Bio217: Pathophysiology Class Notes
Professor Linda Falkow

Unit VIII: Urinary (Renal) System Disorders and Reproductive System Disorders

Chapter 28: Structure & Function of Renal & Urologic Systems
Chapter 29: Alterations of Renal & Urinary Tract Function
Chapter 31: Structure and Function of Reproductive Systems
Chapter 32: Alterations of the Reproductive Systems

• Kidneys (2)
  • Retroperitoneal
  • Renal capsule
  • Adipose capsule
  • Renal fascia
  • Hilum
• Ureters (2)
• Urinary Bladder (1)
• Urethra (1)

Structures of Urinary System

• 1.2 million nephrons per kidney
• Functional unit of the kidney
  — Cortical nephrons
  — Juxtamedullary nephrons
• Parts of nephron
  — Renal corpuscle (=glomerulus + Bowman capsule)
  — Renal tubules
    • Proximal tubule (pct)
    • Loop of Henle
    • Distal tubule (dct)

Structures of the Kidney

• Cortex
• Medulla
• Pyramids
• Calyces
  — Minor and major
• Renal pelvis

Nephron

• Glomerular filtration membrane
  — Blood passes through the three layers and forms the filtrate

Nephron
- Juxtaglomerular apparatus
  - Juxtaglomerular cells (\(\rightarrow\) renin)
  - Macula densa (sense changes in Na+)

  - Renin-angiotensin pathway: reg. BP
    • Decr. blood vol. or decr. Na+ \(\rightarrow\) incr. renin \(\rightarrow\)
      Angiotensin I \(\rightarrow\) Angiotensin II \(\rightarrow\) aldosterone
      (incr. reabsorption of Na+ and H\(_2\)O)

- Urinary Bladder
  - Detrusor muscle
  - Trigone
  - Micturition reflex

- Urethra
  - Internal and external sphincters
  - 3 to 4 cm in females
  - 18 to 20 cm in males

- Receive 1000 to 1200 mL of blood/min.
- Glomerular filtration rate (GFR)
- Autoregulation
  - Tubuloglomerular feedback

- Neural regulation
- Hormones
  - Renin-angiotensin system
  - Aldosterone
  - ADH (conserves water/incr. water reabsorption)
Renal Blood Flow

Nephron Function

- Filters plasma
- Reabsorbs and secretes
  - Tubular reabsorption and secretion
- Forms a filtrate of protein-free fluid
- Regulates filtrate to maintain fluid volume, electrolytes, and pH

Nephron Function

- Glomerular filtration
  - Net filtration pressure
    - Glomerular capillary oncotic/hydrostatic pressure
    - Bowman capsule oncotic/hydrostatic pressure
  - Filtration rate
    - 180 L/day

Nephron Function

- Countercurrent exchange system
  - Contributes to production of concentrated urine

Concentration and Dilution of Urine

- Aldosterone
- Antidiuretic hormone (ADH)
- Atrial natriuretic peptide (ANP)
  - produced by RA, when RA press. increases, inhibits secretion of renin
- Diuretics
  - enhance urine flow (by disrupting Na+ reabsorption and decr. ECF vol.)

Concentration and Dilution of Urine

- Urinary tract obstruction
  - interference with flow of urine at any site along urinary tract
  - Obstruction can be caused by anatomic or functional defect
  - Obstructive uropathy – changes in urinary system due to obstructions (anatomic)

Urinary Tract Obstruction
Urinary Tract Infection (UTI)

- **UTI** - inflammation of urinary epithelium caused by bacteria
- **Acute cystitis**
- **Interstitial cystitis**
- **Acute and chronic pyelonephritis**

**Acute cystitis**
- Cystitis is an inflammation of the u.b.
- *E. coli* most common cause

  - Manifestations
    - Frequency, dysuria, urgency, and lower abdominal and/or suprapubic pain
  - Treatment
    - Antimicrobial therapy, increased fluid intake, avoidance of bladder irritants, and urinary analgesics

**Interstitial cystitis**
- Nonbacterial infectious cystitis
  - Most common in women 20 to 30 years old
  - Bladder fullness, frequency, small urine vol., chronic pelvic pain
- Immunocompromised (undergoing chemo or radiation therapy)

