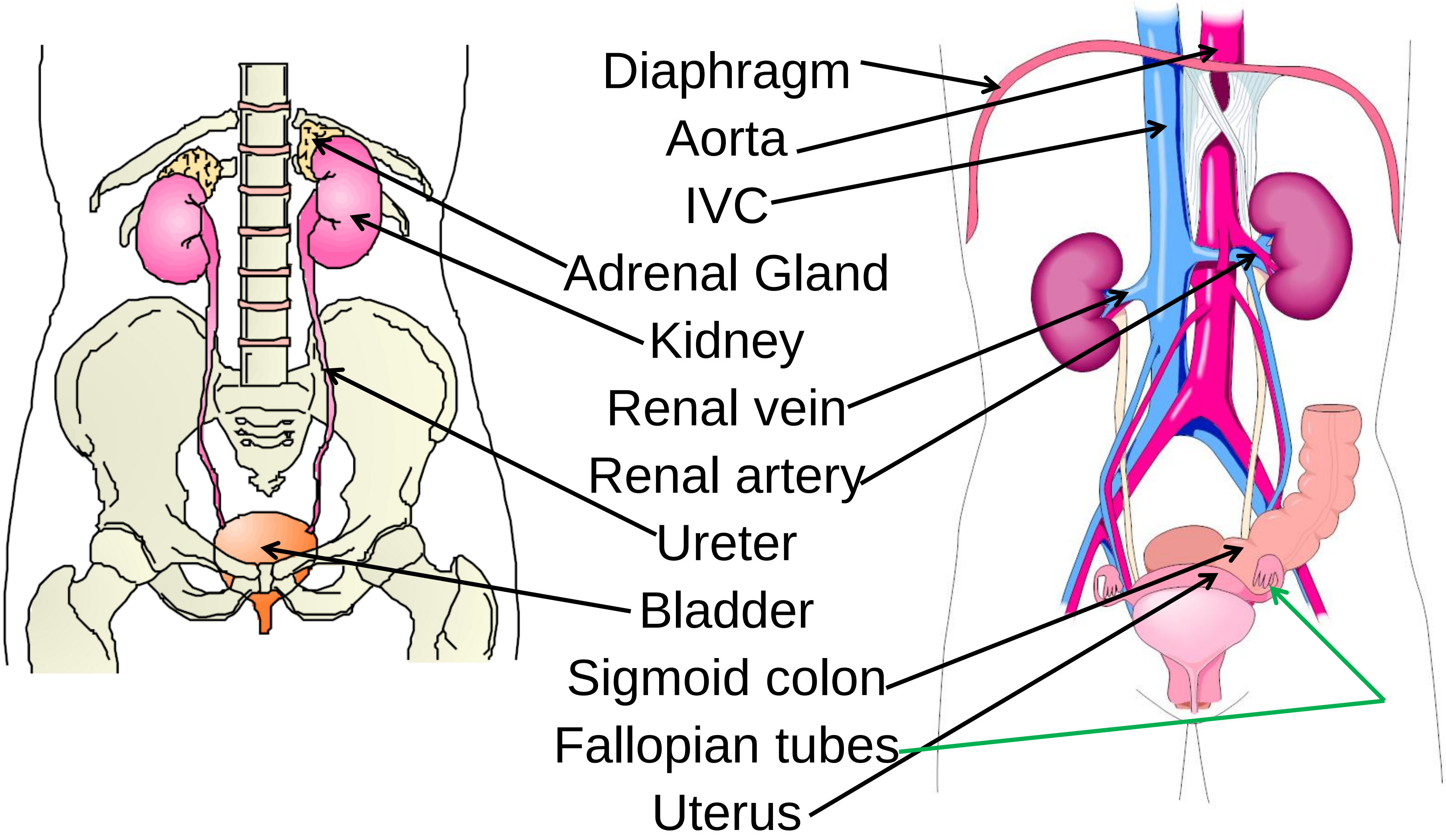
Urinary System

With

The Fetal/Neonatal Kidney

&

Water and Electrolyte Balance



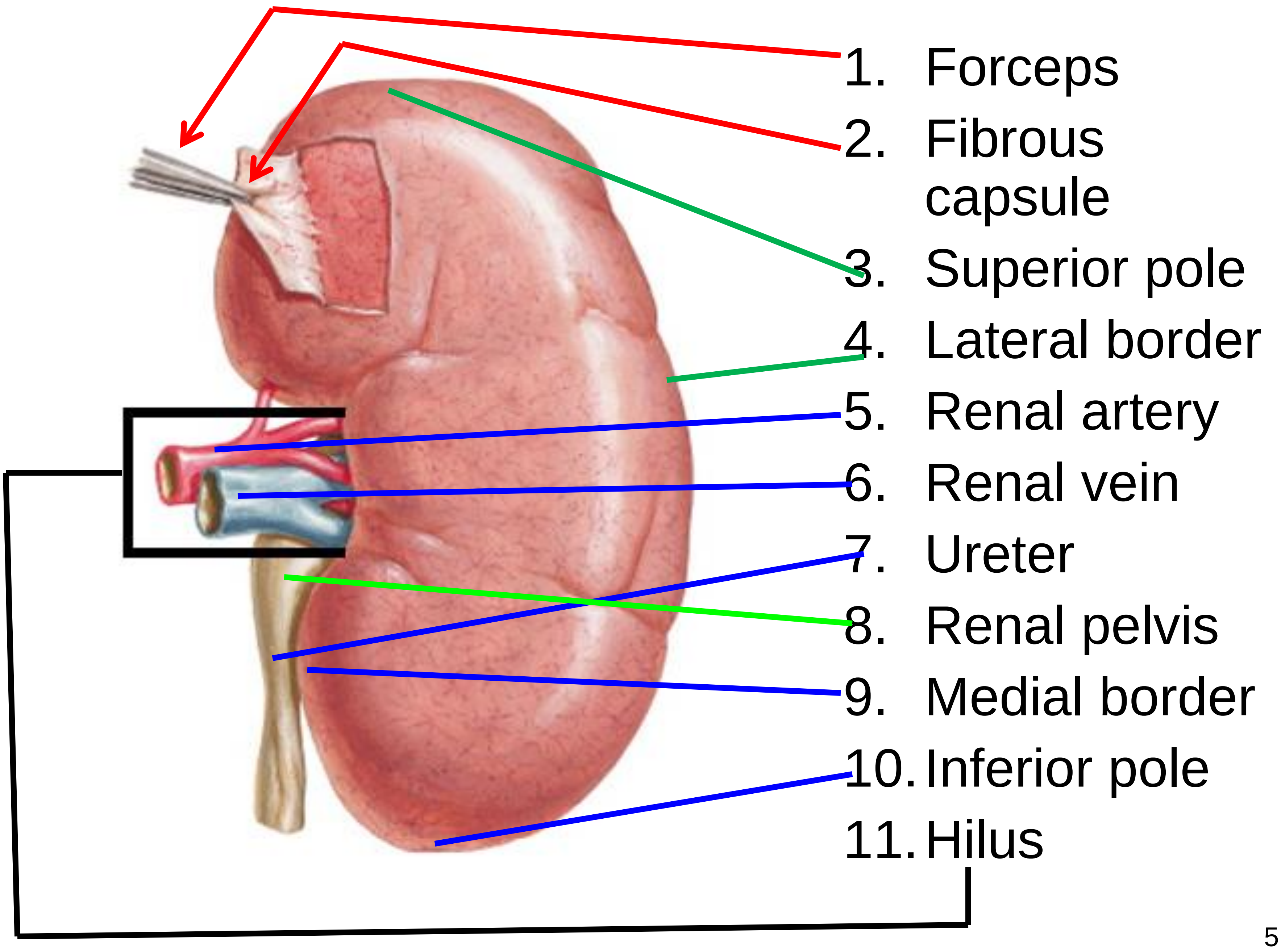
Diaphragm
Aorta
IVC
Adrenal Gland
Kidney
Renal vein
Renal artery
Ureter
Bladder
Sigmoid colon
Fallopian tubes
Uterus

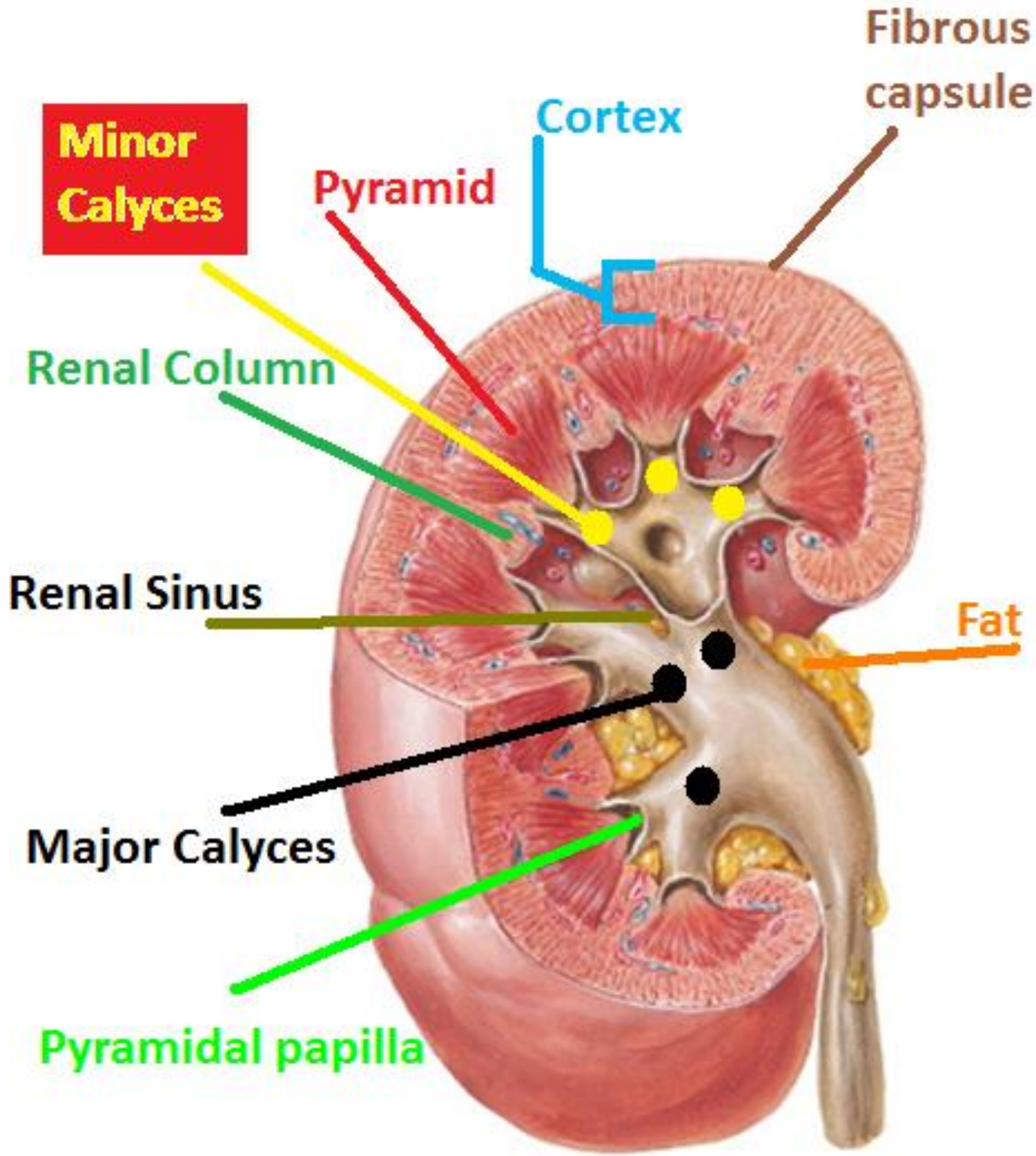
Kidneys

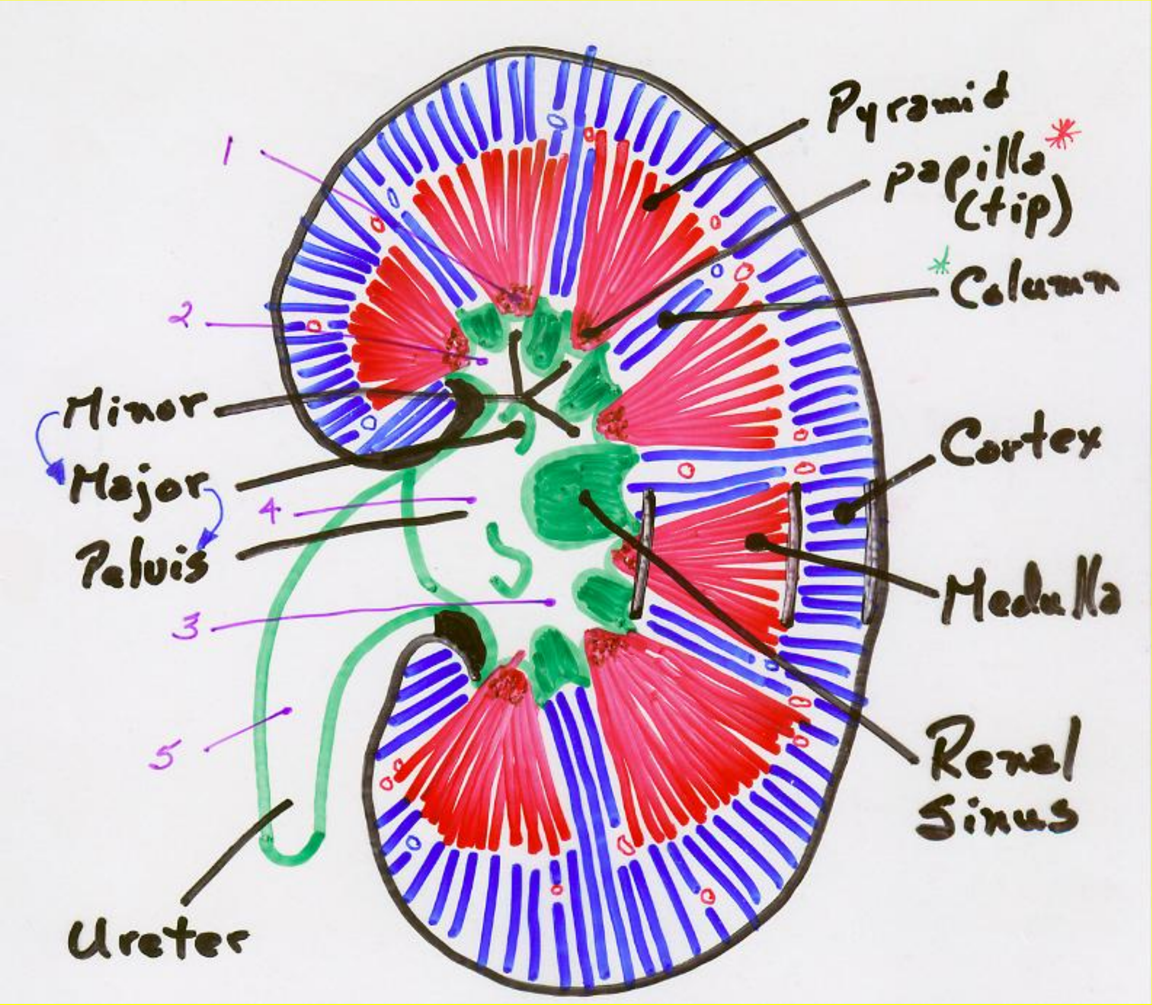
- Are paired, bean-shaped
- Just above the waist behind the parietal peritoneum and posterior wall of the abdominal cavity
- They are <u>retroperitoneal</u>!
- Located between T-12 and L-3
- Right kidney is slightly lower than the left
- 10-12 cm long; 5-7.5 cm wide; 2.5 cm thick
- The HILUS is the center 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 <u>renal sinus</u>

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

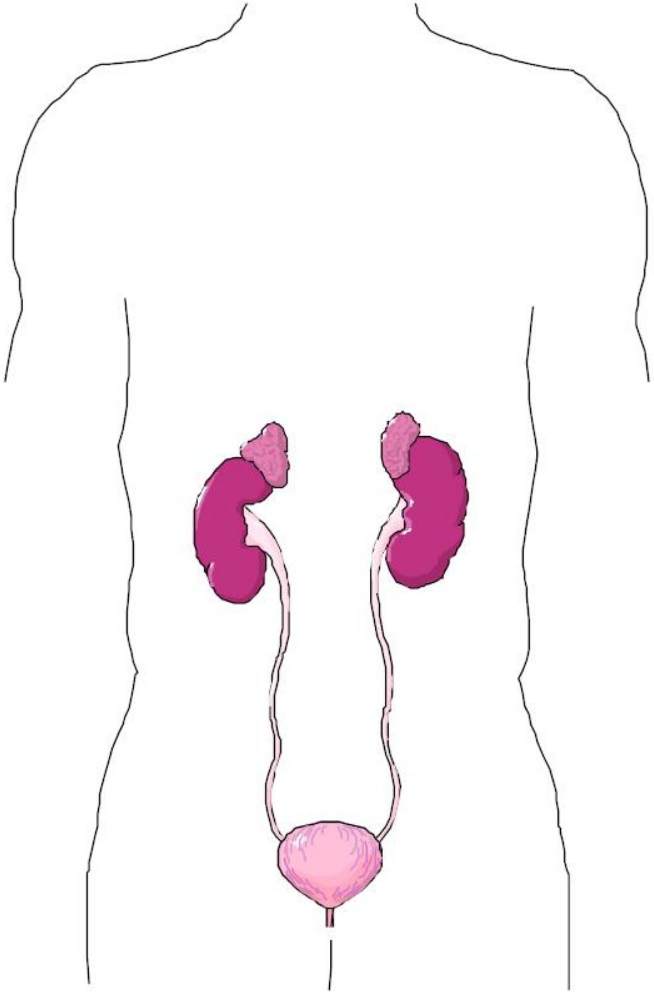

1. Forceps
2. Fibrous capsule
3. Superior pole
4. Lateral border
5. Renal artery
6. Renal vein
7. Ureter
8. Renal pelvis
9. Medial border
10. Inferior pole
11. Hilus


Fibrous
capsule
Cortex
Minor
Calyces
Pyramid
Renal Column
Renal Sinus
Fat
Major Calyces
Pyramidal papilla



- 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:

