Renal insufficiency (failure)
§ 1 Introduction
Urinary system

Kidney
Ureter
Bladder
Urethra
Normal condition: renal blood flow = 20%~30% C.O = 1200 ml/min.
The kidney is the centre of urinary system.
Kidney structure

Nephron (Glomerulus & Tubules)

Renal interstitium

Kidney blood vessels
The **nephron** is the anatomic and functional unit of the **kidney**. It consists of the **glomerulus** and **renal tubule**. Each human kidney has approximately **one million nephrons**.
Figure 22-3. Diagram of the kidney nephron. Water and electrolytes are filtered in the glomerulus and are reabsorbed in the tubular structures. (Chaffee EE, Lytle IM: Basic Physiology and Anatomy, 4th ed. Philadelphia, JB Lippincott, 1980)
The nephron divided into two types
**Types of the Nephron**

- **Cortical nephron**
- **Juxtamedullary nephron**
Blood flow

Cortex: 94%

Medulla: 6%

Blood flow percentages:

Cortex: 85%

Medulla: 15%
Renal function
a. Excretory function
to excrete waste products, drug and toxic substance;

b. Regulatory function
to maintain homeostasis of body fluids, electrolytes and acid-base balance;
Urinary function is finished by the glomerulus and renal tubules.

The glomerular function is to form the original urine by filtration, while reabsorption and secretion are the function of tubules. The terminal urine is determined by the functions of renal tubules.
Excretory function

Filtration function in glomerulus

↓

GFR (125ml/min; 180-200L/d)

↓

Reabsorption and secretion in tubules

↓

Reabsorption of 99% original urine

↓

Urine (1.5~2L / d)

↓

Removal of waste products, drug and toxic substances

Maintenance of water, electrolyte and acid-base balance

Maintenance of volume and composition in urine
c. Endocrine and metabolic function

**Secreting hormone:**
renin, erythropoietin,

**Activated hormone:**
vitamin D, prostaglandin, kallikrein - kinin, ect.,

**Deactivated hormone:**
parathyroid hormone (PTH) and gastrin etc..
Renal failure is a pathological process in which the functions of kidney are severely damaged bilaterally, and thus lead to the accumulation of metabolic products, drugs and poisons, and disorders of water, electrolyte metabolism, acid-base imbalance. And renal endocrine dysfunction.
Causes

a. **Renal diseases (essential):**
   - glomerulonephritis/ pyelonephritis/ acute tubular necrosis / renal tuberculosis / polycystic kidney / renal tumors

b. **Non-renal diseases (secondary):**
   - shock/ heart failure/ hypertension/ arteriosclerosis diabetes/ gout
   - lupus erythematosus/ allergic purpura
   - some drugs/ chemical and biologic poisons/ heavy metals/ urethral calculi/ tumors
Basic pathological taches for renal failure

1. Dysfunction of glomerular filtration
   (1) Decrease of renal blood flow
   (2) Decrease of glomerular effective filtration pressure
   (3) Decrease of glomerular capillary surface area

   They (GFR↓) can lead to oliguria, anuria, azotemia, hyperkalemia, metabolic acidosis, water intoxication.

   (4) Alterations of permeability of glomerular filtration membrane → hematuria and proteinuria.
2. Renal tubular dysfunction

(1) Dysfunction of the proximal convoluted tubules →
renal diabetic urine, amino acid urine, sodium and water retention, renal tubular acidosis etc.

(2) Dysfunction of Henle’s loop →
polyuria, hypotonic or isotonic urine (polyuria/ Hyposthenuria /Isostheuria)

(3) Dysfunction of the distal convoluted tubules and collecting ducts →
disorders of sodium, potassium metabolism and acid-base balance;
determine final quantity and quality of daily urine
3. Renal endocrine dysfunction

(1) Renin-angiotensin-aldosterone system $\uparrow \rightarrow$ Na\(^+\) and water retention, Renal hypertension

(2) Erthropoietin (EPO) $\downarrow \rightarrow$ Renal anemia

(3) 1,25-dihydroxyvitamin D\(_3\) $\downarrow \rightarrow$ Renal osteodystrophy, hypocalcemia

(4) Kallikrein-kinin-prostaglandin-system $\downarrow \rightarrow$ Renal hypertension

(5) Parathyroid hormone and gastrin $\uparrow \rightarrow$ Renal osteodystrophy, digestive ulcer
Regulation of Na and water by the kidney

This is achieved by the mineralocorticoid aldosterone acting on the distal tubule/collecting duct.

