Urinary System

With

The Fetal/Neonatal Kidney

&

Water and Electrolyte Balance
Kidneys

• Are paired, bean-shaped
• Just above the waist behind the parietal peritoneum and posterior wall of the abdominal cavity
• They are retroperitoneal!
• Located between T-12 and L-3
• Right kidney is slightly lower than the left
• 10-12 cm long; 5-7.5 cm wide; 2.5 cm thick
• The HILUS is the center of the concave border of the kidney through which the ureter exits the kidney – is also the entrance to a cavity within the kidney called the renal sinus
Three Layers of Tissue Surround the Kidney

1. Inner most: renal capsule – continuous with the outer coat of the ureter; serves as a trauma barrier and infection barrier for the kidney

2. Adipose capsule: fatty capsule around the renal capsule; holds firmly in place within the abdominal cavity

3. Outer most: renal fascia; anchors kidney to surrounding structures and abdominal wall
1. Forceps
2. Fibrous capsule
3. Superior pole
4. Lateral border
5. Renal artery
6. Renal vein
7. Ureter
8. Renal pelvis
9. Medial border
10. Inferior pole
11. Hilus
• Flow of urine through the kidney
• *papilla project into minor calyx
• *extension of cortex of kidney
Ureters

- 2 each – one for each kidney
- Is extension of renal pelvis and extends 25-30 cm to bladder
- Enter bladder at superior lateral angle of its base
Ureters, Continued

- There is no anatomical valve at ureteral openings into bladder
- There IS a FUNCTIONAL valve
- Because the ureters pass obliquely through and into the bladder, the pressure of the urine compresses the ureters and prevents urine reflux as pressure increases in the bladder
- “kinks the hose” and prevents “backwashing”
- If valve is not working, bladder infections can travel superiorly to become kidney infections
Ureters, Continued

• Primary function: transport urine from renal pelvis to bladder

• Three mechanisms accomplish this:
  1. Peristalsis
  2. Hydrostatic pressure
  3. Gravity
Urinary Bladder

- Shape is dependent on volume of urine
- Walls are thicker when empty
- Walls are thinner when full
- Spherical when slightly distended
- Pear-shaped as volume of urine increases and rises into abdominal cavity
- Muscular layer that allows for bladder stretch is the **detrusor muscle**
- Detrusor also used in the construction of the internal sphincter (sphincter vesiculi)
Urinary Bladder, Cont’d

• At base of bladder internally is a smooth triangular area: trigone
• Trigone points anteriorly like a funnel
• The three points of the trigone are the 2 ureteral openings posteriorly and the internal urethral orifice, anteriorly
Male, Continued

- Sphincter vesiculi
- Urogenital Diaphragm (External Sphincter)
- Cowper's Gland
Urachal Abnormalities

• Patent urachus
• Cyst
• Internally blind
• Externally blind
Bladder Innervation -- Normal

- Descending pathways have arrows going down (motor)
- Ascending pathways have arrows going up (sensory)
- From cerebral cortex is voluntary sphincter relaxation
- From lower cord is sympathetic inhibitory innervation to squeeze sphincter shut
- Pudendal nerve gives voluntary control
- Pelvic nerve provides parasympathetic innervation to relax bladder and contract detrusor
- **Primitive reflex loop that initiates micturition**
- Detrusor muscle
- Sphincter vesiculae (exaggerated for this graphic)
- External sphincter (likewise)
- Sacral innervation in cord S_{2,3,4}
Bladder Innervation -- Anomaly

- Lesion above $S_2$
- Innervations same as on previous slide
- NOTE: reflex loop is primarily active in pre-potty trained kids AND with lesions above $S_2$
  1. Voluntary connection severed
  2. No sphincter relaxation
  3. Reflex loop is back within a few days after injury
     1. Leads to NO voluntary sphincter release
     2. Leads to NO voluntary sphincter suppression
     3. Causes **SPASTIC neurogenic bladder**
     4. Due to hyperactive detrusor reflex
  4. Bladder incompletely empties
  5. Increased UTI’s
Bladder Innervation – Anomaly 2

Lesions:
• Sacral segment lesion
• Cauda equina lesion
• Voluntary connection is severed
• Sympathetic innervation is severed (add to notes to correct graphic!!)
• Reflex loop is severed
• Voluntary micturition is “blocked”
• So, no urine release OR suppressed
• Leads to FLACCID neurogenic bladder due to a diminished detrusor reflex
• Which leads to incomplete emptying and increased UTI’s
Urethra: A small tube that leads from the floor of the bladder to the exterior of the body

- **Female**
  - Urethra lies directly posterior to the symphysis pubis
  - Lies in front of the anterior wall of the vagina
  - Is about 1.5 inches in length
  - About 0.25 inches in width
  - External opening is the urethral meatus and is located between the clitoris and the vaginal opening
  - NOTE: about 40% of women have their urethral meatus inside their vagina

- **Male**
  - Urethra is about 8 inches long
  - Immediately below the bladder, it passes through the prostate (remind students of seminalplasmin)
  - Pierces the urogenital diaphragm
  - Finally pierces the penis and exits at the urethral meatus
  - Serves as the tube through which urine passes
  - The male urethra also serves as the tube through which semen is ejaculated
  - Urethra (for both genders) is the final portion of the urinary system
Urinary Incontinence Classification - 1

Urge Incontinence
• Most common in senior citizens
• Minimal warning before involuntarily voiding
• Is due to detrusor overactivity (uninhibited bladder contractions)
Stress Incontinence

- Due to sneezing, laughing, coughing in daytime
- Due to a “sloppy” sphincter vesiculi
- May follow prostatectomy, childbirth
Overflow Incontinence

- Leak minute amounts in day and noc
- Due to a distended bladder
- Due to an inability to empty bladder completely (underactive detrusor)
Detrusor Hyperactivity with Impaired Contractility (DHIC)

