Urinary system disorders
Chapter 29
The Nephron Anatomy
Physiology

1.25 L per minute blood flow
25% of Cardiac Output
1. Filtration
2. Reabsorption
   - Diffusion
   - Osmosis
   - Active Transport
3. Secretion
   - Diffusion
   - Osmosis
   - Active Transport
4. Excretion
Glomerular Filtration

- Driven by pressure through glomerular membrane
Glomerular Filtration

- Through 3 Selectively Permeable Layers
  - Capillary endothelium
  - Basement membrane
  - Epithelium of Bowman’s capsule
    - podocytes
Glomerular Filtration

- Basement Membrane
  - Selective Filter
    - Slightly porous
    - Repels proteins (negative charge)
    - Allows only water, ions, and small molecules
Renin-Angiotensin-Aldosterone System

Angiotensinogen → Renin → Angiotensin I → ACE → Angiotensin II → Aldosterone Release

Vasoconstriction

Efferent Arterioles

Systemic Arteries
Renin-Angiotensin-Aldosterone System

Liver

Angiotensinogen

Angiotensin I

Angiotensin II

Lungs

Kidney

Surface of pulmonary and renal endothelium: ACE

Decrease in renal perfusion (juxtaglomerular apparatus)

Renin

Kidney

Adrenal gland: cortex

Aldosterone secretion

Arteriolar vasoconstriction. Increase in blood pressure

Pituitary gland: posterior lobe

ADH secretion

Collecting duct: H₂O absorption

Sympathetic activity

Tubular Na⁺ Cl⁻ reabsorption and K⁺ excretion. H₂O retention

Legend

- secretion from an organ
- stimulatory signal
- inhibitory signal
- reaction
- active transport
- passive transport

Water and salt retention. Effective circulating volume increases. Perfusion of the juxtaglomerular apparatus increases.
Renal Cystic Disease

- Fluid filled sacs or Dilated nephrons
  - Four types
    - Simple kidney cysts
    - Acquired cystic disease
    - Medullary sponge kidney
    - Polycystic kidney disease
- Result of tubular obstruction
  - Enlarging cysts
  - Compresses vessels and renal tissue
Autosomal dominant disorder characterized by multiple bilateral grapelike cysts that enlarge and replace functioning kidney tissue

- Grossly enlarged kidneys
- Slowly progressive
- Destruction of renal tissue
Polycystic Kidney Disease

- Complications
  - Pain from enlarging cysts
  - Hematuria from bleeding into a cyst
  - Pyelonephritis from ascending UTI
  - Hypertension due to compression of intrarenal blood vessels and activation of R-A-A System
  - End stage renal failure after age 40
Polycystic Kidney Disease

- Diagnosis and Treatment
  - Ultrasonography
  - Abdominal CT scanning

- Supportive treatment
- Control hypertension
- Prevention of ascending UTIs
- Dialysis and Transplant
Obstruction

- Urine accumulates behind blockage
  - Infection
  - Damage due to backpressure

- Classification
  - Site of obstruction
  - Degree of obstruction
  - Duration of obstruction
Obstruction

- Site of Obstruction
  - Renal Pelvis
  - Ureter
  - Bladder and Urethra
Obstruction

- Common Causes of Obstruction
  - Stones (Renal Calculi)
  - Pregnancy
  - Ureteral Stricture
  - Prostatic Hyperplasia or Cancer
Obstruction

- Mechanisms of Damage
  - Stasis of urine
    - infection
    - stone formation
  - Back pressure
    - interferes with blood flow
    - destroys renal tissue
    - kidney atrophies
Obstruction

- Back Pressure (location is important)
  - Urethral Obstruction
    - Accommodated in the bladder
    - Mild discomfort, Frequency
  - Bladder or Ureter Obstruction
    - More severe
    - Pressure can irreversibly stretch the ureters and renal pelvis
      - (hydroureter & hydronephrosis)
    - May alter tubular transport and compromises blood flow to the kidney
Hydronephrosis
Obstructive Disorders

- Clinical Features
  - Vary depending on site, cause and rapidity of onset
    - Pain
    - UTIs
    - Indications of Renal Dysfunction
    - Hypertension
Kidney Stones

