia, renal tissue has been damaged to the point at which the patient develops intrinsic renal failure.

We can compare this situation to a car. The car will not run without gasoline but the car itself is in good condition, and the only thing we have to do to make it work is to fill up the tank. But if we keep the car in the garage for too long, even if we fill up the tank, it will not run because the battery will be dead. In summary, prerenal acute renal failure is an easily reversible situation if we can correct the cause, but it may lead to intrinsic renal failure if it lasts too long.

We can include in this section the acute renal failure caused by the use of both angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers in patients with bilateral renal artery stenosis, or in patients with solitary kidneys with renal artery stenosis. When renal artery stenosis is present, the kidney produces excess renin, which eventually increases the production of angiotensin II via the angiotensin converting enzyme. Angiotensin II elevates systemic blood pressure to try to increase the blood flow through the stenosis and increase renal perfusion. Furthermore, it increases intra glomerular pressure by constricting the post glomerular (efferent) arteriole much more than the pre glomerular (afferent) arteriole; and it is in this way that the kidney maintains its filtration pressure, the glomerular filtration rate and normal renal function. However, when either an ACE inhibitor or an angiotensin II receptor blocker is given, the intraglomerular pressure drops, because the post glomerular arteriole dilates more than the pre glomerular arteriole. Thus,

the glomerular filtration pressure, the glomerular filtration rate and renal function drop as well. If the patient has two kidneys with bilateral renal artery stenosis or a solitary kidney with renal artery stenosis and receives an ACE inhibitor, the hemodynamic changes described above occur and the patient develops acute renal failure. Because these are hemodynamic changes produced by these medications, stopping them results in resolution of the acute renal failure. However, the artery stenosis persists.

It is, therefore, very important to avoid these type of drugs in patients with these conditions. On the other hand, development of acute renal failure in a patient on either an ACE inhibitor or an angiotensin II receptor blocker may be a clue for the diagnosis of renal artery stenosis.

Intrinsic Acute Renal Failure

In this situation the kidney gets a direct insult that produces acute damage of the renal tissue (Fig. 4). The anatomic location of the lesion can be: glomeruli, vessels, interstitium and tubules.

Glomeruli. Acute poststreptococcal glomerulonephritis, idiopathic rapidly progressive glomerulonephritis, systemic lupus erythematosus etc.

Vessels. Polyarteritis nodosa, scleroderma, hemolytic uremic syndrome, etc.

Interstitium. Acute allergic interstitial nephritis, infections, infiltration (sarcoidosis, lymphoma etc.)

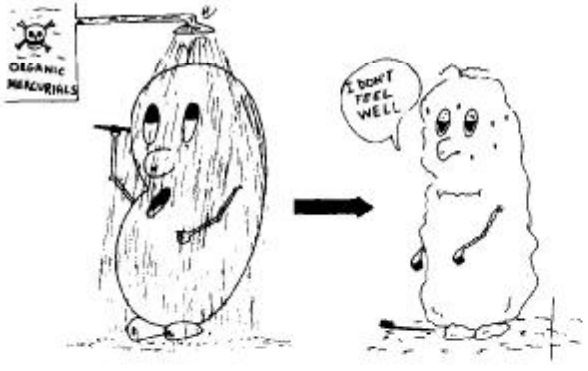

Figure 4 Intrinsic acute renal failure: Organic mercurials produce tissue damage.

Tubules. Acute tubular necrosis (ATN) secondary to long periods of hypotension, nephrotoxic drugs (antibiotics, contrast agents, etc.), multiple myeloma, myoglobinuria and hemoglobinuria associated with renal hypoperfusion, etc.

Postrenal Acute Renal Failure

This is usually a urological problem (Fig. 5). Obstruction can happen at different levels: ureter, bladder, and urethra.

The main causes of renal obstruction are: Prostatic hypertrophy, bladder carcinoma, neurogenic bladder, stones, gynecological tumors, retroperitoneal fibrosis, etc.

If the obstruction lasts too long the kidney may develop permanent damage secondary to increase in intrarenal pressure and/or recurrent infections.

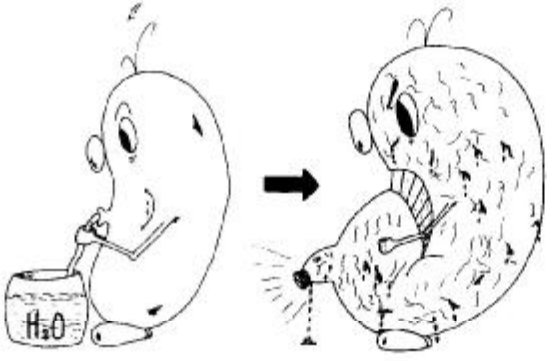

Figure 5 Postrenal acute renal failure: There is an obstruction of the kidney that eventually may produce tissue damage.

CHAPTER II

ETIOLOGY, PATHOPHYSIOLOGY AND PATHOLOGY

From now on, when I speak about intrinsic acute renal failure I will be referring to acute tubular necrosis (ATN). I will not include systemic diseases and/or glomerulonephritis.

The causes of intrinsic acute renal failure can be divided into three main groups:

1. *Direct insult to the kidneys (nephrotoxins).* Mercury, antibiotics, carbon tetrachloride, phenylbutazone, etc. (Fig. 6).

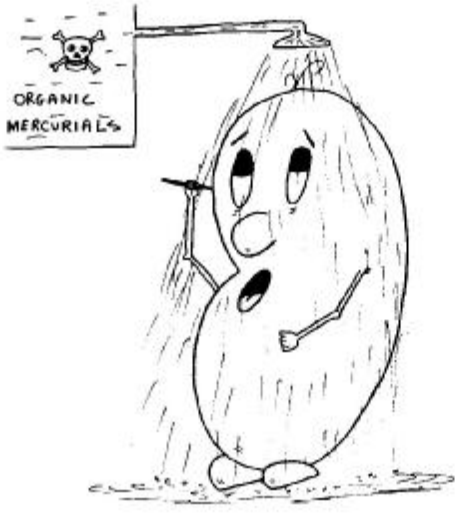

Figure 6 Nephrotoxins

2. *Hemolysis.* Transfusion reactions, venoms, fava beans, glycerol, etc. Hemoglobinuria and myoglobinuria do not appear to be toxic themselves; but there are two factors that may contribute to the development of ATN in these cases: intravascular volume status (e.g., hypotension) and urine pH (acid urine) (Fig. 7).

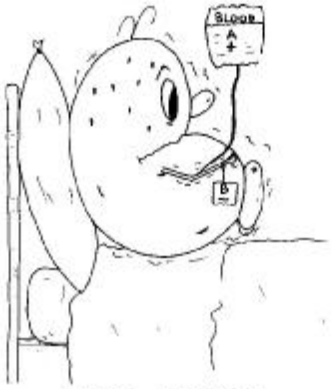

Figure 7 Hemolysis

3. ***Indirect insult to the kidney.*** Shock or renal ischemia (trauma, thrombosis of renal artery, pancreatitis, septic shock etc.) (Fig. 8).

The etiology of cortical necrosis is multifactorial, including severe shock with blood loss, profound intravascular volume depletion, septic abortion and poisoning (snake venoms). All these acutely compromise the blood flow to the cortex, and even more so, if they occur in an already damaged or hypoperfused kidney.

Figure 8 Shock

PATHOPHYSIOLOGY AND PATHOLOGY

The pathogenesis of ATN is not clearly understood (Fig. 9). There are three main hypotheses that attempt to explain the pathophysiology

Figure 9 Pathophysiology of ATN is unclear

of intrinsic acute renal failure and it may well be that all three play a role in its development (Fig. 10).

1. *Changes in the glomeruli.* Decreased glomerular perfusion (e.g., redistribution of blood from cortex to medulla), vasoconstriction of the afferent arteriole or vasodilatation of the efferent arteriole that would decrease filtration pressure; constriction of the mesangium that would decrease glomerular surface area and, finally, decreased permeability of the glomerular capillary wall. In summary, the result of the changes described above would be reflected in a decrease in glomerular filtration rate (GFR).

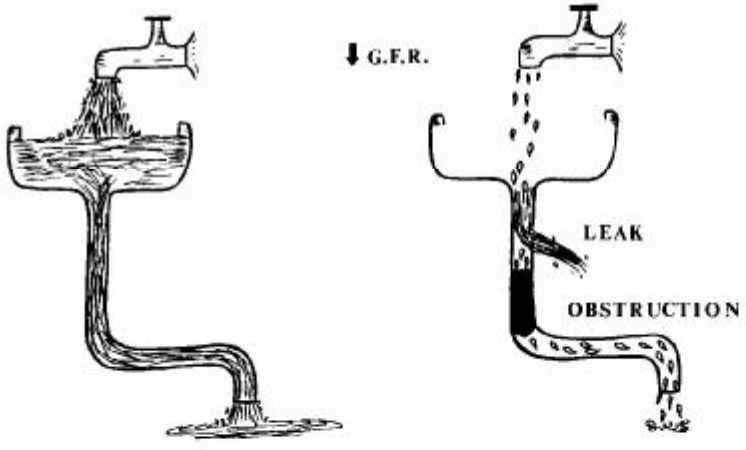

Figure 10 Left side shows "a normal nephron". Right side shows the three main hypotheses involved in the pathophysiology of ATN.

