INTRODUCTION

Urinary System Basics

A. Concept

1. Kidneys
2. Ureters
3. Urinary bladder
4. Urethra

B. Importance

Homeostasis

1. General meaning -- maintenance of life requirements within narrow tolerance limits, given continual variable influences.
2. Specific urinary application -- overall homeostasis of body fluids
    a. Direct -- blood & ECF
    b. Indirect -- ICF, from contact with ECF

C. Functions

1. Fluid balance *[details later]*
    a. Volume maintenance
    b. Solute amounts
    c. Acid-base maintenance
    d. Transport between ECF & ICF -- osmotic context
2. Excretion
    a. Fluid balance -- in order to maintain homeostasis, elimination of excesses required
    b. Toxicity -- elimination of toxins

Excretion

A. Meaning

1. Separation from body fluids & ejection out of body of metabolic waste products

2. Must have been involved in metabolic reactions to be an excretion

B. Systems Represented

1. Urinary -- full-time, primary function

2. Integumentary -- part-time, but very significant function

3. Respiratory -- part-time, significant function

4. Digestive -- part-time, secondary function

C. Substances Excreted

1. General

   a. Due to varying homeostatic needs, some substances which are considered valuable metabolites may at times be excreted

   b. Other, usually toxic, substances are always excreted in greater quantities

2. Water -- from ingestion & cellular respiration

   a. Urine

      - 1200-1400 ml/day
      - Less in hot weather & strenuous exercise

   b. Skin, via sweat glands & diffusion

      - 450-750 ml/day
      - Up to 10x more in hot weather & exercise

   c. Expired as water vapor

      - 350-450 ml/day
      - May double during exercise

   d. Feces -- 100-150 ml/day under all conditions

3. CO_2 -- from cellular respiration
    a. Overwhelming majority expired
    b. Some via urine, feces & sweat -- $CaCO_3$
4. Nitrogenous organic compounds
    a. From amino acid metabolism in the liver
        - General
            - Most via urine
            - Some via bile & sweat
        - Urea -- 90% of total
        - Urate (uric acid)
        - Ammonia (NH_3) -- quite toxic
        - Excess amino acids -- only 1-2 g/day
    b. From muscle metabolism -- creatinine
        - From unique high energy creatine-PO_4
        - Some excreted via urine
    c. From benzoic acid detoxification
        - Hippuric acid -- benzoic acid + glycine
        - Via urine
5. Non-nitrogenous organic compounds
    a. General
        - Most via urine
        - Slight via sweat & oil glands, & feces
        - Quite variable in types & amounts
    b. Glucose -- barely perceptible amounts
    c. Ketone bodies
        - From fatty acid metabolism

- Minute amounts

d. Oxalates -- small amounts

e. Citrate -- small amounts

f. Vitamins -- excess water soluble

g. Hormones

h. Enzymes -- only a few

6. Inorganic salts (electrolytes)

a. General

- Most via urine -- exceptions noted
- Some in sweat & feces

b. In decreasing amount:

Chloride
Sodium
Potassium
Sulfate
Phosphate
Calcium -- more via feces
Magnesium -- more via feces

7. Heat

a. Not a chemical substance, but there is elimination of the excess not utilized to maintain body temperature

b. From cellular respiration

c. Most via skin

- Sweat carries away more heat than dry skin
- Extra vessels deliver more heated blood

d. Some via urine, feces & expired air

D. Basic Processes *[all details later]*

1. Filtration

a. Removes majority of substances from blood

b. Substances now in space which eventually leads outside of

the body

2. Reabsorption

   a. Removal of most components from what was filtered & return to body fluids

   b. Selectivity is its importance

3. Secretion

   a. Addition of extra amounts of some substances to what was filtered

   b. From body fluids via different route

Gross Kidney Structure *[details from lab]*

A. Regions

1. Cortex

   a. Outer

   b. Columns

2. Medulla

   a. Inner

   b. Pyramids

      - Divisions -- 8-15
      - Apex -- papilla

B. Urine Collecting Structures

1. Calyces

   a. Minor

      - One per pyramid -- funnel-shaped
      - Receives urine from papillary ducts *[later]*

   b. Major -- confluence of several minor

2. Pelvis -- receives major calyces
3. Ureter
    a. Tube from narrowing of pelvis
    b. Exits kidney through hilus
    c. Represents duct for entire kidney
    d. Takes urine to bladder

