How Not to Die of Thirst:

a handy guide for getting lost in the desert or at sea

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BSCI 279

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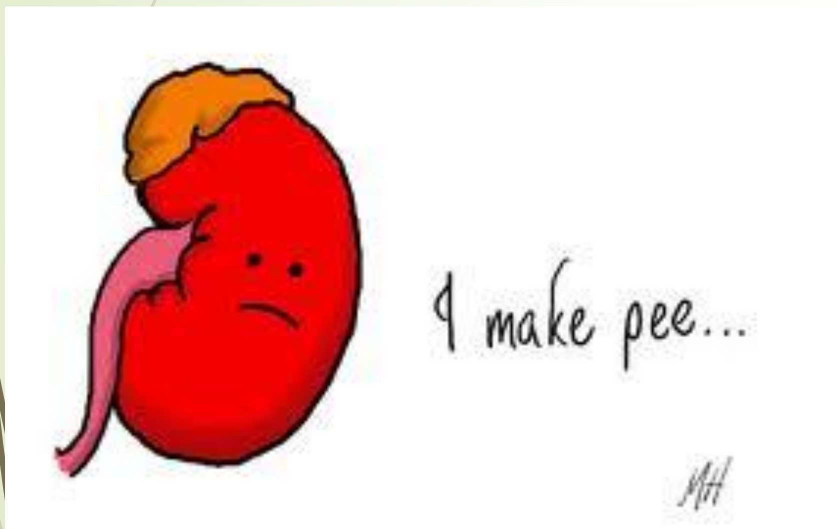
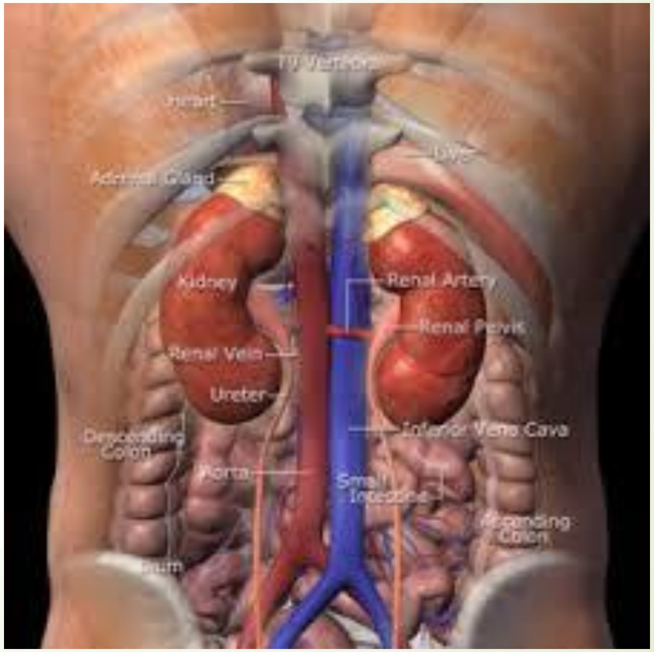
Outline

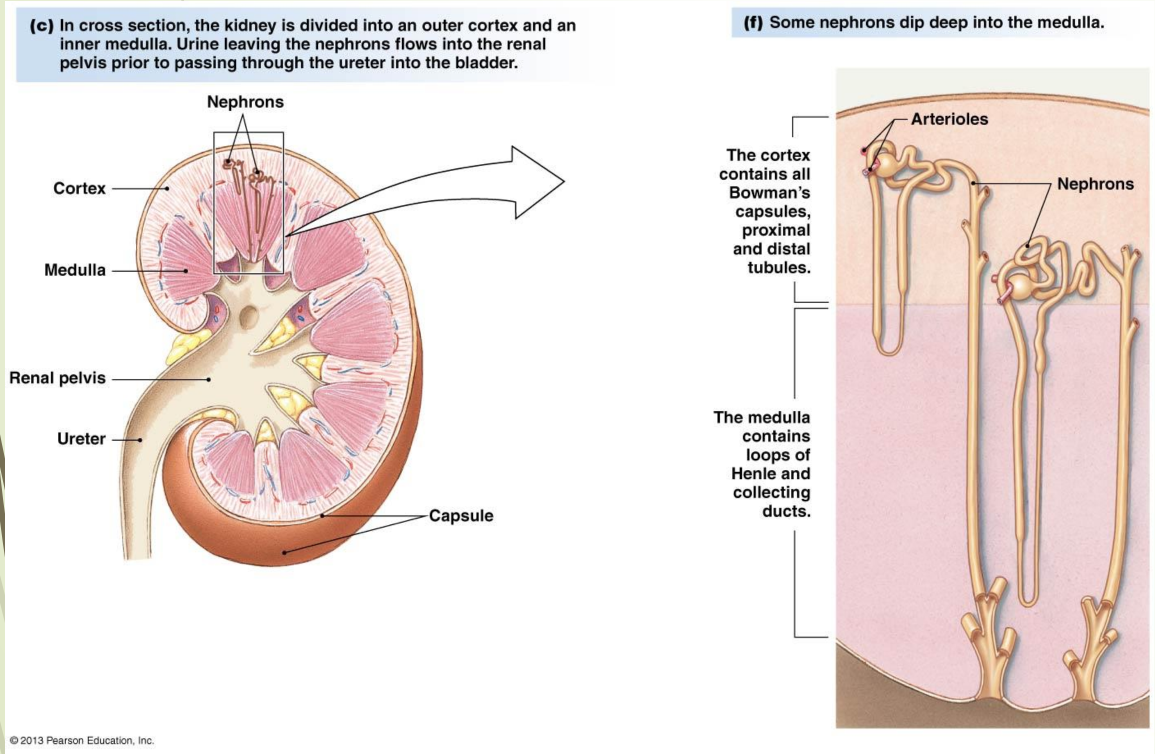
- Renal Review
- Osmoregulation in the desert
- Osmoregulation at sea

What are the functions of the kidneys?

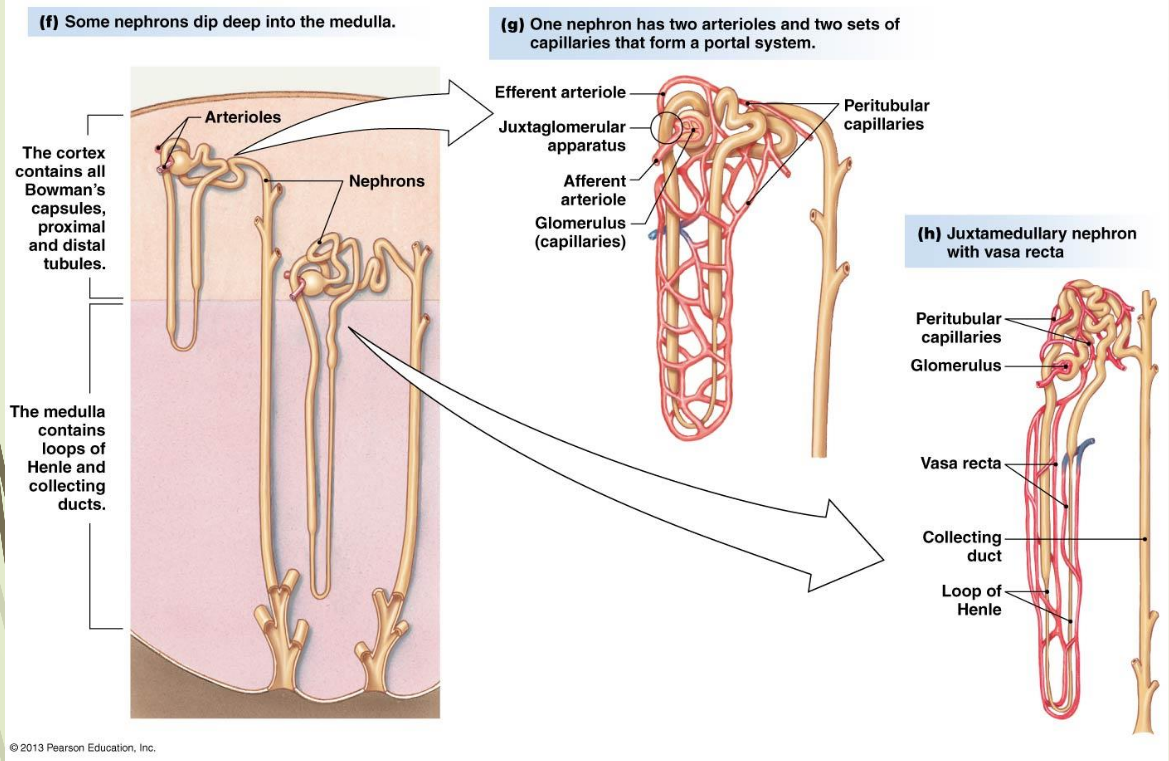




Anatomy of the Kidney



Structure of the Nephron



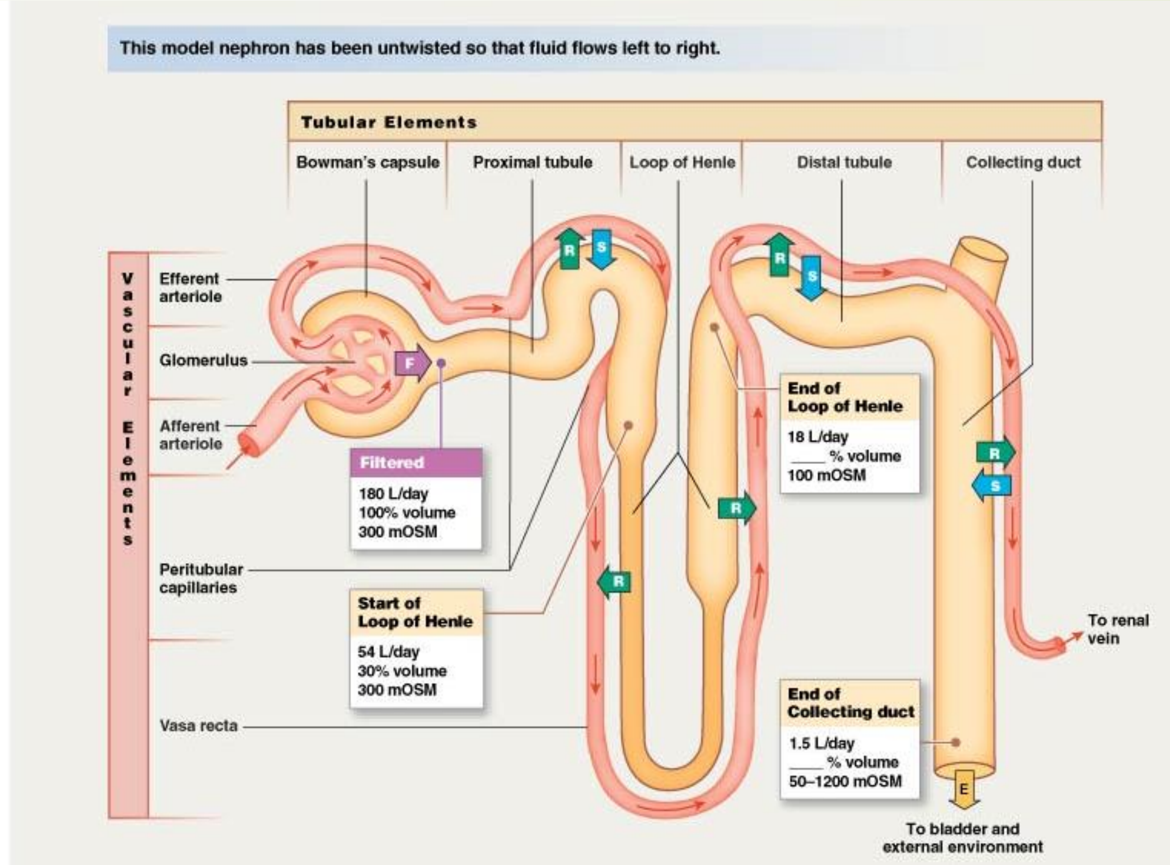
? What is a portal system?

Afferent arteriole → glomerulus→ efferent arteriole→ peritubular capillaries/ vasa recta

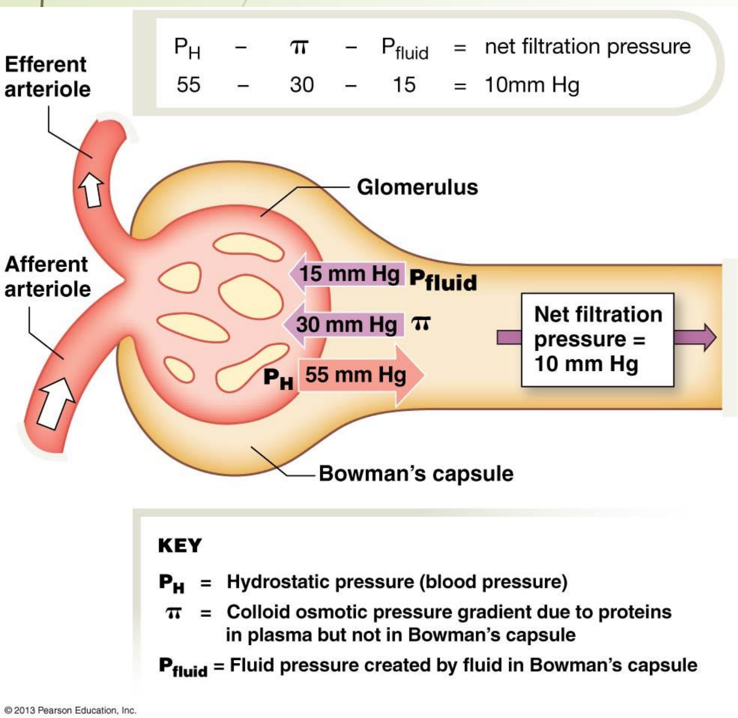
? What is the difference between the peritubular capillaries and the vasa recta?

Four Processes of Nephron

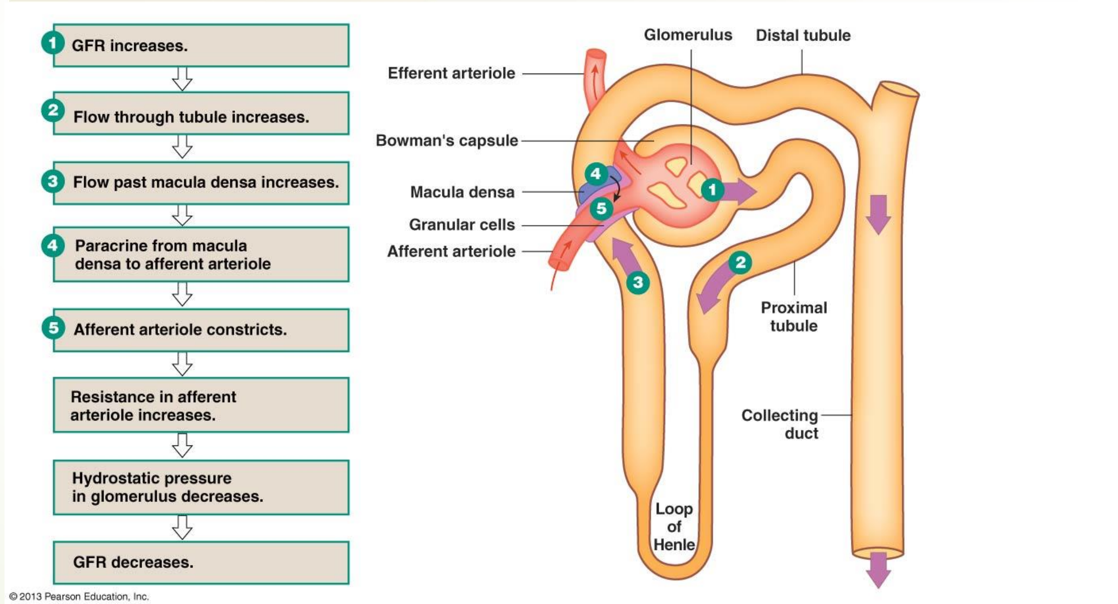
- Filtration
- Reabsorption
- Secretion
- Excretion



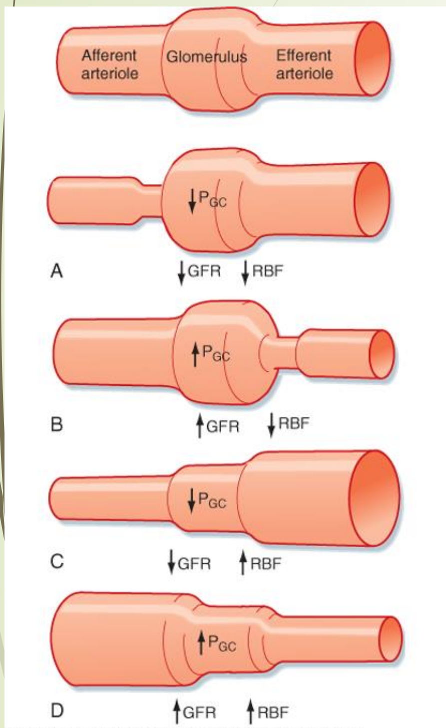
Glomerular Filtration

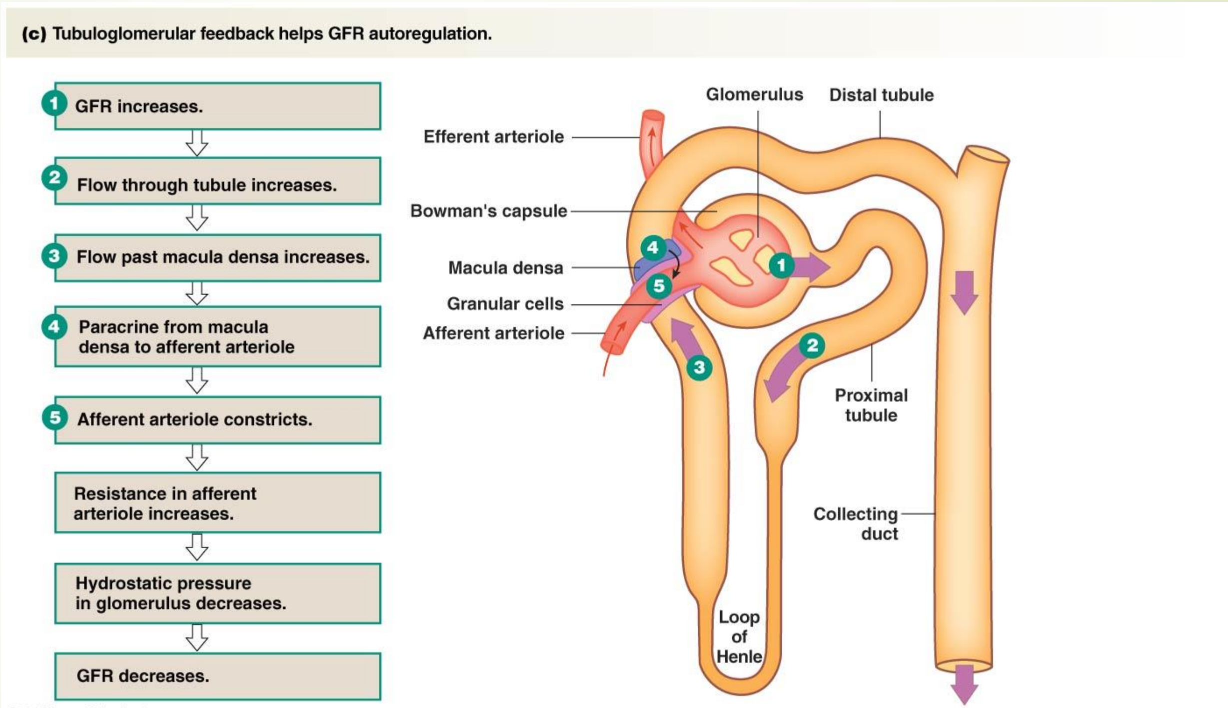


(c) Tubuloglomerular feedback helps GFR autoregulation.



