General Principles of Pathophysiology

- The Cellular Environment
- Fluids & Electrolytes
- Acid-base Balance & Maintenance

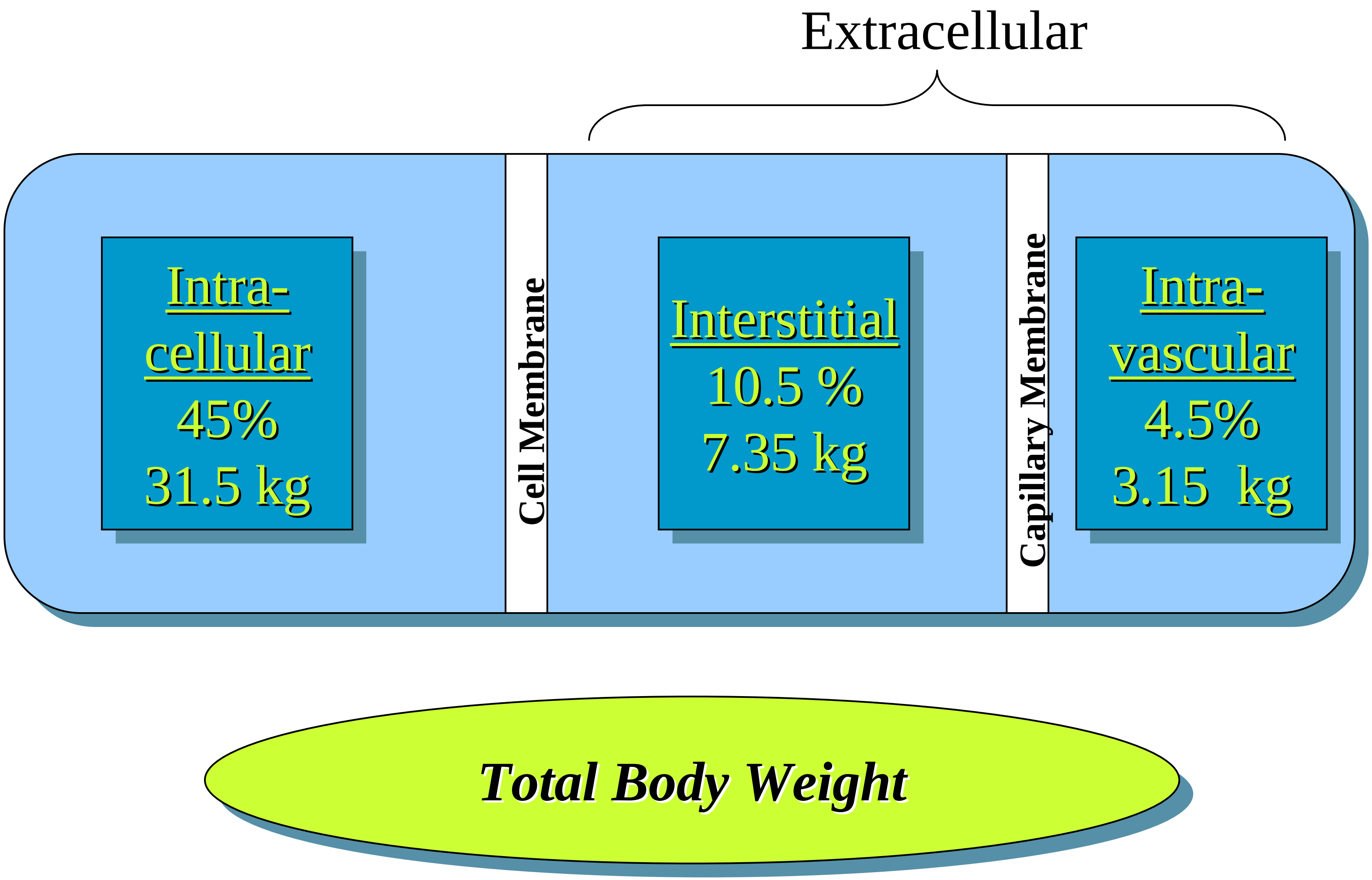
Topics

- Describe the distribution of water in the body
- Discuss common physiologic electrolytes
- Review mechanisms of transport
  - osmosis, diffusion, etc
- Discuss hemostasis & blood types
- Discuss concepts of acid-base maintenance

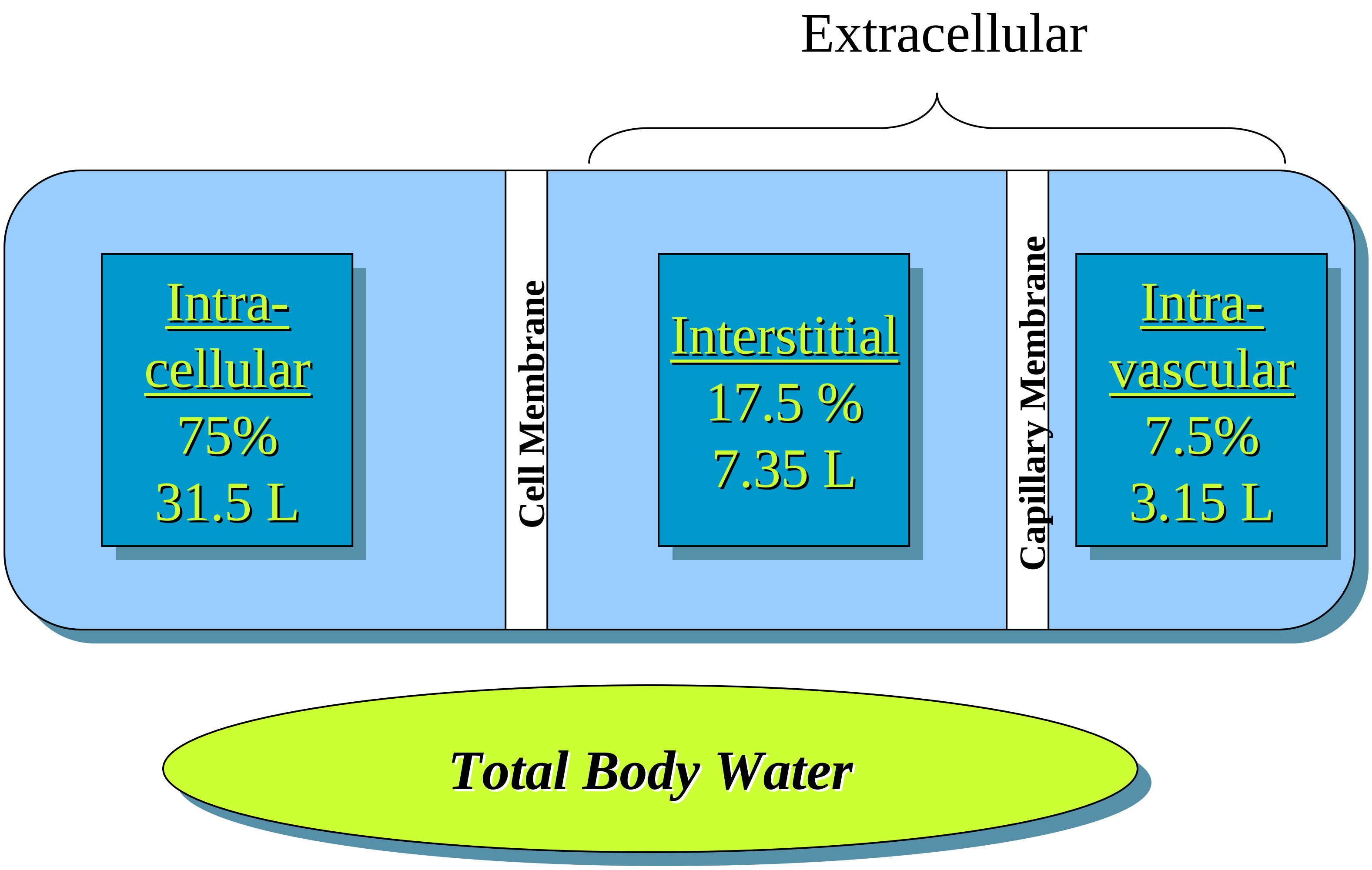
Distribution of Water

- Total Body Weight/ Total Body Water
- Intracellular - ICF (45%/75%)
- Extracellular - ECF (15%/25%)
  - Intravascular (4.5%/7.5%)
  - Interstitial (10.5%/17.5%)