C. Blood vessels

1. Renal artery & vein
2. Interlobar arteries & veins
    a. Branches from renals
    b. Run through columns
3. Arcuate arteries & veins
    a. Perpendicular branches from interlobars
    b. Run along cortical-medullary border
4. Interlobular arteries & veins
    a. Perpendicular branches from arcuates
    b. Run through cortex outwardly
5. Other branches from interlobulars
    a. Run through cortex and under capsule
    b. Example -- intralobulars

Microscopic Kidney Structure

A. Nephron

1. General
    a. Basic structural & functional unit
    b. 1.5 million per kidney

c. Essentially a tubular glandular unit

d. 2 types

- Cortical
  - Majority
  - Shorter -- 35 mm
  - Mostly within cortex
- Juxtamedullary
  - Longer -- 50 mm
  - Over half its length runs through pyramid, almost to apex (papilla)

2. Bowman's (renal) capsule

a. Double-walled rounded cup-like

b. 200 µm across

c. Squamous parietal wall

d. Visceral wall of unique podocytes -- cling to & follow contours of enclosed glomerulus *[not part of nephron* per se *-- later]*

e. Beginning portion

3. Proximal convoluted tubule

a. About 15 mm (L) x 60 µm (D)

b. Simple cuboidal cells with microvilli

c. Completely within cortex

4. Thick descending (straight proximal) tubule

a. About 2 mm (L) x 30 µm (D)

b. Low cuboidal cells with microvilli

c. Enters medulla in juxtamedullary nephrons

5. Loop of Henle (thin portions)

a. General

- About 5-15 mm (L) x 15 µm (D)
- Longer in juxtamedullary nephrons
- Squamous cells

b. Descending portion -- longer

c. Ascending portion -- shorter

6. Thick ascending (straight distal) tubule

a. About 7 mm (L) x 60 µm (D)

b. Cuboidal cells with short microvilli

c. Runs back into cortex

7. Distal convoluted tubule

a. About 10 mm (L) x 60 µm (D)

b. Cuboidal cells with sparse (beginning) to no microvilli (end)

c. Last portion of nephron

B. Excretory Ducts

1. General

a. Take liquid from nephron

b. Chemical adjustments to produce final urine

c. Pass urine to minor calyces

d. Total length of one pathway of this highly branched & interconnected complex -- 20 mm

2. Collecting tubule

a. Begins at end of distal convoluted tubule

b. Same diameter as DCT

c. Simple cuboidal cells

3. Collecting ducts

a. Smallest formed by confluence of several collecting tubules

b. Several levels of branching to larger ducts

c. Up to 100 μm diameter

d. Cells from simple cuboidal to simple columnar

4. Papillary duct (of Bellini)

a. Largest ducts -- confluence of several of largest collecting ducts

b. 200 μm diameter

c. 10-25 per papilla of a pyramid

d. Final ducts - empty into minor calyx

C. Capillaries & Arterioles

1. General

a. Supply nephron with blood for filtering

b. Receptacle for reabsorbed substances

c. Source for secreted substances

2. Glomerulus

a. Balled-up capillary bed

b. Nestled within Bowman's capsule -- tightly adherent to visceral wall

c. Special lining squamous cells -- fenestrated & extremely permeable

3. Afferent arteriole

a. Branches from “other” arteries after interlobular

b. Joins glomerulus

4. Efferent arteriole

a. Joins opposite end of glomerulus

b. Carries blood from glomerulus

c. Exception to venule draining capillaries

d. Smaller than afferent

5. Peritubular capillaries

a. Capillary bed surrounding cortical nephron portions

b. Variations in 2 nephron types

- Cortical -- around straight proximal & distal, & most of thin loop of Henle
- Juxtamedullary -- only around convoluted portions

c. Receive blood from efferent arterioles

d. Join venules which eventually lead to interlobular vein

6. Vasa recta

a. Only in association with juxtamedullary nephrons

b. Origin from efferent arterioles, just like peritubular

c. Descend into medulla, paralleling straight tubule portions & thin loop of Henle

d. Hairpin turn, just like loop of Henle

e. Lateral interconnections among vasa recta form plexuses in medulla

e. Join same venules as peritubular capillaries

D. Renal (Malpighian) Corpuscle

1. Concept -- term applied to glomerulus & the attached Bowman' capsule which surrounds it

2. Significance -- represents vital link between nephron & its initial blood supply

URINE FORMATION

Filtration

A. Introduction

1. Location -- renal corpuscles
2. Concept
    a. Filtration (diffusion under pressure) of substances from blood circulating through glomerulus into capsular space of nephron.
    b. Involves passage through glomerular endothelium, a basement membrane & the capsule's visceral wall of podocytes.
3. Significance
    a. Rapid removal of diffusible substances from blood
    b. No selectivity as to importance -- basically just size
    c. Later, more leisurely selective processes in other parts of nephron