Factors that Affect GFR





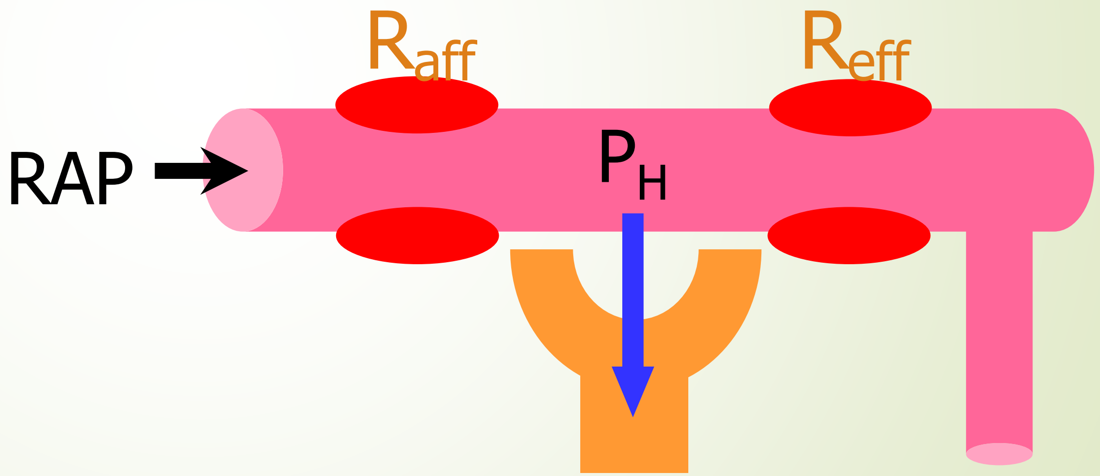
? How would glomerular nephritis affect GFR?

Determining Renal Blood Flow

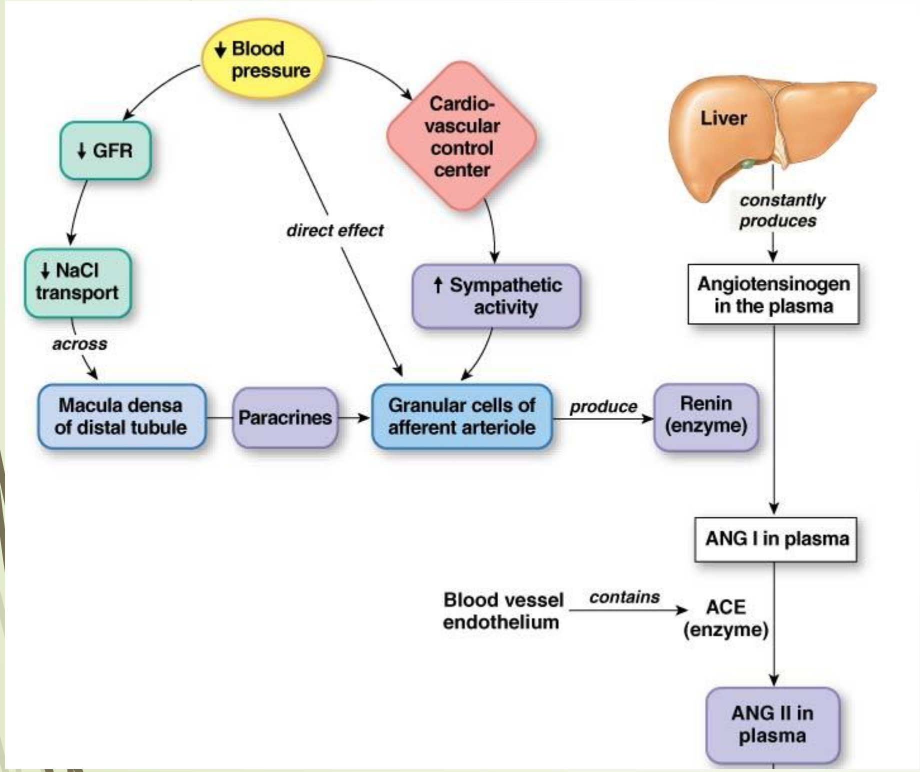
$$F = \Delta P / R$$

$$RBF = \frac{RAP - RVP}{R_{aff} + R_{eff}}$$

$$\boxed{RBF \simeq \frac{RAP}{R_{aff} + R_{eff}}}$$



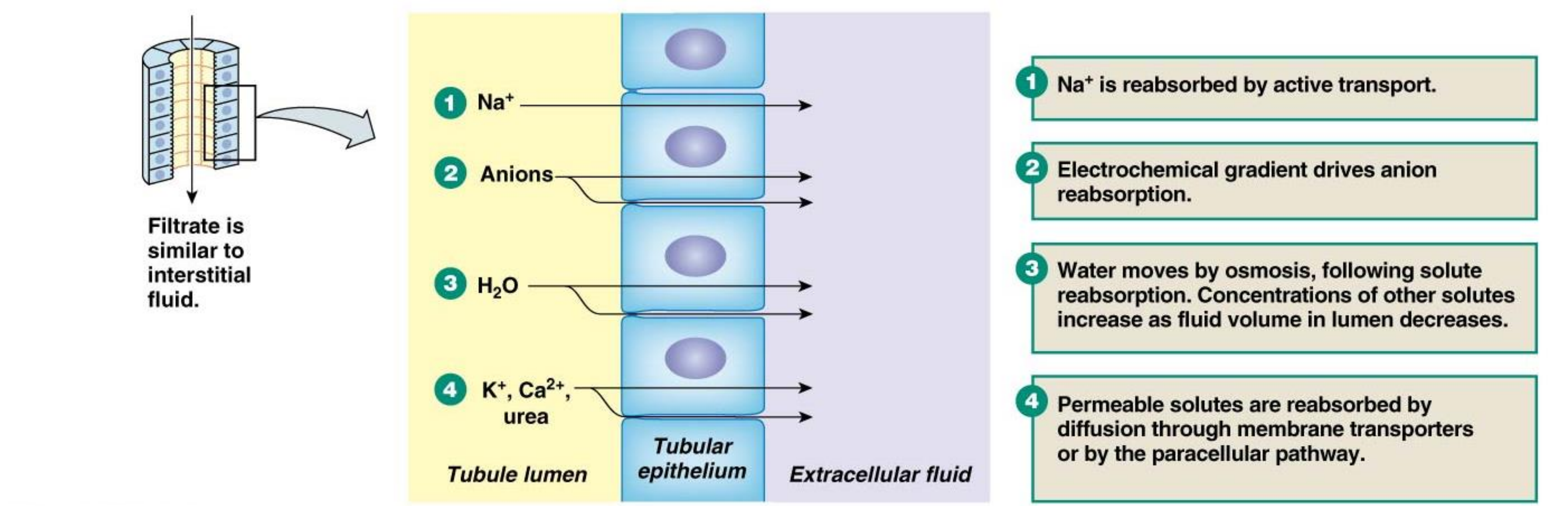
Renin-Angiotensin System Pathway



- Renin
  - Released from granular cells
  - Converts angiotensinogen to ANG I → ANG II (by ACE)
  - Causes:
    - vasoconstriction of arterioles = increase GFR
    - Increases BP

Reabsorption

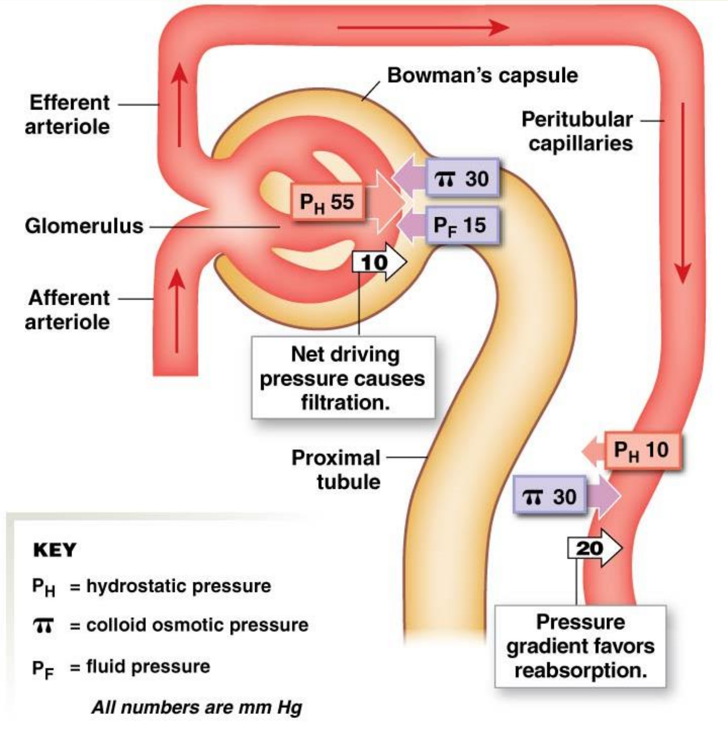
- Proximal tubule
  - Movement of Na



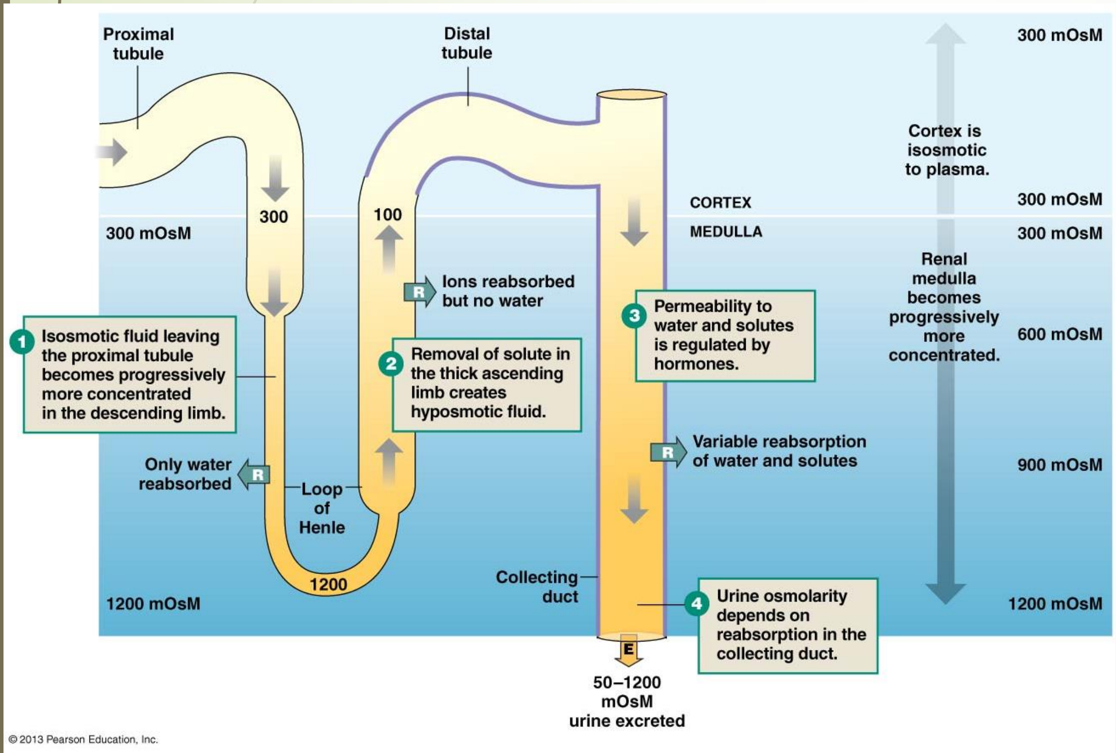
Reabsorption of Water

Balance of Colloid Osmotic Pressure and Hydrostatic Pressure

? Why is hydrostatic pressure lower in the peritubular capillaries than the glomerulus?



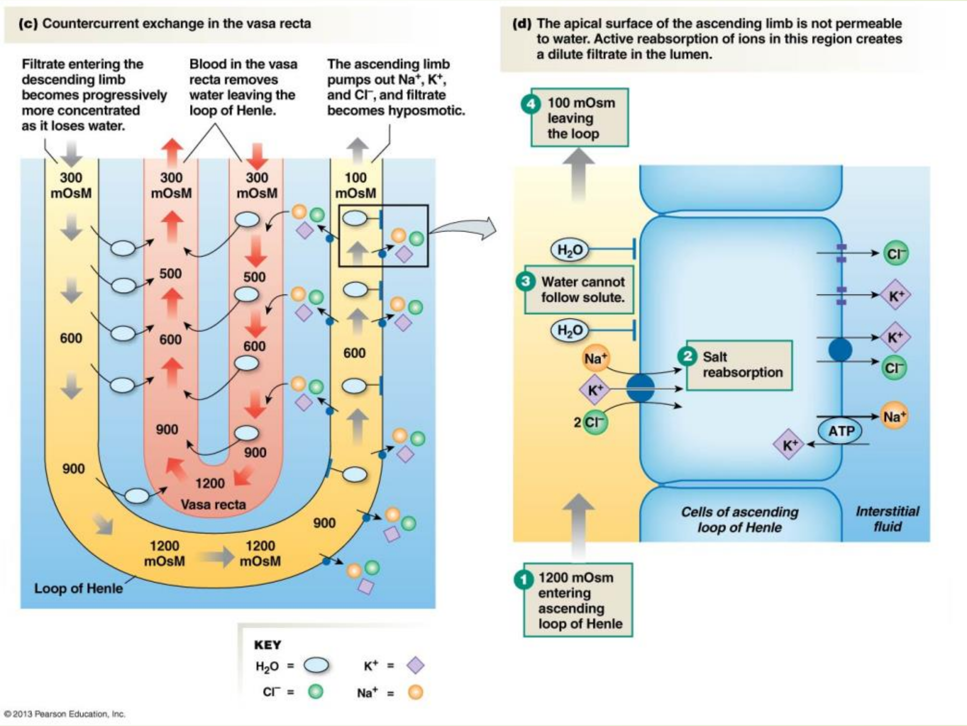
Concentrating Urine



- Osmotic gradient through medulla
  - Maintained by transport of urea out of nephron

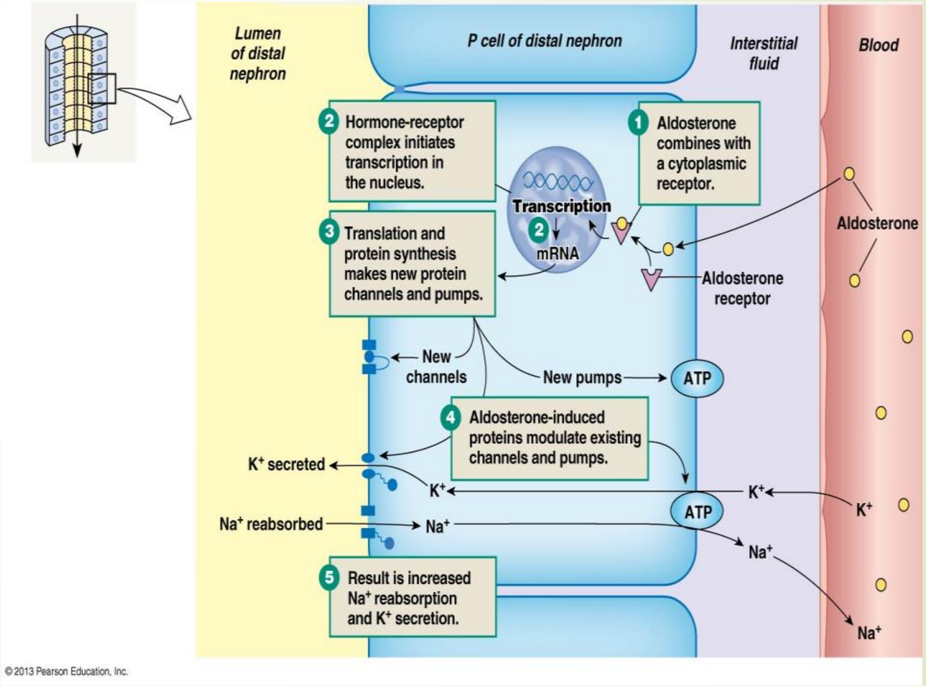
Countercurrent Multiplier

- Ascending limb: permeable to solutes
- Descending limb: permeable to water
- Vasa recta: blood flows in opposite direction