  - Treatment
    - No single treatment effective, symptom relief

**Pyelonephritis**
- Acute pyelonephritis
  - Acute infection of the renal pelvis & interstitium
    - Vesicoureteral reflux (urine reflux up ureter into kidney), *E. coli, Proteus, Pseudomonas*
  - Chronic pyelonephritis
    - Persistent or recurring episodes of acute pyelonephritis that leads to scarring
    - Risk of chronic pyelonephritis increases in individuals w/ renal infections and some type of obstructive pathologic condition

**Chronic Pyelonephritis**

- Normal size - scarring on upper surface
- Shrunken size - scarring
**Glomerular Disorders**

- **Glomerulonephritis**
  - Inflammation of the glomeruli (typically after a strep infection)
  - Immunologic abnormalities (most common)
  - Drugs or toxins
  - Vascular disorders
  - Systemic diseases
  - Viral causes
  - Most common cause of end-stage renal failure

- **Mechanisms of injury**
  - Immune response - deposition of antigen-antibody complexes in glomerular capillaries
  - Formation of antibodies against the glomerular basement membrane → break down cells → incr. permeability

**Glomerulonephritis**

- **Acute poststreptococcal glomerulonephritis**
- **Rapidly progressing glomerulonephritis (RPGN)**
  - Antiglomerular basement membrane disease (Goodpasture syndrome) – rare

- **Chronic glomerulonephritis**

**Glomerulonephritis**

- **Uremia**
  - accumulation of N-wastes and metabolic toxins in plasma
  - Symptoms: confusion, GI complaints, fluid in lungs, infection
  - Describes clinical manifestations of CRF (chronic renal failure)

**Chronic Renal Failure**

- **Chronic renal failure (CRF)**
  - progressive, irreversible loss of renal function that affects nearly all organ systems

- **Stages**
  - Chronic renal insufficiency (GFR 20-35% of normal)
  - Chronic renal failure (GFR 20-25% of normal)
  - End-stage renal failure (GFR <20% of normal)
• CRF due to:
  – Glomerulonephritis
  – Chronic infections (pyelonephritis or TB)
  – Congential (polycystic disease)
  – Vascular (HT or nephrosclerosis)
  – Obstructions (renal calculi)
  – Diabetic neuropathy

Imbalances in following factors:
• Proteinuria and uremia
• Creatinine and urea clearance
• Fluid and electrolyte balance
  – Sodium and water balance
  – Phosphate and calcium balance
  – Potassium balance
  – Acid-base balance

• Alterations seen in following systems:
  – Musculoskeletal
  – Cardiovascular and pulmonary
  – Hematologic
  – Immune
  – Neurologic

– Gastrointestinal
  • Alteration in protein, carbohydrate, and lipid metabolism
– Endocrine and reproduction
– Integumentary

• 1. Which is an abnormal substance of urine?
  – A. Urea
  – B. glucose
  – C. NaCl
  – D. Creatinine

• 2. The presence of albumin in urine would indicate damage to:
  – A. Glomeruli
  – B. Collecting ducts
  – C. pyramids
  – D. None of the above

• 3. GFR is regulated by
  – A. ANS
  – B. ANF
  – C. Renin-angiotensin system
  – D. All of the above
4. An increase in permeability of the dct and cd is due to:
   - A. Decrease in ADH production
   - B. Increase in ADH
   - C. Decrease in blood plasma osmolality
   - D. Increase in water content in blood

5. UTIs occur:
   - A. Only in the kidneys
   - B. Anywhere but the kidneys
   - C. Anywhere in the urinary system

Matching:
   - ___ 6. acute cystitis  a. Infection of renal pelvis & interstitium
   - ___ 7. uremia               b. Inflamm. that is most common cause of end-stage renal failure
   - ___ 8. glomerulonephritis  c. Renal failure w/ elevated blood urea and creatinine
   - ___ 9. pyelonephritis      d. U.b. inflam. ranging from hyperemic mucosa to necrosis of u.b. wall

Development of the Reproductive System
   - Dependent on sex hormones
     - Males—testosterone
     - Females—estrogen, FSH, and LH

Female Reproductive System
   - External genitalia (vulva)
     - Mons pubis
     - Labia majora
     - Labia minora
     - Clitoris
     - Vestibule