- Occurs in the elderly
- Due to decreased bladder contractility with urine retention
Urinary Incontinence Classification - 5

• Other contributing factors to incontinence
  – Drugs
  – Suprasacral cord lesion
  – Pelvic trauma
  – GU surgery
  – Congenital sphincter vesiculi weakness
  – Malignancy
  – Advance age
  – Benign prostatic hypertrophy (BPH)
Nephron

• Functional unit of kidney
• Functions in:
  – Filtration
  – Acid-base balance
  – Toxic waste removal from blood
• Eliminated materials are collectively called urine
• Total volume of blood in our bodies is filtered by the kidneys approximately 60 times a day
Nephron -- generic

- Afferent arteriole in
- Efferent arteriole out
- Glomerulus between the two
- Bowman’s capsule around the glomerulus
- Hooked to PCT
- Hooked to LoH
- Hooked to DCT
- Connects to collecting tubule
- Vasa recta interwoven through and around PCT, LoH, DCT
Nephron and Acid-Base Balance

Normal

Acidosis

Alkalosis
Blood Flow Through Kidney

- Lobar arteries are also known as segmental arteries
- Note difference between interLOBAR and interLOBULAR
- Efferent arteriole is smaller than the afferent arteriole
Juxta-medullary nephron

1. Interlobular artery
2. Afferent arteriole
3. Efferent arteriole
4. Peritubular capillaries
5. Interlobular vein
6. Glomerulus
7. Bowman’s capsule
8. PCT
9. Descending limb
10. LoH
11. Ascending limb
12. DCT
13. Collecting tubules
14. Papillary duct
Urine Formation

• Requires three processes:
  – Glomerular filtration
  – Tubular reabsorption
  – Tubular secretion

• All processes depend necessarily on blood flow into and out of the kidney
1. Glomerular blood hydrostatic pressure – the chief pressure; hydrostatic pressure is the force that a fluid under pressure exerts against the walls of its container; glomerular blood hydrostatic pressure means the blood pressure in the glomerulus; this pressure tends to move fluid out of the glomeruli at a force averaging about 60 mm Hg.
2. Blood colloidal osmotic pressure – opposes the GBHP; because the blood has a much higher concentration of protein than filtrate, water would move out of the filtrate and back into the blood vessel if the GBHP were not greater than the BCOP; this pressure generally runs about 30 mm Hg
3. Capsular hydrostatic pressure – opposes GBHP; when the fluid is forced into the capsular space of the Bowman’s capsule, it meets the walls of the capsule and the fluid which has already filled the renal tubule. Due to this, some filtrate is pushed back into the capillary. The amount of “push” is the CHP, and is generally around 20 mm Hg
Pressures, Cont’d

Effective Filtration Pressure: $P_{\text{eff}}$

- Is the difference between the sum of the CHP and BCOP and the GBHP:

\[
P_{\text{eff}} = \text{GBHP} - (\text{CHP} + \text{BCOP})
\]

\[
60 - (20 + 30) = 10 \text{ mm Hg}
\]

- The $P_{\text{eff}}$ is about 10 mm Hg
- This amount of pressure produces about 125 mL of filtrate per minute in both kidneys
- Also called the Net Filtration Pressure (NFP)
Effective Filtration Pressure

- GBHP = 60 mm Hg
- BCOP = 30 mm Hg
- CHP = 20 mm Hg

$$60 - (30 + 20) = 10 \text{ mm Hg}$$

$$= P_{\text{eff}}$$
Altered $P_{\text{eff}}$ in Selected Disease States

- **Increased** in glomerulonephritis
- **Reduced** in hemorrhage – if $P$ goes less than 50 mm Hg, no urine is produced = anuria
- **Reduced** in flight or fight – secondary to reduced flow through the afferent arteriole because of blood shunting
Filtration Fraction

- The % of plasma entering the nephrons that actually becomes glomerular filtrate
- Averages about 16-20%
Renal Corpuscle = Glomerulus + Bowman’s Capsule

- Filtrate is similar to plasma without the formed elements and with less protein concentration
- 99% of plasma forced into Bowman’s capsule returned to blood via peritubular capillary -- ARROW
Three Major Mechanisms of Renal Plasma Composition Adjustment

1. Glomerular filtration
2. Tubular reabsorption
3. Tubular secretion
Proximal Convoluted Tubule -- PCT

- PCT is ALWAYS permeable to water!
- 80% of water reabsorbed, here, follows Na\(^+\) reabsorption – obligatory water reabsorption
- Na\(^+\) reabsorption under aldosterone regulation
- Ca\(^{2+}\) removed from “pre-urine” via tubular reabsorption under PTH control
Distal Convoluted Tubule -- DCT

- $K^+$ reabsorbed in a passive manner
- $Na^+$ reabsorbed in a passive manner
- $Cl^-$ reabsorbed in an active manner
- Aldosterone causes $Na^+$ retention and excretes $K^+$ -- otherwise, we reabsorb $K^+$ and excrete $Na^+$ with water and $Cl^-$
Dialysis

- Dialysis is a process in which solvent molecules, other small molecules and hydrated ions pass from a solution through a membrane.
- Dialysis is used to purify proteins and is used in patients with renal failure to clean their blood, i.e., remove toxins that would have, otherwise, been removed by their kidneys, were they functioning.
Hyponatremia

1. Low blood levels of Na$^+$
2. Causes ANG II secretion which constricts the efferent arteriole and increases glomerular pressure
3. Also causes aldosterone secretion which increases Na$^+$ reabsorption
4. Both mechanisms increase blood [Na$^+$]
AVP/ADH and Water Reabsorption

- AVP “opens” membranes to “let water out” of the DCT and back into the blood
- Second messenger is cAMP
Juxtaglomerular Apparatus

- JG cells = smooth muscle cells
- Macula densa cells = chemoceptors
Blood Pressure Regulation -- Kidneys