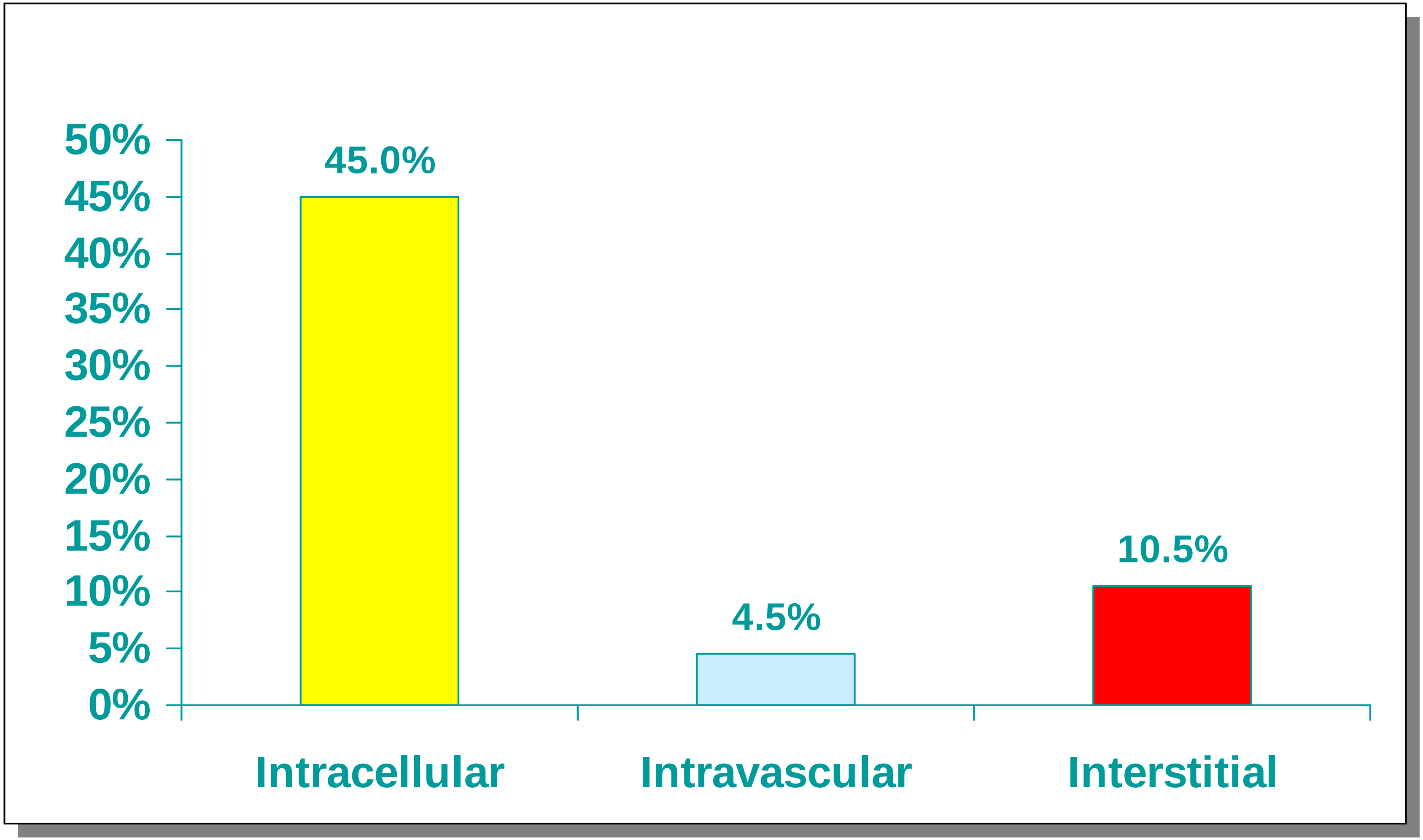
Fluid Distribution



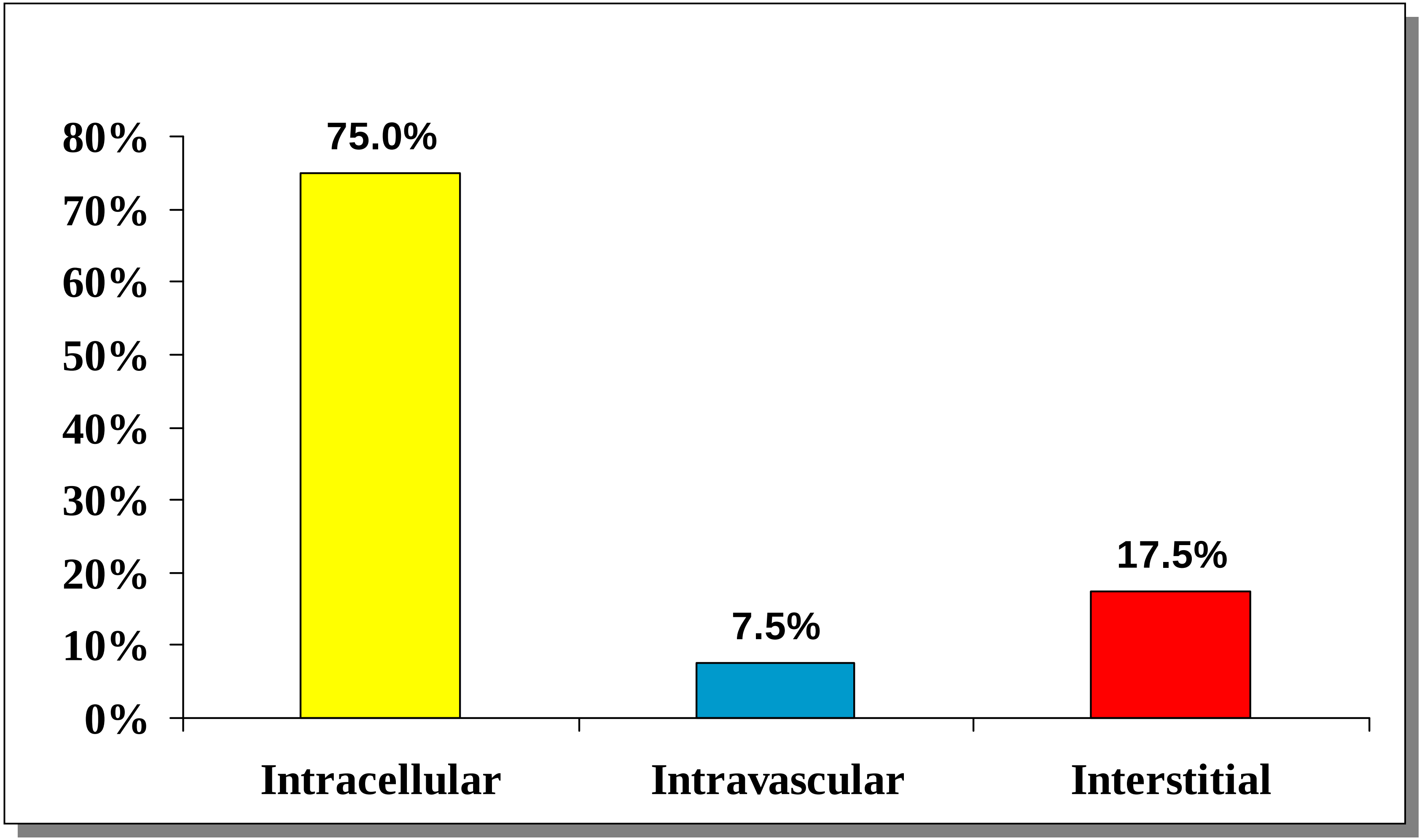
Fluid Distribution



Total Body Weight



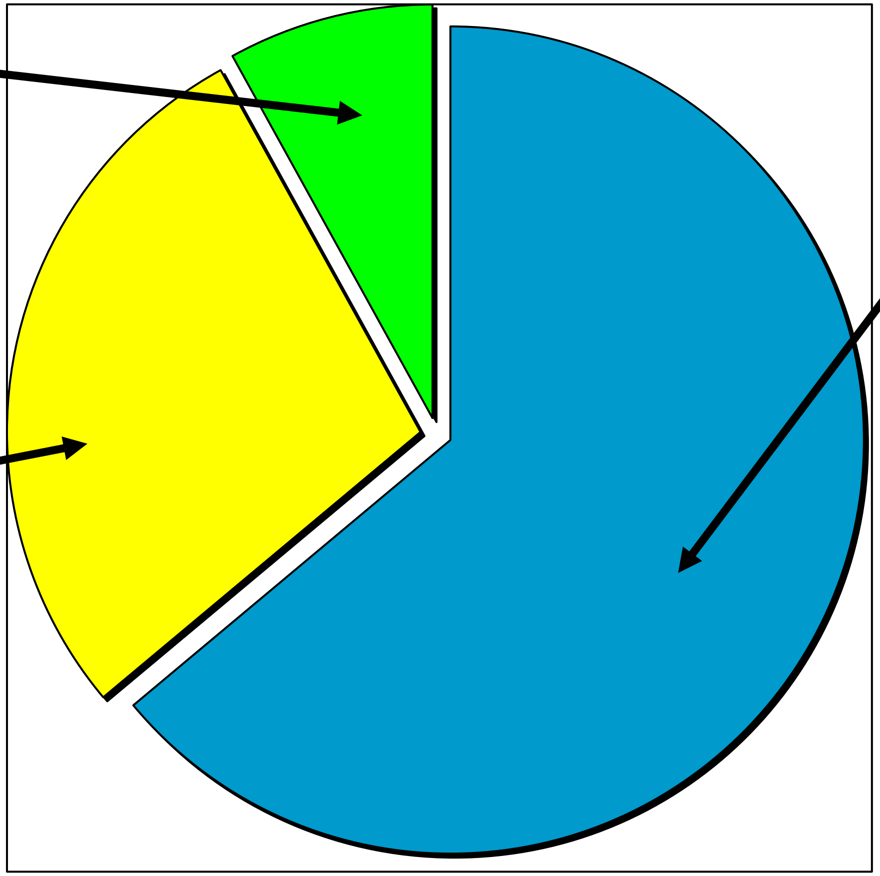
Total Body Water



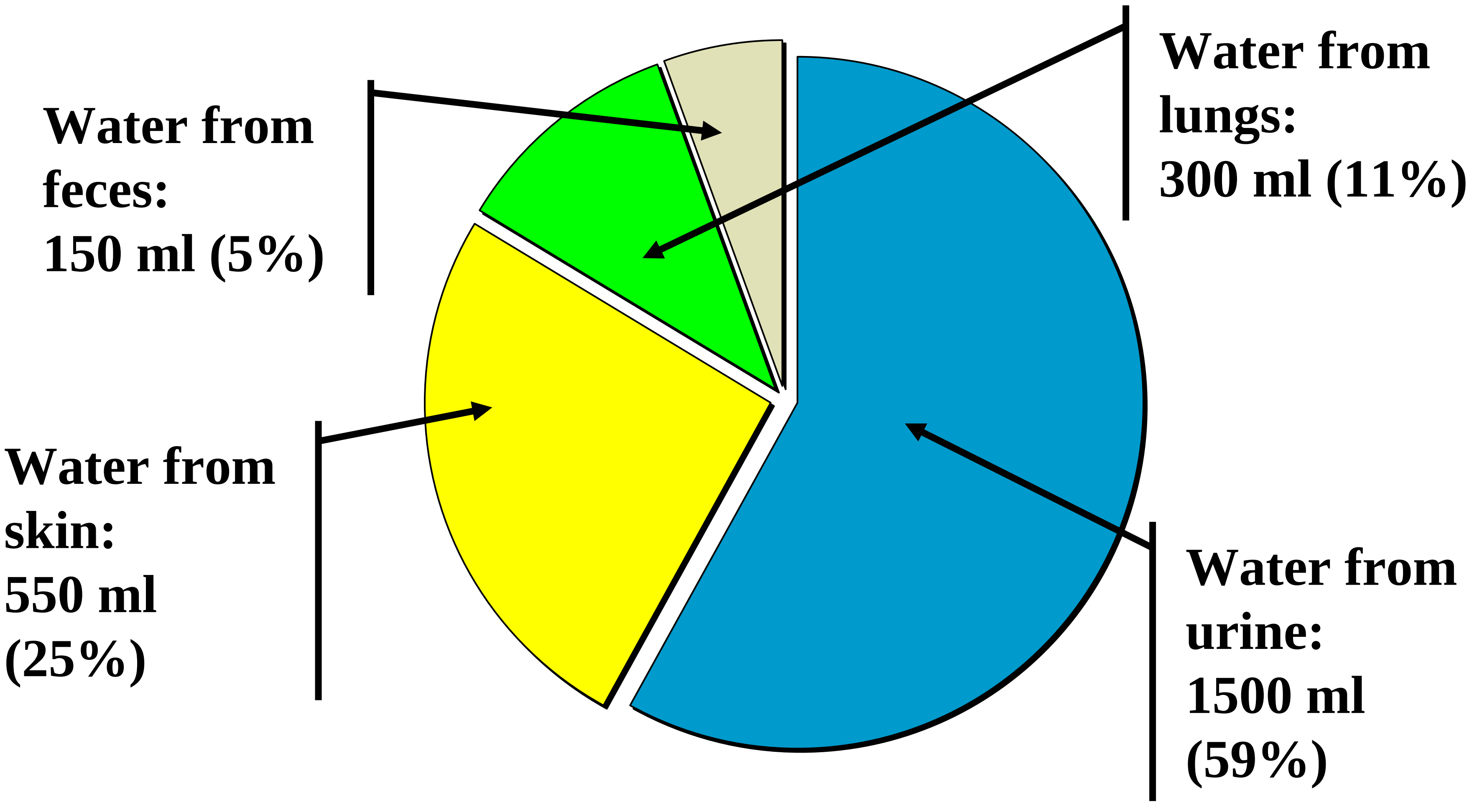
Edema

- Fluid accumulation in the interstitial compartment
- Causes:
  - Lymphatic ‘leakage’
  - Excessive hydrostatic pressure
  - Inadequate osmotic pressure

Fluid Intake



Fluid Output



Osmosis versus Diffusion

- Osmosis is the net movement of water from an area of **LOW** solute concentration to an area of **HIGHER** solute concentration across a semi-permeable membrane.
- *diffusion of water*
  - – in terms of [water]