B. Ultrafiltrate

1. Concept -- filtrate contains same concentration of substances as blood
2. Significance -- this direct quantitative reflection permits kidneys to accurately determine the homeostatic fates of the various substances
3. Exclusions -- non-permeable materials
    a. Formed elements
    b. Plasma proteins
    c. Lipids -- e.g. cyclomicrons

C. Physical Mechanisms

1. Glomerular endothelium

a. Many large fenestrations

b. Only formed elements not permeable

2. Basement membrane

a. Ionized -- highly negative

b. Repels plasma proteins -- negatively ionized

3. Visceral wall of capsule

a. Podocytes

- Branching major & minor processes -- wrap around glomerulus
- Terminals -- feet (pedicels)
- Feet from different podocytes interdigitate

b. Diffusion through gaps between feet

D. Pressures Responsible

1. Blood

a. Glomerular hydrostatic (blood) pressure at afferent arteriolar end about 60 mmHg

b. Much higher than body's other capillaries

c. This force necessary to drive filtration

2. Colloid osmotic

a. From blood's non-diffusible plasma proteins -- about 25 mmHg

b. Opposes blood pressure & filtration

3. Capsular hydrostatic

a. From filtrate constantly within capsule, between visceral & parietal walls -- about 10 mmHg

b. Opposes filtration

4. Net filtration pressure

a. Blood - (colloid osmotic + capsular)

b. 60 mmHg - (25 mmHg + 10 mmHg) = 25 mmHg

E. Rate

1. Basic
    a. 125 ml/min from all nephrons in both kidneys
    b. 180 L per day
    c. Represents 20% of the plasma
2. Variations
    a. Sex -- lower in women
    b. Variable under different conditions in same person

F. Unique Variables

1. General -- necessary to form sufficient filtrate quickly
2. To maintain high net filtration pressure
    a. Glomerulus between 2 arterioles
        - Only place in body
        - Efferent (2nd) arteriole's resistance helps maintain higher pressure than venule would
    b. Difference in afferent/efferent diameters
        - Efferent smaller
        - Increased resistance to flow raises pressure
    c. Renal blood pressure -- higher than other organs
3. Permeability -- glomerular endothelium 100x more than other capillaries

Reabsorption

A. Introduction

1. Concept -- selective removal of substances from filtrate
2. Amount -- of 180 L/day filtrate, only 1.0-1.8 L urine

3. Locations

    a. From filtrate in rest of nephron & collecting lumen -- mostly proximal

    b. To interstitial (tissue) fluid around nephron

    c. Into peritubular capillaries & vasa recta to be carried away

4. Significance

    a. Filtration was massive, but nonselective

    b. Reabsorption determines urine composition -- mostly *[secretion later]*

    c. Not inefficient, despite having to reverse most of filtration -- *[evidence later -- counter-current]*

B. Water

1. General

    a. Normally 97-99% reabsorbed from filtrate

    b. 65% from proximal convoluted & straight

2. Obligatory

    a. This must be reabsorbed

    b. Majority -- from proximal

    c. Passive -- from osmotic gradient created by reabsorption of solutes from filtrate *[details later]*

3. Facultative

    a. Variable amounts, depending on homeostatic needs

    b. From distal convoluted & collecting

    c. Controlled by ADH

        - Permeability in direct proportion
        - Reason for osmotic gradient *[later -- counter-current]*

    d. Diabetes insipidus

        - Absence of ADH

- Excretion of 15-20 L/day of mostly aqueous urine

4. Membrane mechanisms

   a. Aquaporins – water channels

   b. Membrane proteins – all body cells have these

   c. 4 subunits with channel between

   d. 8 distinct types – some also handle small solutes (e.g. glycerol)

   e. Cells of proximal convoluted and straight, and descending just thin follow sodium gradient

   f. Collecting duct cells regulated by ADH

C. Minerals

1. Sodium

   a. 99% reabsorbed from filtrate

   b. Mechanisms

      - Actively transported from tubule cell cytoplasm into interstitial fluid

      - Concentration gradient causes diffusion from tubule lumen -- most facilitated by carrier, which makes it more efficient

   c. Significance

      - Its movement is basis for co-transport of other solutes & part of osmotic reabsorption of water