- (____) renin-angiotensin mechanism

- (- - - - -) tubuloglomerular feedback mechanism (renal autoregulation)
## Urine Chromo-Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>State</th>
<th>Color</th>
<th>State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pale yellow or amber</td>
<td>Normal</td>
<td>Colorless</td>
<td>Dilute with low SpG PROBABLY; 1 exception: polyuria due to osmotic diuresis because of glycosuria</td>
</tr>
<tr>
<td>Brown-black</td>
<td>Hg, Pb poisoning, phenol poisoning, hemorrhage, melanotic CA (black)</td>
<td>Brown/tea</td>
<td>Blood or free Hgb; alkaptonuria</td>
</tr>
<tr>
<td>Orange red</td>
<td>Conjugated bilirubin</td>
<td>Dark orange</td>
<td>Pyridium</td>
</tr>
<tr>
<td>Pink</td>
<td>Beets, blackberries, vegetable dyes (food colorings, candy, sodas), rhubarb, phenolphthalein</td>
<td>Blue</td>
<td>Trp $\rightarrow$ indican + [O] $\rightarrow$ indigo blue: causes blue discoloration of diaper after several hours; urine isn’t blue</td>
</tr>
<tr>
<td>Milky</td>
<td>Fatty globules, GU pus (infection)</td>
<td>Greenish</td>
<td>Bile pigments, generally with jaundice</td>
</tr>
<tr>
<td>Red</td>
<td>Blood, urates</td>
<td>Violet</td>
<td>May be caused by turpentine</td>
</tr>
</tbody>
</table>
What Causes Urine to Turn Red?

- RBC in urine
- Analgesics (aminopyrine)
- HgB
- Bile products
- Flagyl
- Beets
- Laxatives (Ex-Lax type that had phenolphthalein in them – not sold any more)
- S. marcescens: implications in nursery
Patient “Qualifications” for Urine Cultures*

- ALL children with positive Dip Sticks
- ALL men with positive Dip Sticks
- Women who have been hospitalized
- Women with pyelonephritis
- Women with hx of renal anomalies
- Women with hx of D. mellitus
- Women with hx of more than 3 UTI’s in the past 12 months

*NOT INCLUSIVE
### Casts

| Casts: mucoprotein matrix; as they are dehydrated, they lose their shape and take on the shape of their renal "tubule" origin |
|---|---|
| Hyalin | contain albumin, IgG, transferrin and other proteins; from normal renal tubule mucoprotein secretion; occasionally observed |
| Granular (waxy) | contain albumin, IgG, transferrin and other proteins; suggestive of renal parenchymal disease |
| Broad | renal failure casts; an advanced form of granular casts; typical in end-stage renal disease |
| RBC | contain 10-50 discrete RBC; suggestive of glomerular disease |
| WBC | contain discrete WBC; due to pyelonephritis, polyarteritis, etc |
| Hematin | orange to brown in color; due to acute renal tubular injury and chronic failure |
| Fatty | contain fat bodies; when illuminated, appear to have maltese crosses with polarized light; due to nephrotic syndrome |
Hematuria

• 0-5 RBC/HPF are considered normal
• Microscopic hematuria may be caused by fever, exercise and/or urinary tract lesion
• Gross hematuria may be due to coagulation defects, renal infarct, sickle cell disease, calculus, CA, prostatitis – AND! menstruation
Remember: in females, menses may get in urine; 40% of women’s urethral meati are inside the vagina

Hosp Prac, ca Oct 1992
Hematuria

Macroscopic examination may reveal gross hematuria throughout urination, only at the beginning, or only at the end, and may also reveal clots.

- Bleeding throughout urination? Consider a bladder lesion or upper tract pathology.
- Last few drops (terminal hematuria)? This suggests the bladder neck or prostate as the site.
- At onset of urination only (initial hematuria)? Think of lesions below the bladder (especially the prostatic urethra in males).
Etiological Clues in Hematuria

Hosp Prac ca Oct 1992

PATIENT HISTORY IN HEMATURIA

A thorough, detailed history remains paramount in the work-up of hematuria. It can give many clues about the probable bleeding site.

- Documentation of easy bruising or prolonged bleeding after a simple cut should direct efforts toward seeking a bleeding or coagulation disorder.

- Hematuria associated with colicky pain radiating from loin to groin strongly suggests passage of a ureteral stone.

- Hematuria developing after trauma involving the flank probably indicates a contusion or other injury.

- A history of sore throat, hypertension, and facial and peripheral edema in an adolescent suggests acute glomerulonephritis.

- An episode of painless gross hematuria has a 20% chance of indicating a kidney or bladder tumor.

- Hematuria accompanied by lower urinary tract symptoms and signs (such as frequency, dysuria, and pyuria) points to a diagnosis of cystitis (particularly common in females).

- A sexually active young woman with hematuria in all likelihood has intercourse-related ("honeymoon") cystitis.

Note: The patient's age and occupation may shed light on the cause of bloody urine.

Figure 2
Pyuria

- WBC in urine
- 0-10 WBC/HPF are considered normal
- > 10 WBC/HPF is pyuria; find site of infection
Crystalluria