2. *Tubular obstruction*. From cellular and other debris coming from damaged tubular cells and protein precipitation.

3. *Tubular damage*. Causing tubular dysfunction and back leak of urine ultrafiltrate into the renal circulation.

Light microscopy usually shows patchy tubular cell necrosis and cast formation. Proximal tubular areas may show no necrosis but loss of brush border. Interstitial edema and/or cellular infiltrate may also be observed.

The pathology of cortical necrosis shows basically infarction of renal cortex with intravascular thrombi.

CHAPTER III

SIGNS AND SYMPTOMS OF INTRINSIC ACUTE RENAL FAILURE

We are going to divide the progression of ATN into five different periods.

Period I: the kidney is in danger.

Period II: the kidney is in intrinsic acute renal failure (ATN).

Period III: the kidney begins to open up.

Period IV: the kidney is working again!.

Period V: the kidney is back to normal.

PERIOD I

(The Kidney is in Danger)

As we can see in Figure 11 the kidney is in a dangerous situation and at any time, if we do not help it, "it will fail and develop ATN". This period lasts about 24 hours after a primary insult to the kidney. During this time severe renal tissue damage has not yet occurred. When a patient goes through a situation that may cause ATN (trauma, surgery etc.) we should pay special attention to three main signs:

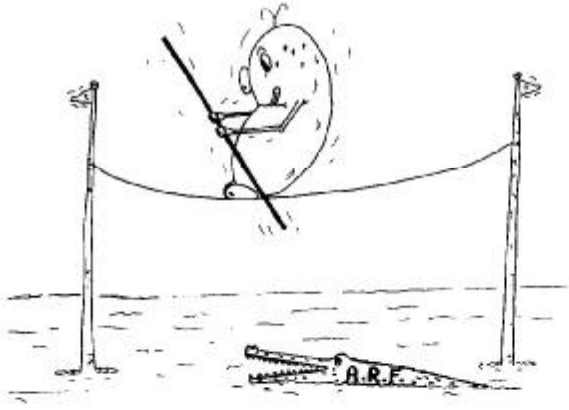

Figure 11 After the insult, the kidney is in a period of danger in which prompt therapeutic intervention may change the course of ATN.

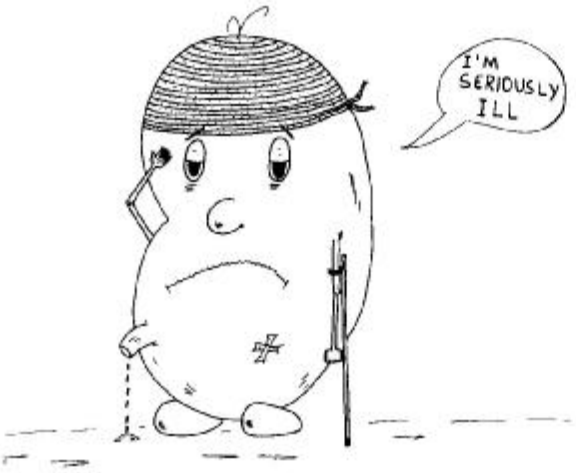

Figure 12 Oliguria without history of intravascular depletion or obstruction, is suspicious of intrinsic acute renal failure.

1) *Oliguria.* (Fig 12). To evaluate this sign we have to measure the urine output hourly. Sometimes the amount of urine made by the kidney is so small that the patient does not feel the need to urinate, or the patient has bladder atony after surgery and cannot empty the bladder. In these cases, the placement of a urethral catheter is very helpful in the evaluation of the oliguria.

2) *Increased plasma BUN, creatinine, K^+, etc.* (Fig. 13).

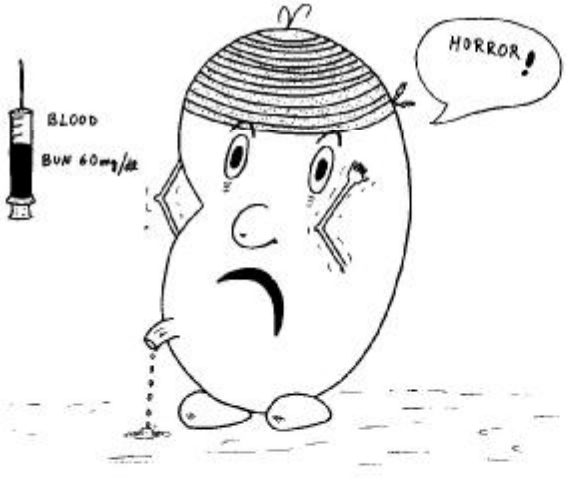

Figure 13 Oliguria and increase in plasma BUN, creatinine, potassium etc.

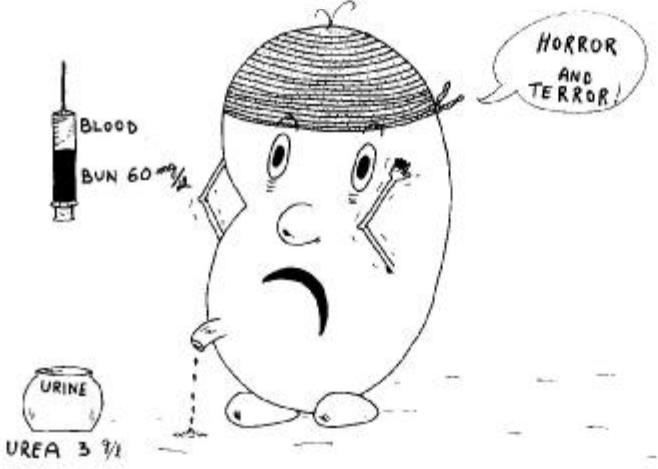

Figure 14 Oliguria, increase in plasma BUN and decrease in urinary urea. (the patient is in ARF).

3) *Decreased urinary urea, creatinine, K^+, etc.* (Fig. 14). Urinary urea and creatinine decrease in proportion to the increase in plasma BUN and creatinine.

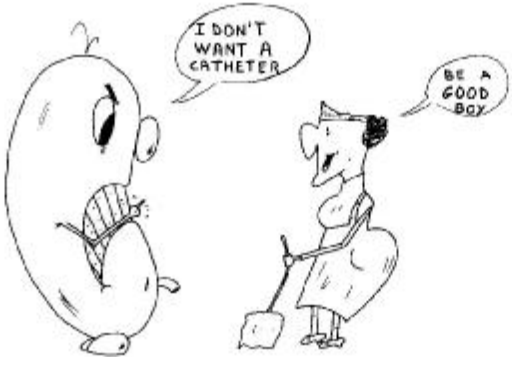

Figure 15 Use the urethral catheter only if needed and avoid unnecessary urinary tract infections.

PERIOD II

(The Kidney is in Intrinsic Acute Renal Failure (ATN)).

During this period several body systems are affected by the decrease of renal function. We see an increase in blood concentration of toxins (BUN, creatinine, middle molecules etc.), fluid overload, acidosis, electrolyte imbalance and a decrease in endocrine renal function.

A review of the main symptoms associated with intrinsic acute renal failure follows.

During this period the patient has oliguria. However, the incidence of non-oliguric acute renal failure has increased in recent years. Although, it is important to know the urine output in patients with ATN in order to maintain fluid balance, we have to be aware of the risk of developing urinary tract infections with the placement of urethral catheters. Therefore, we do not advise the use of urethral catheters unless it is absolutely necessary (Fig. 15).

Figure 16 Blood chemistry in intrinsic acute renal failure.

Blood shows: (Fig. 16)

Increase in BUN and creatinine
Increase in uric acid
Decrease in pH (acidosis)
Hyponatremia
Hyperkalemia
Hypocalcemia
Hyperphosphatemia
Anemia
Leukopenia
Platelet dysfunction

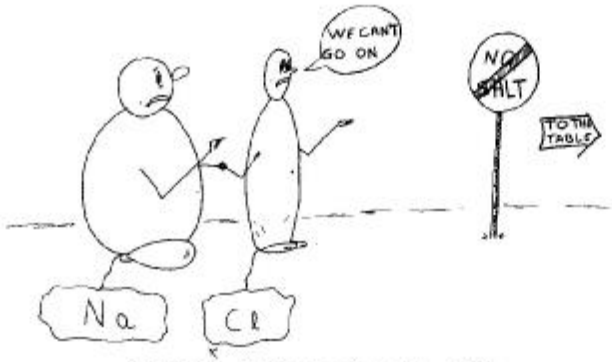

Figure 17 Avoid excessive salt restriction.