- Most Common Cause of Obstruction
  - Nephrolithiasis – stone within the kidney
  - Urolithiasis – stone anywhere in the urinary system
- Calcium Stones are Most Common
- Theories of Stone Formation?
  - Calcium: idiopathic, hypercalciuria, alkaline urine
  - Struvite: from urease-producing bacteria, acidic urine
- Contributing Factors
  - immobilization
  - bone disease
  - vitamin D intoxication
  - decreased fluid intake
Staghorn Kidney Stones
Renal Colic

- Pain that accompanies urinary obstruction caused by kidney stones
- Symptoms: acute, intermittent, excruciating, upper quadrant/flank pain that may radiate to other areas; nausea/vomiting; cool, clammy skin
Lower Urinary Tract Obstruction

- Neurogenic bladder often due to injury of urinary system or neurologic dysfunction

- **Dyssynergia**: dyscoordination of the detrusor muscles of the bladder and the external urethral sphincter muscles

- **Detrusor hyperreflexia**: AKA overactive bladder. Lesions above C2, pontine micturation center, upper motor neuron disease, Guillain-Barre

- **Detrusor areflexia**: muscle fails to contract in response to the stretch of filling urine. MS, spinal lesion below S1, lower motor neuron disorder
Compensatory hypertrophy: the functional side increases in size and “makes up for” the loss of function on the other side. Due to
- Obligatory growth: due to growth hormone
- Compensatory growth: hormones unknown

Postobstructive diuresis: large increase in excretion of urine after obstruction is removed
**Urge incontinence:** I feel like I need to go but the bladder is not as full as it feels, maybe nervous or inflammatory stimulus

**Stress incontinence:** weak muscles and fascia so coughing, laughing, jumping results in urine leaks

**Overflow incontinence:** bladder is just too full to hold that much urine, you waited too long to void

**Functional incontinence:** urinary system and nerves going to and from it work, but you are cognitively demented (Alzheimer’s)
Urinary Tract Infections

- Etiology
  - Escherichia coli (E. coli)
  - Any microorganism that has contaminated or colonized in the urethra, vaginal or perineal area can cause an UTI
Urinary Tract Infections

- Acute Cystitis
  - Lower UTI of the bladder
  - Symptoms: increased frequency of urination, burning & pain on urination, lower abdominal discomfort
  - Also associated with urethritis or vaginitis

- Acute Pyelonephritis
  - Upper UTI that affects the tubules and interstitium of the kidneys
  - Bacterial infection caused by catheterization and urinary instrumentation, vesicoureteral reflux, pregnancy, neurogenic bladder
Urinary Tract Infections

- Host Defenses
  - Washout phenomenon
  - Protective mucin layer of the bladder and urethra
    - Estrogen may play a role in women
  - Local immune response
    - IgA as an antibacterial defense
  - Prostatic secretions in men
  - Genetic polymorphism increases *E. coli* ability to attach in some women
Urinary Tract Infections

• Women
  – Shorter urethra
  – Urethra proximity to openings of vagina and rectum leads to easy contamination
  – Hormonal and anatomical changes during puberty and sexual activity contribute to UTI
  – Common during pregnancy

• Men
  – Longer urethra
  – Prostatic secretions help protect from UTI until age 50 when prostatic hypertrophy leads to obstruction and UTI
Urinary Tract Infection (UTI)

- Nonbacterial infectious cystitis: viral, fungal, chlamydia

- Interstitial cystitis: cause???

  unknown, though several theories have been put forward (these include autoimmune theory, nerve theory, mast cell theory, leaky lining theory, infection theory and a theory of production of a toxic substance in the urine. Other theories are neurologic, allergic, genetic and stress-psychological

  - Manifestations
    - Most common in women 20 to 30 years old
    - Bladder fullness, frequency, small urine volume, chronic pelvic pain

  - Treatment
    - No single treatment effective, symptom relief
Glomerulonephritis

- Bilateral inflammation of the glomeruli
- Most common cause of chronic renal failure
- Uncertain cause but immune mechanism is likely (Type 2 cell lysis Strep A ab, Type 3 SLE immune complex)