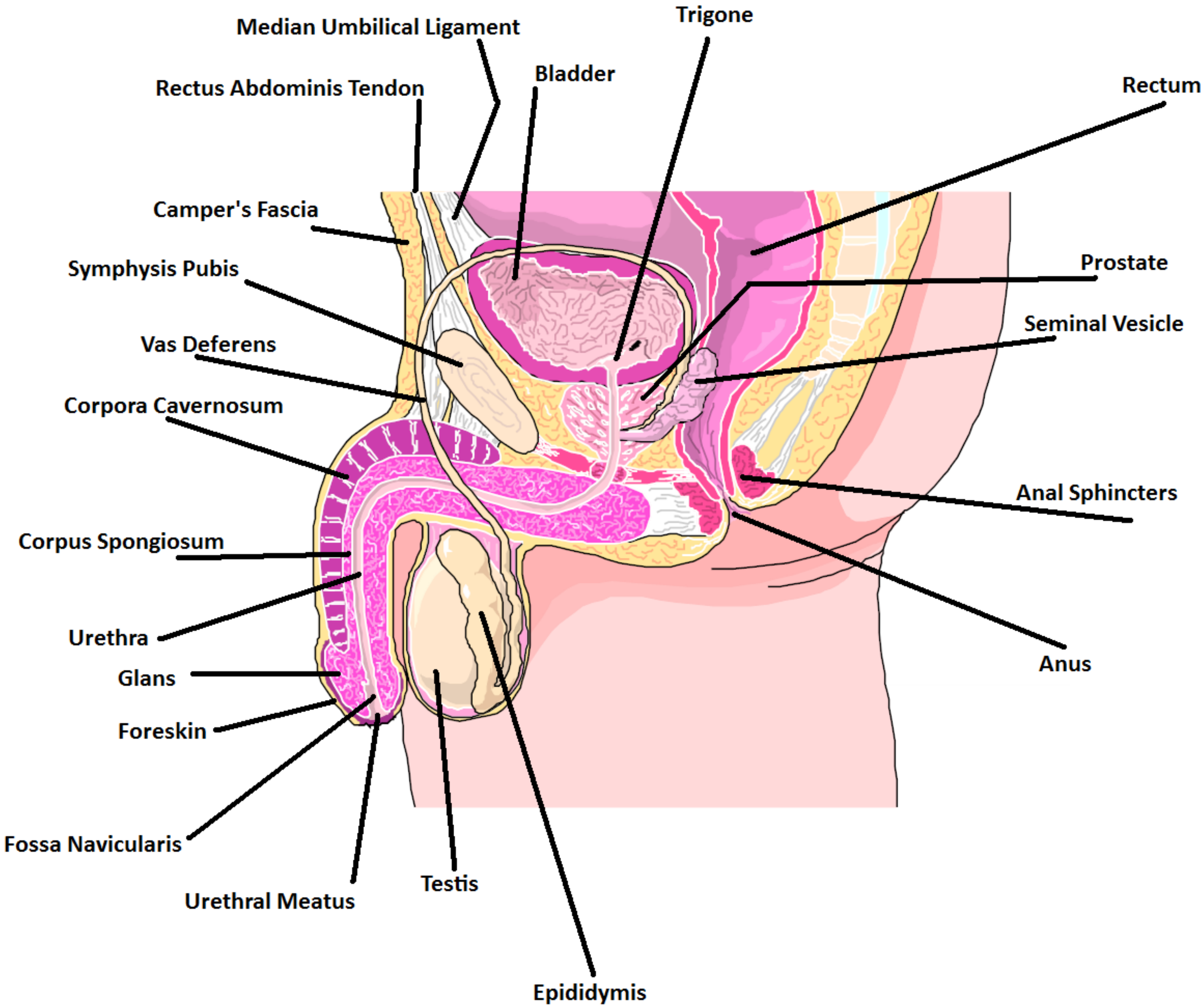
1. Peristalsis
2. Hydrostatic pressure
3. Gravity

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 <u>detrusor muscle</u>
- Detrusor also used in the construction of the internal sphincter (sphincter vesiculi)

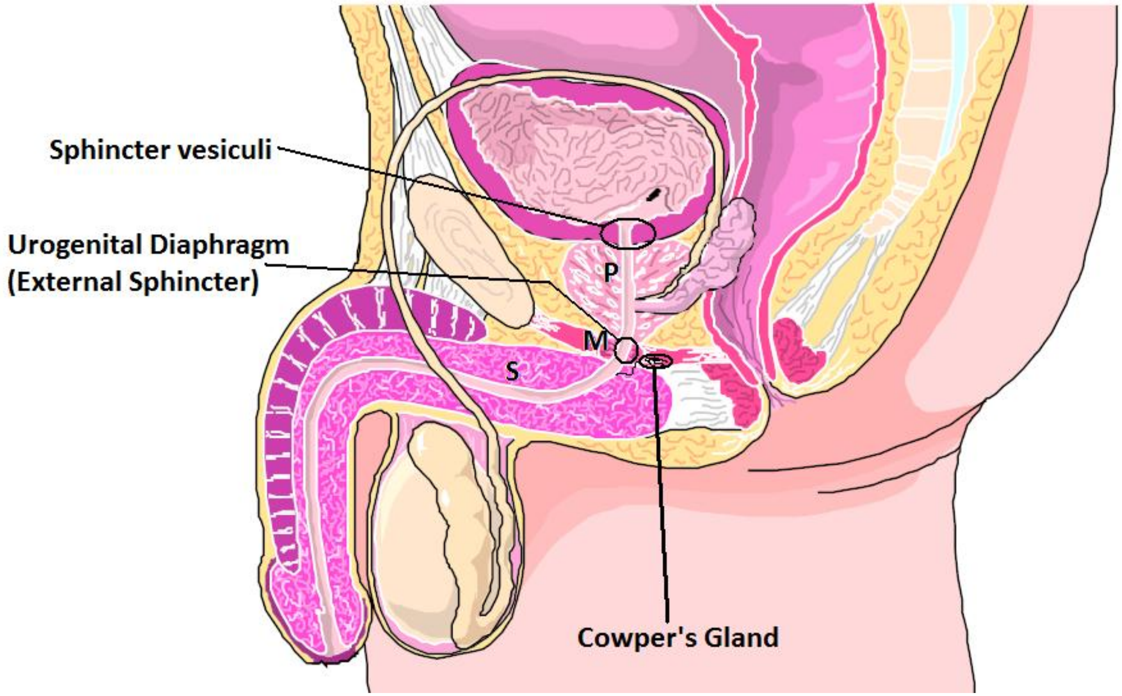
Urinary Bladder, Cont'd

- 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

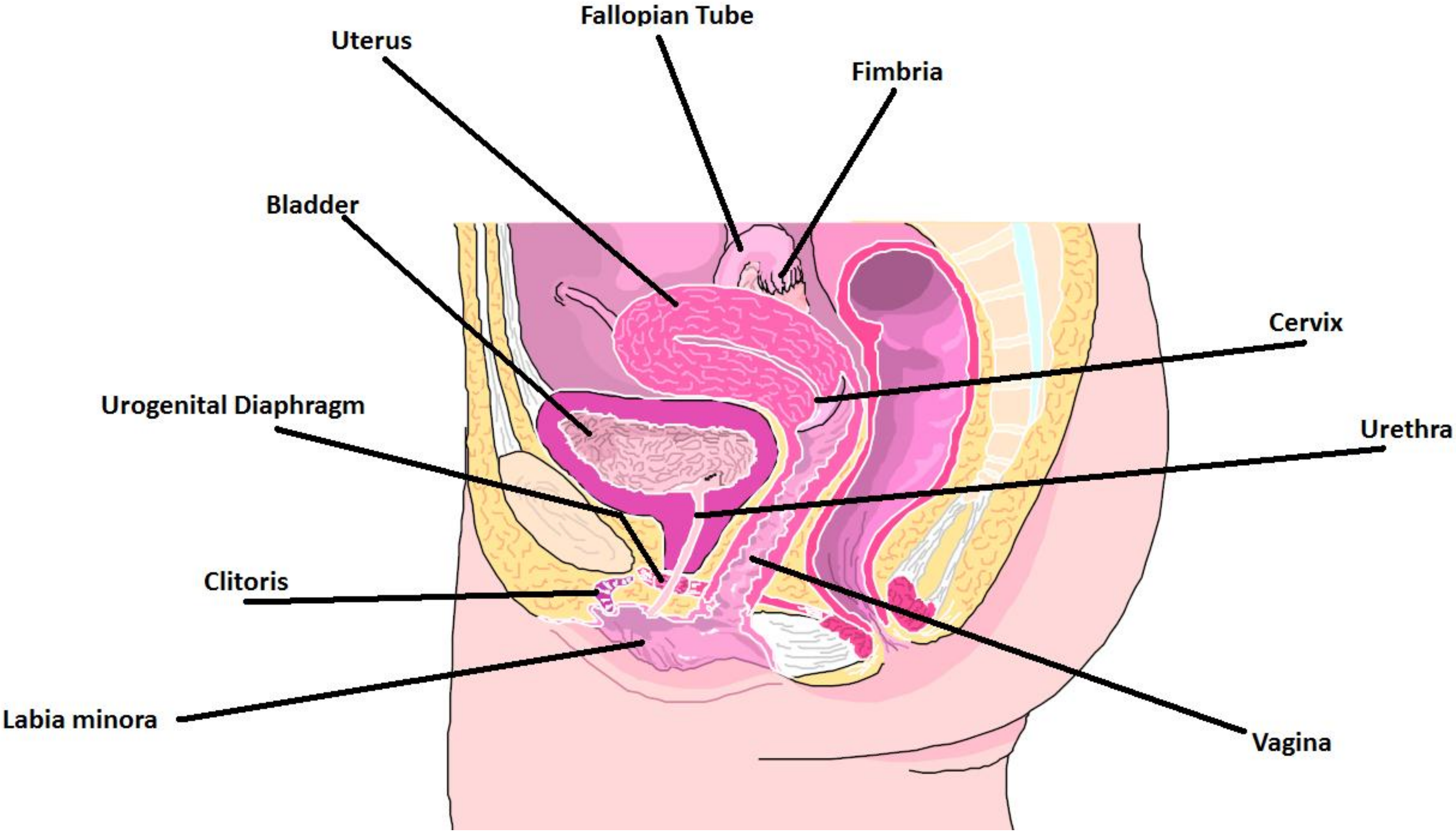


Median Umbilical Ligament
Trigone
Bladder
Rectus Abdominis Tendon
Rectum
Camper's Fascia
Symphysis Pubis
Prostate
Seminal Vesicle
Vas Deferens
Corpora Cavernosum
Anal Sphincters
Corpus Spongiosum
Urethra
Anus
Glans
Foreskin
Fossa Navicularis
Testis
Urethral Meatus
Epididymis

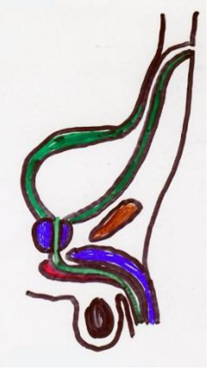
Male, Continued



Female


Fallopian Tube
Uterus
Fimbria
Bladder
Cervix
Urogenital Diaphragm
Urethra
Clitoris
Labia minora
Vagina

Urachal Abnormalities



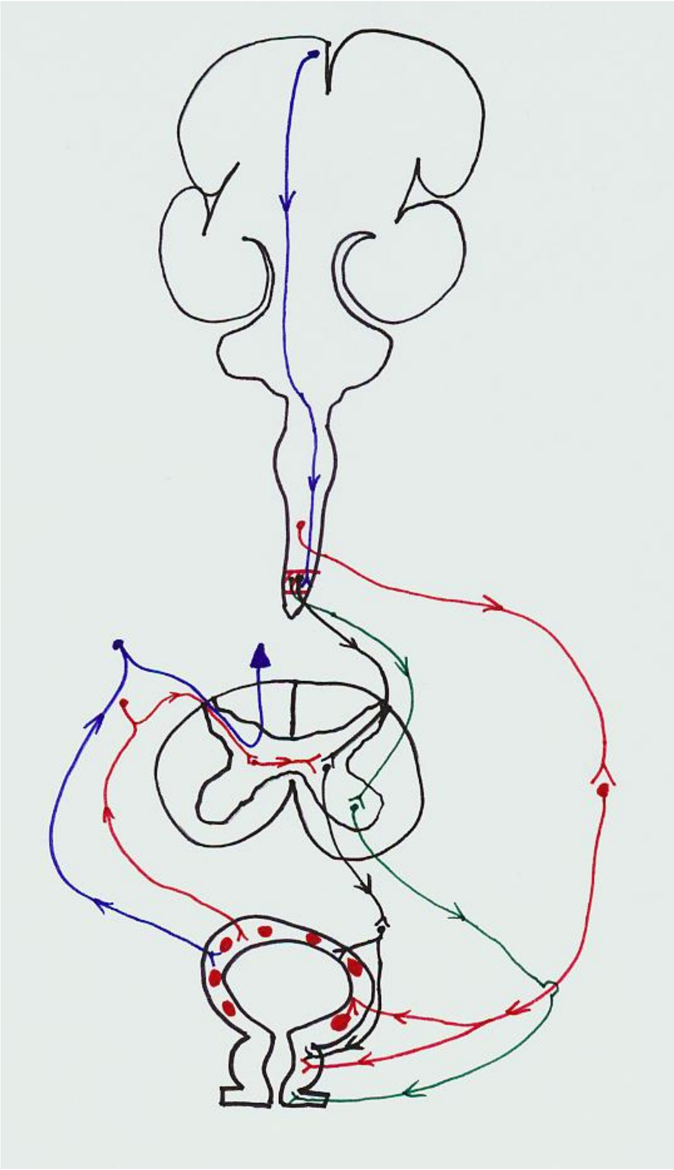
- Patent urachus

- Cyst

- Internally blind

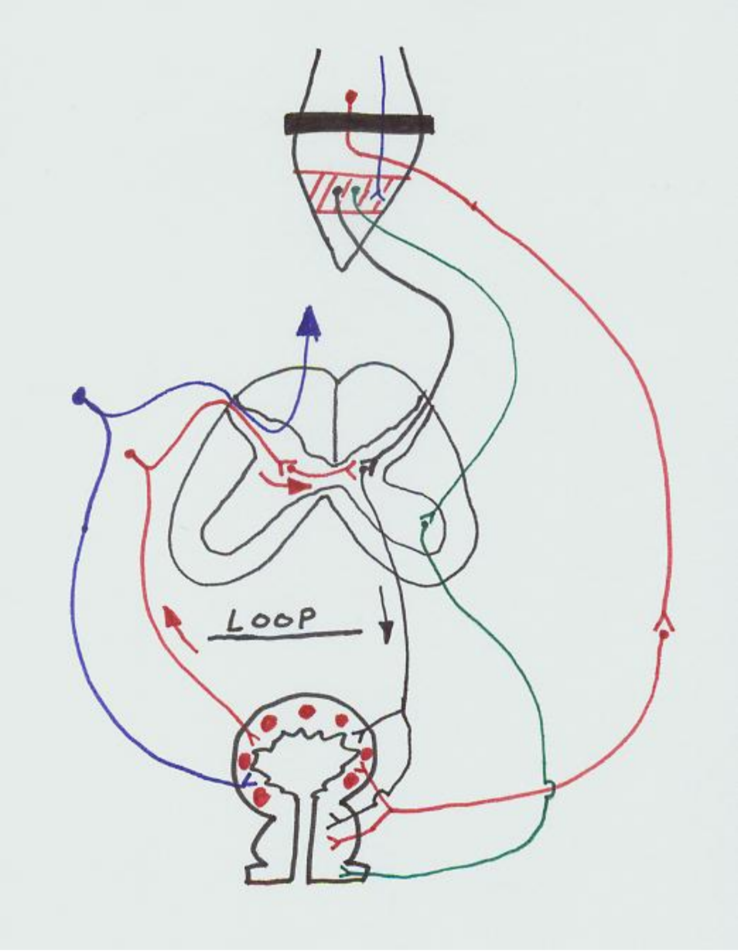
- Externally blind

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 intiates micturition**
- Detrusor muscle
- Sphincter vesiculae (exaggerated for this graphic)
- External sphincter (likewise)
- Sacral innervation in cord $S_{2,3,4}$

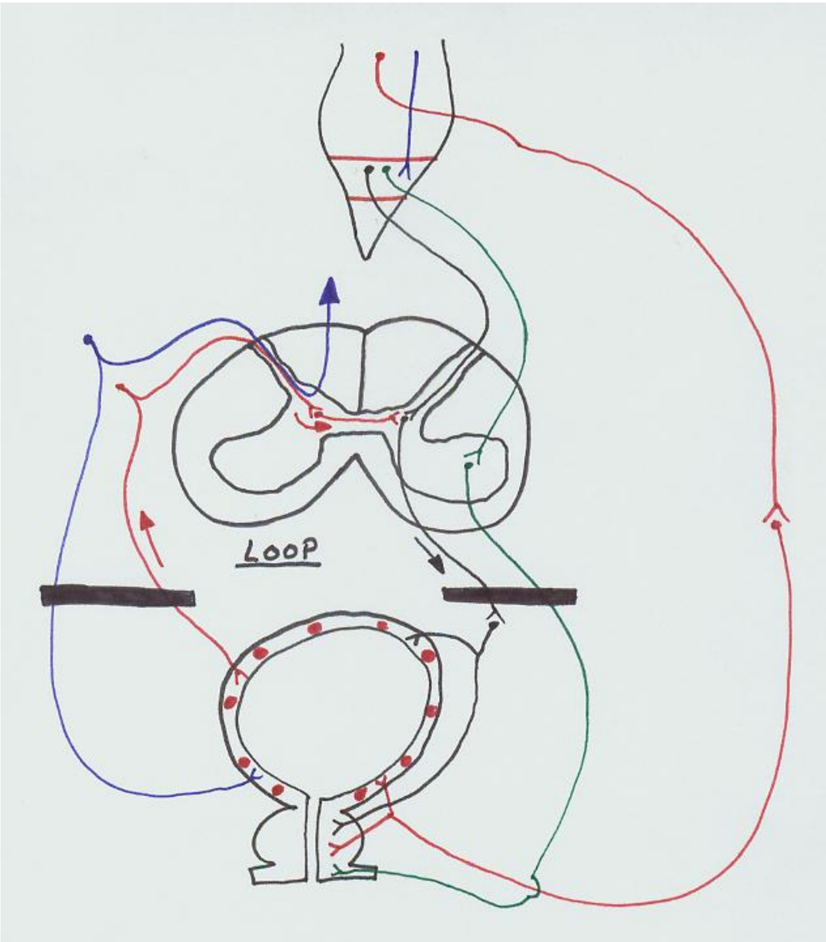
Bladder Innervation -- Anomaly



- 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)

Urinary Incontinence Classification - 2

Stress Incontinence

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

Urinary Incontinence Classification - 3

Overflow Incontinence

- Leak minute amounts in day and noc
- Due to a distended bladder
- Due to an inability to empty bladder completely (underactive detrusor)

Urinary Incontinence Classification - 4

Detrusor Hyperactivity with Impaired Contractility (DHIC)

- Occurs in the elderly
- Due to decreased bladder contractility with urine retention