- Diffusion is the net movement of solutes from an area of **HIGH** solute concentration to an area of **LOWER** solute concentration.

Silly definition stuff

- Osmolarity = osmoles/L of solution

- Osmolality = osmoles/kg of solution

Where an osmole is 1 mole (6.02×10^{23} particles)

The bottom line?
Use them synonymously!

Tonicity

- Isotonic
- Hypertonic
- Hypotonic

Isotonic Solutions

- Same solute concentration as RBC
- If injected into vein: no net movement of fluid
- Example: 0.9% sodium chloride solution
  - aka Normal Saline

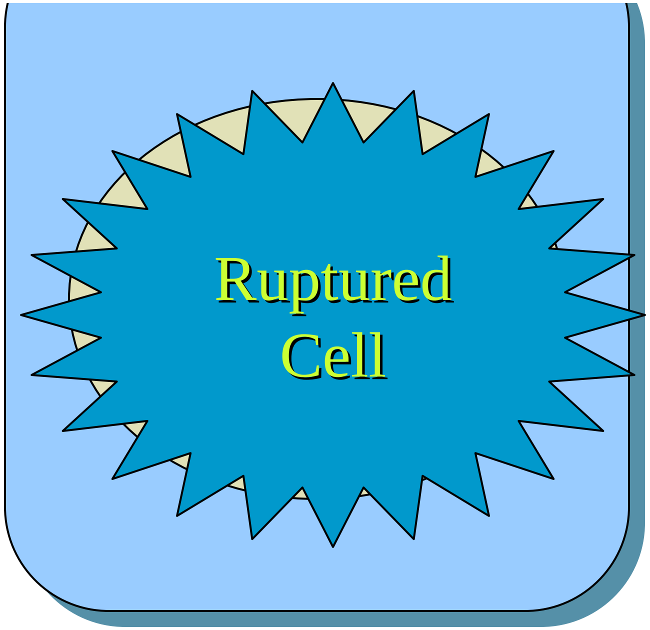
Hypertonic Solutions

- Higher solute concentration than RBC
- If injected into vein:
  - Fluid moves INTO veins