Hyponatremia is commonly seen in ATN. This is usually due to administration of too much free water, endogenous free water production from tissue catabolism and/or the prescription of excessive salt restriction (Figs. 17 & 18).

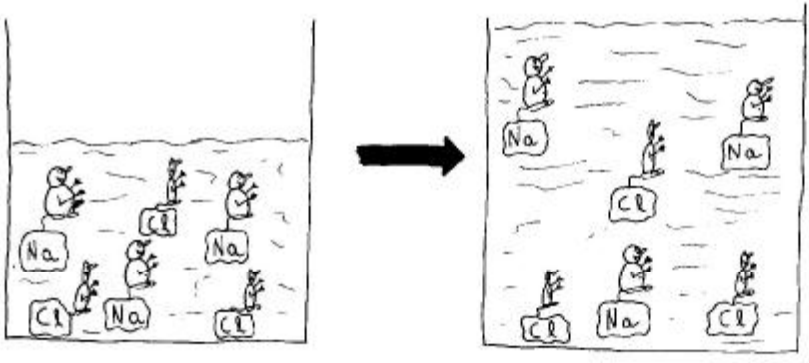

Figure 18 Avoid excessive free water intake.

Hyperkalemia is often seen in ATN and may cause cardiac arrest. If, in spite of medical treatment, plasma potassium continues to increase, the only solution is dialysis (Fig. 19).

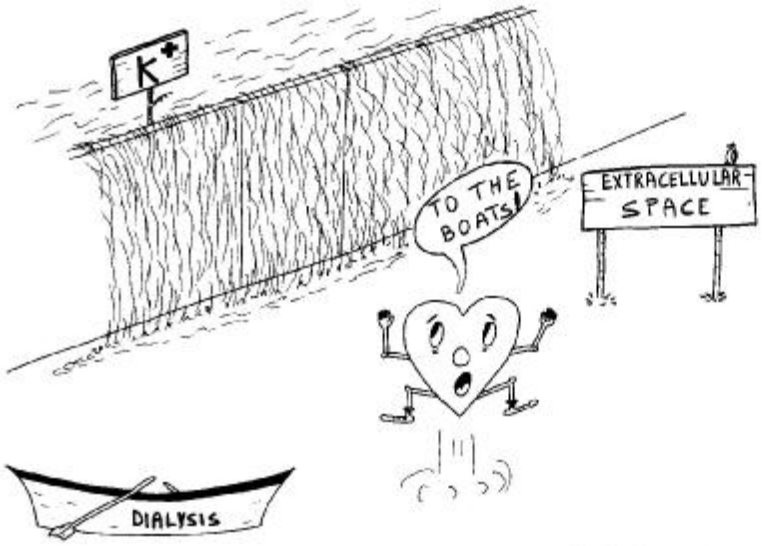

Figure 19 Acute potassium overload is dangerous for the heart.

Anemia is a constant clinical feature in ATN and usually in two weeks the hematocrit is down in the 20's (Fig 20). This is usually secondary to decreased erythropoiesis, hemolysis and blood loss.

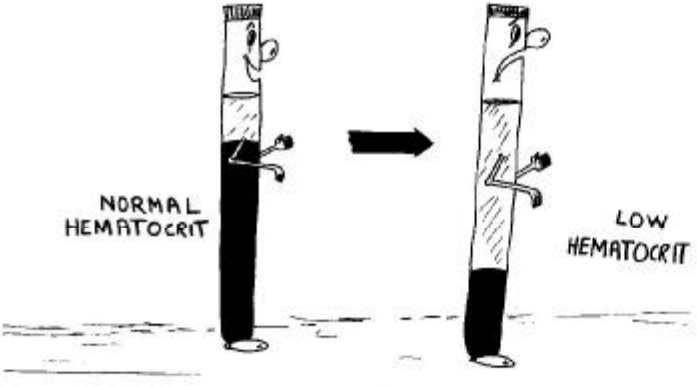

Figure 20 Hematocrit decreases

There are changes in the metabolism of carbohydrates, lipids and proteins, but clinical manifestations secondary to these disorders are not obvious because of the general condition of the patient.

Changes in the endocrine system occur but I will not discuss them here since they are beyond the scope of this book.

In patients with ATN the urine shows (Fig. 21):

Decreased urea and creatinine
Proteinuria
Red blood cells
Decreased excretion of Cl^-, Na^+ and K^+
Casts

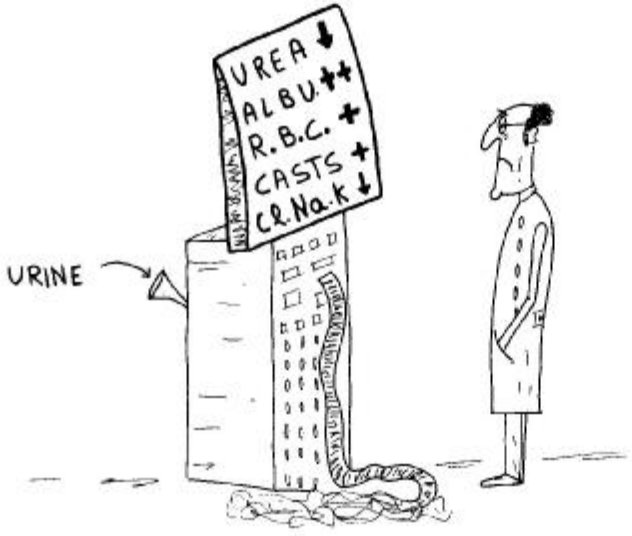

Figure 21 Urinalysis in ATN

Symptoms Due to Organ System Involvement

Gastrointestinal (G.I.)

A dry brown tongue is present in uremic patients regardless of their hydration state (Fig. 22).

Figure 22 Uremic tongue: dry and brown tongue regardless of hydration state.

Nausea, vomiting and anorexia are usually present (Fig. 23).

G.I. bleeding is frequent in patients with ATN and can be very severe. Hematocrit drops acutely, melena (Fig. 24) may be present and

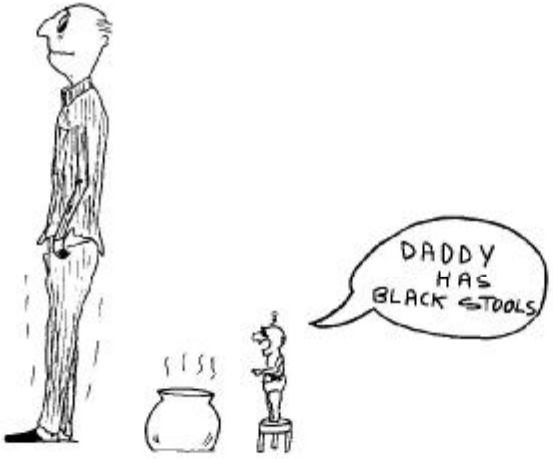

Figure 24 G.I. bleed.

induce a further increase in BUN and K^+, secondary to plasma protein digestion and destruction of blood cells in the G.I. tract respectively (Fig. 25). Therefore, in ATN it is very important to avoid the

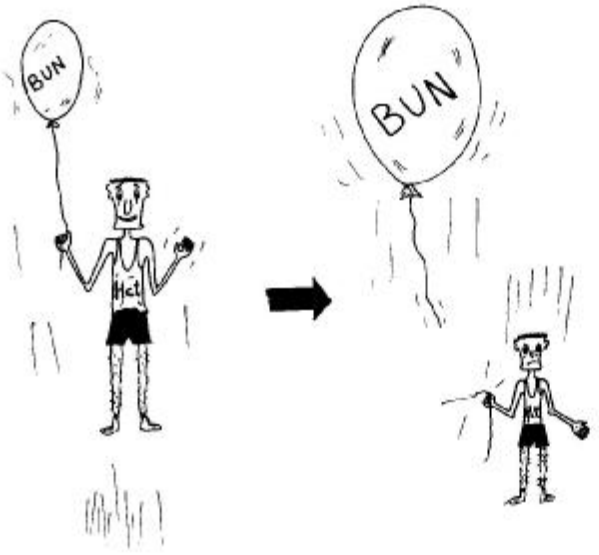

Figure 25 With G.I. bleed, plasma BUN increases due to absorption of nitrogen from plasma proteins digestion while the hematocrit decreases.

administration of drugs that can cause massive G.I. bleeding, as may be seen with aspirin (Fig. 26). The use of histamine two receptors inhibitors (e.g. cimetidine and ranitidine) for prophylaxis of peptic ulcers secondary to stress, may be very useful.