- Injury to Glomeruli (Glomerulopathies)
  - Allows Proteins to enter tubules with filtrate
    - Proteinuria
  - Allows RBC’s to enter tubules with filtrate
    - Hematuria
Glomerular Disorders

- Increased glomerular capillary permeability and loss of negative ionic charge barrier result in passage of plasma proteins into the urine
- Resulting hypoalbuminemia encourages plasma fluid to move into the interstitial spaces
  - Edema
Glomerular capillaries and Bowman’s capsule are both made of epithelial cells sitting on a basement membrane. They are so tightly attached to each other that they share one basement membrane. The epithelial cells of Bowman’s capsule stand up from the basement membrane on foot processes, leaving pores between the feet for filtration.
Circulating immune complexes lodge in glomerular membrane

Antibodies to glomerular basement membrane proteins

Immune Damage to the Glomerulus
Acute Proliferative Glomerulonephritis

- The most common form of glomerulonephritis
- Follows infections caused by strains of group A Strep
- Inflammatory response due to an immune reaction
  - Capillary membrane swells
  - Becomes permeable to plasma proteins and cells
- Also called post-streptococcal glomerulonephritis
  - Occurs 7 – 12 days post infection
  - Oliguria is first sign followed by proteinuria and hematuria
  - Approximately 95% full recovery - spontaneously
Glomerulonephritis

- Rapidly progressing glomerulonephritis
  - Antiglomerular basement membrane disease (Goodpasture syndrome: *glomerulonephritis* and *hemorrhaging of the lungs*), autoimmune Type II hypersensitivity reaction
- Chronic glomerulonephritis, diabetes mellitus, SLE
Rapidly Progressive Glomerulonephritis

- Unknown cause
  - Perhaps - immunologic mechanism
    - Immune complex: Strep A
    - Anti-glomerular membrane: Goodpasture’s
- Rapidly progressive

- Treatment
  - Plasmapheresis
  - Immunosuppressive drugs
IgA Nephropathy

- Primary glomerulonephritis
- IgA containing immune complexes
- Unknown cause
  - Possible defect in IgA molecule
  - Slowly progressive
- No known treatment
Nephritic Syndrome

- Glomerular disorders in which inflammatory process damages the glomerular membrane
- Mild protein loss
  - Red and white blood cells escape into the urine
    - Hematuria with red and white cell casts
  - Hemodynamic changes can decrease permeability of glomerular membrane and decreases the GFR
- Low proteinuria
Nephritic Syndrome

- Complications
  - Renal Failure
    - Pulmonary edema
    - Heart failure
    - Hypertension
Nephrotic Syndrome

- **Collection of clinical findings** associated with glomerular disease characterized by marked proteinuria, hypoalbuminemia, hyperlipidemia and edema

- Increased glomerular permeability causes massive loss of plasma proteins
  - proteinuria

- Edema is common
  - Hypoalbuminemia allows plasma to leak into tissues
  - Reduced intravascular volume lowers GFR triggering Angiotensin II and Aldosterone which increase sodium and water retention
Nephrotic Syndrome

- Other proteins lost in urine:
  - Immunoglobulins and complement $\rightarrow$ immune suppression
  - Clotting and anti-clotting proteins $\rightarrow$ thrombosis
  - Proteins that carry other blood components $\rightarrow$ imbalances in blood components; altered drug dosages

- Glomerular damage
  - Increased permeability to proteins
  - Proteinuria ($\geq 3.5 \text{ g/24 h}$)
  - Hypoproteinemia
    - Decreased plasma oncotic pressure $\rightarrow$ Edema
    - Compensatory synthesis of proteins by liver $\rightarrow$ Hyperlipidemia
Nephrotic Syndrome

Glomerular Damage

↑ Permeability to Protein

Proteinuria > 3.5 g/24hr

Hypoproteinemia (Albumin < 3 g/100ml)

Compensatory Protein Synthesis including Lipoproteins

Hyperlipidemia

Plasma leaks into tissues

↓ Plasma Osmotic Pressure

↓ Plasma Volume

↓ GFR

↑ Na / Water Retention

↑ Aldosterone

EDEMA
Nephrotic Syndrome

- Complications
  - Malnutrition
  - Infection
  - Coagulation disorders
  - Thromboembolic vascular occlusion
  - Accelerated atherosclerosis
  - Acute renal failure
Nephrotic Syndrome

- Treatment
  - Correct underlying cause
  - Diuretics
Nephrotic Syndrome

- Membranous glomerulonephritis: one of the more common forms of nephrotic syndrome. Caused by immune complexes binding to the glomerular basement membrane.