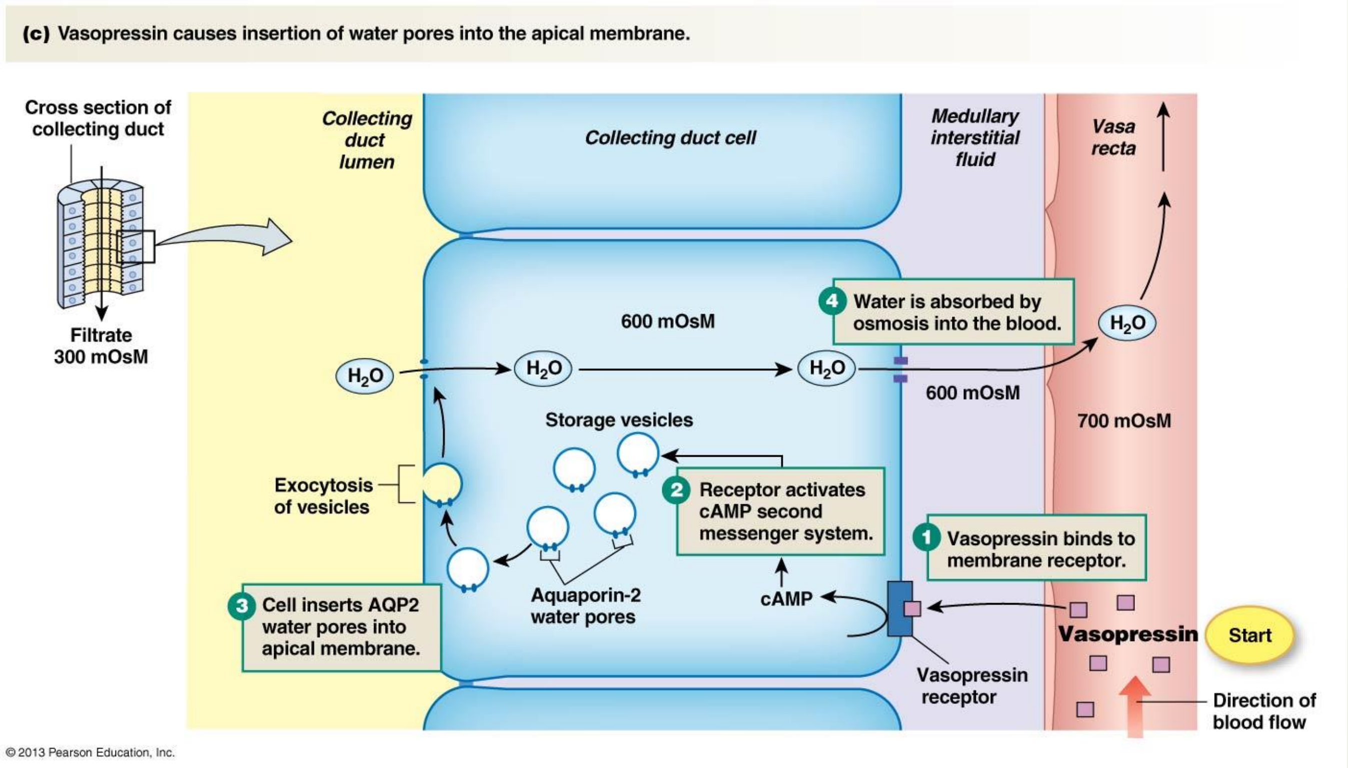


Reabsorption in the Distal Tubule and Collecting Duct

- Aldosterone
  - Initiates transcription of Na K ATPase pumps, ENaC and ROMK (K leak) channels
  - Increases activity of existing pumps and channels

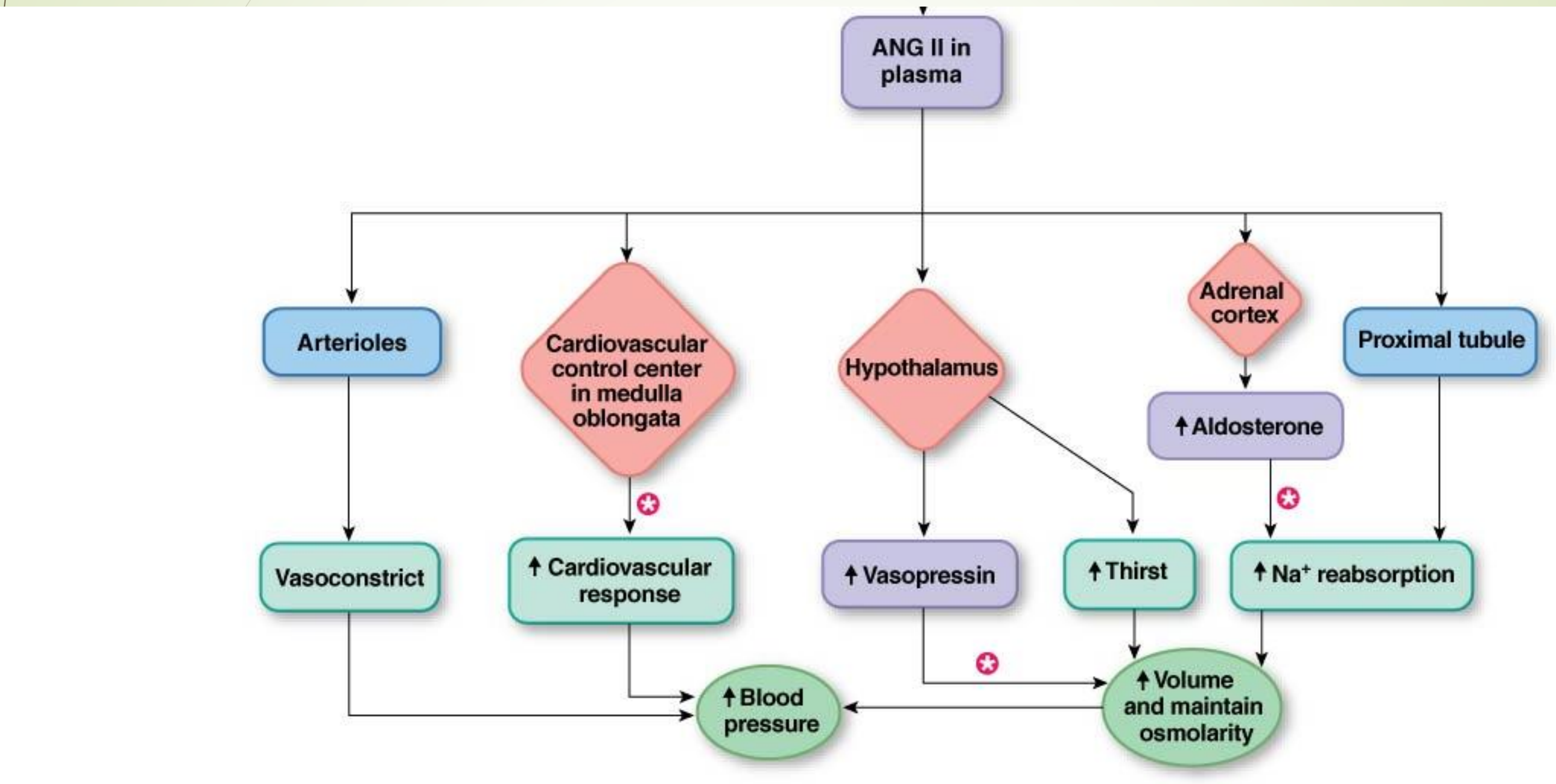


Reabsorption in the Collecting Duct

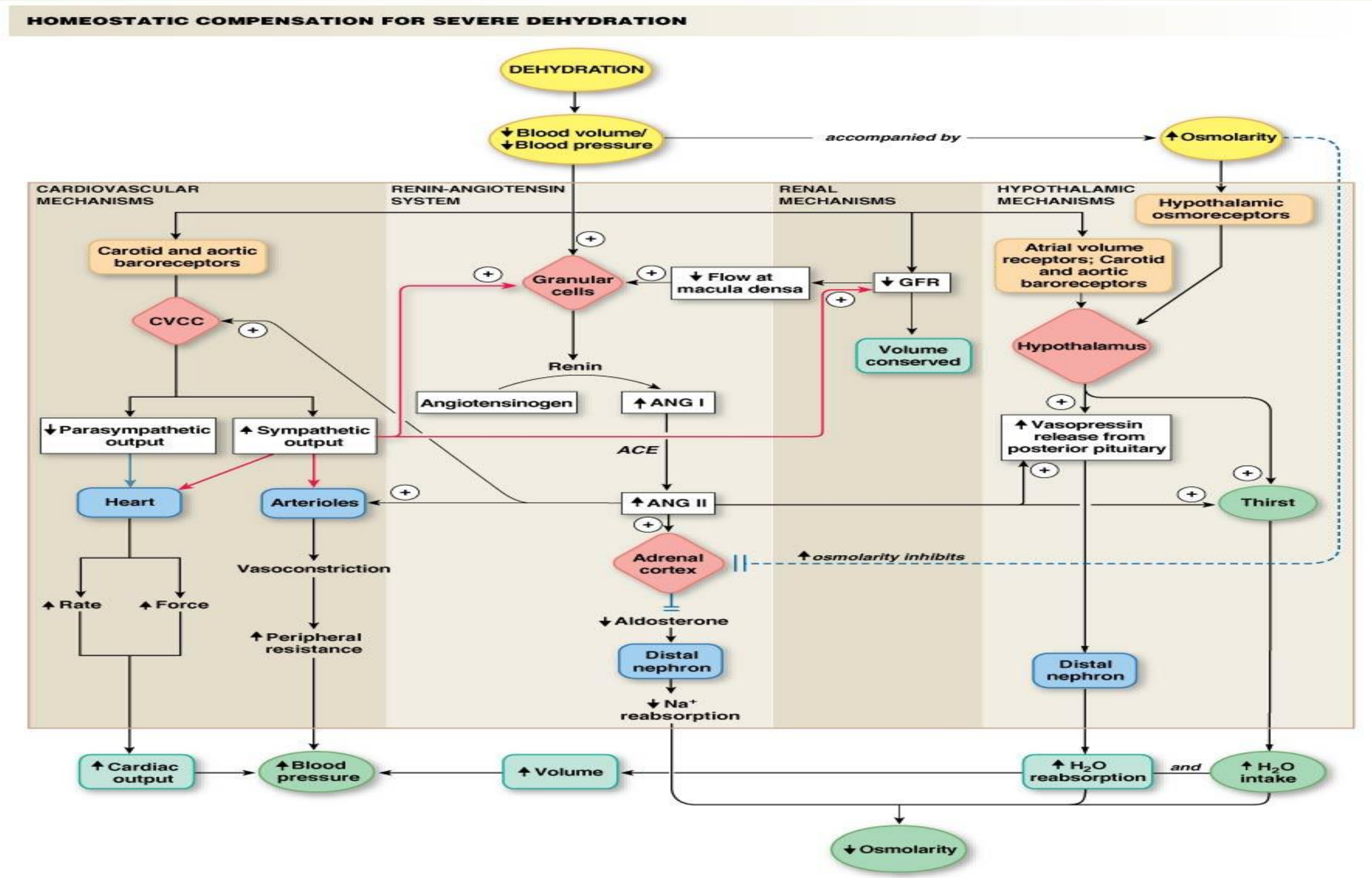


- Release ADH→ binds to receptors→ activates cAMP pathway (gSa) → Inserts aquaporins→ H_2O reabsorbed

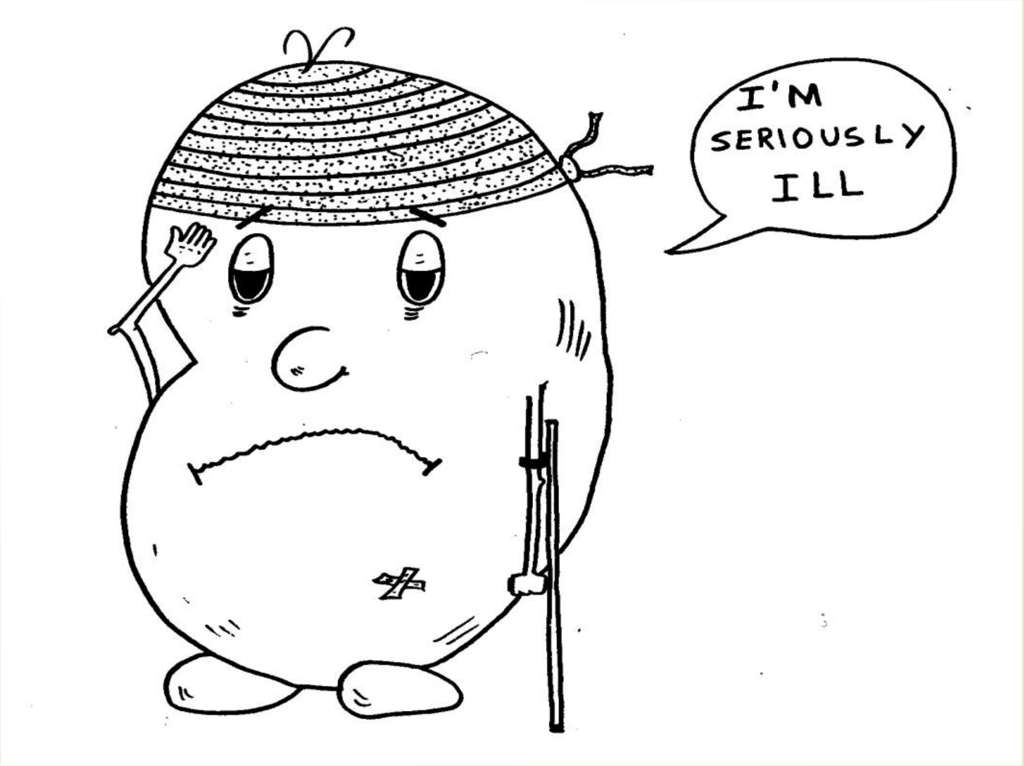
Modulation of Renal System



How Everything Comes Together



Kidney Failure



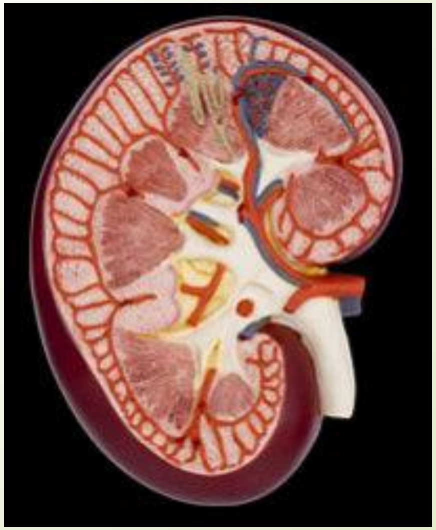
Acute vs. Chronic Kidney Failure

Acute

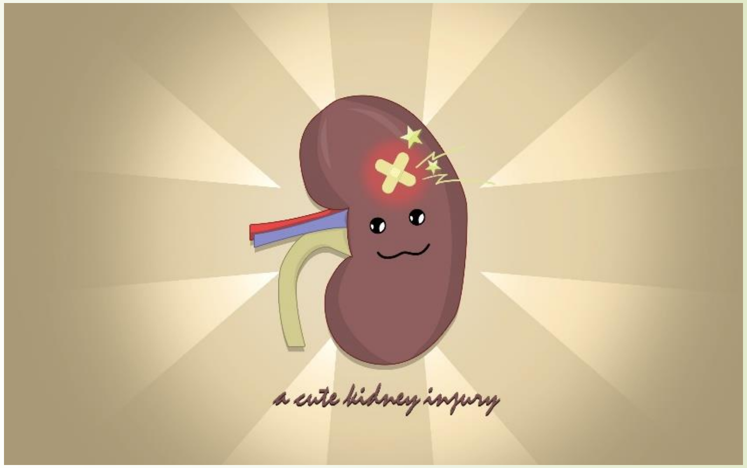
- Sudden Onset
- Rapid Reduction in urine output
- Usually reversible

Chronic

- Progressive
- Not Reversible
- Nephron Loss



Causes of ARF



- Pre-Renal
  - Cardiac failure, Dehydration, Vomiting, Diarrhea, Drugs
- Renal-Intrinsic
  - Interstitial nephritis, Acute Tubular Necrosis, ischemia, obstruction
- Post-renal
  - Cancer of the prostate or cervix, neurogenic bladder, bladder carcinoma

Risk factor for ARF

- Advanced age
- Preexisting renal disease
- Diabetes mellitus
- Underlying cardiac or liver disease

Old age, liv

Symptoms of ARF

- Decrease urine output (oliguria, anuria)
- Edema
- Heart Failure
- Nausea, vomiting
- Hyperkalemia