Internal Genitalia
   - Vagina
   - Uterus
     - Cervix
   - Fallopian tubes
   - Ovaries
Female Sex Hormones

- Estrogens
  - Estradiol (E2): 95% produced by ovaries
  - remainder by adrenal gland & placenta (pregnancy)
  - Estrone
  - Estriol
- Progesterone – from corpus luteum
- Androgens – small amt. from ovaries & adrenal cortex

Menstrual Cycle

- Menarche
- Menopause
- Phases
  - Menstruation (menses)
  - Follicular/proliferative phase
  - Luteal/secretory phase
  - Ischemic/menstrual phase
**Menstrual Cycle**
- Ovarian cycle
- Uterine phases
- Vaginal response
- Body temperature change
  - BBT (basal body temp.) biphasic
  - Follicular phase $\approx 98^\circ F$
  - Luteal phase $\approx 0.4 - 1.0 ^\circ F$ elevation

**Menstrual Cycle**
- External genitalia
  - Testes
    - Produce gametes and sex hormones
  - Epididymis
    - Vas deferens
  - Scrotum
  - Penis
    - Glans and prepuce

**Male Reproductive System**
- Internal genitalia
  - Ducts
    - Vas deferens and ejaculatory duct
  - Accessory Glands
    - Seminal vesicles
    - Prostate gland
    - Bulbourethral glands

**Spermatogenesis**
- Spermatogonia
- Primary spermatocytes
- Secondary spermatocytes
- Spermatids
- Sertoli cells
  (Sustentacular cells)
Male Sex Hormones

- **Androgens**
  - Primary androgen—testosterone
  - Produced mainly in (interstitial cells of) Leydig cells of testes
  - Testosterone
    - Sexual differentiation
    - Urogenital system dev.
    - Nervous and skeletal tissue dev.
    - Libido

Disorders of the Female Reproductive System

- Hormonal and menstrual alterations
  - **Primary dysmenorrhea** (painful menstruation)
    - Painful menstruation associated with prostaglandin release in ovulatory cycles
  - **Secondary dysmenorrhea**
    - Painful menstruation related to pelvic pathology (endometriosis, PID, fibroids)
  - **Pathophysiology**
    - Excess PGF from endometrium; GI upset, headaches, syncope
  - Treatment: Hormones, PG inhibitors, exercise, heat

Hormonal and Menstrual Alterations

- **Primary amenorrhea**
  - Absence of menstruation by age 14 (& no secondary sex characteristic dev. by age 16)
  - Pathophysiology:
    - Dysfunctional H-P-O axis; congenital or hypoplasia of uterus; genetic (Turner’s syndrome XO)
- **Secondary amenorrhea**
  - Absence of menstruation for three or more cycles or 6 months in women who have previously menstruated

Amenorrhea

With high gonadotropin levels
- Menopause
- Congenital ovarian failure caused by: Immune system
  - Resistance to gonadotropins
  - Autoimmune disease
  - Chemotherapy
  - Resistance to gonadotropins
  - Environmental factors

Increased ovarian hormone secretion
- Ovarian dysfunction caused by: Menstruating tumors
  - Polycystic ovary syndrome

With low gonadotropin levels
- Hypogonadism
  - Hypothalamic-pituitary disorders (e.g., Turner, Kallmann’s)
  - Dystrophic hyperplasia of uterine disorders (e.g., adrenarche, psychogenic disorder, endocrine disease)

Increased ovarian hormone secretion
- Ovarian dysfunction caused by: Menstruating tumors

Hormonal and Menstrual Alterations

- **Secondary amenorrhea**
  - Causes
    - Pregnancy (normal)
    - Dramatic weight loss
      - Malnutrition or excessive exercise
      - Anovulation
      - Hirsutism (increased testosterone)

Hormonal and Menstrual Alterations

- **Abnormal uterine bleeding**
  - Menstrual irregularity
  - Dysfunctional uterine bleeding
Infection and Inflammation

- **Pelvic inflammatory disease (PID)**
  - Acute inflammatory disease due to infection
  - May involve any organ of reproductive tract
  - Salpingitis (inflam. of fallopian tubes)
  - Oophoritis (inflam. of ovaries)
  - STDs migrate from vagina to the upper genital tract
  - Polymicrobial infection (due to gonorrhea or chlamydia)
  - Can lead to infertility, ectopic pregnancy, abscess, septic shock (death)