- Urates/carbonates/ammonium salts from end products of metabolism
- Calcium, phosphorus, amino acids due to excesses of nutrients
- Crystals MAY be a clue to stone formation and to some metabolic disorders
<table>
<thead>
<tr>
<th>Crystal</th>
<th>Illustration</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid</td>
<td><img src="image1" alt="Uric acid" /></td>
<td>&quot;football&quot;; hyperuricemia causes uric acid crystalluria; problem with patients with leukemia types of CA due to cytotoxic drugs (with increased cell death, have an increase in nucleic acids); treat with bicarbonate or citrate; milk, veggies, fruits (except plum, prunes, cranberries)</td>
</tr>
<tr>
<td>Amorphus urates</td>
<td><img src="image2" alt="Amorphus urates" /></td>
<td>Not considered to have any particular clinical relevancy</td>
</tr>
<tr>
<td>Calcium oxalate</td>
<td><img src="image3" alt="Calcium oxalate" /></td>
<td>opaque &quot;X&quot; through center; about 2/3 of all calcium containing stones; treat with veggies, milk, fruit (except plums, prunes, cranberries)</td>
</tr>
<tr>
<td>Sodium urate</td>
<td><img src="image4" alt="Sodium urate" /></td>
<td>&quot;Zinnia&quot;</td>
</tr>
<tr>
<td>Tyrosine</td>
<td><img src="image5" alt="Tyrosine" /></td>
<td>Rare; &quot;dandelion puffs&quot;; metabolic disorder; liver disease</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td><img src="image6" alt="Sulfonamides" /></td>
<td>&quot;wheat shock&quot;; treat with bicarbonate; not as common nowadays</td>
</tr>
<tr>
<td>Cystine</td>
<td><img src="image7" alt="Cystine" /></td>
<td>&quot;Wheat cracker&quot;; rare; metabolic disorder; treat with bicarbonate, lots of water or Diamox; may be present with or WITHOUT stones</td>
</tr>
<tr>
<td>Leucine</td>
<td><img src="image8" alt="Leucine" /></td>
<td>&quot;poker chips&quot;; rare; metabolic disorder; liver disease</td>
</tr>
<tr>
<td>Crystal</td>
<td>Illustration</td>
<td>Comment</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Ammonium urate</td>
<td></td>
<td>&quot;Thorn-apple&quot;; tx by increasing fluid intake</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td></td>
<td>&quot;Stake&quot;; due to hypercalciuria; over extended immobility; tx with increased fluid intake</td>
</tr>
<tr>
<td>Hypercalciuria: associated with hyperparathyroidism and bone resorption (prolonged immobilization)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple phosphate: MgNH₄PO₄</td>
<td></td>
<td>Due to UTI -- especially Proteus and some strains of Staphylococci (urease activity); treat with meat, bread, protein foods, cranberry juice, plums, prunes; increase fluid intake; may cause &quot;Staghorn&quot; calculus formation -- another form of triple phosphate crystal; this form of calculus &quot;almost always&quot; due to UTI</td>
</tr>
<tr>
<td>Amorphous phosphate</td>
<td>&quot;Leaves&quot;</td>
<td>Larger than amorphous urates; not considered to have any particularly clinical relevancy; increase fluid intake</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>&quot;Dumb-bell&quot;</td>
<td>&quot;Dumb-bell&quot;; increase fluid intake</td>
</tr>
</tbody>
</table>
Urolithiasis

- Men affected more than women
- Tend to be older than 30 YOA
- Tend to be unilateral in about 80% of patients
- Stones provide for UTI, as well:
  - Due to the obstruction they cause
  - Due to trauma they cause to the tissue
- About 20% of calcium stones are due to increased uric acid excretion with OR without hypercalciuria
Urolithiasis – “Mechanism”

- Uric aciduria
- Flows to collecting ducts
- Uric acid precipitates
- The solid uric acid binds with calcium oxalate
- And forms a stone with a uric acid core ("nucleus")
Magnesium ammonium phosphate

• aka triple phosphate
• “almost always” due to UTI with Proteus or some Staphylococci with urease activity
• $\text{MgNH}_4\text{PO}_4$
IVP: IntraVenous Pyelogram

- Discuss allergies to shellfish, iodine
- Media given slow IV push
- Taste in mouth after injection
- Visualization and why
- Voiding cystourethrogram can be difficult – may still want one
Fetal/Neonatal Kidney
Introduction

1. Fetal urine formation begins during the 9th-11th week of gestation.
2. New glomeruli formation ceases between a fetal weight of 4.6-5.5 lbs.
3. More than 90% of newborns urinate within 24 hours of birth.
4. Approximately 100% of newborns urinate within 48 hours of birth.
• The cortex of the kidney is NOT as mature as the medulla at birth.
• The glomerular filtration rate (GFR; the rate at which glomerular filtrate is formed -- generally around 130 mL/min) increases rapidly in the first 7 days of life.
• This is probably due to the increase in GFR in the juxtamedullary nephrons.
• After day 7, the GFR increases more gradually.
• This effect is probably due to an increase in GFR in the cortical nephrons.
• The GFR gets to the adult level by about 1 year of age.
Concentrating Ability of The Fetal/Neonatal Kidney

- The day an infant is born, the concentrating ability of the kidney, i.e., to make adult-like urine, is about 45% of the concentrating ability of the adult.
- The maximal urine concentrations observed in the newborn is about 650 mOsm/L (refer back to CHEM 121 for information on osmolarity).
- This ability approximates half that of the adult's ability.
- This is NOT due to an inability of the immature kidney, rather it is reflective of the infant's anabolic state, i.e., with increased anabolism (refer to your A&P I notes for anabolism), the greatest percent of dietary protein is used in synthesis and NOT catabolism.
- Hence, there is a concurrent decrease in urea excretion (review your BIOL 224 notes on the urea cycle and protein catabolism).
- If a high protein diet is fed to a two-week old infant, it will produce the concentrated urine that an adult will produce.
The graphic relationships between the amount of ECF as a percent of total Body Weight and the concentrating ability of the kidneys during the first week of age.