Hypotonic Solutions

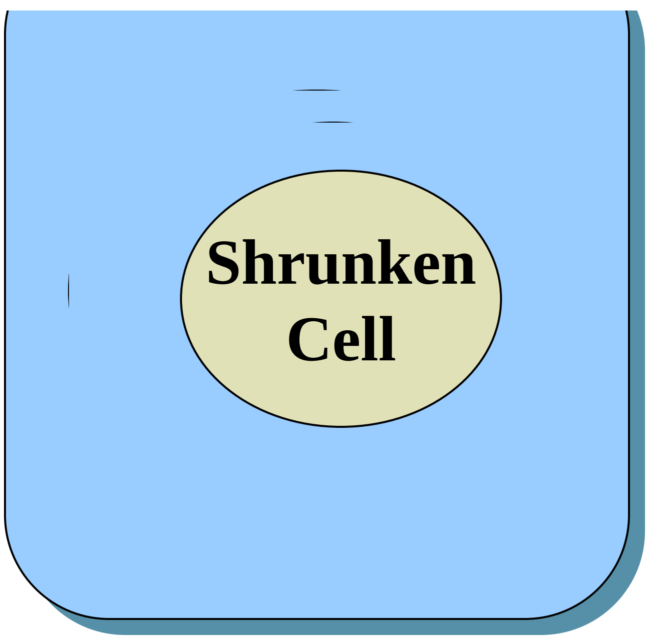
- Lower solute concentration than RBC
- If injected into vein:
  - Fluid moves OUT of veins

Affects of Hypotonic Solution on Cell



- The [solute] outside the cell is lower than inside.
- Water moves from low [solute] to high [solute].
- The cell swells and eventually bursts!

Affects of Hypertonic Solution on Cell



- The [solute] outside the cell is higher than inside.
- Water moves from low [solute] to high [solute].
- The cell shrinks!