- Hypovolaemia
- Reduced renal perfusion
- Juxtaglomerular apparatus
- Renin
- Angiotensinogen → Angiotensin I → Angiotensin II
- Adrenal cortex, Aldosterone
- Distal tubule/collecting duct
- Increased Na\(^+\) and water reabsorption - K\(^+\) loss
The content of renal failure

Acute renal failure (ARF)
Chronic renal failure (CRF)
Uremia
§ 2 Acute Renal Failure (ARF)

1. Concept

ARF is a complex pathophysiologic process and is an important clinical syndrome. It is characterized by sudden decline in renal excretory function over a period and usually associated with oliguria, anuria (partly non-oliguria), Alteration of composition in urine, the clinical manifestations appear azotemia, hyperkalemia, metabolic acidosis and water intoxication.
2. **Classification**

(1) Urine:
   a. **Oliguric type ARF** ( \(< 400 \text{ml/d} \) )
   b. **Non-oliguric type ARF** (dysfunction of concentration urine by renal tubules)

(2) Damage:
   a. **Functional** ARF (Prerenal causes → Renal ischemia)
   b. **Parenchyma** ARF (Acute renal tubule necrosis)

(3) Causes:
   a. **Prerenal** ARF
   b. **Intra**renal ARF
   c. **Post**renal ARF
3. **Causes**

(1) **Prerenal causes** → **Prerenal ARF**

**Renal hypoperfusion** (Blood supply to nephron ↓)

- Cardiac output ↓
- Blood pressure ↓
- Blood volume ↓
- Constriction of kidney blood vessels.

**Prerenal ARF** is divided into two type. Namely, **Functional ARF** and **Parenchyma ARF**. Their clinic manifestations is obviously different.
Alterations of volume and composition in urine

Prerenal causes

Renal perfusion ↓ → GFR ↓

ADH ↑, ADS ↑

Oliguria (<400ml/d) or
Anuria (<100ml/d)
Urinary Na⁺ ↓ (<20mmol/L)
Urine specific gravity ↑ (>1.020)
Urine osmolality ↑ (>400mosm/L)
Ucr / Pcr ↑ (>40:1)
RFI < 1
FE₉₉ < 1
Urine sedimentary assay: (-)

RFI = Urinary Na⁺ / Ucr / Pcr
FE₉₉ = Urinary Na⁺ / blood Na⁺ / Ucr / Pcr
Alteration of volume and composition in urine

Severe renal ischemia

Renal poisoning

→ Renal perfusion ↓

→ GFR ↓

→ ATN

Oliguria, Anuria or

Non-oliguria (≈1000ml/d)

Urinary Na⁺ ↑ (>40mmol/L)

Urine specific gravity ↓ (<1.015)

Urine osmolarity ↓ (<350mOsm/L)

Ucr / Pcr ↓ (<20:1)

RFI > 1

FE_Na > 2

Urine sedimentary assay:
Proteinuria, Cylindruria, Blood urine.
Distinguish of functional ARF and Parenchyma ARF

### Functional ARF
- **Causes**
  - Prerenal causes → ischemia
- **Mechanism**
  - ECBV ↓
  - Renal perfusion ↓
  - ADH ↑
  - ADS ↑
  - GFR ↓
  - Oliguria/anuria

### Parenchyma ARF
- **Intriarenal causes → ATN**
  - (ischemia, toxin)
- **Mechanism**
  - Renal perfusion ↓
  - ATN
  - GFR ↓
  - Oliguria/anuria/non-oliguria

### Treatment
- Improve microcirculation
- Restore renal perfusion

### Prognosis
- Reperfusion in time
- Function restore
- Realize balance between output and infusion
- The course divided into three stages (about 3 months to one year)
- Non-oliguria prognosis good
**Distinguish of functional ARF and Parenchyma ARF**

<table>
<thead>
<tr>
<th>Urine index</th>
<th>Functional ARF</th>
<th>Parenchyma ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td>U. S.G</td>
<td>&gt; 1.020</td>
<td>&lt; 1.015</td>
</tr>
<tr>
<td>Osmolality</td>
<td>&gt; 400 mmol/L</td>
<td>&lt; 350 mmol/L</td>
</tr>
<tr>
<td>Urinary Na⁺</td>
<td>&lt; 20 mmol/L</td>
<td>&gt; 40 mmol/L</td>
</tr>
<tr>
<td>UCr/PCr</td>
<td>&gt; 40 : 1</td>
<td>&lt; 20 : 1</td>
</tr>
<tr>
<td>RFI</td>
<td>&lt; 1</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>FENa⁺</td>
<td>&lt; 1</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Sediment</td>
<td>Bland</td>
<td>proteinurine, cast of RBC/ WBC/ epithelial cell/granular</td>
</tr>
<tr>
<td>Diuretic effect of</td>
<td>good</td>
<td>worse</td>
</tr>
<tr>
<td>mannitol</td>
<td></td>
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</tr>
</tbody>
</table>

\[
\text{Una}^+ = \frac{\text{(RFI)}}{\text{UCr/PCr}}
\]

\[
\text{(FENa)} = \frac{\text{Una}^+/\text{Pna}^+}{\text{UCr/PCr}} \times 100
\]
(2) Intrarenal causes (intrinsic renal injury)