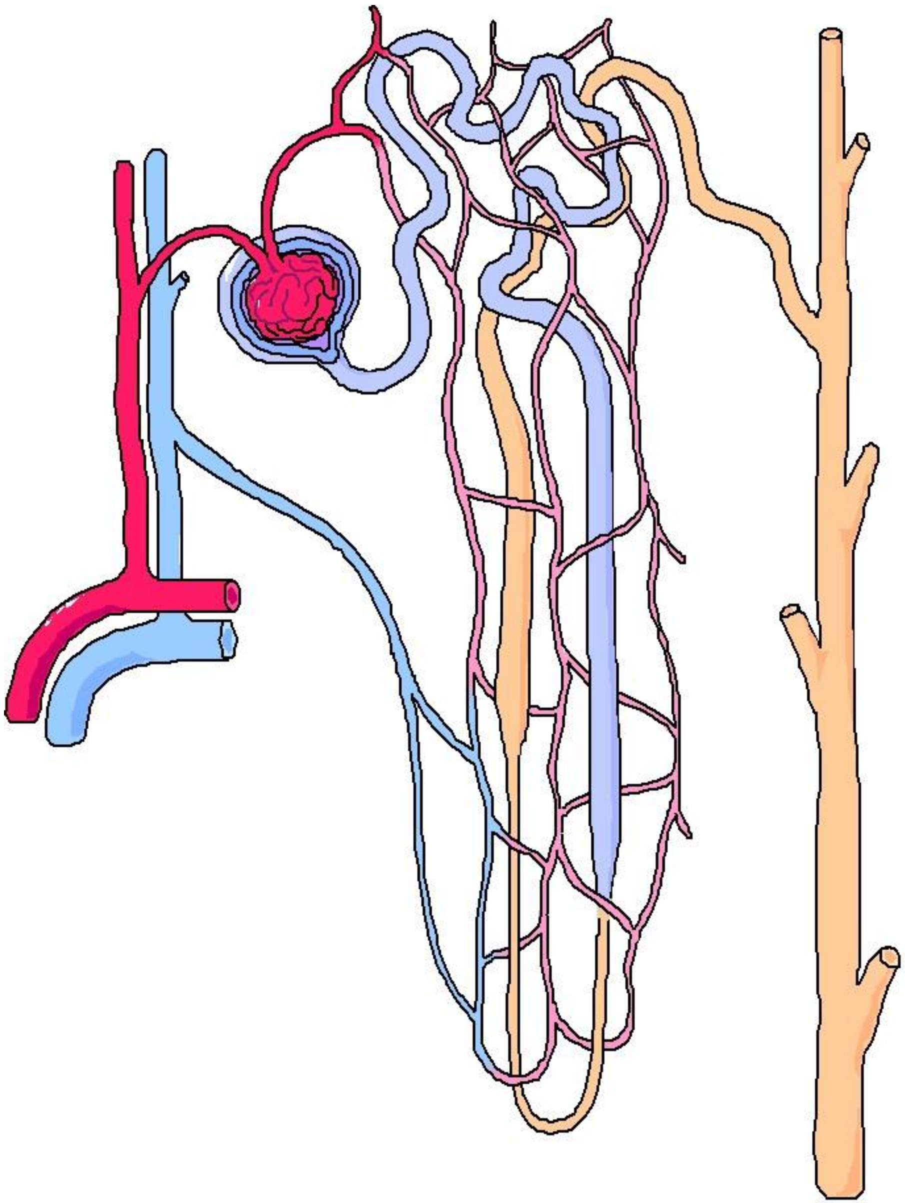
Urinary Incontinence Classification - 5

- 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

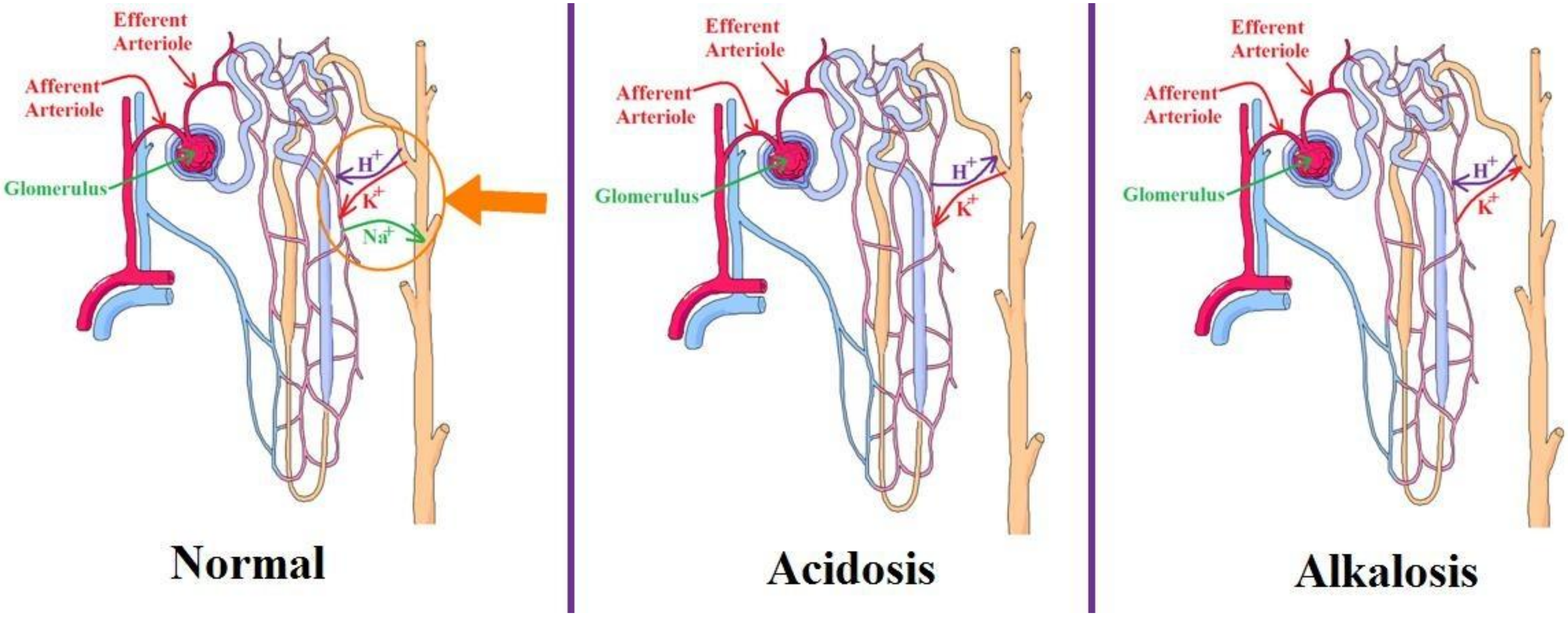
- Functional unit of kidney
- Functions in:
  - Filtration
  - Acid-base balance
  - Toxic waste removal from blood
- Eliminated materials are collectively called urine
- Total volume of blood in our bodies is filtered by the kidneys approximately 60 times a day

Nephron -- generic

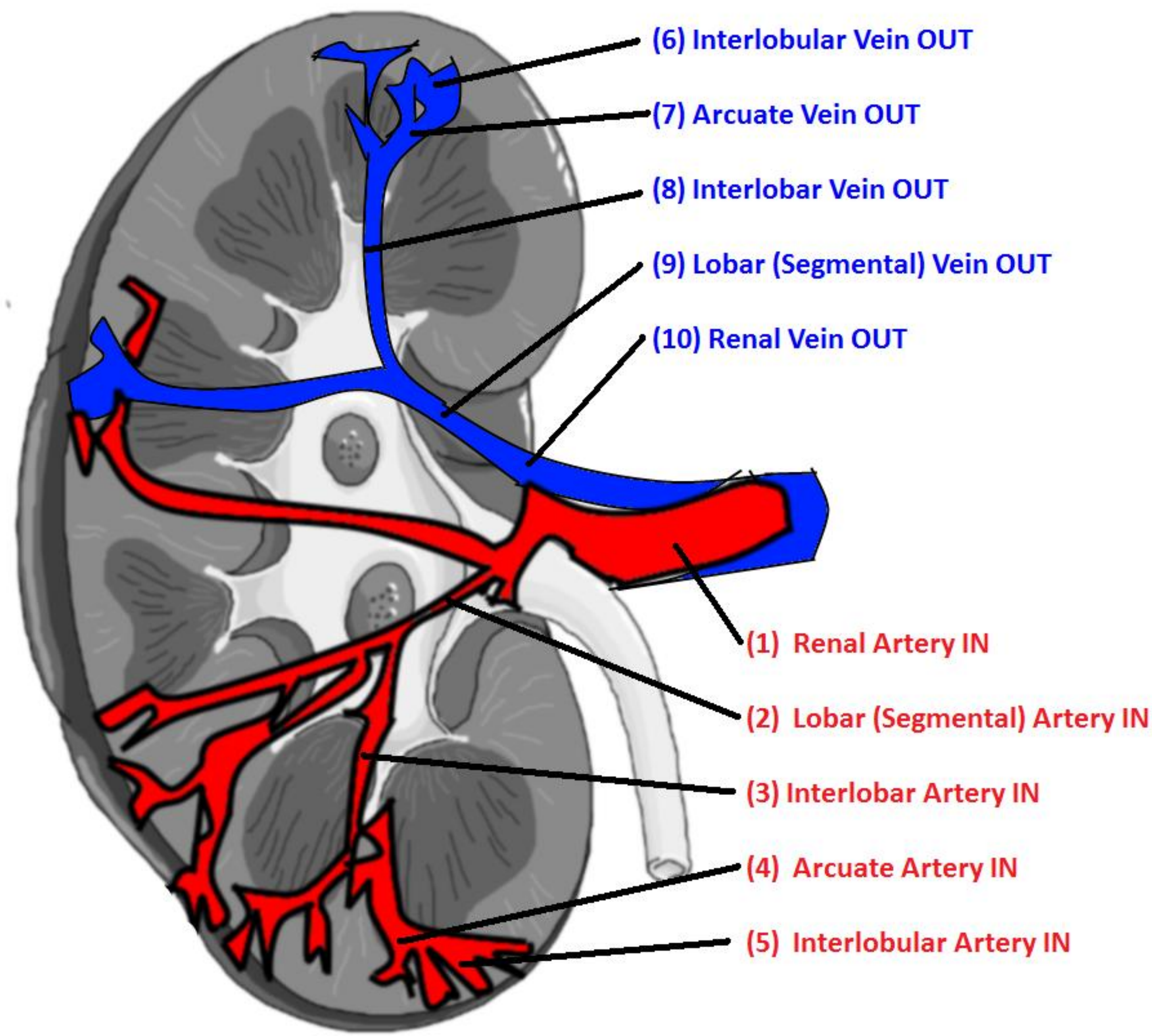


- Afferent arteriole in
- Efferent arteriole out
- Glomerulus between the two
- Bowman's capsule around the glomerulus
- Hooked to PCT
- Hooked to LoH
- Hooked to DCT
- Connects to collecting tubule
- Vasa recta interwoven through and around PCT, LoH, DCT

Nephron and Acid-Base Balance



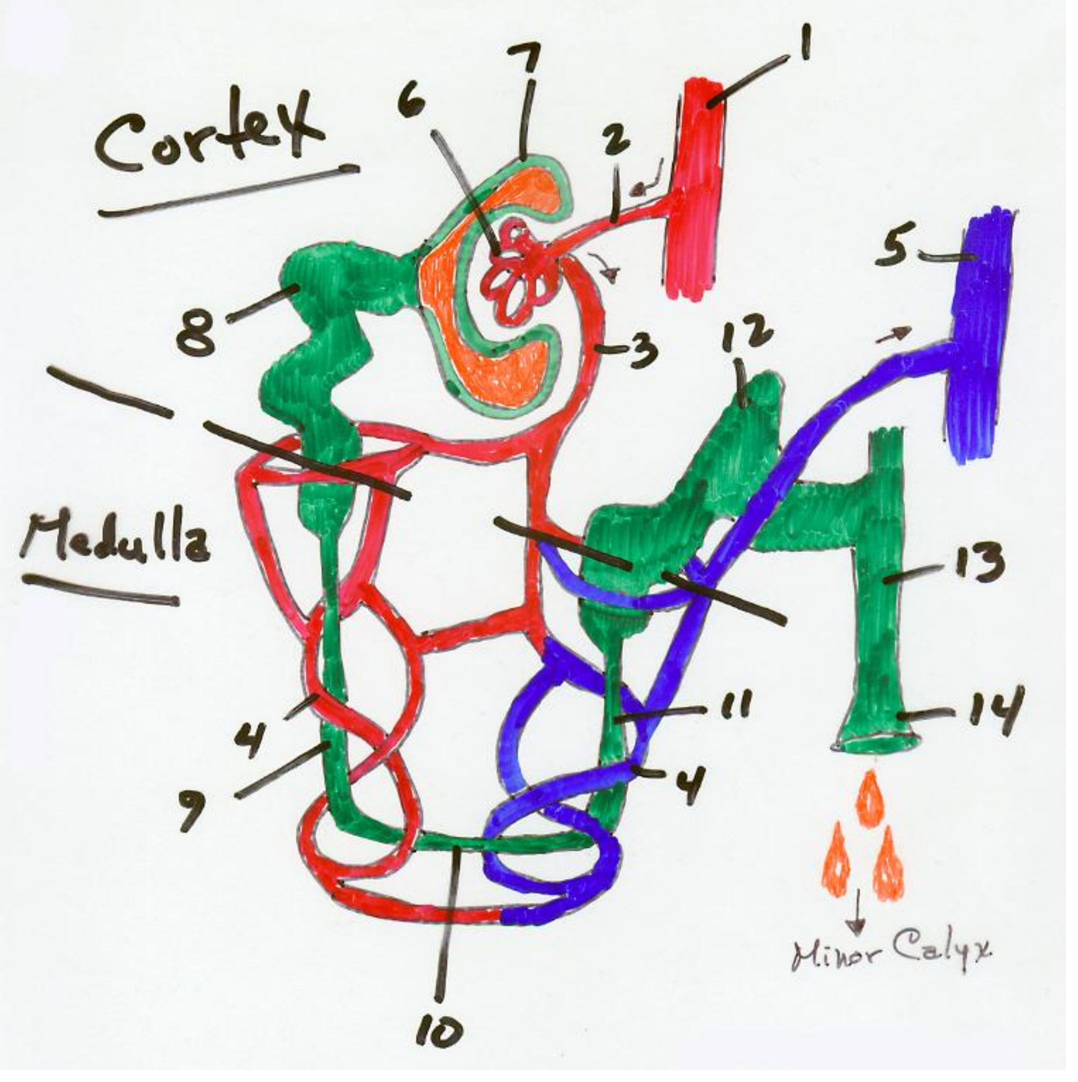
Blood Flow Through Kidney



Interlobular Artery to Afferent Arteriole to Efferent Arteriole to Vasa Recta to Interlobular Vein

- Lobar arteries are also known as segmental arteries
- Note difference between interLOBAR and inter LOBULAR
- Efferent arteriole is smaller than the afferent arteriole

Juxta-medullary nephron

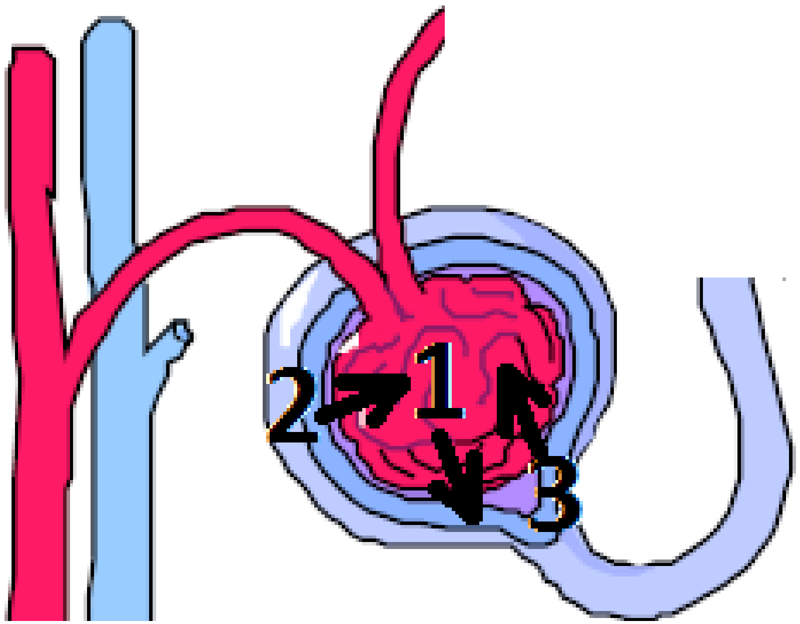


1. Interlobular artery
2. Afferent arteriole
3. Efferent arteriole
4. Peritubular capillaries
5. Interlobular vein
6. Glomerulus
7. Bowman's capsule
8. PCT
9. Descending limb
10. LoH
11. Ascending limb
12. DCT
13. Collecting tubules
14. Papillary duct

Urine Formation

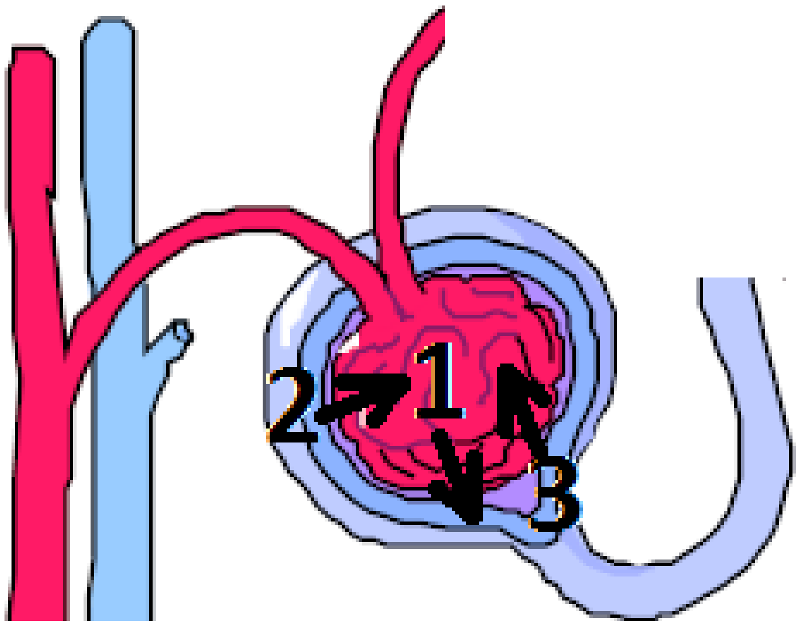
- Requires three processes:
  - Glomerular filtration
  - Tubular reabsorption
  - Tubular secretion
- All processes depend necessarily on blood flow into and out of the kidney

Filtration Pressures -- 1



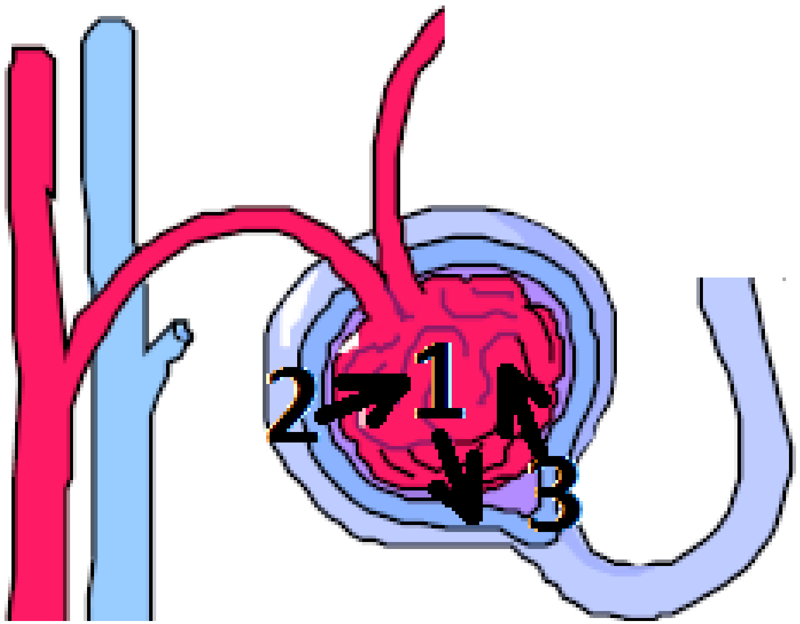
1. Glomerular blood hydrostatic pressure – the chief pressure; hydrostatic pressure is the force that a fluid under pressure exerts against the walls of its container; glomerular blood hydrostatic pressure means the blood pressure in the glomerulus; this pressure tends to move fluid out of the glomeruli at a force averaging about 60 mm Hg