- Infusion of isotonic solution into veins

→

- No fluid movement

- Infusion of hypertonic solution into veins

→

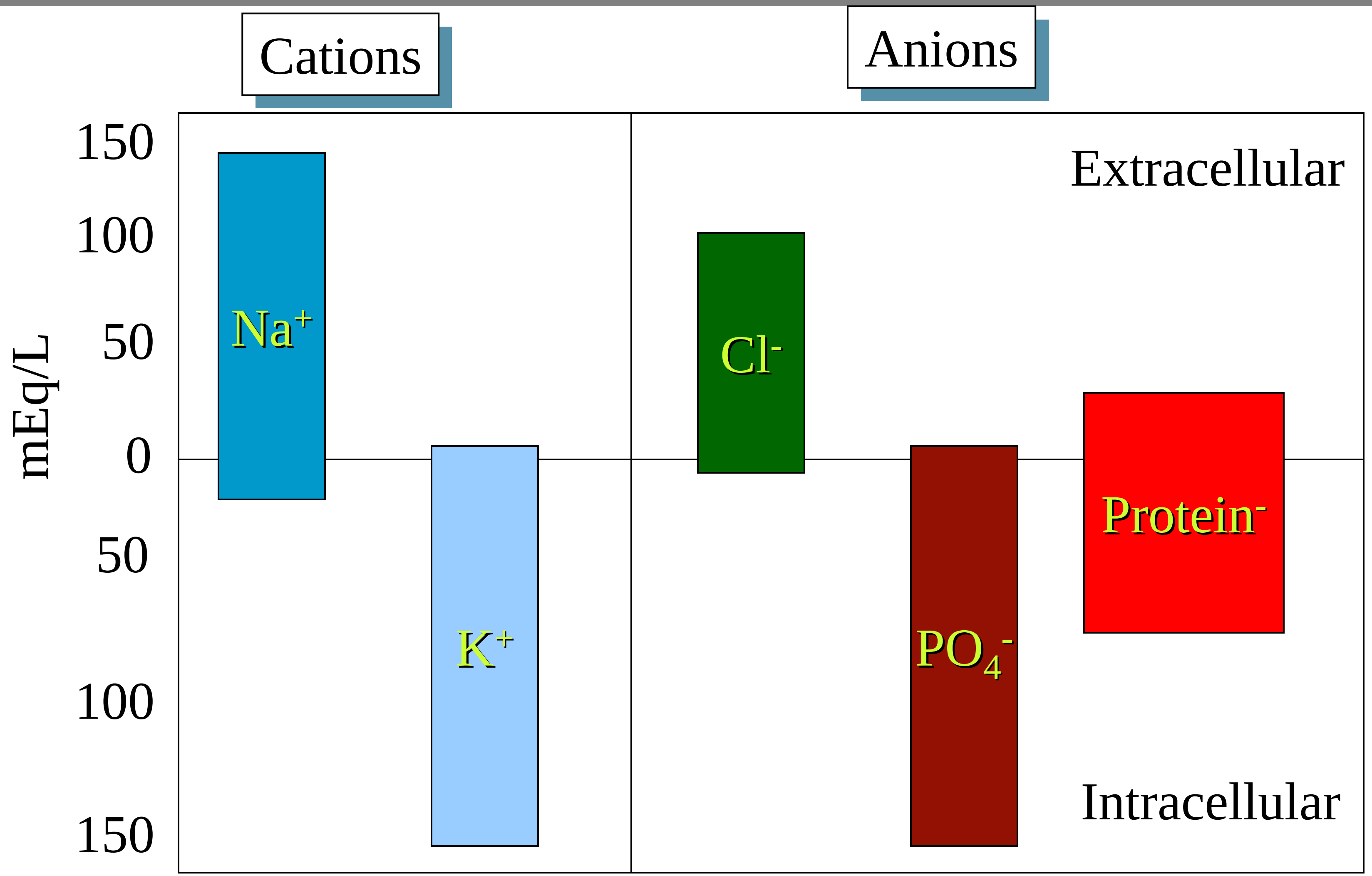
- Fluid movement into veins

- Infusion of hypotonic solution into veins

→

- Fluid movement out of veins

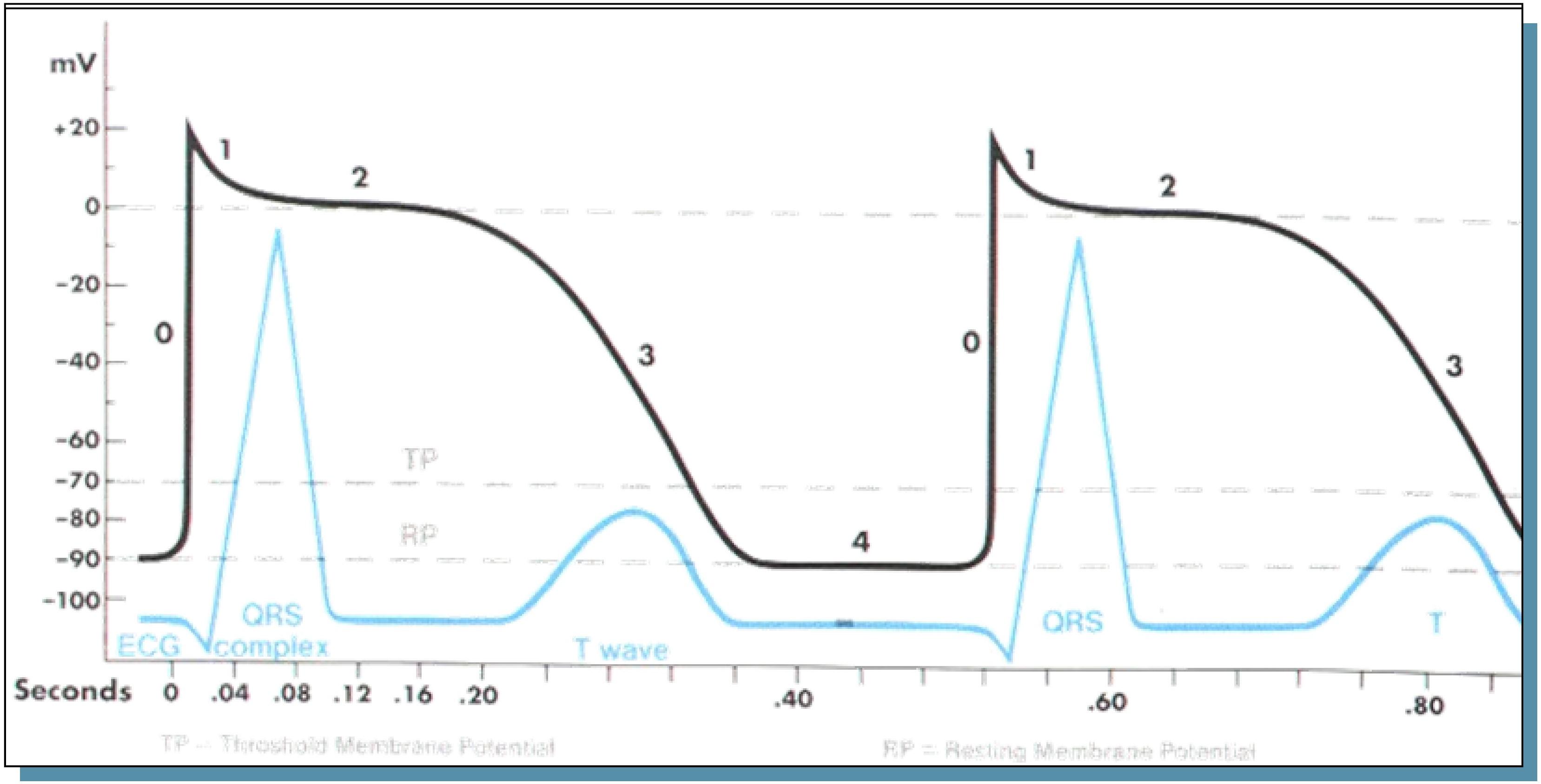
Ion Distribution



Example of Role of Electrolytes

- Nervous System
  - – Propagation of Action Potential
- Cardiovascular System
  - – Cardiac conduction & contraction

Cardiac Conduction / Contraction



Composition of Blood

- 8% of total body weight
- Plasma: 55%
  - Water: 90%
  - Solutes: 10%
- Formed elements: 45%
  - Platelets
  - Erythrocytes

Hematrocrit

- % of RBC in blood
- Normal:
  - 37% - 47% (Female)
  - 40% - 54% (Male)

Blood Components

- Plasma: liquid portion of blood
- Contains Proteins
  - Albumin (60%) contribute to osmotic pressure
  - Globulin (36%): lipid transport and antibodies
  - Fibrinogen (4%): blood clotting

Blood Components

- Formed Elements
  - Erythrocytes
  - Leukocytes
  - Thrombocytes

Erythrocytes

- ‘biconcave’ disc
- 7-8 mcm diameter
- Packed with hemoglobin
- 4.5 - 6 million RBC/mm^3 (males)
- Anucleate
- 120 day life span
- 2 million replaced per second!

Leukocytes

- Most work done in tissues
- 5,000 - 6,000/mm^3
  - – Neutrophils (60-70%)
  - – Basophils (Mast Cells) (<1%)
  - – Eosinophils (2-4%)
  - – Lymphocytes (20-25%)
  - – Monocytes (Macrophages) (3-8%)

Thrombocytes

- Platelets
- Cell fragments
- 250,000 - 500,000/mm^3
- Form platelet plugs

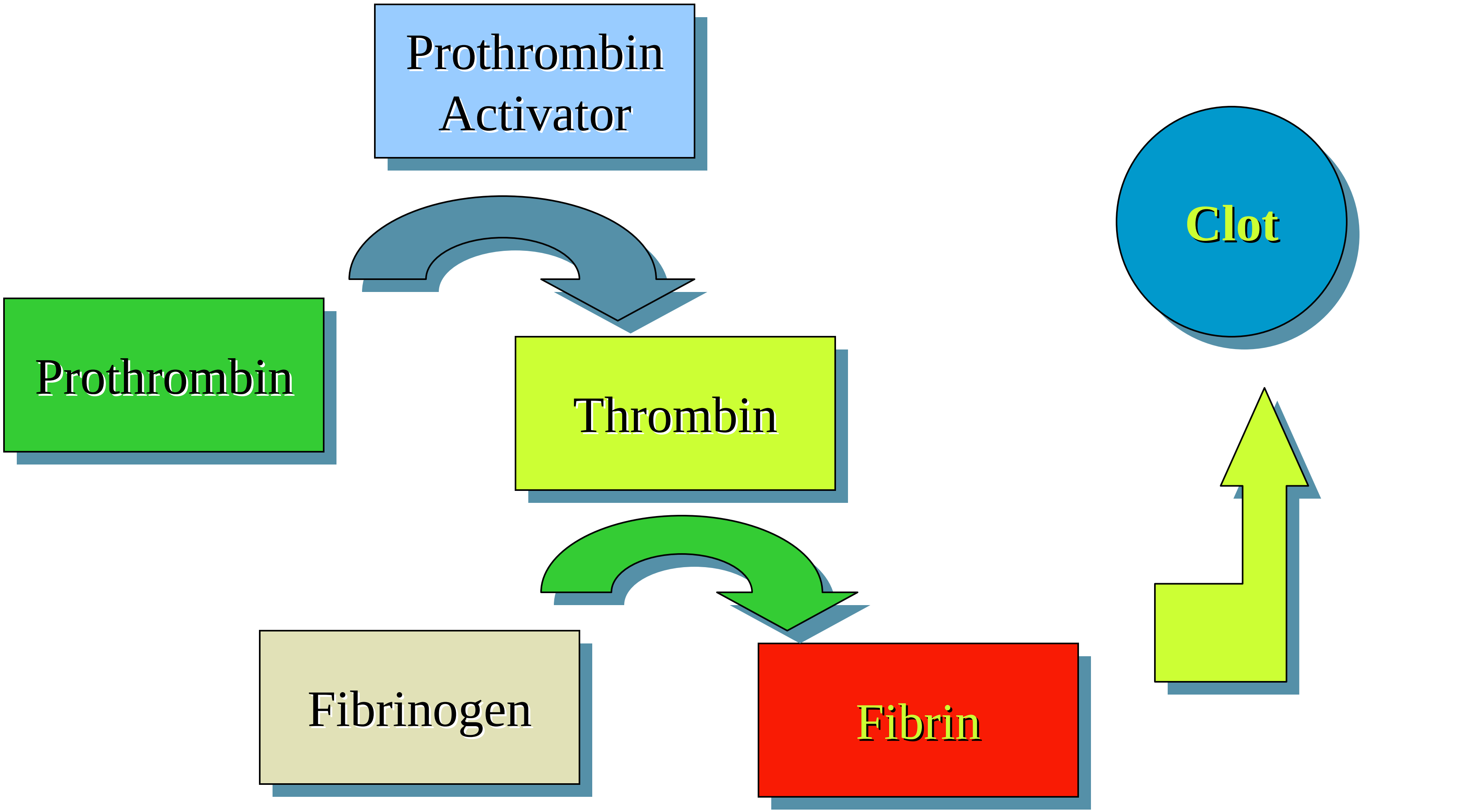
Hemostasis

- The stoppage of bleeding.
- Three methods
  - Vascular constriction
  - Platelet plug formation
  - Coagulation

Coagulation

- Formation of blood clots
- Prothrombin activator
- Prothrombin $\Rightarrow$ Thrombin
- Fibrinogen $\Rightarrow$ Fibrin
- Clot retraction

