specific immunity to genetics

specific resistance
(the immune response)

functionally, the third line of defense against infections

non innate, but adaptive:
- carefully targeted
  - recognizes a specific foreign substance and
  - acts to immobilize or neutralize it
- amplifies the immune response, complement reactions, etc

has the following characteristics:
1. Response to a Specific Antigen
   - protein or organic molecule,
   - free or attached to bacterial cell or other pathogen
2. Systemic Response
   - effective throughout the entire body
3. Has Memory
   - resistance lasts a long time

antigens

any substance that can mobilize the immune system
- ie. provoke an immune response

can be free molecules or attached to cells of bacteria, fungi, etc

the ability of a molecule to act as an antigen depends on its size and complexity

most are large complex organic molecules (MW >10,000), not normally found in the body
- ie. intruders = nonself

especially immunogenic:
- foreign proteins
- nucleic acids
- some lipids
- many large polysaccharides

but large simple molecules of many small repeating units (eg. plastics) have little or no immunogenicity
must be foreign to the host
our body is programmed to recognize our own proteins as “self” ie. not immunogenic

but these same proteins may be strongly immunogenic to others eg. transfusions, transplants

microorganisms and pollen grains are immunogenic because their surface membranes have many such foreign molecules on them

examples of antigen containing structures:
- bacterial capsules
- cell wall lipopolysaccharides of G- bacteria
- glycoproteins in cell membranes
- attachment sites for viruses
- bacterial toxins and extracellular enzymes

small molecules such as peptides, nucleotides, and many hormones are NOT immunogenic but may become so by attaching to the body’s own proteins (=Haptens)

eg. chemicals in poison ivy, animal dander, some detergents, cosmetics, etc

actually, only certain parts of an entire antigen are immunogenic usually a small sequence of amino acids (~10) that triggers an immune reactions

→ = antigenic determinants (=epitopes)

most naturally occurring antigens have a variety of antigenic determinants eg. large proteins have 100’s

specific immunity involves two different kinds of lymphocytes: T cells and B cells:
- both originate in bone marrow
- T cells move to thymus for further maturation
- B cells develop further in bone marrow
- after development both are dispersed to lymph nodes and spleen until needed
The immune response (specific immunity) involves the interaction of two major processes in the body, directed by two different kinds of **lymphocytes** (WBC’s):

**A. Antibody Mediated Immunity**  
(AMI; Humoral Immunity)

**B. Cell Mediated Immunity**  
(CMI)

**Antibody Mediated Immunity**

=AMI; =Humoral Immunity

involves the release of proteins called antibodies

Mediated by B lymphocytes (B-cells)

**B-Cell Development & Activation**

1. by the time an infant is a few months old
   B lymphocytes (B cells) have completed the 1\textsuperscript{st} stage of their development:
   manufactured in fetal liver
   they synthesize up to 100,000 antibody molecules that they hold in the cell membrane

2. The next stage of development occurs in lymph nodes and spleen and only occurs if B cell encounters an antigen it recognizes:

   a. specific B cells activated by exposure to an antigen
      \( \rightarrow \) antigen binds to antibodies on cell membrane of B cell
   b. triggers clonal selection and multiplication
      \( \rightarrow \) produces numerous copies of identical cells with identical antibodies on cell membranes
   c. differentiation into **plasma cells** and **memory cells**
   d. **plasma cells** secrete **antibodies**
      2,000 Ab/sec over few (4-5) days, then dies
   e. **memory cells** do not secrete antibodies
      but if later exposed to same antibody they can develop into plasma cells and secrete antibodies
ie. they “remember” an earlier encounter with the antigen

**Antibodies**

antibodies are proteins called immunoglobins
= gamma globulin of plasma proteins

each of us has ~ a billion different kinds of antibodies
and each of these has a unique shape

each immunoglobulin molecule consists of 4 polypeptide chains joined together to form a “Y” shaped molecule

each antibody has 2 or more **combining sites**
→ small concave areas at tip of arms of “Y” that are uniquely shaped and complementary to the epitope

two long (= heavy, ~400 AA’s) chains and two short (= light, ~200 AA’s) chains linked by disulfide bonds
constant region → same AA sequence for all in same class
variable region → = antigen binding sites (tips of Y)
the body uses ~300 gene “pieces” to make >1 Billion different kinds of antibody molecules

the amino acid sequence determines the specific shape of these polypeptide chains
this unique shape allows a specific antibody to combine with specific antigen

**Classes of Antibody Molecules:**

**IgG**

most abundant antibody in plasma
75-80% of gamma globulin
also found in internal secretions (synovial fluid, spinal fluid, peritoneal fluid)
effective against bacteria, viruses, and toxins
plasma levels increase dramatically during secondary responses
only Ig that can cross placenta

**IgM**

largest of the antibodies
only found in blood
5-10% of plasma immunoglobins
1st antibody released to blood by plasma cells during primary response
attacks specific toxins eg. diphtheria, tetanus, botulism toxin
blood group antibodies belong to this group
→ cause agglutination

**Ig A**
dimer
10-25% in serum
also found in body secretions: mucus, saliva, urine, milk, tears
active against bacterial and viral infections
inhibits attachment of parasites in gut
1st to encounter bacteria in GI tract
passed to nursing child in mothers milk

**Ig E**
associated with allergies
causes certain WBC’s to release histamine
→ dilates capillaries
→ constricts bronchi

**Ig D**
very low concentrations in serum
levels increase during chronic infections

formation of the antigen/antibody complex by B-cell activity does not generally destroy the invader
→ it prepares it for destruction by
  non-specific phagocytosis (WBC’s)
  triggering complement fixation
  CMI (T-cell activity)

antibodies bind to antigens to cause a variety of possible effects:

1. **Agglutination**
   bind to antigens on cells to cause them to clump together
   makes it easier for WBC’s to remove

2. **Precipitation**
   binds soluble antigens together causing them to precipitate out of solution
   makes it easier for WBC’s to remove them

3. **Neutralization**
   binds to bacterial toxins (esp. exotoxins) and
4. **Prevents viral attachment**
   binds to viral receptor sites to prevent viral invasion of cells
   (doesn’t work for latent viruses)

5. **Stimulates Natural Killer Cells**
   antibodies coat and mark a cell for destruction by the NK cells
   =antibody dependent cell mediated cytotoxicity

6. **Complement Fixation**
   triggers complement reactions especially against cellular antigens
   cascade reactions can cause:
   - cell lysis
   - opsonization
   - inflammatory enhancement

**primary vs secondary response**
**primary**
→ persons initial exposure to an antigen
   lag of several days before antibodies begin being produced
   peak production in ~10 days

**secondary**
→ reexposure to same pathogen triggers memory cell response
   memory cells can persist for 20 years or more
   much quicker response
   much stronger response

**natural vs acquired immunity**
**natural**
→ immune response is triggered due to natural exposure to a pathogen

**acquired (=artificial)**
→ immune response is triggered by a medical procedure, eg vaccination

**active vs passive immunity**
**active**
→ exposure triggers body’s own immune response including memory cells

**passive**
→ subject receives antibodies from another person or animal, rather than making them himself
   offers immediate protection, short term
no active antibody production is stimulated  
no memory develops

eg. fetus gets antibodies from mom  
eg. gamma globulin to treat hepatitis, botulism,  
snake bites, etc

**monoclonal antibodies**
specific B cell (with desired antibodies) is fused to  
cancer cell
\[ \rightarrow \text{rapid production of large numbers of the} \]
\[ \text{same antibody} \]

**Cell Mediated Immunity**

= CMI

Mediated by T lymphocytes (T-cells)

involves a more diverse group of cells than for B cell activation

usually, slower to respond

antigens are usually larger than in AMI

most active in:
  bacterial infections
  destruction of malignant tumor cells
  transplant rejections

T-cells also contain antigen receptors on their cell membranes

**T-Cell Development & Activation**
1. probably also first develop in fetal liver from stem  
cells

2. then move to thymus where they develop and  
proliferate

3. move into lymph nodes and spleen as T- cells

T-cells cannot recognize **free** antigens in the blood  
generally need cell to cell contact to work

  a. specific T cells activated by exposure to a  
specific antigen (on a cell)
eg. viral infected cell, cancer cell
bacterial cell

b. initiate clonal selection and multiplication
c. differentiation into several cell types
d. various T-cells secrete immunoactive chemicals
   \= \textbf{lymphokines}, NOT antibodies
   \rightarrow which direct the activities of both B and T cells and phagocytes

\textbf{Kinds of T-Cells Produced:}

i. \textbf{Helper T-cells} (esp CD4 cells)
   most prevalent of all kinds of T cells, 65%
   directly helps T and B cells to function
   releases lymphokines:
   \rightarrow recruit lymphocytes
   \rightarrow stimulate differentiation of lymphocytes
   \rightarrow help B cells recognize antigens
   there can be no immune response without them

ii. \textbf{Cytotoxic T- cells} (CD8 cells)
   directly kill specific target cells by lysis
   especially effective against foreign cells, cancer cells, fungi, some protozoa and helminths
   recognizes virally infected cells by viral antigens on cells surface

iii. \textbf{Suppressor T-cells} (CD8 cells)
   restricts rampant uncontrolled immune response
   dampens activity of T and B cells
   brings immune response to an end

iv. \textbf{Delayed Hypersensitivity Cells}
   chronic infections
   cell mediated allergies

v. \textbf{Memory Cells}

\textbf{Lymphokines:}
various T-cells secrete immunoactive chemicals
   \= \textbf{lymphokines} = \textbf{cytokines}

   soluble chemical messengers by which cells of the immune system communicate with each other