- Note that the ECF decreases from approximately 60% of the total body weight at about 20 weeks of gestation to around 40% by one week of age.
- Note also that from term to one week of age that the reduction in ECF is very gradual (from about 45% to 40% at one week).
- During that same time, note the rapid increase in concentrating ability of the kidneys.
- The overall increase in osmolarity in the first week is probably due to correction of the infant's INITIAL hypo-osmotic (i.e., expanded) ECF volume.
- The kidney is necessary in transitional changes from the expanded ECF volume of the fetus/newborn to the POST-NATAL ECF volume homeostasis.
• When the infant is 3 months old, more or less, its kidneys are at about 100% of the concentrating ability of the adult.
• Maximal urinary concentration observed in adults is about 1400 mOsm/L.
• Both levels (half and 100%) are dependent upon nutrition and development.
Water Requirements

- Water requirements for infants are dependent upon water loss from the skin, lungs, feces and urine.
- The NRC recommends 0.05 oz/kcal/d.
## General Suggestions for Water Intake for Infants and Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Requirements For Water (oz/lb/d)</th>
<th>Avg weight lbs; (50th Percentile)</th>
<th>E.g., vol/d (oz/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.33 mo</td>
<td>2.15</td>
<td>8.8</td>
<td>19</td>
</tr>
<tr>
<td>0.25 yr</td>
<td>2.31</td>
<td>14</td>
<td>32</td>
</tr>
<tr>
<td>0.5 yr</td>
<td>2.15</td>
<td>17.6</td>
<td>38</td>
</tr>
<tr>
<td>1 yr</td>
<td>1.92</td>
<td>23</td>
<td>44</td>
</tr>
<tr>
<td>2 yrs</td>
<td>1.85</td>
<td>27.6</td>
<td>51</td>
</tr>
</tbody>
</table>
NOTE

• Although it appears that the daily water requirements are going down as the baby ages, they are really requiring MORE water as they are at heavier weights as they get older.
In General

• As a general rule, breast milk and formula GENERALLY supply appropriate amounts of water to/for the infant.
• In general, if "X" amount of milk (breast or formula) is fed to an infant, the infant's body responds with cell growth and has normal water excretion at about 100% that of an adult at one month of age.
• On the other hand, if the volume of water in "X" amount of milk WITHOUT the milk solids is fed to the baby, the baby's body responds by having NO cellular growth, decreased water excretion which leads to INcreased water retention.
• This retained water is NOT in the cells, rather it is in the interstitium.
• This causes a dilutional hyponatremia (too much water dilutes the sodium ion concentration).
• This is common in early infancy -- particularly in first babies as parents are learning how to care for the baby.
NOTE

• NOTE: In a hot environment, the baby DOES require more water.

• In addition, with vomiting and/or diarrhea, watch the baby for fluid/electrolyte disorders/imbalances as they will dehydrate very rapidly.

• PediaLyte is a good fluid and electrolyte replacement for infants and kids.
Dehydration

- Infants can get into serious water depletion within 36 hours similar to that observed in adults who have been without water for 5 days.
- Dehydration occurs faster in infants than adults because water reserves are decreased relative to the BMR.
- An increased BMR leads to increased urine volume and increased skin/lung water losses.
Over Hydration (Hyperhydration) of Infants

- If a water load is given to an infant that causes the infant's kidneys to reduce their absolute rate of urine formation.
- This makes the infant more vulnerable to over-hydration which leads to water intoxication.
- With water intoxication, sodium ion levels are lowered, the baby becomes restless, may develop N/V, diarrhea, poly/oliguria and may develop convulsions.
- Water intoxication develops when water is fed to a baby in place of milk or formula or if the formula is diluted excessively.
- BUT, if the infant is thirsty, let him or her drink water AFTER milk/formula until his or her thirst is quenched –
  - THEY WILL AUTO- REGULATE!!!!!!!!!!!!!!!!!!!!!

- When, then ought one add water to the infant's diet?
- Somewhere around 1-3 months of age or prn infant's needs.
- REMEMBER: An infant is better able to withstand the stress of water DEPRIVATION than the stress of HYPERHYDRATION.
For the first week or so, excreted urine is weakly acid to neutral or slightly alkaline. After the first week, it's about the pH of older children and adult urine.
Water and Electrolyte Balance and Regulation
- Water makes up 55-60% of the average adult's body weight.
- It makes up a greater percentage of a child's total body weight.
- The reductions observed as we age are due to a reduced lean body mass and increased adipose tissue.
- Adipose tissue is water free tissue.
- LBM has a higher water content.

<table>
<thead>
<tr>
<th>Total Body Water</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Newborn infant</strong></td>
<td>75-80% of total body weight (50% in ECF and 50% in ICF)</td>
</tr>
<tr>
<td><strong>Average adult male</strong></td>
<td>60% of total body weight (about 35% in ECF and 65% in ICF)</td>
</tr>
<tr>
<td><strong>Average adult female</strong></td>
<td>50% of total body weight (Ibid)</td>
</tr>
<tr>
<td>In Elderly</td>
<td>45-50% of total body weight</td>
</tr>
</tbody>
</table>

These reductions are due to two things: 1) reduced LBM as we age and 2) increased adipose tissue as we age.

Adipose tissue is water free tissue; LBM has a higher water content.
- The dynamic nature of the total water in our bodies.
- When we think of water stores in our bodies, it's easy to visualize water in the plasma (7% of total body water), in the cells (62.5% of total body water) and water in between the cells (18% of the total body water).
- Water, though, is also found in connective tissues (5%), water moving between the cells (2.5% ) and in bone (5%).
In terms of "compartmentalization", the fluid "spaces" are subdivided into extra-cellular fluid (ECF) and intracellular fluid (ICF).

<table>
<thead>
<tr>
<th>Compartmentalization of &quot;Body&quot; Waters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECF</strong></td>
</tr>
<tr>
<td>pH about 7.4</td>
</tr>
<tr>
<td>Glucose about 90</td>
</tr>
<tr>
<td>Na⁺</td>
</tr>
<tr>
<td>Cl⁻</td>
</tr>
<tr>
<td>HCO₃⁻</td>
</tr>
<tr>
<td><strong>Primary lytes</strong></td>
</tr>
<tr>
<td>Cation</td>
</tr>
<tr>
<td>Anion</td>
</tr>
<tr>
<td><strong>ICF</strong></td>
</tr>
<tr>
<td>pH about 6.7</td>
</tr>
<tr>
<td>Glucose about 0-20</td>
</tr>
<tr>
<td>K⁺</td>
</tr>
<tr>
<td>HPO₄²⁻</td>
</tr>
</tbody>
</table>

Na⁺: regulates total body fluid volume
K⁺: regulates cellular volume
The minimal amount of water required per day to get rid of water and toxins via our kidneys is 500 mL.