Filtration Pressures -- 2



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

Filtration Pressures -- 3



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_{eff}

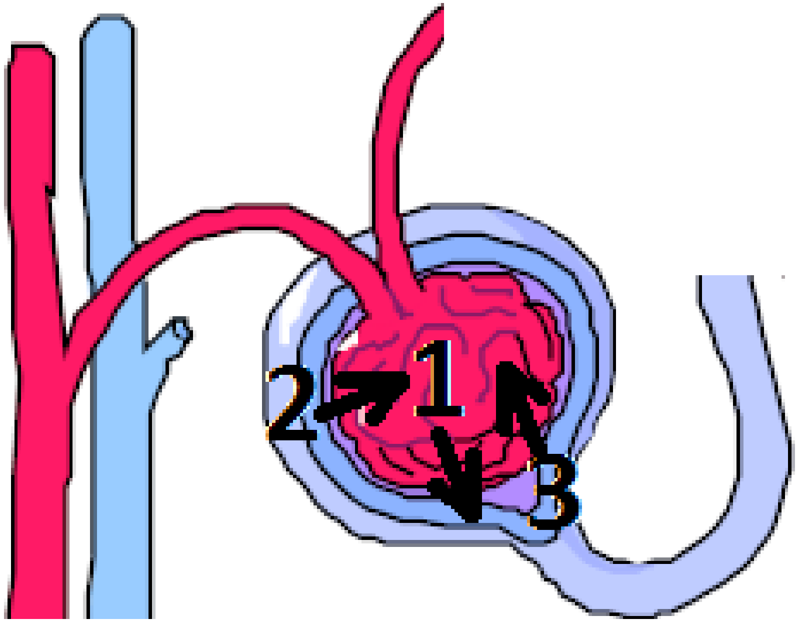
- Is the difference between the sum of the CHP and BCOP and the GBHP:

$$P_{eff} = GBHP – (CHP + BCOP)$$

$$60 – (20 + 30) = 10 \text{ mm Hg}$$

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

Effective Filtration Pressure



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

60 – (30 + 20) = 10 mm Hg

= P_{eff}

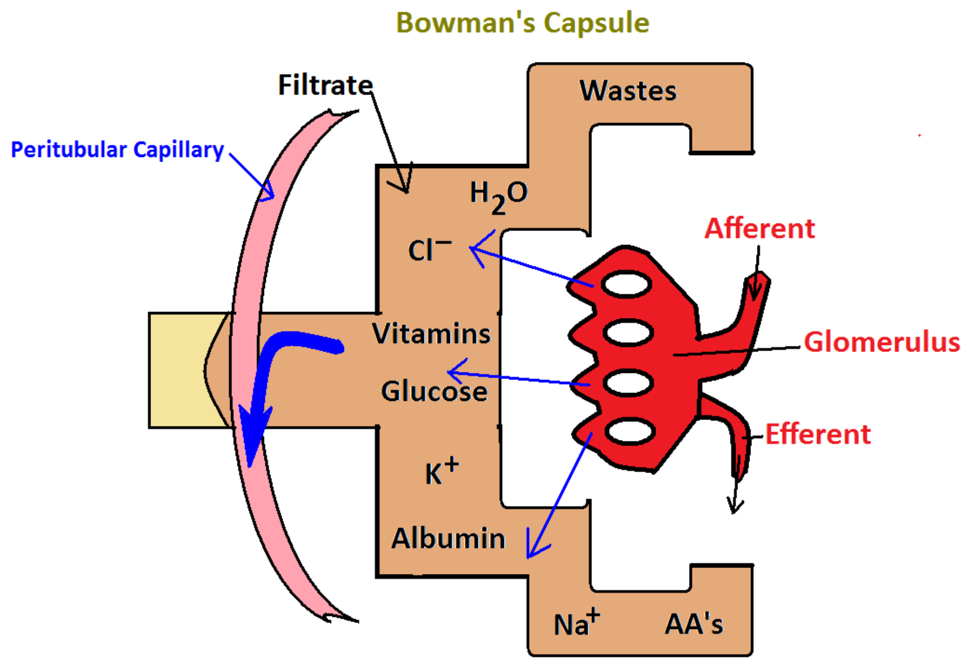
Altered P_{eff} in Selected Disease States

- 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

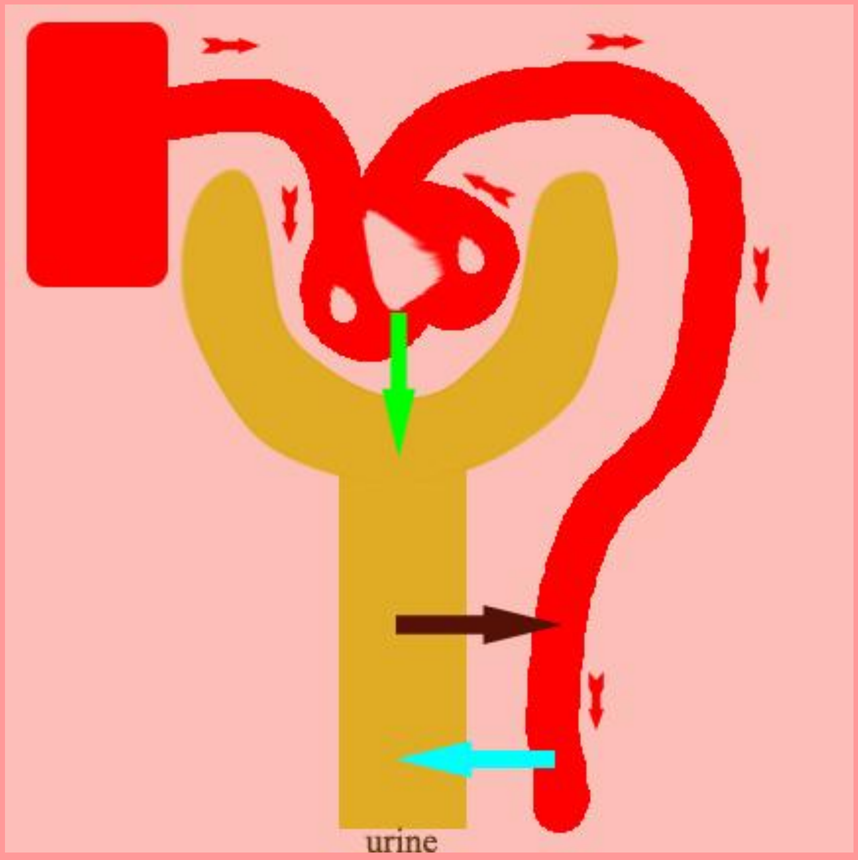
- The % of plasma entering the nephrons that actually becomes glomerular filtrate
- Averages about 16-20%

Renal Corpuscle = Glomerulus + Bowman's Capsule



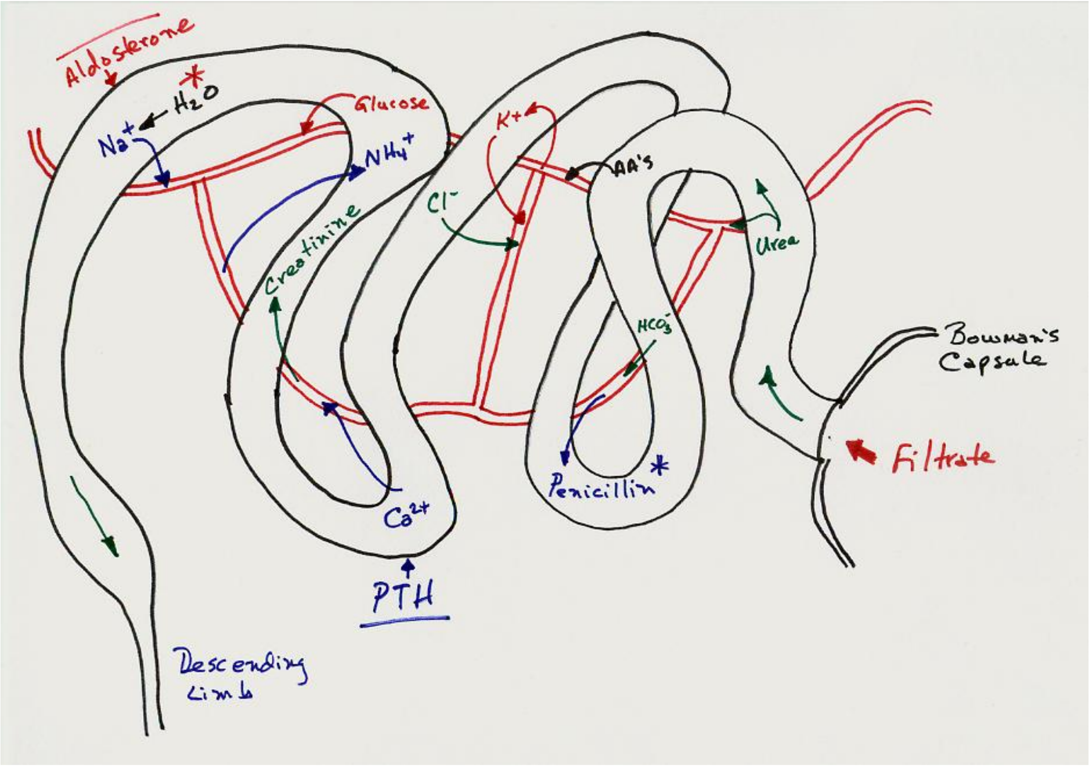
- Filtrate is similar to plasma without the formed elements and with less protein concentration
- 99% of plasma forced into Bowman's capsule returned to blood via peritubular capillary -- ARROW

Three Major Mechanisms of Renal Plasma Composition Adjustment



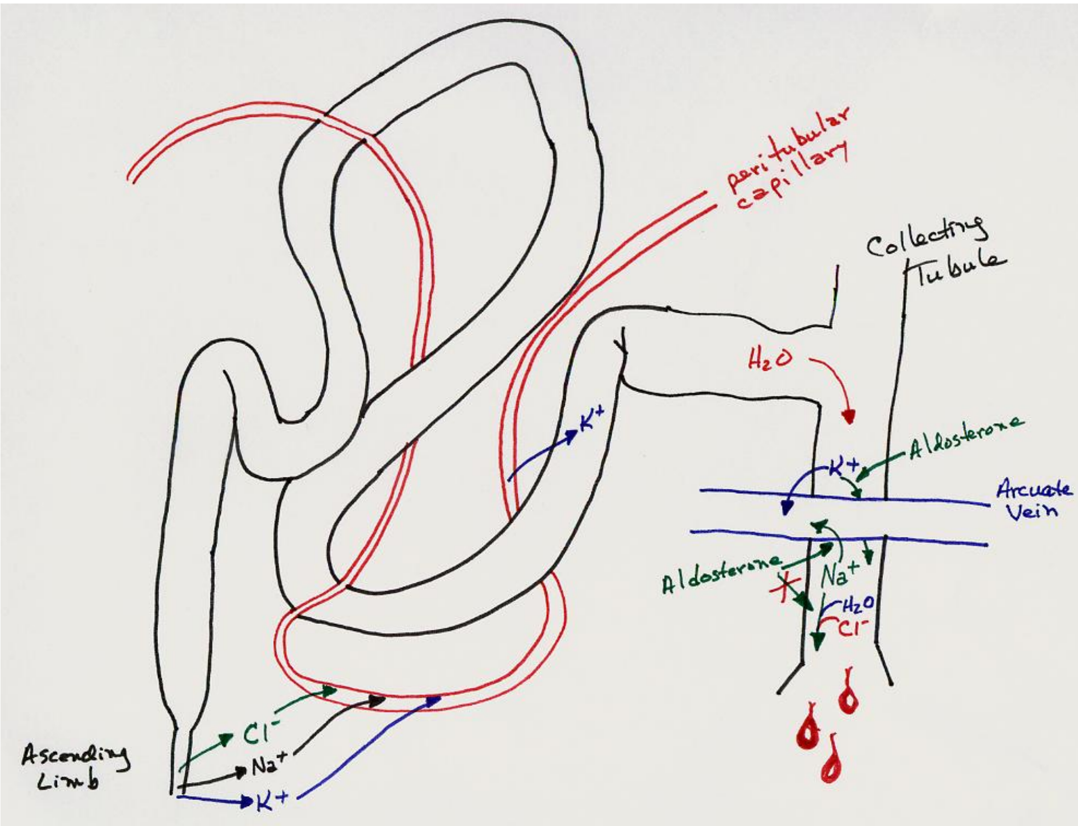
1. Glomerular filtration
2. Tubular reabsorption
3. Tubular secretion

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

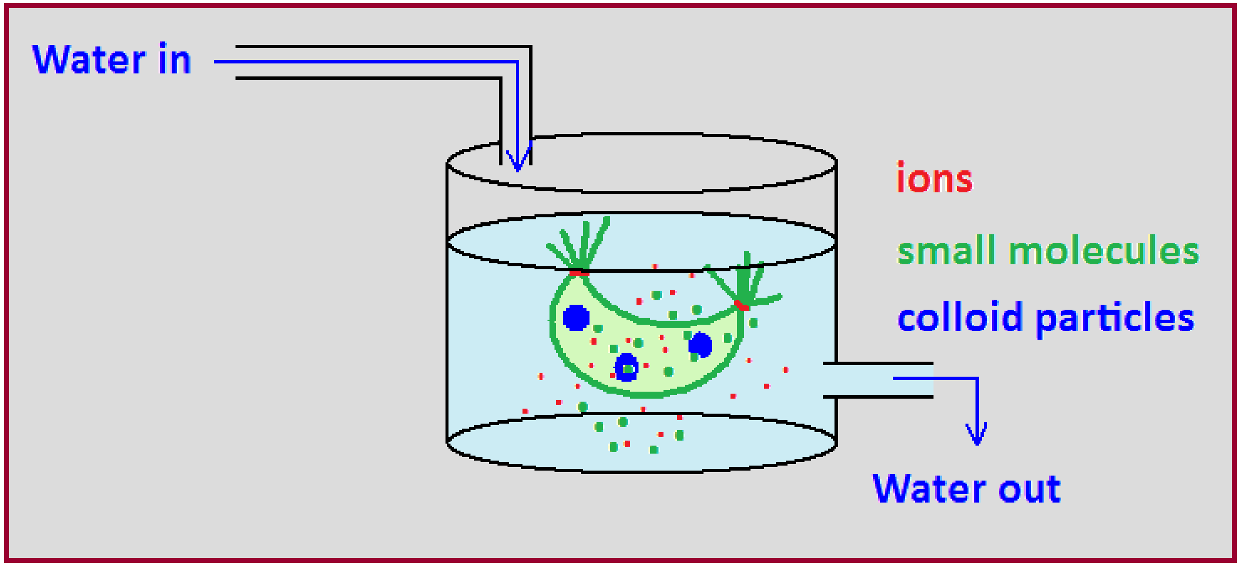
Distal Convoluted Tubule -- DCT



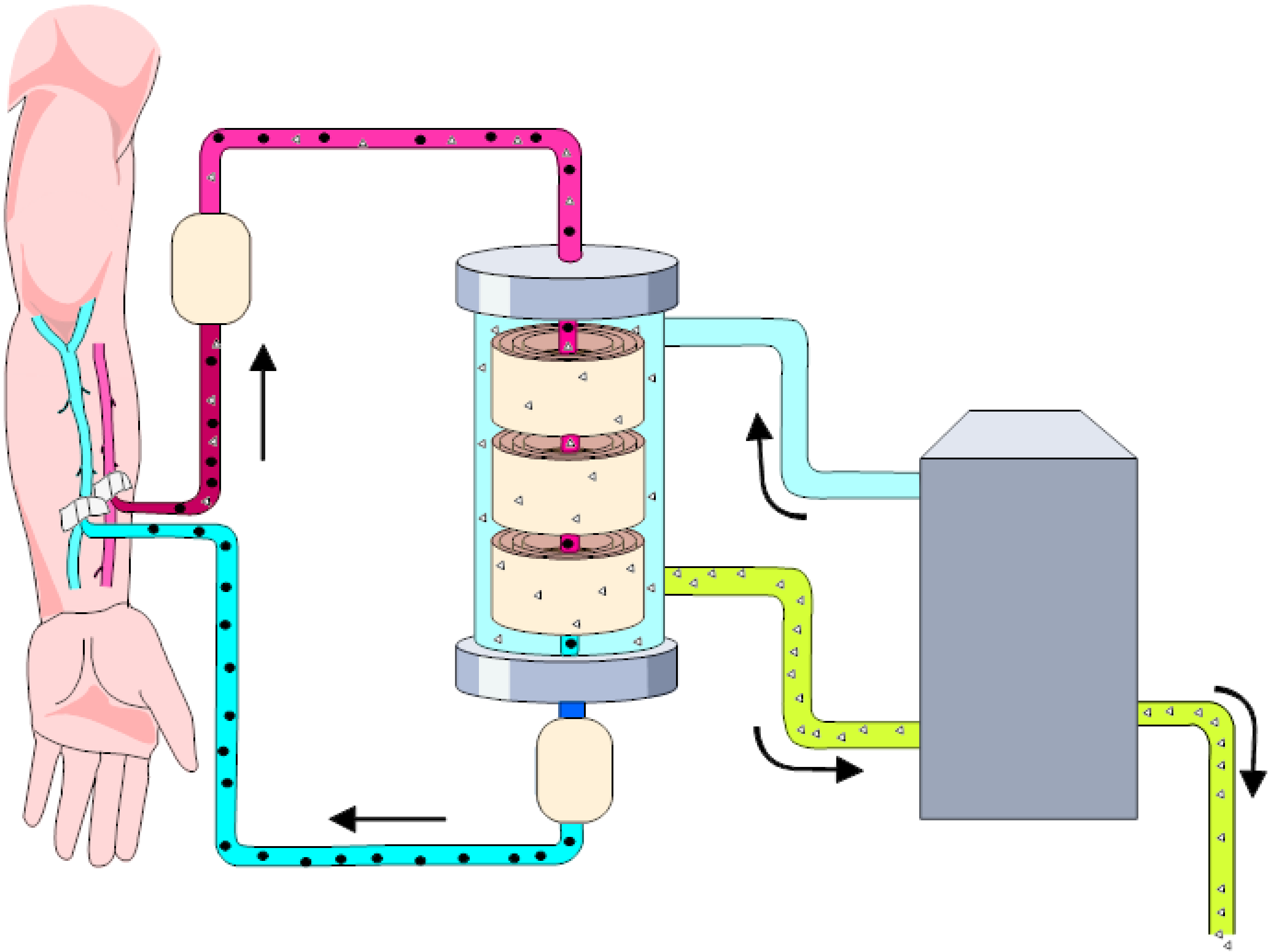
- K^+ reabsorbed in a passive manner
- Na^+ reabsorbed in a passive manner
- Cl^- reabsorbed in an active manner
- Aldosterone causes Na^+ retention and excretes K^+ -- otherwise, we reabsorb K^+ and excrete Na^+ with water and Cl^-

