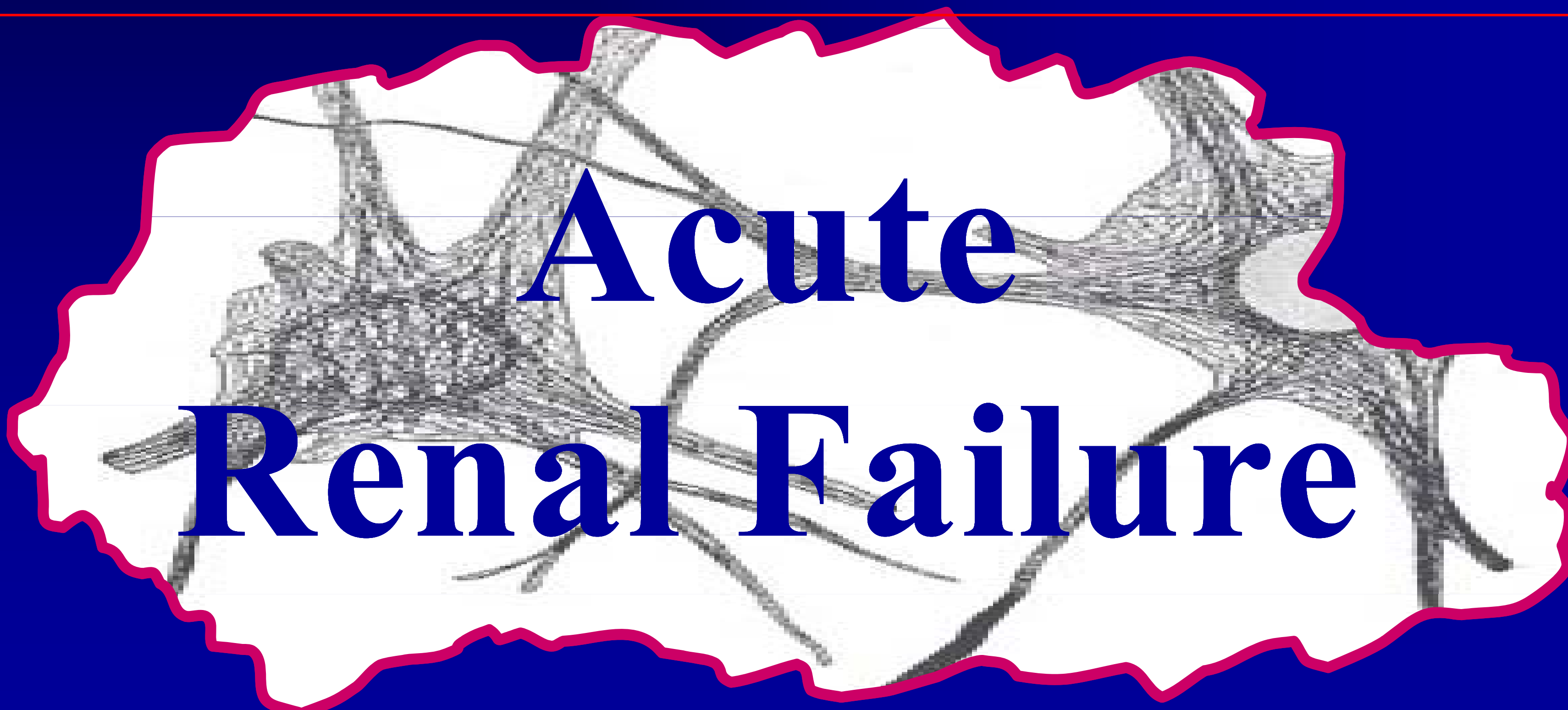
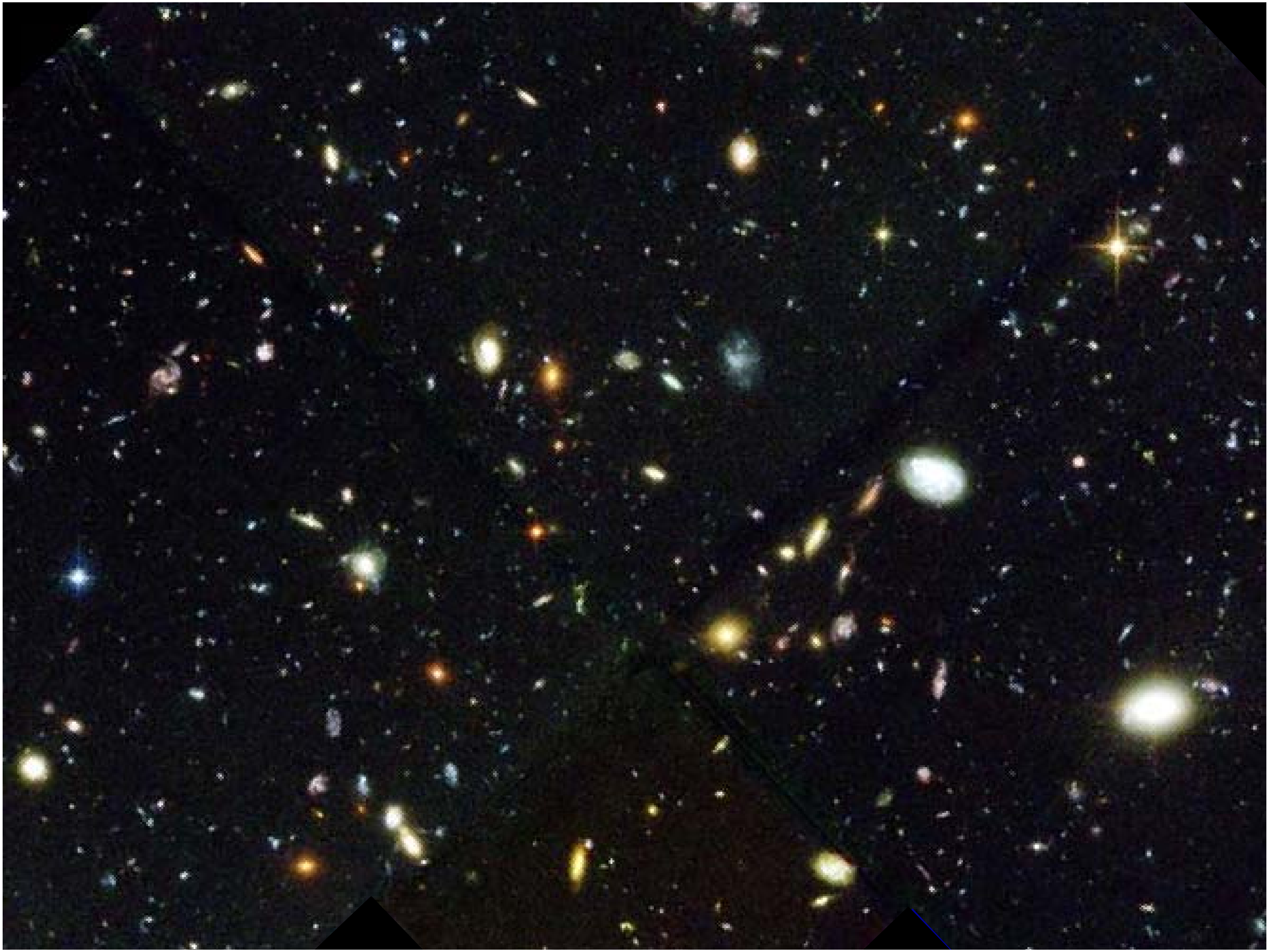
A Four Dimensional Approach to

Acute Renal Failure



The track of understanding renal physiology takes us through a convoluted journey

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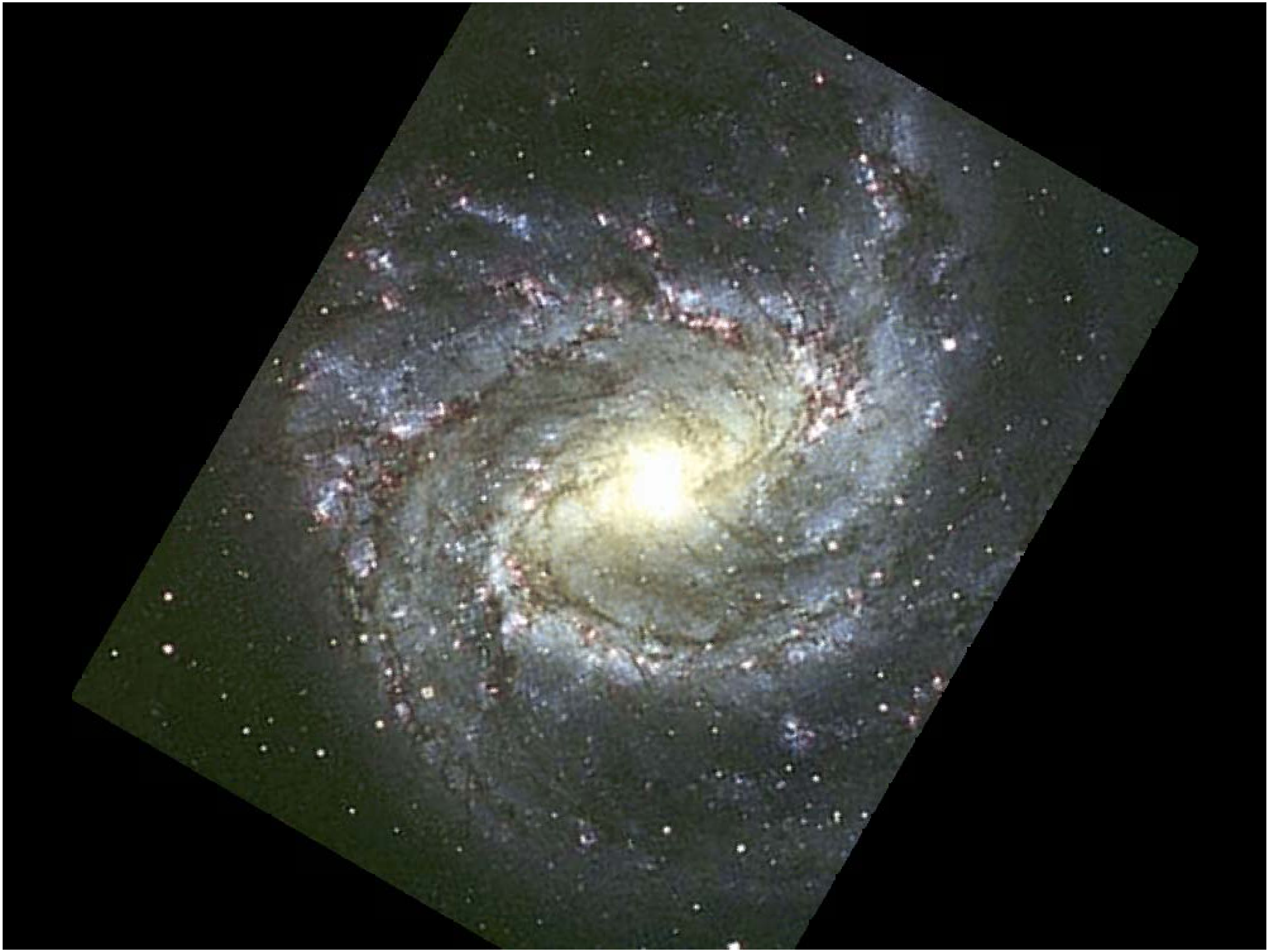
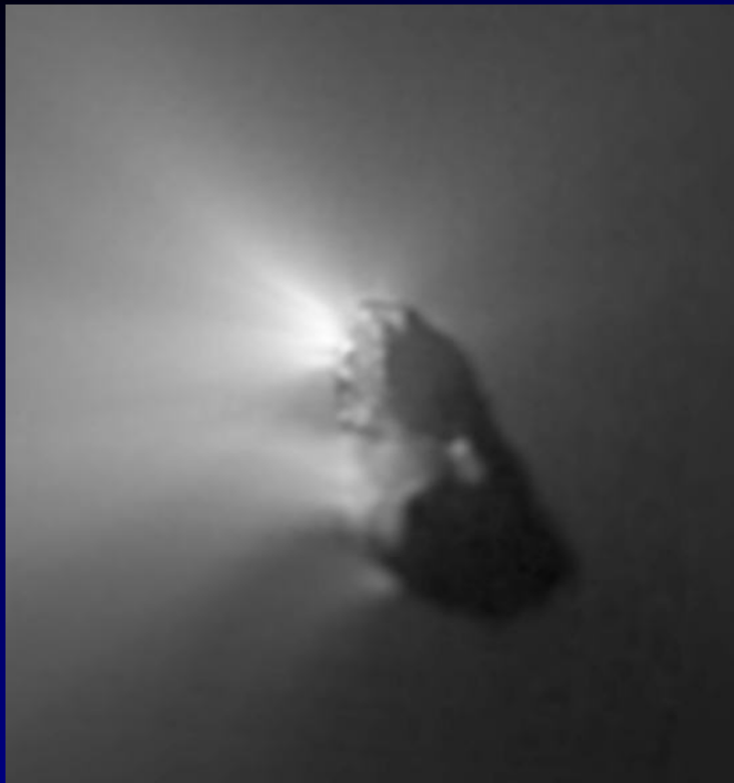
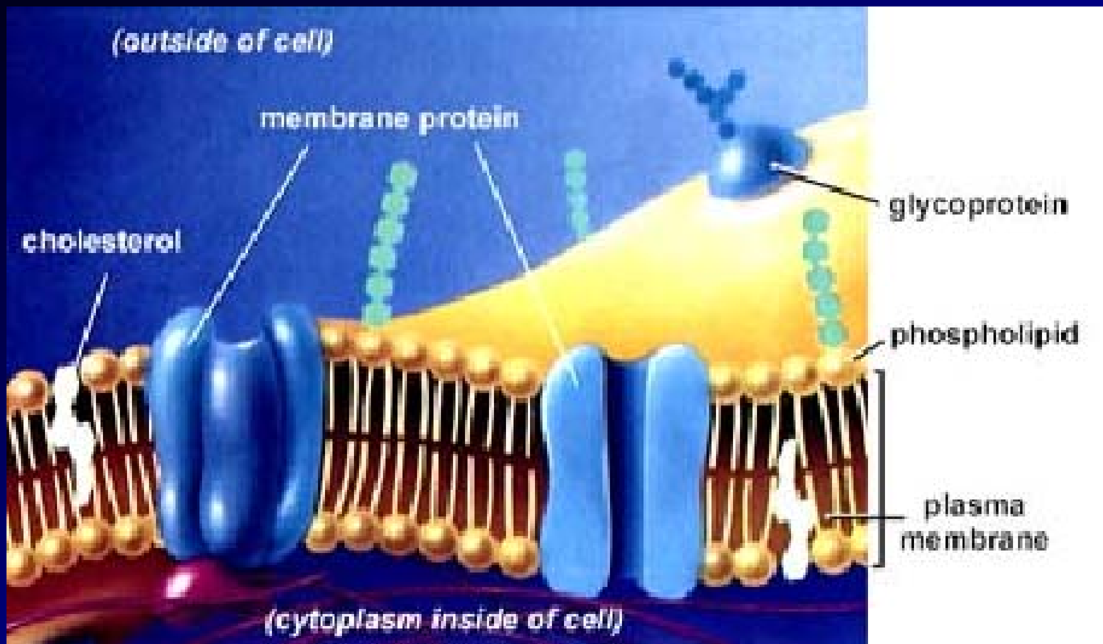
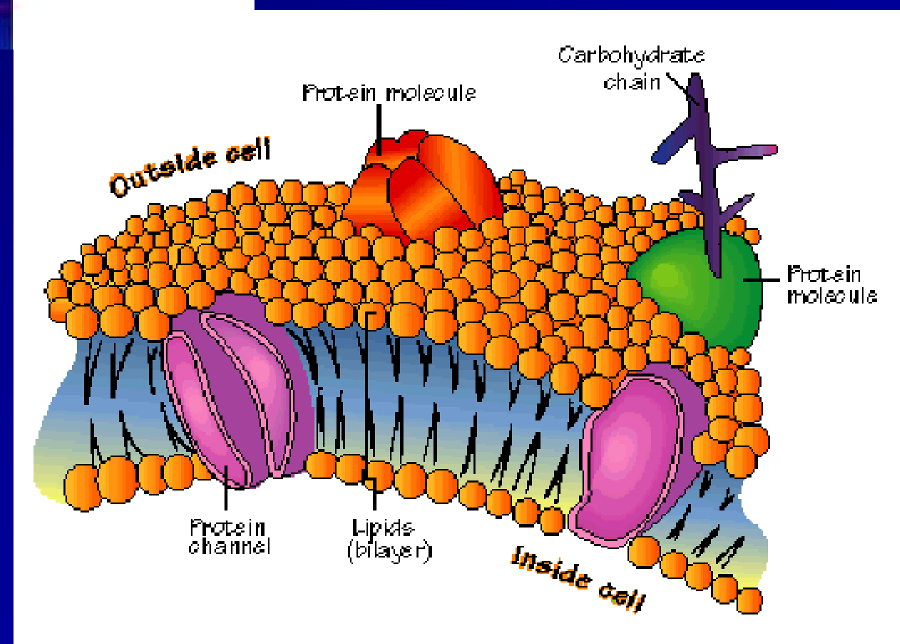
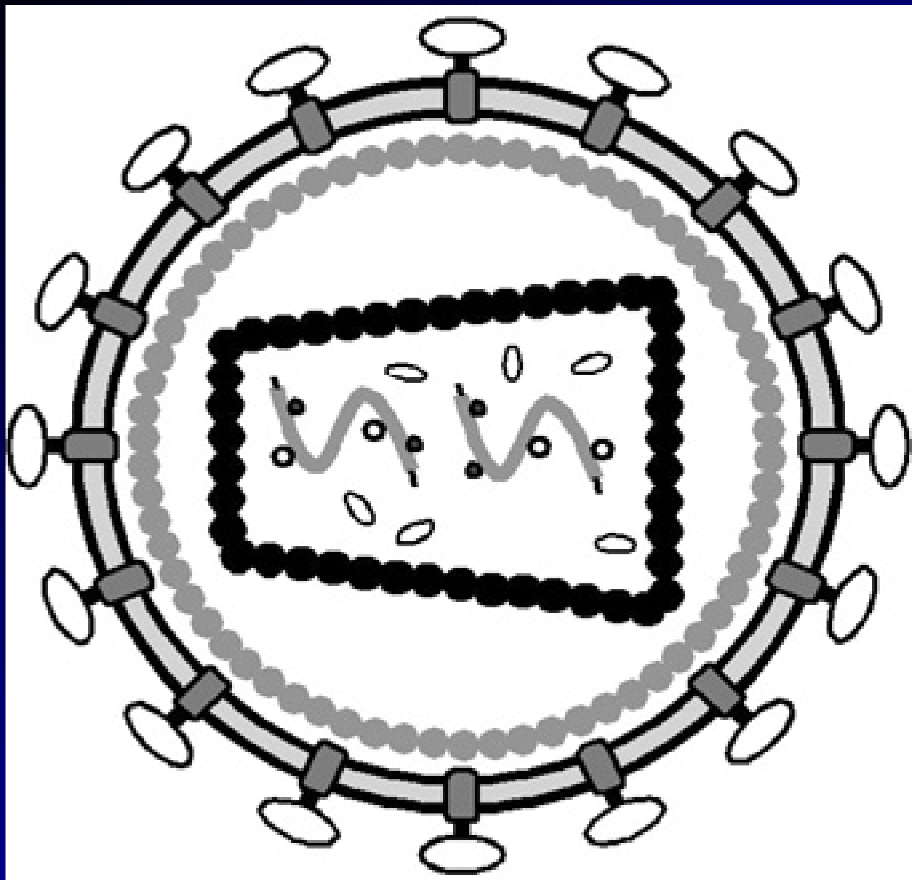