\textbf{1. chemotactic factor}
→ attracts macrophages to invaders

2. **macrophage activating factor**
   → tells macrophages to destroy antigen
   gives them enhanced antibacterial activity:
   increased metabolic activity
   more lysosomes
   increased phagocytosis

3. **lymphotoxin**
   → poison which kills any cell it contacts
   requires direct cell contact

4. **migration inhibition factor**
   → halts macrophage migration

????
lymphokines: soluble chemical messengers by which cells of the immune system communicate with each other

**a. Interleukin 1**
→ stimulates helper T-cells in presence of antigen
→ attracts macrophages in inflammatory response

**b. Interleukin 2**
→ proliferation of TH cells
→ proliferation and differentiation of B-cells
→ activation of Tc and NK cells

**c. alpha interferon**
→ inhibits intracellular viral replication
→ increases activity of macrophages against microbes and tumor cells

**d. Tumor Necrosis Factor**
→ toxic to tumor cells
→ enhances activity of phagocytic cells

**e. GM-CSF (Granulocyte Macrophage-Colony Stimulating Factor)**
→ stimulates the formation of RBC’s and WBC’s from stem cells
Interactions of AMI and CMI Systems:

both systems work together to increase the immune response against specific foreign antigens

eg. production of antibodies by B-cells often requires helper T-cells
    esp. “T-dependent antigens” – proteins such as viruses, bacteria, foreign RBC’s, hapten–carrier combinations

eg. stimulate B-cells to differentiate into plasma cells and produce antibodies

Neuroendocrine-Immune Interactions

all three systems are interconnected
    neural links:
        neurons innervate immune system organs such as spleen and lymph nodes
    chemical links:
        all three produce active chemicals
        neurotransmitters, hormones, lymphokines
        sometimes one chemical can have effect in all three systems

all three coordinate and control the responses to the outside world

the immune system acts as a “diffuse sense organ”

relays data about inflammation or infections to brain

Examples of interactions:

eg. Brain might respond to an infection by causing fever and achy feeling (part of nonspecific defense)

eg. stress can activate parts of same pathway

eg. mental state can influence the body’s resistance to disease: anxiety or psychological stress increased severity of a cold

    hypothalamus → pituitary → adrenal → stress
>bld sugar → reduced inflammatory response

e.g. immune system can be taught to react to visual
cue with an allergic reaction = conditioned response

Clinical Applications of Immunity

1. Vaccinations

based on primary vs secondary response

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  produced
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passive
→ subject receives antibodies from another person or
  animal, rather than making them himself
  offers immediate protection, short term
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  e.g. fetus gets antibodies from mom
  e.g. gamma globulin to treat hepatitis, botulism,
  snake bites, etc
2. **Monoclonal Antibodies**  
   specific B cell (with desired antibodies) is fused to cancer cell  
   → rapid production of large numbers of the same antibody

3. **Organ Transplants and Rejections**  
   same principle as blood transfusions  
   usually need immunosuppressive drug therapy

4. **Allergies**  
   immediate (acute) hypersensitivity  
   mediated by B cells  
   IGE → mast cells → histamine  
   anaphylactic shock

   delayed hypersensitivities  
   mediated by T cells  
   antihistamines don’t work  
   use corticosteroids

5. **Immunodeficiencies**  
   congenital  
   eg. SCID  
   
   acquired  
   eg. AIDS

6. **Autoimmune Diseases**

5% of adults in North America
→ 2/3rd of victims are women

normal state of self tolerance breaks down due to:
→ self reactive lymphocytes are normally silenced during development  
   in this case some escape and attack body  
   → new self antigens (?antibodies) appear due to gene mutation or hapten binding  
   → foreign antigens resembling self antigens trigger antibodies that not only attack foreign antigens but self antigens as well

autoantibodies & sensitized T-cells
some of most common autoimmune diseases:

**eg. Multiple Sclerosis**
- destruction of myelin sheath of brain and spinal cord
- especially in young adults
- nerve fibers are severed
- neurons short circuit
- cycles of remission and relapse

**eg. Myasthenia Gravis**
- destruction of neuromuscular junctions
  - Ach receptors
- results in muscle weakness
- typical symptom = droopy eyelids

**eg. Graves Disease**
- increased thyroid activity
  - thyroid produces excessive amounts of thyroxine

**eg. Juvenile Onset Diabetes Mellitis**
- destruction of beta cells in Islets of Pancreas
- results in insulin deficiency

**eg. Rheumatoid Arthritis**
- joint inflammation and destruction

**eg. Lupus**
- attacks kidneys, heart, lungs, skin

**The Respiratory System**

Respiratory system functions as gas exchange system for oxygen and carbon dioxide

- **cellular respiration** (energy production)

closely tied to circulatory system

**Physiology of Respiration**

**External Respiration**

= pulmonary ventilation

we move ~500 ml of air in and out of lungs with each breath
breathing involves 2 processes:
- inspiration
- expiration

involves moving air down a **pressure gradient**

**Inspiration**
- an active process
- involves contraction of diaphragm
  - → innervated by phrenic nerve
  - may also involve external intercostals

  contraction of diaphragm lowers pressure in thoracic cavity:
  - outside pressure > pressure in lungs → lungs inflate

  outside: 760 mmHg → inside: 754 mmHg

**Expiration**
- mainly a passive process
- relaxation of diaphragm
- volume of chest decreases, forcing air out of lungs
- may also involve contraction of internal intercostals
- inside: 763 mmHg → outside: 760 mmHg
  - (forced=up to 790 mmHg)

**Factors that affect pulmonary ventilation:**

1. **Resistance to airflow**
   - in respiratory passages
   - constriction increases resistance (=drag)
   - mainly in bronchi and bronchioles

2. **Compliance**
   - lungs are >100 x’s more distendable than a balloon
   - lungs increase in volume passively as chest cavity expands

   Pulmonary fibrosis reduces compliance

3. **Elasticity of lungs**
   - elasticity = tendency of organ to return to normal position or shape
   - lungs contain lots of elastin fibers
Emphysema = less elastic and more collagen fibers → requires 3-4x’s more energy to breath (15-20% vs 5% normal)

4. Surface Tension

outer surface of lungs and inner surface of alveoli are covered with thin film of water
water has a high surface tension (very “sticky”)

on outer surface of lungs:
→ visceral pleura tends to stick to parietal pleura
   creates slight negative intrapleural pressure
   helps to inflate lungs during inspiration

on inside of alveoli:
→ tends to cause the alveoli to collapse upon themselves

counteracted by:

a. lungs never completely deflated;
   always contain some air

b. secrete surfactant
   a lipoprotein
   reduces surface tension in alveoli
   not produced until 8th month of pregnancy
   → respiratory distress syndrome

pneumothorax
opening in chest cavity
eliminates pressure differential
causes lungs to collapse

Respiratory Volumes

the volume of air exchanged in breathing is measured with a spirometer
provides information on pulmonary functions

Tidal Volume (TV)
normal volume of air with each breath
small part of total lung capacity (~10%)
~500 ml

**Expiratory Reserve Volume (ERV)**
- additional air one can expire after releasing tidal volume
- use internal intercostals to forcibly expire additional air
- ~1000-1200 ml

**Inspiratory Reserve Volume (IRV)**
- additional amount of air that can be inspired in addition to tidal volume
- use external intercostals to lift rib cage
- ~3300 ml

**Residual Volume**
- air that cannot be removed from lungs
  - ~1200 ml
  - removed in pneumothorax

**Vital Capacity (VC)**
- largest volume of air that can be moved into or out of lungs
  - VC = IRV + TV + ERV

vital capacity is affected by:
  a. overall size of individual, gender → size of lungs
  b. volume of blood in lungs → eg congestive heart failure
  c. excess fluid in pleural or abdominal cavity
  d. loss of lung elasticity → eg. emphysema
  e. misc health related factors → eg. smoking, exercise, etc

**Forced Expiratory Volume (FEV)**
- time required to exhale vital capacity

**Total Lung Capacity (TLC)**
- maximum amount of air the lungs can hold
  - TLC = VC + RV
  - ~5700-6200 ml

**Minute Respiratory Volume (MRV)**
- amount of air that ventilates lungs each minute
  - index of respiratory efficiency
  - = TV x Breathing rate
  - = ~500 ml x 12
= \sim 6000 \text{ ml/min} \ [6 \text{ l/min vs exercise} = \sim 100-200 \text{ liters/min}]

But of the Tidal Volume (\sim 500 \text{ ml})
about 150 \text{ ml} never gets to alveoli
remains in air passages

**Alveolar Ventilation Rate**
= \sim 350 \text{ ml} \times 12
= \sim 4200 \text{ ml/min} \ (\sim 70\% \text{ of MRV})
= 63 \text{ gallons/hr}
= 1512 \text{ gallons/day}
a better index of effective ventilation
\to eliminates “dead space”
deeper breaths more effective than more frequent breaths