Dialysis

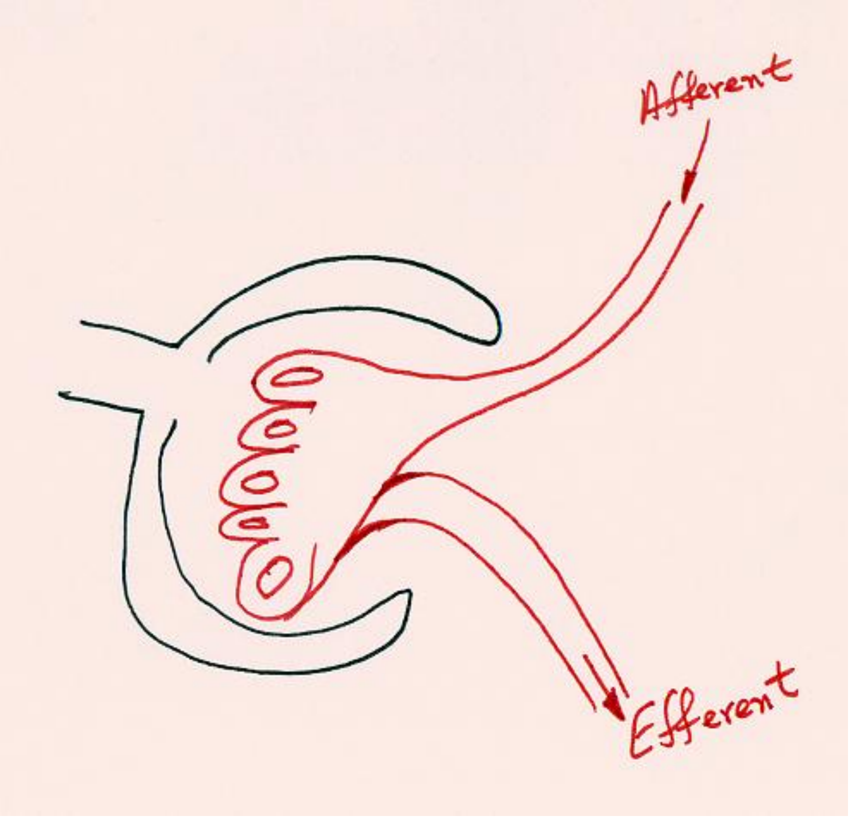
- Dialysis is a process in which solvent molecules, other small molecules and hydrated ions pass from a solution through a membrane.
- Dialysis is used to purify proteins and is used in patients with renal failure to clean their blood, i.e., remove toxins that would have, otherwise, been removed by their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



Dialysis

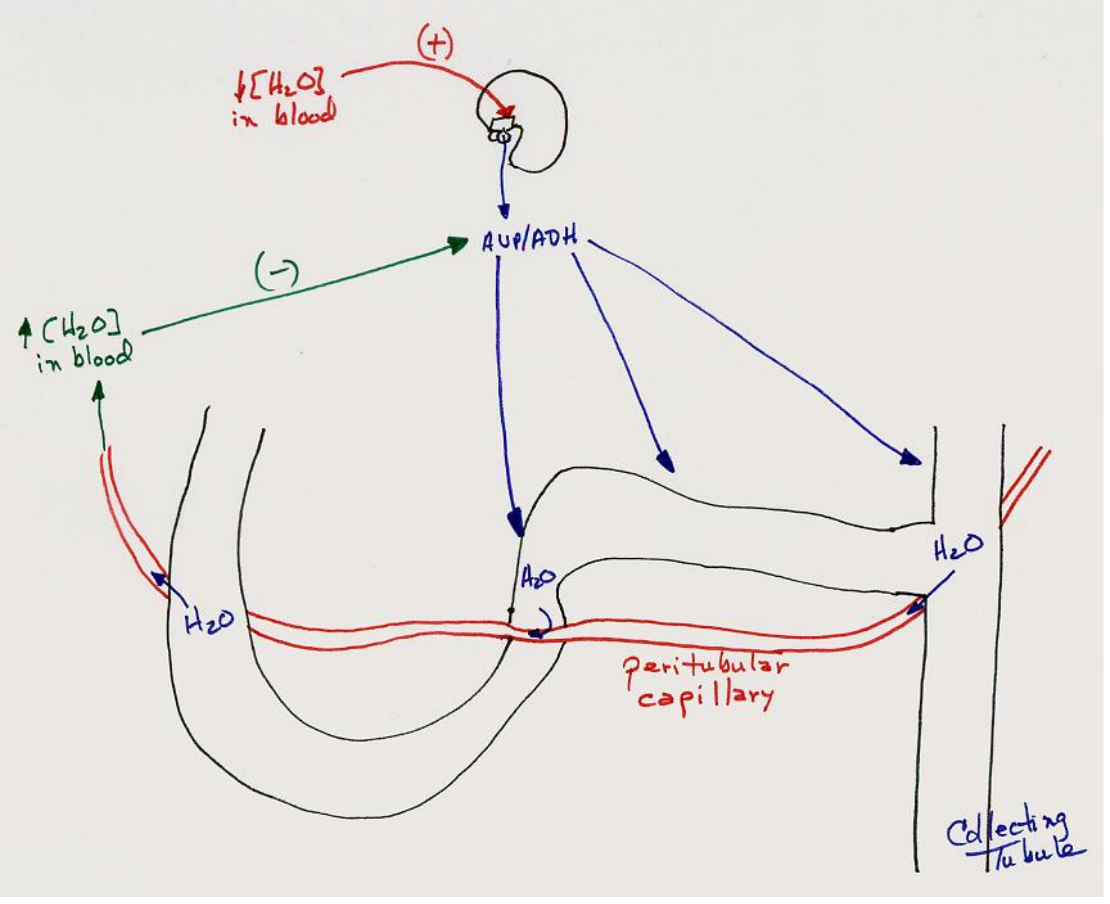


Hyponatremia



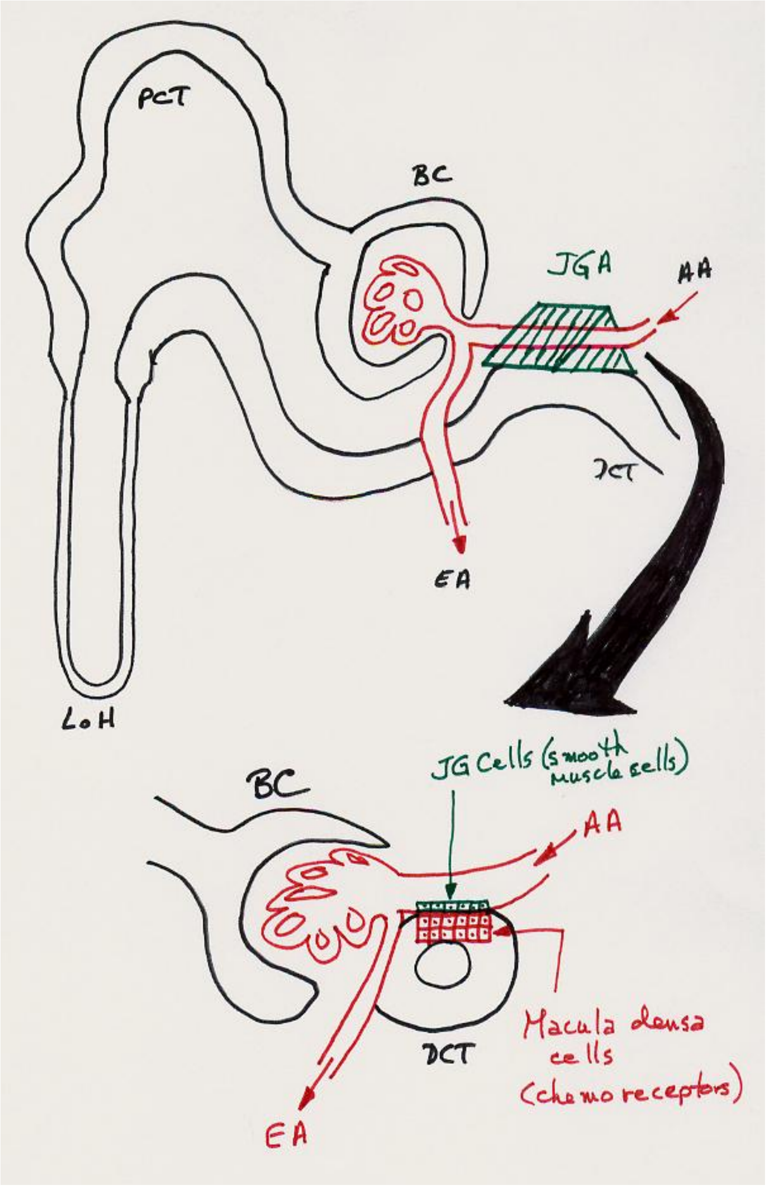
1. Low blood levels of Na^+
2. Causes ANG II secretion which constricts the efferent arteriole and increases glomerular pressure
3. Also causes aldosterone secretion which increases Na^+ reabsorption
4. Both mechanisms increase blood $[Na^+]$

AVP/ADH and Water Reabsorption



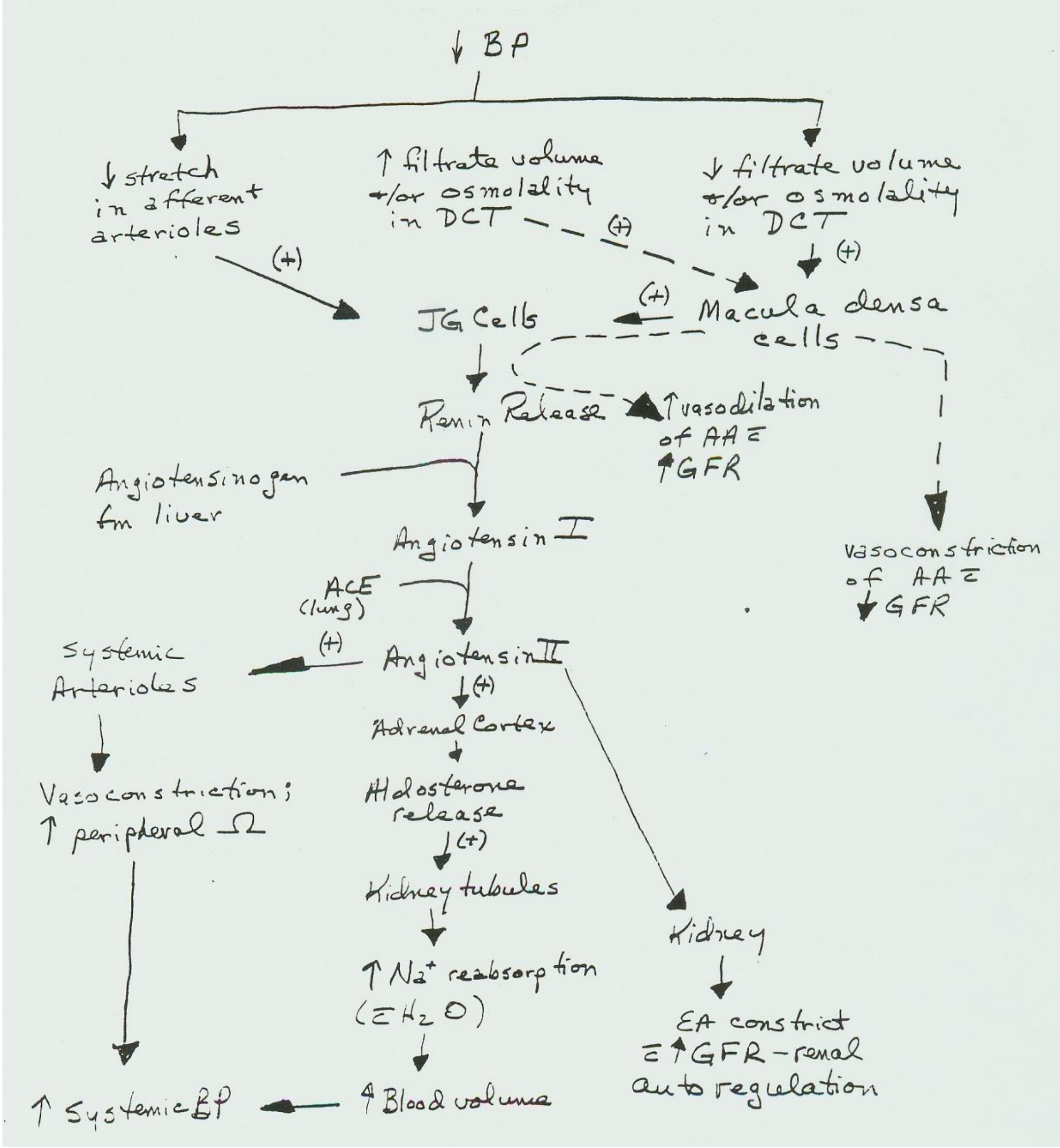
- AVP "opens" membranes to "let water out" of the DCT and back into the blood
- Second messenger is cAMP

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

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

What Causes Urine to Turn Red?

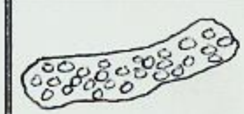
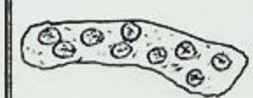
- RBC in urine
- Analgesics (aminopyrine)
- HgB
- Bile products
- Flagyl
- Beets
- Laxatives (Ex-Lax type that had phenolphthalein in them – not sold any more)
- S. marcescens: implications in nursery

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

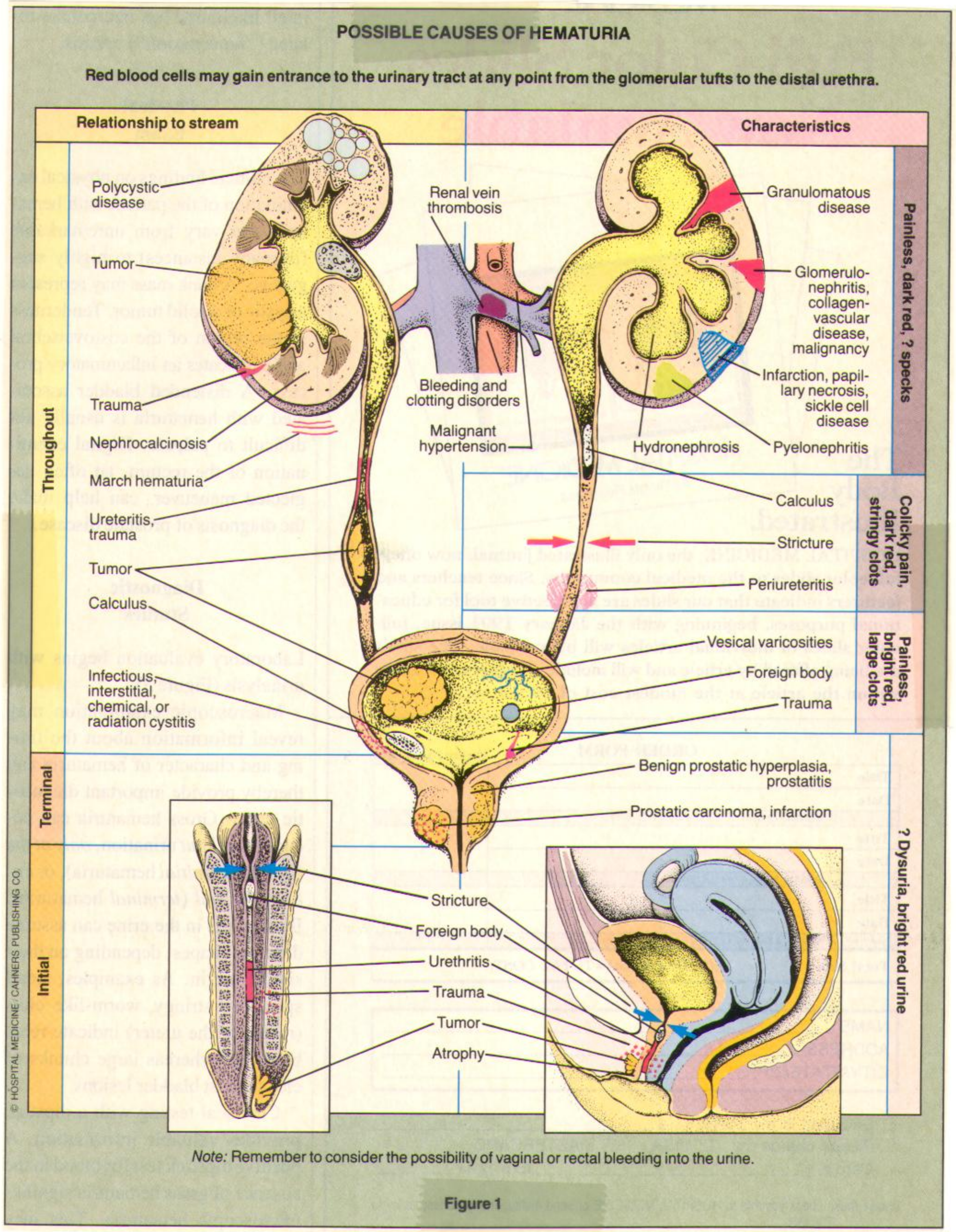
*NOT INCLUSIVE

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

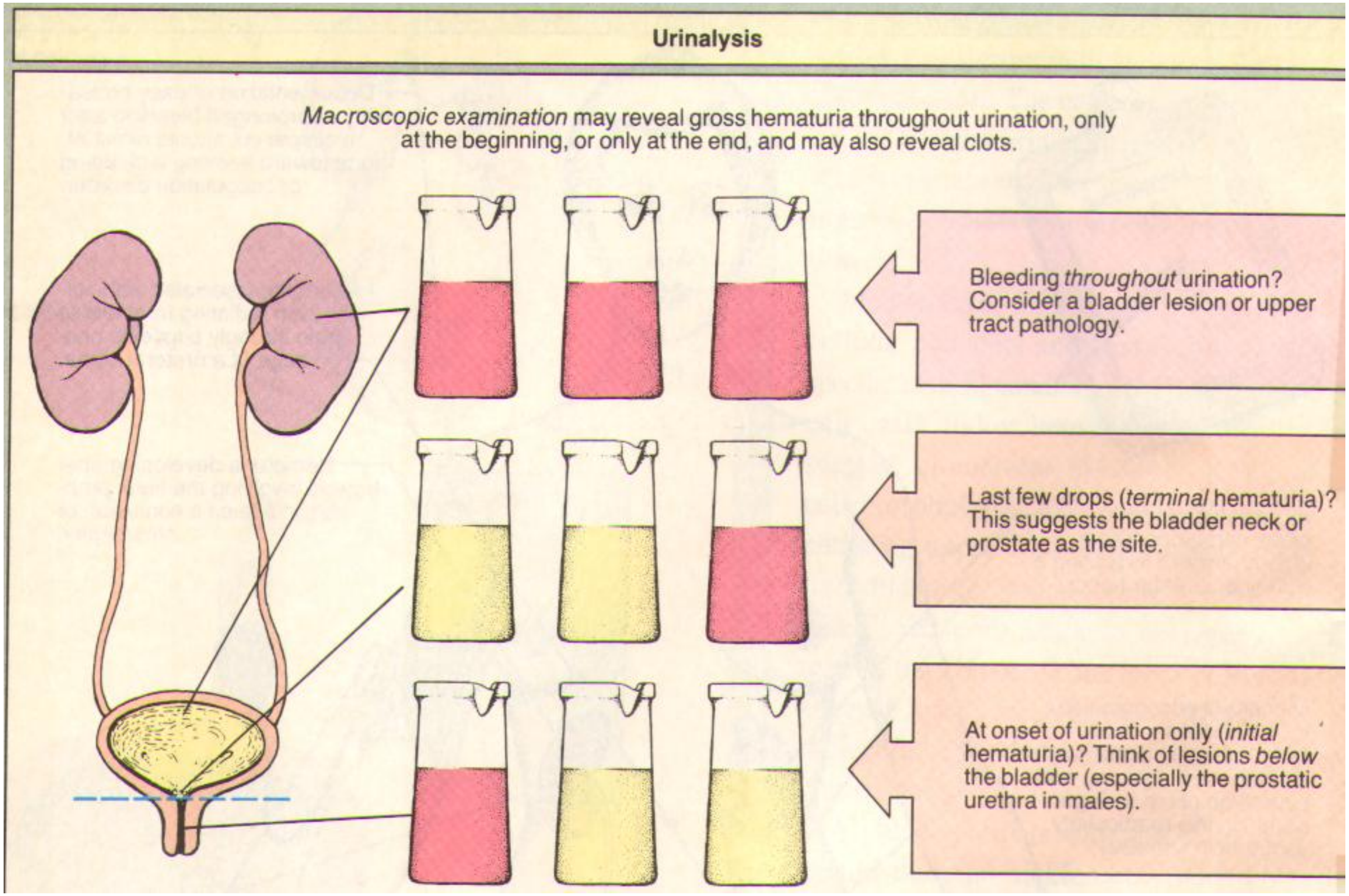


Remember: in females, menses may get in urine; 40% of women's urethral meati are inside the vagina