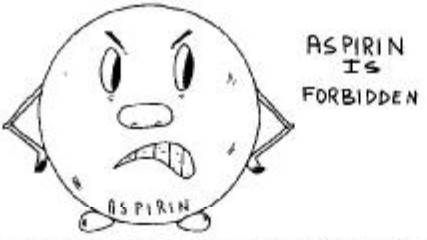

Figure 26 Aspirin should be avoided in patients with ARF.

Respiratory System

Fluid overload and pulmonary edema are frequent problems for patients with ATN. It is very important to keep accurate records of fluid intake and output, as well as daily weights, to avoid "drowning" of the lungs (Fig. 27). Cough, orthopnea and bilateral rales are the usual signs of pulmonary edema.

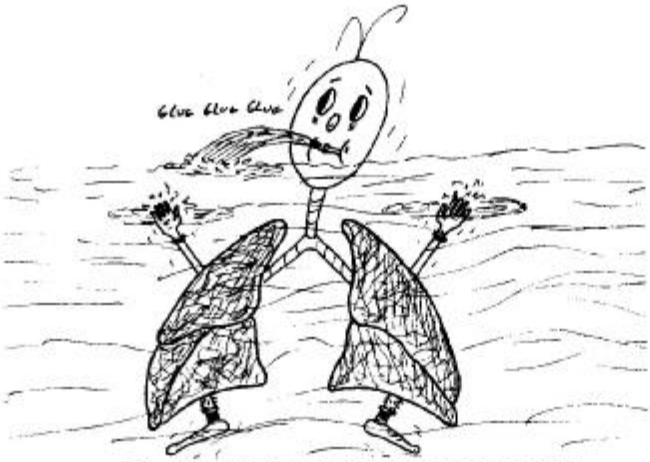

Figure 27 Fluid overload and pulmonary edema.

Cardiovascular System

There are two main problems that involve the heart. Increase in left ventricular work secondary to fluid overload and hypertension, and inflammation of the pericardium (pericarditis). Congestive heart failure (CHF) is usually related to fluid overload. As can be seen in Figure 28, "the left heart gets tired of fighting against the increase in intravascular volume", causing acute pulmonary edema.

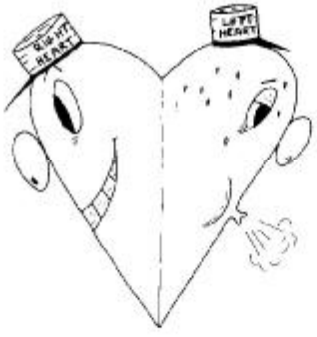

Figure 28 Heart failure.

Hyperkalemia may cause cardiac arrest as I mentioned before (Fig. 29).

Figure 29 Hyperkalemia may cause cardiac arrest.

Neurologic System

The main neurological symptoms are twitching (Fig. 30), myo-

Figure 30 Twitching and myoclonus are signs of nervous system involvement.

clonus, lassitude, fatigue (Fig. 31), decreased ability to concentrate,

Figure 31 Lassitude

confusion, somnolence (Fig. 32), lethargy, seizures and coma. Some patients may develop symptoms of euphoria and hallucinations.

Peripheral neuropathy may be present, as well as the so-called "restless leg syndrome", in which the patients are unable to keep their legs at rest.

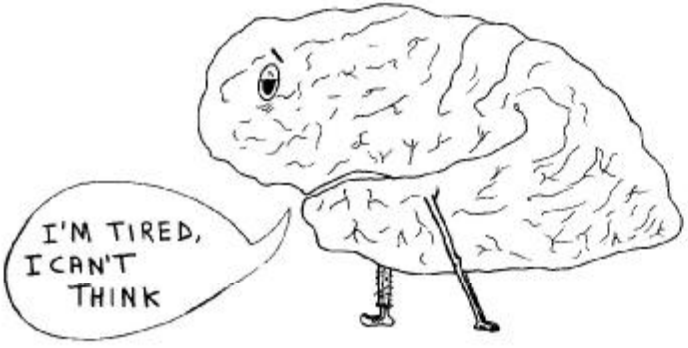

Figure 32 Decreased ability to concentrate.

Immune system

Cellular and humoral immunity are altered in patients with renal failure. Infection is frequent and is the major cause of mortality in ARF patients. Physicians have to be aware of this eventuality and use appropriate antibiotics promptly. The dose of antibiotics (and other drugs)

should be adjusted for the degree of renal function (see recommended readings).

Weight

It is very important to weigh the patients daily to assess adequacy of fluid balance. Patients with ARF have an increase in catabolism which should be reflected in a decrease in tissue mass. The dry weight should fall around 0.2-0.5 kg/day and even more in patients with hypercatabolism. Tissue catabolism produces "endogenous" water which is different for carbohydrates, lipids and proteins (see appendix). The weight reflects fluid intake, output and catabolism. Therefore, a patient with ARF should lose ~0.5 kg/day if his fluid balance is well managed. However, hypercatabolism in these patients can be halted with early and continuous high caloric intake.

PERIOD III

(The Kidney Begins to Open Up)

Right!. The kidney is opening up and it begins to make more urine. During this period the kidney eliminates water and not toxic products. In other words, the urine increases in quantity but not in quality (Fig. 33). Therefore, the patient is still uremic, but an increase in urine output decreases any fluid overload which, usually, had complicated the oliguric period in spite of efforts to maintain good fluid balance.

Figure 33 Increased urine output does not mean urine of good quality.

PERIOD IV

(The Kidney is Working Again!)

This period is called polyuric. Here, the urine output increases further but now the kidney is making urine of better quality than in the previous period, and concentrating mechanisms recover slowly. There is an increase in the excretion of urea, creatinine, potassium etc. (Fig. 34). During this period the urine output can be very high (10 liters per 24 hours or even more). This tremendous urine output is secondary to both the increase in urinary urea, that acts as an osmotic diuretic, and to the fact that the concentrating mechanisms of the kidney are not, yet, fully recovered. We have to watch the patient very closely, because the increase in urine output will increase electrolyte excretion and cause severe hypokalemia, hyponatremia and hypomagnesemia as well as orthostatic hypotension.

During this period the uremic symptoms improve slowly.

Figure 34 Polyuric phase: increase of urine output (polyuria: >2 liters/24hrs) with increase of elimination of substances (urea, creatinine, electrolytes etc.).

PERIOD V

(The Kidney is Back to Normal)

Two to three weeks after "the kidney starts opening up" renal function is almost back to normal. However, the anemia and a decrease in the ability to maximally concentrate or dilute the urine may last longer. Therefore, the patient has to be careful with excessive fluid and salt intake, while the kidney completely recovers its concentrating mechanisms.

CHAPTER IV

DIFFERENTIAL DIAGNOSIS AND PROGNOSIS

The differential diagnosis includes prerenal, intrinsic and postrenal acute renal failure.

First obtain a good medical history and perform a physical examination. This gives an idea of what is happening to the patient, e.g., excessive fluid losses (diarrhea), weight loss and orthostatic hypotension suggests dehydration (Fig. 35). A history of heart disease with acute

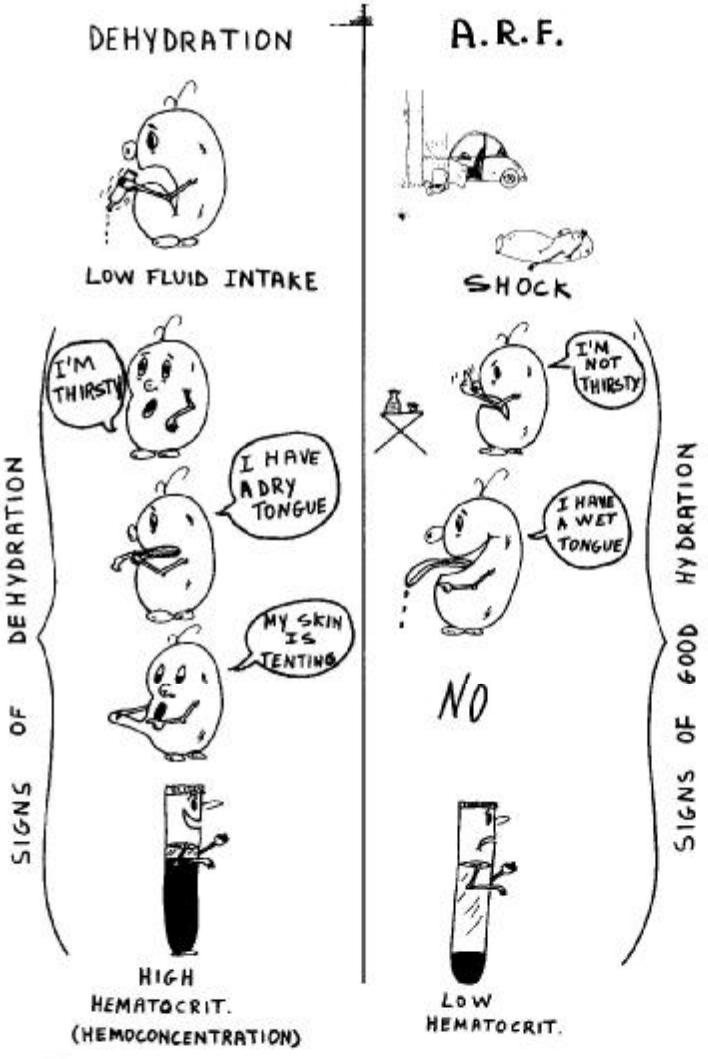

Figure 35 Differential diagnosis between ARF and dehydration.

decrease in cardiac function will make renal hypoperfusion secondary to decrease in cardiac output very likely (Table I).