      - Central role in counter-current mechanism *[later]*

   d. Variations in nephron segments

      - Proximal -- as described above

      - Distal -- variable

        - Less permeable cell membranes

        - Hormonal control -- aldosterone

2. Chloride

    a. 99% reabsorbed

    b. Mechanisms

        - Most directly follows sodium, to maintain electrical balance

        - Some by co-transport

3. Potassium

    a. Some reabsorbed

    b. Mechanisms

        - Due to Na^+/K^+ pump, transported opposite sodium -- into tubule cells from interstitial fluid

        - Tends to diffuse back out through sides at intercellular junctions, though

4. Calcium

    a. Most reabsorbed

    b. Mechanism -- co-transport

5. Magnesium

    a. Some reabsorbed

    b. Mechanism -- co-transport

6. Bicarbonate

    a. Almost all reabsorbed

    b. Mechanism -- complicated

        - Tubule lumen -- CO_2 diffuses out

        - In cell -- $CO_2 + H_2O = H_2CO_3 = H^+ + HCO_3^-$

        - Bicarbonate into interstitium by co-transport

7. Others

    a. Phosphate, sulfate & nitrate -- some reabsorbed

    b. Mechanism -- co-transport

D. Nitrogenous Wastes

1. Urea

    a. 50% reabsorbed

    b. Mechanism -- passive, follows water

2. Urate

    a. 98% reabsorbed

    b. Mechanism -- co-transport

3. Creatinine

    a. None is reabsorbed

    b. *[see below -- secretion]*

E. Organic Nutrients

1. General

    a. Glucose, amino acids, vitamins (water soluble), & ketone bodies

    b. Normal amounts completely reabsorbed -- vital

    c. Mechanisms

        - Co-transport from lumen into tubule cells
        - Facilitated diffusion from cells into interstitium

2. Proteins

    a. Completely reabsorbed

    b. Mechanism -- special handling, since non-permeable

        - From tubule lumen by pinocytosis
        - Hydrolyzed into amino acids -- now handled as already described

3. Sucrose, oxalates & citrates

   None reabsorbed

Secretion

A. Introduction

1. Concept

   a. Addition to filtrate of substances which were not filtered

   b. Opposite direction from reabsorption

      - From peritubular capillary blood
      - Into interstitial fluid
      - Enters tubule lumen

2. Locations

   a. Distal convoluted tubule

   b. Collecting tubule & duct

3. Significance

   a. Permits maximum excretion of certain substances, making up for ultrafiltrate inadequacy

   b. Some toxic substances cannot be filtered

B. Substances

1. Ammonia

   a. Too toxic for body fluids

   b. NH_3 + glutamic acid = glutamine (nontoxic)

   c. DCT reverses reaction

   d. Excreted as ammonium ion – $NH_3 + H^+ = NH_4^+$

2. Hippuric acid

   a. Benzoates -- toxic

b. Benzoic acid (e.g.) + glycine = hippuric acid (nontoxic)

c. DCT reverses reaction

3. Creatinine

a. None was reabsorbed -- secretion adds to amount excreted in urine

b. Mechanism -- active transport

4. Potassium & hydrogen

a. DCT & collecting tubules

b. Mechanisms

- Counter-transport -- earlier portions
  - From active sodium reabsorption
  - More negative tubule lumen attracts positive ions
- Active transport -- latter portions
  - K^+ -- aldosterone control
  - H^+ -- special cells, for pH homeostasis

5. Others

a. e.g. -- organic acids & bases; neurotransmitters

b. Mechanism -- active transport

6. Abnormal

a. e.g. -- drugs

b. Mechanism -- active transport

Counter-current Mechanism

A. Introduction

1. Urine/filtrate difference
    a. Urine typically hyperosmotic to original filtrate
    b. Most water usually needed in body fluids
2. Progressive concentration
    a. Would seem to occur from capsule to collecting
    b. Not possible
        - Would require active transport of water
        - Osmotic gradient 900x greater than exists
3. Variable filtrate osmotic conditions