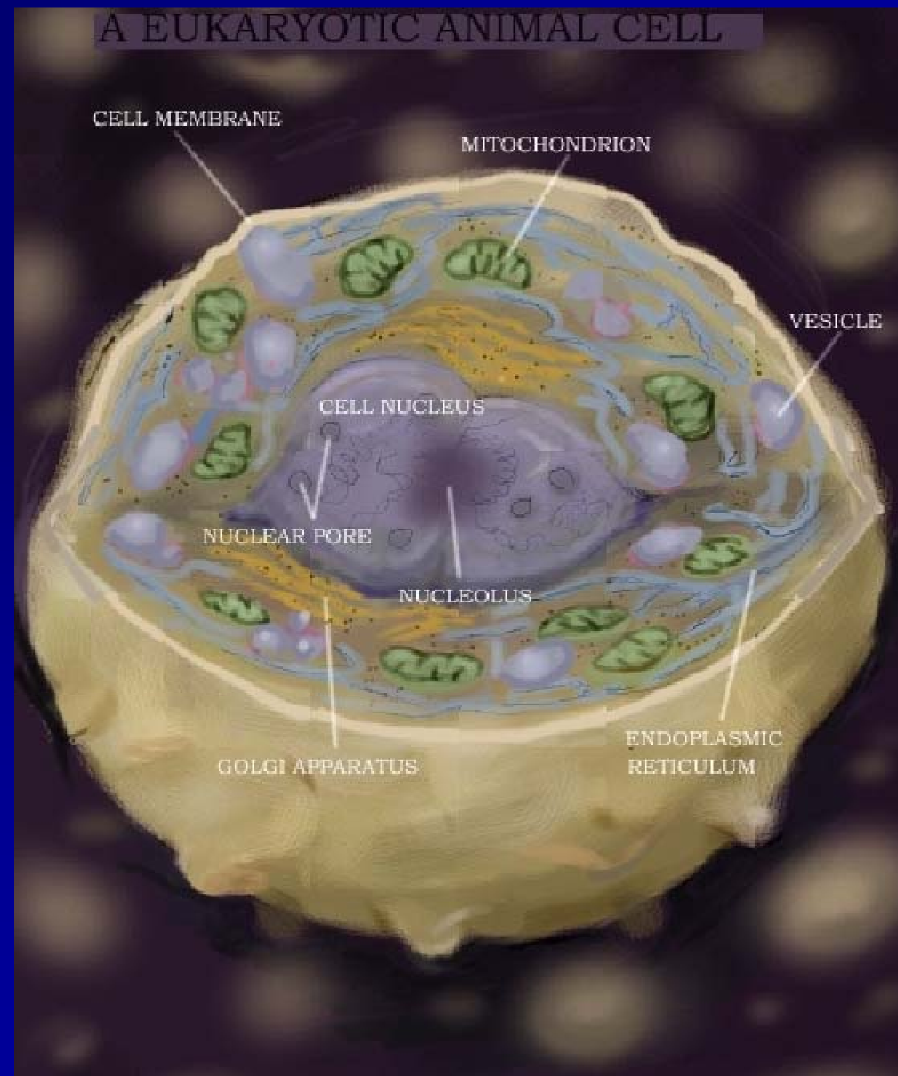


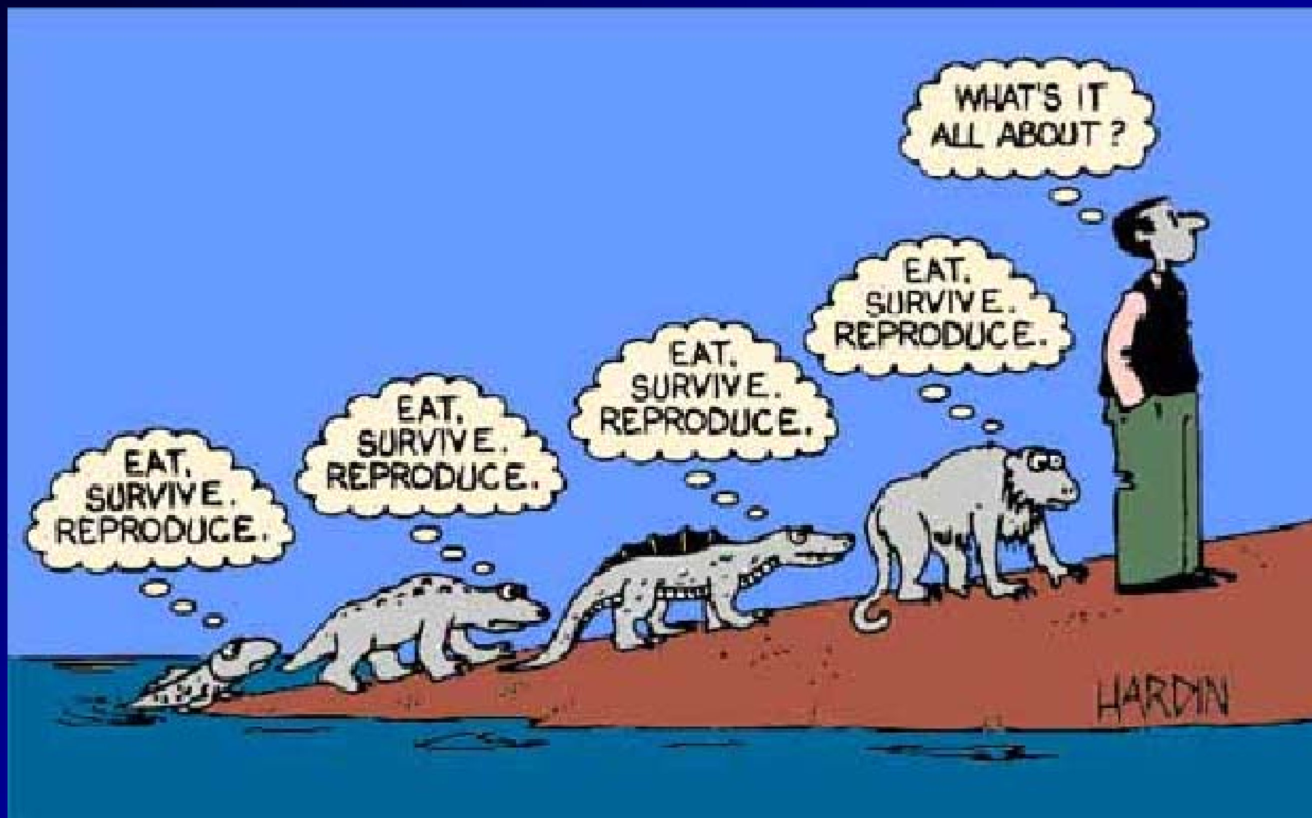

Network BBS
3.0 Gigabytes
les for PCs
Conferences
72-6099


(outside of cell)
membrane protein
cholesterol
glycoprotein
phospholipid
plasma membrane
(cytoplasm inside of cell)


Carbohydrate chain
Protein molecule
Outside cell
Protein molecule
Protein channel
Lipids (bilayer)
Inside cell




A EUKARYOTIC ANIMAL CELL
CELL MEMBRANE
MITOCHONDRION
VESICLE
CELL NUCLEUS
NUCLEAR PORE
NUCLEOLUS
ENDOPLASMIC RETICULUM
GOLGI APPARATUS


EAT, SURVIVE, REPRODUCE.
EAT, SURVIVE, REPRODUCE.
EAT, SURVIVE, REPRODUCE.
EAT, SURVIVE, REPRODUCE.
WHAT'S IT ALL ABOUT?
HARDIN


MAHER
PHYSICIAN
Emergency
Pharmacy Services

Electrolytes are charged particles **(ions)** that are dissolved in body fluids.