Table I: PRERENAL

Diseases of Renal Artery	Dehydration	Fluid Redistribution	Decreases in Heart Function
Thrombosis Stenosis, etc.	Low fluid intake Fluid Losses (diarrhea, etc.)	Sepsis Burns	C.H.F. Tamponade, etc.

Good fluid balance, normal heart function and use of nephrotoxic drugs suggests intrinsic acute renal failure (Table II).

Table II: INTRINSIC ACUTE RENAL FAILURE

Glomeruli	Vessels	Interstitium	Tubule (ATN)
Glomerulonephritis	Vasculitis	Allergic interstitial nephritis	Prolonged renal ischemia Nephrotoxins

Once we have an idea of what is happening clinically, we should proceed to order a few tests that will help us to make a final diagnosis. **Always** look at a **fresh** urine sample under the microscope and send some to the laboratory to measure the urinary parameters shown in Table III.

Table III: URINE SEDIMENT

Prerenal	Intrinsic Acute Renal Failure	Postrenal
Unremarkable	Granular casts Epithelial cell casts WBC casts RBC casts	Unremarkable

URINE ELECTROLYTES

	Prerenal	Intrinsic Acute Renal Failure	Postrenal	
			Acute	Chronic
Na mEq/L	< 20	> 40	< 20	> 40
FeNa%[1]	< 1	>1–2	< 1	> 1
Osmolality	>500	<300	>500	<300
Urine/plasma creatinine	> 40	< 20	> 20	< 20
Plasma BUN/ plasma creatine[2]	> 20	< 20	> 20	< 20

WBC = White blood cells. RBC = Red blood cells.
[1]FeNa is the percentage of the total Na^+ filtered by glomeruli, that is excreted in the urine
[2]This ratio may be increased by high protein intake, use of steroids, G.I. bleeding, tetracyclines and hypercatabolism.

Always obtain a renal ultrasound to rule out obstruction (postrenal acute renal failure) (Table IV).

Table IV: POST ACUTE RENAL FAILURE

Gynecological tumors
Blood clots
Papillary necrosis
Prostatic tumors
Neurogenic bladder
Ureteral obstruction (bilateral)
Urethral obstruction (stricture)

A diuretic phase is usually seen after releasing the obstruction. This is secondary to a decrease in concentrating ability and to an increase in excretion of urea that usually has accumulated during the obstruction.

If we suspect that the patient has intravascular volume depletion, a fluid challenge should be given, e.g., infusion of 500 ml of half normal or normal saline in one hour and watch the patient closely for an increase in urine output. The fluid challenge can be repeated but there is the risk of developing acute pulmonary edema.

Suspicion of renal artery obstruction should lead to a radioisotope renal scan.

If renal artery stenosis is suspected because a patient develops acute renal failure after the use of either an ACE inhibitor or an angiotensin II receptor blocker, a renal scan with and without captopril may help in the diagnosis. The renal scan after captopril should show worsening function in the kidney with the stenosis compared to the renal scan without captopril.

It is difficult to make the diagnosis of cortical necrosis without a renal biopsy. However, we can suspect it by the history, when the patient has very low urine output (0–50ml/day) and when the ARF persist for more than 6 weeks without continuous insult to the kidneys. Sometimes one or two months after the acute event we can see a granular calcification outlining the periphery of the kidneys.

We should avoid the use of i.v. contrast in patients with acute or chronic renal failure (e.g., serum creatinine > 1.5 mg/dl).

However, if the patient needs the use of i.v. contrast to diagnose an acute event (e.g., cerebral hemorrhage), we can perform a CAT scan with contrast knowing that it may prolong the ARF.

First we have to save the patient and then the kidneys.

In some circumstances, in which ATN is unlikely and obstruction has been ruled out, it may be necessary to perform a renal biopsy to diagnose some of the other intrinsic causes of acute renal failure (e.g., idiopathic rapid progressive glomerulonephritis, Wegener's granulomatosis, polyarteritis nodosa etc).

Transplanted kidneys can suffer acute renal failure due to any of the etiologies discussed previously and the approach to diagnosis and treatment are the same as for native kidneys. However, in the differential diagnosis we have to add two major situations in which the acute renal failure is directly related to the fact that we are dealing with a transplanted kidney. These are: acute transplant rejection and acute cyclosporine toxicity. Sometimes it is difficult to differentiate between the two and a renal biopsy may be necessary for final diagnosis. Cyclosporine blood levels are measured routinely for dose adjustment and high levels should alert the physician to possible cyclosporine induced renal failure. The treatment in this case is to decrease the cyclosporine dose. Acute rejection is treated with high doses of steroids and/or administration of other immunosuppressive drugs (e.g., monoclonal antibodies).

Prognosis (Fig 36)

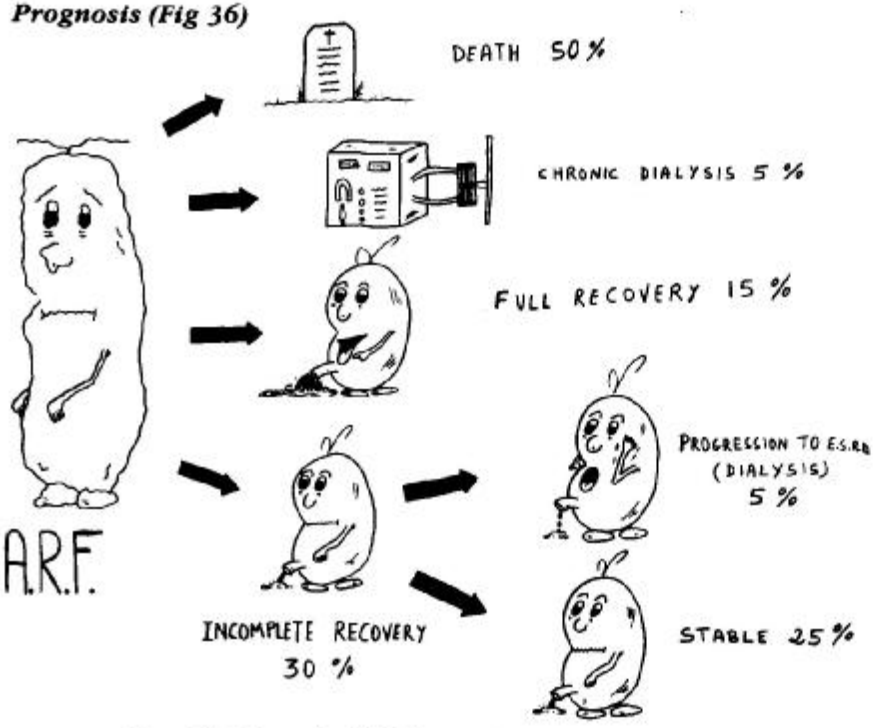

Figure 36 Prognosis. (E.S.R.D. = end stage renal disease).

CHAPTER V

PROPHYLAXIS AND TREATMENT

We should avoid any insults to the kidneys (e.g., nephrotoxic drugs, iodine dye etc.) in high risk patients (e.g., diabetics, open heart surgery, multiple myeloma, dehydration, CHF, pre-existing renal failure, elderly patients, etc.). In a high risk patient that may go through a situation that may cause acute renal failure (e.g., i.v. contrast load), we should take the following precautions. The patient should be well hydrated prior to the test, even with i.v. fluids if necessary, and mannitol may be infused prophylactically (25 grams of mannitol in 500 ml of normal saline to be started one hour before the procedure at a rate of 100 ml/hr (Fig. 37)). It is very important that i.v. fluids be continued to avoid negative fluid balance secondary to the increased diuresis from the mannitol and the iodine-containing dye (high dose furosemide can also be used).