    [all will be compared with original capsular filtrate]

    a. Isosmotic (no change) -- PCT & thick descending
    b. Hyperosmotic (more concentrated) -- loop of Henle
    c. Isosmotic (same as filtrate) -- thick ascending
    d. Hypoosmotic (more dilute) -- DCT
    e. Hyperosmotic -- latter DCT & collecting
4. Significance
    a. Permits concentration of solute wastes
    b. Conserves water
    c. Accomplished via simple fluid principles
    d. Variable due to hormonal influences -- more dilute urine <u>can</u> be produced if excess water excretion needed *[later]*

B. Underlying Principles

1. Concentration gradients

a. Increased when gong from cortex into medulla

b. Decreased when going from medulla into cortex

2. Innate behavior from physical relationships

a. Physical setup

- Parallel tubes
- Hairpin connections
- Solution flowing in opposite directions
- Semipermeable walls
- Fluid surrounding tubes

b. Results

- Setup will cause a small concentration difference to be multiplied continuously through the tubes
- <u>Must</u> be this type of setup for production of concentrated urine -- straight, or differently configured tubes would work poorly or not at all

3. Gradient maintenance

a. Loop of Henle

- <u>Establishes</u> gradient
- From descending/ascending differences *[later]*

b. Vasa recta

- <u>Maintains</u> gradient established by loop
- Own separate counter-current multiplier -- coordinated with nephron/collecting, though

c. Collecting tubule & ducts

- <u>Finish</u> the process, producing final urine
- Variable, due to ADH *[later]*

4. Osmotic counter “currents”

a. Entire mechanism based on osmotic currents

b. Created by continuously circulating filtrate, interstitial fluid & blood -- form positive feedback loops

c. Opposite currents in descending & collecting as compared with ascending

d. Opposite currents in ascending & descending limbs of vasa recta

C. Mechanisms of Action

1. Proximal convoluted tubule

   a. Results

      - 65^{+}% volume reduction of capsular filtrate
      - Proportional, though -- isosmotic to filtrate

   b. Events

      - Active sodium (with chloride) reabsorption
      - Passive osmosis of water -- follows sodium

2. Ascending thin & thick

   a. This <u>is</u> the next logical step

      - Filtrate itself is next in descending portions
      - Ascending events control those in descending

   b. Results

      - Change to isosmotic -- was hyper- at bottom of loop
      - Hypoosmotic by DCT

   c. Events

      - Active chloride (with sodium) transport out
      - No osmosis follows -- <u>impermeable</u> to water

3. Descending thick & thin

   a. Results -- very hyperosmotic by bottom of loop

   b. Events

      - Sodium diffuses in

- Water diffuses out by osmosis

c. Cause -- hyperosmotic medullary fluid *[later]*

4. Distal convoluted & collecting tubules

a. Results

- Progressively less hypoosmotic
- Variable -- from hypo- to hyperosmotic

b. Events

- Osmosis out -- no longer impermeable
- ADH responsible for variable amount -- direct proportion

c. Causes

- Active sodium (with chloride) transport out
- Hyperosmotic medullary fluid attracts water

5. Medullary tissue fluid

a. Result

- Perpetually kept hyperosmotic
- More hyperosmotic higher to lower

b. Causes

- Active salt transport out of thick ascending
- Active salt transport out of collecting
- Passive salt transport out of thin descending
- Passive urea transport out of collecting -- follows water, from ADH increase
- Vasa recta leaves behind excess sodium *[later]*

6. Vasa recta

a. Result -- prevents medullary blood from removing excess solutes

b. Causes

- Sluggish blood flow -- only 1-2% of kidney total
- Counter-current exchange mechanism
  - Removes excess water from medulla -- recall diffusion from descending
  - Leaves behind excess sodium

D. Summary

1. Production of concentrated urine
   a. Basic counter-current mechanism
   b. Increased ADH
2. Production of dilute urine
   a. Basic counter-current mechanism
   b. Decreased ADH

MICTURITION

A. Concept

1. Expulsion of urine from the bladder
2. Commonly termed urination or voiding

B. Mechanisms

1. Muscles
   a. Detrusor -- general smooth muscle of bladder wall
   b. Internal urethral sphincter
      - Smooth muscle
        - Around beginning of urethra

c. External urethral sphincter

- Skeletal muscle
- Below internal sphincter

d. Rectus abdominis

2. Volumes

a. 200-300 ml -- threshold for initiation

b. 500 ml

- Total effective capacity
- Very little ability to retain more without considerable discomfort