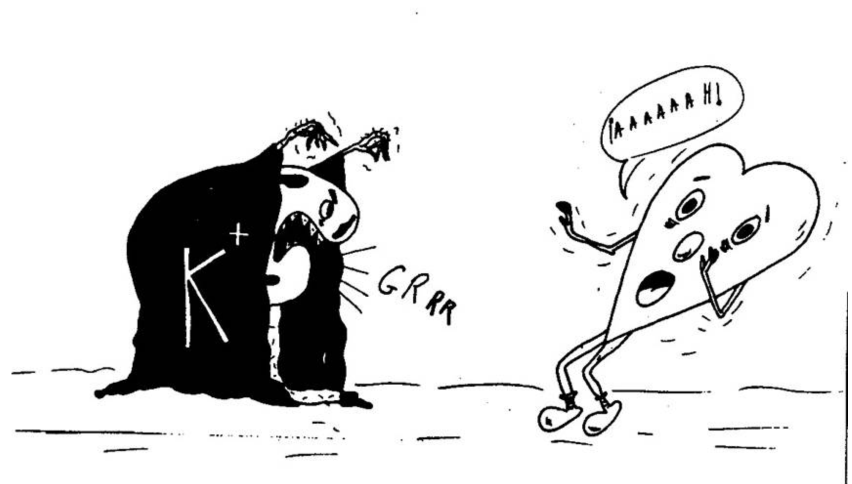
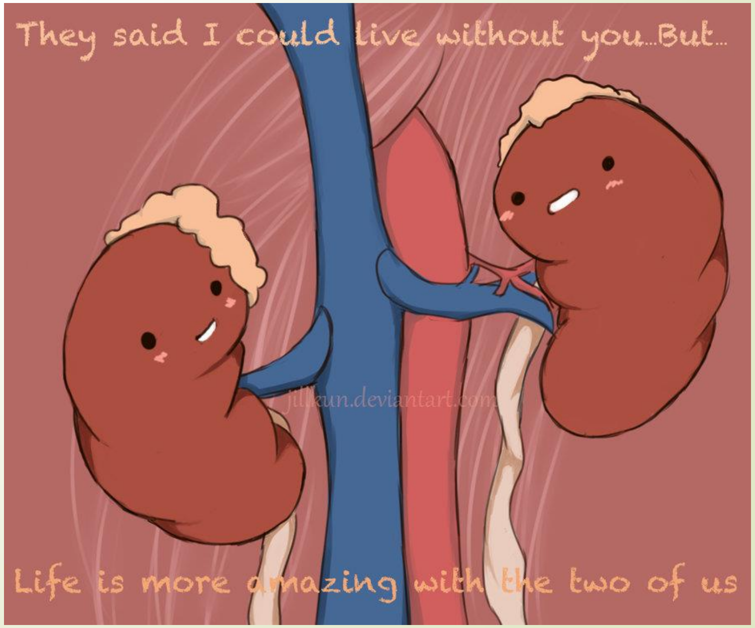


Figure 29 Hyperkalemia may cause cardiac arrest.

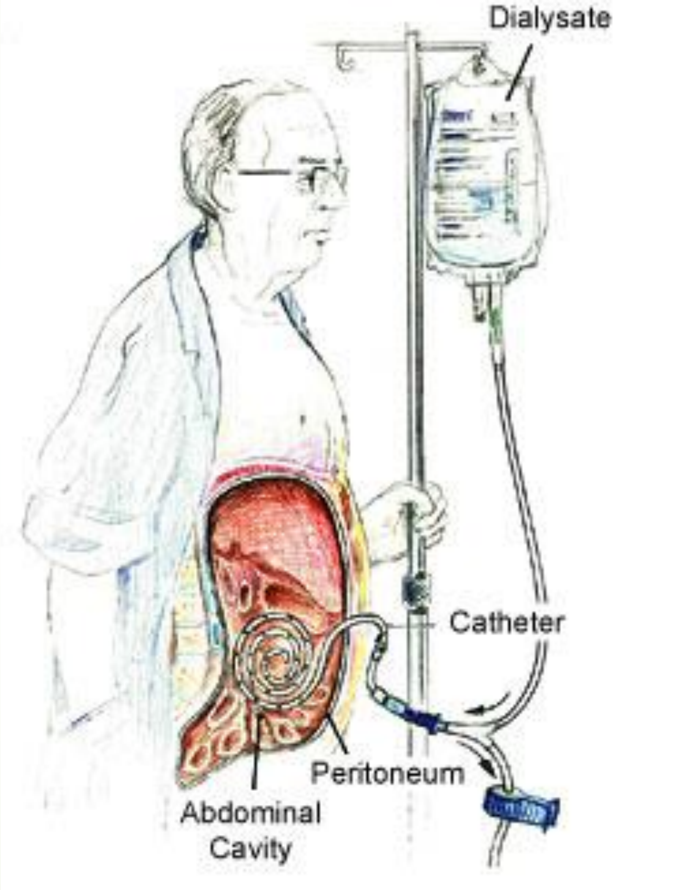
Physical Exam

- Vital Signs:
  - Elevated BP: Concern for malignant hypertension
  - Low BP: Concern for hypotension/hypoperfusion (acute tubular necrosis)
- Neurological:
  - Confusion: uremia, malignant hypertension, infection, malignancy
- ENT:
  - Dry mucus membranes: Concern for dehydration (pre-renal)
- Exterior:
  - Edema: Concern for nephrotic syndrome



Treatment of ARF

- Treat Underlying Cause
  - Blood Pressure
  - Infection
  - Remove obstruction
- Hydration
- Diuresis
- If severe,
  - Dialysis
  - Renal transplant



Continuous Ambulatory Peritoneal Dialysis

Chronic Renal Failure

- Affects more than 2 out of 1,000 people in the U.S.
- Mortality 20%
- Classified by 3 months of renal failure

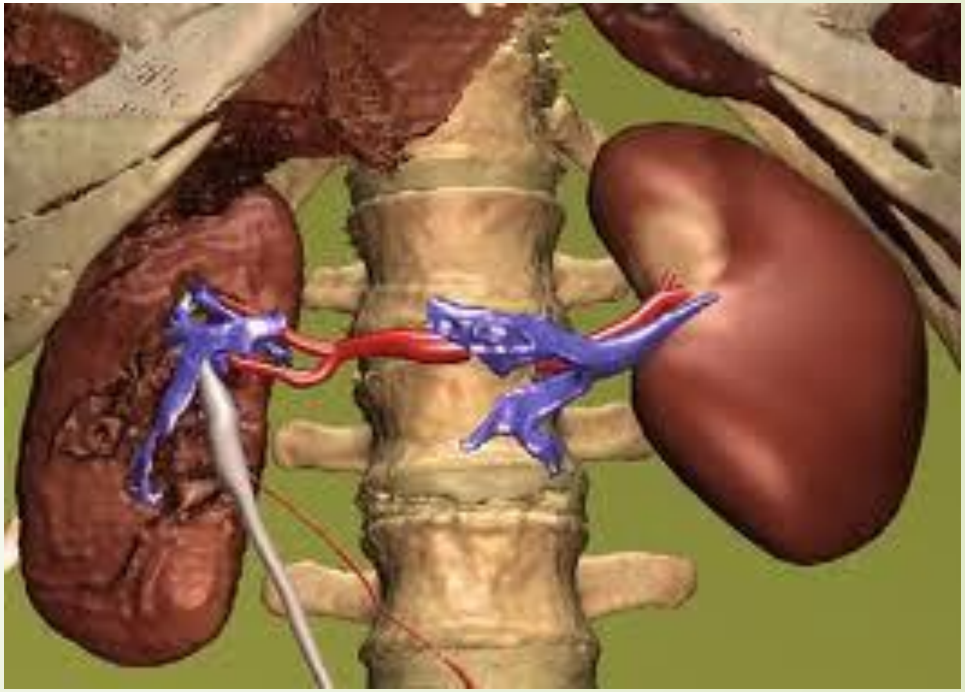
	STAGES OF CRF	
Stage	Description	GFR (mL/min/1.73 m2)
1	Kidney damage with normal or increased GFR	≥ 90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney Failure	< 15

Causes of CRF

- Diabetic Nephropathy
- Hypertension
- Chronic glomerulonephritis
- Polycystic kidney disease
- Kidney obstructions

CRF Symptoms

- Weakness
- Fatigue
- Neuropathy
- Nausea
- Vomiting
- Seizure
- Cardiac Failure



Treatment

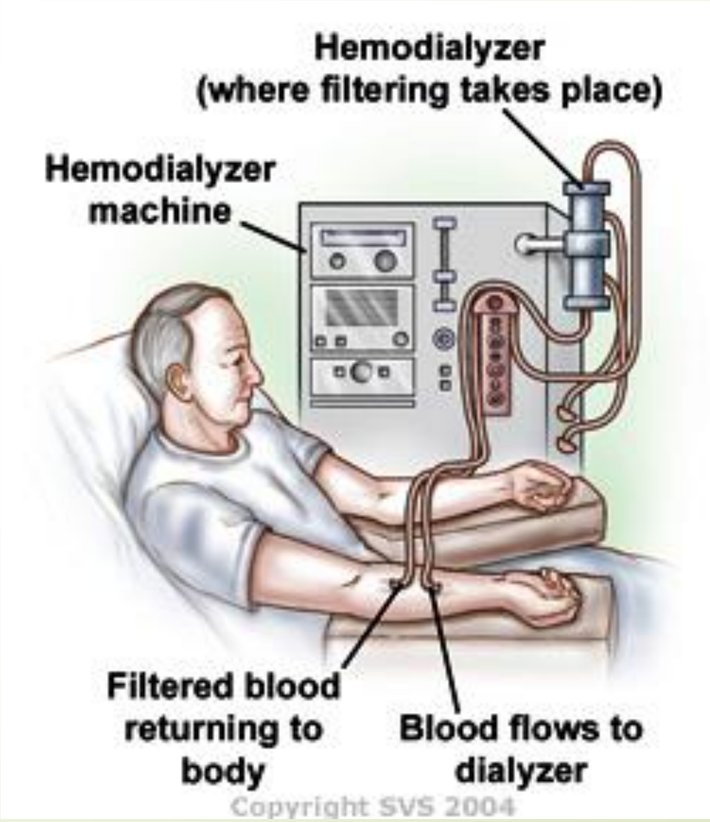
- Blood Pressure Control –diuretics
- Ace Inhibitors
- Diabetes Control
- Smoking cessation
- Bicarbonate therapy for acidosis
- Dialysis
- Renal Transplant

Stage	Description	GFR	Evaluation	Management
	At increased risk		Test for CKD	Risk factor management
1	Kidney damage with normal or ↑ GFR	>90	Diagnosis Comorbid conditions CVD and CVD risk factors	Specific therapy, based on diagnosis Management of comorbid conditions Treatment of CVD and CVD risk factors
2	Kidney damage with mild ↓ GFR	60-89	Rate of progression	Slowing rate of loss of kidney function [1]
3	Moderate ↓ GFR	30-59	Complications	Prevention and treatment of complications
4	Severe ↓ GFR	15-29		Preparation for kidney replacement therapy Referral to Nephrologist
5	Kidney Failure	<15		Kidney replacement therapy

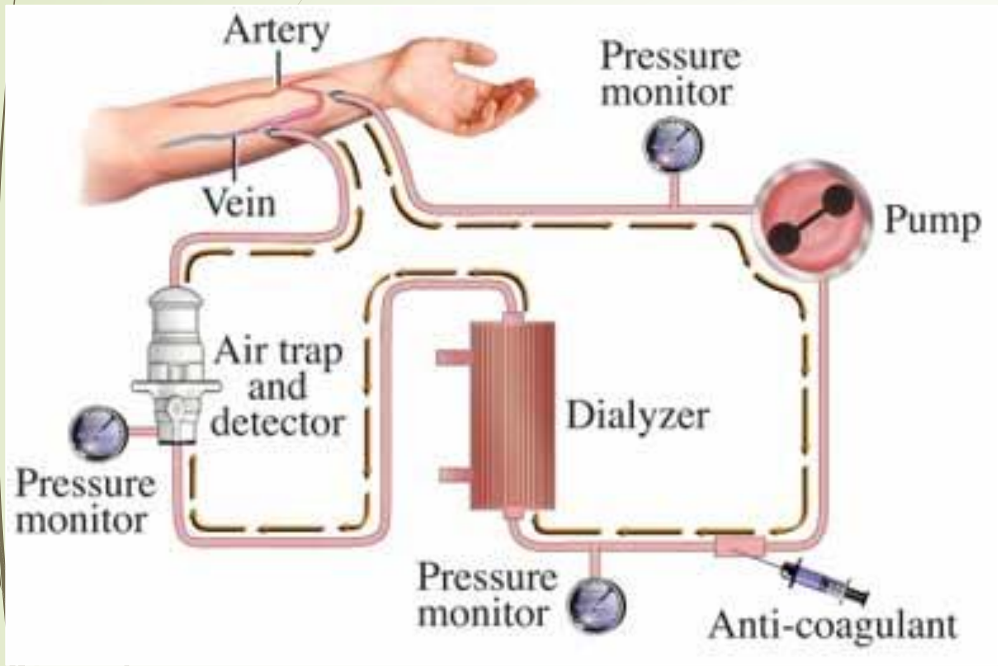
[1]Target blood pressure less than 130/80 mm Hg. Angiotension converting enzyme inhibitors (ACEI) or angiotension receptor blocker (ARB) for diabetic or non-diabetic kidney disease with spot urine total protein-to-creatinine ratio of greater than 200 mg/g.

Treatment

- Dialysis
  - Diffuse harmful waste out of body
- Indications for Dialysis
  - Acidosis (metabolic)
  - Electrolytes (hyperkalemia)
  - Ingestion of drugs/Ischemia
  - Overload (fluid)
  - Uremia

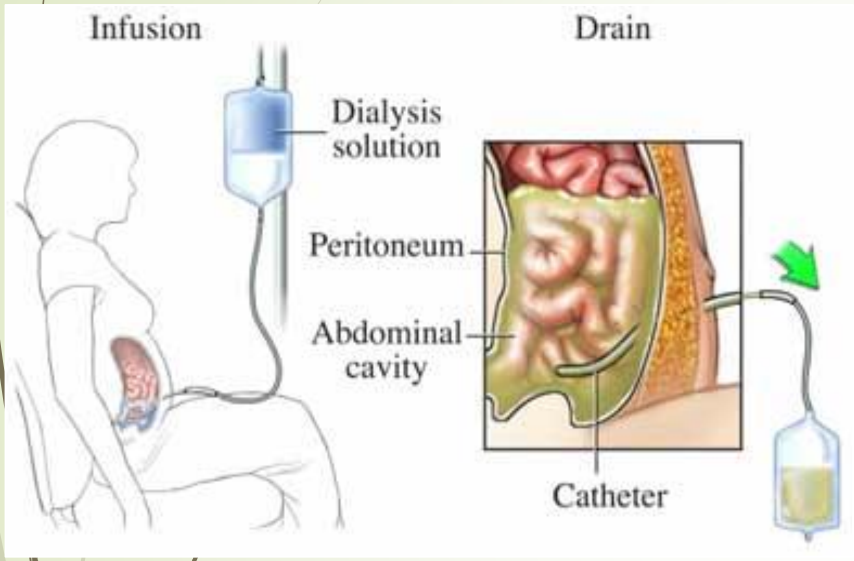


Hemodialysis



- Hemodialysis
  - 3-4 times per week
  - Machine filters blood
- Types of Access Points:
  - Temporary
  - AV Fistula
  - AV Graft

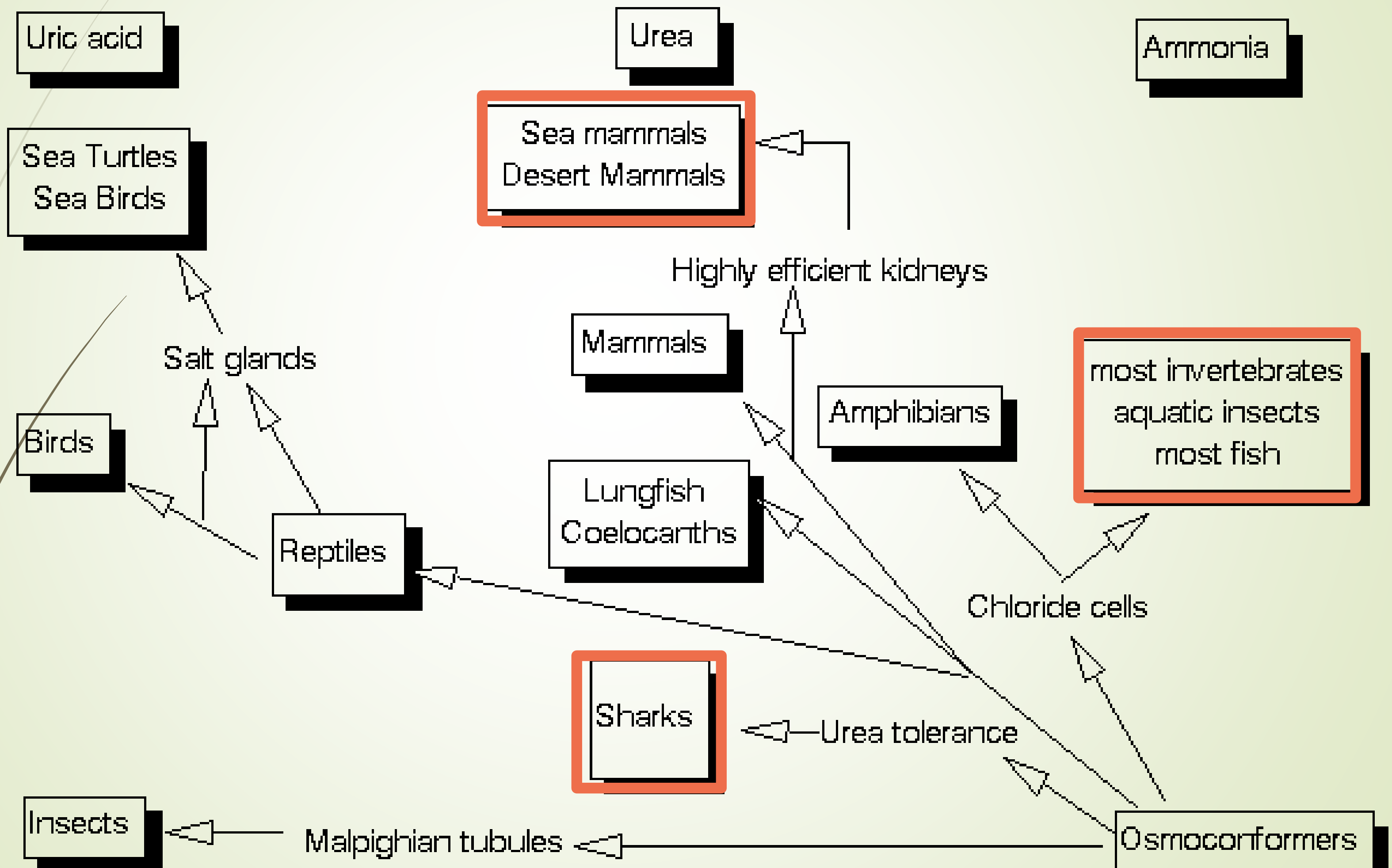
Peritoneal Dialysis



- Peritoneal Dialysis
  - Filter waste through intestinal lining
- Types:
  - Continuous Ambulatory Peritoneal Dialysis (CAPD)
  - Continuous Cycling Peritoneal Dialysis (CCPD)