- Focal glomerulosclerosis: common in kids, scarring of some of the glomeruli, there are several genetic causes.

- Minimal change disease (lipoid nephrosis): in kids, cause is idiopathic, diffuse loss of (podocyte) foot processes, vacuolation, and growth of microvilli on the visceral epithelial cells.
Damage to tubules and surrounding tissues

Generally due to:

- Pyelonephritis
- Toxic substances such as medications or ischemic injury

Urinalysis is neither nephrotic nor nephritic in Character
- Mild Proteinuria ( < 1 gm/day )
Renal Failure

- Inability of kidney to maintain homeostasis and eliminate nitrogenous wastes
- Decline in GFR leading to azotemia
  - ↑ Creatinine
  - ↑ Urea
- Generally a decline in urine output
  - Oliguria = < 500 mL/day
  - Anuria = < 100 mL/day
- Non-oliguric failure is possible
Acute Renal Failure

- Sudden interruption of renal function
  - Classified as prerenal, postrenal & intrarenal
  - Often reversible if treated early
- Three phases
  - Oliguric phase
  - Diuretic phase
  - Recovery phase
Acute Renal Failure

- Oliguric phase
  - Lasts for a few days to several weeks
  - Urine output drops to below 400 ml/day
  - Patient may become fluid overloaded
  - Cellular injury and necrosis of kidney

- Diuretic phase
  - Lasts days to weeks
  - Kidneys become unable to conserve sodium & water
  - Urine output increases
Acute Renal Failure

- **Recovery Phase**
  - Lasts 3 to 12 months
  - Renal function gradually returns to normal
Acute Renal Failure

- Prerenal failure: most common
  - Caused by diminished blood flow to the kidney
  - Kidney becomes ischemic
  - Damages kidney tubules
Acute Renal Failure

- Intrinsic failure (intrarenal failure)
  - Damage to the filtering structures of the kidney
  - May be nephrotoxic, inflammatory or ischemic
Acute Renal Failure

- **Postrenal failure**
  - Bilateral obstruction to urine outflow
### Causes of Acute Renal Failure

<table>
<thead>
<tr>
<th>Prerenal</th>
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<tbody>
<tr>
<td>Hypovolemia</td>
<td>Heart failure</td>
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<tr>
<td>Decreased vascular filling</td>
<td>Vasoconstrictive drugs</td>
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<table>
<thead>
<tr>
<th>Postrenal</th>
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<tbody>
<tr>
<td>Bilateral ureteral obstruction</td>
<td>Bladder outlet obstruction</td>
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<table>
<thead>
<tr>
<th>Intrinsic (ATN)</th>
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</thead>
<tbody>
<tr>
<td>Prolonged ischemia</td>
<td>Acute renal disease</td>
</tr>
<tr>
<td>Nephrotoxins</td>
<td></td>
</tr>
</tbody>
</table>
Acute Renal Failure

- Complications
  - Infection
  - Heart failure
  - Hypertensive crisis
  - Electrolyte imbalance

- Diagnostic test findings
  - Elevated BUN, creatinine and potassium
  - Abnormal urinalysis
Acute Renal Failure

- **Treatment**
  - Reverse the cause
  - Electrolyte and I.V. therapy
Acute Tubular Necrosis

- Intrarenal acute renal failure
- Injury to the nephron’s tubular segment
- Resulting from ischemia or nephrotoxic injury
Acute Tubular Necrosis

- **Causes**
  - **Ischemic injury**
    - Hypotension
    - Trauma, hemorrhage, dehydration
    - Shock
  - **Nephrotoxic injury**
    - Toxic chemical ingestion or inhalation
    - Hypersensitivity reaction to antibiotics etc.
Acute Tubular Necrosis