3. Pressure receptors

a. Within bladder wall

b. Respond to stretch from filling

c. Impulses to sacral segments of spinal cord

d. Initiate reflex muscle responses eventually leading to micturition

e. May completely occur locally -- brain <u>may</u> intervene

4. Muscle responses

a. Detrusor

- Parasympathetic impulses from spinal cord
- Wave-like rhythmic contractions
  - Towards urethral outlet
  - Periodic & widespread until maximum capacity reached

b. Internal sphincter

- Remains contracted via sacral reflex to prevent micturition
- Relaxation under different conditions
  - <500 ml -- only when external sphincter relaxed

- >500 ml -- from intense detrusor contractions

c. External sphincter

- Remains contracted via sacral reflex -- inhibition causes relaxation
- Relaxation under different conditions
  - <500 ml -- conscious decision
  - >500 ml -- unconscious, along with internal sphincter

d. Rectus abdominis

- Contracted to increase intra-abdominal pressure
- Pressure on full bladder assists

5. Brain centers

a. Cerebral cortex

- Responsible for learned reflex which contracts external sphincter
- Initiates conscious relaxation of external sphincter for micturition
- Can override spinal micturition reflex, if volume not extreme

b. Brainstem

- Pons & medulla
- Unconscious facilitation or inhibition of spinal reflex

C. Pathology

1. Incontinence

a. Concept

- Loss of bladder control
- From slight to inability to retain any urine

b. Normal in infants -- insufficient development of nervous pathways between brain & sacral cord

c. Abnormal

- Several sites of damage -- bladder, cord or brain
- Would determine severity

2. Retention

a. Concept -- inability to void

b. Causes

- Obstruction
- Spasmodic sphincter contraction
  - Nerve damage
  - Psychological factors -- e.g. stress

FLUID BALANCE & DYNAMICS

Blood Pressure Regulation -- Urinary Related

A. Autonomic Nervous Control

1. General

a. Affects kidneys only -- rest of body unaffected

b. Sympathetic division alone -- parasympathetic not utilized to produce opposite effects

2. Pressure increase

a. Moderate impulse level

b. Afferent & efferent constricted proportionately

c. Vasoconstriction raises glomerular pressure

3. Pressure decrease

a. Intense impulse level

b. Afferent more constricted than efferent

c. Arteriolar diameters closer to the same

d. Pressure lowered -- size disparity negated

B. Autoregulation

1. General

a. Local -- not from outside (e.g. nervous) influences

b. Purpose -- maintains constant effective filtration rate

c. Mechanism

- Involves nephron & arterioles
- Accomplished chemically

d. Significance

- More important than nervous
- More attuned to needs
- More effective (accurate)

2. Structure -- juxtaglomerular apparatus (JGA) or complex

a. Indistinct -- merger of 3 parts of larger structures

- First part of distal convoluted tubule
- Afferent arteriole
- Efferent arteriole

b. Each JGA from parts of same nephron/corpuscle

c. Modified cells in wall of contact areas

- Macula densa -- distal tubule
- Juxtaglomerular cells -- arterioles

3. Mechanisms

a. Sodium & chloride levels monitored -- distal filtrate

- Too low if insufficient filtration pressure -- too much reabsorption in ascending
- Too high if excessive filtration pressure -- insufficient reabsorption in ascending

b. To increase pressure & filtration rate

- Afferent arteriole dilated by macula densa
- Efferent arteriole constricted by juxtaglomerular cells -- indirect
  - Increased renin secretion into blood
  - Plasma angiotensinogen converted to angiotensin
  - Angiotensin targets efferent arteriole

c. To decrease pressure & filtration rate

- Afferent arteriole constricted
- Efferent arteriole dilated

C. Systemic Control

1. General

a. Overall BP changes throughout body

b. Kidneys affected as well

c. Sympathetic & autoregulation can counteract

2. Causes

a. Cardiac output influences on BP

b. Peripheral resistance -- e.g. widespread autonomic

c. Respiratory needs requiring BP adjustments

Osmotic Pressure Regulation

A. Scope

1. Affects the entire body
2. Important homeostatic mechanism -- controls ECF/ICF interchanges
3. Intricate & interrelated -- very simple consideration here