The significance of water is at least 5-fold:
1) water actively participates in many chemical reactions;
2) water is solvent for minerals, vitamins, amino acids, glucose and other small molecules;
3) water acts as a lubricant and cushion around joints;
4) water acts in regulating the body's temperature;
5) water provides the solvent for the fluids used as shock absorbers inside the eyes, spinal cord and amniotic sac surrounding the fetus in the womb.
## Daily Water "Balance"

<table>
<thead>
<tr>
<th>Intake</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intake</strong></td>
<td><strong>Output</strong></td>
</tr>
<tr>
<td>Metabolism</td>
<td>Sweat 8% 200 mL</td>
</tr>
<tr>
<td>Moist foods</td>
<td>Feces 4% 100 mL</td>
</tr>
<tr>
<td>Beverages</td>
<td>Skin/lung loss 28% 700 mL</td>
</tr>
<tr>
<td>TOTALS</td>
<td>Urine 60% 1500 mL</td>
</tr>
</tbody>
</table>

**Intake:**
- Metabolism: 10% 250 mL
- Moist foods: 30% 750 mL
- Beverages: 60% 1500 mL
- TOTALS: 100% 2500 mL

**Output:**
- Sweat 8% 200 mL
- Feces 4% 100 mL
- Skin/lung loss 28% 700 mL
- Urine 60% 1500 mL
- TOTALS 100% 2500 mL
Sweat and Body Heat

- Sweat is a fluid unto itself.
- It is hypo-tonic (hypo-osmotic) and is primarily water with very low concentrations of Na⁺ and Cl⁻.
- When a person exercises in the heat, it is not unusual for that person to lose 1 L of sweat per hour.
- When a person has a fever between 101° and 103° F, they need their fluid intake increased by 500 mL per 24 hour period.
- When a person has a fever greater than 103° F, they need their fluid intake increased by 1000 mL per 24 hour period.

<table>
<thead>
<tr>
<th>Sweat</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPOtonic (HYPO-osmotic) -- primarily water with LOW Na⁺ and Cl⁻</td>
</tr>
<tr>
<td>When exercising in heat: 1 L sweat lost per hour</td>
</tr>
<tr>
<td>With fever between 101 and 103 F: increase fluids by 500 mL per 24 hour period</td>
</tr>
<tr>
<td>With fever greater than 103 F: increase fluids by 1000 mL per 24 hour period</td>
</tr>
</tbody>
</table>
Osmosis

- Osmosis is defined as the movement of water from a region of higher water concentration to a region of lower water concentration across a semi-permeable membrane.

- Osmotic pressure is the pressure required to halt the net flow of water through a semi-permeable membrane into a solution.

- Osmolarity is a function of osmotic pressure:
  \[ \pi = nMRT \]

- Where \( \pi \) is the osmotic pressure, \( n \) is the number of mols of solute, \( M \) is the molarity of the solution, \( T \) is the absolute temperature and \( R \) is the gas constant (0.0821 \( \text{L-atm/mol-K} \) or 62.4 \( \text{torr-L/mol-K} \)).
Effects on the Body from Altered Osmotic Solution Infusion
Biological Application

- One classical application of osmosis is the effects of different fluids on cells in the human body.
- As you can see in the graphic, cells bathed in hypotonic (dilute) solutions rupture if not done with care, cells bathed in hypertonic (concentrated) solutions shrink and cells bathed in isotonic solutions exhibit no changes, at all.

```
Normal Cell

- in hypotonic medium < 0.9% Saline
- in isotonic medium 0.9% Saline
- in hypertonic medium > 0.9% Saline
```
Isotonic Solutions

- Remember that a solution that is isotonic has the same amount of water AND solutes as whatever it is being mixed with.
- In the case of humans, when a solution is isotonic, it is at about 0.9% saline (aka normal saline; NS).
- When NS is infused into the body, there is an increased ECF volume with no change in ICF volume OR osmotic pressure.
- Isotonic fluids are used to treat hypovolemic shock to increase the ECF volume (a fluid volume expander) and to restore perfusion throughout the body.
Hypotonic Fluids

- Sometimes fluids are isotonic in the bottle (or bag, now), but become hypotonic following metabolism, e.g., 5% dextrose in water (D5W).
- When this is infused into the body, the ECF expands about 33%.
- The ICF expands about 67%.
- The infusion of this solution reduces the osmotic pressure of these two fluid compartments.
- Hence, the water infused is "free" water.
- Therefore, it maintains fluid needs and is used for replacing volume loss.
Hypertonic Solutions

- The last fluid for consideration is the hypertonic solution.
- An excellent example of this is 3% saline.
- When this fluid is infused into the body, the ECF volume increases dramatically.
- The ICF volume, however, is drastically reduced.
- The volume effects are due to an increase in Na\(^+\), therefore, osmosis forces water out of the ICF into the ECF, i.e., osmotic pressure in the ECF increases (due to the hypertonic fluid infusion) until water from the ICF flows out to reduce the osmotic pressure to "normal".
- This effect is very useful in treating situations like cerebral edema, i.e., forces fluid out of the neurological tissue, reducing the extent of injury to that delicate tissue.
Regulation of Water Intake

- Specific sequences are followed by the body when it requires water.
- The body, first, must lose 1-2% of its water.
- Once that happens, osmoreceptors (review notes on the hypothalamus) in the thirst centers are stimulated by an increase in osmotic pressure of the ECF due to water loss.
- Hypothalamic activity, then, stimulates thirst feelings for us to seek out water.
- The actual act of drinking the water and the physical distention of the stomach by water stimulates nerve endings (similar to the Hering-Breuer reflex in the lungs and the stretch receptors in the pregnant uterus) that inhibit the thirst centers.
- Water is absorbed across the stomach and small bowel and large bowel.
- The last event is that the osmotic pressure in the blood is reduced by the addition of water.
Sodium Ion and Water Balance Regulation

- The first mechanism for consideration is that of the release and inhibition of anti-diuretic hormone (aka arginine vasopressin; ADH or AVP).
Sodium Ion and Water Balance Regulation

• A 5-10% reduction in ECF is all it takes to cause an increase in AVP release and thirst stimulation.
• AVP is primarily involved with osmoregulation.