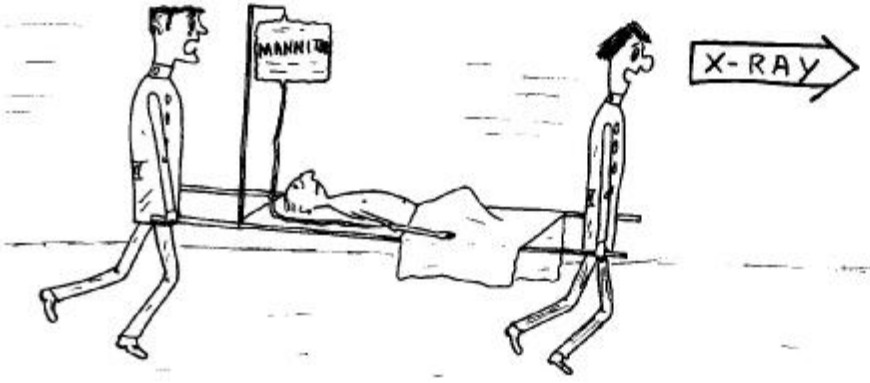

Figure 37 Mannitol infusion as prophylaxis.

TREATMENT

PERIOD I

(The Kidney is in Danger)

This period starts at the time the kidney receives the insult and continues until intrinsic acute renal failure develops. The length of this period varies from one patient to another. During this time therapeutic

intervention may reverse and/or diminish the severity of the ARF (Fig. 38). During this period, that may last 24 hours, we can use mannitol 25 grams in 500 ml of normal saline (n.s.) to be given in 40 minutes, or high dose furosemide (300 mg in 0.5 liter of n.s. to be given in 60 minutes; or chlorothiazide 500 mg i.v. followed by furosemide 300 mg i.v.). It is unclear by which mechanism these measures may change the course of the ATN.

In some circumstances the patients may respond to the use of diuretics with an increased urine output, but without a significant increase in the clearance of toxins. This is important because, although the patient may still need dialysis, fluid management becomes much easier. In patients with renal failure the loop diuretics (e.g., furosemide) are the most effective, however higher doses than normal are required (e.g., furosemide 200 mg every 12 hours). It is also important to remember that there are circumstances in which the response to diuretics is decreased. Some patients that do not respond to high doses of oral diuretics because of decreased bowel absorption (e.g., intestinal wall edema) will respond to intravenous administration. The combination of different classes of diuretics may also be helpful in increasing urine output because they block sodium reabsorption at different sites of the nephron. For example, loop diuretics block sodium reabsorption primarily in the loop of Henle. Therefore, sodium can be reabsorbed distally either in the distal tubule or the collecting duct, decreasing the efficacy of the loop diuretic. In this situation, adding a thiazide (distal diuretic) or spironolactone (aldosterone antagonist) may increase urine output. Hypoalbuminemia is another circumstance in which the diuretic response may be decreased. The majority of diuretics are bound to plasma proteins which transport them to the kidney where they are secreted into the tubular lumen. If hypoalbuminemia is present, only a small amount of diuretic binds to protein while the rest leaves the intravascular space and does not reach the kidney. This can be solved by intravenous administration of albumin previously mixed with furosemide. Finally, the addition of low dose dopamine (1 to 3 ug/kg/min) may potentiate the effect of diuretics.

The use of atrial natriuretic peptide is still experimental and the effect of calcium channel blockers has not yet been established.

Special mention should be made about what has been called heme-pigment-associated acute renal failure. In this setting acute renal fail-

ure is associated with either myoglobinuria or hemoglobinuria due to rhabdomyolysis or hemolysis respectively. In this setting the use of intravenous fluids with mannitol and urine alkalinization has shown to provide renal protection (for instance: 1/2 normal saline with 10 gm of mannitol and 50 mEq of sodium bicarbonate to maintain both a urine output of 200 to 300 cc/hr and a urine pH above 6.5). If good urine output is not obtained within several hours the forced diuresis should be discontinued.

During this period substitution of renal function is required to correct the fluid and electrolyte imbalance.

Initiate dialysis if the patient becomes uremic.

Water Balance

Records of fluid intake and output to maintain adequate balance and avoid fluid overload are essential.

Intake: I.V. fluids
Food and drinks
Production of water from catabolism of carbohydrate, protein and lipids (see appendix).

Output: Insensible losses (respiration and perspiration)
Urine
Stool
Others (vomiting, nasogastric suction, etc.) (Fig. 39).

Daily weights are essential since it is important to keep in mind that patients with ATN are usually in a catabolic state and, without adequate caloric intake, they lose 0.2-0.5 kg/day, even one kilogram in

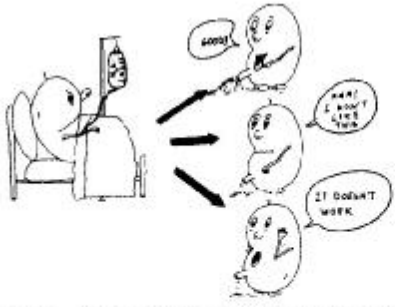

Figure 38 Responses to mannitol or furosemide (Lasix) challenge.

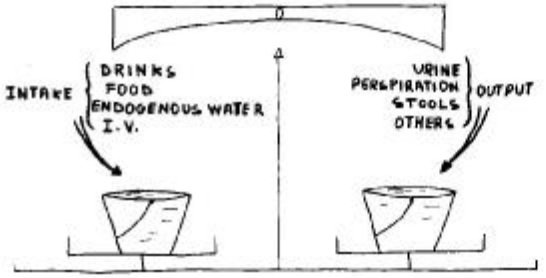

Figure 39 We should maintain adequate fluid balance.

hypercatabolic situations. Therefore, if the weight of the patient remains the same (without good nutrition) it means that he is becoming fluid overloaded (Fig. 40). Good caloric intake decreases catabolism and, therefore, the production of endogenous water.

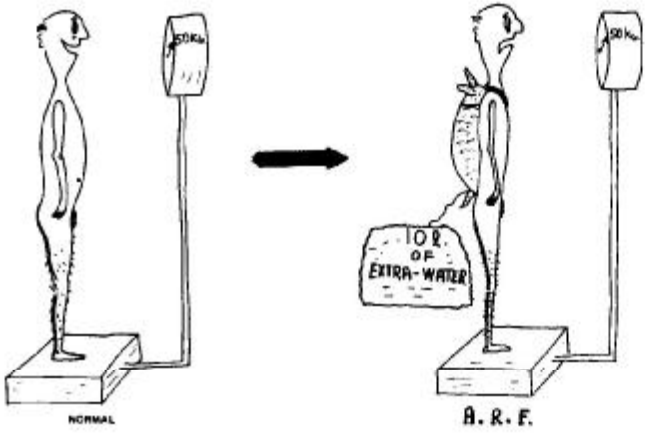

Figure 40 Weight increases or remains the same, because of fluid overload (unless there is high caloric intake).

Sodium and Chloride Balance

Usually patients in ATN excrete constant amounts of salt regardless of the intake. Therefore, to avoid Na^+ and Cl^- imbalance we have to maintain some salt intake. Excessive salt restriction should not be

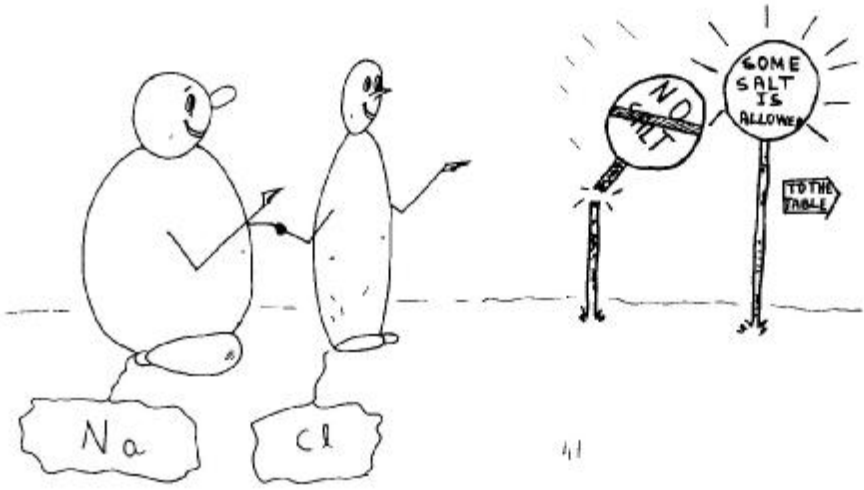

Figure 41 Avoid excessive salt restriction.

prescribed. (Fig. 41). Furthermore, we should avoid an excessive intake of free water (water without salt).