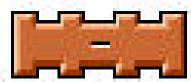
Electrolytes (Dissolved Ions)

Major Positive Ions **(Cations)**

- Sodium ion, Na^{+}
- Potassium ion, K^{+}
- Calcium ion, Ca^{2+}
- Magnesium ion, Mg^{2+}

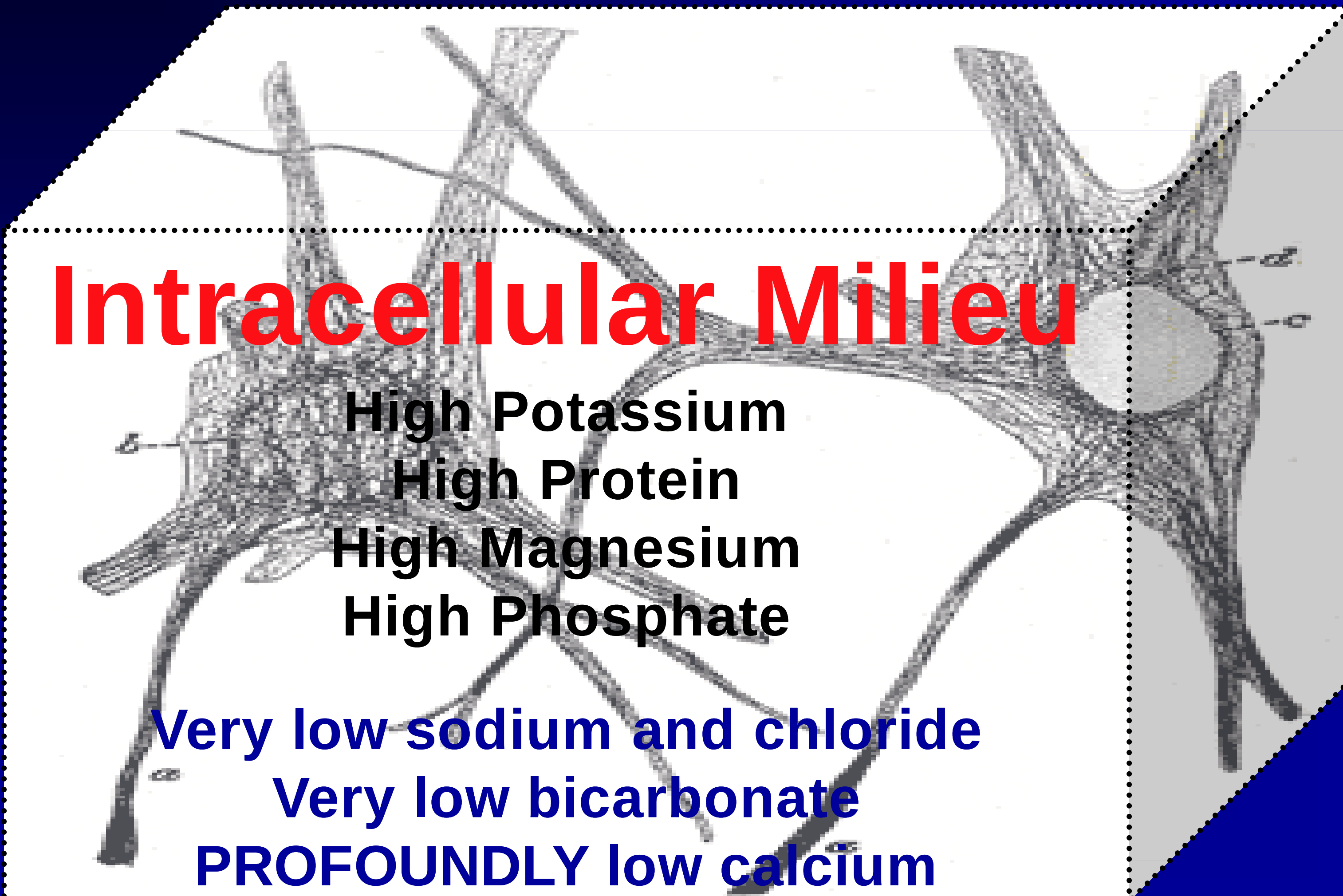
Major Negative Ions **(Anions)**

- Chloride ion, Cl^{-}
- Bicarbonate ion, HCO_3^{-}
- Phosphate ions, HPO_4^{2-} & $H_2PO_4^{-}$
- Sulfate ion, SO_4^{2-}



Organic acids

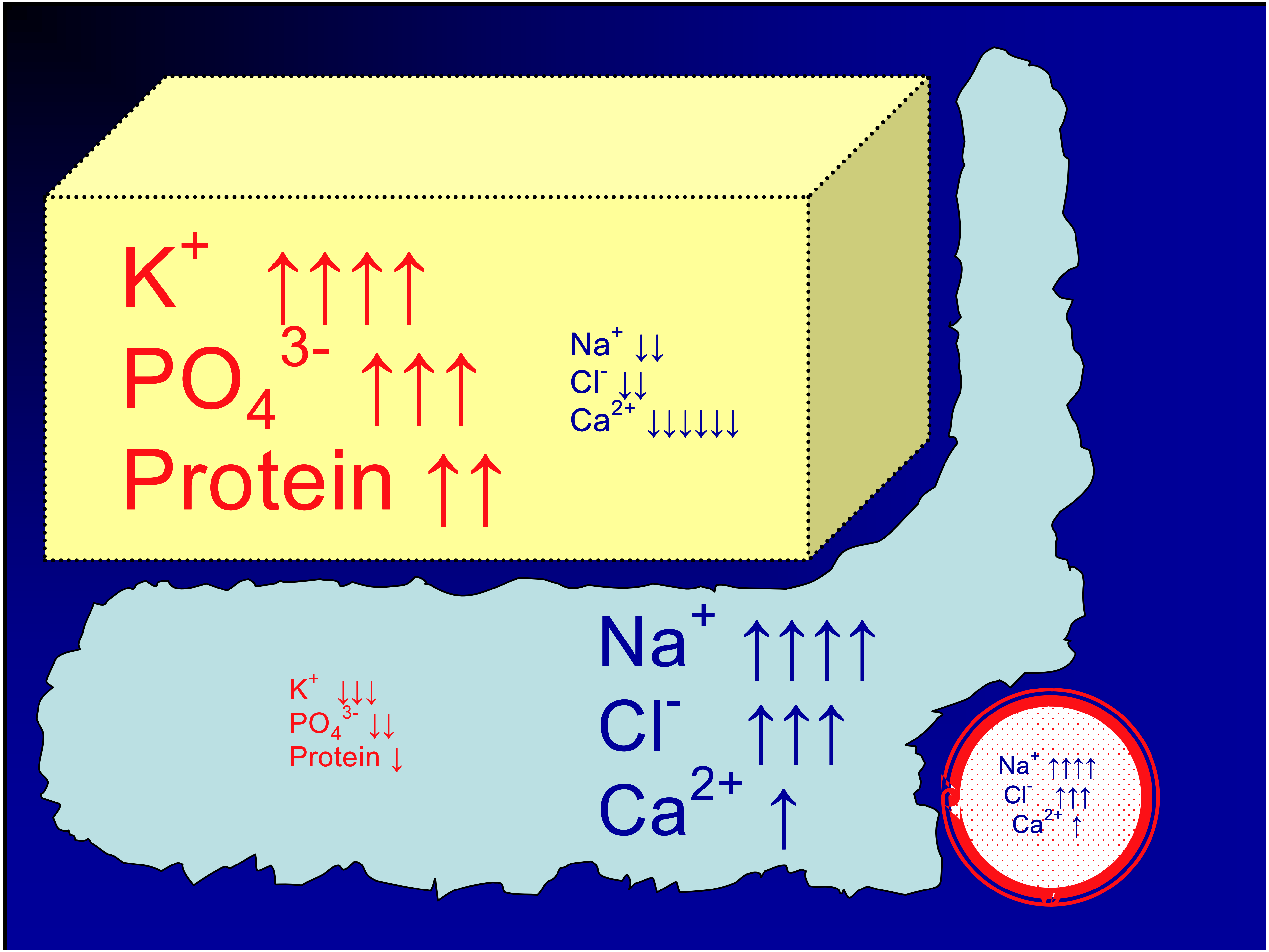
Proteins



Intracellular Milieu

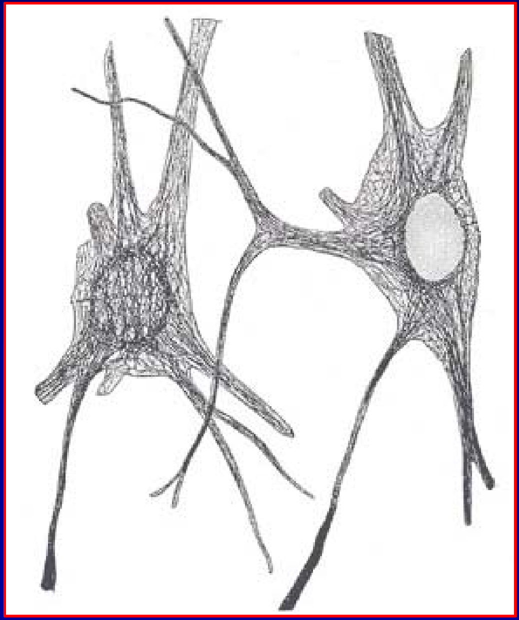
High Potassium
High Protein
High Magnesium
High Phosphate

Very low sodium and chloride
Very low bicarbonate
PROFOUNDLY low calcium



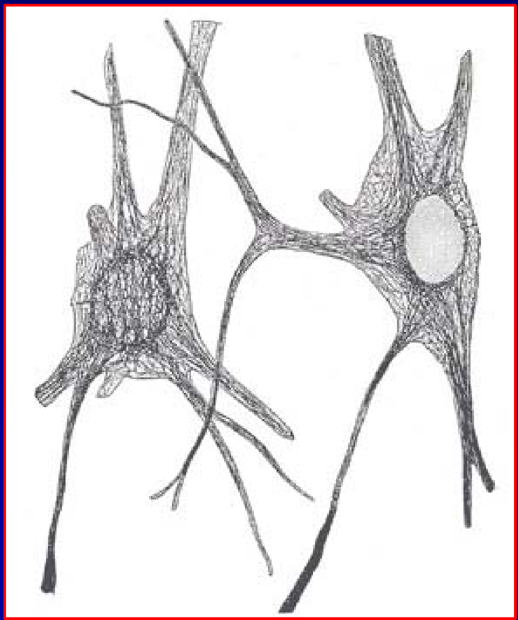
K+ ↑↑↑↑
PO4 3- ↑↑↑
Protein ↑↑
Na+ ↓↓
Cl- ↓↓
Ca2+ ↓↓↓↓↓↓
K+ ↓↓↓
PO4 3- ↓↓
Protein ↓
Na+ ↑↑↑↑
Cl- ↑↑↑
Ca2+ ↑
Na+ ↑↑↑↑
Cl- ↑↑↑
Ca2+ ↑

The Inside of the Cell is a Protein rich, high potassium, high phosphate, and high magnesium environment

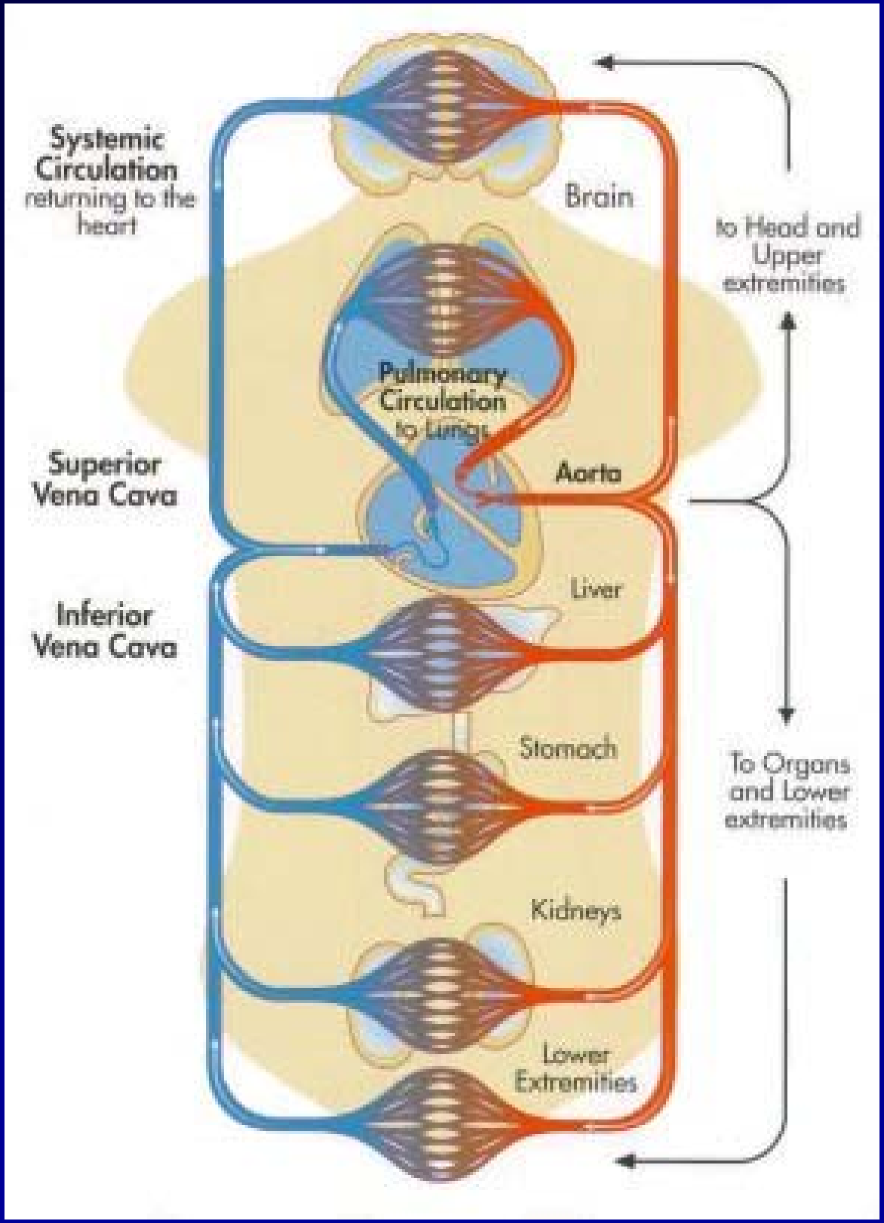


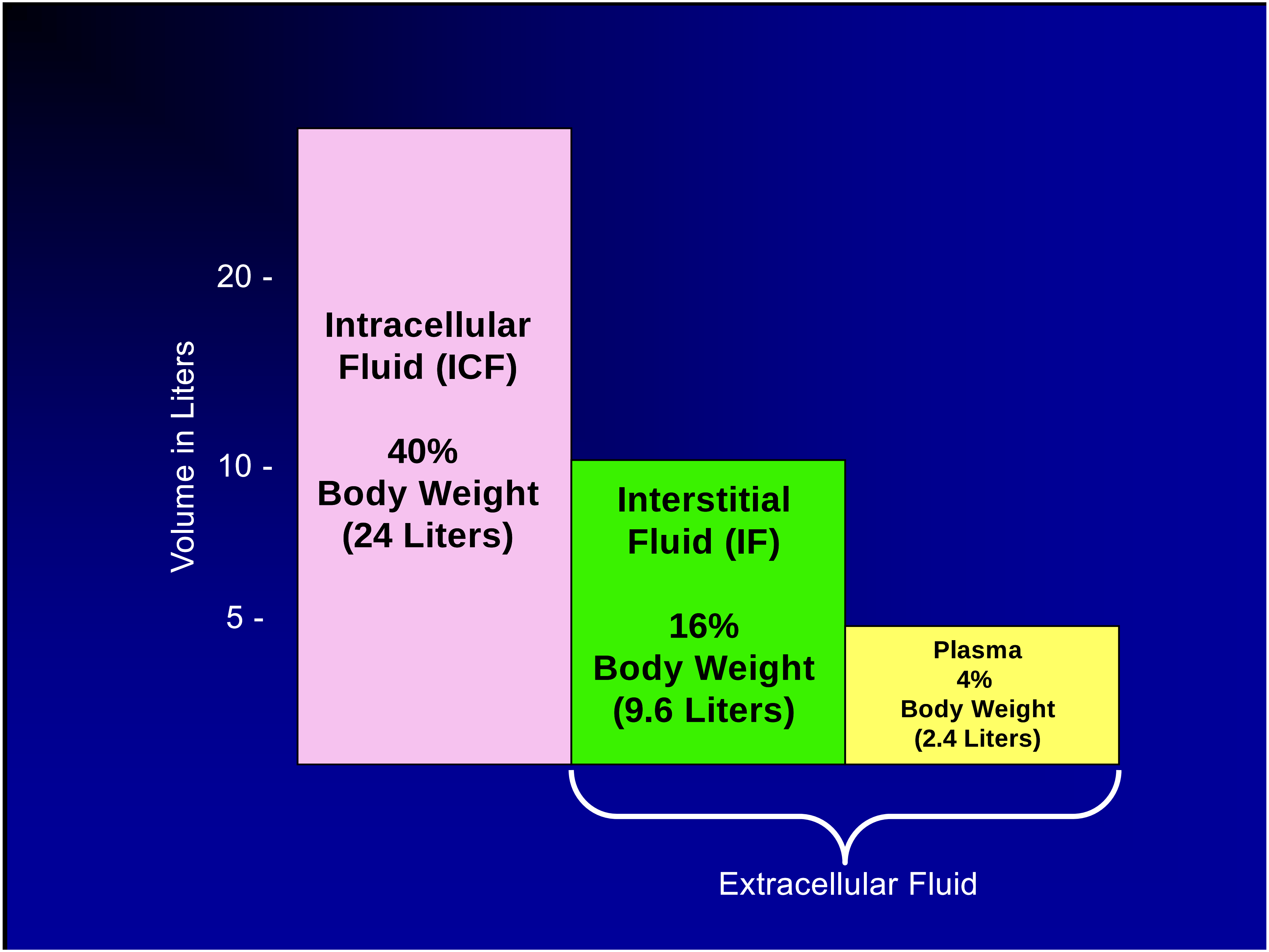
…this is where the processes of creating energy and life take place!!

