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LECTURER

ICON

Acute tubular necrosis

1. Introduction

Acute tubular necrosis is a kidney disorder involving damage to the tubule cells of the kidneys, which can lead to acute kidney failure. Tubular cells continually replace themselves and if the cause of ATN is removed then recovery is likely. ATN presents with acute renal failure (ARF) and is one of the most common causes of ARF. Acute tubular necrosis (ATN) is the most common cause of acute kidney injury (AKI) in the renal category. AKI is commonly defined as an abrupt decline in renal function, manifested by acute elevation in plasma blood urea nitrogen (BUN) and serum creatinine, occurring in hours to days to weeks, and usually reversible. Acute tubular necrosis (ATN) is usually caused by lack of oxygen to the kidney tissues (ischemia of the kidneys). It may also occur if the kidney cells are damaged by a poison or harmful substance.

2. Definition

It is a medical condition involving the death of tubular cells that form the tubule that transports urine to the ureters while reabsorbing 99% of the water (and highly concentrating the salts and metabolic byproducts).

3. Risk factors and incidence

Acute kidney injury (AKI) is observed in about 5% of all hospital admissions and in up to 30% of patients admitted to the intensive care unit (ICU). ATN is the most common cause of AKI in the renal category, and the second most common cause of all categories of AKI in hospitalized patients, with only prerenal azotemia occurring more frequently. Risk factors for ATN include

- ♣ Pre-existing liver disease
- ♣ Pre-existing renal disease
- ♣ Concomitant use of other nephrotoxins [eg, amphotericin B, radiocontrast media, cisplatin]
- ♣ Advanced age
- ♣ Shock
- ♣ Female sex

- ♣ A higher aminoglycoside level 1 hour after dose
- ♣ Blood transfusion reaction
- ♣ Injury or trauma that damages the muscles
- ♣ Low blood pressure (hypotension) that lasts longer than 30 minutes
- ♣ Recent major surgery
- ♣ Septic shock due to severe infection

4. Classification

It may be classified as either toxic or ischemic. Toxic ATN occurs when the tubular cells are exposed to a toxic substance (nephrotoxic ATN). Ischemic ATN occurs when the tubular cells do not get enough oxygen, a condition that they are highly sensitive and susceptible to, due to their very high metabolism.

4.1 Toxic ATN

Toxic ATN can be caused by free hemoglobin or myoglobin, by medication such as antibiotics such as aminoglycoside and cytoxic drugs such as cisplatin, or by intoxication (ethylene glycol, "anti-freeze").

a) Causes of nephrotoxic acute tubular necrosis

The kidney is a particularly vulnerable target for toxins, both exogenous and endogenous. Not only does it have a rich blood supply, receiving 25% of cardiac output, but it also helps in the excretion of these toxins by glomerular filtration and tubular secretion.