Hosp Prac, ca Oct 1992

Hematuria

Hosp Prac ca Oct 1992



Etiological Clues in Hematuria

Hosp Prac ca Oct 1992

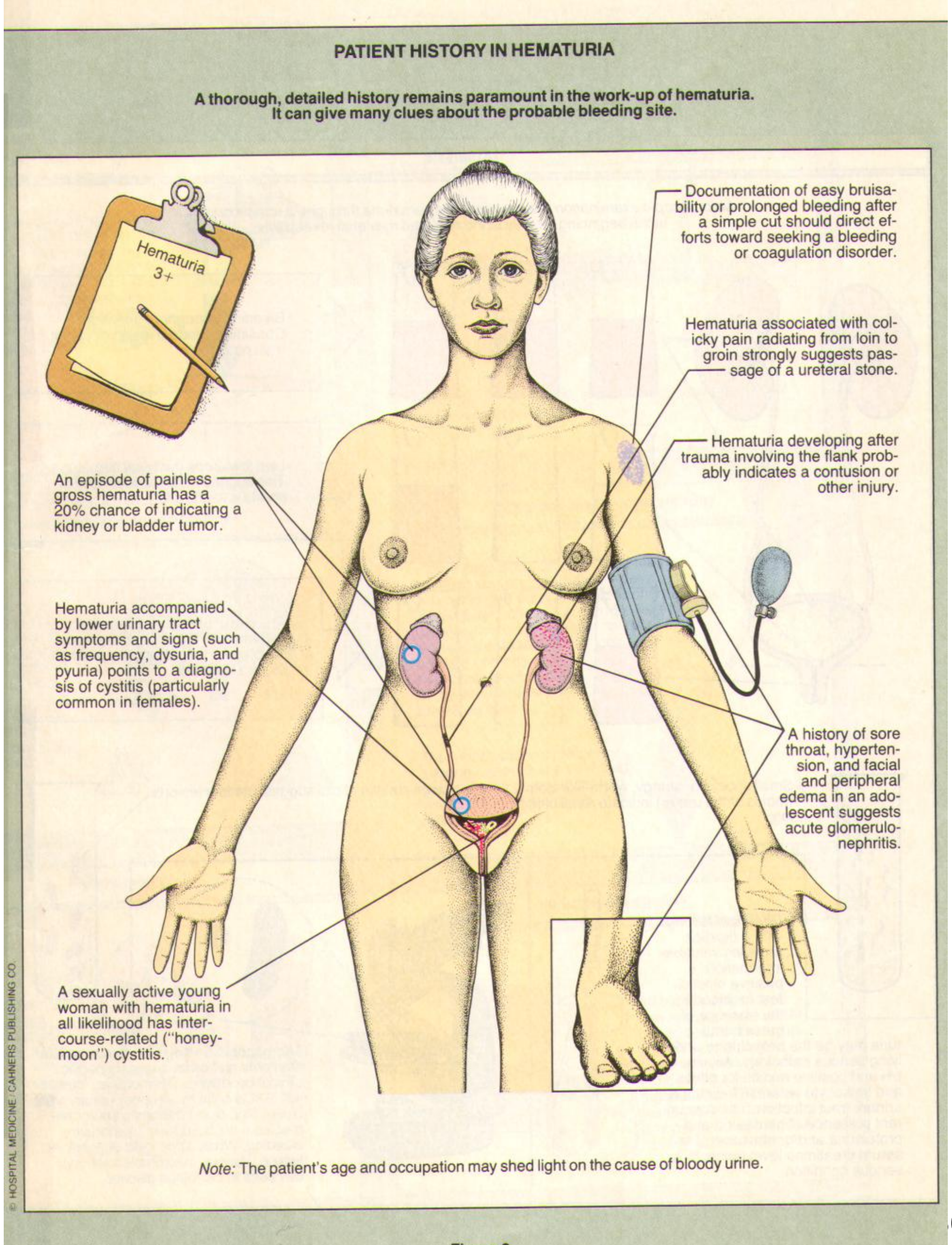


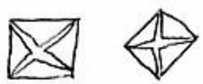
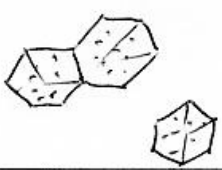
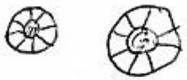
Figure 2

Pyuria

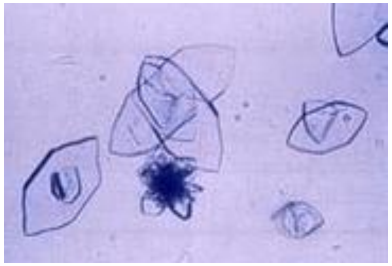
- WBC in urine
- 0-10 WBC/HPF are considered normal
- > 10 WBC/HPF is pyuria; find site of infection

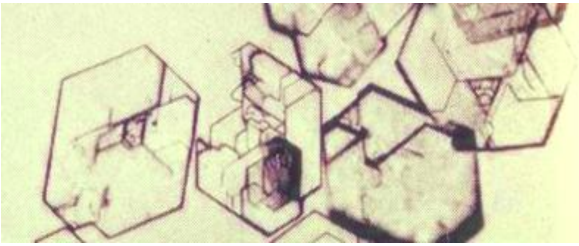
Crystalluria

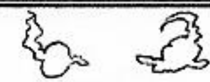
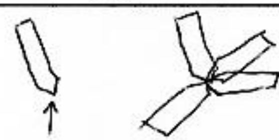
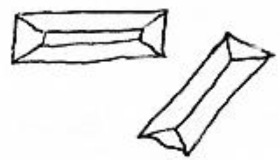
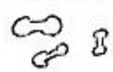
- Urates/carbonates/ammonium salts from end products of metabolism
- Calcium, phosphorus, amino acids due to excesses of nutrients
- Crystals MAY be a clue to stone formation and to some metabolic disorders

Crystals in Acid Urine		
Crystal	**Illustration**	**Comment**
Uric acid		"football"; 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)
Amorphus urates		Not considered to have any particular clinical relevancy
Calcium oxalate		opaque "X" through center; about 2/3 of all calcium containing stones; treat with veggies, milk, fruit (except plums, prunes, cranberries)
Sodium urate		"Zinnia"
Tyrosine		Rare; "dandelion puffs"; metabolic disorder; liver disease
Sulfonamides		"wheat shock"; treat with bicarbonate; not as common nowadays
Cystine		"Wheat cracker"; rare; metabolic disorder; treat with bicarbonate, lots of water or Diamox; may be present with or WITHOUT stones
Leucine		"poker chips"; rare; metabolic disorder; liver disease

http://www.ndt-educational.org/fogazzislidepart1.asp
http://www.ndt-educational.org/fogazzislidepart2.asp
http://www.ndt-educational.org/fogazzislidepart3.asp





Crystals in Alkaline Urine			
Crystal		**Illustration**	**Comment**
Ammonium urate			"Thorn-apple"; tx by increasing fluid intake
Calcium phosphate			"Stake"; due to hypercalciuria; over extended immobility; tx with increased fluid intake
Hypercalciuria: associated with hyperparathyroidism and bone resorption (prolonged immobilization)			
Triple phosphate: $MgNH_4PO_4$	Common	"Coffin" 	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 "Staghorn" calculus formation -- another form of triple phosphate crystal; this form of calculus "almost always" due to UTI
	Rapidly ppt'd form	 "Leaves"	
Amorphous phosphate			Larger than amorphus urates; not considered to have any particularly clinical relevancy; increase fluid intake
Calcium carbonate			"Dumb-bell"; increase fluid intake

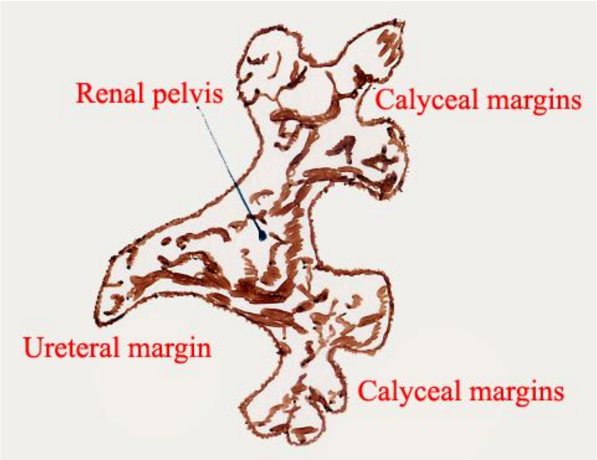
Urolithiasis

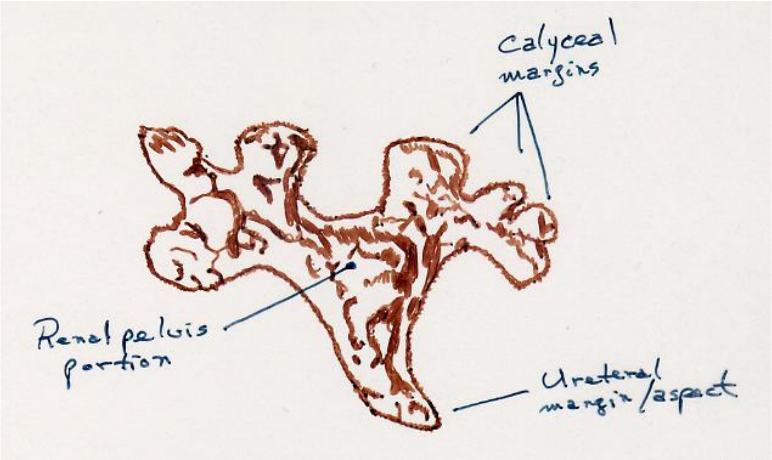
- Men effected more than women
- Tend to be older than 30 YOA
- Tend to be unilateral in about 80% of patients
- Stones provide for UTI, as well:
  - Due to the obstruction they cause
  - Due to trauma they cause to the tissue
- About 20% of calcium stones are due to increased uric acid excretion with 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
- $MgNH_4PO_4$

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

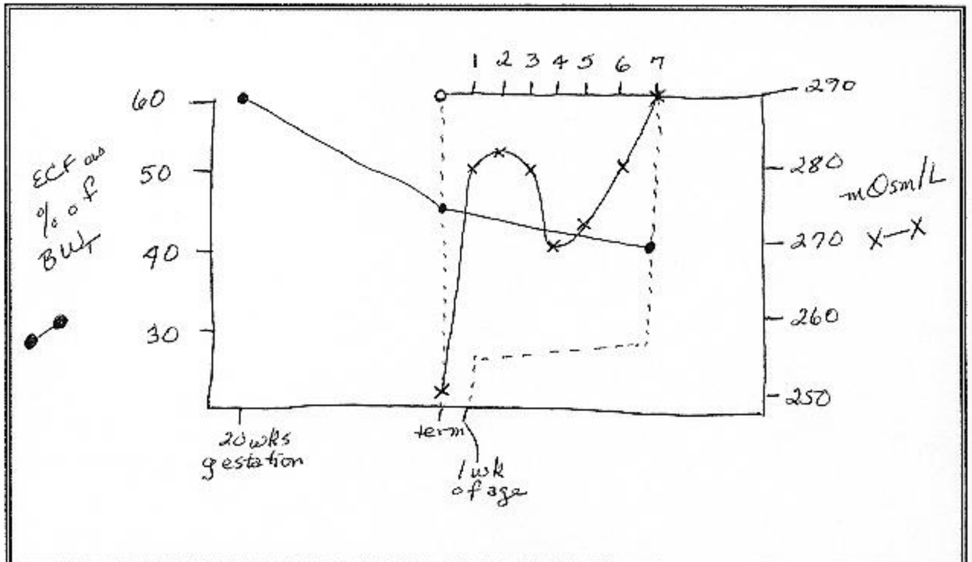
Introduction

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 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 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 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 (hypo-tonic; 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

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

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.

Neonatal Renal Acid-Base Regulation

- 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.

Total Body Water	
Newborn infant	75-80% of total body weight (50% in ECF and 50% in ICF)
Average adult male	60% of total body weight (about 35% in ECF and 65% in ICF)
Average adult female	50% of total body weight (Ibid)
In Elderly	45-50% of total body weight
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.	

Total Body Water			
	Connective tissue: 5%		
	↓↑	↓↑	
Plasma water: 7% →	Interstitial fluid: ← 18%	Intracellular water: 62.5% →	Transcellular ← water: 2.5%
	↓↑	↓↑	
	Bone water: 5%		

- 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).

Compartmentalization of "Body" Waters		
ECF	Primary lytes	ICF
pH about 7.4		pH about 6.7
Glucose about 90		Glucose about 0-20
Na^+	Cation	K^+
Cl^-	Anion	HPO_4^{2-}
HCO_3^-		
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"

Daily Water "Balance"					
Intake			Output		
Metabolism	10%	250 mL	Sweat	8%	200 mL
			Feces	4%	100 mL
Moist foods	30%	750 mL	Skin/lung loss	28%	700 mL
Beverages	60%	1500 mL	Urine	60%	1500 mL
TOTALS	100%	2500 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.

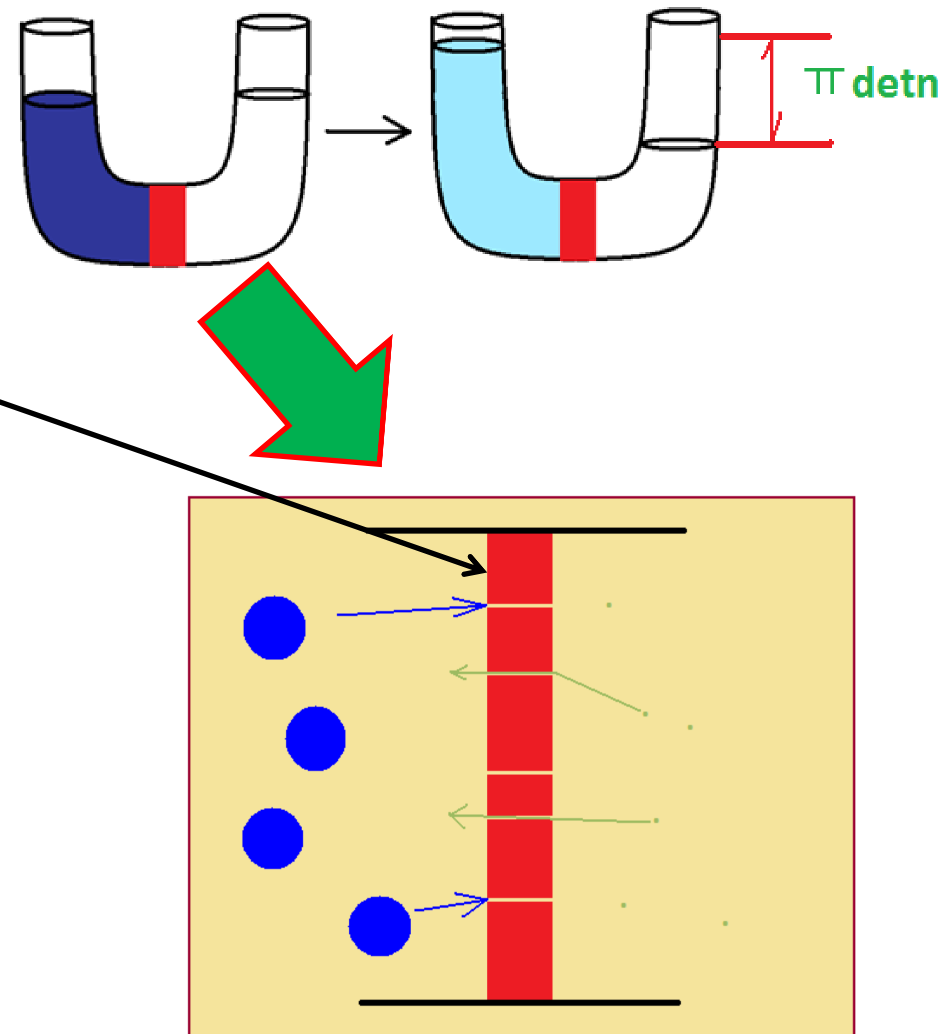
Sweat
HYPOtonic (HYPO-osmotic) -- primarily water with LOW Na^+ and Cl^-
When exercising in heat: 1 L sweat lost per hour
With fever between 101 and 103 F: increase fluids by 500 mL per 24 hour period
With fever greater than 103 F: increase fluids by 1000 mL per 24 hour period

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:

$$\pi = nMRT$$

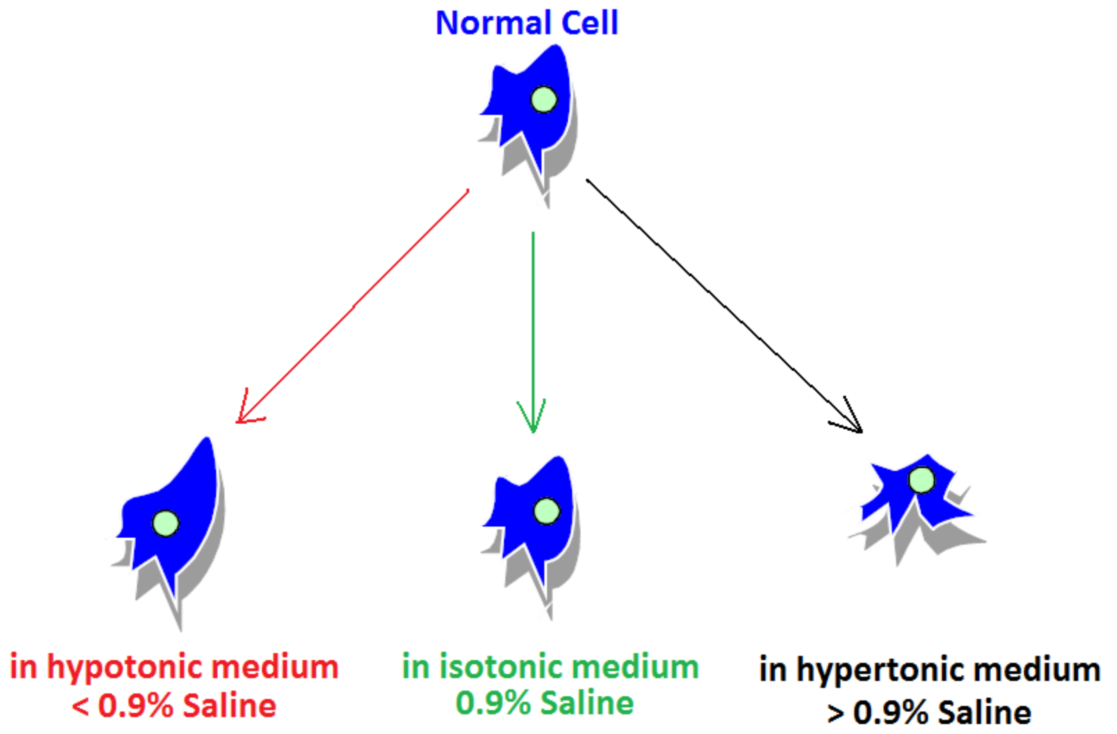
- Where π is the osmotic pressure, n is the number of mols of solute, M is the molarity of the solution, T is the absolute temperature and R is the gas constant (0.0821 L-atm/mol-K or 62.4 torr-L/mol-K).