**Disorders indicated with pulmonary functions tests:**

**Restrictive Disorders**
diseases interfering with inspiration
pulmonary fibrosis \to lowers VC
emphysema \to lowers minute volume

**Obstructive Disorders**
diseases interfering with expiration
asthma (bronchiole constriction)
\to normal VC
\to but lower forced expiratory volume
emphysema

**Alveolar Gas Exchange**
composition of air:

<table>
<thead>
<tr>
<th>air entering lungs</th>
<th>air exiting lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>[78% \text{ N}_2]</td>
<td>14% \text{ O}_2</td>
</tr>
<tr>
<td>21% \text{ O}_2</td>
<td>5.6% \text{ CO}_2</td>
</tr>
<tr>
<td>0.04% \text{ CO}_2</td>
<td></td>
</tr>
</tbody>
</table>

the exchange of gasses in the lungs takes place between alveolar air and venous blood
gas exchange occurs across the lining of the alveoli and capillaries (2 cell layers thick)
\to respiratory membrane
total surface area \(\sim 70 \ (60-80) \text{M}^2\)
\(\approx 760 \text{ ft}^2 \sim 20’x38’\)

Gas exchange is the result of simple diffusion down oxygen and carbon dioxide concentration gradients:

**Concentrations of Gasses Usually Measured in Partial Pressures**
- \(\text{PO}_2 = 21\% \text{ of } 760 \text{ mmHg} = 160 \text{ mmHg}\)
- \(\text{PCO}_2 = 0.04\% \text{ of } 760 \text{ mmHg} = 0.3 \text{ mmHg}\)

<table>
<thead>
<tr>
<th>Alveoli</th>
<th>Blood Entering Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO2</td>
<td>105mmHg</td>
</tr>
<tr>
<td>PCO2</td>
<td>39mmHg</td>
</tr>
</tbody>
</table>

Amount of O2 diffusing into blood depends on:
1. **Oxygen Pressure Gradient**
2. **Surface Area of Lungs**
3. **Respiratory Rate**

Oxygen binds to hemoglobin inside RBC’s
\(=\) oxyhemoglobin

The exchange of gasses in tissues is also by simple diffusion:

<table>
<thead>
<tr>
<th>Blood leaving lungs</th>
<th>Tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO2</td>
<td>(\leq 40\text{mmHg})</td>
</tr>
<tr>
<td>PCO2</td>
<td>(\geq 45\text{mmHg})</td>
</tr>
</tbody>
</table>

The amount of oxygen delivered to tissue cells is affected by:
1. **Rate of Oxygen Utilization**
   - Regulates the rate of delivery by controlling size of gradient
   - As conc of O2 in tissues decreases; the bonds between O2 and Hb weaken
2. **Carbon Dioxide Concentration**
   - More CO2 \(\rightarrow\) more O2 released
3. **pH**
   - Lower pH \(\rightarrow\) more O2 released
4. **Temperature**
   - Higher temp \(\rightarrow\) more O2 released

**Dissociation Curve for Hemoglobin:**
1st O2 on and off is hardest
other 3 are easier to bind or remove

eg. creates differential release of oxygen to cells needing it most

eg. More oxygen is released to active muscle cells

**Myoglobin** → has 1 heme group
holds onto O2 longer
accepts O2 from Hemoglobin
“middleman”

**Transport of Gasses in Blood**

**Oxygen**

almost all hemoglobin in blood going through lungs manages to pick up oxygen
→ 97-99% saturation
    versus ~70% saturation in venous blood

→ hemoglobin has a very **high affinity** for O2

only ~1-1.5% of O2 is carried dissolved in plasma

Hyperventilation doesn’t increase PO2 of blood
only slightly increases dissolved O2 concentrations
→ may deliver a little more O2 to tissues
but not much

the amount of oxygen carried in the blood then is mainly dependent on the
amount of hemoglobin in blood

4 O2/hemoglobin → 250 Million Hb/RBC → 1 Billion O2/RBC

anemia decreases oxygen transport

Only 20-25% of oxygen is unloaded per circuit of bloodflow
→ venous reserve
   “holding breath”

Hemoglobin saturation reduced to ~70%:
   high altitudes
   CV disease

CO binds to Hemoglobin even more strongly than does oxygen
→ CO poisoning (takes very little, but continuous
Carbon Dioxide

transported in blood three major ways:
1. 7% dissolved in plasma
   → >20x’s more soluble than O2
2. 20-23% bound to hemoglobin
   CO2 binds to amino group of hemoglobin
   (O2 binds to heme portion)
   = carbaminohemoglobin
3. 70% converted to bicarbonate ions

   carbonic anhydrase
   \[
   \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-
   \]

   this reaction occurs mainly inside RBC’s
   bicarbonate ions are then released into the plasma

   oxygen release is enhanced by CO2 loading

Regulation of Respiration

normal breathing is automatic, rhythmic

Skeletal muscles of diaphragm and intercostals are innervated by somatic motor neurons

controlled by respiratory reflex centers in brainstem

Three reflex centers in brain that regulate breathing:

1. respiratory center: medulla

   (medullary rhythmicity area)

   establishes basic rhythm of breathing

   maintains automatic breathing rate
   → 12-15 breaths/min

   a. contain chemoreceptors that are sensitive
      to changes in CO2
   b. chemoreceptors in aorta and carotid sinus
      also monitor CO2 levels in arterial blood
elevated blood CO₂ ➔ faster breathing

c. other chemoreceptors in aorta and carotid sinus also monitor pH

more acidic ➔ faster breathing

d. O₂ sensors in aorta and carotid sinus detect slight reductions in O₂ and cause reflex stimulation of respiratory center

more of a backup system

→ rarely is the most important control

if cells in respiratory become hypoxic they may fail

Hypoxic drive: people with respiratory disease these O₂ sensors become more important

2. apneustic: pons

promotes inspiration, breath holding
forceful, prolonged inspiration

3. pneumotaxic center: pons

antagonist to apneustic
inhibits inspiration
fine tunes, prevents overinflation

the two centers in pons insure a smooth transition between inspiration and expiration

helps maintains rhythmicity of breathing

when connection between medulla and pons are cut breathing becomes abnormal

→ gasps

“inflation & deflation reflexes” alternate activity

helps regulate depth of breathing

occurs when stretch receptors in pleura, bronchioles and alveoli are stimulated during inspiration
prevents overinflation when stretch receptors are no longer stimulated
prevents further expiration

**Hypothalamus**
irritant receptors trigger bronchiole constriction, coughing etc

**Cerebrum**
emotional state, eg fear, pain, can speed up breathing
can voluntarily speed up or slow down breathing
but can’t overpower reflex controls

**Pulmonary Blood Pressure**
heart pumps ~5l of blood per minute
5 liters in systemic circuit
5 liters in pulmonary circuit

change in pressure:
**systemic circuit:**
averages 100 \[\rightarrow\] 0
\[\rightarrow\text{difference} = 100 \text{ mmHg}\]
high resistance

**pulmonary circuit:**
averages 15 \[\rightarrow\] 5
\[\rightarrow\text{difference} = 10 \text{ mmHg}\]
low resistance
no pulmonary edema

**alveolar airflow – blood flow coupling**
if low O2/high CO2 get
\[\rightarrow\] arterial constriction
\[\rightarrow\] bronchial dilation
improves gas exchange in alveoli
Digestive System

We need food for cellular utilization:
- nutrients as **building blocks** for synthesis
- sugars, etc to break down for **energy**

most food that we eat cannot be directly used by the body
  - too large and complex to be absorbed
  - chemical composition must be modified to be useable by cells

digestive system functions to altered the chemical and physical composition of food so that it can be absorbed and used by the body; ie
  - **physical and chemical digestion**
  - **absorption**
  - **collect & eliminate nonuseable components**

Digestive Physiology

lumen of GI tract is continuous with outside of body
  - food being digested must be isolated from body cells since it’s the same composition as rest of body
  - digestion occurs OUTSIDE the internal environment of cells and tissues

digestive system functions to
  - digest or break down food
  - absorb nutrients

as materials are being processed they are moved through alimentary canal by:
  - **peristalsis**
  - **segmentation**

Digestion

digestion = all food changes that occur in the alimentary canal

need to convert food into a form that can be absorbed and used by body cells

two types of digestion:
  - **physical digestion**
    - breaking large pieces down into smaller pieces
  - **chemical digestion**
    - breaking large molecules
(proteins, fats, starches, etc)
into small molecules
(amino acids, fatty acids, sugars, etc)

Mouth
food entering mouth is physically broken down
tooth mixed with saliva lubricant enzyme = amylase
→ begins carbohydrate digestion most (60%) of starch digestion by amylase from saliva occurs in stomach after swallowing bolus at end of digestion in mouth food = bolus

Pharynx
bolus is swallowed on swallowing
uvula closes off nares epiglottis closes off glottis of larynx

