Acute renal failure (ARF) is responsible for 5% of emergency hospitalization cases. ARF is classified into prerenal, intrinsic, or postrenal, depending on etiology. Prerenal ARF is the most common type. Etiology is determined through a systematic approach involving blood tests, urine tests, and abdominal ultrasonography. Treatment focuses on supportive therapy based on fluid and electrolyte replacement to reduce waste accumulation and sustain nutrition.

Definition of Acute Renal Insult

The 3 Criteria for Defining Acute Renal Insult

According to Kidney Disease Improving Global Outcomes (KDIGO), ARF is defined by one of the following 3 criteria:
Increase in creatinine serum level of more than 0.3 mg/dl (within 48 hours)

- Increase in creatinine serum level by more than 50% (within the prior 7 days)
- Decrease in urine volume (oliguria) to less than 0.5 ml/kg body weight/hour for 6 hours

Although oliguria or anuria is considered the preeminent symptom of ARF, many patients also present with polyuria or normuria (see below). In these cases, the measurement of creatinine serum levels (especially over the course of the illness) may provide the only indication of ARF and become undergoing dialysis.

Epidemiology of Acute Renal Insult

Acute Renal Failure as a Common Disease

ARF is a relatively common disease, with an incidence of 2,000—3,000 million inhabitants. Older people and toddlers are particularly susceptible, as they can dehydrate quickly when experiencing acute water loss (e.g., due to infections or heavy sweating). Patients in intensive care can also develop the disease, as kidney problems in this unit are frequent; approximately about 5% of all intensive care patients suffer from ARF.

Etiology and Pathophysiology of Acute Renal Insult

Causes of Acute Renal Insult

Because of various pathophysiologic processes, kidney function can diminish rapidly. As a consequence, uremic substances accumulate and alter water, electrolyte, and acid-base balances. Usually, this loss of function is reversible, as long as the underlying cause or structural processes do not become chronic.

Types of Acute Renal Insult

Etiologically, ARF can be subdivided into 3 types. Each type encompasses different pathophysiological processes, so understanding the type of ARF presenting in a patient is crucial to identifying the choice of treatment:

- Prerenal ARF
- Intrinsic ARF
- Postrenal ARF

Prerenal ARF (about 60 % of all cases)
Prerenal ARF is the result of reduced renal perfusion, with the glomerular and tubular structures initially being completely intact. It may be caused by actual hypovolemia (e.g., due to exsiccosis, diarrhea, or pancreatitis), but also relative hypovolemia stemming from e.g., cardiac insufficiency, shock, or sepsis. Prerenal ARF may lead to a reduction in renal perfusion. Diseases that cause renal vasoconstriction may result also in prerenal failure. Hepatorenal syndrome is evident.

Through the regulation mechanisms of the kidney, reduced perfusion activates the renin-angiotensin-aldosterone system (RAAS). At the same time, the body experiences a release of catecholamine and ADH. This reaction is a vasoconstriction with simultaneous retention of sodium and water in order to compensate for the hypovolemic condition.

In the case of exsiccosis, these reactions are appropriate. However, in the presence of cardiac insufficiency, actual reduced perfusion does not involve a lack of water. Clinically, signs of hyperhydration predominate. The activation of RAAS erroneously increases the intracorporeal water concentration, and hyperhydration increases. If diuretics are administered in this situation, renal perfusion will be reduced even more, increasing the risk of ischemia and intrinsic renal failure.

**Intrinsic Renal Insult (about 35 % of all cases)**

Acute damage to the glomeruli or tubular cells leads to structural damage of the kidney itself. Usually, an acute tubular necrosis brought about by, e.g., different (micro- and macroangiopathic) ischemic processes such as thromboembolism or a thrombotic microangiopathy will occur. Gomerulonephritides may also lead to reduced kidney function.

Toxic damage, especially iatrogenic damages, are frequent. Contrast agents or other medications play an important role here. In addition, myoglobinuria due to rhabdomyolysis, hemoglobinuria due to hemolysis, or uric acid salts due to gout or tumor lysis are potential causes.

A number of frequently administered drugs can also cause damage to the kidneys, including nonsteroidal anti-inflammatory drugs, aminoglycosides, cephalosporin, vancomycin, amphotericin B, cisplatin, methotrexate, cyclosporine, diuretics, X-ray contrast agents, and angiotensin-converting-enzyme inhibitors.