Pelvic Inflammatory Disease (PID)

Pelvic Inflammatory Disease (PID) (Salpingitis)

Leiomyomas (benign fibroid tumors)

- Developed from SMC

Benign Growth and Proliferative Conditions

- **Endometriosis**
  - Presence of functioning endometrial tissue or implants outside the uterus (retrograde menses)
  - Responds to hormone fluctuations of the menstrual cycle
  - Occur mostly in abdominal & pelvic cavities

Female Reproductive Cancer

- **Cervical cancer** (2% of cancers in women)
  - Cervical dysplasia (CIN – cervical intraepithelial neoplasia – precancerous)
  - Invasive carcinoma of the cervix
- **Risk factors**
  - HPV and HIV
  - Multiple sexual partners
  - Poor nutrition and smoking
- **Vaccine (2006)**
  - Gardasil (Merck) against HPV 6,11,16,18
- **Pap smear – screening test**
Cervical Cancer

A: progressive degrees of CIN  
(cervical intraepithelial neoplasia)

B: Normal multiparous cervix

C: CIN Stage 1  
(cancer only in cervix)

Female Reproductive Cancer

- Ovarian cancer (> 5% of all female cancer deaths)
- Cause — unknown; incr. risk with age, family history (breast or ovarian cancer)
- Pathophysiology:
  - Arise from epithelial cells (on outside of ovary, or stroma)
  - Associated with BRCA genes (breast cancer)
- Symptoms: abdominal pain & swelling (ascites)
- Metastasis: pelvis, colon, stomach, pleura

Disorders of the Testis

- Orchitis
  - Acute inflammation of the testis
  - Complication of a systemic disease or related to epididymitis
  - Mumps most common cause

Disorders of the Testis

Cancer of the testis

- Among the most curable of cancers (>95% cure)
- Common in men between ages 15 and 35
- Causes painless testicular enlargement
- Risk factors
  - History of Cryptorchidism (undescended testes)
  - Abnormal dev. of testes
  - Klinefelter (XXY)
  - History of testicular cancer

Disorders of the Prostate Gland

- Benign prostatic hyperplasia (BPH)
  - Enlargement of the prostate gland
  - Symptoms associated with urethral compression
  - Relationship to aging
  - Evaluation
    - Digital rectal exams
    - Prostate-specific antigen (PSA) monitoring

Disorders of the Prostate Gland

- Cancer of the prostate
  - Accounts for 29% of all cancers in males
  - Prostatic cancer is asymptomatic until adv. stages
  - Symptoms are similar to BPH
- Pathophysiology
  - 95% of neoplasms are adenocarcinomas
  - Related to steroid hormone use
  - \(T \rightarrow DHT\) and estradiol (in animal studies: both \(\rightarrow\) carcinogenic effect)
  - Action of IGF (insulin growth factor) potent mitogen (increase cell prolif. and decr. apoptosis)
  - Cancer cell lives and multiplies
Disorders of the Prostate Gland

- Cancer of the prostate
  - Dietary factors (high sat. fat, incr. calcium levels → decr. Vit. D which protects against prostate cancer, low fiber and complex CHO, incr. protein
  - Hormones (anabolic steroids)
  - Vasectomy (possibly due to elevated androgens, antisperm antibodies)
  - Chronic inflammation
  - Familial factors (5-10%)

Benign Breast Lesions

- Nonproliferative breast lesions
  - Fibrocystic changes (FCC)

- Proliferative breast lesions without atypia
  - Epithelial hyperplasia
  - Florid hyperplasia
  - Sclerosing adenosis
  - Complex sclerosing lesion
  - Papillomas

Breast Cancer

- Most common cancer in American women
- Leading cause of death from ages 40 to 44
- Second most common killer after lung cancer
- Black women more likely to die from it

Breast Cancer

- Reproductive factors (early 1st pregnancy lowers risk)
- Hormonal factors (ovarian androgen excess, HRT incr. risk)
- Environmental factors and lifestyle
  - Radiation
  - Diet (high intake fruits, veg., whole grains, low fat)
  - Chemicals (xenoestrogens – mimic estrogens, found in pesticides, plastics, detergents, drugs) (PCBs, DDT)
- Physical activity
- Familial factors and tumor-related genes