• Hypo-osmolality is synonymous with hyponatremia (it is NOT the same as Na⁺ depletion!!!!!!).
• Generally, hypo-osmolality goes along with intracellular water excess.

• Hyper-osmolality is synonymous with hypernatremia (RARELY is hypernatremia due to an ABSOLUTE Na⁺ excess).
• Generally, hyper-osmolality goes along with intracellular water loss.

• As a general rule, the plasma osmolality is equal to 2 times the serum sodium ion concentration.
• In normal patients, the sodium ion levels are held in check with AVP.
• The second mechanism for consideration involves the renin-angiotensin-aldosterone axis

• Aldosterone binds to receptors in the kidneys and causes Na\(^+\) retention -- with some secondary water retention and K\(^+\) loss.

• A Na\(^+\) reduction of only 4-5 mEq/L stimulates aldosterone secretion in ILL patients.

• Aldosterone secretion is elevated in patients with decreased Na\(^+\) levels in volume depletion; aldosterone secretion is reduced in patients with reduced Na\(^+\) levels with water RETENTION.
Potassium Ion Regulation

- Potassium ion regulation is regulated with Na+ regulation via aldosterone.
- $K^+$ also plays a role in/with acid/base balance.
The Inter-Relationship Between Ca\(^{2+}\), Mg\(^{2+}\) and PO\(_{4}^{3-}\)

- All three of these ions are tightly regulated together.
- The first mechanism under consideration is that of Ca\(^{2+}\) regulation by calcitonin (CT)
The Inter-Relationship Between Ca\textsuperscript{2+}, Mg\textsuperscript{2+} and PO\textsubscript{4}\textsuperscript{3-}

- The second mechanism under consideration is that of parathyroid hormone (aka parathormone; PTH) secretion
The serum levels of Ca\(^{2+}\) and PO\(_4^{3-}\) are inversely related: if Ca\(^{2+}\) is high, PO\(_4^{3-}\) is low; if Ca\(^{2+}\) is low, then PO\(_4^{3-}\) is high.

If this relationship was not maintained, soft tissue precipitation of Ca\(_3\)(PO\(_4\))\(_2\) would result, causing ossification/calcification of these soft tissues.

This precipitation occurs when the cross product of the two ions' levels is equal to OR greater than 60.
The effects of Mg$^{2+}$ on Ca$^{2+}$ levels is best demonstrated by examining three clinical states:

• First two:
  1) Acute hypomagnesemia
     - PTH release, CT release and Ca$^{2+}$ levels are ALL elevated.
     - This results in the formation of weak bones.
  2) Chronic hypomagnesemia
     - PTH secretion and Ca$^{2+}$ levels are both reduced.
3) Hypermagnesemia.
   - CT secretion and Ca\(^{2+}\)/Mg\(^{2+}\) urinary excretions are all elevated.

The bottom line is that when one of these three minerals is out of whack, the other two are, also.
## Sources and Needs of for Electrolytes and Water

<table>
<thead>
<tr>
<th>In General</th>
<th>When, specifically</th>
<th>How much</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before exercise</td>
<td>2 hours</td>
<td>500-750 mL water</td>
</tr>
<tr>
<td></td>
<td>0.25 hours</td>
<td>500 mL refrigerator cold water</td>
</tr>
<tr>
<td>During exercise</td>
<td>q 0.25 hours</td>
<td>250-500 mL of refrigerator cold water</td>
</tr>
<tr>
<td>After you’re done exercising</td>
<td>q 0.25 hours or prn for own comfort</td>
<td>250 mL until you’ve drunk 500 mL for every 0.454 kg lost</td>
</tr>
</tbody>
</table>
Ibid
<table>
<thead>
<tr>
<th>Foods</th>
<th>Fluids</th>
<th>Metabolic Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>Lyte Intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>Lyte Output</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweat</td>
<td>Feces</td>
<td>Urine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
While We’re At It

\[
\frac{m \text{Eq}}{L} = \frac{\text{mg ion/L solution}}{\text{atomic wt}} \times \frac{\# \text{charges}}{\text{ion}}
\]

E.g.
- \( \frac{\# \text{charges}}{\text{ion}} \) for \( \text{Na}^+ \) = 1
- \( \frac{\# \text{charges}}{\text{ion}} \) for \( \text{Mg}^{2+} \) = 2
- \( \frac{\# \text{charges}}{\text{ion}} \) for \( \text{Cl}^- \) = 1
- \( \frac{\# \text{charges}}{\text{ion}} \) for \( \text{NH}_4^+ \) = 1

For \( \text{Ca}^{2+} @ 100 \text{ mg/L} \)

\[
\frac{m \text{Eq}}{L} = \frac{100 \text{ mg Ca}^{2+}/L}{40 \text{ mg/mmol}} \times 2 \frac{m \text{Eq}}{\text{mmol}} = 5 \frac{m \text{Eq}}{L}
\]