Effects on the Body from Altered Osmotic Solution Infusion

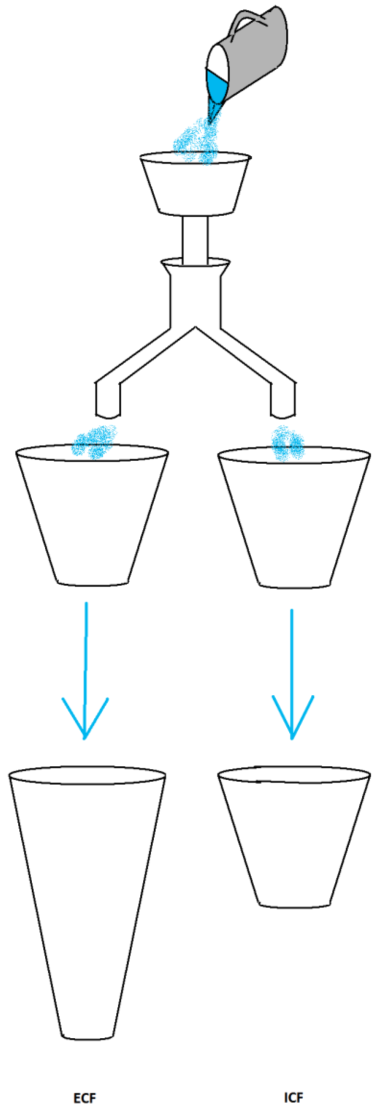
Biological Application

- 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.



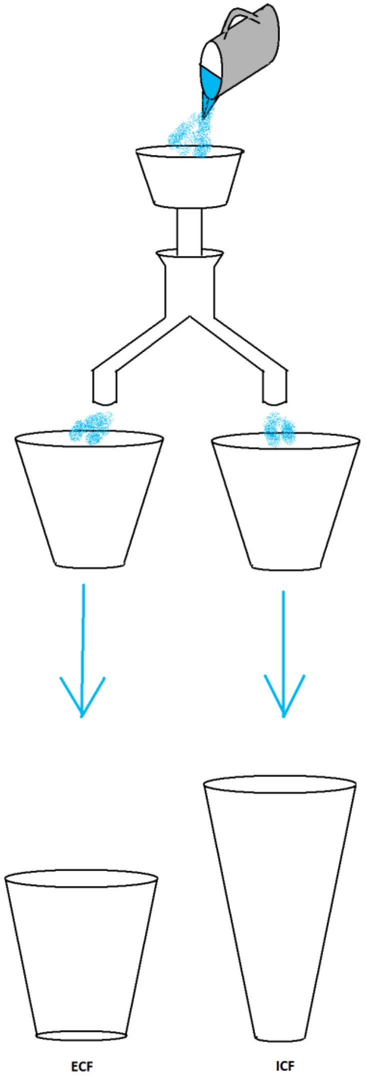
Isotonic Solutions

- 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 treat hypovolemic shock to increase the ECF volume (a fluid volume expander) and to restore perfusion throughout the body.



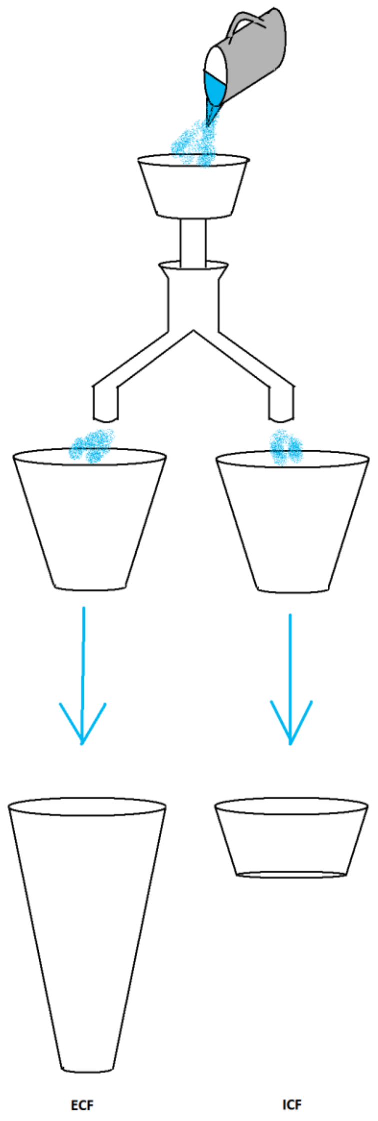
Hypotonic Fluids

- 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.

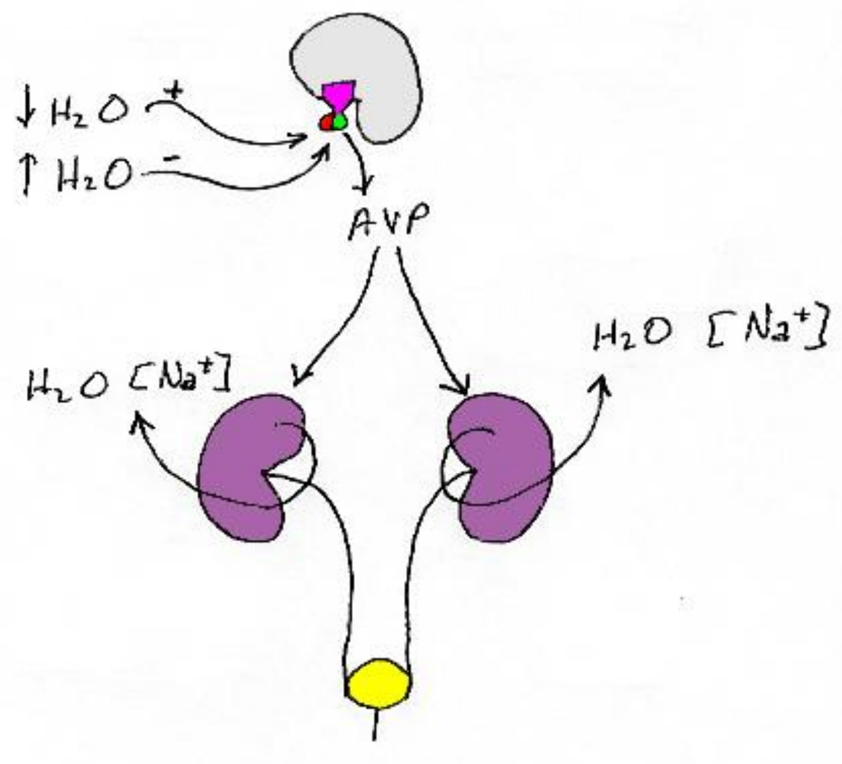


Regulation of Water Intake

- 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

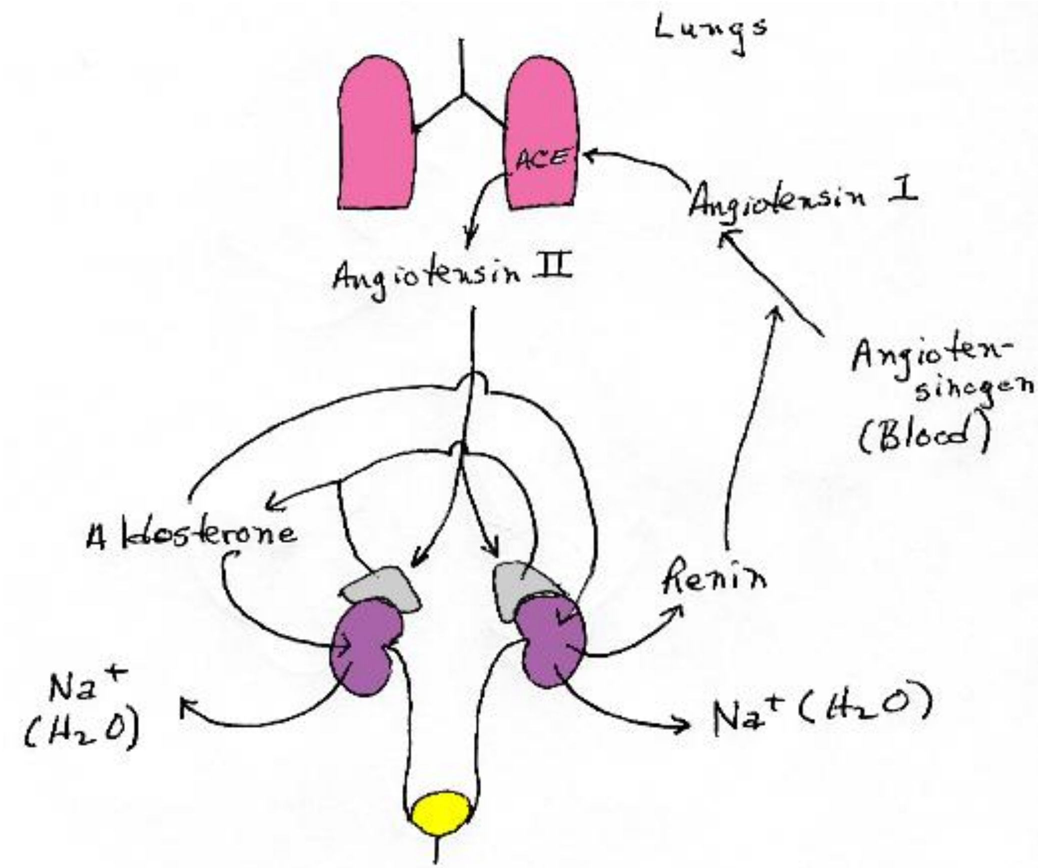
- A 5-10% reduction in ECF is all it takes to cause an increase in AVP release and thirst stimulation.
- AVP is primarily involved with osmoregulation.

- 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.

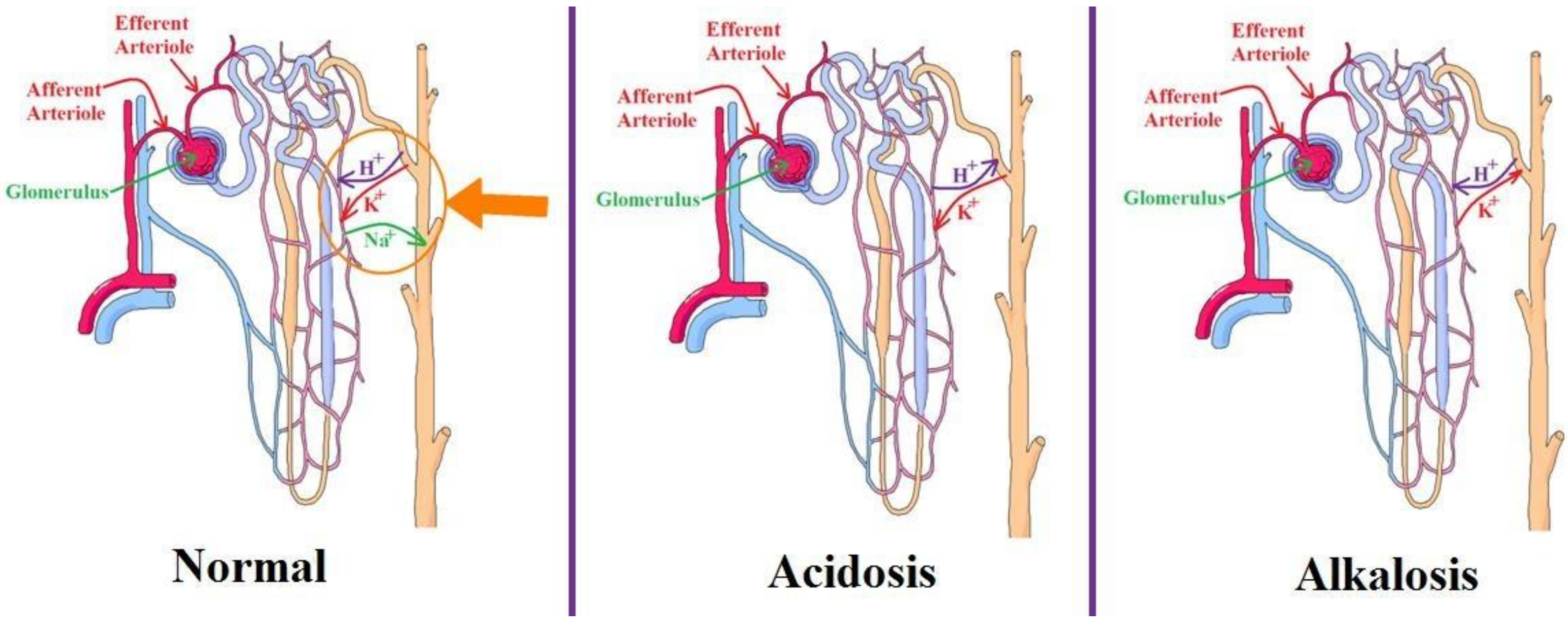
- As a general rule, the plasma osmolality is equal to 2 times the serum sodium ion concentration.
- In normal patients, the sodium ion levels are held in check with AVP.

- 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.



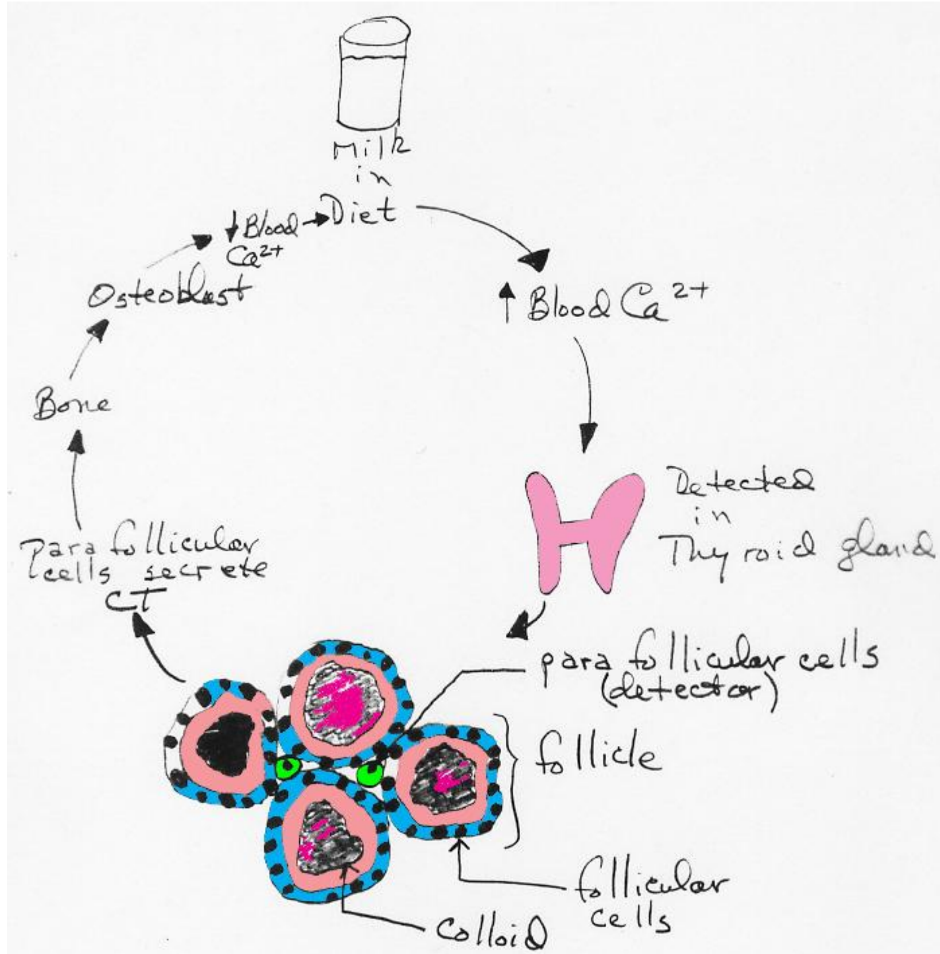
Potassium Ion Regulation

- Potassium ion regulation is regulated with Na+ regulation via aldosterone.
- K^+ also plays a role in/with acid/base balance.