- **Pathophysiologic Changes**
  - Decreased urine output, hyperkalemia and elevated renal function tests

- **Complications**
  - Heart failure
  - Pulmonary edema
  - Anorexia and vomiting
Acute Tubular Necrosis

- **Diagnostic test findings**
  - Abnormal urinalysis
  - Abnormal blood tests of renal function

- **Treatment**
  - Reverse cause
  - Long term fluid management
Chronic Renal Failure

- End result of gradual tissue destruction and loss of renal function
  - Occasionally due to acute destruction of kidney
  - Fatal without treatment
- Nephron damage is progressive and permanent
- Relatively asymptomatic until 75% loss of nephrons
Chronic Renal Failure

- **Diminished renal reserve**
  - Nephrons are working as hard as they can
  - GFR is 50 – 89% of normal

- **Renal insufficiency**
  - Nephrons can no longer regulate urine density
  - GFR is 20 – 50% of normal

- **Renal failure**
  - Nephrons can no longer keep blood composition normal
  - GFR is 5 – 20% of normal

- **End-stage renal disease**
  - GFR is Less than 5% of normal
Chronic Renal Failure

- As GFR decreases azotemia and uremia develops
  - Azotemia = accumulated nitrogenous wastes in blood
    - Early asymptomatic sign of renal failure
    - Elevated BUN
  - Uremia = urea and other nitrogenous wastes increase in blood
    - Constellation of symptoms due to systemic complications attributed chronic renal failure (increased BP, edema, nausea, vomiting, neurological problems due to toxic levels of nitrogenous wastes)
  - These appear when azotemia becomes significant
Chronic Renal Failure

- Renal filtering function decreases
  - Altered fluid and electrolyte balance
    - Acidosis, hyperkalemia, salt wasting, hypertension
- Wastes build up in blood
  - Increased creatinine and BUN
    - Toxic to CNS, RBCs, platelets
- Kidney metabolic functions decrease
  - Decreased erythropoietin
  - Decreased Vitamin D activation
## Chronic Renal Failure

*These are not usually seen in Acute Renal Failure*

<table>
<thead>
<tr>
<th>Body System</th>
<th>Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic</td>
<td>Anemia, bleeding tendencies, immunocompromised</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Hypertension, CHF, pulmonary edema, arrhythmias</td>
</tr>
<tr>
<td>Gastrointestinal (GI)</td>
<td>Anorexia, nausea, vomiting, GI bleeding</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Muscle weakness, bone pain, spontaneous fractures</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Headache, anorexia, lethargy, delirium, coma, seizures</td>
</tr>
<tr>
<td>Body fluids</td>
<td>Metabolic acidosis, hyperkalemia, hypocalcemia</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Impotence, amenorrhea, loss of libido</td>
</tr>
</tbody>
</table>
Chronic Renal Failure

• Causes
  • Endocrine disease (diabetes)
  • Chronic glomerular disease (glomerulonephritis)
  • Chronic infection
  • Congenital anomalies
  • Vascular disease (hypertension etc.)
  • Obstruction
  • SLE
Chronic Renal Failure

- **Treatment**
  - Low protein, high calorie, fluid restricted diet
  - Medications
  - Dialysis
  - Kidney transplant
Acute Renal Failure (ARF)

Ischemia or nephrotoxins

Possible glomerular injury

Intrarenal vasoconstriction

Decreased vasoconstriction and decreased surface area

Tubular injury (i.e., acute tubular necrosis)

Cellular cast formation

Obstruction

Increased intraluminal pressure

Tubular back leak

Decreased GFR

Oliguria
Chronic Renal Failure

Renal injury

Loss of nephrons → Angiotensin II

Glomerular capillary hypertension

Glomerular permeability and filtration

Proteinuria

Tubular protein reabsorption

Tubulointerstitial inflammation and fibrosis

Renal scarring

Systemic hypertension
Tumors

- Renal tumors
  - Renal adenomas
  - Renal cell carcinoma (RCC)
- Bladder tumors
  - Transitional cell carcinoma
  - Gross, painless hematuria
  - Most common in males older than 60 years
  - Chronic heavy smokers