Osmoregulation at Sea

Evolution of excretory and osmoregulatory strategies



Pinnepids

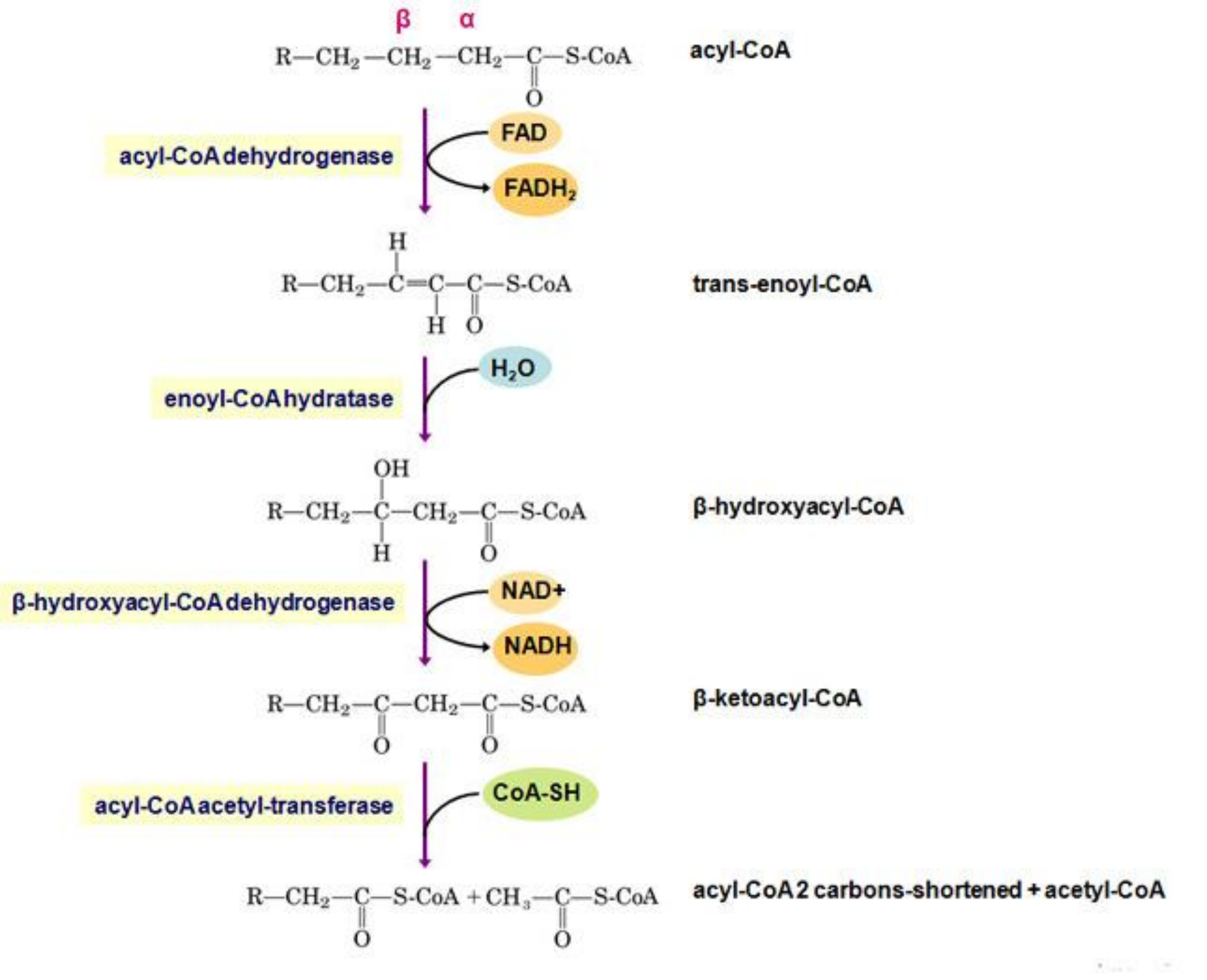
Water Sources

- Marine mammals rarely drink

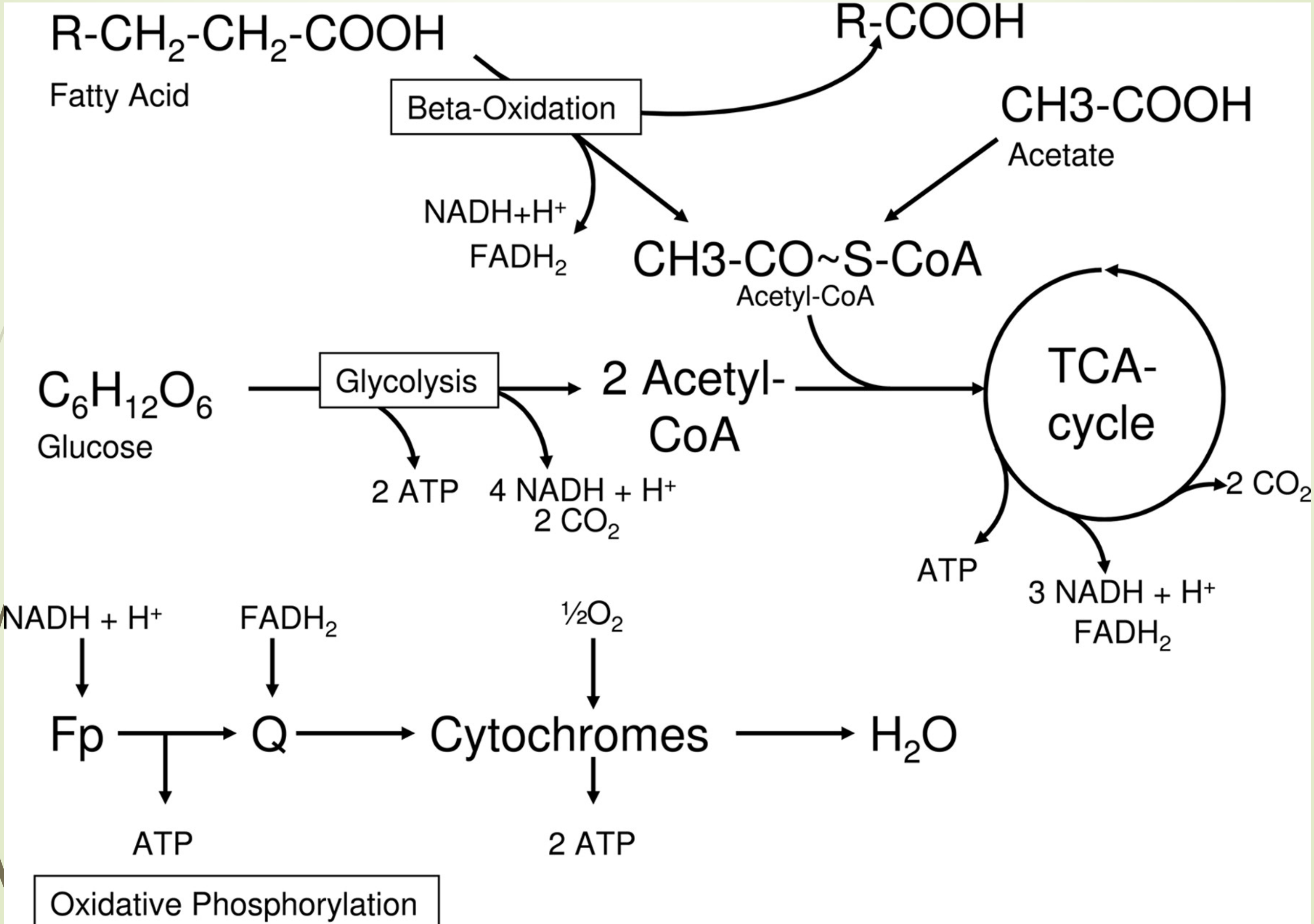
? How can animals obtain water without drinking?

- Sea water from food (60-80% water), fat metabolism, or accidental drinking
- Drinking helps with thermoregulation & electrolyte homeostasis

β oxidation


β
α
R—CH2—CH2—CH2—C—S-CoA
O
acyl-CoA
acyl-CoA dehydrogenase
FAD
FADH2
H
R—CH2—C═C—C—S-CoA
H O
trans-enoyl-CoA
enoyl-CoA hydratase
H2O
OH
R—CH2—C—CH2—C—S-CoA
H O
β-hydroxyacyl-CoA
β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH
R—CH2—C—CH2—C—S-CoA
O O
β-ketoacyl-CoA
acyl-CoA acetyl-transferase
CoA-SH
R—CH2—C—S-CoA + CH3—C—S-CoA
O O
acyl-CoA 2 carbons-shortened + acetyl-CoA

The Full Cycle



Reniculate Kidney

- Multi-lobed kidney found in aquatic mammals
- Compound or discrete

? Why?

- Increased surface area removes toxins
- Sporta perimedullaris:
  - smooth muscle between cortex and medulla, large glycogen reserves, unique blood vessels

? Why?

  - keep kidneys functioning during dives

Urine Concentration

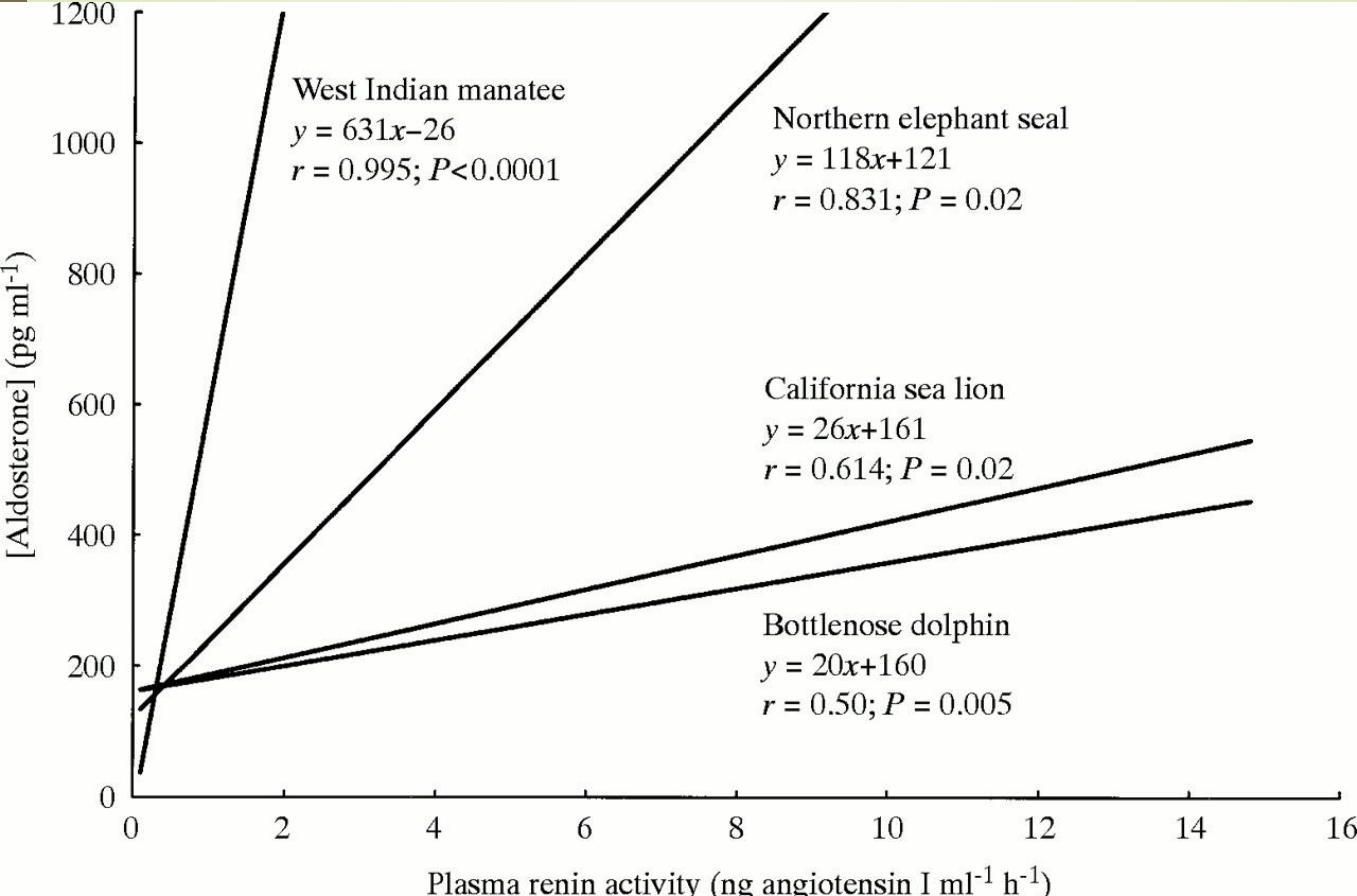
- All marine mammals can produce urine as least as concentrated as sea water (1000 mosM)
  - However, most excrete urine the same concentration as sea water

? What are two ways to concentrate urine?

- Anatomical:
  - Because of multiple reniculi, loops of Henle are relatively short, so they cannot achieve the same osmolality as desert rodents
- Hormonal:
  - Increase in Na+ availability decreases the sensitivity of the RAS

	Urine osmolality (mosmol l^{-1})	Urine: plasma ratio
Terrestrial		
Human	1400	4.6
Dog	1800	6
Camel	2800	7
Domestic cat	3100	10
Kangaroo rat	5500	14
Hopping mouse	9400	25
Marine/aquatic		
West Indian manatee	1158	3.7
Sei whale	1353	3.8
American river otter	1482	4.8
Rough-toothed dolphin	1700	5.0
Bottlenose dolphin	1815	5.3
Weddell seal	1760	5.6
Northern elephant seal	1850	5.9
Grey seal	2161	6.0
Harbor seal	2050	6.2
Sea otter	2130	6.7
Ringed seal	2420	6.8
Baikal seal	2374	6.9
Cape fur seal	2364	7.0

Order Common name	Na^+ (mmol l^{-1})	K^+ (mmol l^{-1})	Cl^- (mmol l^{-1})	Urea (mmol l^{-1})
Sea water	470	10	548	NR
Pinnipedia				
Baikal seal	244	137	202	1817
California sea lion	442	118	608	65
Cape fur seal	368	216	567	1640
Harbor seal	523	370	508	NR
Northern elephant seal	80	230	NR	490
Northern fur seal	160	129	140	833
Ringed seal	297	157	267	1351
Weddell seal	330	125	NR	1248
Cetacea				
Bottlenose dolphin	460	179	632	1345
Beluga whale	NR	NR	39	570
Blue whale	NR	NR	450	NR
Finback whale	330	72	850	430
Pilot whale	263	NR	NR	NR
Sei whale	330	82	370	650
Sirenia				
West Indian manatee	31	60	406	NR
Fissipedia				
American river otter	31	19	16	NR
Sea otter	505	117	555	953


1200
1000
800
600
400
200
0
[Aldosterone] (pg ml-1)
0
2
4
6
8
10
12
14
16
Plasma renin activity (ng angiotensin I ml-1 h-1)
West Indian manatee
y = 631x–26
r = 0.995; P<0.0001
Northern elephant seal
y = 118x+121
r = 0.831; P = 0.02
California sea lion
y = 26x+161
r = 0.614; P = 0.02
Bottlenose dolphin
y = 20x+160
r = 0.50; P = 0.005

Elephant Seals:
Herp Derpiest Animals of the Sea

Preventing Water Loss

- Elephant seals fast for 2-3 months after weaning

? How?

- ↓ protein metabolism leads to ↓ nitrogen load
- ↓ GFR and ↑ urine osmolality lead to ↓ water loss

? Which hormones?