The Outside of the Cell is the Salt of the Sea from which Life Sprang Forth



…bathing the cells in the liquid from which they were born


Systemic Circulation returning to the heart
Brain
to Head and Upper extremities
Pulmonary Circulation to Lungs
Superior Vena Cava
Aorta
Inferior Vena Cava
Liver
Stomach
To Organs and Lower extremities
Kidneys
Lower Extremities


Volume in Liters
20 -
10 -
5 -
Intracellular Fluid (ICF)
40% Body Weight (24 Liters)
Interstitial Fluid (IF)
16% Body Weight (9.6 Liters)
Plasma
4% Body Weight (2.4 Liters)
Extracellular Fluid

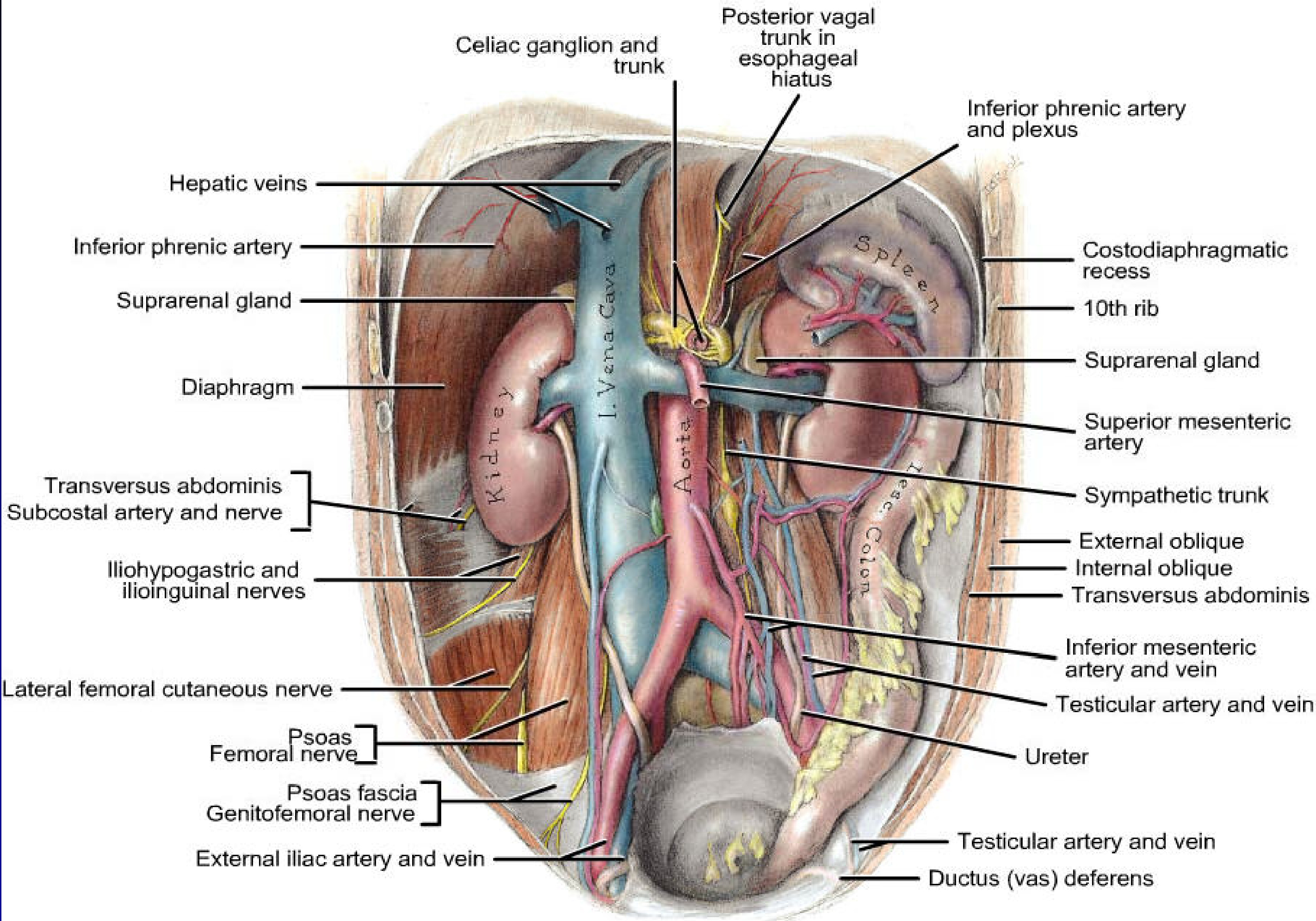
Body Fluid Compartments		
Total Body Water	Body Weight (%)	Total Body Water (%)
Total	60	100
Intracellular	40	67
Extracellular	20	33
Intravascular	5	8
Interstitial	15	25

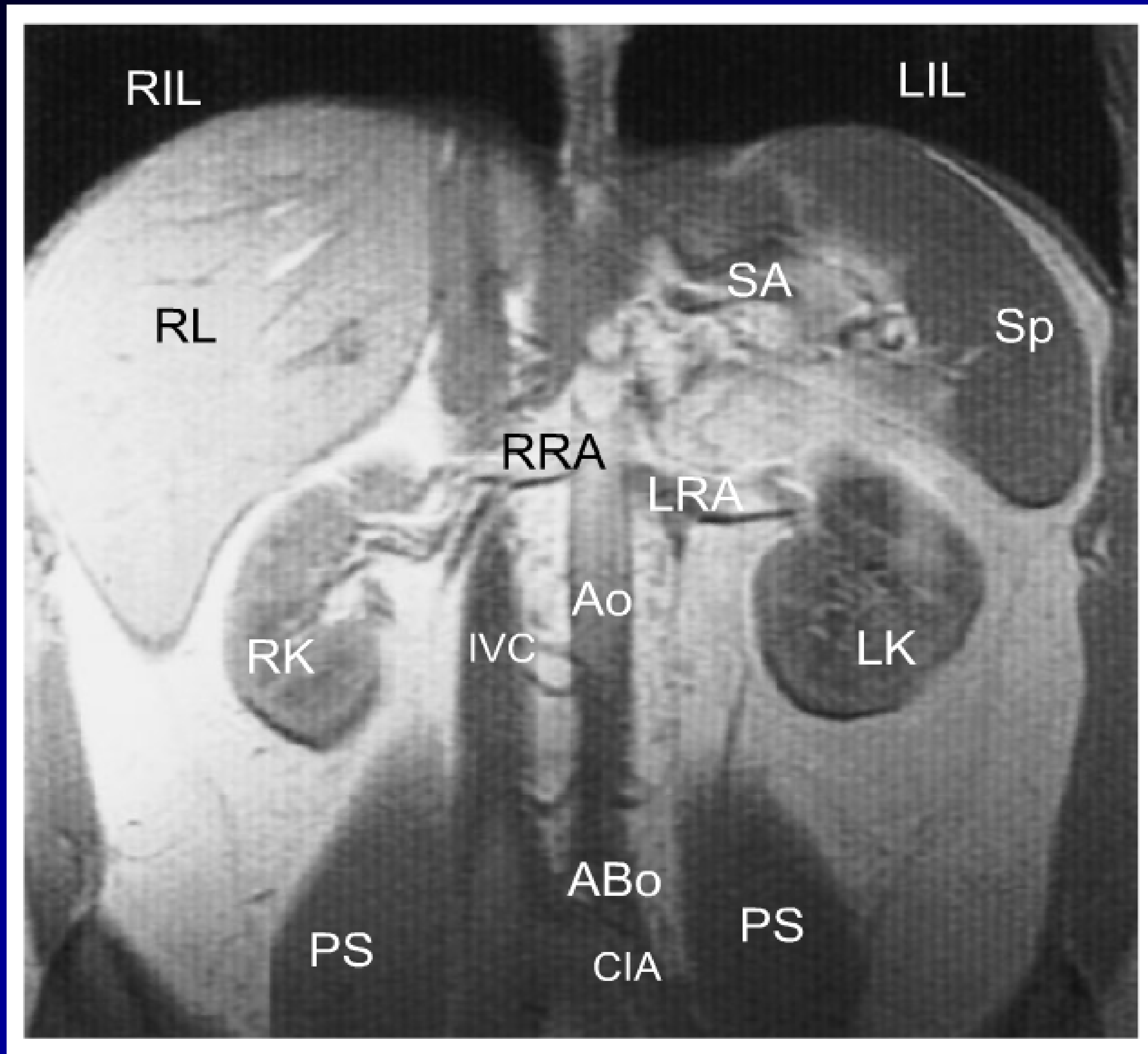
Body Fluid Compartments			
Age	Total Body Water As % Body Weight	Extracellular Fluid As % Body Weight	Intracellular Fluid As % Body Weight
Premature	75 - 80	50	35
Newborn	70 – 75	50	35
1 Year Old	65	25	40 – 45
Adolescent Male	60	20	40 – 45
Adolescent Female	55	18	40

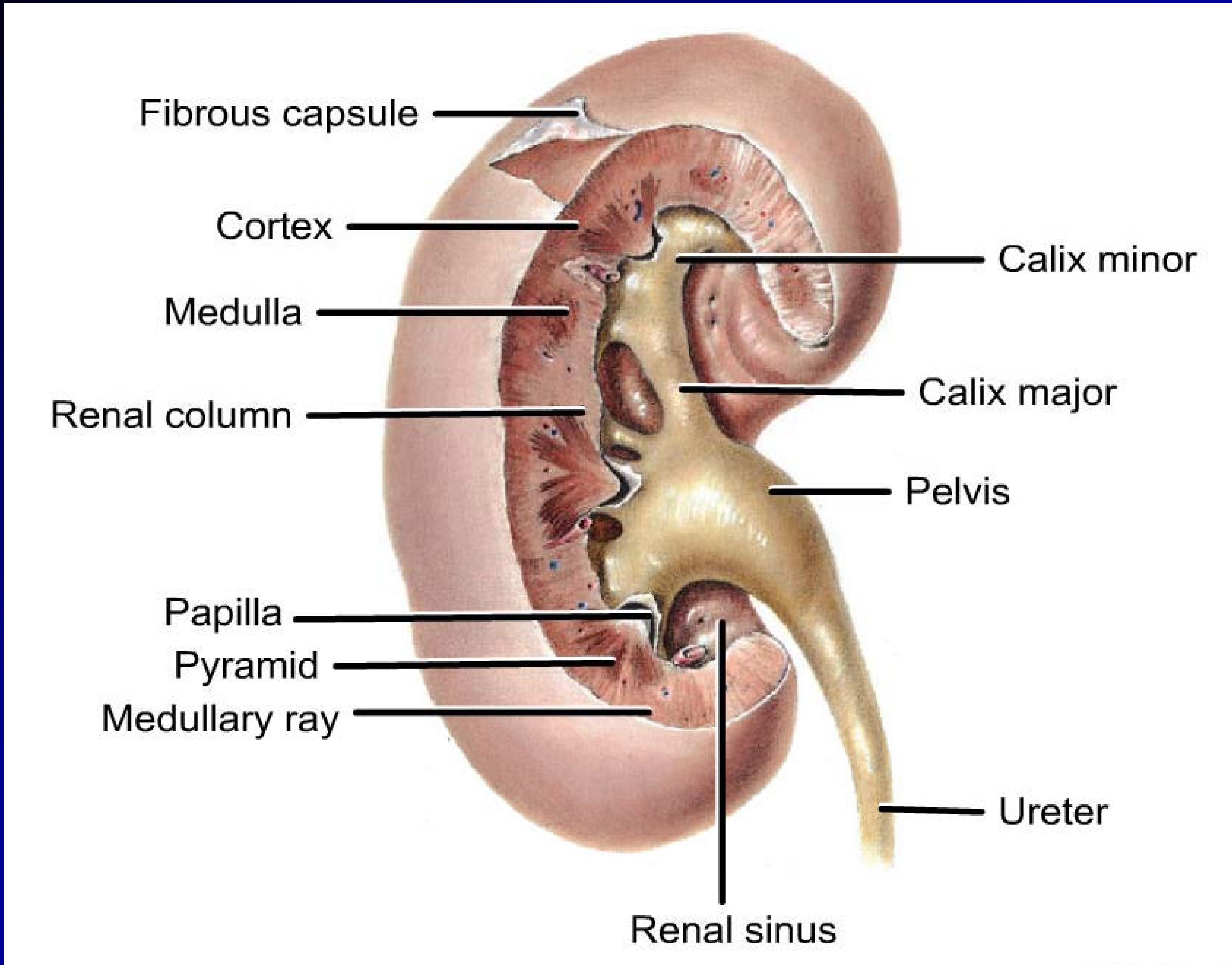
Electrolyte Concentration in Fluid Compartments (meq/L)			
	Plasma	Interstitial Fluid	Intracellular Fluid
Cations			
Na^{+}	140	146	12
K^{+}	4	4	150
Ca^{2+}	5	3	10^{-7}