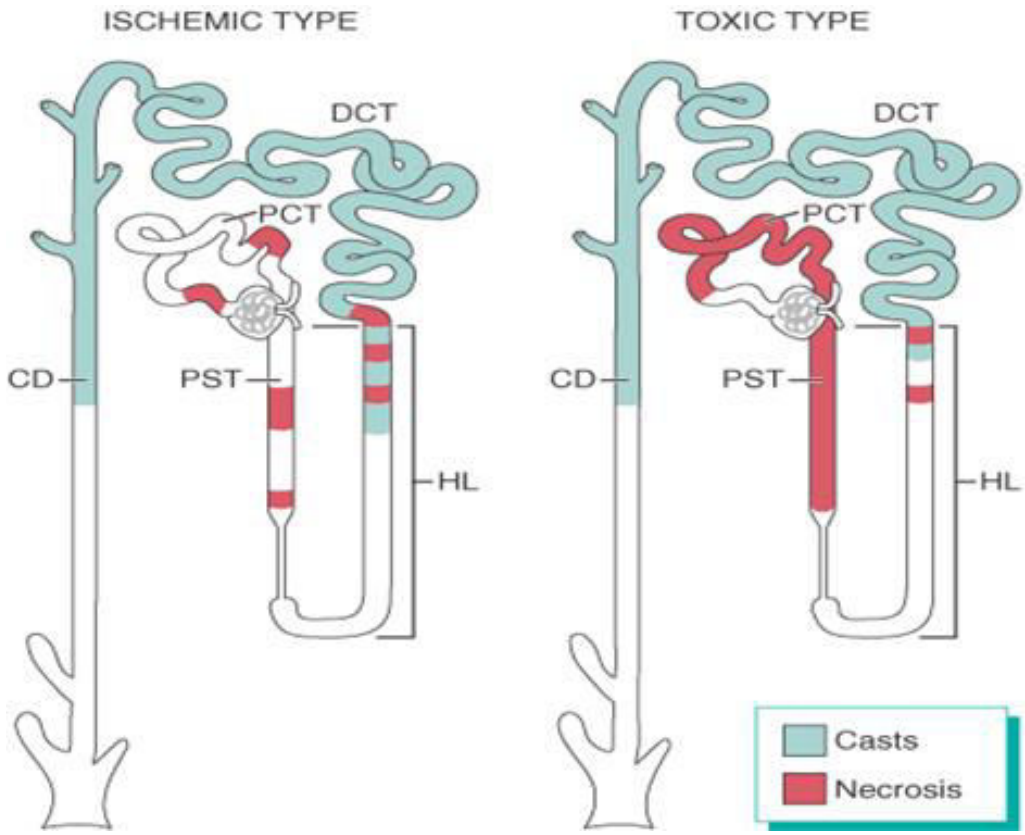
Exogenous nephrotoxins that cause ATN include the following:

- **Aminoglycoside**-related toxicity occurs in 10-30% of patients receiving aminoglycosides, even when blood levels are in apparently therapeutic ranges.; a high trough level has not been shown to be an independent risk factor)
- **Amphotericin B** nephrotoxicity risk factors include male sex, maximum daily dose (nephrotoxicity is more likely to occur if >3 g is administered) and duration of therapy, hospitalization in the critical care unit at the initiation of therapy, and concomitant use of cyclosporine
- **Radiographic contrast** media can cause contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN) (commonly occurs in patients with several risk factors, such as elevated baseline serum creatinine, preexisting renal insufficiency, underlying diabetic nephropathy, congestive heart failure [CHF], or high or repetitive doses of contrast media, as well as volume depletion and concomitant use of diuretics, ACE inhibitors, or ARBs).

- Cyclosporine and tacrolimus (calcineurin inhibitors)
- Cisplatin
- Ifosfamide
- Foscarnet
- Pentamidine, which is used to treat *Pneumocystis carinii* infection in individuals who are immunocompromised (risk factors for nephrotoxicity include volume depletion and concomitant use of other nephrotoxic antibiotic agents, such as aminoglycosides, which is common practice in the immunosuppressed)
- Sulfa drugs, acyclovir, and indinavir

Endogenous nephrotoxins that cause ATN include the following:

- In, **myoglobinuria, rhabdomyolysis** is the most common cause of heme-pigment associated AKI and can be caused by traumatic or nontraumatic injuries
- In **hemoglobinuria**, AKI is a rare complication of hemolysis and hemoglobinuria, and most often, it is associated with transfusion reactions
- **Acute crystal-induced nephropathy** occurs when crystals are generated endogenously due to high cellular turnover (ie, uric acid, calcium phosphate), as observed in certain malignancies or the treatment of malignancies, but this condition is also associated with ingestion of certain toxic substances (eg, ethylene glycol) or nontoxic substances (eg, vitamin C).
- **Multiple myeloma**



4.2 Ischemic ATN

Ischemic ATN can be caused when the kidneys are not sufficiently perfused for a long period of time (i.e. renal artery stenosis) or during shock. Hypoperfusion can also be caused by embolism of the renal arteries. Ischemic ATN specifically causes *skip lesions* through the tubules.

a) Causes of ischemic acute tubular necrosis

Ischemic ATN may be considered part of the spectrum of prerenal azotemia, and indeed, ischemic ATN and prerenal azotemia have the same causes and risk factors. Specifically, these include the following:

- **Hypovolemic states**: hemorrhage, volume depletion from gastrointestinal (GI) or renal losses, burns, fluid sequestration
- **Low cardiac output states**: heart failure and other diseases of myocardium, valvulopathy, arrhythmia, pericardial diseases, tamponade
- **Systemic vasodilation**: sepsis, anaphylaxis
- Disseminated intravascular coagulation

- **Renal vasoconstriction**: cyclosporine, amphotericin B, norepinephrine, epinephrine, hypercalcemia
- **Impaired renal autoregulatory responses**: cyclooxygenase (COX) inhibitors, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs)

5. Pathophysiology

Acute tubular necrosis (ATN) follows a well-defined 3-part sequence of initiation, maintenance, and recovery. The tubule cell damage and cell death that characterize acute tubular necrosis usually result from an acute ischemic or toxic event. Most of the pathophysiologic features of ischemic ATN, as described below, are shared by the nephrotoxic forms.

Initiation phase

Ischemic ATN is often described as a continuum of prerenal azotemia. Indeed, the causes of the 2 conditions are the same. Ischemic ATN results when hypoperfusion overwhelms the kidney's autoregulatory defenses. Under these conditions, hypoperfusion initiates cell injury that often, but not always, leads to cell death.

Injury of tubular cells is most prominent in the straight portion of the proximal tubules and in the thick ascending limb of the loop of Henle, especially as it dips into the relatively hypoxic medulla. The reduction in the glomerular filtration rate (GFR) that occurs from ischemic injury is a result not only of reduced filtration due to hypoperfusion but also of casts and debris obstructing the tubule lumen, causing back-leak of filtrate through the damaged epithelium (ie, ineffective filtration).

The earliest changes in the proximal tubular cells are apical blebs and loss of the brush border membrane followed by a loss of polarity and integrity of the tight junctions. This loss of epithelial cell barrier can result in the above-mentioned back-leak of filtrate.

Another change is relocation of Na^+/K^+ -ATPase pumps and integrins to the apical membrane. Cell death occurs by both necrosis and apoptosis. Sloughing of live and dead cells occurs, leading to cast formation and obstruction of the tubular lumen

In addition, ischemia leads to decreased production of vasodilators (ie, nitric oxide, prostacyclin [prostaglandin I_2, or PGI_2]) by the tubular epithelial cells, leading to further vasoconstriction and hypoperfusion.

On a cellular level, ischemia causes depletion of adenosine triphosphate (ATP), an increase in cytosolic calcium, free radical formation, metabolism of membrane phospholipids, and abnormalities in cell volume regulation. The decrease or depletion of ATP leads to many problems with cellular function, not the least of which is active membrane transport.

With ineffective membrane transport, cell volume and electrolyte regulation are disrupted, leading to cell swelling and intracellular accumulation of sodium and calcium. Typically, phospholipid metabolism is altered, and membrane lipids undergo peroxidation. In addition, free radical formation is increased, producing toxic effects. Damage inflicted by free radicals apparently is most severe during reperfusion.

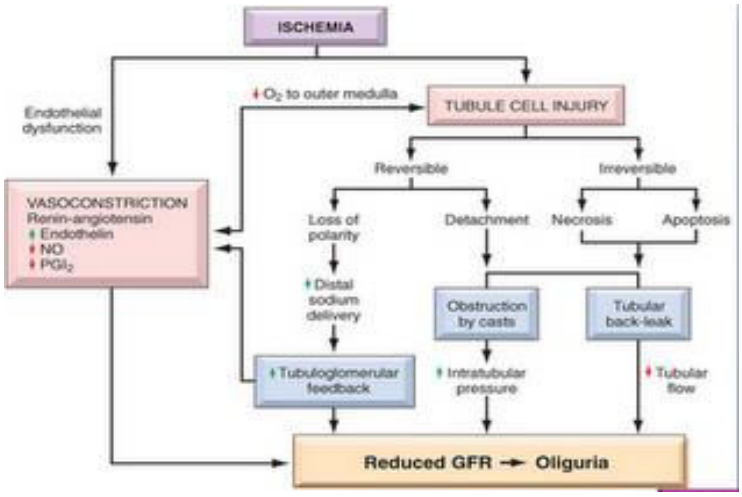
Maintenance phase

The maintenance phase of ATN is characterized by a stabilization of GFR at a very low level, and it typically lasts 1-2 weeks. Complications (eg, uremic and others) typically develop during this phase.