Coagulation



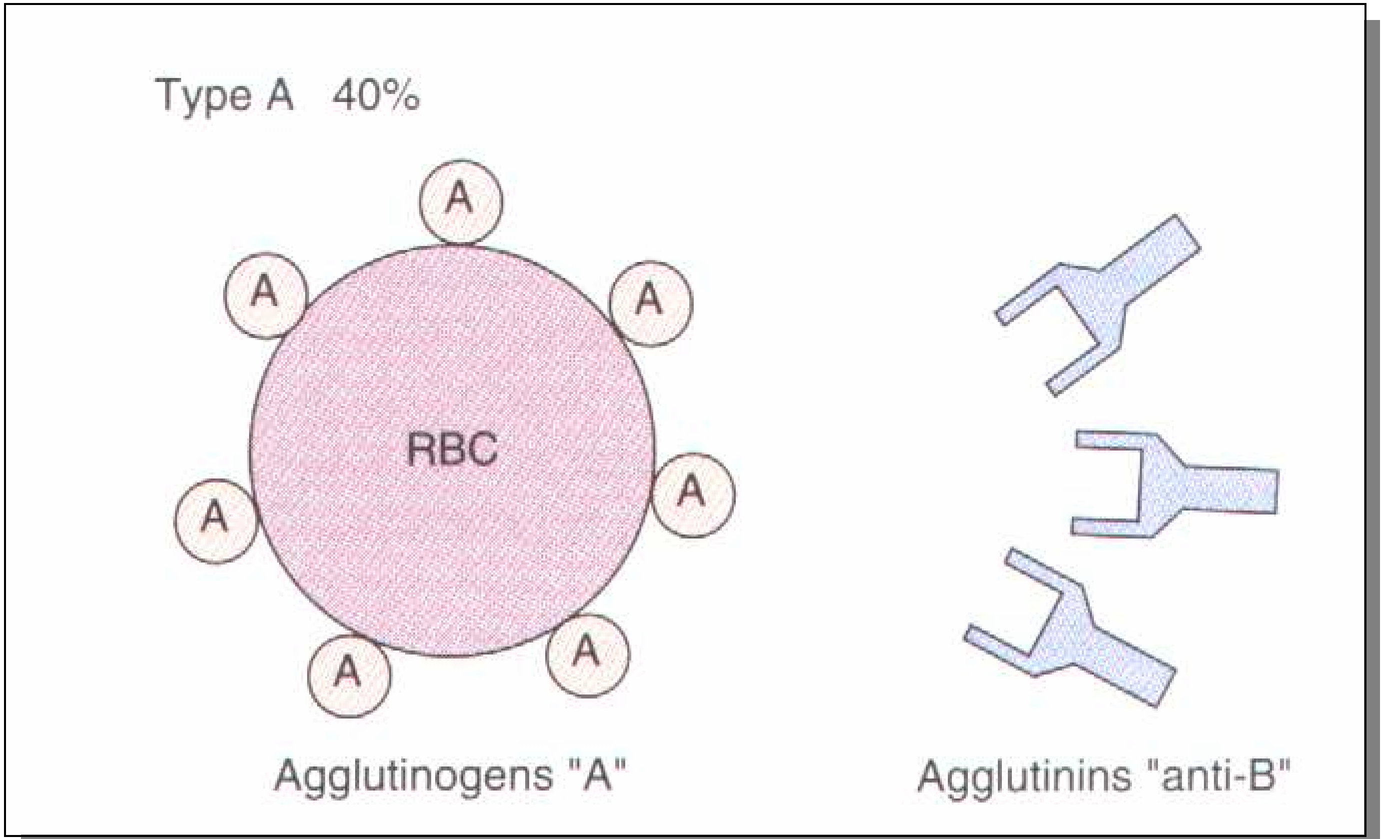
Fibrinolysis

- Plasminogen
- tissue plasminogen activator (tPA)
- Plasmin

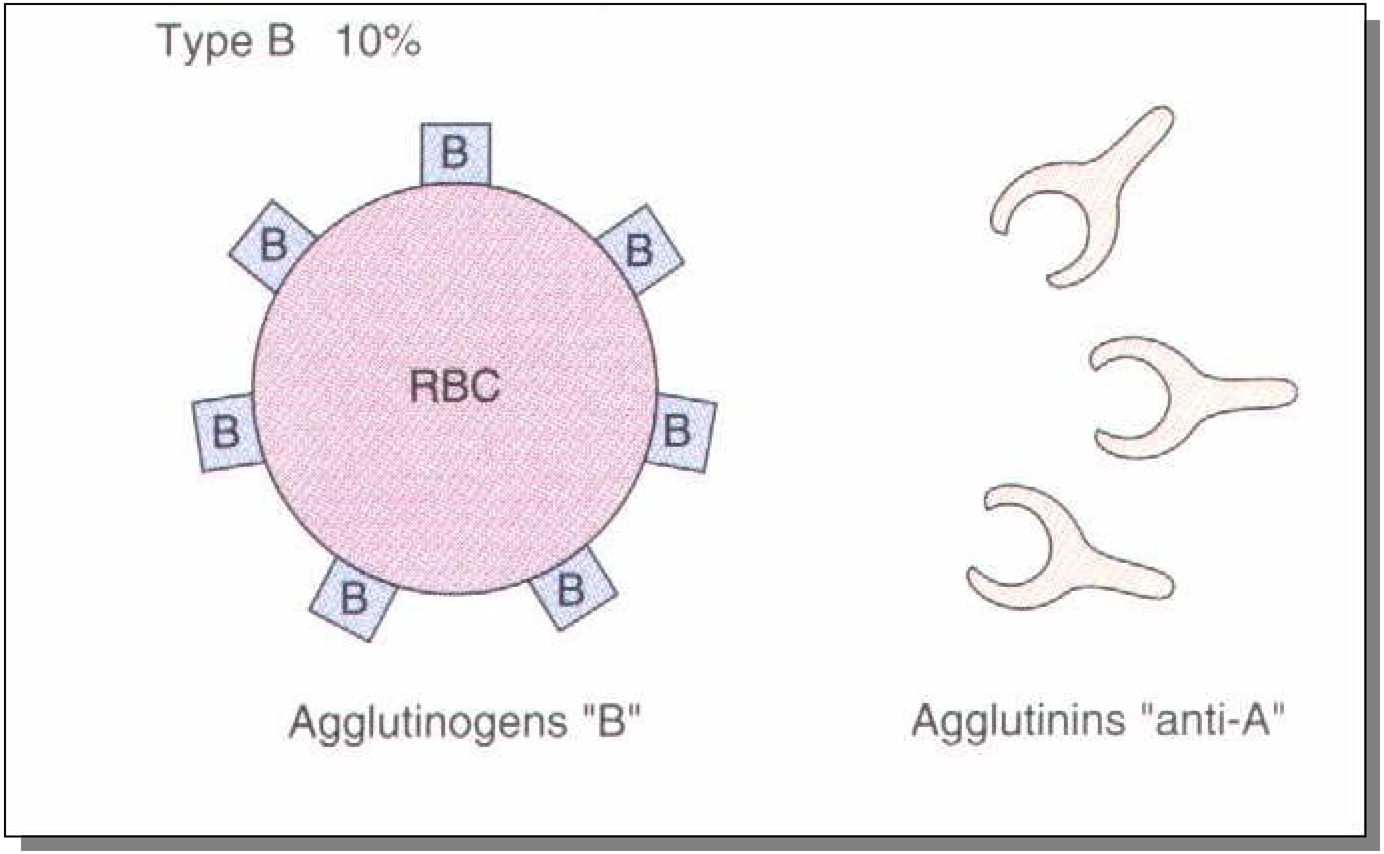
Blood Types

- Agglutinogens (Blood Antigens)
- Agglutinins (Blood Antibodies)
- Agglutination (RBC clumping)
- ABO
- Rh Antigens