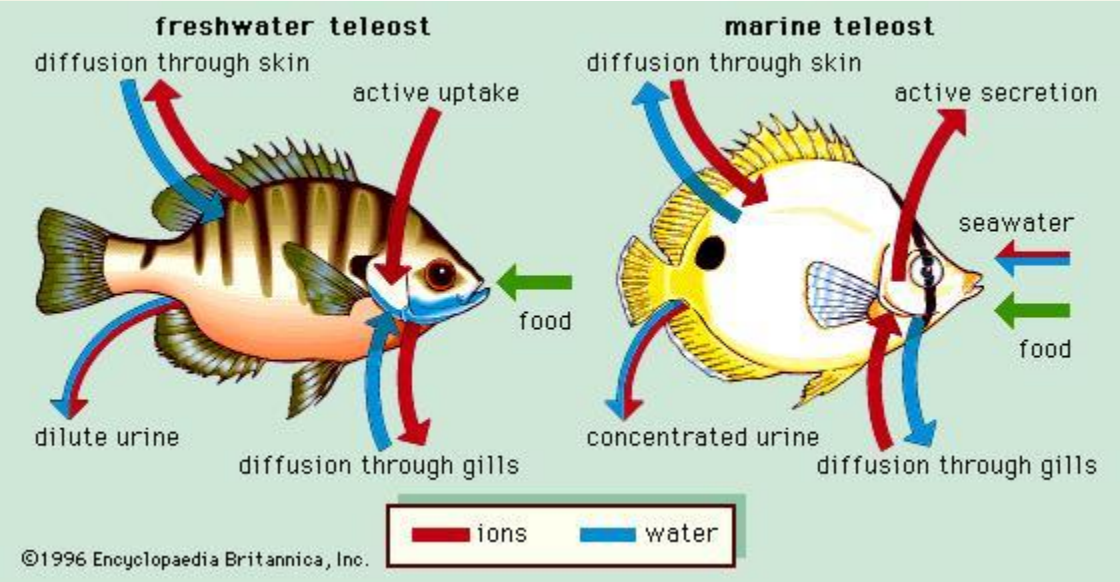
- Henry-Gauer reflex: increase in MAP → arterial distension → diuresis

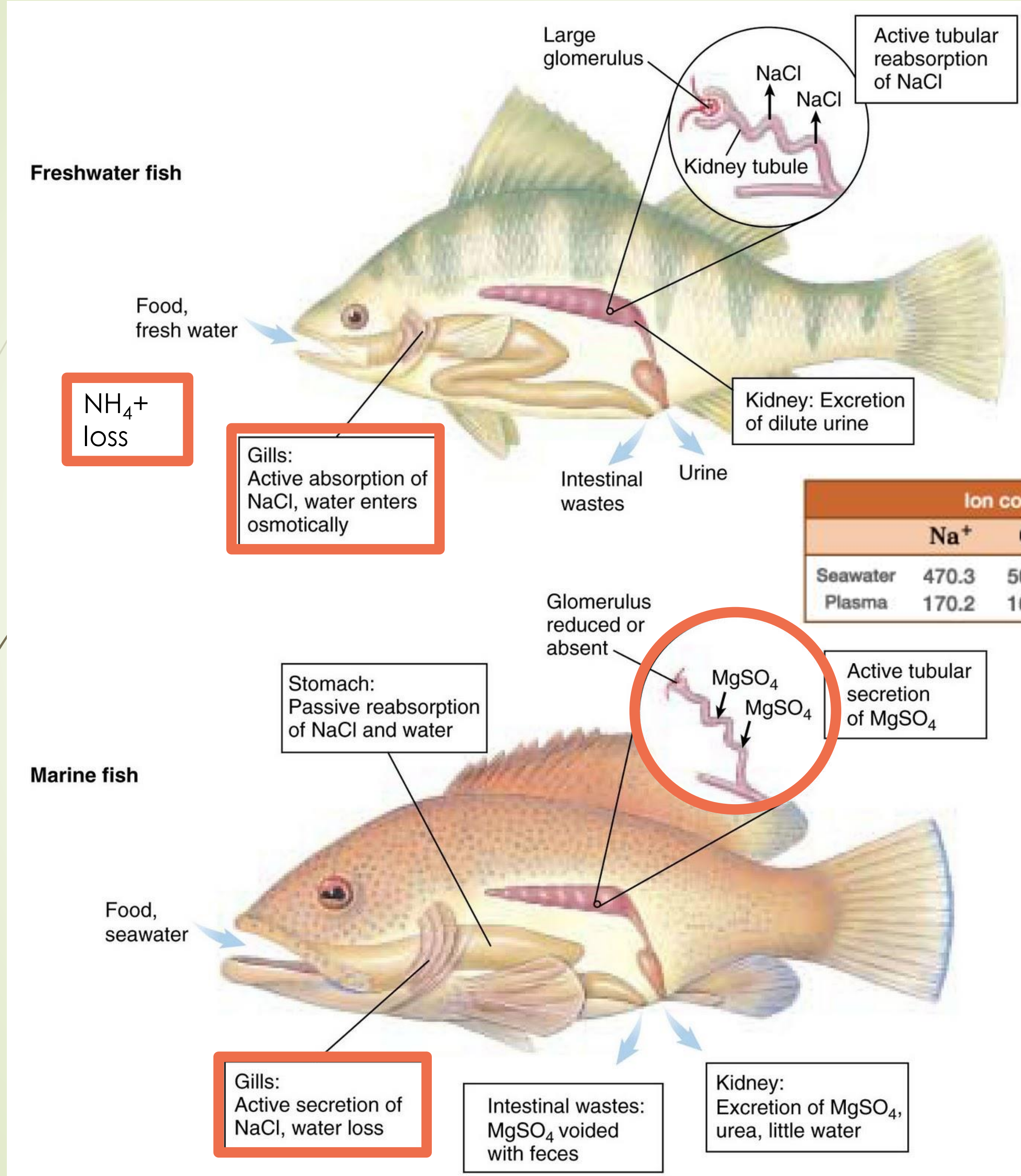
? Which hormones?

Freshwater vs Marine Teleosts

Freshwater vs Marine Teleosts

Freshwater:		**Marine:**
	Gills?	
	Water source?	
	Urine concentration?	
	Nitrogenous waste removal?	



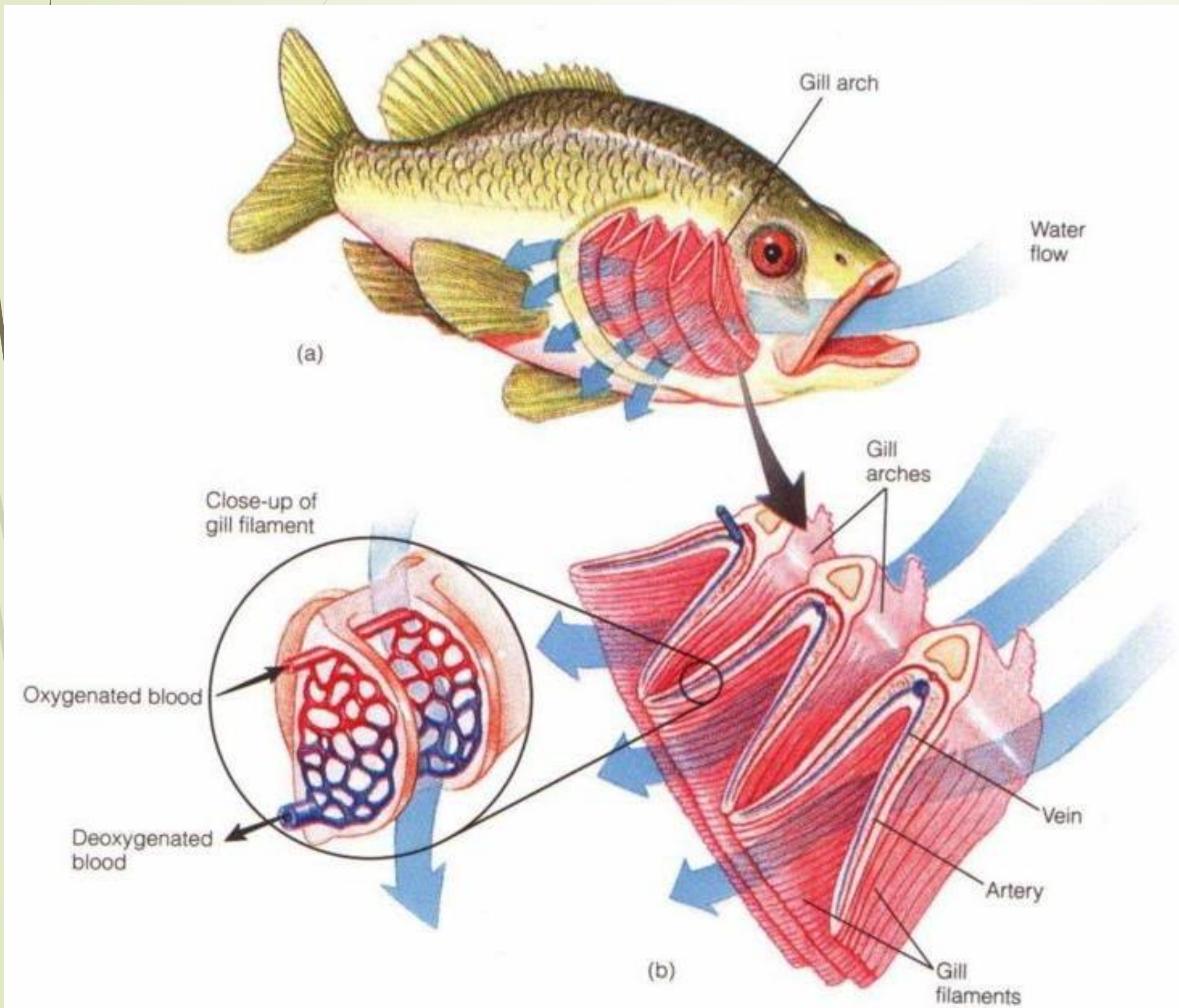


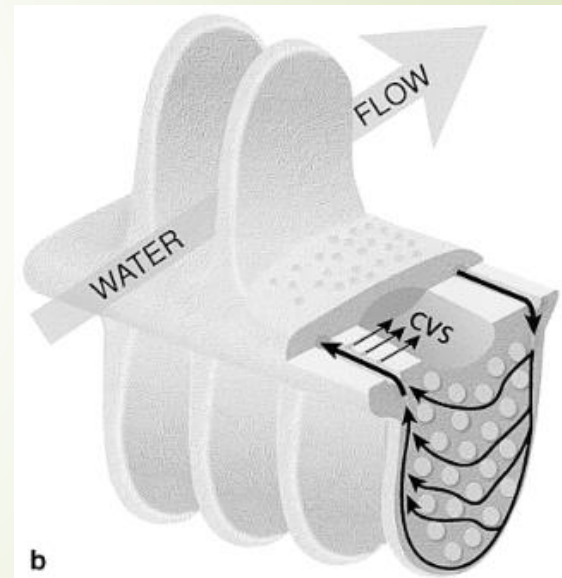
Ion concentration (mM)					
	Na^+	Cl^-	Mg^{2+}	Ca^{2+}	SO_4^{2-}
Seawater	470.3	508.2	54.5	10.5	30.4
Plasma	170.2	162.0	1.4	1.8	0.7

Blood Plasma Compositions

	Concentration (mM kg water^{-1})								
	Na^+	Cl^-	K^+	Mg^+	Ca_2^+	SO_4	Urea	TMAO	Osmolality
Seawater	439	513	9.3	50	9.6	26	–	–	1050
Hagfish	549	563	11.1	18.9	5.1	3	2.8	0	1152.9
Lamprey (SW)	156	159	32	7	3.5		–	–	333
Coelacanth	197	187	5.8	5.3	4.8	4.8	377	122	942
Shark	255	241	6	3	5	0.5	441	72	1118
Teleost (SW)	180	196	5.1	2.5	2.8	2.7	–	–	452
Freshwater (soft)	0.25	0.23	0.005	0.04	0.07	0.05	–	–	1
Lamprey (FW)	119.6	99.6	2.3	1.5	1.8	–	–	–	224.8
Stingray (FW)	164	151.7	4.45	–	3	–	1.1	–	282
Teleost (FW)	130	125	2.9	1.2	2.7	–	–	–	261.8
Euryhaline fishes									
Stingray (FW)	211.9	207.8	5.2	–	4.3	–	196	–	625.2
Stingray (SW)	310	300	6.95	–	3.1	–	394.5	–	1034
Teleost (FW)	124	132	2.9	–	2.7	–		–	274
Teleost (SW)	142	168	3.4	–	3.3	–	–	–	297

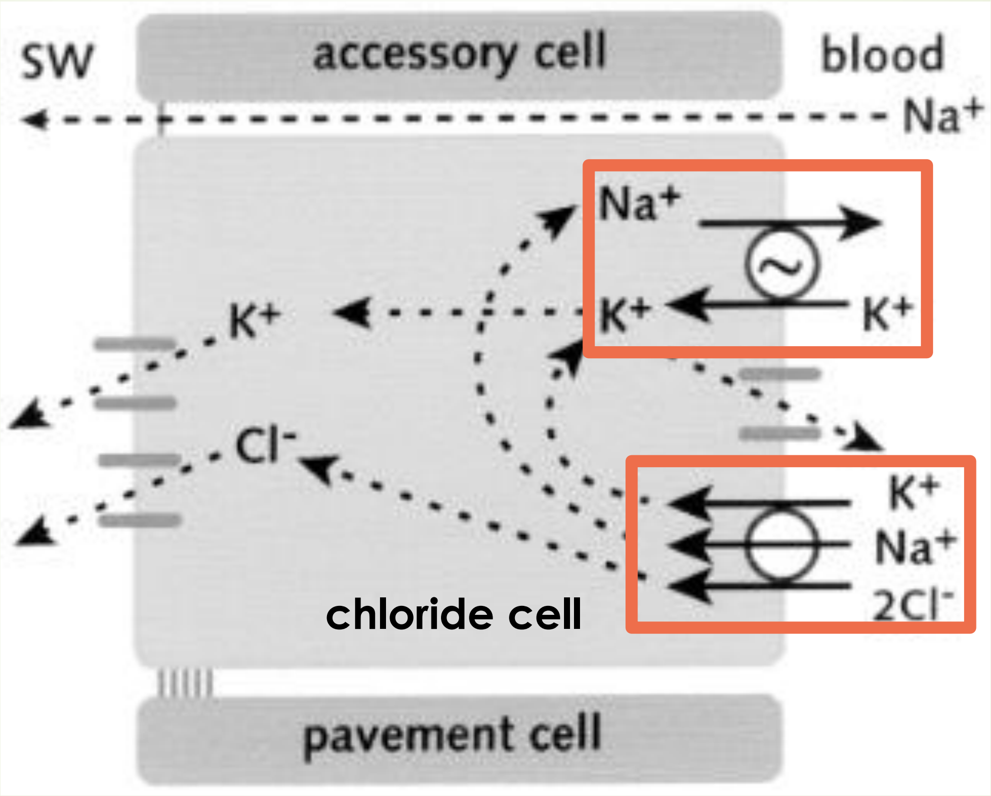
Gill Ion Pumps





Marine Gill Ion Pumps

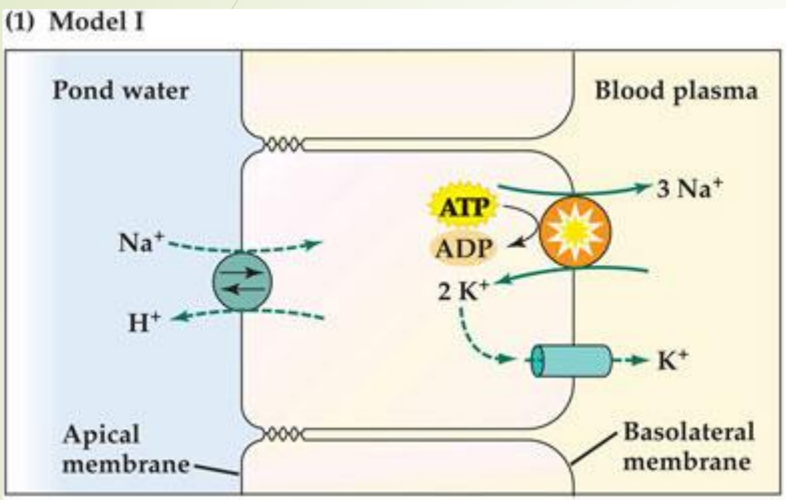
High [Na+]
High [Cl-]

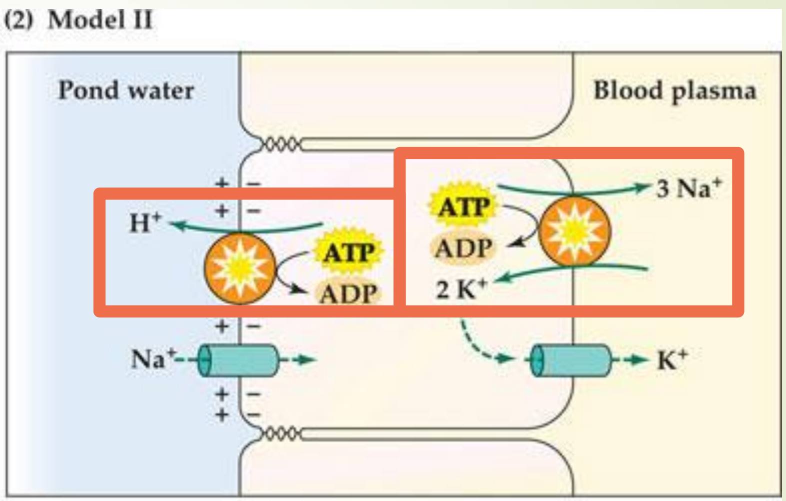


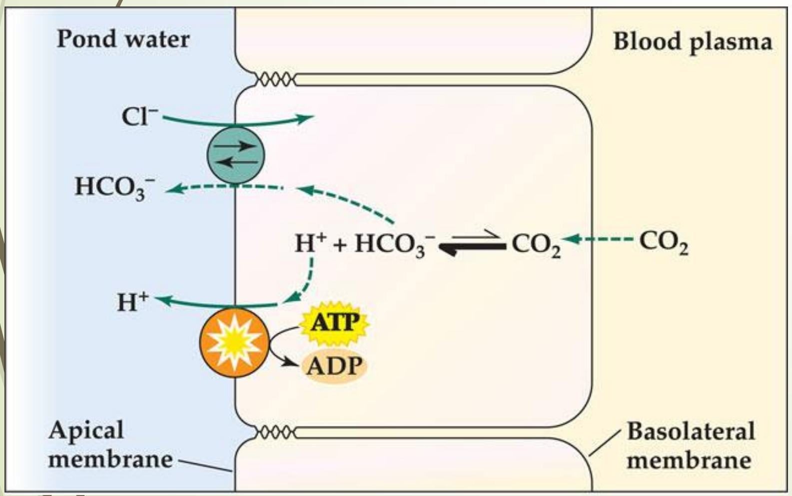
Mid [Na+]
Mid [Cl-]