→ Intrarenal ARF

Injury of renal tissue itself (glomerulus, tubules, blood vessels)

1) Diseases of glomerulus --- Acute streptococcal glomerulonephritis

2) Acute tubular necrosis (ATN) --- Severe renal ischemia, Renal poisoning (Heavy metals, Insecticide, Poisonous mushrooms, Carbon tetrachloride)

A number of chemical agents can selectively and critically destroy renal tubular cells.

3) Renal vessel injury --- Embolism of renal artery, DIC

4) Renal interstitial injury --- Acute interstitial nephritis, Bilateral pyelonephritis
Postrenal causes → Postrenal ARF

Obstructive disorders in urinary tract---bladder stone, prostate, tumor, Blood clots, Scarring of injury or surgery.
Acute renal failure

Prerenal causes

Tubular necrosis

Ischemia (50% of cases)

Intrinsic causes

Interstitial nephritis (10% of cases)

Toxins (35% of cases)

Postrenal causes

Acute glomerulonephritis (5% of cases)
3. Pathogenesis of ARF

1. Renal hemodynamic alterations (Vasomotor theory) → GFR↓↓↓↓ (key)

(1) Decrease of renal perfusion pressure → GFR↓
   Arterial blood pressure ↓ → Decrease of renal perfusion pressure

(2) Renal vasoconstriction → GFR↓
   Renin-angiotensin system ↑ → AT II ↑
   Sympathetic adrenomedullary system ↑ → Catecholamine ↑,
   Prostacyclin ↓, Endothelin (ET) ↑, Nitric oxide (NO) ↓,
(3) Renal vascular **endothelial swelling** → GFR↓
   a. Renal ischemia → failure of Na\(^+\)-K\(^+\)-ATPase
   b. Ischemia/reperfusion → oxygen free radical↑
These cause renal vascular endothelial swelling and capillary luminal narrow.

(4) Intrarenal disseminated intravascular coagulation (DIC) → GFR↓
Hemodynamic and hemorheological alteration
   a. increased blood viscosity
   b. decreased transformable ability
   c. platelets activated
   d. adhibition and wedge of leucocytes
2. Renal glomerular injury

Acute glomerulonephritis, lupus nephritis → glomerular membrane damage → filtration area ↓
→ GFR ↓
3. **Renal tubular injury**

1. Renal tubular occlusion (**Tubule obstruction theory**)


3. Tubuloglomerular feedback (imbalance)
4. **Renal cell injury**

Except ATN, it contains endothelial, mesangial cells etc.

**Mechanisms:**

1. Reduction of ATP synthesis and **dysfunction** of ion pumps
2. Increase of oxygen free radical
3. Decrease of reduced glutathione
4. Increased **activity** of phospholipases
5. Cytoskeletal structural changes
Renal ischemia / renal poisons

\[ \downarrow \]

RAS↑ ET↑; NO↓ PGE2↓

\[ \downarrow \]

Renal arteriolar vasoconstriction

\[ \downarrow \]

Necrosis and degeneration of renal Tubular

\[ \downarrow \]

Cellular debris
Tubular obstruction

\[ \downarrow \]

Lost tubule integrity
Back-leakage of crude urine

\[ \downarrow \]

\[ \downarrow \]

\[ \downarrow \]

GFR

\[ \downarrow \]

Oliguria

\[ \downarrow \]

Azotemia, Hyperkalemia, Metabolic acidosis, Water intoxication

\[ \downarrow \]

Acute renal failure

**Mechanism of acute renal failure**
Acute renal failure may be divided into **Oliguric type ARF** and **Non-oliguric type ARF** according to urine in clinic.

First, we discuss **development** of **Oliguric type ARF** and **alterations** of **Metabolism and Function** in the body.