The mechanisms of injury described above may contribute to continued nephron dysfunction, but tubuloglomerular feedback also plays a role. Tubuloglomerular feedback in this setting leads to constriction of afferent arterioles by the macula densa cells, which detect an increased salt load in the distal tubules.

Recovery phase

The recovery phase of ATN is characterized by regeneration of tubular epithelial cells. During recovery, an abnormal diuresis sometimes occurs, causing salt and water loss and volume depletion. The mechanism of the diuresis is not completely understood, but it may in part be due to the delayed recovery of tubular cell function in the setting of increased glomerular filtration. In addition, continued use of diuretics (often administered during initiation and maintenance phases) may also add to the problem.



6. Clinical manifestations

- Decreased consciousness

- Coma
- Delirium or confusion
- Drowsy, lethargic, hard to arouse

- Decreased urine output or no urine output
- General swelling, fluid retention
- Nausea, vomiting

7. Diagnostic investigations

- ♣ History collection
- ♣ Physical examination
- ♣ Kidney biopsy
- ♣ Laboratory investigations which includes

- BUN and serum creatinine
- Fractional excretion of sodium
- Urinalysis
- Urine sodium
- Urine specific gravity and osmolarity urine

8. Treatment

In most people, ATN is reversible. The goal of treatment is to prevent life-threatening complications of acute kidney failure. Treatment focuses on preventing the excess build-up of fluids and wastes, while allowing the kidneys to heal. Patients should be watched closely for deterioration of kidney function.

Treatment can include:

- Identifying and treating the underlying cause of the problem
- Restricting fluid intake to a volume equal to the volume of urine produced
- Restricting substances normally removed by the kidneys (such as protein, sodium, potassium) to minimize their buildup in the body
- Taking medications to help control potassium levels in the bloodstream
- Medicines taken by mouth or through an IV to help remove fluid from the body

a) Medical management

Temporary dialysis can remove excess waste and fluids. This can make you feel better, and may make the kidney failure easier to control. Overall, medical management includes maintaining fluid balance, avoiding fluid excesses, or possibly performing dialysis.
Maintenance of fluid balance is based on daily body weight,
Serial measurements of central venous pressure

Serum and urine concentrations, fluid losses, blood pressure, and the clinical status of the patient. The parenteral and oral intake and the output of urine, gastric drainage, stools, wound drainage, and perspiration are calculated and are used as the basis for fluid replacement. The insensible fluid lost through the skin and lungs and produced through the normal metabolic processes is also considered in fluid management. Dialysis may not be necessary for all people, but is often lifesaving, especially if serum potassium is dangerously high.

Dialysis may be needed in the following cases:

- Decreased mental status
- Fluid overload
- Increased potassium levels
- Pericarditis
- To remove toxins that are dangerous to the kidneys
- Total lack of urine production
- Uncontrolled buildup of nitrogen waste products

Pharmacologic Therapy

- Because hyperkalemia is the most life-threatening of the fluid and electrolyte disturbances, the patient is monitored for hyperkalemia through serial serum electrolyte levels (potassium value more than 5.5 mEq/L [5.5 mmol/L]), electrocardiogram changes (tall, tented, or peaked T waves), and changes in clinical status.
- The elevated potassium levels may be reduced by administering cation-exchange resins (sodium polystyrene sulfonate [Kayexalate]) orally or by retention enema. Kayexalate works by exchanging a sodium ion for a potassium ion in the intestinal tract. Sorbitol is often administered in combination with Kayexalate to induce a diarrhea-type effect (it induces water loss in the GI tract).
- If a retention enema is administered (the colon is the major site for potassium exchange), a rectal catheter with a balloon may be used to facilitate retention if necessary. The patient should retain the resin 30 to 45 minutes to promote potassium removal.
- Afterward, a cleansing enema may be prescribed to remove the Kayexalate resin as a precaution against fecal impaction.