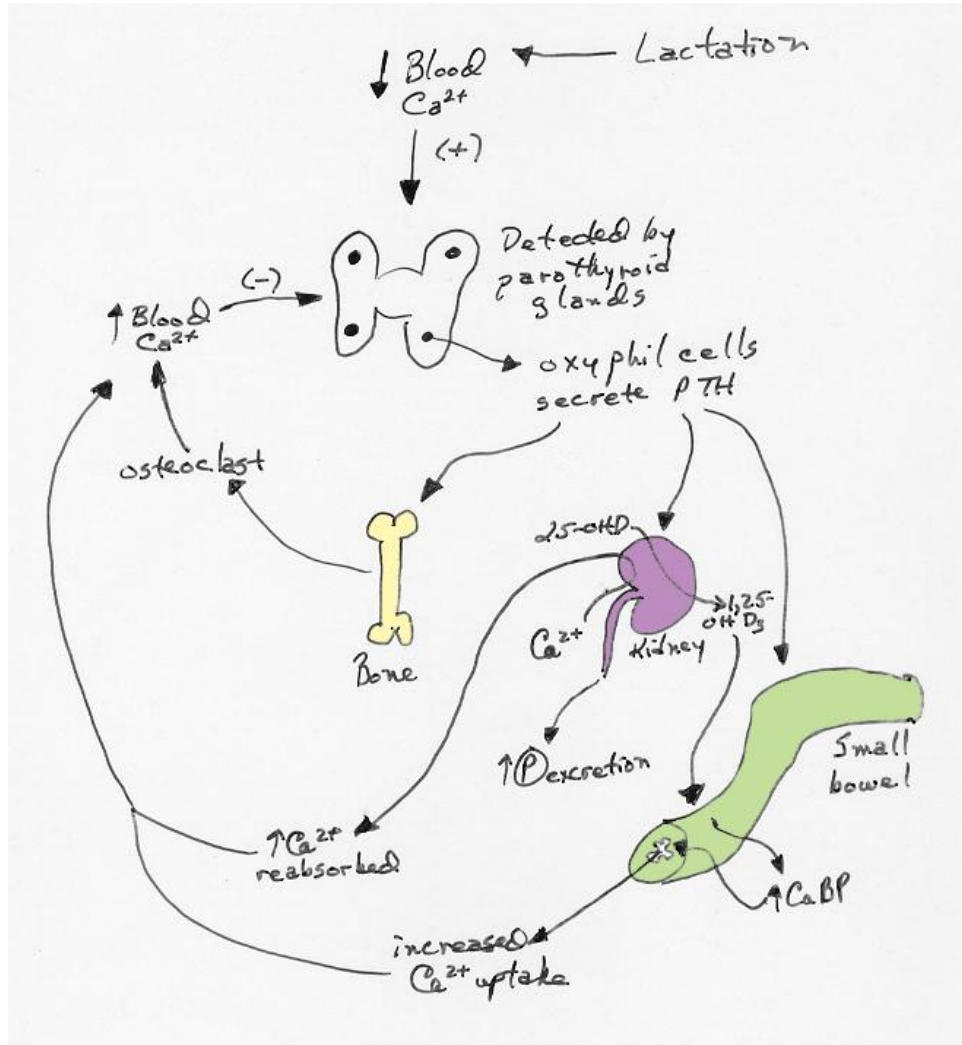
The Inter-Relationship Between Ca^{2+}, Mg^{2+} and PO_4^{3-}

- 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^{2+} , Mg^{2+} and PO_4^{3-}

- The second mechanism under consideration is that of parathyroid hormone (aka parathormone; PTH) secretion



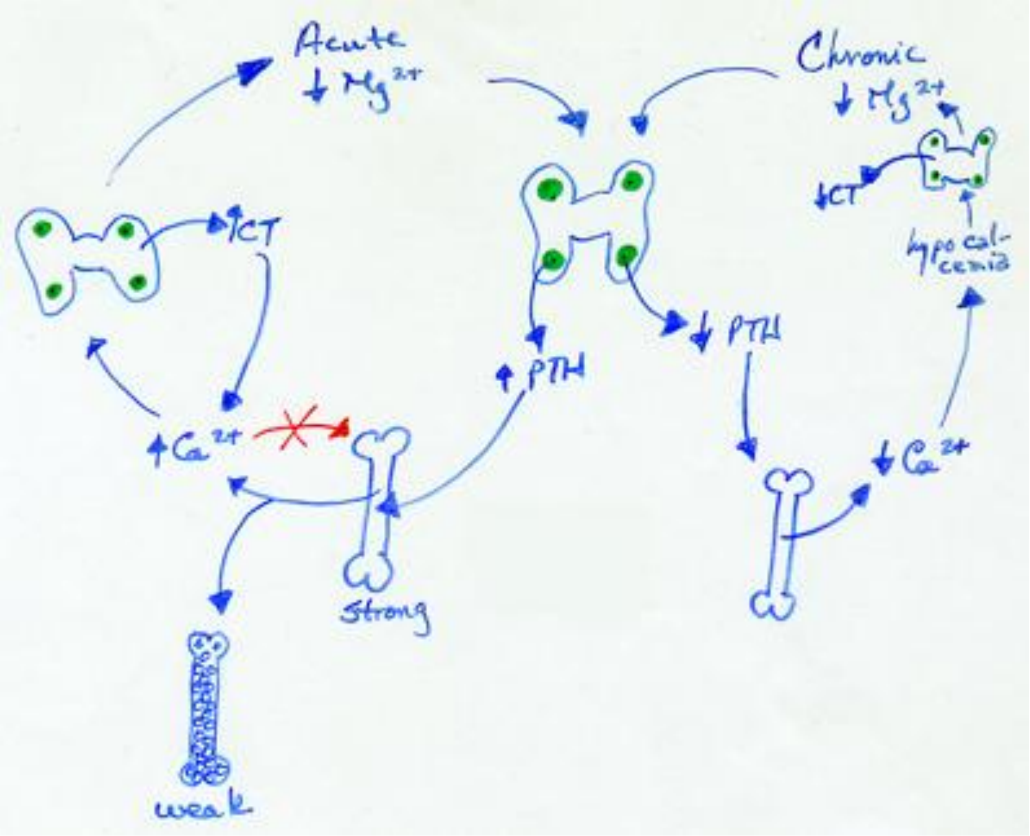
Ibid

- 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:

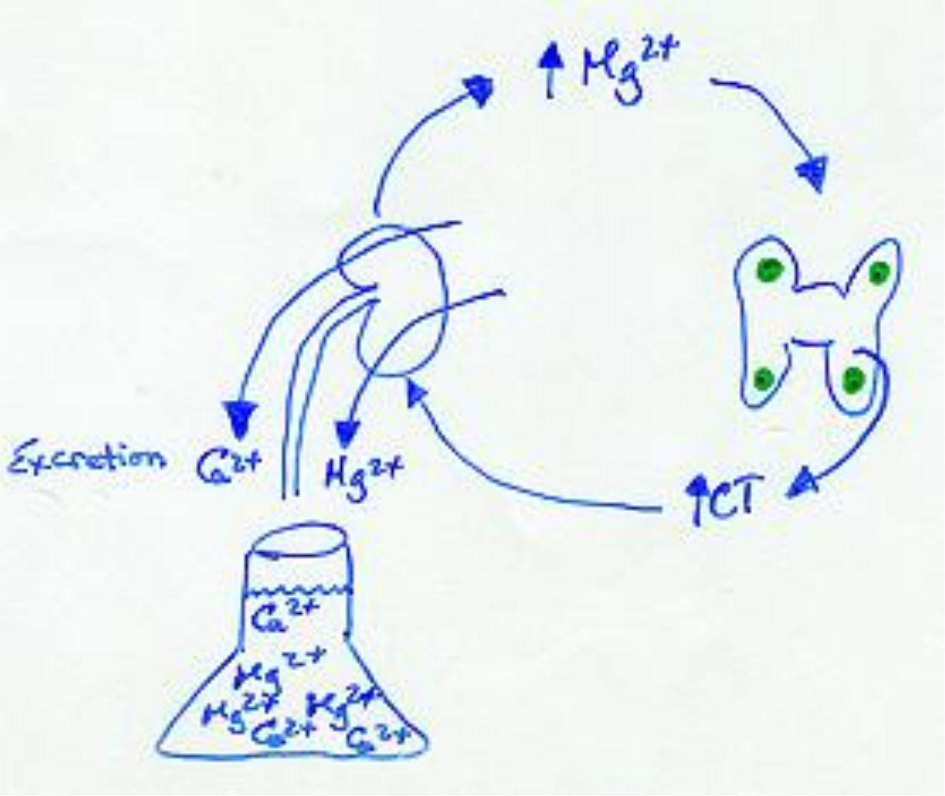
1) Acute hypomagnesemia
   - PTH release, CT release and Ca^{2+} levels are ALL elevated.
   - This results in the formation of weak bones.
2) Chronic hypomagnesemia
   - PTH secretion and Ca^{2+} levels are both reduced.



Ibid

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.

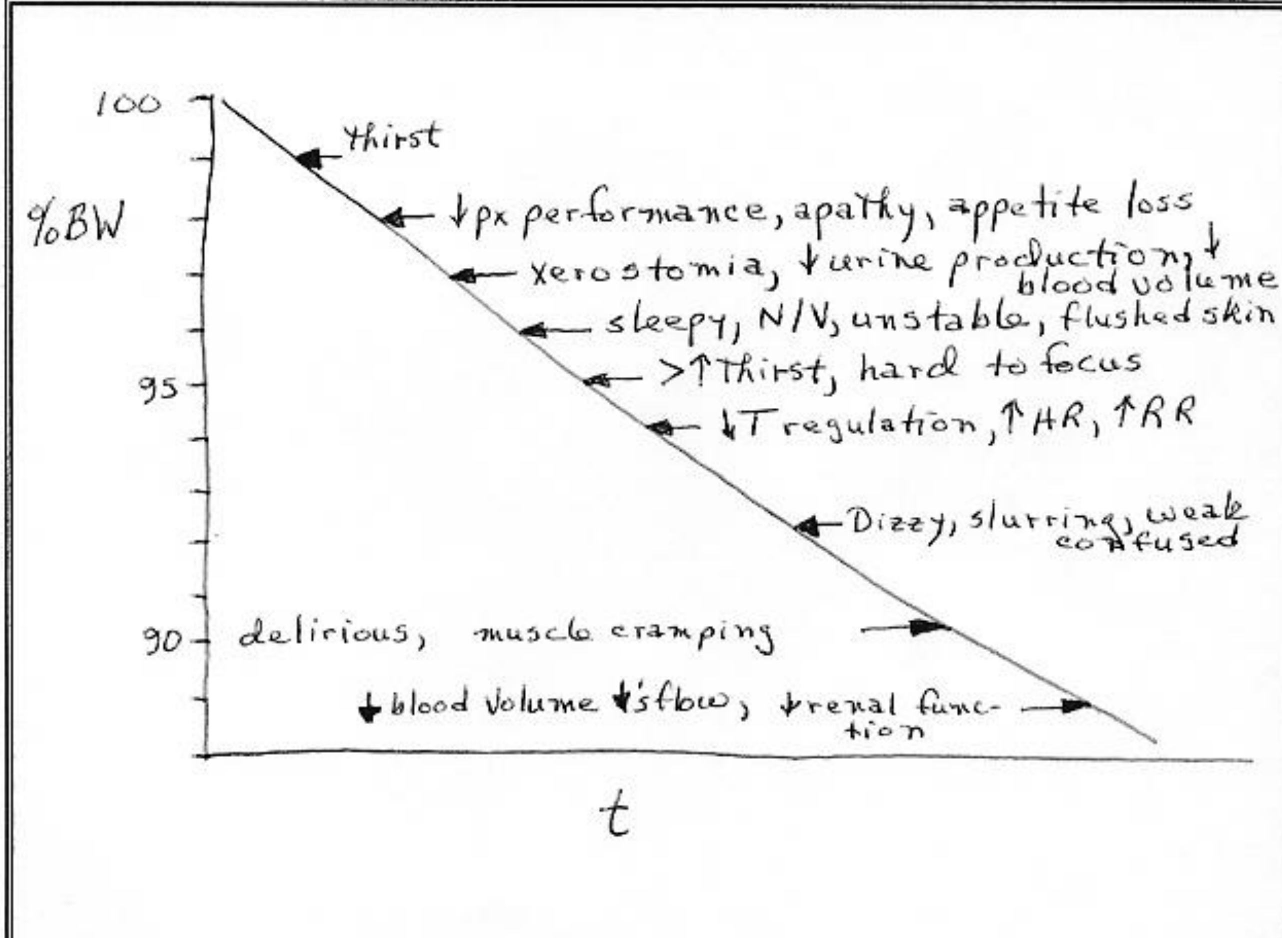


Sources and Needs of/for Electrolytes and Water

When you need water/How much to drink		
In General	**When, specifically**	**How much**
Before exercise	2 hours	500-750 mL water
	0.25 hours	500 mL refrigerator cold water
During exercise	q 0.25 hours	250-500 mL of refrigerator cold water
After you're done exercising	q 0.25 hours or prn for own comfort	250 mL until you've drunk 500 mL for every 0.454 kg lost

Ibid

The Effects of Not Drinking Water Appropriately, i.e., Dehydrating Yourself



Ibid – Sources – I & O

Foods	Fluids	Metabolic Reactions
↓	↓	↓
	Lyte Intake	
	↓	
	Lyte Output	
↓	↓	↓
Sweat	Feces	Urine

While We're At It

$$\frac{mEq}{L}$$

$$\equiv \frac{\text{mg ion / L solution}}{\text{atomic wt}} \times \frac{\#\text{charges}}{\text{ion}}$$

$$\frac{\#\text{chg's}}{\text{ion}}$$

E.g. $Na^{+} = 1$

$Mg^{2+} = 2$

$Cl^{-} = 1$

$NH_4^{+} = 1$

$\frac{mEq}{L}$ for Ca^{2+} @ 100 mg/L

$$\frac{mEq}{L} = \frac{100 \text{ mg } Ca^{2+}/L}{40 \text{ mg/mmol}} \times 2 \frac{mEq}{mmol} = 5 \frac{mEq}{L}$$

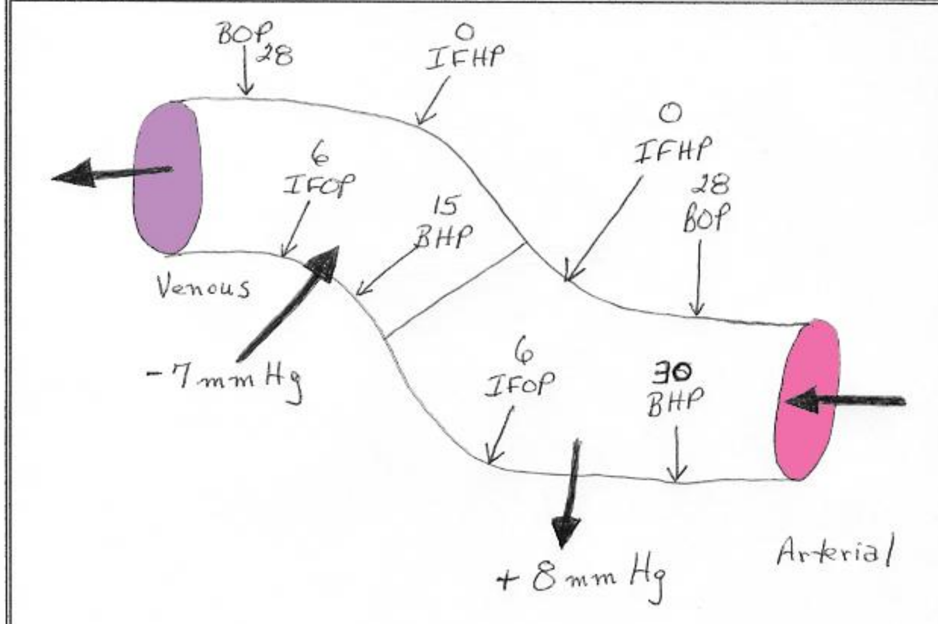
for Na^{+} @ 3300 mg/L

$$\frac{mEq}{L} = \frac{3300}{23} \times 1 = 143 \text{ mEq/L}$$

Cardiovascular Role in Fluid Balance

- Fluid imbalances can create problems, as well.
- Starling's Law of the Capillary explains what happens under normal hydrated states.

Blood/Fluid Pressures Received by Capillaries			
BHP	IFHP	BOP	IFOP
Outward pressure on the walls of the capillary; about 15 mm Hg Venous	Inward pressure on the walls of the capillary; about 0 mm Hg	Inward pressure on the walls of the capillary; about 28 mm Hg	Outward pressure on the walls of the capillary; about 6 mm Hg



Net INWARD Pressure:	Net OUTWARD Pressure:
$(6 + 15) - (28 + 0) = -7$ mm Hg	$(6 + 30) - (28 + 0) = 8$ mm Hg
"Forces" into the blood cellular wastes	"Forces" nutrients from the vessel into the interstitium

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

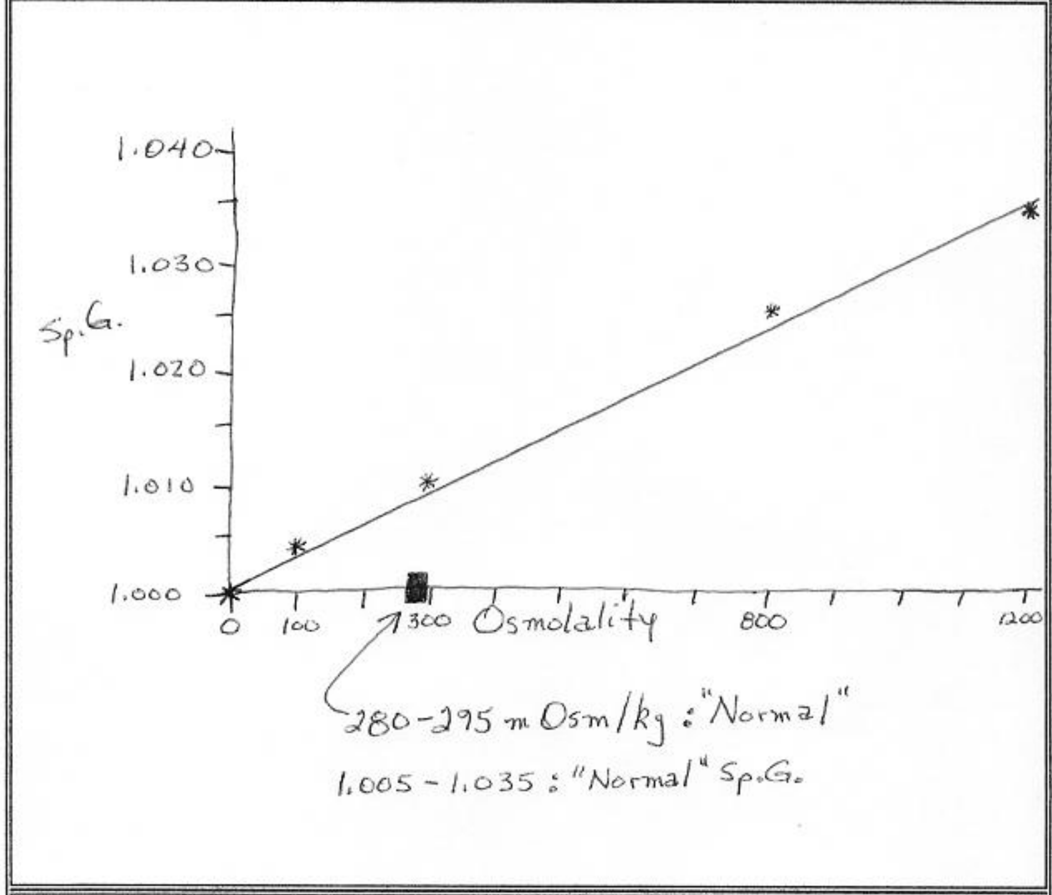
Water/Lyte Guide for Assessment of Disorders

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

Dry conjunctiva	reduced fluid volume	Increased ICP	reduced Na^+
Periorbital edema	fluid volume excess	Seizures	Decreased Ca^{2+}
Dry lips	reduced fluid volume (or mouth breather)	Hand veins	↑ fill time with hypovolemia; ↑ EMPTYING time with hypervolemia
Decreased skin turgor	reduced fluid volume	Hypochloremia	associated with metabolic alkalosis and hypokalemia
Temperature	101-103 F, increase volume requirements X 500 mL/24 hours	Hyperchloremia	associated with metabolic acidosis and hyperkalemia
Rapid heart rate	reduced fluid volume	Elevated BUN	osmotic diuresis with reduced fluid volume
GI system	NO bowel sounds = hypokalemia; Bowel sounds with diarrhea = hyperkalemia	Elevated creatinine	hypovolemia
Urinary Na^+/K^+	2:1 is normal; hyperaldosteronism: Na^+/K^+ reversed; Adrenal insufficiency: Na^+/K^+ elevated	Decreased creatinine	hypervolemia

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^+])



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.