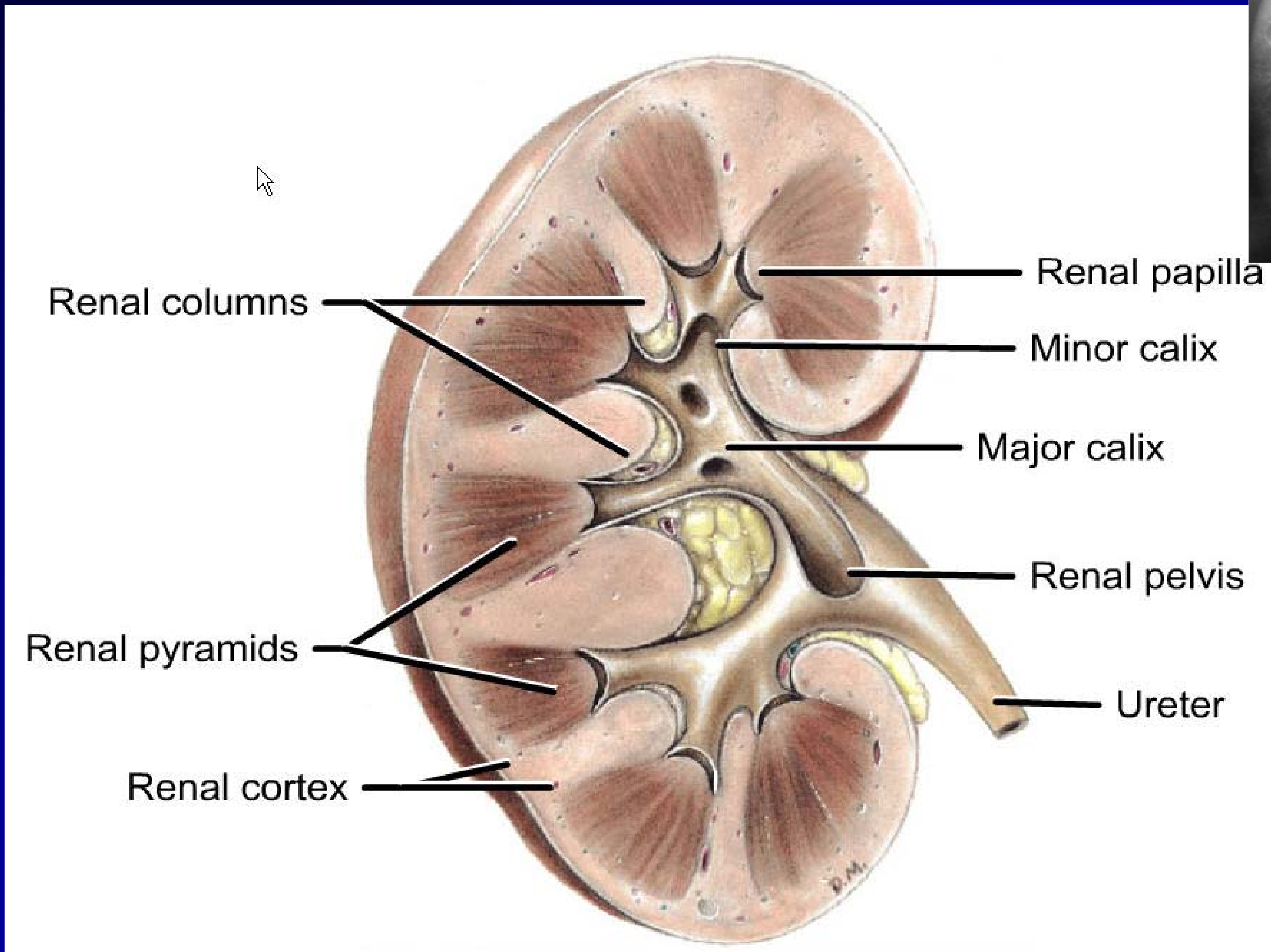
Electrolyte Concentration in Fluid Compartments (meq/L)

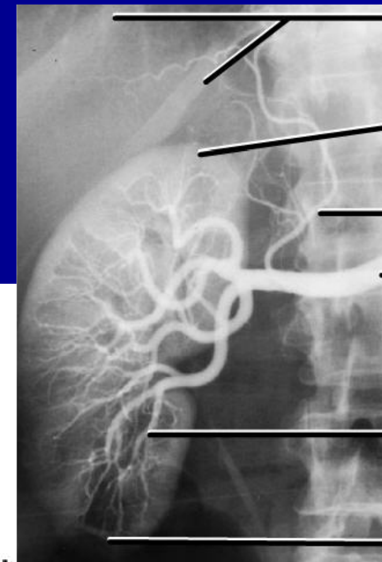
	Plasma	Interstitial Fluid	Intracellular Fluid
Anions			
Cl^-	103	114	3
HCO_3^-	24	27	10
SO_4^{2-}	1	1	---
HPO_4^{3-}	2	2	116
Protein	16	5	40
Organic anions	5	5	---


Celiac ganglion and trunk
Posterior vagal trunk in esophageal hiatus
Inferior phrenic artery and plexus
Hepatic veins
Inferior phrenic artery
Suprarenal gland
Diaphragm
Transversus abdominis
Subcostal artery and nerve
Iliohypogastric and ilioinguinal nerves
Lateral femoral cutaneous nerve
Psoas
Femoral nerve
Psoas fascia
Genitofemoral nerve
External iliac artery and vein
Costodiaphragmatic recess
10th rib
Suprarenal gland
Superior mesenteric artery
Sympathetic trunk
External oblique
Internal oblique
Transversus abdominis
Inferior mesenteric artery and vein
Testicular artery and vein
Ureter
Testicular artery and vein
Ductus (vas) deferens
Spleen
I. Vena Cava
Kidney
Aorta
Desc. Colon


RIL
LIL
SA
RL
Sp
RRA
LRA
Ao
IVC
RK
LK
ABo
PS
PS
CIA


Fibrous capsule
Cortex
Medulla
Renal column
Papilla
Pyramid
Medullary ray
Calix minor
Calix major
Pelvis
Ureter
Renal sinus


Renal columns
Renal papilla
Minor calix
Major calix
Renal pelvis
Renal pyramids
Ureter
Renal cortex



V

!!

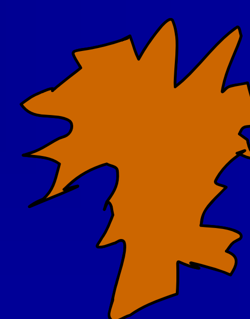
Water is constantly being lost

Urine

Feces

Sweat

Spit (south Georgia)

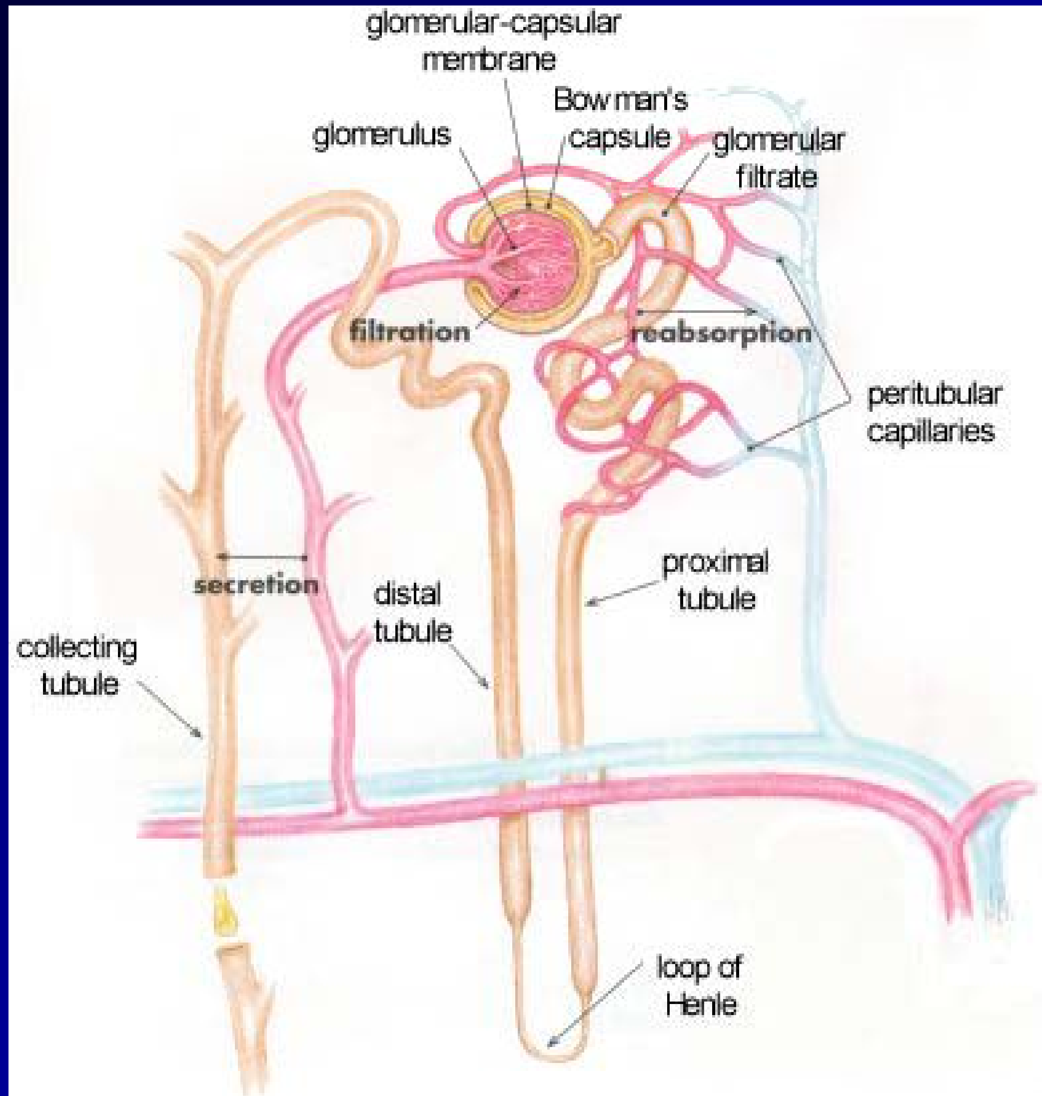


Exercise, fever, vomiting, diarrhea
NG suction, other tubes…

All remove volume from the body, initially from the circulating vascular volume, then from the interstitium and cells

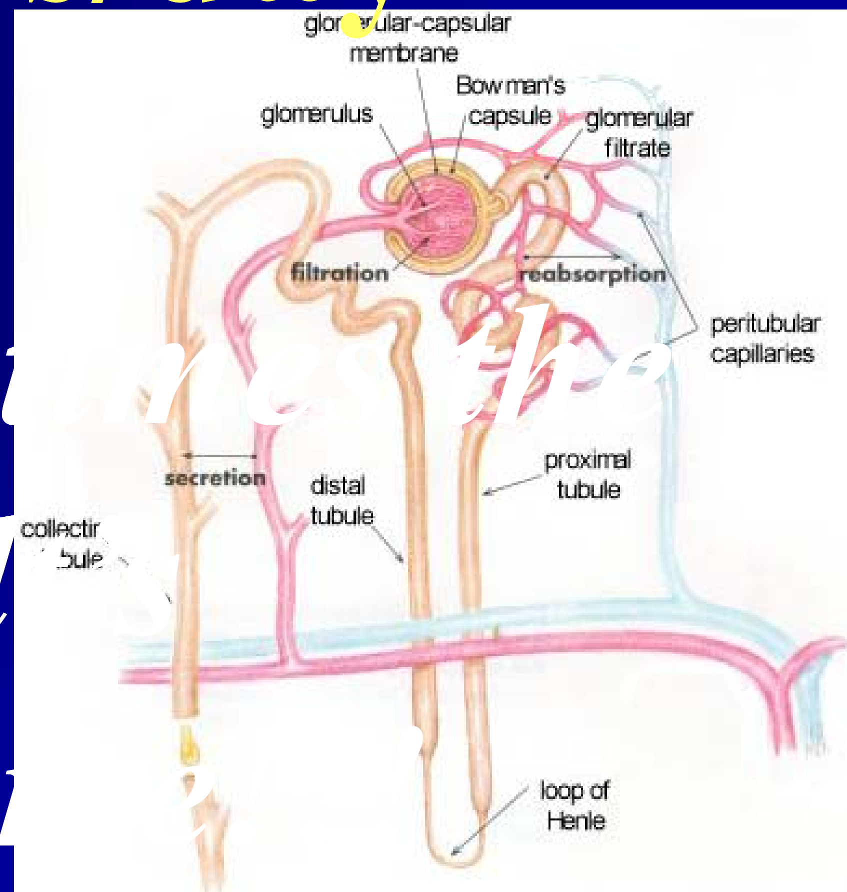
Water Losses in a 60 – 80 Kg Man

	Average Daily Volume (mL)	Minimal Daily Volume (mL)
Sensible Losses		
Urinary	800 - 1500	300
Intestinal	0 - 250	0
Sweat	0	0
Insensible Losses		
Lungs and Skin	600 – 900	600 - 900


glomerular-capsular
membrane
Bowman's
capsule
glomerulus
glomerular
filtrate
filtration
reabsorption
peritubular
capillaries
secretion
distal
tubule
proximal
tubule
collecting
tubule
loop of
Henle

The nephron leaks out 180 liters/day

…that is 60 t mes the normal adul plasma volu



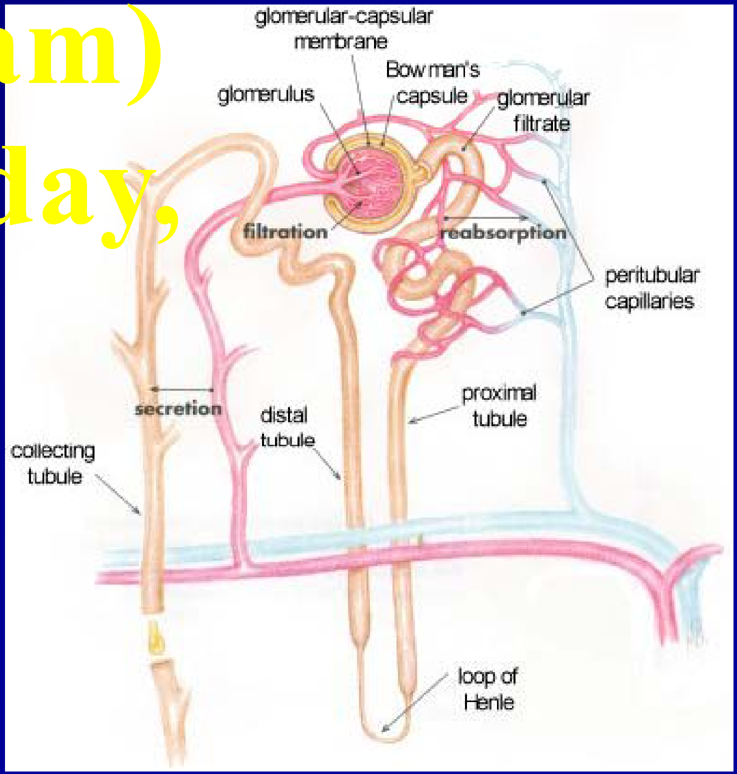
We literally pour out our entire PLASMA VOLUME every 30 minutes

…that's a powerful organ!