B. Increases

1. Concept -- hyperosmotic condition in body fluids
2. Causes
    a. Solute retention
        - Ingestion -- more salt (solute) intake
        - Kidney diseases -- excessive reabsorption
        - Hormonal
            - Hyperglycemia
            - Aldosterone hypersecretion & no ADH change -- usually vary together
    b. Water loss
        - Ingestion -- too little intake
        - Fluid loss -- solutes lost as well, but water causes more dramatic effects
            - Diarrhea
            - Vomiting
            - Excess sweating
        - Hormonal
            - Hyperglycemia -- water drawn from tissues
            - Hyposecretion of ADH -- diabetes insipidus

C. Decreases

1. Concept -- hypoosmotic condition in body fluids
2. Causes
    a. Solute loss
        - Ingestion -- insufficient salt (solute) intake
        - Kidney infection -- e.g. glomerulonephritis
        - Hormonal
            - Hypoglycemia
            - Aldosterone hyposecretion
    b. Water retention
        - Ingestion -- excess intake
        - Kidney failure
        - Hormonal -- ADH hypersecretion

D. Control Mechanisms

1. Osmoreceptors
    a. Within hypothalamus
    b. Monitor osmotic pressure of body fluids
    c. Activity level
        - Hyperosmotic causes more activity
        - Hypoosmotic causes less activity
2. Antidiuretic hormone (ADH)
    a. Secreted by hypothalamus
    b. Stored within pars nervosa
    c. Amounts
        - More from increased osmoreceptor activity

- Less from decreased osmoreceptor activity

3. Water reabsorption

   a. In DCT & collecting tubules/ducts

   b. Direct proportion with ADH amount

      - More reabsorption dilutes hyperosmotic body fluids
      - Less reabsorption excretes excess water from hypoosmotic body fluids

4. Drinking center

   a. Within hypothalamus

   b. Controls thirst

   c. Precise amount needed consumed

      - Immediate relief -- prevents further desire
      - Takes 30^{+} min. for ingested water to actually dilute body fluids, though

Extracellular Fluid Volume Regulation

A. Scope

1.

2. *[same as for osmotic pressure]*

3.

4. Not any particular component of fluids as in osmotic changes -- the water is of critical importance, though

B. Increases

1. General -- all produce solute and water retention

2. Ingestion

   a. Increased solutes & water

b. Malnutrition

3. Hormonal -- aldosterone & ADH hypersecretion

4. Kidney diseases -- e.g. chronic renal failure (insufficiency)

5. Cardiovascular diseases

   a. Hypertension

   b. Congestive heart failure

6. Drugs

   a. All would increase ADH

   b. e.g. -- nicotine, morphine, barbiturates, anesthetics

C. Decreases

1. General -- caused by <u>any</u> general body fluid loss

2. Ingestion -- general decrease (e.g. undernourishment)

3. Hormonal -- aldosterone &/or ADH hyposecretion

4. Diseases

   a. Kidney reabsorptive deficiencies

   b. Systemic infections

5. Fluid losses

   a. Excessive sweating or severe burns

   b. Vomiting or diarrhea

   c. Hyperventilation

6. Drugs

   a. All diuretics

   b. e.g. -- alcohol, caffeine, lithium

D. Control Mechanisms *[Example of fluid volume <u>decrease</u>]*

1. Sodium reabsorption

    a. Renin -- secretion from JGA

    b. Angiotensin I -- renin converts from angiotensinogen

    c. Angiotensin II

        - More active form
        - Derived from angiotensin I
        - Converted by lung enzyme

    d. Aldosterone

        - Secretion stimulated by angiotensin II
        - Increased sodium/chloride reabsorption

    e. Atrial natriuretic factor

        - Secreted by heart wall
        - Proportionate with blood volume
        - <u>Inhibits</u> sodium/chloride reabsorption

    f. Salt appetite

        - Hypothalamic center
        - Regulates desire to consume salt
        - More active under 2 body fluid conditions
            - Less sodium concentration
            - Decreased fluid volume

2. Water reabsorption

    a. Osmoreceptors

        - Detect hyperosmotic body fluids
        - Gradient purposely caused by sodium/chloride reabsorption

b. ADH

- Secretion increased
- Water reabsorption increased
- Counteracts hyperosmolality
- Increases body fluids -- ultimate goal