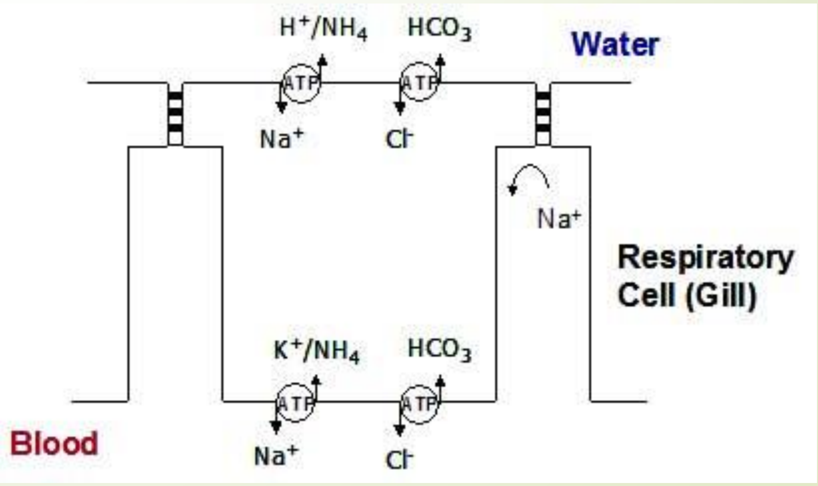
High [K+]

Freshwater Gill Ion Pumps

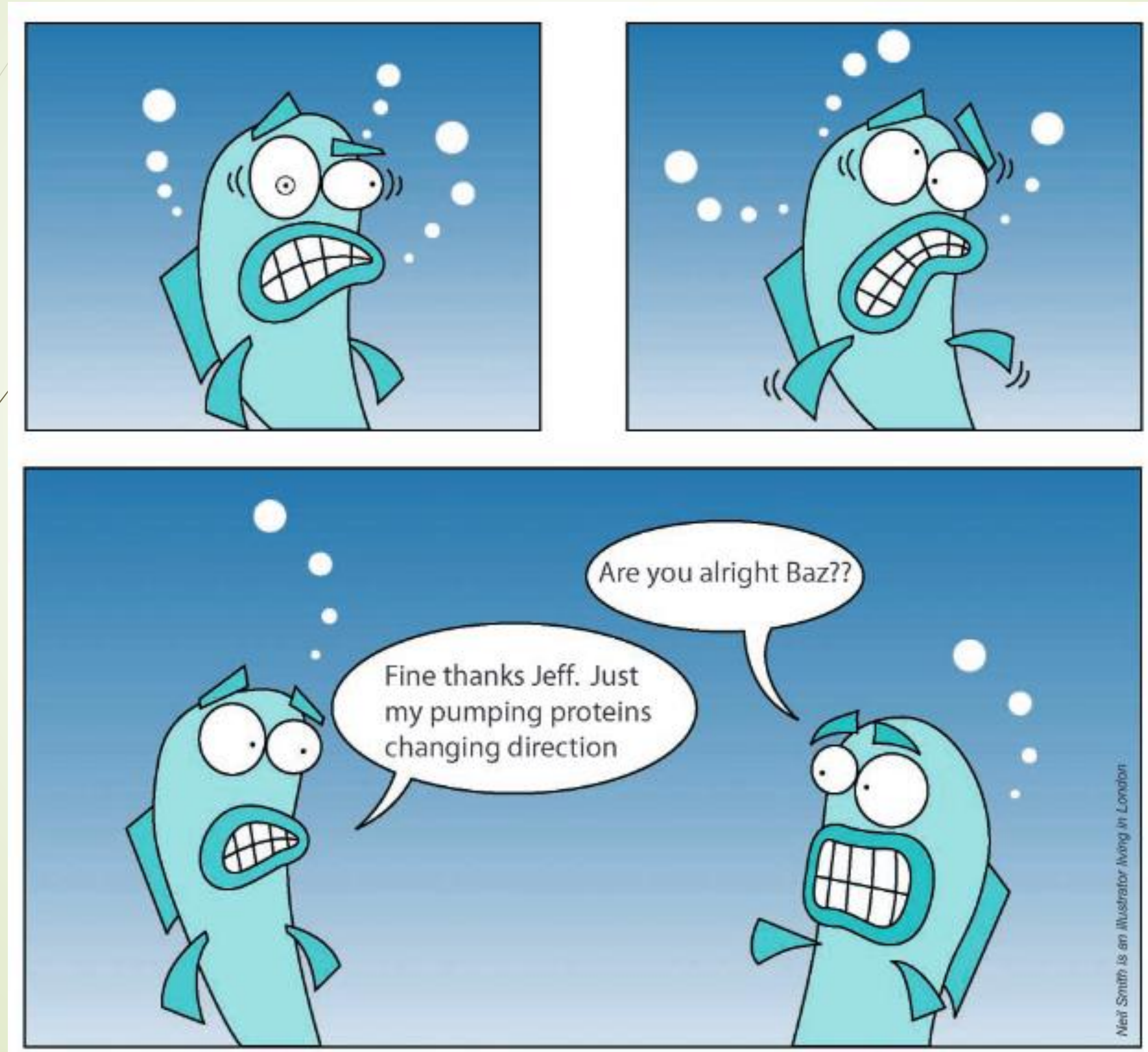








Euryhalinity



Euryhalinity

Freshwater:

- **Prolactin**
- ↓ Branchial permeability
- ↓ ATPase activity
- ↓ Chloride cell size & density
- ↑ Proton pu
- **Local mediators (prostaglandins, NO, endothelin)**
- ↓ salt extrusion

Marine:

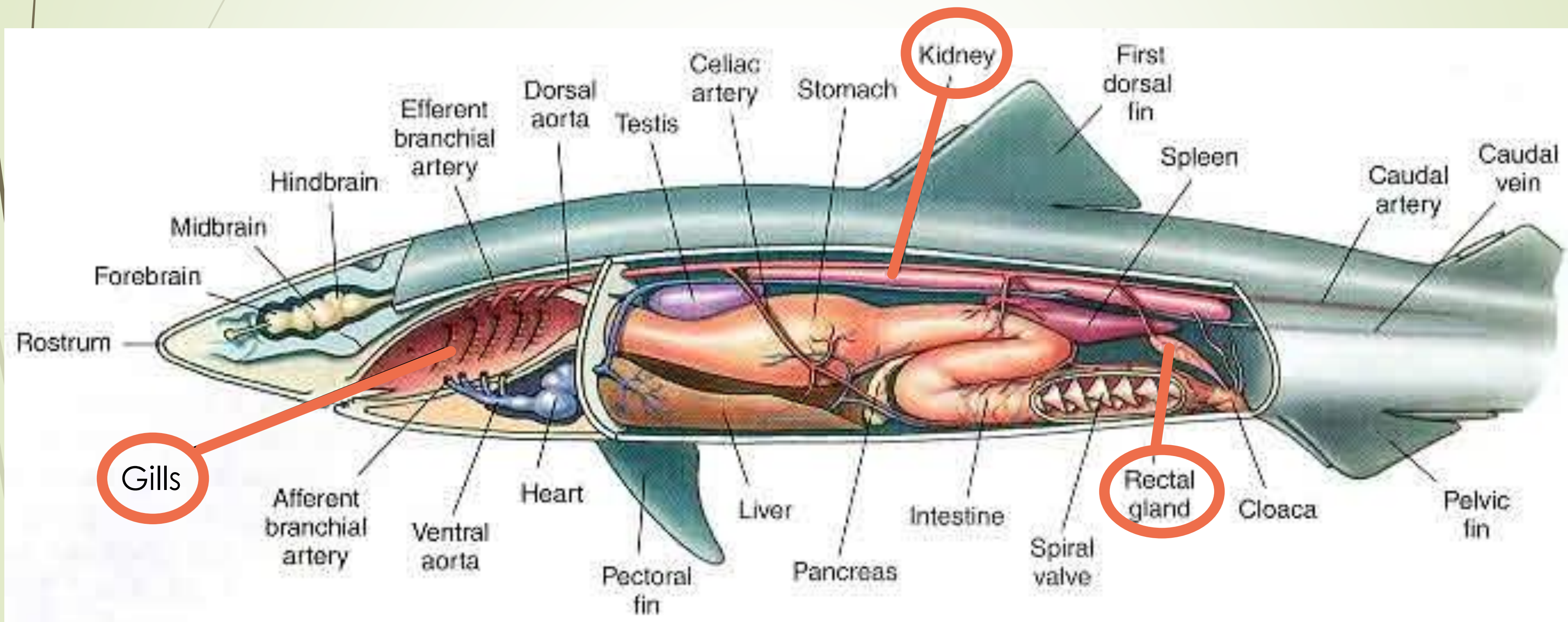
- **Growth hormone (GH)/insulin-like growth factor (ILGF)**
- ↑ ATPase activity
- ↑ Chloride cell size & density
- **Natriuretic peptides**
- ↓ salt loading by reducing oral ingestion & intestinal uptake

? What changes would you expect?

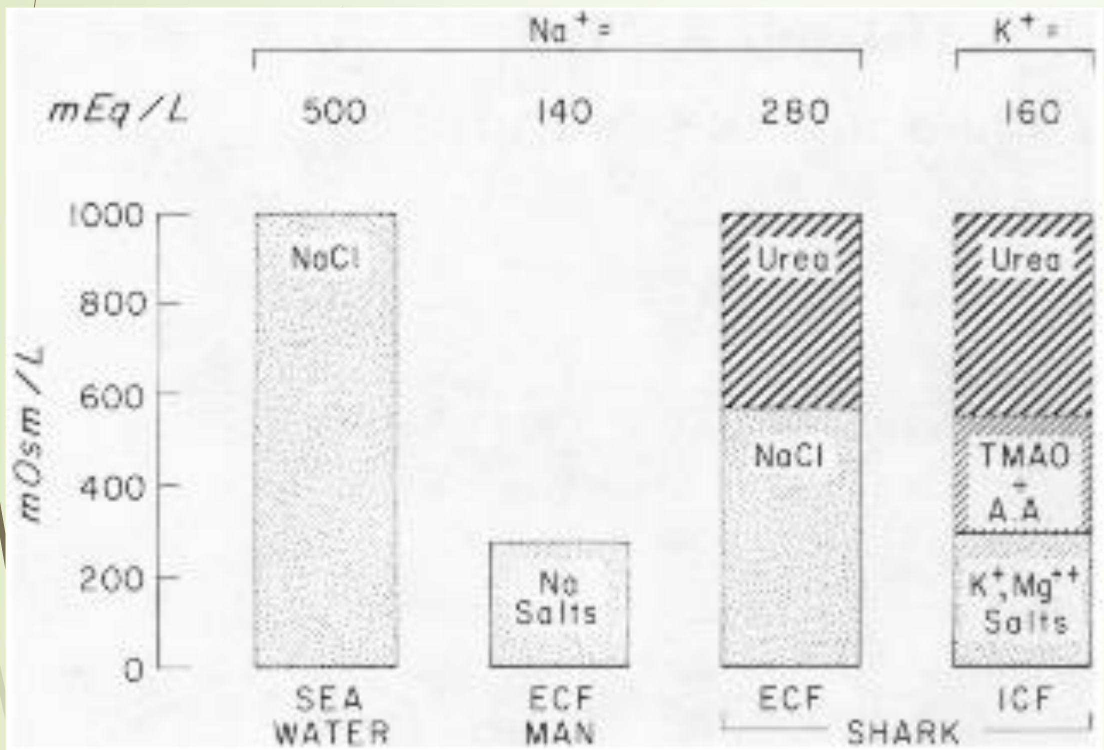
Cortisol works like prolactin in freshwater and works synergistically with GH & ILGF in seawater

Elasmobranches

Shark Anatomy



Urea & TMAO

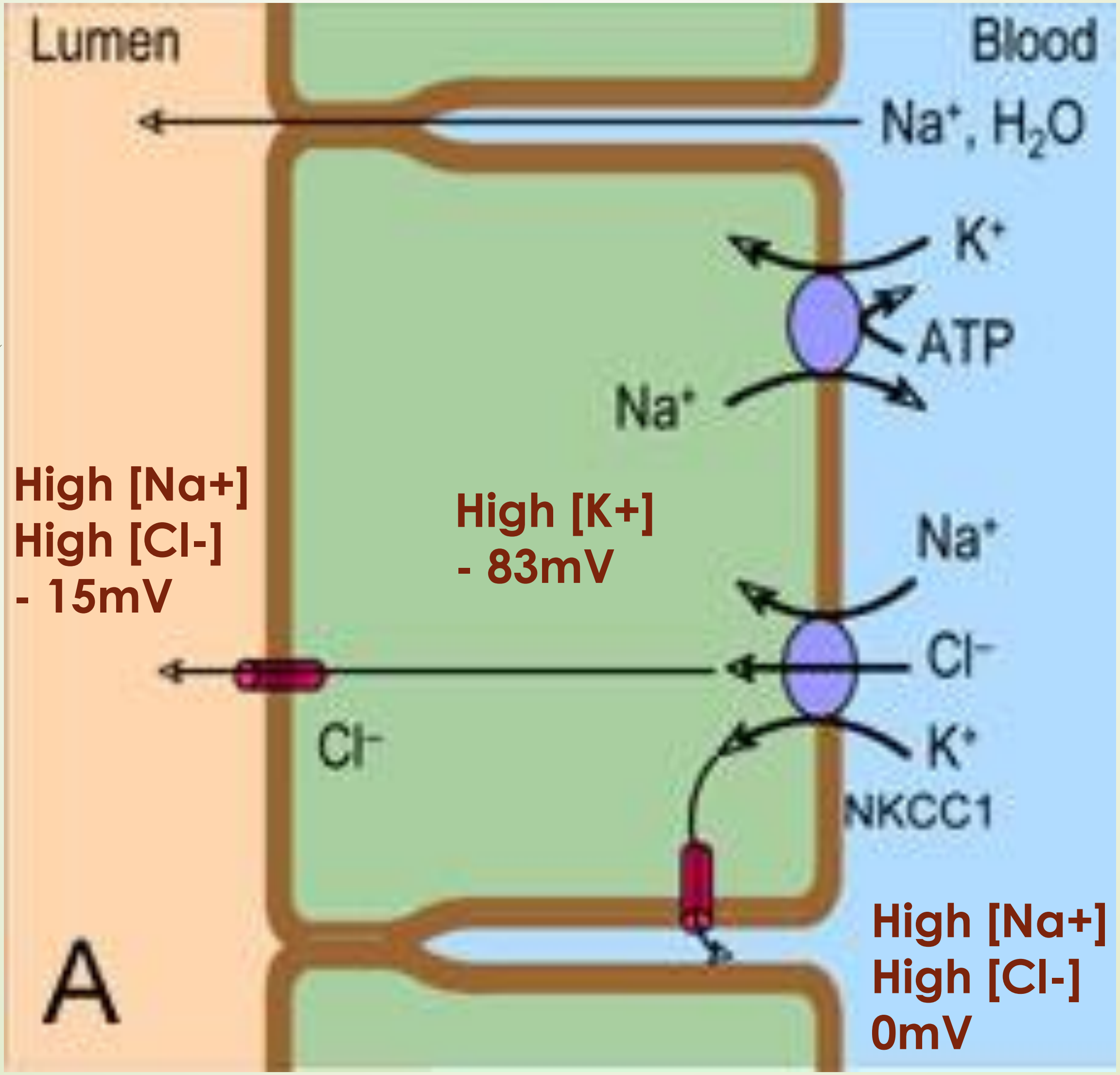


- High urea levels (2.5% vs 0.01-0.03%) in blood makes isotonic to seawater
- Urea actively pumped out of cells
- Gills are impermeable to urea, unlike in other marine species
- Trimethylamine N-oxide protects proteins from harmful effects of urea

Osmoconformers that decouple osmotic & electrolyte regulation

? Urine concentration? Water source?

Shark Rectal Glands



Rectal Gland Hormones

- Atrial natriuretic peptide stimulates vasoactive intestinal peptide release, which stimulates prolactin release
  - Rectal gland secretion
  - Diuresis

? Why?

