No matter in which clinical field you will be working in the future, you will be confronted with cases of acute renal failure. In this acute emergency illness, various pathomechanisms come together and lead to a principally reversible decrease in renal function, often involving disbalances of water and electrolytes. The different types of acute renal failure have to be understood well in order to develop an adequate treatment strategy. This article presents the main aspects of acute renal failure clearly and comprehensively.

**Definition of Acute Renal Failure**

**The 3 Criteria for Defining Acute Renal Failure**

According to the **KDIGO**, acute renal failure is defined by one of the following criteria:
Increase in creatinine serum level by more than 0.3 mg/dl (within 48 hours); or

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

Even tough oliguria or anuria is considered the cardinal symptom of acute renal failure; many patients present with polyuria or normuria (see below). In these cases, the measurement of creatinine serum levels (especially during the course of the illness) may provide the only indication of acute renal failure and become undergoing dialysis.

Epidemiology of Acute Renal Failure

Acute Renal Failure as a Common Disease

Acute renal failure (ARF) is a relatively common disease with an incidence of 2.000—3.000/million inhabitants, especially older people and also toddlers can dehydrate quickly when experiencing acute water loss (e.g., due to infections or heavy sweating) and are then facing the risk of acute renal failure. Also in intensive care, kidney problems are frequent, and about 5 % of all intensive care patients suffer acute renal failure.

Etiology and Pathophysiology of Acute Renal Failure

Causes of Acute Renal Failure

Because of various pathophysiologic processes, kidney function can diminish rapidly. As a consequence, uremic substances accumulate and alter the 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 Failure

Etiologically, acute renal failure can be subdivided into 3 types. This subdivision also encompasses different pathophysiological processes, which makes knowing and identifying them essential for the choice of treatment:

- Prerenal ARF
- Intrinsic ARF
Prerenal ARF (about 60 % of all cases)

Prerenal ARF follows from a **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**, a shock, or sepsis and may lead to a reduction of renal perfusion. Also, diseases that cause renal vasoconstriction may result in prerenal failure. In this context, the **hepatorenal syndrome** is noticeable.

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

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

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

Acute damage to the *glomeruli* or *tubular cells* leads to a structural damage of the kidney itself. Most frequently, an acute tubular necrosis brought about by, for instance, different (micro- and macroangiopathic) ischemic processes such as *thromboembolisms* or a *thrombotic microangiopathy*, will be the consequence. Of course, *glomerulonephritides* may also lead to a reduced functioning of the kidney.

Furthermore, toxic damages, 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 *tumorlysis*, are potential causes.

**Note:** The following (frequently administered) drugs can cause relevant damage to (inter alia) the kidney: NSAIDs, aminoglycosides, cephalosporin, vancomycin, amphotericin B, cisplatin, methotrexate, cyclosporine, diuretics, X-ray contrast agents and ACE inhibitors.

If you want to shine in your exams, remember the following: The *renal tubules* are responsible for reabsorption. If an intrinsic renal dysfunction affects mostly the tubules, this may cause severe *polyuria* as part of the acute renal failure.

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

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

All possible diseases that might *impair the drainage of urine from the kidney* can lead to urinary retention with subsequent postrenal failure. Any *congenital malformations* of the urinary tract must be excluded as a cause.

Furthermore, there are various *acquired urinary obstructions*: tumors, gynecological conditions, urinary catheters, outflow obstructions due to medication, prostate enlargement, and ureteric stones.

**Clinical Presentation and Symptoms of Acute Renal Failure**

**Clinical Manifestation of Acute Renal Failure**

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

1. **Initiating stage:** Before the manifestation of actual acute renal failure, it remains
mostly asymptomatic. Possible symptoms of an underlying disease predominate.

2. **Oliguric stage**: The cardinal symptom of ARF is oliguria or anuria. It leads to a corporeal hyperhydration which involves many complications: hypertension, pulmonary edema, pleural effusion, left ventricular heart failure, ascites, cerebral edema, and much more. A consequence of the urinary retention may be hyperkalemia with acidosis. Nevertheless, as mentioned above, there are many normuric or polyuric courses.

3. **Diuretic or polyuric stage**: Usually, the glomeruli recover faster than the tubular system, which means that during the recovery, the reabsorption might be disturbed a while longer, while the filtration capacity of the kidney is already functioning again. This marks the polyuric stage involving the loss of water and electrolytes.

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

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**Complications of Acute Renal Failure**

**Possible Complications with Acute Renal Failure**

Complications follow from the above-mentioned pathophysiological processes. Many organ systems may be affected.

- The **lung** might be affected by hyperhydration, including edema and effusion. ARDS is also possible.
- In the **cardiovascular system**, there might develop a heart insufficiency due
to hypertension or hyperhydration, or arrhythmias due to the imbalanced electrolyte concentrations.

- Because of the heart insufficiency, there is a risk of **congestion in the venous circuit** causing gastritis, ulcerations, or gastrointestinal bleeding. The stress-associated release of hormones increases the tendency for gastrointestinal bleeding.
- **Neurologically**, seizures may occur caused by the cerebral edema or the electrolyte imbalance. In addition, vigilance can be impaired.