Esophagus
wave of reflex contractions = peristalsis

Stomach
muscular contractions separate and mix food particles
in stomach bolus is mixed with gastric juices
gastric juices low pH ~2 hydrochloric acid pepsin
→ ideal for breaking proteins into smaller fragments
body must be protected from harsh pH of gastric juices:
a. thick coating of bicarbonate rich mucous
b. tight junctions join epithelial cells to help prevent leakage
c. pepsin and HCl are secreted in inactive forms
d. stomach lining is rapidly replaced
→ renewed every 3-6 days
heartburn = cardiac valve doesn’t close completely

vomiting = medullary reflex:
- triggered by irritants in stomach
- closing nose and glottis
- relaxes cardiac sphincter
- spasm of diaphragm

gastric ulcers: *Helicobacter pylori*
- part of normal flora of stomach
- can neutralize stomach acids
- excessive growth can irritate stomach lining to produce ulcers

physical digestion is completed in stomach

once digestion in stomach is competed have a white milky liquid = chyme

stomach takes about 2-6 hours to empty after a meal

gastric emptying is controlled by
- enterogastric reflex:
  - periodic opening/ closing of pyloric valve
  - prevents overburdening smaller duodenum

Duodenum
- all physical digestion has been completed

Completes chemical digestion of food

most chemical digestion occurs here

enzymes secreted from pancreas and gall bladder

intestinal and pancreatic juices are alkaline → neutralize acidity of chyme

presence of chyme in duodenum triggers:
- release of bile from liver & gall bladder
- release of pancreatic secretions
- release of duodenal secretions

1. Bile
- contains no enzymes
contains
- **bile salts** – made from cholesterol in liver
- **bile pigments** (bilirubin, biliverdin)
- **cholesterol** – normally remains in solution
  may precipitate out as **gall stones**

is a surfactant → emulsifies fats into smaller fat
droplets to speed their digestion

2. **Pancreatic Juices**

pancreas is an endocrine gland (insulin, glucagon)
but 98% of its tissues make and secrete digestive
juices through ducts to the duodenum

include:
- **bicarbonates** – to neutralize gastric acids
- **proteinases** (esp trypsin and chymotrypsin)
  - breaks proteins into peptides and amino acids
- **lipases** – fats to fatty acids and glycerol
- **amylase** – starches to mono & disaccharides
- **nucleases** – nucleic acids into nucleotides

3. **Duodenal Secretions**

include:
- **peptidases** – breaks polypeptides into amino acids
- **disaccharidases** – disaccharides into monosaccharides
- **nucleosidases & phosphatases** – break nucleotides into component parts

**Large Intestine**

some digestion occurs here due to bacteria
esp in caecum
esp herbivores → large caecum
  carnivores → small or no caecum

**Control of Digestive Secretions**

secretions from digestive glands is under nervous and hormonal control
digestion begins as mainly an autonomic nervous reflex
digestion is completed due mainly to hormonal controls

1. **Saliva**

strictly a nervous reflex
reflex is triggered by:
mechanical and chemical presence of food in mouth
olfactory stimulation
visual stimulation
salivation can also be a learned response
→ learned by association: eg. Pavlov’s dog

2. Gastric Secretions
A. secretions occur in three separate phases:
   cephalic phase
   secretions first activated by sight, smell, taste and thoughts of food
   gastric phase
   continued secretion is triggered by presence of polypeptides in pyloric region of stomach
   stimulates parietal cells to secrete hormone = gastrin
   gastrin circulates within capillaries of stomach and enhance secretions from gastric glands in stomach wall
   gastrin is secreted as long as there is food in stomach
   Intestinal Phase
   chyme is released into duodenum duodenum presence of chyme causes release of intestinal gastrin
   this further stimulates gastric secretions

B. Enterogastric Reflex
   slows stomach emptying to once/∼20 seconds
   signaled by stretch receptors induodenum
   speed of reflex varies by types of foods
   eg. fats - slow; proteins – fast
   fluidity
   solids – slower; liquids – quicker
   age
   infant – fast; adult – slower
C. Presence of fat (fats float → last to leave stomach) in duodenum stimulates release of GIP (gastric inhibitory peptide)
   → shuts down gastric secretions

4. Bile
   when chyme enters duodenum
   → secretes cholecystokinin
   → stimulates peristalsis of gall bladder

5. Pancreatic Juices
when chyme enters duodenum it causes the release of:

**cholecystokinin**
- stimulates pancreas to release enzymes

**secretin**
- stimulates pancreas to release bicarbonates

6. **Duodenal Enzymes**
   - may be another hormone that stimulates release of duodenal enzymes
   - don’t know now

**Absorption**

~9-10 liters (2.5 gallons) of food, liquids and GI secretions enter tract/day

~500 – 1000 ml reaches the large intestine

150 ml is expelled as feces

~half of that is bacteria from intestines

→ 75 ml wastes

absorption occurs throughout digestive tract but most (90%) occurs in small intestine; 10% in large intestine and stomach

**Stomach**
- some water
- alcohol
- a few drugs

**Small Intestine**
- absorb ~90% of materials
- absorbs virtually all foodstuffs
- absorbs 80% of electrolytes
- absorbs most water

**Jejunum**
- all food stuffs
- most water
- most electrolytes

**Ileum**
- reclaim some additional bile salts
Small intestine is greatly modified for absorption

→ epithelial cells are joined by tight junctions
  substances cant move between cells
  materials must pass through cells to get to
  interstitial spaces
  = transepithelial transport

→ surface area is greatly increased for more efficient absorption of nutrients:

  1” diameter x 10’ long
  → if smooth tube = 0.33 m² (3 sq ft)

  but: interior is folded
  → increases area ~3 x’s

  also: fingerlike projections = villi
  ~1mm tall
  contain capillary beds
  contain lacteals
  → increases area another 10x’s

  also: each epithelial cell of villus has microvilli
  up to 1700/cell
  = brush border
  → increases area another 20x’s

  →→→ 200 m² (1800 sq ft)

Large Intestine
  excess water and some additional nutrients

absorption can be an active or passive process:
  1. most nutrients are absorbed by active transport
     eg. glucose
     amino acids
     some minerals
  2. some lipids are absorbed by diffusion to lacteals
     eg. fats
     fat soluble vitamins
  3. water is absorbed by osmosis
  4. large molecules are absorbed by pinocytosis
     eg. a few large fats and proteins
passed to lacteals with other fats

**Absorption of Specific Nutrients**

especially in jejunum

1. **Carbohydrates**
   mono → facilitated diffusion → capillaries

2. **Proteins**
   amino acids → active transport → capillaries
   each requires a specific carrier
   eg. genetic diseases

   whole proteins → endocytosis → capillaries
   rarely absorbed,
   but more common in newborns
   results in food allergies
   may also be how IgA are absorbed from
   mothers milk

3. **Lipids**

   micelles → diffusion → chylomicrons → lacteals

   bile salts are essential for absorption as well as
   digestion

   micelles = collections of fatty elements clustered
   together with bile salts
   polar on outside
   nonpolar core

   micelles are much smaller than emulsion droplets
   and easily diffuse between microvilli to come in contact with cell
   surface

   fats, cholesterol, fat soluble vitamins then leave
   the micelles and move through the cell membrane by diffusion into
   epithelial cells of villi

   fat absorption is completed in ileum

   in absence of bile, (eg gall stones), most fat passes
   to large intestine

   once inside epithelial cells:
   triglycerides are coated with proteins to
   produce **chylomicrons**

   **golgi bodies** process and secrete them
a few enter capillary beds (too large)
most enter lacteals in villi

once in blood:
hydrolyzed back into free fatty acids that can be used by
cells for energy production or converted to fat in adipose tissue

4. Nucleic Acids

nucleotides → active transport → blood

5. Vitamins

water soluble → diffusion → blood
except B12, very large, charged molecule
bonds to intrinsic factor produced by stomach
taken in by endocytosis

fat soluble → micelles → etc

6. Electrolytes

most are actively absorbed throughout the length
of intestine

Fe and Ca++ mainly in duodenum
for most nutrients the amount reaching the intestine is the
amount absorbed
But absorption of Fe and Ca is closely tied to body’s need:

Fe
is actively transported into mucosal cells
binds to protein ferritin
stored until needed or lost as cells sloughed off
women have 4x’s more transport proteins than
men
in blood Fe binds to protein = transferrin, for
transport

Ca
regulated by Vitamin D
acts as a cofactor to facilitate Ca absorption
eg. <Bld Ca → >PTH:
→ >Ca release from bone
→ >reabsorption of Ca by kidney
→ renal activation of Vit D to increase
absorption in intestine

Na\(^+\) is coupled with active absorption of glucose and Amino acids
K\(^+\) moves in by simple diffusion
most anions passively diffuse along a gradient but Cl\(^-\) is actively transported

7. Water
9 L of water enters small intestine daily
95% is absorbed by small intestine (osmosis) coupled to solute uptake
rest is absorbed by large intestine of ~ 500 ml of chyme entering large intestine
~150 ml of feces is produced
Liver

is the largest gland in body
lies immediately under the diaphragm
consist of 2 lobes

Functions of Liver:
1. store carbohydrates, iron, vitamin A, B12 & D
2. metabolize fats, carbos and proteins
3. detoxify blood from digestive system
4. secrete bile to aid in digestion (~1pt/day)

Food, Nutrition, Metabolism

the food that we eat must do 2 things:
1. serve as building blocks, ie. nutrients
   used to maintain and build tissues

2. release energy when metabolized in cells
   breaking bonds releases energy
   we break down large organic molecules to
   release their energy and make ATP

food

\[ \text{matter} \text{ (building blocks)} \]

\[ \text{energy} \text{ (metabolism, ATP)} \]