Yet, the "beans" reabsorb some 99% of this volume

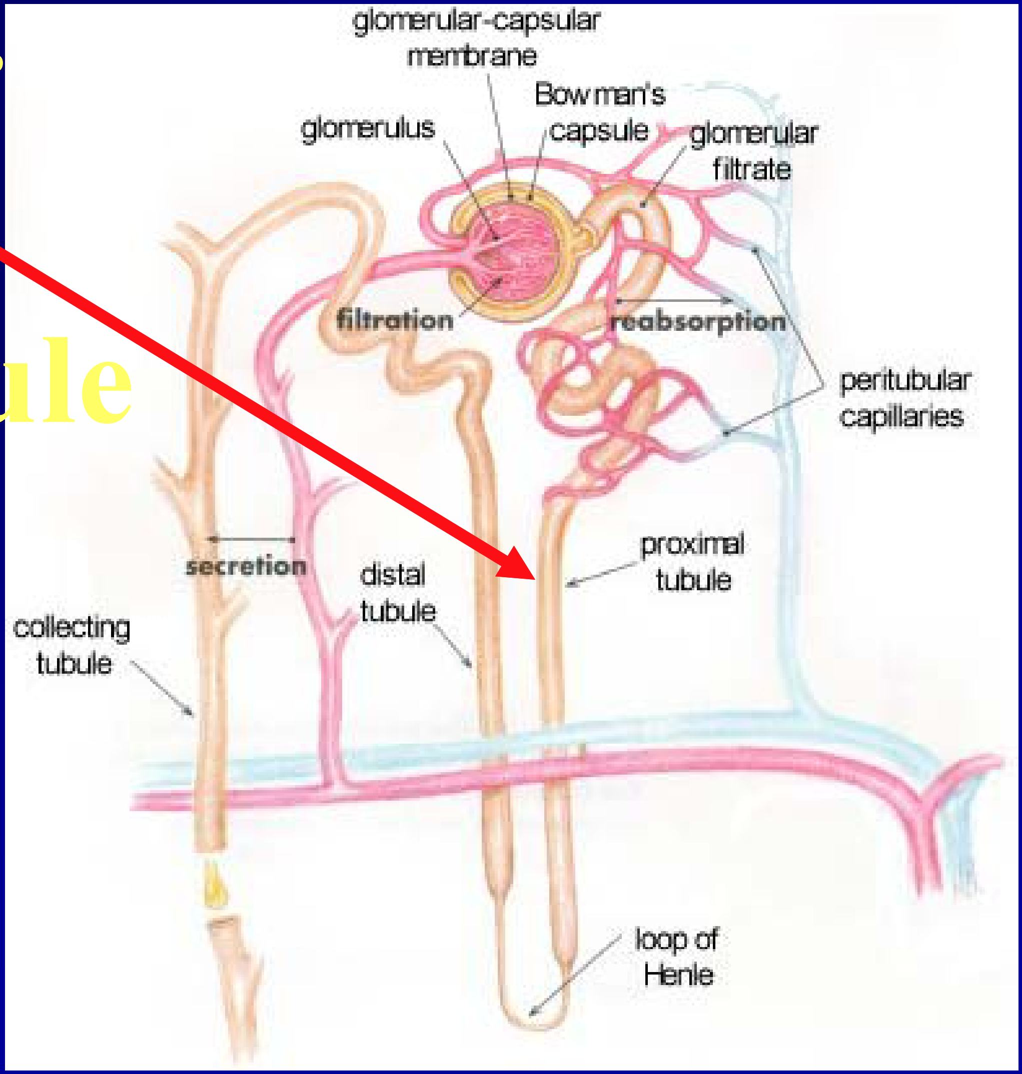
…that is some refining power

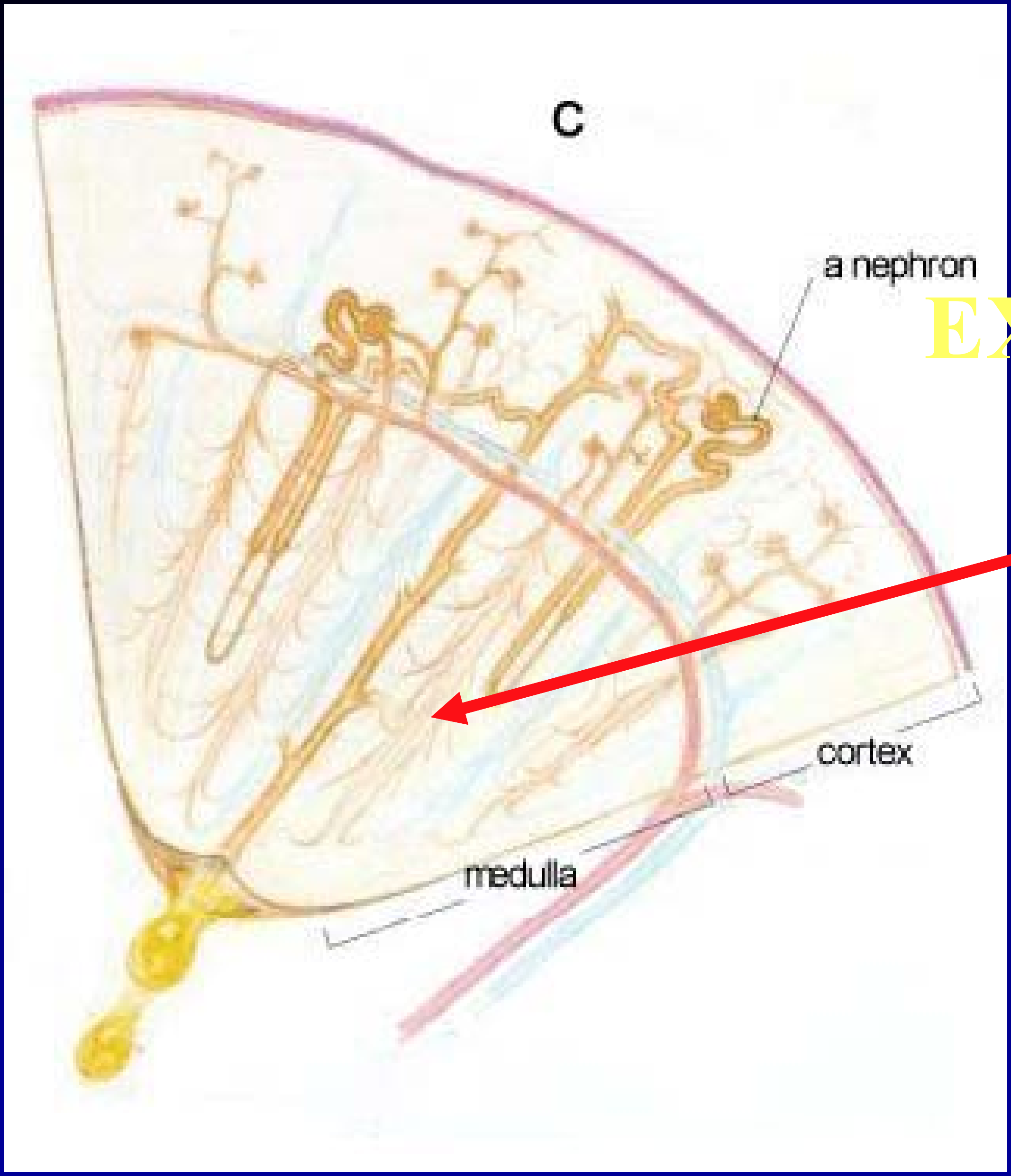
With a GFR of 120 ml/min (180 L/day) 25,000 mEq of sodium (about half a kilogram) are filtered out per day, almost all of which are reabsorbed



A “Trip through the Tubules”

Tubular fluid is iso-osmolar in the proximal tubule

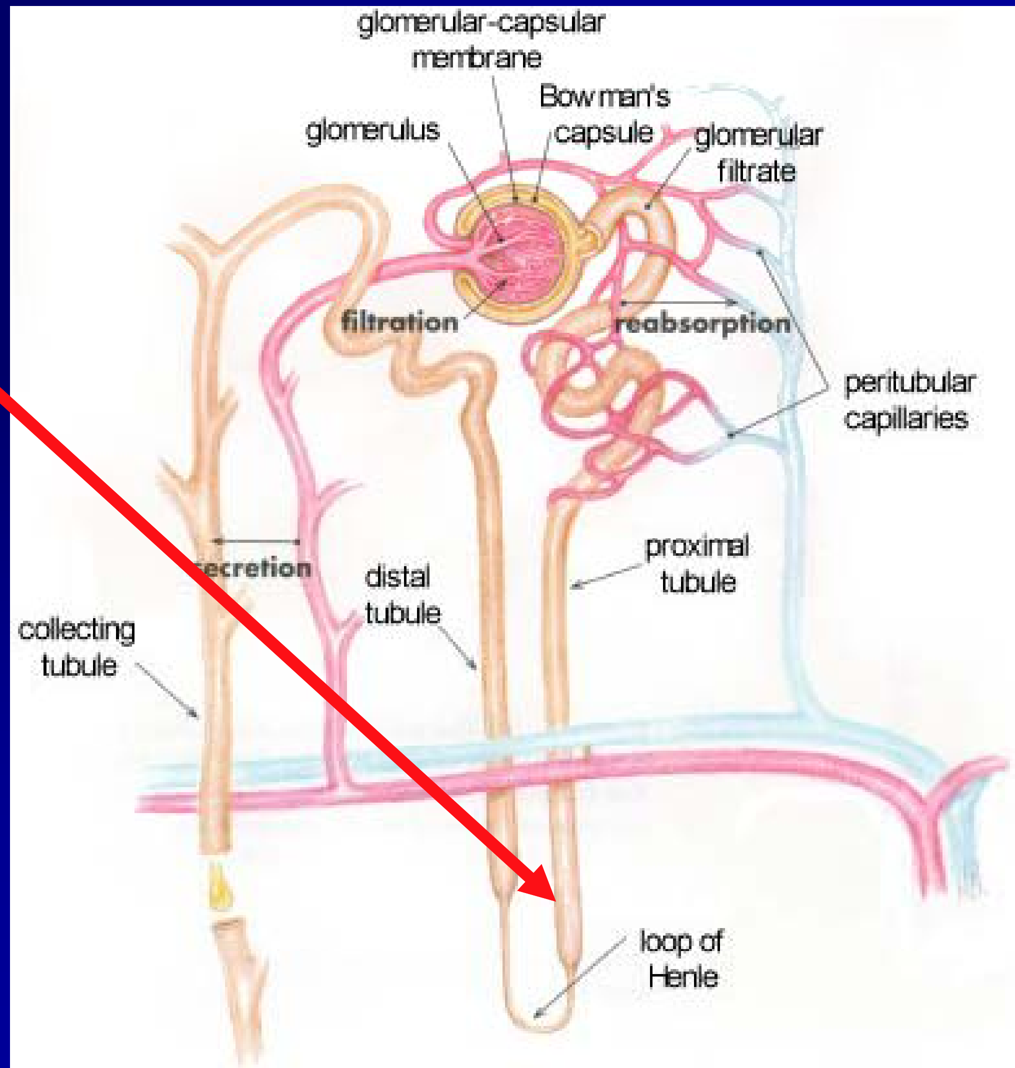




The Renal Medulla is EXCEEDLINGLY concentrated and highly osmotically concentrated

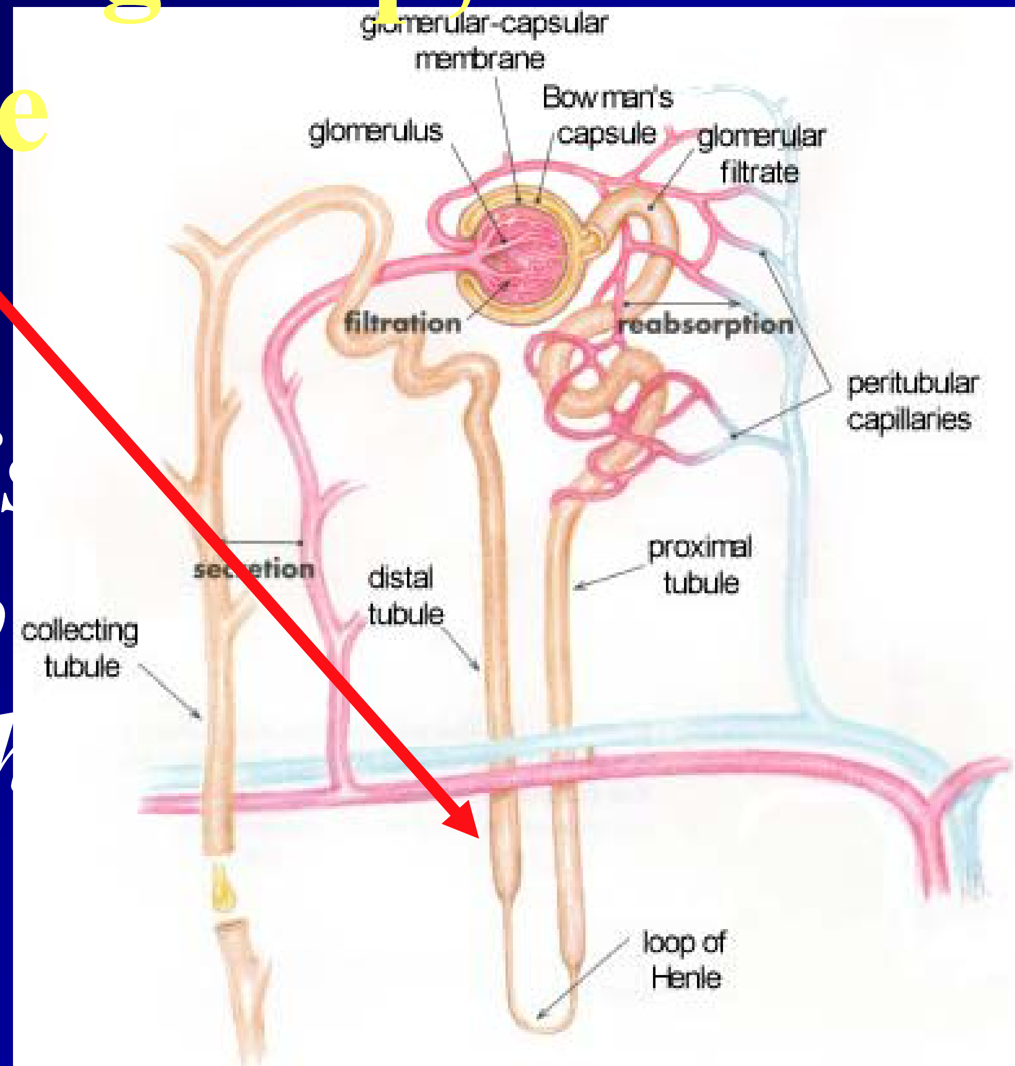
…2 – 4 times the osmolarity of the filtrate