The progress course of oliguric type ARF may be divided into three stages:

1. **Oliguric stage** (persistence 1-2 week)
2. **Diuretic stage** (persistence 2 week)
3. **Recovery stage** (persistence 3 months to one year)
Alterations of Metabolism and Function

1. The Oliguric stage

(1) Urinous alterations
   ① **Oliguria** (<400ml/24h) or **anuria** (100/24h)
   ② **Hematuria**, albuminuria and **cylindruria**
(2) **Water intoxication**

a. Oliguria or anuria $\rightarrow$ **Excretory H\textsubscript{2}O↓**

b. **Increase** of endogenous water from catabolism

c. **Increase** of water **intake** and **infusion**

*Cerebral edema, Pulmonary edema, Cardiac insufficiency*
(3) **Hyperkalemia** → **cardiac arrest**
① **Oliguria** → decreased potassium excretion;  
② Tissue **injury** and increased **catabolism** promote release of potassium;  
③ **Acidosis** causes the exchange between extracellular H\(^+\) and intracellular K\(^+\);  
④ **Hyponatremia** causes the decreased K\(^+\)-Na\(^+\) exchange in the distal renal tubules;  
⑤ **Perfuse** the storage blood.
4) Metabolic acidosis

1. GRF ↓ → excreting H⁺ ↓
2. Decreased capability of excreting acids and conserving base by renal tubules
3. Increased catabolism → fixed acids ↑
Azotemia

*The marked increase of non protein nitrogen (NPN) content, such as urea, creatinine, uric acid, etc., is called *azotemia.*

**BUN (＞20mg/dl); NPN (＞40mg/dl)**

**Mechanisms:**

① **Protein catabolism increased**

② **GRF ↓ → exclude inadequately**
Acute renal failure \(\rightarrow\) Acid retention \(\rightarrow\) Metabolic-acidosis

- Hyperkalemia
- Urinary sediment
- Iso-osmolar urine
- Increased urinary sodium excretion

Fluid-retention

- Edema
- Hyponatremia

Increased serum creatinine
2. The Diuretic stage

When the urine output elevates more than 400ml/d, it means the polyuric stage coming.

Mechanisms:

① The renal blood stream and GFR gradually restore normal;

② Function of the neonatal renal tubular epithelia is still immature, so the sodium and water reabsorbing capacity is low yet;

③ Renal interstitial edema fade away and the casts in renal tubules are swept and the obstruction of renal tubules is released;

④ Osmotic diuresis
The clinical manifestations of diuretic stage in ARF

In the early phase, Azotemia, Hyperkalemia and Acidosis do not receive melioration at once, because renal function does not completely restore immediately.

Dehydration, Hypokalemia and Hyponatremia are easy to occur in the late stage.
3. Recovery stage

In this stage the urine output begins to decrease and gradually restores. NPN in the blood decreases, and disorders of water, electrolyte and acid-base balance are corrected.
Nonoliguric ARF

Nonoliguric ARF is another type of ARF, in which renal pathological changes and clinical exhibition are relatively slight, so the process is shorter, and Prognosis is better.

Its main characters include:
① urinary volume not decreased (400~1000ml/d);
② special gravity of urine is low and fixed, and urinary sodium is low; (disorder of concentration urine)
③ The azotemia results from GFR↓.
## Distinction of Oliguria ARF and non-Oliguria ARF

<table>
<thead>
<tr>
<th></th>
<th>Oliguria ARF</th>
<th>Non-Oliguria ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causes</strong></td>
<td>ischemia</td>
<td>Renal poisoning</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>High incidence</td>
<td>Lower incidence</td>
</tr>
<tr>
<td></td>
<td>About 2/3→1/2</td>
<td>About 1/3→1/2</td>
</tr>
<tr>
<td><strong>Course stages</strong></td>
<td>3 months to 1 year</td>
<td>Relatively shorten</td>
</tr>
<tr>
<td></td>
<td>Divided three stage</td>
<td>No obvious</td>
</tr>
<tr>
<td><strong>Urine</strong></td>
<td>(&lt;400\text{ml/d Start})</td>
<td>(&gt;400\text{ml/d Begining})</td>
</tr>
<tr>
<td><strong>GFR</strong></td>
<td>↓↓↓</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>before renal tubule injury</td>
<td>After renal tubule injury</td>
</tr>
<tr>
<td><strong>Tubules Dysfunction</strong></td>
<td>Severity damage</td>
<td>Mild injury(\text{dysfunction of urinous concentration})</td>
</tr>
<tr>
<td><strong>Symptom</strong></td>
<td>Severity with hyperkalemia</td>
<td>Azotemia without hyperkalemia</td>
</tr>
<tr>
<td><strong>Nephron(N)</strong></td>
<td>(&lt;1%)</td>
<td>(&gt;10%)</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>50%</td>
<td>30%</td>
</tr>
</tbody>
</table>
Pathophysiological basis of prevention and treatment

For the treated of ARF are as following:

1. To maintain fluid and electrolyte, acid-base, and solute homeostasis, such as treating hyperkalemia and correcting metabolic acidosis

2. To control the level of blood nonprotein nitrogen.

3. To prevent subsequent infection.

4. To promote healing and renal recovery.

5. To permit other support measures, such as nutrition to proceed without limitation.

6. Renal replacement therapy may be provided by peritoneal dialysis or intermittent hemodialysis.