1. Building Blocks

nutrients \( \rightarrow \) the most basic atoms or molecules
that we need to survive

essential vs nonessential nutrients
the body can make some nutrients itself given
proper elements
some nutrients the body cannot make
\( \rightarrow \) must be in food
45 –50 different nutrients are essential
nutrients
\( \rightarrow \) can’t make them ourselves
eg. elements, vitamins, some AA’s

elements:

<table>
<thead>
<tr>
<th>macronutrients</th>
<th>micronutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 18.5%</td>
<td>Cr, Co</td>
</tr>
</tbody>
</table>
H 9.5%  Cu, F
O 65%   Mo, Se
N 3.2%  Si, Sn (tin)
P 1.0%  Zn, V
Ca 1.5%

molecules:
O2 (oxygen gas)
vitamins
8 amino acids
2 fatty acids

2. energy

we break down organ foods (sugars, lipids, etc) to extract energy

chemical bond energy: break bonds
→ release energy

most cells prefer glucose but can also use lipids, proteins, etc

some cells can only use glucose

glucose + O2 → CO2 + H2O + ATP

most foods are a combination of essential and nonessential nutrients that we use as building blocks and as energy

as a general rule the foods we eat contain the essential nutrients and energy sources in roughly similar amounts as they are found in the body

→ we are what we eat!

but if our diets aren’t carefully selected:
→ can get too little or too much of a particular nutrient
  eg. deficiencies may cause diseases
  eg. excesses may be toxic

→ can get too much or too little energy
  need ~ 2000 Cal/day
→ may contain various additives that could be beneficial, neutral or toxic to body

Carbohydrates
Kinds in food:

mainly from plants (fruits, vegetables, and grains)

simple sugars: mono & disaccharides (honey, fruits, lactose is from milk)

complex carbohydrates = polysaccharides: starches and fiber from plants; glycogen from meats

“starch”

virtually all starchy foods come from plants
plant cells store glucose as starch
long branched or unbranched chains
packed tightly in wheat and rice grains and tubers
also high in legumes (peas, beans)
almost all “starchy foods” are from plants
provide much of the food energy for people worldwide:
  rice → Asia
  wheat → Canada, US, Europe
  corn → Central and South America
  millet, rye, oats, barley

glycogen

= animal starch
long heavily branched polymer
animal cells store a small amount of sugar as glycogen
meats only contain a limited amount since its broken down quickly after slaughter
not found in plant cells
important in our bodies
  each of our cells stores some sugar in form of glycogen
  ~1lb/person
  ~1/3" in liver cells
  liver glycogen plays critical role in glucose homeostasis
  can quickly release glucose into blood when levels drop
  ~2/3" in muscle tissue
  muscles can respond to energy demands quickly by converting it to glucose for energy production

“fiber”

structural part of plant
not same thing as starch → undigestible
eg. cellulose – cannot digest but essential for digestion
= roughage, fiber [“natural fiber” = sawdust]
cellulose, hemicellulose, pectins, lignins, cutins, tannin, gums
different kind of linkages between subunits
→ body lacks enzymes to split them apart
fibers important nutritionally:
affect time to absorb other nutrients from GI tract
improves flow of materials through intestine
used as fiber in breads etc = “sawdust”
some may be fermented by gut bacteria to produce
additional nutrients

soluble fibers:  fruits, oats, barley, legumes
               slow stomach emptying
               delay glucose absorption
               lower cholesterol levels

insoluble fibers: veggies, wheat, cereal
                 accelerates chyme thru intestine
                 ?delays? glucose absorption

pectins
   = jellies and jams

lignins
→ resist decomposition

**Uses in body**

energy
all carbohydrates are polymers of monosaccharides
are main energy source of all cells

ribose and deoxyribose to synthesize DNA and RNA

fiber enhances digestion
complex carbohydrates, the body cannot digest
but required for digestion

excess sugars converted to: glycogen & fats

glycogen
   each cell, esp liver and muscle can store some
   excess glucose as glycogen
   ~ 1lb/person
   1/3rd in liver
   2/3rd s in muscle tissue
provides quick energy in muscle cells
in liver helps maintain glucose blood levels
fats
   all excess is converted to fats (adipose tissue)

Requirements

no essential carbohydrates

the amount in diet is not critical for essential nutrition

recommend 45 – 65% SN03 of diet is carbohydrates;
   120-175 g/day

minimum 100g/d to prevent shift to proteins and fat catabolism

a diet high in complex carbohydrates helps control body weight
   crowds out fat
   reduces hunger
   reduces “empty calorie” intake

enough fiber to promote digestion

recommended sugar intake ≤ 10% total energy intake

US consumption

carbohydrates comprise 51-33%SN03 of food we eat

about half of our sugar intake is natural and half consists of refined sugar (sucrose)

200-300 g/day
   much refined sugar
   (45 lbs/yr); >46% caloric intake

Imbalances

Deficiencies:
   if not enough carbo’s the body shifts to fats and proteins for energy
   but some cells cannot effectively do this and may become energy starved

   tissue wasting,
   metabolic acidosis (from excessive fat breakdown)
**Excesses:**

- Cells convert some to glycogen (animal starch)
  - Esp liver and muscle cells
  - Allows a quicker response to energy demands
  - Glycogen in liver plays critical role in maintaining blood sugar levels between meals

Sugar:

- US $\rightarrow$ 45 lbs/yr
- “Empty calories” $\rightarrow$ Contribute to energy needs but no nutrients
- Therefore, need to consume even more calories to get proper nutrients
  - Eg. soda: 200 cal $\rightarrow$ ~0 nutrients
  - 3 slices bread: 200 Cal $\rightarrow$ Includes 9g proteins and some B vitamins

Even being careful in food selection it takes at least 1500 calories to get all needed nutrients.

The less active a person is the more critical this becomes.

Sugar isn’t bad, but nutrients must come 1st.

Dental caries (refined sugar)

Obesity

- Not only getting more calories
- But most foods with added sugar are also high in fats

Heart disease

- (In carbohydrate sensitive people)

Hyperactivity in children, criminal behavior

No confirming data; just anecdotes

**Starch & fiber:**

- Generally, high carbohydrate diets benefit by reducing fat intake and obesity,
- Reduce risk of heart disease,
- Reduce risk of cancer,
- Reduced risk of diabetes,
- Better GI tract health,

But excessive fiber intake in malnourished, elderly & children can reduce mineral absorption

**Lipids**

A diverse group of compounds including:

- Triglycerides
- Phospholipids
- Sterols (including cholesterol)
- Eicosinoids, prostaglandins
most are polymers of fatty acids

**Kinds in foods**

95% of dietary fats & oils are triglycerides

responsible for much of the flavor, tenderness, aroma of food

plants high in lipids

- nuts,
- vegetable oils \(\uparrow\) [mainly polyunsaturated fats]

animal products high in lipids

- meats, esp organ foods
- dairy products \(\downarrow\) [most saturated fats]
- eggs

animal products are only dietary source of cholesterol

fats carry with them fat soluble vitamins (A,D,E & K)

polyunsaturated fats mostly in plant oils (grains, seeds, nuts, leafy vegetables)

cholesterol: animal foods only, not plants

- esp. egg yolks, organ meats such as liver, whole milk, butter, cheese

**Uses in Body**

triglycerides:

- alternate fuel (concentrated stored energy)
- shock protection pads
- insulation from cold
- insulation around neurons and nerves

phospholipids:

- cell membranes
- emulsifiers to keep fats suspended in blood and fluids

sterols:

- hormones (adrenal cortex, gonads)
- bile salts
- cell membranes (0.9 of all body cholesterol)

**Requirements**

2 essential fatty acids: linoleic and linolenic acids
(high in fish, grains, seeds, nuts, leafy veggies) → needed for
normal brain development
maintain cell membrane
make hormones
immune response

Fat soluble vitamins are usually dissolved in fats ad oils we eat.

80-100g/d; 25 - 35% of calories should be from fats
unsaturated better than saturated fats
≥3% required Fatty Acids (1-1.5 g/day)
<250 mg/d cholesterol

**US Consumption**

32 - 34% of calories in our diets are from fats
only get 10% of required amount of linoleic acid

**Imbalances**

(of all nutrients fats are most often linked to chronic diseases)

**Deficiencies:**

mainly due to inadequate amounts of essential fatty acids;
mainly seen in infants and young children fed nonfat milk and low-fat diets

retarded growth
reproductive failure
skin lesions
kidney and liver disorders
neurological and visual problems

**Excesses:**

of all nutrients, excess fat is most often linked to chronic diseases:

obesity
>50% of those in US are overweight
obesity costs ~$117 Billion/yr in USS

cardiovascular disease
(esp. high cholesterol & high LDL)
some cancers (total fat intake)

**Nutritional BS**

1. Lecithin supplements
   a phospholipid
   not essential
   body digests it like other fats
   taken at “dosages” recommended; 7g/d
   → can alone add 6.5 lbs/yr excess fats
   large doses may cause GI tract distress

2. All cholesterol is bad for you
   its made and used by liver
   liver makes much more cholesterol than we get in diet
   50,000 trillion (50 quadrillion) molecules/second
   or 800-1500mg/d
   need cholesterol for cell membranes
   synthesis of steroid hormones
   to make bile salts

   cholesterol in blood:
   LDL’s = bad guys
   linked to increased risk of heart attack