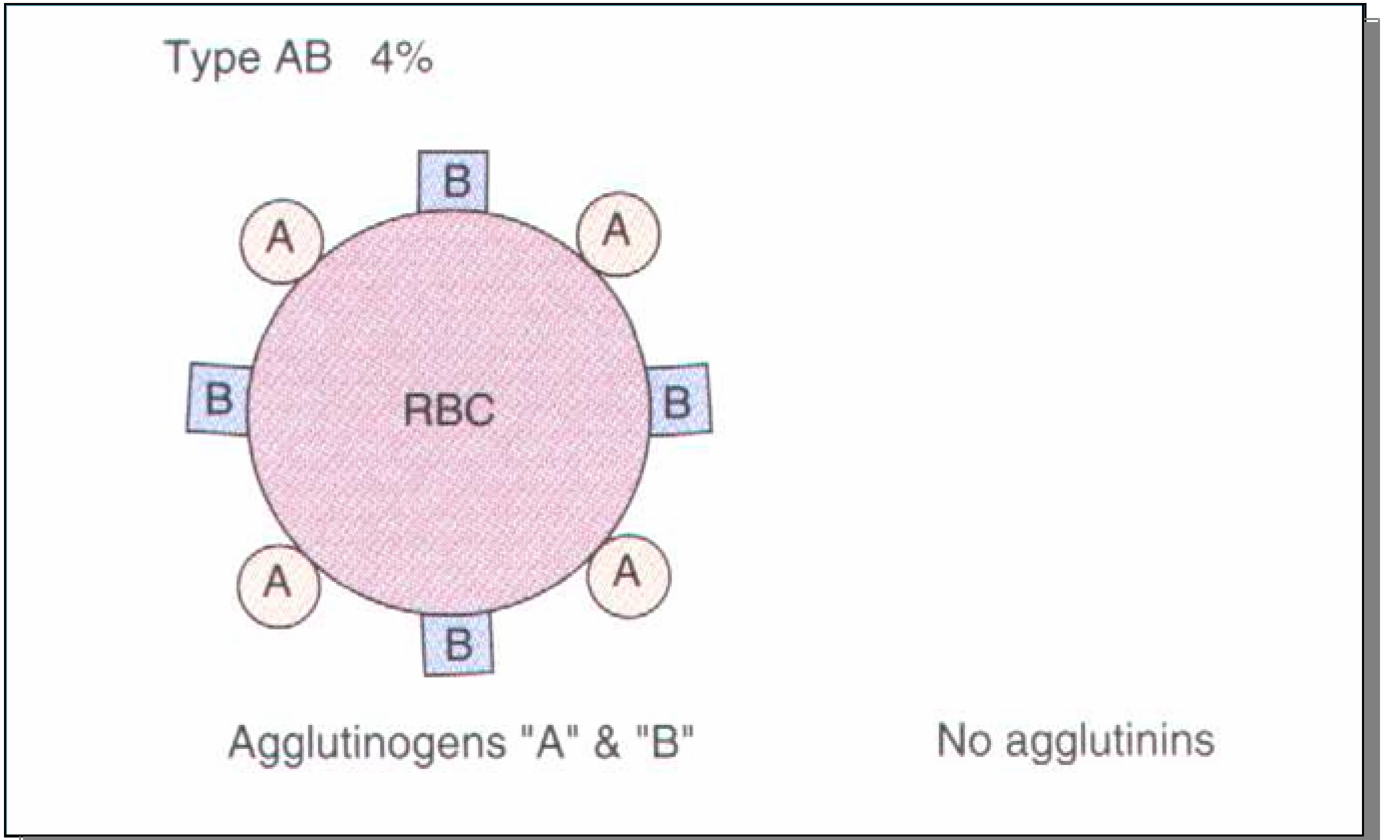
Type A Blood



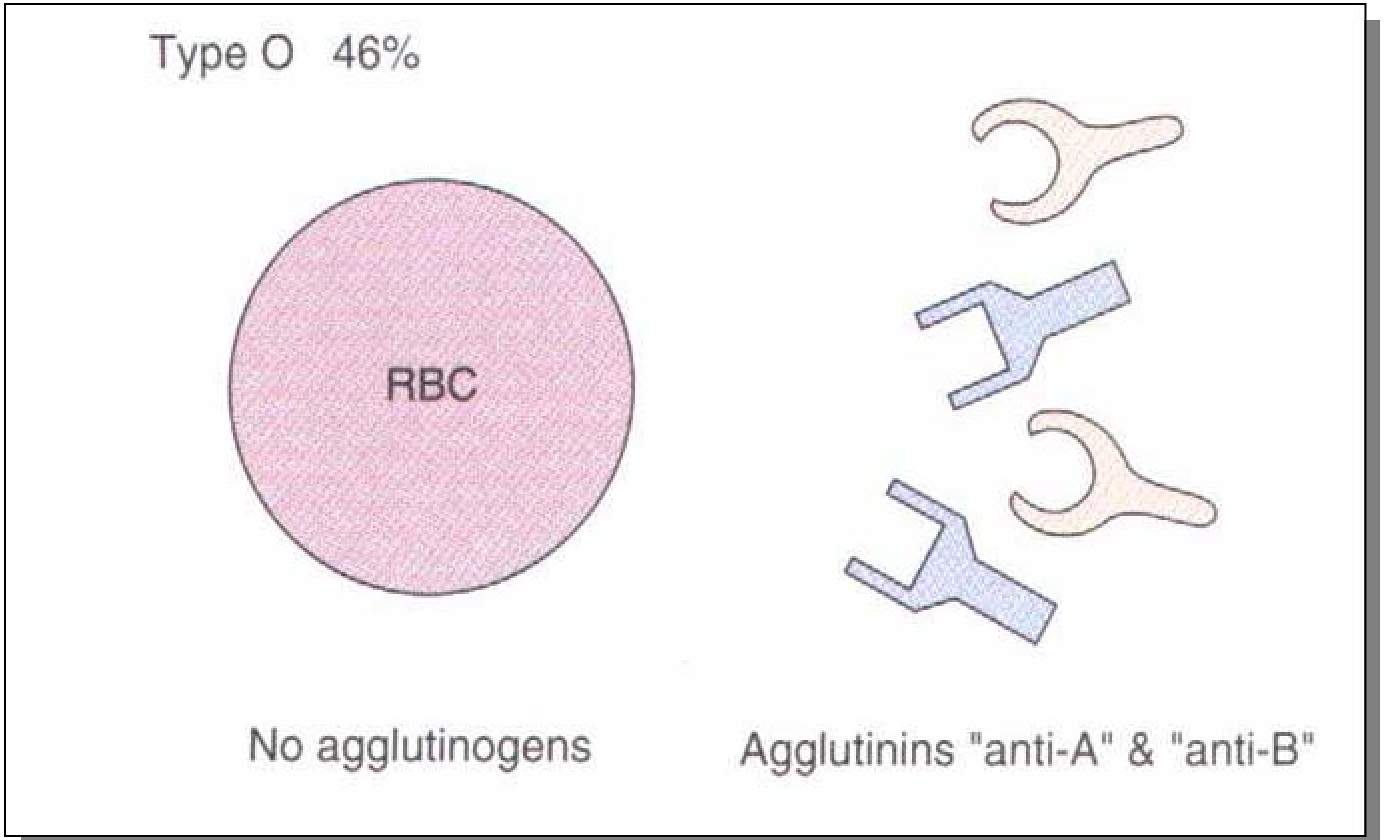
Type B Blood



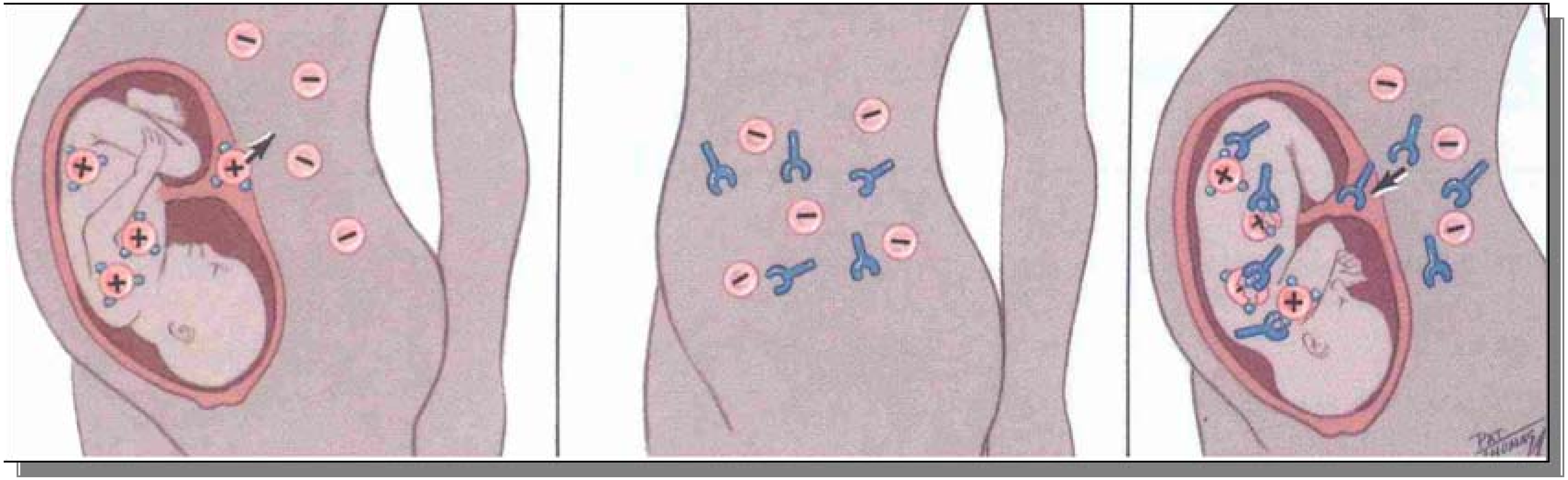
Type AB Blood



Type O Blood



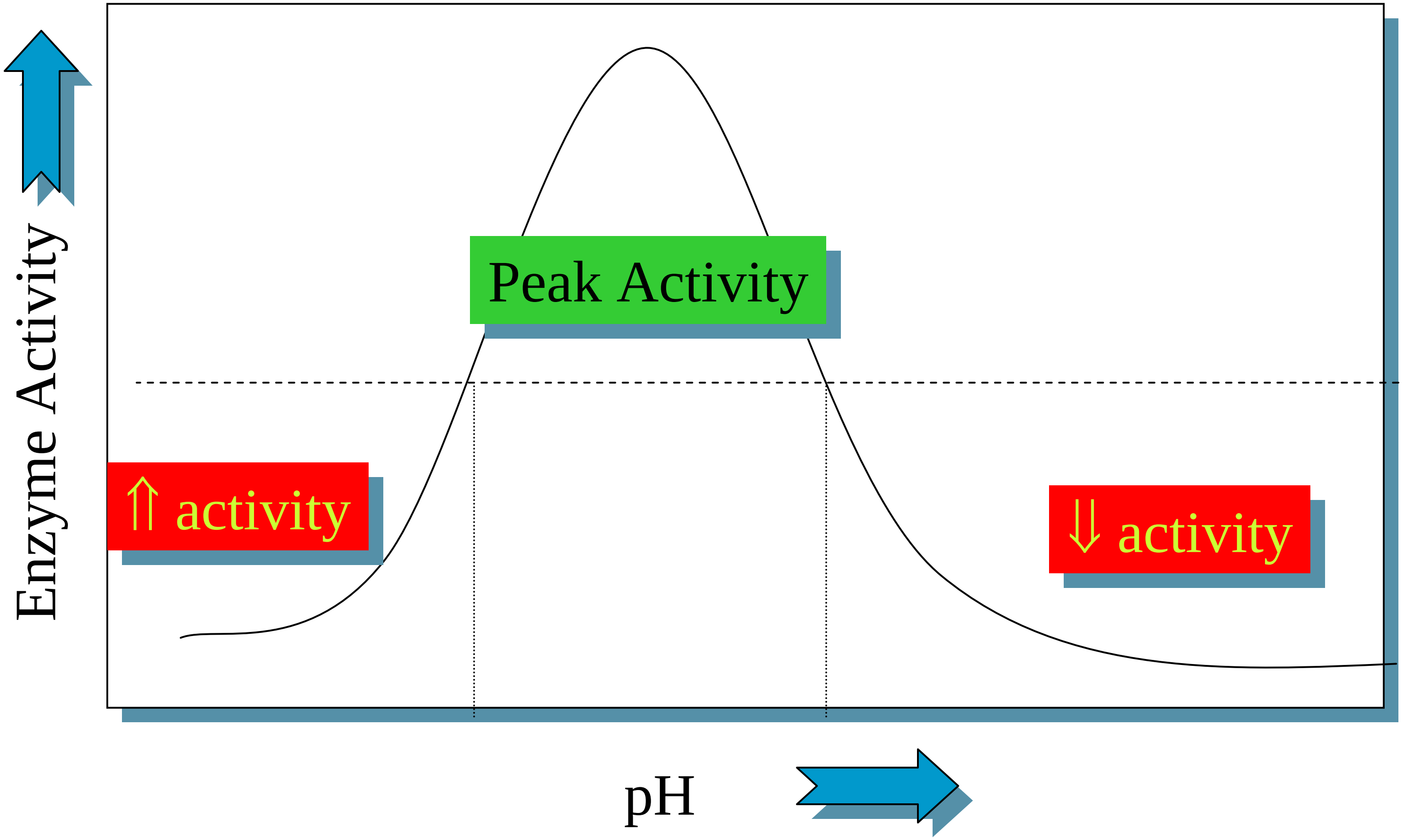
Rh Antigens



Bottom line of Acid-Base

- Regulation of [H+]
  - normally about 1/3.5 million that of $[Na^+]$
  - 0.00004 mEq/L (4×10^{-8} Eq/L)
- Dependent upon
  - Kidneys
  - Chemical Buffers
- Precise regulation necessary for peak enzyme activity

pH Effects on Enzyme Activity



Acid Base

- Acids release H^+
  - example: $HCl \rightarrow H^+ + Cl^-$
- Bases absorb H^+
  - example: $HCO_3^- + H^+ \rightarrow H_2CO_3$

pH is logarithmic

- pH = log $1/[H^+]$
- = - log $[H^+]$
- = - log 0.00000004 Eq/L
- pH = 7.4
- Think of pH as 'power of $[H^+]$

pH is Logarithmic

pH is inversely related to [H+]

→

as
[H+] ⇑
pH ⇓

&

as
[H+] ⇓
pH ⇑

Small Δ pH mean large Δ $[H^+]$

→

pH 7.4 = 0.00000004
pH 7.1 = 0.00000008
(it doubled!)

Buffers Resist pH Changes

- Weak acid & conjugate base pair
- $H_2CO_3 \Leftrightarrow HCO_3^- + H^+$
- Conjugate Acid ⇔ conjugate base + acid

Henderson-Hasselbalch Equation

- $pH = pK_a + \log [base]/[acid]$
  - Ex:
    - $= 6.1 + \log 20/1$
    - $= 6.1 + 1.3$
    - $= 7.4$
- Key ratio is base: acid
  - HCO_3^- : CO_2 (standing in for H_2CO_3)

pH Scale

- 0 : Hydrochloric Acid
- 1: Gastric Acid
- 2: Lemon Juice
- 3: Vinegar, Beer
- 4: Tomatoes
- 5: Black Coffee
- 6: Urine
- 6.5: Saliva

- 7: Blood
- 8: Sea Water
- 9: Baking Soda
- 10: Great Salt Lake
- 11: Ammonia
- 12: Bicarbonate
- 13: Oven Cleaner
- 14: NaOH

Acid Base Compensation

- Buffer System
- Respiratory System
- Renal System

Buffer System

- Immediate