Water, then, is reabsorbed in the descending loop of Henle



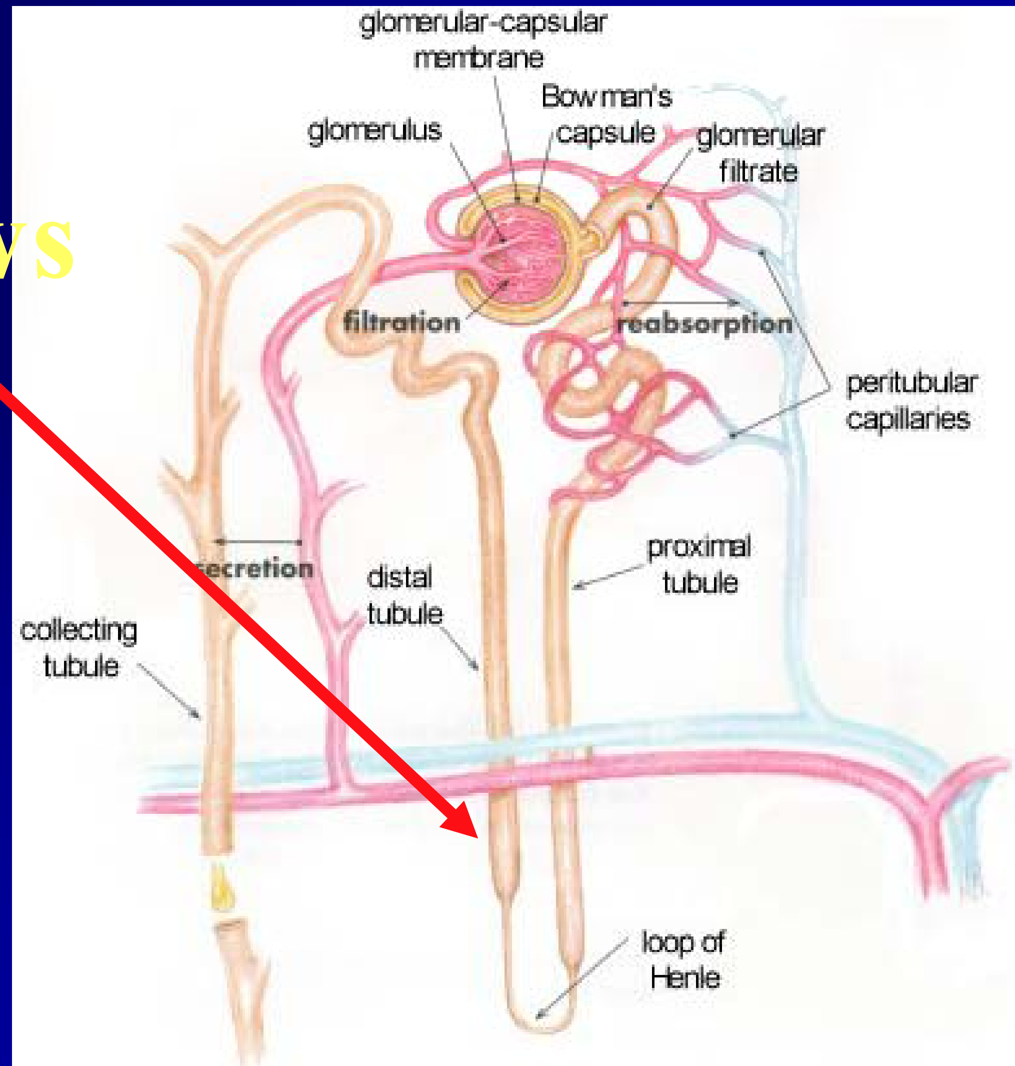
In the ascending loop, Na / K / Cl are reabsorbed

…this portion i
impermeable to
water, even with
↑↑ ADH

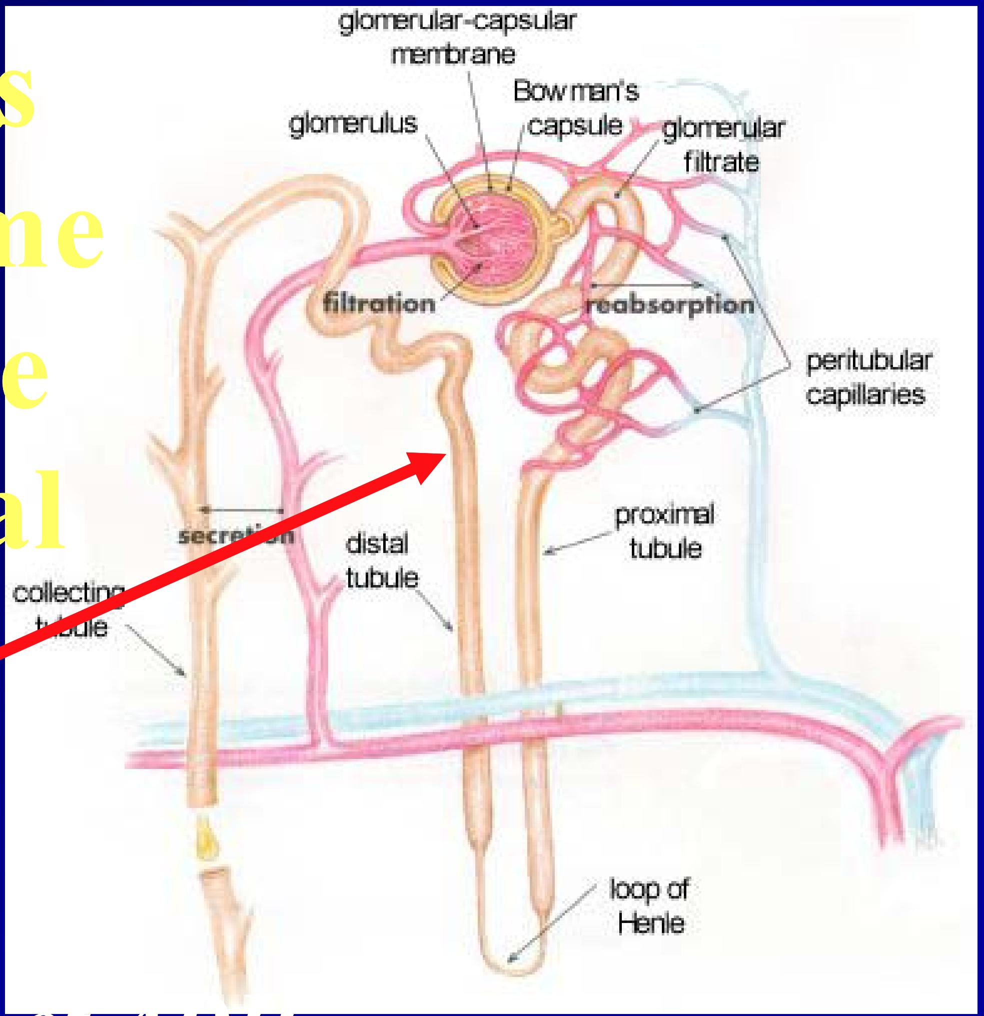


Tubular fluid becomes more dilute as it flows up the ascending loop

…osmolarity of 100 mOsm/L



In the Distal Tubules and Collecting Ducts fluid may become even more dilute due to additional reabsorption of NaCl



…impermeable
to water in ABSENCE of ADH
(osmolarity ↓ to 50 mOsm/L

Urine Sodium is the

"signal"

of what the body is trying to do

…unless the kidneys are failing

Look at
the BODY…

…then look
at the SIGNAL!

Look at Hydration and Hemodynamic Status

…and then look at the fluid being eliminated

How effective is the SIGNAL?

We can excrete as little as 1 meq Na^+ per day

…or as much as 5000 meq Na^+

How effective is the SIGNAL?

We can dilute urine
to as little as
50 mOsm/L of solute
in 300 cc urine

…or concentrate as much
as 1400 mOsm/L

It's what 2 million nephrons with multiple hormal signals will do for you

…and, it's what an organ that processes 36 times your blood volume per day can do

The renal excretion of water is independent of solute excretion

…the primary effector or water excretion is ADH (vasopressin)

When Osmolarity is greater than normal, the posterior pituitary secretes ADH

…increases permeability of the distal tubules and collecting ducts to water

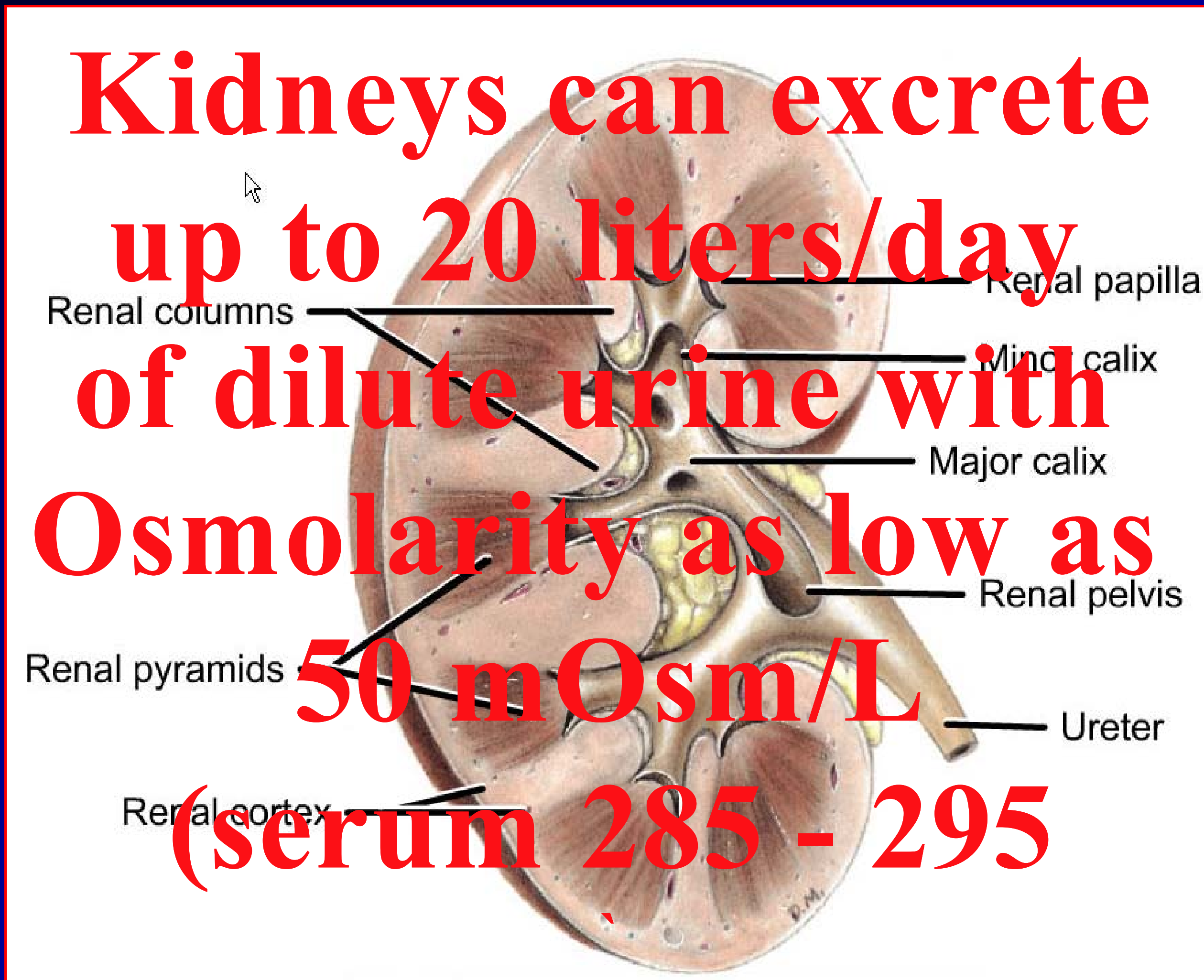
When Osmolarity is greater than normal, the posterior pituitary secretes ADH

- ↑ ***Water absorption***
- ↓ ***Urine volume***
- ***Does not markedly alter rate of renal excretion of solute***

When Osmolarity is less than normal, the posterior pituitary secretes less ADH

…reduces the permeability of distal tubules and collecting ducts to H_2O

Kidneys can excrete up to 20 liters/day of dilute urine with Osmolarity as low as 50 mOsm/L (serum 285 - 295



After drinking a liter of H_2O, within 45 minutes urine volume ↑ by 600%

…with urine concentration falling from 600 mOsm/L to 100 mOsm/L

The kidneys can concentrate the urine to 1400 mOsm/L

…desert animals can concentrate urine to 10,000 mOsm/L, surviving in the desert without drinking water, getting water only from food

Sea water has 2400 mOsm/L

…but the lowly Australian hopping mouse can excrete the salt load in a liter of sea water in 200 cc of urine and could thus drink sea water with impunity

A normal human excretes 600 mOsm of solute per day

…if maximum concentrating ability is 1200 – 1400 mOsm/L, then: 600/1200 = 0.5 L/day minimal urine volume to excrete normal solute waste

Electrolyte Requirements

Sodium – 1.0 – 1.5 mEq/Kg (43.4 mEq/gram)

Potassium – 0.5 – 0.75 mEq/Kg (~ ½ Sodium)

Chloride - 1.0 – 1.5 mEq/KG

Common IV Solutions

Solution	Glucose (g/L)	Na^+	K^+	Ca^{2+}	Cl^-	Lactate	PO_4^{3-}	Mg^{2+}
5% Dextrose (D5W)	50	0	0	0	0	0	0	0
10% Dextrose (D10W)	100	0	0	0	0	0	0	0
Normal Saline (NS)	0	154	0	0	154	0	0	0
D5NS	50	154	0	0	154	0	0	0
D5 ½ NS	50	77	0	0	77	0	0	0
0.2% NS	0	31	0	0	31	0	0	0
3% NaCl	0	513	0	0	513	0	0	0
Ringer's Lactate (RL)	0	130	4	3	109	28	0	0
D5 RL	50	130	4	3	109	28	0	0

Urine Sodium

is the *"sign"* of what the body is trying to do

…unless the kidneys are failing…

Fractional excretion of sodium

The fraction of sodium actually excreted by the body relative to the amount filtered by the kidney.