   HDL’s = good guys
   represent cholesterol being returned to liver for breakdown
   high levels → decreased heart attack risk

<table>
<thead>
<tr>
<th>optimal ranges</th>
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<tbody>
<tr>
<td>total cholesterol</td>
</tr>
<tr>
<td>LDL</td>
</tr>
<tr>
<td>HDL</td>
</tr>
<tr>
<td>Triglycerides</td>
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</tbody>
</table>

food cholesterol does not raise blood cholesterol as much as saturated fat in diet does
→ sat fats are main cause of >LDL & <HDL

**Proteins**

**Kinds in food:**
animal proteins: meats, fish, poultry, cheese, milk, eggs
plant proteins: nuts, cereals & grains, legumes
**Uses in Body**

amino acids to synthesize the 50,000 or so proteins in our cells
- enzymes
- hormones
- regulators
- transport
- antibodies
- actin/myosin
- fiber(collagen)
- buffers
- complement
- active transport
- hemoglobin
- clotting
- salt/water

balance
- energy alternative (last resort, muscle wasting)

**Requirements**

~half of 20 amino acids are essential, must be gotten in diet
- 10 essential in children
- 8 essential in adults

(body cant make proteins if any one of the Amino Acids are in short supply)

**complete protein** (generally animal protein)
- = all essential amino acids
- (meats, fish, cheese, milk, eggs)

**incomplete protein** (most plant protein)
- = missing 1 or more essential amino acids
- (nuts, cereals, legumes)

a few plant foods have complete proteins but even then most are “lower quality” → essential AA’s not present in adequate amounts
- (eg. soybeans have complete proteins)

vegetarians must plan meals well to get complete complement of essential AA’s:
- eg. blackbeans and rice
- eg. peanut butter on wheat bread
- eg. tofu & veggies on rice

need to maintain nitrogen balance:
- within each cell, proteins are constantly being made and broken down
- body can’t store excess amino acids, it converts them to lipids
- free amino acids may be used immediately released into blood used for energy
<table>
<thead>
<tr>
<th>+ Nitrogen Balance (synthesis &gt; decomposition)</th>
<th>- Nitrogen Balance (synthesis &lt; decomposition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>increased GH, Sex Hormones</td>
<td>increased glucocorticoids</td>
</tr>
<tr>
<td>children</td>
<td>physiological or emotional stress</td>
</tr>
<tr>
<td>pregnant women</td>
<td>poor dietary intake</td>
</tr>
<tr>
<td>repair of injury</td>
<td>starvation</td>
</tr>
<tr>
<td>recovery from illness</td>
<td></td>
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</tbody>
</table>

when glucose and FA’s are not available cells use AA’s for energh and to make glucose over time, wasting of lean body tissue carbo’s and fats “spare” proteins

recommend 10 - 35%SN03 of calories from proteins

(0.8g/kgwt/day ≈ 1 - 8oz serving of meat/d)

**US Consumption**

15%SN03 of calories from proteins
1.5 - 2 lbs per day, also mostly also high in fats

**Imbalances**

**Deficiencies:**

can have devastating effects, esp on children
eg. Protein-Energy Malnutrition

**Marasmus & Kwashiorkor**
affect >500 mil children worldwide;
includes most of 40,000 children who die PER DAY

impaired brain and learning development
GI tract fails
anemia
edema
due to deficits of plasma proteins
during pregnancy – miscarriage or premature birth

**Excesses:**

may be risk factor in heart disease
some cancers (colon, breast, pancreas, prostate, kidney)
adult bone loss and calcium loss increases with
excessive animal (not plant) proteins in diet
obesity (protein rich foods are usually fat rich foods)

**Nutritional BS**

1. Protein and amino acid supplements:
   all reasons touted for their use are unfounded
   a. athletes take them to build muscle
   b. dieter to spare protein while losing weight
   c. women to strengthen fingernails
   d. individual AA’s to
cure herpes (lysine)
sleep better (tryptophan)
to lose weight
to relieve pain and depression (tryptophan)

normal healthy people NEVER need protein supplements
they are expensive
they are less completely digested
when used as “replacement” they are dangerous
eg. liquid protein diets
→ caused death in many users
single AA’s do not occur naturally in foods ad offer no benefit to
the body
the body was not designed to handle the large amounts of
individual AA’s in supplements
→ can create such a demand for a carrier that it
prevents the absorption of other AA’s
some can be toxic at high levels

**Vitamins**

vitamins are organic molecules:
1. other than proteins, carbohydrates, lipids and nucleic acids
2. used in very small amounts
3. most cannot be made by body
4. don’t form polymers
5. cannot be broken down for energy

categorized as:
water soluble and fat soluble vitamins
→ affects: what foods they are found in
if and where they are stored in body
toxicity
how they are eliminated

**Water Soluble**
- dissolve easily in water, not fat
- sensitive to heat and light
  - generally don’t store well
  - lost in cooking
- absorbed directly into blood and travel freely
  - throughout the body
- generally not stored well in body
  - eliminated daily by kidneys
  - fewer toxicities
  - needed in frequent, small doses
- B’s, C

**B Vitamins**
- (B1, B2, Niacin, Biotin, Pantothenic Acid, B6, Folic Acid, B12)
- not used directly as fuel
  - but help body *use* fuel
- act as coenzymes in many energy reactions
  - eg. NAD, NADP
- others help in new cell formation
- deficiencies cause major shutdown in body systems
- toxicities are uncommon but do occur in “pill takers”
- toxicities when obtained from food alone are unknown

**Vitamin C**
- coenzyme
- collagen formation
- antioxidant

**Fat Soluble vitamins**
- dissolve easily in fat, not water
- generally more heat and light stable
  - not destroyed by cooking or storage
- first enter lymphatic system
- generally require protein transport molecules to travel in blood
- blood concentrations are maintained because body retrieves them from storage as needed
- stored in liver and fat cells and accumulate; not readily excreted
  - don’t need every day
  - easier to have toxicity: can reach toxic levels
if consumed in excess
→ needed in less frequent doses

play major roles in growth and maintenance
their presence affects health and functions of
eyes
skin
GI tract
lungs
bones and teeth
nervous system
blood

tend to appear in different foods than water soluble vitamins

A, D, E, K

**Vitamin A**
promotes
vision
growth
bone remodeling
immune system

animal foods, liver, fish, butter, eggs
fast foods often lack vitamin A
Vit A for acne → no effect (altered form = accutane is)
retin A for wrinkles, long term effects unknown

**Vitamin D**
not essential
body can synthesize it with UV
UV and liver ad kidney convert precursor
to active form
liver and kidney disease can cause symptoms of deficinency
acts like hormone
increases Calcium absorption and raises blood calcium levels

egg yolks, liver, fish, butter, fortified milk
sunscreen >spf 8 prevents activation
whites just need 15 minutes of sun on hands, face and arms
darks need up to 3 hours of exposure
**Vitamin E**
- antioxidant: protects lipids and cell membrane
- vegetable oils, fruits
- does NOT:
  - improve physical performance
  - enhance sexual performance
  - slow aging
  - prevent gray hair
  - prevent wrinkles
  - slow parkinsons

**Vitamin K**
- blood clotting
- synthesized by bacteria in GI tract
- liver, leafy green veggies, cabbage

**Minerals**
- inorganic elements
- cannot be changed or broken down
  - → no special care to preserve during storage or prep
  - → but may leach into water and be lost during cooking
- 4% of body weight
- some minerals are easily absorbed into blood and transported
- others need carriers to be absorbed and transported

body requires relatively large amounts of 7 minerals:

- **Calcium** [2.5lbs/132lbs]
- **Phosphorus** [1.3 lbs/132 lbs]
- **Sulphur** [1/3rd lb/132 lbs]
- **Sodium**
- **Potassium** [1/2 lb/132 lbs]
- **Cloride**
- **Magnesium**

**Calcium**:
- bones and teeth
- membrane transport
- nerve transmissions
- muscle contractions
- heart rhythm
blood clotting
enzyme cofactor

**Phosphorus**:  
bones and teeth  
ATP  
creatine phosphate  
DNA & RNA  
phospholipids  
active transport

**Sulphur**  
most proteins

**K, Cl, Na**  
osmotic balance  
nerve impulses  
muscle contractions

**Magnesium**  
coenzymes

trace amounts of 12 others:

F, I, Fe,
F → strengthens bones
I → thyroid hormones
Fe → hemoglobin

Co, Cr, Cu, Mn, Se, Zn  
cofactors for enzymes

in general, the body absorbs nutrients best from foods in which they are diluted and dispersed.

taken in pure concentrated form they are more likely to interfere with absorption other nutrients:

eg.  > Zn → hinders Cu and Ca absorption
    > Fe → hinders Zn absorption
    > Ca → hinders Mg and Fe absorption
    > Mg → hinders Ca and Fe absorption

eg. even fortified foods can cause problems  
> ß carotene → interferes with Vit E metabolism  
> Vit E → interferes with Vit K activity
several professional nutritional societies have indicated that people should ordinarily SHOULD NOT use supplements when one does need nutrients

1st try to get them from foods
2nd multivitamin, mineral supplements
   betw 50-150% RDA for each nutrients are best
   (these are ranges normally found in foods and are therefore within tolerances)
3rd treat any supplement like medicine