b) Nursing Management

- The nurse has an important role in caring for the patient with ARF. In addition to directing attention to the patient's primary disorder (which may be a factor in the development of ARF), the nurse monitors for complications, participates in emergency treatment of fluid and electrolyte imbalances, assesses progress and response to treatment, and provides physical and emotional support.

- Additionally, the nurse keeps family members informed about the patient's condition, helps them understand the treatments, and provides psychological support. Although the development of ARF may be the most serious problem, the nurse must continue to include in the plan of care those nursing measures indicated for the primary disorder (eg, burns, shock, trauma, obstruction of the urinary tract).

Monitoring Fluid And Electrolyte Balance

- Because of the serious fluid and electrolyte imbalances that can occur with ARF, the nurse monitors the patient's serum electrolyte levels and physical indicators of these complications during all phases of the disorder. Hyperkalemia is the most immediate life threatening imbalance seen in ARF. Parenteral fluids, all oral intake, and all medications are screened carefully to ensure that hidden sources of potassium are not inadvertently administered or consumed. Intravenous solutions must be carefully selected according to the patient's fluid and electrolyte status. The patient's cardiac function and musculoskeletal status are monitored closely for signs of hyperkalemia.
- The nurse monitors fluid status by paying careful attention to fluid intake (intravenous medications should be administered in the smallest volume possible), urine output, apparent edema, distention of the jugular veins, alterations in heart sounds and breath sounds, and increasing difficulty in breathing. Accurate daily weights, as well as intake and output records, are essential.
- Indicators of deteriorating fluid and electrolyte status are reported immediately to the physician, and preparation is made for emergency treatment. Hyperkalemia is treated with glucose and insulin, calcium gluconate, cation-exchange resins (Kayexalate), or dialysis. Fluid and other electrolyte disturbances are often treated with hemodialysis, peritoneal dialysis, or other continuous renal replacement therapies.

Reducing Metabolic Rate

- The nurse also directs attention to reducing the patient's metabolic rate during the acute stage of renal failure to reduce catabolism and the subsequent release of potassium and accumulation of endogenous waste products (urea and creatinine). Bed rest may be indicated to reduce exertion and the metabolic rate during the most acute stage of the disorder. Fever and infection, both of which increase the metabolic rate and catabolism, are prevented or treated promptly.

Promoting Pulmonary Function

- Attention is given to pulmonary function, and the patient is assisted to turn, cough, and take deep breaths frequently to prevent atelectasis and respiratory tract infection. Drowsiness and lethargy may prevent the patient from moving and turning without encouragement and assistance.

Preventing Infection

- Asepsis is essential with invasive lines and catheters to minimize the risk of infection and increased metabolism. An indwelling urinary catheter is avoided whenever possible because of the high risk for UTI associated with its use.

Providing Skin Care

- The skin may be dry or susceptible to breakdown as a result of edema; therefore, meticulous skin care is important. Additionally, excoriation and itching of the skin may result from the deposit of irritating toxins in the patient's tissues. Massaging bony prominences, turning the patient frequently, and bathing the patient with cool water are often comforting and prevent skin breakdown.

Nursing Diagnosis: Excess fluid volume related to decreased urine output, dietary excesses, and retention of sodium and water

Goal: Maintenance of ideal body weight without excess fluid

Nursing Interventions

1. Assess fluid status:
a. Daily weight
b. Intake and output balance
c. Skin turgor and presence of edema
d. Distention of neck veins
e. Blood pressure, pulse rate, and rhythm
f. Respiratory rate and effort
2. Limit fluid intake to prescribed volume.
3. Identify potential sources of fluid:
a. Medications and fluids used to take medications: oral and intravenous
b. Foods
4. Explain to patient and family rationale for restriction.
5. Assist patient to cope with the discomforts resulting from fluid restriction.
6. Provide or encourage frequent oral hygiene as it minimizes dryness of oral mucous membranes.