- $CO_2 + H_20 \Leftrightarrow H_2CO_3 \Leftrightarrow H^+ + HCO_3^-$
- Equilibrium: 20 HCO_3^- to 1 CO_2 (H_2CO_3)
- Excessive $CO_2 \Rightarrow$ acidosis
- Excessive $HCO_3^- \Rightarrow$ alkalosis

Simplified:
$CO_2 \Leftrightarrow H^+$

Question...

Is the average pH of the blood lower in:

a) arterie

b) veins

Because veins pick up the byproducts of cellular metabolism, including…

CO_2!

Respiratory System

- Minutes
- $CO_2 \Leftrightarrow H^+$
- Respiration ⇑: CO_2 ⇓: H^+ ⇓
- Respiration ⇓: CO_2 ⇑: H^+ ⇑

Renal System

- Hours to days
- Recovery of Bicarbonate
- Excretion of H^+
- Excretion of ammonium

Disorders

- Respiratory Acidosis
- Respiratory Alkalosis
- Metabolic Acidosis
- Metabolic Alkalosis

Respiratory Acidosis

- ⇑ CO_2 + H_20 ⇔ ⇑ H_2CO_3 ⇔ ⇑ H^+ + HCO_3

- Simplified:
- ⇑ CO_2 ⇔ ⇑ H^+

Respiratory Alkalosis

- $\Downarrow CO_2 + H_20 \Leftrightarrow \Downarrow H_2CO_3 \Leftrightarrow \Downarrow H^+ + HCO_3$

- Simplified:
- $\Downarrow CO_2 \Leftrightarrow \Downarrow H^+$

Metabolic Acidosis

- ⇑ $H^+ + HCO_3 \Leftrightarrow$ ⇑ $H_2CO_3 \Leftrightarrow H_20 +$ ⇑ CO_2

•Simplified:

•Producing too much H^+

Metabolic Alkalosis

- $\Downarrow H^+ + HCO_3 \Leftrightarrow \Downarrow H_2CO_3 \Leftrightarrow H_20 + \Downarrow CO_2$

•Simplified:

•Too much HCO_3

Normal Values

- pH: 7.35 - 7.45
- PCO_2: 35 - 45

Abnormal Values

	pH	PCO_2
Respiratory Acidosis	⇓	⇑
Respiratory Alkalosis	⇑	⇓
Metabolic Acidosis	⇓	Normal ⇓ if compensating
Metabolic Alkalosis	⇑	Normal ⇑ if compensating

All Roads Lead to Rome!

Respiratory Opposes

Metabolic Equals
(or doesn't oppose)

Example:

- pH = 7.25
- PCO_2 = 60

Example:

- pH = 7.50
- PCO_2 = 35

Example:

- pH = 7.60
- PCO_2 = 20

Example:

- pH = 7.28
- PCO_2 = 38