**Vitamin & Mineral Supplements BS**

~40% of US population takes supplements regularly
~$4 Billion/year spent

~20% take multivitamins

others take large doses of single nutrients

especially:
   Vit C
   Iron
   Calcium

Most are self prescribed; only a few are physician recommended

why:
   dietary insurance -just in case not getting adequate amounts
to protect against certain diseases
vitamins are best taken as supplements:
   after complete nutritional assessment
   in such cases mineral supplements may be as important as vitamin supplements
   → people whose diet lacks certain vitamins probably lack several minerals as well

**Arguments Against taking supplement:**

1. **Toxicity**

   Often goes unrecognized, esp if chronic
Eg. A woman took 1000 RE vitamin A/day for > 10 years (75-750 RE is safe range)
   Was diagnosed with liver disease
   Condition cleared up when she discontinued supplements

toxic overdoses in children are fairly common
  poison control center gets >30,000 calls/yr on children <6yrs old swallowing large doses of supplements
  fruit flavored, shaped like cartoon characters

Iron containing supplements are esp toxic and fatal

some believe supplements should have warning labels

2. **Often accompanied by life threatening misinformation**
   some ill people believe high doses of a vitamin or mineral can be therapeutic

false claims are exceedingly common
  eg. member of Consumer Health Education Council called 41 Houston area health food stores
  asked to speak to person who provided nutritional advice
  caller said that they had brother sick with AIDS
  All 41 offered products they said could “strengthen the immune system
  30 said they sold products that would cure AIDS

  similar inquiries found people who said they could treat:
  headaches dizziness fatigue
  kidney stones glaucoma sudden wt loss
  stress cancer

  none recommended callers obtain medical advice

people with health problems are more likely to take supplements than others
  yet, today’s health problems un US ar more likely to be due to overnutrition and poor lifestyle choi8ces than to nutritional deficiencies

many falsely believe that
  the food supply contains inadequate nutrients
  that supplements provide energy
  supplements can enhance athletic performance
  supplements can build lean body mass without work or
faster than work alone

3. **On individual basis we have Unknown Needs**
   no one knows how to formulate the ideal supplement:
   what nutrients should be included
   how much of each for each person

   surveys have shown no relationship between the supplements
   people take and the nutrients they actually need

4. **May give a false sense of security**
   may lull people into eating irresponsibly
   produce self diagnosis when symptoms of a disease come on

**Good Reasons to take Supplements:**

1. **To Correct Overt Deficiencies**
   eg. scurvy, pellagra, rare but still occur
   may require therapeutic doses 2-10x’s RDA’s

2. **Improve Nutritional Status**
   subclinical deficiencies are more difficult to see and
   are probably much more common
   eg. habitual dieters, vegetarians, elderly
   few people get RDA for all nutrients every day
   but most receive average needs for all nutrients

3. **Reduced Disease Risk**
   may help,
   eg. may be susceptible to osteoporosis
   esp if lactose intolerant or allergic to
   milk

4. **To Support Increased Nutritional Needs**
   eg. in certain stages of life cycle
   eg women of childbearing age → folate
   eg pregnant or breast feeding women
   → Fe, Ca++, folate
   eg. newborns → Vit K
**Metabolism**

Digestion breaks down complex organic molecules into their component parts: glucose, glycerol, fatty acids, amino acids, nucleotides

metabolism focuses on what happens to these substances in the body cells

**metabolism** = sum of all chemical reactions that occur in the body

*anabolism* = synthesis; requires energy

*catabolism* = decomposition; releases energy

energy transfer

couples anabolism to catabolism: \( \text{ADP} \xrightarrow{\text{coupled}} \text{ATP} \)

often an energy releasing step is **coupled** with a energy requiring step

**Metabolic Pathways**

Metabolism in most cells is a collection of groups of enzymes forming a metabolic pathway

many of the reactions occurring in cells occur in a sequential, stepwise fashion = **metabolic pathways**

→ *intermediate products*
→ branching
→ end product inhibition
→ genetic errors

Most chemical reactions and entire metabolic pathways that occur in cells are **reversible**: same enzyme may catalyze reaction in either direction

reaction rate and direction depends partly on the concentrations of substrates and products = Law of Mass Action

\[
\text{carbonic anhydrase}
\]

eg. \( \text{H}_2\text{CO}_3 \xleftrightarrow{\text{rate & direction of reaction depends on substrate concentrations}} \text{H}_2\text{O} + \text{CO}_2 \)
Major Catabolic Pathways
(energy producing)

Carbohydrates

Carbohydrates are broken down into simple sugars (=monosaccharides) by digestion and absorbed into the body.

Most cells use glucose as their main energy source.

Complete breakdown involves 3 metabolic pathways:
1. Glycolysis
2. Krebs Cycle
3. Electron Transport Chain

1. Glycolysis

Glucose is broken down into 2 pyruvic acids.

2 ATP’s are made in the process.

If free oxygen is available, pyruvic acid is converted to Acetyl CoA.

If no free oxygen is available, it is converted to lactic acid (toxic waste product).

Fatty acids and amino acids can also be broken down into Acetyl CoA:

\[
\begin{align*}
\text{Glucose} & \xrightarrow{\text{2 ATP’s}} \text{pyruvate} \\
\text{pyruvate} & \xrightarrow{\text{2 ATP’s}} \text{lactic acid} \\
\text{lactic acid} & \xrightarrow{\text{2 ATP’s}} \text{Acetyl CoA} \\
\text{Acetyl CoA} & \xrightarrow{\text{2 ATP’s}} \text{Krebs Cycle}
\end{align*}
\]
**Fats**

most (95%) are triglycerides;  
→ digested to glycerol and fatty acids

glycerol is converted to pyruvate

fatty acids are taken apart 2 Carbons at a time to make Acetyl CoA

cells can make glucose form pyruvate and other 3-C compounds, but NOT from 2-C fatty acid fragments
	herefore, for the most part, fat cannot provide energy for RBC’s or the brain and nervous system  
→ only glycerol from fats can be converted  
(≈5% of wt of triglyceride)

**Amino Acids**

if consumed in excess of need to make new proteins they are 1st deaminated:

\[ \text{AA} \rightarrow \text{ketoacid} + \text{ammonia (alkaline)} \]

\[ \text{urea} \]

liver takes the ammonia to make urea

most are glucogenic  
→ can provide glucose to body

some are ketogenic  
→ can be used to make body fat, not glucose

some enter Krebs Cycle directly  
→ or can be used to make glucose

Therefore, proteins, not fats are a fairly good source of glucose when carbohydrates are not available

only some AA’s are essential; others can be made given a source of Nitrogen:  
= Transamination
transfer amino group from one AA to a keto acid
mainly occurs in the liver
liver makes ammonia $\rightarrow$ kidney excretes urea
high bld ammonia $\rightarrow$ liver disease
high bld urea $\rightarrow$ kidney disease

need water to excrete urea (osmosis):
with high protein diet excess water is lost as more urea is excreted
$\rightarrow$ apparent weight loss with high protein fad diets

2. Krebs Cycle & Electron Transport
if energy is needed, Acetyl CoA will enter the Krebs Cycle and ETS
In Krebs cycle H’s, CO2 and ATP are made
ETS involves a series of proteins that serve as electron carriers
electrons are removed from hydrogen atoms
energy is removed from electrons
last step requires O2 to form water
process cannot occur without adequate O2

**The Body’s Energy Budget**

energy is measured in unites called kcals = Calories
the more H’s a molecule contains the more ATP (energy) can be generated
of the various energy pathways:
  fat provides the most energy for its weight
  note all the H’s $\rightarrow$ more oxidation can occur
  eg: glucose has 12 H’s $\rightarrow$ 38ATP’s
  a 16-C FA has 32 H’s $\rightarrow$ 129ATP’s

we take in energy continuously
we use energy periodically
optimal body conditions when **energy input = energy output**

any excess energy intake is stored as fat

average person takes in ~1 Million Calories and expends 99% of them → maintains energy stability

1 lb of body fat stores 3500 Calories

```
| 454g:  87% fat |
| 395g x 9 Cal/g = 3555 kcal |
```

would seem if you burn an extra 3500 Cal you would lose 1 lb; and if you eat an extra 3500 Cal you would gain 1 lb

not always so:
1. when a person overeats much of the excess energy is stored; some is spent to maintain a heavier body
2. People seem to gain more body fat when they eat extra fat calories than when they eat extra carbohydrate calories
3. They seem to lose body fat most efficiently when they limit fat calories

**For overweight people a reasonable rate of wt loss is**

1/2 – 1 lb/week → can be achieved with Cal intake of ~ 10 Cal/lb of body wt.