## Diagnosis of Acute Renal Failure

### Laboratory Diagnosis and Medical History

The basis of diagnosis is a focused **medical history** with the corresponding **clinical presentation** and determination of the **diuretic level**. Laboratory tests should include urinalysis. **Retention parameters** can be measured in the blood, especially the electrolyte concentrations have to be checked regularly. In accordance with an assumed or manifesting underlying condition, lab tests can provide valuable information.

![Diagram of renal failure indices](Picture: "Laboratory evaluations used to diagnose acute kidney injury" by Rajitbasu. License: CC BY-SA 3.0)

### Determining the Fractional Sodium Excretion in Acute Renal Failure

In clinical practice, the **determination of the fractional sodium excretion** represents an important examination. It is also a popular topic in exams! The fractional sodium excretion is based on the clearance of sodium in relation to the clearance of creatinine.
The results of this test help to distinguish between a prerenal and an intrinsic AFR. It is based on the following assumptions:

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

Other Examination Methods for Acute Renal Failure

Besides these basic diagnostic methods, **imaging techniques** can provide useful additional information (also for differential diagnosis). **Sonography** can be used to detect enlarged kidneys in case of acute renal failure, and a rather small, thinned and hyperechoic kidney in case of a chronic renal disease or failure.

An enlarged renal pelvis points to urinary obstruction related to postrenal AFR. **MRI** and **CT scans** are particularly suited for the more specific assessment of structural lesions (tumors, thrombosis and perfusion dysfunctions).

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

Differential Diagnosis of Acute Renal Failure

Differential diagnosis is mostly concerned with which type of acute renal failure it is. Medical history, premedication, and pretreatment are especially useful here. **Chronic renal failure** must be excluded.

An important differential diagnosis is a **functional oliguria**. This disorder might stem from a long period of thirst and is usually accompanied by a hardly increased **creatinine level**, but also functional oliguria can eventually lead to acute renal failure.

Treatment of Acute Renal Failure

Substitution of Fluids and Electrolytes for Acute Renal Failure of Prerenal Genesis

The kidney function can only recover when the underlying pathophysiological mechanism has been eliminated. As a principle, **nephrotoxic** substances are to be avoided, and the **fluid and electrolyte balances** have to be thoroughly controlled and treated, then the adequate treatment form has to be chosen in accordance with the underlying genesis.

In case of **prerenal genesis**, the reason for the hypoperfusion must be found and treated. Accordingly, the **substitution of fluids and electrolytes** is a suitable option. The administration of **loop diuretics** can be helpful in maintaining diuresis.

Here, it is important to note that while this medication measurably increases **diuresis**, it does not increase the **glomerular filtration**; neither do diuretics have any impact on the recovery of kidney functions.

Patients with sepsis, or with a severe heart insufficiency, often require intensive care
Immunosuppressive Therapy and Revascularization for Acute Renal Failure of Intrinsic Genesis

Also for AFR of intrinsic genesis, the treatment of the underlying disease comes first. Accordingly, an 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 cannot be generally recommended. The only absolute indication for the administration of diuretics is hyperhydration.

Treatment of Acute Renal Failure of Postrenal Genesis

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

Extracorporeal Treatment of Acute Renal Failure

There is always the possibility of an extracorporeal treatment with hemodialysis or hemofiltration for electrolyte imbalances, water overloads, or acid-base imbalances that cannot be compensated any other way or are life-threatening.

Image: “Simplified Hemodialysis Circuit.” by YassineMrabet. License: CC-BY 3.0
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 Failure

Acute renal failure is a dangerous disease with a high mortality; even the progress that have been made in intensive care have not changed this fact. The mortality rate of intensive care patients with acute renal failure is about 60%! This high mortality can often be explained by a serious underlying disease or the often 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 failure?

   A. Pleural effusions
   B. Hyperkalemia
   C. Increased vulnerability to infections
   D. Combined respiratory and metabolic alkalosis
   E. Stress-related ulcers and bleedings in the upper gastrointestinal tract

2. You work at the emergency room. Your next patient supposedly has 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 failure from a prerenal failure. In patients with intrinsic renal failure, ...

A. ...the fractional sodium excretion is increased.  
B. ...the urine osmolarity is increased.  
C. ...the 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 internistic consult. Your patient...

A. ...probably suffers from postrenal failure.  
B. ...suffers from irreversible renal failure.  
C. ...probably has a rhabdomyolysis with acute intrinsic renal failure.  
D. ...should have decreasing potassium levels in his serum.  
E. ...will probably not develop any further complications.

References

Bienholz, A., Kribben, A., Leitlinien der KDIGO in der deutschen Übersetzung zum akuten Nierenversagen, Nephrologe 2013  

Herold, G. und Mitarbeiter, Innere Medizin, 2014  


AMWF Leitlinien akutes Nierenversagen  

Correct answers: 1D, 2A, 3C  

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