- Somatostatin inhibits VIP signal cascade

Bull Sharks

Salt to Fresh Water Transition

Metric	Fresh Water	Sea Water
Water osmolarity	3 mOsm	980-1000 mOsm
Plasma osmolarity	642 ± 7 mOsm	1067 ± 21 mOsm
Na+	208 ± 3 mM	289 ± 3 mM
Cl-	203 ± 3 mM	296 ± 6 mM
Urea	192 ± 2 mM	370 ± 10 mM
TMAO	13.2 mM	46.6 mM
Rectal gland Na(+)/K(+)-ATPase	5.6 ± 0.8 (mmol*Pi)/(mg* protein h)	9.2 ± 0.6 (mmol*Pi)/(mg* protein h)
Kidney Na(+)/K(+)-ATPase	8.4 ± 1.1 (mmol*Pi)/(mg* protein h)	3.3 ± 1.1(mmol*Pi)/(mg* protein h)

Bull Sharks

- Transition from hypoosmotic in sea water to hyperosmotic in fresh water
- Kidney secretes urea & TMAO
- Rectal gland shrinks
- Direction of salt flow in gills reverses
- Bull sharks found in rivers are usually juveniles

? Why?

- Predator avoidance and increased food abundance

Dessert Animals

Adaptations

- Morphological
- Physiological

Morphological: Kidney

- Wider and Thicker Medulla
- Long loops of Henle
- Long proximal tubule
- Long collecting tubule
- Small renal corpuscles
- Elongated papillae

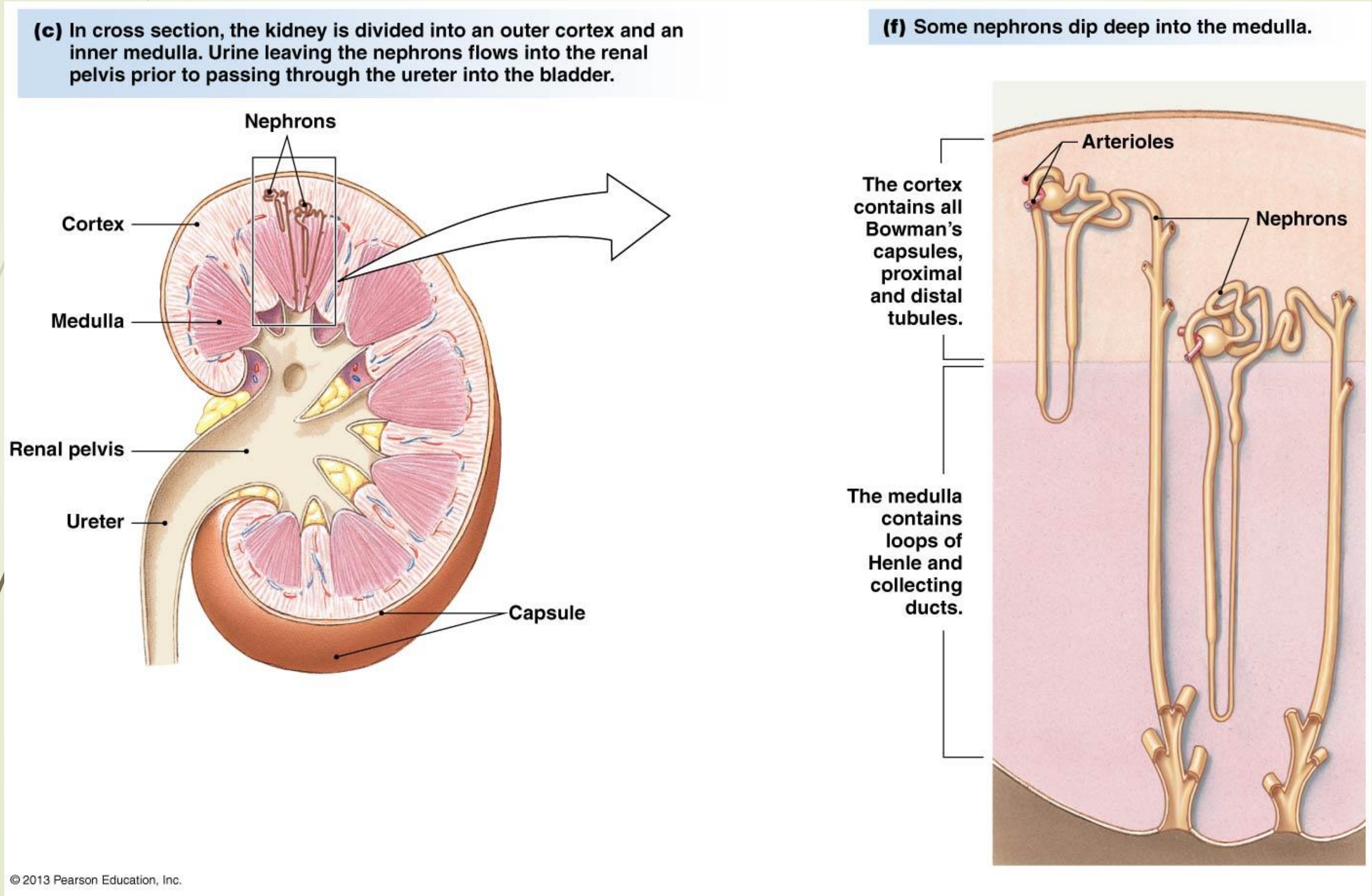
? Why?

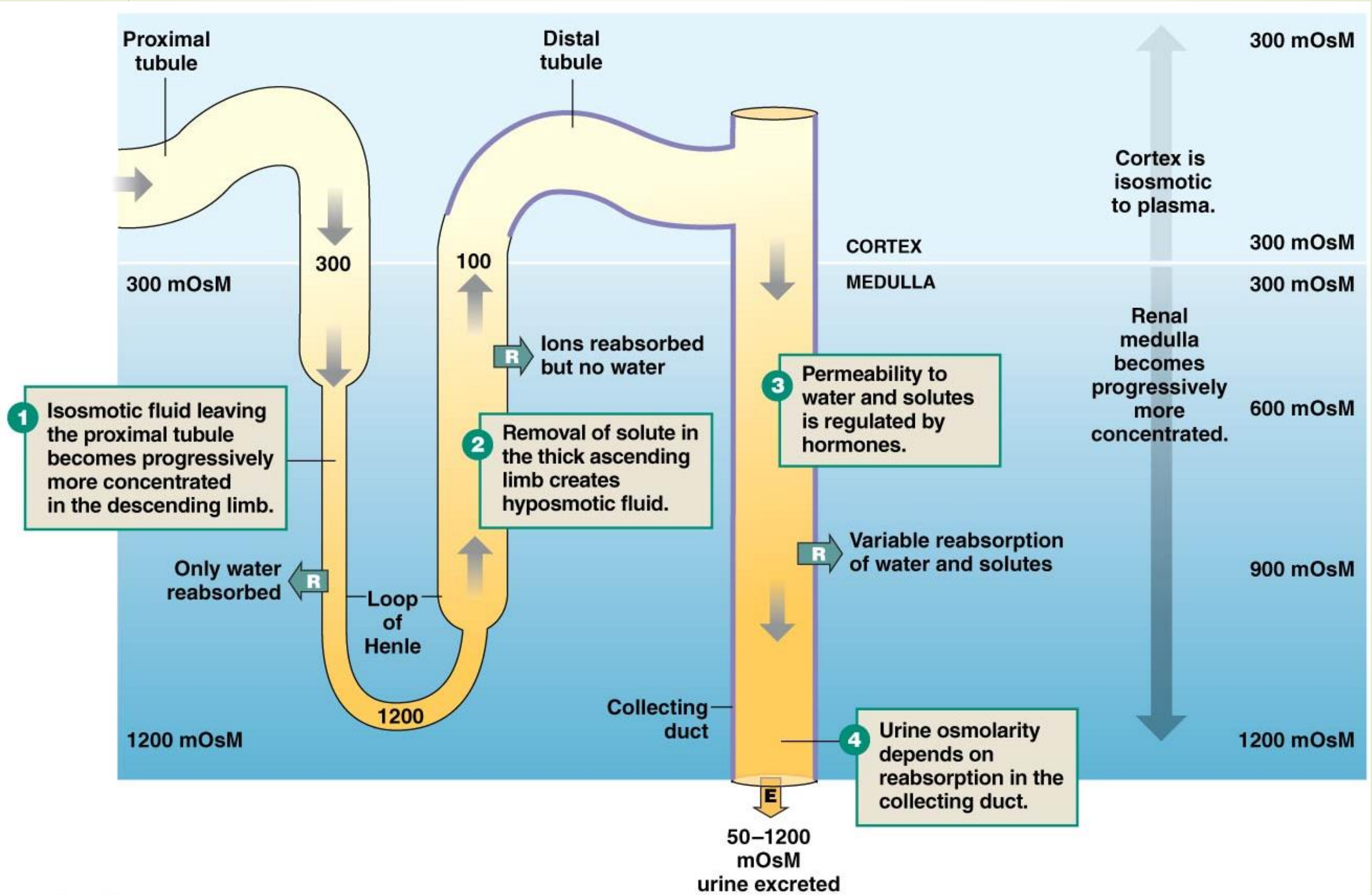
Morphological: Other

? Why?

- Short reflecting coat
- Apocrine sweat glands
- Respiratory system
- Lower metabolic rate
- Colon water retention
- Urea recycling

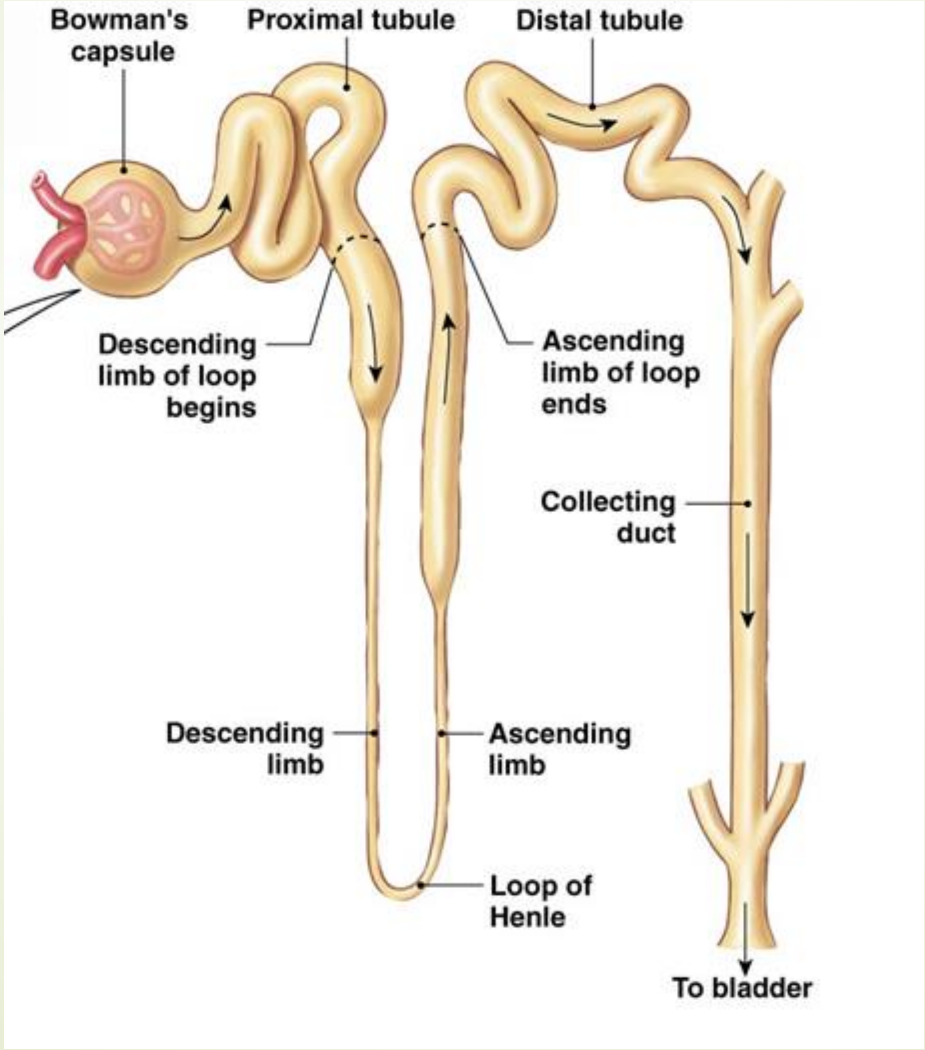
Renal Medulla



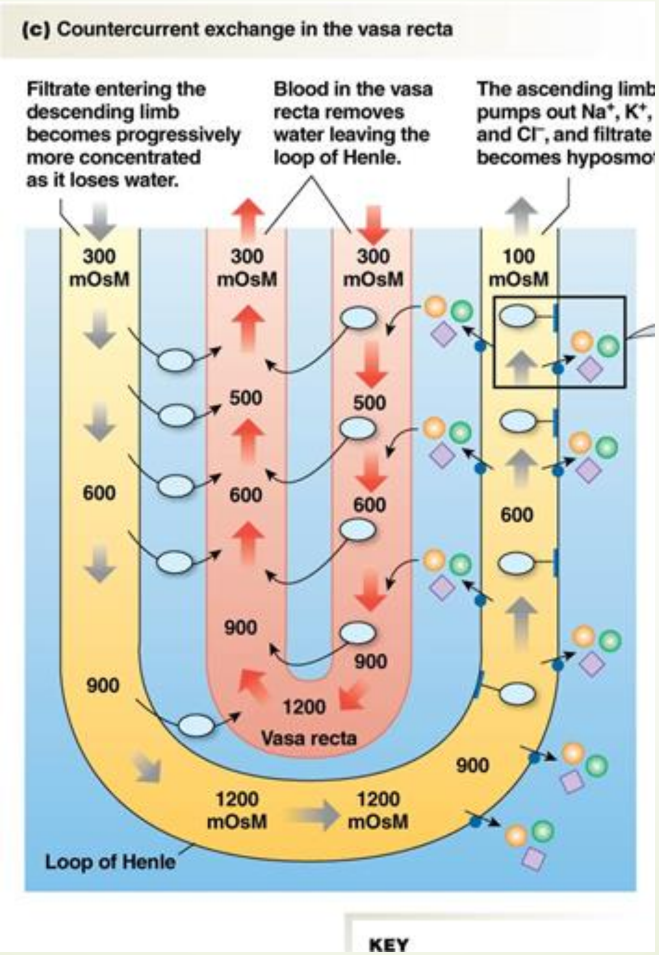


Proximal tubule
Distal tubule
300 mOsM
Cortex is isosmotic to plasma.
300 mOsM
CORTEX
MEDULLA
300 mOsM
300
100
300 mOsM
Ions reabsorbed but no water
Renal medulla becomes progressively more concentrated.
1 Isosmotic fluid leaving the proximal tubule becomes progressively more concentrated in the descending limb.
2 Removal of solute in the thick ascending limb creates hyposmotic fluid.
3 Permeability to water and solutes is regulated by hormones.
600 mOsM
Variable reabsorption of water and solutes
900 mOsM
Only water reabsorbed
Loop of Henle
1200
Collecting duct
1200 mOsM
1200 mOsM
4 Urine osmolarity depends on reabsorption in the collecting duct.
50–1200 mOsM urine excreted

Proximal Tubule



Loop of Henle

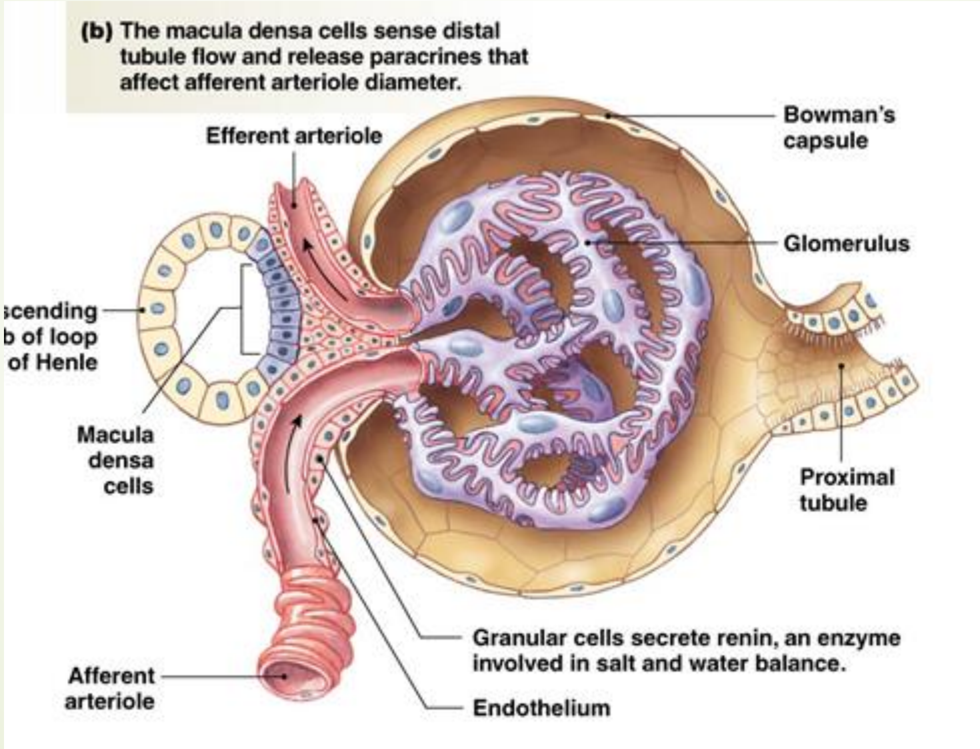


Urea recycling

- Reuse the solute into the counter-current exchange

? Why?

Glomerulus



(b) The macula densa cells sense distal tubule flow and release paracrines that affect afferent arteriole diameter.
Efferent arteriole
Bowman's capsule
Glomerulus
scending
b of loop
of Henle
Macula densa cells
Proximal tubule
Granular cells secrete renin, an enzyme involved in salt and water balance.
Afferent arteriole
Endothelium

Juxtaglomerular Apparatus

- Sense Na+
- RAS pathway
- Not as pronounced in desert animals

Physiological

- GFR
- ADH
- RAS