Breast Cancer

- Manifestations
  - Painless lump, dimpling of skin, edema
- Pathophysiology:
  - 70% arise from ductal (glandular) epithelium
  - Genetic alterations of DNA, chromosomes, suppression of apoptosis
  - 1/3 are hormone dependent (Progesterone or estrogen receptor positive)
- Treatment
  - Based on stage of cancer
  - Surgery, radiation, chemotherapy, hormone therapy, biologic therapy and bone marrow transplantation
Disorders of the Male Breast

- Gynecomastia
  - Overdevelopment of the breast tissue in a male
  - Results from hormone alterations
    - Idiopathic and system disorders, drugs, or neoplasms

- Male breast cancer
  - Most commonly seen after age 60
  - Tumors resemble carcinomas of breast in women
  - Crusting and nipple discharge are common clinical manifestations

Chlamydia Infections

- Chlamydia (bacterial)
  - Infections caused by *Chlamydia trachomatis*
  - Most common STI in the United States
  - Obligate, gram-negative, intracellular bacterium

Sexually Transmitted Urogenital Infections

- Syphilis
  - *Treponema pallidum*
    - Corkscrew-shaped, anaerobic bacterium that cannot be cultured in vitro
    - Infects any body tissue
    - Syphilis becomes a systemic disease shortly after infection.
      - Maternal-fetal transmission

Sexually Transmitted Viral Infections

- Human papillomavirus (HPV)
  - 120 different types of HPV
    - 30 serotypes are unique to stratified squamous epithelium
    - Divided into high-risk and low-risk serotypes
  - HPV is a nonenveloped, circular double-stranded DNA virus

Sexually Transmitted Parasitic Infections

- Trichomoniasis
  - Caused by *T. vaginalis*
    - Anaerobic, unicellular, flagellated, parasitic protozoan
  - Adheres to and damages squamous epithelial cells
    - Urethra, vagina, and Skene and Bartholin glands
  - Accounts for 25% of infectious vaginitis cases

Sexually Transmitted Viral Infections

- Genital herpes
  - Two serotypes
    - Herpes simplex virus type 1
    - Herpes simplex virus type 2
      - 80% of initial and 98% of recurrent infections are type 2
  - Transmitted through contact with a person who is shedding the virus in a secretion or from a peripheral lesion or mucosal surface
Sexually Transmitted Parasitic Infections

• Pediculosis pubis
  – Caused by the crab louse *Phthirus pubis*
  – Transmitted primarily by intimate sexual contact or contact with infected bed linens or clothing
  – A crab louse has a 25- to 30-day life cycle
  • Stages: egg or nit, three nymphal stages, and an adult stage

• Scabies
  – Caused by the adult female itch mite, *Sarcoptes scabiei*
  – Transmission of scabies requires prolonged close skin-to-skin contact
  • Typically occurs between family members or sexual partners

Concept CHECK

• 1. Progesterone
  – A. Stim. lactation
  – B. Incr. uterine tube motility
  – C. Thins the endometrium
  – D. Maintains the thickened endometrium

• 2. The ovaries produce
  – A. Ova, estrogens, oxytocin
  – B. Ova only
  – C. Ova and estrogens
  – D. Testosterone & semen

• 3. Cells that produce testosterone:
  – A. Interstitial cells
  – B. Testicular endocrine cells
  – C. Sustentacular cells
  – D. Spermatogonia

• 4. The function of testosterone:
  – A. Dev. Of male gonads
  – B. Bone and muscle growth
  – C. Influence sexual behavior
  – D. Growth of testes
  – E. All of the above

• 5. Acute PID
  – A. Mainly affects males
  – B. Is usually caused by viruses
  – C. Neve causes peritonitis
  – D. May cause infertility or tubular pregnancy

• 6. Endometriosis
  – A. Has ectopic endometrium responding to changing hormone levels of the menstrual cycle
  – B. Occurs mainly in the pleural cavity
  – C. Causes infertility in most women
  – D. Does not occur after treatment

• 7. The infectious cause of orchitis is
  – A. Streptococci
  – B. Gonococci
  – C. Chlamydial organisms
  – D. Mumps virus