Fractional excretion of sodium

$$Fe_{Na} = \frac{U_{Na} / P_{Na}}{U_{Cr} / P_{Cr}}$$

Fractional excretion of sodium

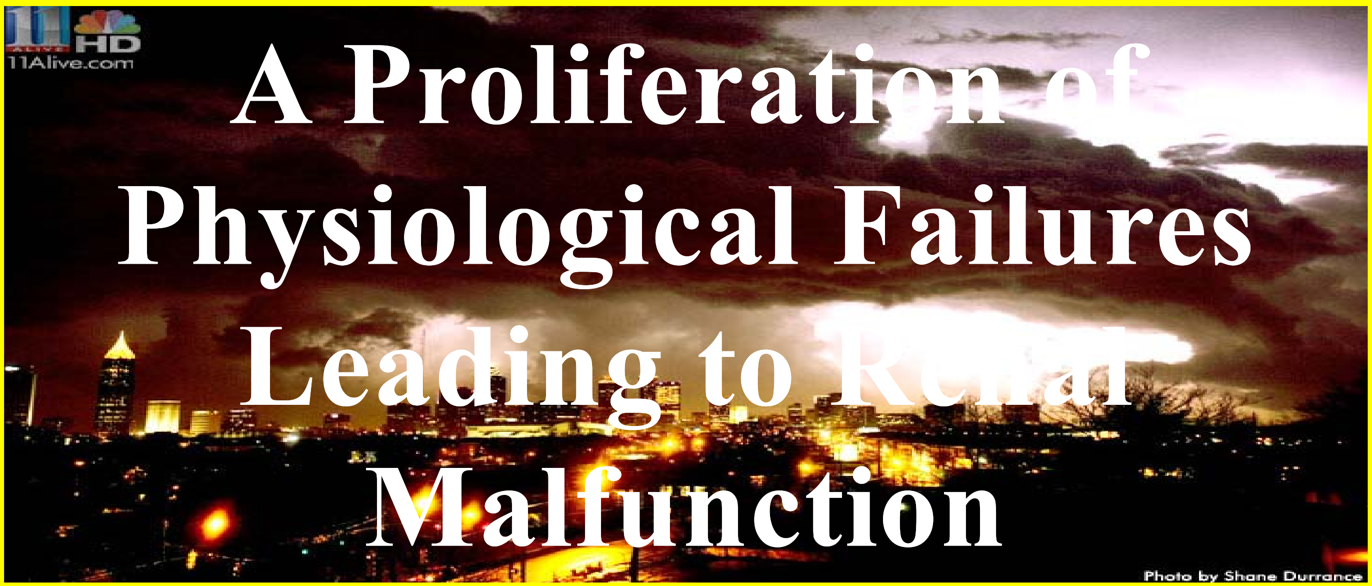
FE_{Na} should be 1% - 3%.

Anything higher than 3% indicates impaired tubular function.

Diuretics <u>MAY</u> elevate this number


...which brings
us to...

Acute Renal Failure



A Proliferation of Physiological Failures Leading to Renal Malfunction

Acute Renal Failure:

- Definition
- Acute Renal Failure vs.
  Chronic Renal Failure
- Etiology
- Pre-renal causes
- Intrinsic Renal Diseases
- Acute Tubular Necrosis
- Presentation of Renal Failure
- Evaluation of the Patient
- Management

Acute Renal Failure:

Definition:

a. A sudden/severe decline in renal function resulting in accumulation of nitrogenous waste products

b. On a continuum with azotemia and renal insufficiency

c. May be accompanied by severe metabolic derangements

- metabolic acidosis, volume overload, and hyperkalemia

Acute Renal Failure:

Acute vs. Chronic Renal Failure

a. Requires review of past history, records or labs

b. Important because aim in ARF is to reverse RF, aim in CRF is to treat complications

c. Consider that ARF may be superimposed on CRF

Type of ARF	Examples
Prerenal Azotemia	•Hypovolemia •Hypoalbuminemia •Heart Failure •Hypotension •Renal artery/vein disease
Intrinsic Renal Disease Vascular	•Vasculitis •Scleroderma •Malignant HTN
Glomerular	•Glomerulonephritis •SLE •Goodpasture's
Interstitial	•Drugs •Toxins •Infections
Acute Tubular Necrosis	•Post Ischemia (post Prerenal) •Myoglobinuria/hemoglobinuria •Toxins (iodine contrast, aminoglycosides)
Post Renal Obstruction	•Extrarenal (tumor, neurogenic, urethral calculi or stricture) •Intrarenal – bilateral or affecting single functioning kidney (calculi, tumor, papillary necrosis

Acute Renal Failure:

Prerenal causes – Due to low blood flow to the kidney

a. Systemic Disease
b. Renal Artery/Vein Disease

Acute Renal Failure:

Systemic Disease

a. Hypovolemia
b. Hypotension
c. Third spacing of fluids
d. Congestive heart failure
e. Hypoalbuminemia – cirrhosis, nephrotic syndrome

Acute Renal Failure:

<u>Renal Artery/Vein Disease</u>

(some classify as *Intrinsic Renal Disease)*

a. Decreased blood flow

(1) ACE inhibitors in the setting of bilateral renal artery stenosis

(2) Prostaglandin Inhibitors – NSAID's and ASA cause renal artery constriction

b. Artery obstruction (disease must be bilateral or affect the single functioning kidney)

(1) Trauma

(2) Aortic Aneurysm/Dissection

(3) Tumor compression

(4) Thromboembolic Disease

Acute Renal Failure:

Intrinsic Renal Disease – 5-10% of ARF in adults, 40-60% of ARF in pediatrics

a. Vascular

(1) Malignant Hypertension
(2) Scleroderma
(3) TTP/Hemolytic Uremic Syndrome (HUS)

Acute Renal Failure:

Intrinsic Renal Disease – 5-10% of ARF in adults, 40-60% of ARF in pediatrics

b. Glomerular

(1) Systemic Vasculitis (polyarteritis, Wegener's, HSP)
(2) Goodpasture's Syndrome
(3) SLE
(4) Glomerulonephritis (Immune complex, post-strep, and rapidly progressive glomerular nephritis)

Acute Renal Failure:

<u>Intrinsic Renal Disease</u> – 5-10% of ARF in adults, 40-60% of ARF in pediatrics

c. Interstitial

(1) Drugs – probably immune related, not dose dependent, reoccurs with repeat exposure
- a. Penicillins
- b. Diuretics
- c. NSAIDS

(2) Toxins
- a. Heavy Metals
- b. Ethylene Glycol

(3) Infections – probably immune related
- a. Bacterial
- b. Rickettsia

Acute Renal Failure:

Acute Tubular Necrosis – most common cause of ARF in adults

1. Post – Ischemic
   - Most commonly results from severe pre-renal azotemia
2. Nephrotoxins
   - a. Antibiotics – aminoglycosides
   - b. NSAIDS
   - c. Iodine contrast
   - d. Myoglobinuria
   - e. Hemoglobinuria
3. Exclude pre-renal, post-renal, and instrinsic disease if ARF continues despite treatment

Presentation of Acute Renal Failure:

No particular clinical presentation is unique to Acute Renal Failure

1. Volume Status
   - Hypovolemic
   - Euvolemic
   - Volume overload

Presentation of Acute Renal Failure:

2. Azotemia
   a. Asymptomatic – only apparent on blood test
   b. Uremic Syndromes
      (1) Altered mental status
      (2) Pericardial disease
      (3) Pruritis
      (4) Nausea/vomiting

Presentation of Acute Renal Failure:

3. Metabolic
   - a. Hyperkalemia - dysrhythmias
   - b. Metabolic acidosis
   - c. Hyponatremia
   - d. Hypocalcemia
     - (1) Usually asymptomatic
     - (2) May result in tetany after bicarb given
   - e. Hyperphosphatemia
   - f. Hypermagnesemia

Presentation of Acute Renal Failure:

4. Hematologic
   a. Anemia – if renal disease is long-standing
   b. Thrombocytopenia
   c. GI bleeding from bleeding diathesis

Presentation of Acute Renal Failure:

5. Active Urinary Sediment
   a. Red cell casts suggest glomerulonephritis
   b. Azotemia in the setting of a normal urinalysis suggests obstruction

Evaluation of the Patient with Acute Renal Failure:

1. *Volume Status!!!!*
2. Physical Exam – distended bladder, pelvic tumor/mass, prostate
3. Uremic Syndrome?
4. Exposure to Toxins?
5. Search for pre-renal and post-renal disease – these are typically reversible
6. Laboratory Results

Test	Pre-renal	Renal	Acute Tubular Necrosis	Post-renal
Urine Sodium (mEq/L)	<20	>40		
Fract Excret of sodium (%)*	<1	>2		
	granular casts	WBC casts	pigmented cellular casts	granular casts
Kidney size	Normal	Normal	Normal	Increased
Radionuclide Study	Poor uptake Delayed excretion	Good uptake Delayed excretion	Variable	Good uptake No excretion

Urine Sodium is Usually Pretty Low!

Thus, a measurement of a HIGH urine Na+ suggests that the kidneys are "wasting salt"

Burton D. Rose, MD

Nephrologist

Boston, MA

"Up to Date"

1998

"Urine sodium concentration — The urine sodium concentration tends to be low in prerenal disease (<20 meq/L) in an appropriate attempt to conserve sodium, and high in ATN (>40 meq/L) due in part to the tubular injury. There is, however, frequent overlap resulting in many cases from variations in water reabsorption which can also affect the urine sodium concentration. As an example, a prerenal patient who is highly water-avid due to increased secretion of antidiuretic hormone may have a higher than expected urine sodium concentration despite excreting relatively little sodium. Conversely, decreased water reabsorption in ATN can lower the urine sodium by dilution. The net effect is that the fractional excretion of sodium (FENa) is a better test, because it evaluates only sodium handling (the fraction of the filtered sodium that is excreted) and is not affected by changes in water reabsorption."

Management of the Patient with Acute Renal Failure:

Remember folks!!

Potassium rises 0.6 mEq/L for every decrease of 0.1 pH on the ABG. So, even if the potassium is 6.4, if the pH is 7.00, then the patient has a corrected K+ of 4.0.

)

(5)Lasix

(6)Albuterol

Management of the Patient with Acute Renal Failure:

1. Treat Complications
   b. Volume Overload
   c. Hypocalcemia
      (1)May be precipitated by Bicarb
      (2)Tetany – calcium gluconate
   d. Hypermagnesemia
      (1)Avoid extra magnesium in antacids or laxatives

Management of the Patient with Acute Renal Failure:

1. Treat Complications

   e. Hyperphosphatemia

      (1)Limit phosphate in diet

      (2)Use phosphate absorbing antacids

   f. Pericarditis

      - In ARF, is indication for urgent dialysis

   g. Correct bleeding diathesis/platelet abn.

      (1)Cryoprecipitate

      (2)DDAVP (raises Factor VIII four-fold)

Management of the Patient with Acute Renal Failure:

2. Pre-renal – improve blood flow to kidney

a. Replace volume

b. Dopamine

c. Relieve compromised blood flow

(1) Renal artery stenosis and ACE inhibitor

(2) Trauma/tumor

•Hyperkalemia

•Volume Overload, with cardiopulmonary compromise

•Acidosis

•Hypertension, severe and uncontrolled

•Drug toxicity – salicylate, lithium, theophylline (charcoal hemoperfusion preferred), methanol, ethylene glycol

•Possible Indications:
Pericarditis, progressive altered mental status from uremia

b. Transfer, if nephrologist or dialysis unavailable

Acute Renal Failure:

Glomerulonephritis

1. Syndrome of hematuria, proteinuria
2. Immune mediated inflam. of glomerulus
3. Post-streptococcal most common in childhood
4. Presentation
   a. Edema
   b. Hematuria
   c. Hypertension
   d. ARF
5. Management
   a. Most admitted =>> Definitely consult!
   b. Manage complications of ARF

MANAGING COMPLICATIONS OF ARF

- Hyperkalemia
- Volume Overload
- Hypocalcemia
- Hypermagnesemia
- Hyperphosphatemia
- Pericarditis
- Pre-renal (Replace volume, dopamine,
- Relieve compromised blood flow)
- Renal
- Post Renal – Relieve obstruction
- Encourage Urine Flow (Mannitol, Lasix)
- Possible need for Dialysis

Acute Renal Failure:

Nephrotic Syndrome

1. Syndrome of proteinuria, hypoalbuminemia, edema, hyperlipidemia
2. Glomerular disease causing protein leaking
3. Peak: Ages 2-7 years – minimal change nephrotic syndrome most common
4. Clinical Presentation
   a. Edema
   b. Hematuria and hypertension unusual
5. Management
   a. Most admitted – definitely consult
   b. Manage complications of ARF
   c. Lasix is diuretic of choice

Chronic Renal Failure

1. Irreversible renal function loss
2. Kidneys usually small and scarred
3. GFR > 25% normally tolerated well
4. GFR < 25% caused end-stage renal disease
5. Evaluation is centered around ruling ARF and ARF superimposed on CRF
6. Treatment
    a. Dialysis
    b. Transplant

Hemodialysis Complications

1. Vascular Access
   a. Fistula is vein redirected, vs. graft is artificial
   b. No blood draw, tourniquet or BP in extremity with shunt
   c. In life-threatening emergency, can access shunt:
      (1) Sterile technique
      (2) DO NOT PUNCTURE BACK WALL
      (3) Will need pump for IV fluid
      (4) Use non-occlusive pressure to halt bleeding

Hemodialysis Complications

1. Vascular Access
   d. Shunt thrombosis – loss of thrill, then consult vascular surgeon: Some are using thrombolytics
   e. Shunt infection
      (1) Red, warm, tender
      (2) IV antibiotics to cover skin flora
      (3) Likely admission

Hemodialysis Complications

2. Bleeding – Platelet dysfunction and/or heparin complications
3. Hypotension – must search for cause
   a. MI
   b. Pericardial Tamponade
      (1) Due to bleeding
      (2) Symptomatic with volume reduction
   c. Sepsis
   d. Bleeding secondary to anticoagulation
   e. Excessive fluid removal

Hemodialysis Complications

4. Hypokalemia
   a. Only occurs during dialysis
   b. Causes ventricular irritability
   c. With Ventricular fibrillation during dialysis, think about hypokalemia
   d. Digitalis toxicity may be precipitated by hypokalemia from dialysis

Hemodialysis Complications

5. Disequilibrium syndrome
    a. Due to rapid change in osmolality
    b. More common during first dialysis session
    c. Nausea, vomiting, headache
    d. Altered mental status, seizure may occur
    e. Treatment – infuse osmotically active substance
    f. Consider other causes of CHS dysfunction, especially in previously stable dialysis patient

Synthesis

The understanding of renal physiology connects us directly to the evolution of the universe

As with ALL subjects in science, if you don’t give this connection a REGULAR CONSIDERATION…

You'll

LOSE

IT!!!

DON'T

LOSE

IT!!!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and good morning!