Potassium Balance

Plasma potassium increases quite rapidly in patients with ATN. Hyperkalemia can cause cardiac arrest, therefore, it must be closely followed. Potassium intake should be lower than 40-60 mEq/24 hr; cation exchange resins (Kayexalate) (1) (Fig. 42) and dialysis should be used as needed.

In patients with severe hyperkalemia (muscle weakness and EKG changes), temporary measures to decrease plasma potassium should be used until hemodialysis is started: Ca^{++} i.v. can block the effects of K^+ on the heart; glucose infusion with insulin and correction of acidosis with i.v. bicarbonate shift K^+ from the extracellular to the intracellular space.

Calcium, Phosphate and Magnesium Balance

Hypocalcemia, hyperphosphatemia and hypermagnesemia develop in acute renal failure.

(1) :1 gram of Kayexalate binds 1 mEq of potassium from the G.I. secretions. In patients with vomiting, Kayexalate can be given as an enema. Kayexalate can be administered with or without 30% sorbitol.

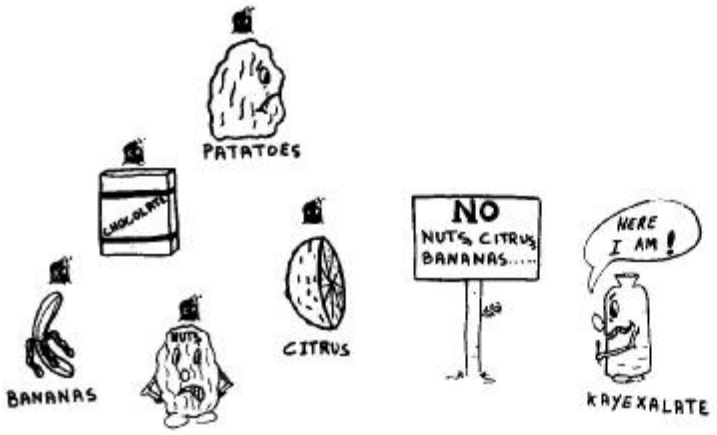

Figure 42 Control of hyperkalemia includes: diet and Kayexalate.

Hypocalcemia occurs as a consequence of decreased production of 1,25 $(OH)_2$ vitamin D_3 and skeletal resistance to parathyroid hormone. Both hyperphosphatemia and hypermagnesemia are the result of decreased urinary excretion in the presence of persistent dietary intake. Oral calcium salts (calcium carbonate, calcium citrate or calcium acetate) and aluminum salts can be given to control the hyperphosphatemia. Decrease of both oral phosphate and magnesium should be prescribed.

In rhabdomyolysis, both severe hyperphosphatemia and hyperkalemia can occur due to the release of phosphate and potassium from the damaged muscle.

In the rhabdomyolysis recovery phase, hypercalcemia can occur as a result of calcium mobilization (previously deposited in the damaged muscle), decrease of serum phosphate due to increase of urinary phosphate and increase of calcitriol. Aggressive calcium replacement in the hypocalcemic phase in this setting can lead to severe hypercalcemia in the recovery phase.

Indications for Acute Dialysis

BUN > 100 mg/dl and/or severe uremic symptoms
K^+ > 7 mEq/l
Fluid overload (pulmonary edema)
Severe acidosis (Fig. 43)

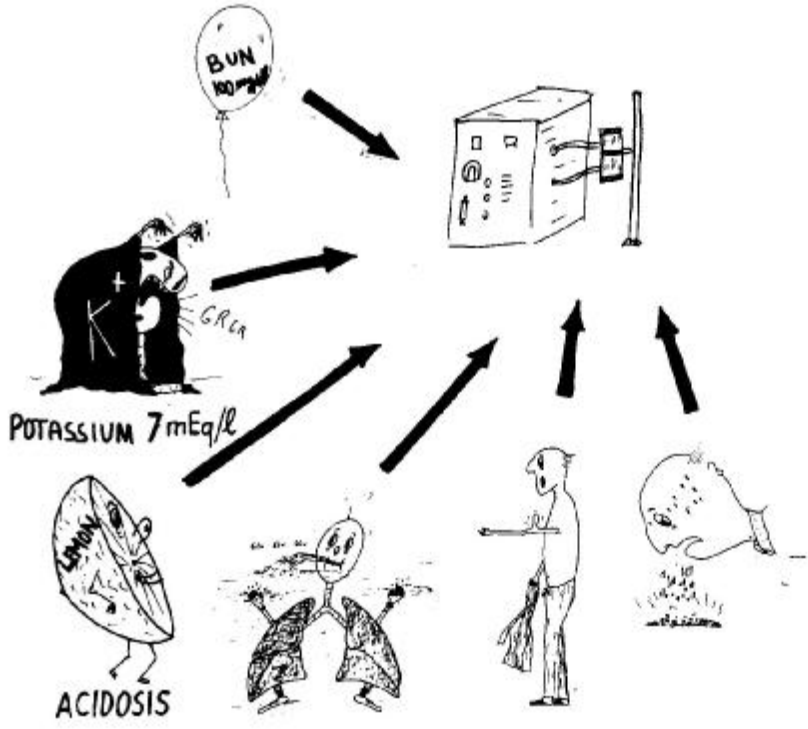

Figure 43 Indications for dialysis.

Usual Complications of Hemodialysis

Hypotension

Bleeding

Arrhythmias

Disequilibrium syndrome. Usually occurs at the end of the first and second dialysis. The symptoms includes headache, muscle twitching, nausea, vomiting, somnolence, confusion, coma and seizures.

This syndrome is caused by brain edema secondary to a decrease in plasma osmolality that occurs during hemodialysis, which is not followed by the same decrease in brain cell osmolality. The more uremic the patients are, the more likely they are to develop this syndrome (changes in blood and brain pH may also play a role in this syndrome). Therefore, dialysis should be performed "gently" in the first two or three days by using small dialyzers, low blood flows and short dialysis times.

The most widely used vascular access for acute dialysis are double lumen subclavian and femoral catheters.

Dialysis Methods

Hemodialysis. An intermittent procedure performed with high blood flows (250-300 ml/min) for 3-4 hours per day as needed. Requires the use of a dialysis machine to deliver dialysis fluid at a rate of 500 ml/min. This technique is based on the physical concept of diffusion. Diffusion transfer is a **passive transfer of solutes across a membrane,** in the absence of net solvent transfer.

Peritoneal Dialysis. Performed continuously with hourly exchanges as needed.

CAVH. (Continuous arteriovenous hemofiltration). Continuous blood (<100 ml/min) filtration through a high permeability membrane to accomplish ultrafiltration rates between 200-800 ml/hr. Requires continuous fluid replacement and does not need dialysis fluid. This technique is based on the physical principle of filtration and it can be performed continuously (twenty four hours a day, seven days a week). Filtration is the simultaneous **transfer of a solvent, with a part of the solutes it contains,** across a membrane.

CAVHD. (Continuous arteriovenous hemodialysis). Continuous procedure performed with low blood flows (<100 ml/min) and peritoneal dialysis fluid as dialysate at a rate of 17 to 300 ml/min. This technique does not require the use of a dialysis machine.

CAVHHD. (Continuous arteriovenous hemodiafiltration). This is a combination of CAVH and CAVHD.

Complications

The most frequent complications of ATN in Period II are: infection, myocardial infarction, heart failure, acute gastrointestinal bleeding, disseminated intravascular coagulation (DIC) and strokes.

Treatment for patients with G.I. bleeding is emphasized in Fig. 44. If the patient needs dialysis, low dose heparin or no heparin (with some special dialyzers) can be used. We can perform hemodialysis with the so-called

Figure 44 Therapy for G.I. bleed.

regional heparinization. Regional heparinization is the continuous infusion of heparin in the blood coming out of the patient, with continuous infusion of protamine in the blood going back into the patient to inhibit the effect of the heparin in the systemic circulation. Infusion of citrate predialyzer and calcium postdialyzer, instead of heparin and protamine, have also been used to perform regional heparinization. In some cases of

severe G.I. bleeding I have used peritoneal dialysis which does not require the administration of any heparin.

PERIOD III

(The Kidney Begins to Open Up)

The patient has an increase in urine output but the urine is still of poor quality. Therefore, he may still require dialysis, though it may be easier to maintain fluid balance (Fig. 45).

Figure 45 More urine does not mean better urine.

PERIOD IV

(The Kidney is Working Again!)

The kidney starts to excrete toxins and copious amounts of water with them (Fig. 46). During this period, the kidney cannot concentrate the urine and loses a lot of water with electrolytes (polyuric phase). Furthermore, the urea and toxins are acting as osmotic diuretics increasing even more the water and electrolyte excretion. The therapeutic measures at this point are directed toward adequate fluid and electrolyte replacement to compensate for the excessive losses. As a rule, aim for a negative fluid balance of about 500 ml to 1000 ml/24 hours (Fig. 47). This decreases the amount of fluid accumulated during the oliguric phase and avoids continuous polyuria secondary to excessive fluid intake. Patients may require i.v. fluids to keep up with the urine output that can be as high as 10 liters/day or even more.