The renal tubules are responsible for reabsorption. If an intrinsic renal dysfunction affects the tubules, this may cause severe polyuria as part of ARF.

If sodium reabsorption is diminished because of damage to the tubular cells, the tubuloglomerular feedback mechanism causes constriction of the afferent glomerular arteriole. This in turn leads to a reduction in the glomerular filtration rate.

**Postrenal Insult (about 5 % of all cases)**

Any disease with the potential to impair the drainage of urine from the kidneys can lead to urinary retention with subsequent postrenal failure. Congenital malformations of the
Clinical Presentation and Symptoms of Acute Renal Insult

Clinical Manifestation of Acute Renal Insult

The clinical manifestation of ARF is very diverse and largely depends on a persistent underlying disease. The clinical course of the disease can be divided into three stages:

1. **Initiating stage:** Before ARF manifests, it is mostly asymptomatic. Possible symptoms of an underlying disease predominate.

2. **Oliguric stage:** The preeminent symptom of ARF is oliguria or anuria. It leads to corporeal hyperhydration with a number of complications, including hypertension, pulmonary edema, pleural effusion, left ventricular heart failure, ascites, cerebral edema, and more. A consequence of urinary retention may be hyperkalemia with acidosis. However, as noted above, there are many normuric or polyuric stages.

3. **Diuretic or polyuric stage:** Usually, the glomeruli recover faster than the tubular system, which means that during recovery, reabsorption may remain disturbed while the filtration capacity of the kidney begins to function again.

Depending on what is causing the ARF, side pain, fever, fatigue, and symptoms relating to complications (see below) may also be present.

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**Picture:** "Renal Symptoms of Renal Failure" by Maen K. Househ. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

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Complications of Acute Renal Insult

Possible Complications with Acute Renal Insult

Complications are due to the above-noted pathophysiological processes. Many organ systems may be affected:

- The lungs can be affected by hyperhydration, including edema and effusion. Acute respiratory distress syndrome may occur.
- Heart failure may develop due to hypertension or hyperhydration, or arrhythmias may develop due to imbalanced electrolyte concentrations.
- If heart failure occurs, there is a risk of congestion in the venous circuit causing gastritis, ulcerations, or gastrointestinal bleeding. The stress-associated release of hormones can increase the likelihood of gastrointestinal bleeding.
- Seizures may occur due to a cerebral edema or electrolyte imbalance. In addition, vigilance can be impaired.

Diagnosis of Acute Renal Insult

Laboratory Diagnosis and Medical History

Diagnosis of ARF is based on a focused medical history with a corresponding clinical presentation and determination of the diuretic level. Laboratory tests should include urinalysis. Retention parameters can be measured in the blood, especially electrolyte concentrations, which should be checked regularly. Depending on the underlying condition, lab tests can provide valuable information.

<table>
<thead>
<tr>
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<tr>
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Table: “Laboratory evaluations used to diagnose acute kidney injury” by Rajitbasu.
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Determining the Fractional Sodium Excretion in Acute
Renal **Insult**

The determination of fractional sodium excretion is an important finding. Fractional sodium excretion is based on the clearance of sodium in relation to the clearance of creatinine. The results of this test help distinguish between a prerenal and an intrinsic ARF. It is based on the following assumptions:

1. In prerenal ARF, the tubular system is still functioning and hypovolemia is counteracted by increased reabsorption. This results in concentrated urine with low sodium content. Fractional sodium excretion < 1%.
2. In intrinsic ARF with acute tubular necrosis, tubular function is impaired and deficient reabsorption results in diluted urine with high sodium content. Fractional sodium excretion > 1%.

Other Examination Methods for Acute Renal Failure

Imaging techniques can also provide useful additional information or a differential diagnosis. Sonography can be used to detect enlarged kidneys and confirm a diagnosis of ARF; in contrast, small, thin, hyperechoic kidneys may indicate chronic renal failure.

An enlarged renal pelvis may indicate urinary obstruction related to postrenal ARF. Magnetic resonance imaging and computed tomography scans are particularly suited to the more specific assessment of structural lesions (tumors, thrombosis, and perfusion dysfunctions).