Nursing Diagnosis: Imbalanced nutrition; less than body requirements related to anorexia, nausea, vomiting, dietary restrictions, and altered oral mucous membranes

Goal: Maintenance of adequate nutritional intake

1. Assess nutritional status:
a. Weight changes
b. Laboratory values (serum electrolyte, BUN, creatinine, protein, transferrin, and iron levels)
2. Assess patient's nutritional dietary patterns:
a. Diet history
b. Food preferences
c. Calorie counts
3. Assess for factors contributing to altered nutritional intake:
a. Anorexia, nausea, or vomiting
b. Diet unpalatable to patient
c. Depression

d. Lack of understanding of dietary restrictions
e. Stomatitis
4. Provide patient's food preferences within dietary restrictions.
5. Promote intake of high biologic value protein foods: eggs, dairy products, meats.
6. Encourage high-calorie, low-protein, low-sodium, and low-potassium snacks between meals.
7. Alter schedule of medications so that they are not given immediately before meals.
8. Explain rationale for dietary restrictions and relationship to kidney disease and increased urea and creatinine levels.
9. Provide written lists of foods allowed and suggestions for improving their taste without use of sodium or potassium.
10. Provide pleasant surroundings at meal-times.
11. Weigh patient daily.
12. Assess for evidence of inadequate protein intake:
a. Edema formation
b. Delayed healing
c. Decreased serum albumin levels
7. Ingestion of medications just before meals may produce anorexia and feeling of fullness.
8. Promotes patient understanding of relationships between diet and urea and creatinine level to renal disease.
9. Lists provide a positive approach to dietary restrictions and a reference for patient and family to use when at home.
10. Unpleasant factors that contribute to patient's anorexia are eliminated.
11. Allows monitoring of fluid and nutritional status.
12. Inadequate protein intake can lead to decreased albumin and other proteins, edema formation, and delay in healing.
Nursing Diagnosis: Deficient knowledge regarding condition and treatment
Goal: Increased knowledge about condition and related treatment
1. Assess understanding of cause of renal failure, consequences of renal failure, and its treatment:
a. Cause of patient's renal failure
b. Meaning of renal failure
c. Understanding of renal function
d. Relationship of fluid and dietary restrictions to renal failure
e. Rationale for treatment (hemodialysis, peritoneal dialysis, transplantation)
2. Provide explanation of renal function and consequences of renal failure at patient's level of understanding and guided by patient's readiness to learn.
3. Assist patient to identify ways to incorporate changes related to illness and its treatment into lifestyle.

4. Provide oral and written information as appropriate about:
a. Renal function and failure
b. Fluid and dietary restrictions
c. Medications
d. Reportable problems, signs, and symptoms
e. Follow-up schedule
f. Community resources
g. Treatment options

9. Prognosis

The patient may make less urine for a few days to 6 weeks or more. This may be followed by a period of high urine output. This occurs because the healed and newly functioning kidneys try to clear the body of fluid and wastes. One or two days after your urine amount rises, symptoms reduce and test results begin to return to normal.

10. Complications

- Bleeding from the gastrointestinal tract
- Chronic kidney disease and permanent kidney damage
- High blood pressure
- Fluid and electrolyte imbalances
- Uremia,
- Anemia.
- Increased risk of infection

11. **Prevention**

Promptly treating conditions that can lead to decreased blood flow and/or decreased oxygen to the kidneys can reduce the risk of acute tubular necrosis.

Blood transfusions are crossmatched to reduce the risk of incompatibility reactions.

Control conditions such as diabetes, liver disorders, and cardiac disorders to reduce the risk of acute tubular necrosis.

Carefully monitor exposure to medications that can be toxic to the kidney. Have your blood levels of these medications checked regularly. Drink a lot of fluids after having any radiocontrast dyes to allow them to be removed from the body and reduce the risk of kidney damage.

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