Figure 46 During the polyuric phase the patient should be kept in relative negative fluid balance.

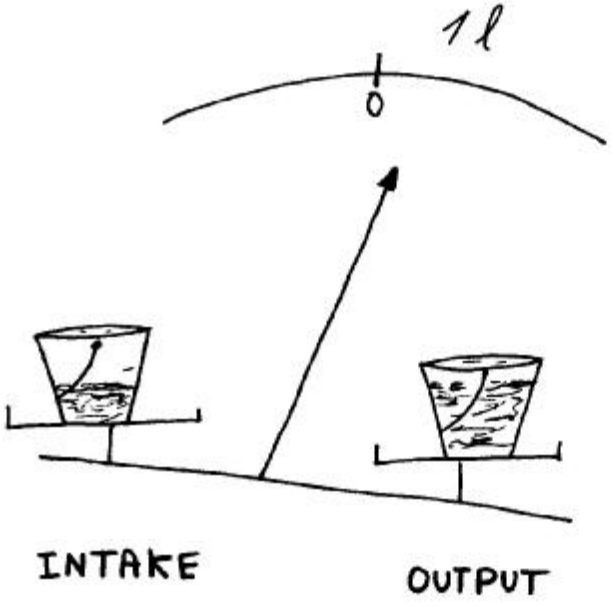

Figure 47 Aim for a negative fluid balance.

PERIOD V

(The Kidney is Back to Normal)

This period may be a long one, in which the renal function is almost normal but the kidney is not yet able to control excessive water (Fig. 48) and salt intake (Fig. 49).

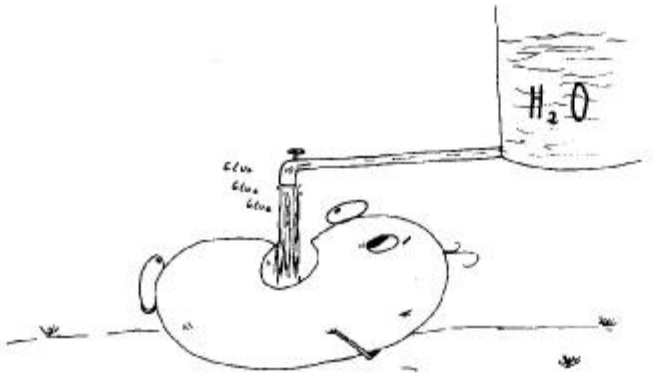

Figure 48 Avoid fluid overload.

Figure 49 Avoid salt overload.

APPENDIX

Normal urine output = 40-60 ml/hr
Anuria: < 100 ml/24 hr
Oliguria: 100-400 ml/24 hr
Polyuria: > 2 liters/24 hr
Plasma osmolality = ~290 = plasma $[Na^+] \times 2 + \frac{\text{glucose}}{18} + \frac{\text{BUN}}{2.8}$

Specific gravity of the urine is the **weight** of the urine compared with that of an equal volume of distilled water.
Urine osmolality is the **number** of particles per kg of water.
Usually there is a correlation between them:

s.g.	osmolality
1000	0
1020	700
1050	1000

However, when the urine has protein, glucose, dye or mannitol; the specific gravity increases more than the osmolality because of their high molecular weight.

Total body water = 60% of total body weight.
Intracellular water = 2/3 of total body water
Extracellular water = 1/3 of total body water:

a) Intravascular ~3 liters
(~5% of total body weight)

b) Interstitial ~12 liters
(~18% of total body weight)

e.g.: Total body weight = 70 kg
Total body water ~42 liters
Intracellular water ~28 liters
Extracellular water ~14 liters:
a) Intravascular ~3 liters
b) Interstitial ~11 liters

Normal Blood Values

Potassium	3.5—4.5 mEq/l (3.5—4.5 mmol/l)
Sodium	135—145 mEq/l (135—145 mmol/l)
Chloride	95—105 mEq/l (95—105 mmol/l)
Urea	25 mg/dl (4.16 mmol/l) (BUN is 1/2 of urea (~10 mg/dl))
Creatinine	0.6—1.3 mg/dl (53.04—114.92 µmol/l)
Hematocrit	40%
pH	7.35—7.45

Normal Urine Values

Chloride	100 mEq/24 hr
Sodium	100 mEq/24 hr
Potassium	30 mEq/24 hr
Urea	30-40 g/24 hrs.

Minimum urine pH is 4.5-5.0
(Urine values change with diet)

Other

Diarrhea	chloride 40 mEq/l sodium 100 mEq/l potassium 30 mEq/l bicarbonate 20 mEq/l
Gastric Secretion	chloride 120 mEq/l sodium 90 mEq/l loss of H^+ (may produce metabolic alkalosis) potassium 6 mEq/l
Saliva	chloride 34 mEq/l sodium 33 mEq/l potassium 20 mEq/l

Intestinal Secretion	chloride 50 mEq/l sodium 90 mEq/l potassium 12 mEq/l bicarbonate 30 mEq/l
Biliary Secretion	chloride 85 mEq/l sodium 140 mEq/l potassium 5 mEq/l bicarbonate 45 mEq/l
Sweat	chloride 50 mEq/l sodium 50 mEq/l potassium 5 mEq/l

Respiration: free water

Endogenous Water

Endogenous water is produced by the catabolism of carbohydrates, lipids, proteins:

100 grams of carbohydrates: 55 ml of water.
100 grams of lipids: 107 ml of water.
100 grams of proteins: 41 ml of water.

How to calculate creatinine clearance

(using plasma creatinine, age and body weight)

$$\frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{Plasma creatinine.}} = \text{Creatinine Clearance.}$$

(times 0.85 for females)

How to calculate deficit of Na^+ and Cl^-

Normal plasma Na^+ — current plasma Na^+ = Na^+ deficit per liter × total body water = total Na^+ needed to correct the plasma Na^+

e.g. normal plasma Na^+ = 140 mEq/l
Current plasma Na^+ = 120 mEq/l
Total body water = about 60% of total body weight (42 liters for a total body weight of 70 Kg).
140 – 120 = 20 mEq/l × 42 liters = 840 mEq of Na^+ needed.
(Same for Cl^-).

Pseudohyponatremia is usually secondary to hyperlipidemia, hyperproteinemia, hyperglycemia or administration of mannitol. Every 62 mg /dl increment in plasma glucose will decrease plasma sodium by 1 mEq/L.

How to correct hypernatremia

$$\frac{\text{About 60\% of body weight} \times (\text{current plasma } Na^+ - 140)}{140} = \text{Total}$$

free water needed to correct the hypernatremia.

e.g.: For a Na^+ of 160 in a man of 70 Kg of weight

$$\frac{42 \times (160-140)}{140} = 6 \text{ liters of free water}$$

How to correct hypokalemia

A decrease of 1 mEq/l in plasma K^+ represents 100-200 mEq of K^+ deficit. Below 3 mEq/l each decrease of 1 mEq/l reflects another 200-400 mEq of K^+ deficit.

I.V. K^+ replacement should not exceed 10 mEq/hour. If higher rates are necessary, patients should be monitored closely.

How to correct hyperkalemia: (See page 41)

Decrease of arterial pH by 0.1 increases plasma potassium 0.6 mEq/l, and vice versa.

Acid base

Metabolic acidosis

Decrease of 1 mEq/l in plasma bicarbonate, decreases pCO_2 1.2 mm Hg

Metabolic alkalosis

Increase of 1 mEq/l in plasma bicarbonate, increases pCO_2 0.6 mm Hg

Respiratory acidosis

Acute: each increase of 10 mm Hg in pCO_2 will increase plasma bicarbonate 1 mEq/l

Chronic: each increase of 10 mm Hg in pCO_2 will increase the plasma bicarbonate 3.5 mEq/l

Respiratory alkalosis

Acute: each decrease of 10 mm Hg in pCO_2 will decrease plasma bicarbonate 2 mEq/l

Chronic: each decrease of 10 mm Hg in pCO_2 will decrease plasma bicarbonate 5 mEq/l

How to correct plasma bicarbonate

(24–current plasma bicarbonate) × 50% of body weight = deficit of plasma bicarbonate.
e.g., if body weight is 70 kg and plasma bicarbonate is 14 mEq/l
10 × 35 = 350 mEq of total bicarbonate deficit.

Relation between plasma calcium and albumin

Every 1 g/dl decrement in plasma albumin will decrease plasma calcium 0.8 mg/dl.

Calories

1 gram of carbohydrates = 4 calories
1 gram of proteins = 4 calories
1 gram of lipids = 9 calories