For \( \text{Na}^+ @ 3300 \text{ mg/L} \)

\[
\frac{m \text{Eq}}{L} = \frac{3300}{23} \times 1 = 143 \frac{m \text{Eq}}{L}
\]
Cardiovascular Role in Fluid Balance

- Fluid imbalances can create problems, as well.
Starling’s Law

• Note that there is a net pressure "out" of the vessels of 1 mm Hg.
• That is actually accounted for by the pressure (-1 mm Hg -- net inward) in the lymphatic vessels.
Starling’s Law and Pathologies

- We can use Starling's Law of the Capillary to explain the formation of edema.
- One manner in which edema forms is by having an elevated CHP.
- In this case, the pressure forces fluids out of capillaries into the interstitial space.
- An example of this is when one has elevated Na\(^+\) levels with water retention or when one has venous blockages.
- A second manner in which we can explain edema formation is by a person having a reduced BOP.
- An example of this is when one has hypoalbuminemia (review your notes from BIOL 224 regarding blood proteins and starvation).
- A third mechanism is caused by increased capillary permeability.
- In this instance, there is an increased IFOP.
- An example of this is an inflammatory reaction (review your BIOL 224 or 251 notes on the immune system).
- The last mechanism occurs when there is either an obstruction of the lymphatics or there is an increased IFOP.
Categories of Changes in Body Fluid Abnormalities

• There are three "big" categories of fluid volume changes:
  – 1) Volume
  – 2) Osmolality
  – 3) Composition
Volume Changes

- Volume changes occur primarily in the ECF.
- They involve an equal loss or gain of Na\(^+\)/water causing an increase or decrease in ECF.
- Examples include diarrhea -- the loss of isotonic ECF fluid causes a decrease in ECF volume but NO decrease in ICF fluid volume; this causes no osmotic pressure changes.
ASIDE: Diarrheas

• Functional diarrhea
  – Due to irritation/stress

• Organic diarrhea
  – Due to a lesion in the bowel

• Osmotic diarrhea
  – Due to gluten, fat, lactose

• Secretory diarrhea
  – Due to bacteria, viruses, bile acids, laxatives, hormones: WORST of the 4 kinds!
Osmolality Changes

• Osmolality changes occur primarily with the ICF.
• They involve unequal gain or loss of Na⁺/water.
• Examples include hypo/hypernatremia.
• This DOES cause osmotic pressure changes. (duh! big red truck!)
Compositional Changes

- Compositional changes occur primarily with the ECF.
- Changes in the concentration of various ions does not lead to changes in osmotic pressure since there is no increase in the number of osmotically active particles (review CHEM 121 notes on osmolality).
- For example, $K^+$ increases from normal (approximately 4.5 mEq/L) to 7.5 will not change osmotic pressure significantly, but WOULD effect the HEART and skeletal muscle.
Third Spacing

• A "fourth" form of fluid volume change is called "third spacing".
• This is a form of compositional changes.
• It involves non-ECF, non-ICF sequestration of fluids generally due to increased or decreased ECF changes.
• Examples include burn fluids, ascitic fluid, soft tissue injuries, peritonitis and blisters on skin.
• This fluid is NOT easily exchanged with the ECF.
## Mini-Guide to Assessing Water/Electrolyte Alterations

| 2% loss in body weight | mild fluid volume deficit |
| 5% loss in body weight | moderate fluid volume deficit |
| 8% loss in body weight | severe fluid volume deficit |

Compare to 150 lb person

- 3 lb loss/gain
- 7.5 lb loss/gain
- 9 lb loss/gain

| 2% gain in body weight | mild fluid volume excess |
| 5% gain in body weight | moderate fluid volume excess |
| 8% gain in body weight | severe fluid volume excess |

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Fluid Volume Abnormality</th>
<th>Increased ICP</th>
<th>Reduced Na⁺</th>
<th>Reduced Ca²⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry conjunctiva</td>
<td>reduced fluid volume</td>
<td>Seizures</td>
<td>Decreased Ca²⁺</td>
<td></td>
</tr>
<tr>
<td>Periorbital edema</td>
<td>reduced fluid volume (or mouth breather)</td>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry lips</td>
<td>reduced fluid volume</td>
<td>Hyperglycemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased skin turgor</td>
<td>reduced fluid volume</td>
<td>Hypochloremia</td>
<td>Increased Na⁺</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>101–103°F, increase volume requirements X 500 mL/24 hours</td>
<td>Hyperchloremia</td>
<td>Decreased Ca²⁺</td>
<td></td>
</tr>
<tr>
<td>Rapid heart rate</td>
<td>reduced fluid volume</td>
<td>Elevated BUN</td>
<td>Osmotic diuresis with reduced fluid volume</td>
<td></td>
</tr>
<tr>
<td>GI system</td>
<td>NO bowel sounds = hypokalemia; Bowel sounds with diarrhea = hyperkalemia</td>
<td>Elevated creatinine</td>
<td>Hypovolemia</td>
<td></td>
</tr>
<tr>
<td>Urinary Na⁺/K⁺</td>
<td>2:1 is normal; hyperaldosteronism: Na⁺/K⁺ reversed; Adrenal insufficiency: Na⁺/K⁺ elevated</td>
<td>Decreased creatinine</td>
<td>Hypervolemia</td>
<td></td>
</tr>
</tbody>
</table>
The relationship between urinary specific gravity (Sp.G.; review CHEM 101 notes on specific gravity) and osmolality (in units of mOsm/kg; this is approximately equal to twice the serum sodium levels)

Plot of Urinary Sp.G. vs Osmolality (mOsm/kg; approximately equal to 2 * [Na\(^+\)])

- 280-295 mOsm/kg: "Normal"
- 1.005 - 1.035: "Normal" Sp.G.

Osmolality is more accurate than Sp.G.
SpG vs Osmolality

- While Sp.G. is used routinely to determine the state of hydration of a person
  - it doesn't cost as much to run
  - osmolarity is by far more accurate.