Electrolyte Balance

A. General

1. Scope
   a. Principal ions only
   b. Others important -- e.g. phosphate, sulfate
2. General effects
   a. Determine water distribution in body
   b. Acid-base balance
   c. Cell membrane irritability -- nerve & muscle

B. Potassium

1. Functions -- principal intracellular cation
   a. Cytoplasmic osmotic pressure maintenance
   b. Membrane electrical potentials -- nerve & muscle
   c. Enzyme activation
2. Influences upon potassium
   a. Aldosterone
      - Sodium reabsorption causes potassium secretion
      - Excess potassium increases aldosterone
   b. pH

- Acidosis causes more K^+ reabsorption
- To cause secretion of H^+ via ion exchange

c. Sodium

- Basically moves opposite from potassium
- Kidneys handle Na^+ better -- if both low, it is more reabsorbed

C. Sodium

1. Functions -- principal <u>extracellular</u> cation

a. Extracellular osmotic pressure maintenance -- tissue fluid & blood

b. Sodium pump

- Establishes basic membrane gradients
- Permits transport of other substances

c. Membrane electrical potentials -- nerve & muscle

2. Influences upon sodium

a. Aldosterone -- *[previously covered]*

b. Atrial natriuretic factor -- *[previously covered]*

c. Glomerular filtration rate (GFR)

- Indirect proportion for GFR : sodium excretion
- Conserves sodium when filtration in excess

d. Other solutes -- glucose (e.g.)

- Hyperglycemia leads to glycosuria
- Sodium displaced by glucose
- More sodium excretion than desirable

D. Calcium

1. Functions -- most abundant cation (most in bones)
    a. Stabilizes membranes
    b. Regulates muscle contraction -- intracellularly
    c. Enzyme regulation -- as co-factor
    d. Adherence of adjacent cells
2. Influences upon calcium
    a. Hormonal
        - PTH -- *[previously covered]*
        - Thyrocalcitonin -- *[previously covered]*
    b. Digestive absorption
        - Vitamin D enhances
        - Phosphates inhibit
    c. Excretion
        - Most via feces -- vitamin D & phosphate control
        - Some via urine -- handled like sodium, under PTH influence

E. Magnesium

1. Functions -- equally distributed
    a. Membrane stabilization -- nerve & muscle
    b. Enzyme co-factor -- e.g. ATPase & peptidases
    c. Calcium antagonist -- often
2. Influences upon magnesium
    a. Hormonal
        - T_3, T_4, GH & PTH -- *[previously covered]*
        - Via movements in/out of cells & bones

b. Excretion

- Most reabsorbed -- PTH control
- Direct nephron effect -- excess excreted

F. Chloride

1. Functions -- principal <u>extracellular</u> anion
   a. Counteracts cations
   b. Osmotic pressure maintenance
   c. Acid-base balance -- usually via HCl
2. Influences upon chloride
   a. Sodium -- follow each other (except nerve/muscle)
   b. Digestive -- part of gastric HCl
   c. Bicarbonate
      - Normally balance each other
      - Excess Cl^- loss (e.g.) -- alkalosis

<u>Acid-Base Balance</u>

A. Extracellular Buffering System

1. Dual function -- absorbs excess ions of opposite types
   a. Acidic -- H^+
   b. Basic -- e.g. OH^-
2. Systems utilized
   a. Bicarbonate -- mixture of H_2CO_3 & $NaHCO_3$
   b. Phosphate
   c. Protein
3. Mechanism -- using bicarbonate system
   a. Acid buffering

$HCL + NaHCO_3 = H_2CO_3 + NaCl$

b. Basic buffering

$NaOH + H_2CO_3 = NaHCO_3 + H_2O$

B. Lung Excretion

1. Frees CO_2 from blood in carbonic acid form
2. Dysfunctions
   a. Respiratory acidosis
      - From hypoventilation
      - Normal correction -- breathing control system increases ventilation
   b. Respiratory alkalosis
      - From hyperventilation
      - Uncommon

C. Kidney Excretion

1. Bicarbonate -- adjusted by varying reabsorption
2. Hydrogen
   a. Exchanged for sodium *[previously covered]*
   b. Secondary frees bicarbonate which was utilized for neutralizing H^+ in body fluids
   c. H^+ neutralized within urine
      - Combined with phosphate
      - Combines with ammonia -- ties up potentially harmful ammonia as well