For a definitive diagnosis of glomerulonephritis, a percutaneous kidney biopsy is indispensable.

**Differential Diagnosis of Acute Renal Insult**

Differential diagnosis is mostly concerned with diagnosing the type of ARF. Medical history, premedication, and pretreatment are especially useful here. Chronic renal failure needs to be excluded.

An important differential diagnosis is functional oliguria. This disorder may occur after a long period of time without water and is usually accompanied by a barely increased creatinine level; functional oliguria can eventually lead to ARF.

**Treatment of Acute Renal Insult**

**Substitution of Fluids and Electrolytes for Acute Renal Insult of Prerenal Genesis**

In prerenal ARF, kidney function can only recover when the underlying pathophysiological mechanism has been eliminated. Nephrotoxic substances should be avoided, and fluid and electrolyte balances must be thoroughly controlled and treated.

The reason for the hypoperfusion must be uncovered and then treated. The administration of fluids and electrolytes is a prudent option. Loop diuretics can also be helpful in maintaining diuresis. (Note that while this medication measurably increases diuresis, it does not increase glomerular filtration or have any impact on the recovery of kidney function.)
Patients with sepsis or with severe heart failure often require treatment in the intensive care unit.

**Immunosuppressive Therapy and Revascularization for Acute Renal Failure of Intrinsic Genesis**

In intrinsic AFI, it is important to first treat the underlying disease. Immunosuppressive treatment is advisable for glomerulonephritis, and revascularization for ischemia.

For raising diuresis, loop diuretics can be administered; however, the use of diuretics is controversial and therefore not generally recommended. The only absolute indication for the administration of diuretics is hyperhydration.

**Treatment of Acute Renal Insult of Postrenal Genesis**

In cases of postrenal ARF, it is imperative to remove the urinary obstruction. If this is not immediately possible, the surgical insertion of an artificial excretory opening (percutaneous nephrostomy) is indicated.

**Extracorporeal Treatment of Acute Renal Failure**

Extracorporeal treatment with hemodialysis or hemofiltration for electrolyte imbalances, water overloads, or acid-base imbalances can also be attempted. This type of renal replacement therapy should be considered only as a temporary measure, and limited accordingly. If kidney function cannot be restored sufficiently, permanent dialysis may become necessary.
This type of renal replacement therapy should be considered only as a temporary measure which must be limited accordingly. If the kidney function cannot be restored sufficiently, permanent dialysis might become necessary.
Prognosis of Acute Renal Insult

Despite the progress that has been made in treating ARF in intensive care units, it is a dangerous disease with a high mortality rate, at approximately 60%. This high rate can often be explained by a serious underlying disease or, sometimes, severe and systemic complications.

Review Questions

The answers are below the references.

1. Which of the following findings is the least likely to be found in the anuric stage of acute renal insult?
   
   A. Pleural effusions
   B. Hyperkalemia
   C. Increased vulnerability to infections
   D. Combined respiratory and metabolic alkalosis
   E. Stress-related ulcers and bleeding in the upper gastrointestinal tract

2. You work in the emergency room. Your next patient supposedly has an acute renal failure. Before you examine the patient, you go over the three different types of acute renal failure and remind yourself which diagnostic criteria distinguish an intrinsic renal insult from a prerenal failure. In patients with intrinsic renal failure, ...

   A. Fractional sodium excretion is increased.
   B. Urine osmolarity is increased.
C. Fractional sodium excretion is decreased.
D. A massively increased proteinuria is typical.
E. Doppler sonography is the most reliable diagnostic method.

3. One week ago, you started working in trauma surgery. Your currently assigned patient is a young extreme athlete who went rock climbing and got stuck in a crevice. He suffered a severe bruising of both thighs. About 2 days after he has been admitted to the hospital, his creatinine level rises extremely. Your patient reports that he hardly ever has to “pee” anymore. You don't want to seem incompetent and scared, so you first think of what might be wrong with your patient before requesting an internist consult. Your patient...

A. Likely suffers from postrenal ARF.
B. Likely suffers from irreversible ARF.
C. Likely has rhabdomyolysis with intrinsic ARF.
D. Should have decreasing potassium levels in his serum.
E. Will probably not develop any further complications.

References


Correct answers: 1D, 2A, 3C

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