Quicker Weight Loss:
1. may lose lean tissue
2. may not get 100% of nutrients
3. may result in binge eating/crash diet cycle
4. quick weight changes are not just fat normal, long-term wt gained or lost = 75% fat, 25% lean starvation: ~ 1/2 and 1/2 fat to lean

eg. **fasting** after a meal:

1. when we eat, excess C, P, F converted to glycogen and fat
2. later (hrs to ~1 day) glycogen and fat are used for energy
3. continued fast (or starvation) proteins and fats are used for energy
low bld glucose → liver begins to make glucose from lactic acid and amino acids

normally, brain and nerve cells consume
~2.3 of daily glucose needs
(400-600 Cal; 20% of all energy used in body/day)

therefore, body protein in muscles and liver always breakdown to some extent during fasting

the amino acids that can’t be used to make glucose are used as energy source by other cells

this breakdown of body protein is an expensive way to get glucose

in 1st few days of a fast:
→ body protein provides ~90% of glucose
→ glycerols provides ~10%

if protein loss were to continue at this rate
→ death would occur in ~3 weeks regardless of the quantity of fat someone had stored

but; as fast continues, fat breakdown also increases (almost doubles)

brain cells adapt:
→ uses AcetylCoA units made from fatty acids to make ketone bodies

brain can use these ketone bodies for energy

after ~10 days ketone bodies are meeting much of the brain’s energy needs

but some areas still rely exclusively on glucose
→ body protein is still needed

ketone bodies ~ ketoacids
→ body goes into acidosis; bld pH declines
→ ketone bodies spill into urine =ketosis
→ ketosis suppresses appetite

this has served as justification for ketosis producing diets
but

1. any kind of food restriction leads to reduced appetite
   $\rightarrow$ a well balanced, low cal diet induces loss of appetite without harmful side effects

2. ketosis reduces metabolism to conserve tissue
   $\rightarrow$ loss of fat is greatly reduced (less than what would be lost on low cal diet)

**Low Carbohydrate Diets**

similar to fasting
glycogen reserves are spent
protein is metabolized to make glucose
eventually get onset of ketosis

hype:
   brings dramatic wt loss in 1\textsuperscript{st} few days

but:
   much of this loss is glycogen and protein and large amounts of water and minerals

   eg. 7 lb loss in 2 days:
   1 or 2 lbs of fat
   5-6 lbs of protein, water, minerals

after diet, weight quickly rebounds

**Protein Sparing Diets**

ingesting only protein
but this protein is used to supply glucose
carries serious health risks:
   ketosis
   vitamin and mineral deficiencies
   fluid loss
poor long term record of success
   $\rightarrow$ people generally regain weight
now sold only to doctors or hospitals and must carry a “Protein Diet Warning”

**Measuring Energy Input (Food Calories)**
Bomb Calorimeter
  → burn food and see how much heat it gives off

  but: body is less efficient than the calorimeter in converting food to energy. Can be corrected

  also varies by proportion of Carbos, Fats, Protein in the food

Food intake:
  controlled by many factors that affect hypothalamus

  most eat at 4 hr intervals; stomach is designed this way

  empty stomach delivers “hungry” message to brain
  → people who restrict their E intake → hunger diminishes with time

  people can adapt to excessive amounts as well

**Measuring Energy Output**

the body converts E in food to ATP at ~50% efficiency

the rest is lost as heat

when ATP is used again to do work (movement, heartbeat, nerve impulses, active transport, etc)
  again ~50% is lost

  → overall efficiency of converting food to work
  ~25%

the other 75% is lost as heat

the work itself also generates heat

therefore, the total amount of heat the body produces reflects the amount of energy it is burning

measured by **direct calorimetry**
  = heat production

or by **indirect calorimetry**
  = amt of O2 consumed or CO2 expelled
  use a respirometer
  → every time 1 L of O2 is consumed,
4.83 Calories of heat har produced

There is a tremendous variation in daily caloric requirements

1300 - 5000 Cal/day

average male = 2900
average female = 2100

affected by:

1. age
   2 yr old burns 2x’s Calories/lb as an adult

2. Weight
   the more a person weighs, the more total energy
   is required but probably less energy/lb
   → normal wt adult may be 1.5x’s more BMR/lb
   than obese person

3. exercise
   strenuous exercise can increase metabolism up to
   40 x’s for a short period

4. stress
   severe stress can increase metabolism over
   160 x’s over short time

5. metabolic hormones
   eg pituitary, thyroid, GH
   eg. GH can raise BMR 15-20% during growth stage

6. body temperature
   1º C → 10% increase in MR
   high fever may double the metabolic rate

7. pregnancy
   20% increase last trimester
   60% increase during lactation

   → difficult to define a “normal” metabolic rate

Components of Energy Expenditure:
1. Basal Metabolism (60-65%)
2. Physical Activity (25-30%)
3. Thermic Effects of food (10%)
4. Adaptive Thermogenesis (?)
1. Basal Metabolic Rate

easier to define a "**Basal Metabolic Rate**" =
   is the metabolic rate
   at rest
   after a 12 hour fast
   after > 1 hour after exercise

is NOT a minimum

at least 2/3rds of energy spent each day
   maintain body temperature
   nerve impulses
   heart beat (100,000x’s/day)
   posture
   kidney filtration
   etc

2/3 – 3/4 of body energy is used for maintenance
   = Basal Metabolism

only 1/4 – 1/3 is used in voluntary muscle activity

BMR represents our major energy expenditure
   ~1 Cal/kg/hr

   eg. 150 lb person = 55 Cal/kg/hr = 1320/day

BMR is highest in people with more lean body mass

BMR is also greater in tall people → >surface area

BMR declines with age ~5%/decade

2. Physical Activity

most variable component of energy expenditure

a heavy person uses more energy/minute than thinner person

3. Thermic Effect of Food

the body uses energy to process food
   eg. GI tract muscles
   eg. secretory cells
eg. active transport is proportional to energy intake

usually ~10% of food intake is used to digest and absorb that food

eg. 2000 Cal $\rightarrow$ 200 Cal used to digest and absorb

4. Adaptive Thermogenesis

some energy is spent when body must adapt to changed conditions

eg. cold

overeating
starvation
trauma
stress

$\rightarrow$ need to build hormones and enzymes necessary to cope

extremely variable

not usually included in calculations

Regulation of Body Temperature

regulation of body temperature is vitally important

$\rightarrow$ enzymes work in narrow temperature range

even slight shifts can disrupt metabolic balance and produce disorders

normal temperature of body core = 98.6º F (37º C)

homeostasis requires that

heat energy output = heat input

skin plays a key role in this process

all chemical reactions produce heat as a byproduct

$\rightarrow$ more activity $\rightarrow$ more heat is produced

muscle cells are the major heat producers

Heat Homeostasis

Excessive Heat (Body Temp Too High)
nerve impulses from skin and body and warmed blood send message to thermostat in hypothalamus

does dilation of blood vessels in skin

also deeper blood vessels constrict
→ blood is diverted to body surface

heat is lost by:

1. **Radiation (IR energy)**
   most heat is lost this way

2. **evaporation**
   nerves stimulate sweat glands in skin to release fluid
   as fluid evaporates it absorbs heat
   eg. sponge bath for fever patients

3. **conduction**
   contact transfer
   eg. chair seat, clothes, etc

4. **convection**
   heated air moves away from body
   cooler air moves in

**Inadequate Heat (Body Temp Too Low)**

brain triggers different response to reduce heat loss
→ skin blood vessels constrict
→ sweat glands become inactive

if the body is still losing too much heat may stimulate muscles to contract slightly
→ increases cell respiration → releases more heat

also may get shivering
→ rhythmic contractions to increase metabolism of muscle cells to produce more heat

**Body Weight, Body Composition & Health**

weight gains and losses tell little about how the body’s composition may have changed
→ but this is how most judge their “fitness”

for most: “overweight” = “overfat”
healthy body weight is defined by 3 criteria:

1. a weight within a suggested range
2. a fat distribution pattern associated with a low risk of illness
3. no medical conditions that would suggest a need for weight loss

Healthy Weight Standards

often do not account for age or gender

based on insurance data which underrepresents minorities and elderly

Body Mass Index

many prefer BMI to Weight tables

\[
\text{BMI} = \frac{\text{kg wt}}{\text{ht in m}^2} \text{ or } \frac{\text{wt (lb x 705)}}{\text{ht in inches}^2}
\]

normal: males 20-25
    females 19-24

overweight if BMI = 25-30
obesity if BMI = >30

if >30 \rightarrow greater risk of premature death
if >35 \rightarrow 2x’s as likely to die prematurely
if >40 \rightarrow greater CV disease

US average BMI = 26.3

studies show a “J” shaped relationship between body weight and mortality
\rightarrow people who are underweight or extremely overweight carry high risks of early death

Health Risks of Underweight

1\textsuperscript{st} to die during famine

more at risk when tests require fasting

in greater danger when fighting a wasting disease like cancer
\rightarrow many people with cancer die not from cancer but from malnutrition
underweight women more likely to be infertile

pregnancy may result in unhealthy infant

**Health Risks of Overweight**

obesity has been declared a “disease” because so many health risks are associated with it:

- diabetes
- cardiovascular disease
- hypertension
- sleep apnea
- osteoarthritis
- abdominal hernias
- some cancers
- varicose veins
- gout
- gall bladder disease
- liver malfunction
- arthritis
- flat feet
- respiratory problems
- complications in surgery and pregnancy
- greater rate of accidents

obesity related illnesses cost $39 Billion/yr (1986)

**Some Examples:**

1. **Cardiovascular Disease**
   - strong relationship
   - central obesity is as important risk factor as high blood cholesterol, hypertension and smoking

2. **Diabetes**
   - Adult Onset (Noninsulin dependent) diabetes is 3x’s more likely to develop in obese than nonobese person
   - Central body fat cells appear to be larger and more insulin resistant than lower body fat cells

3. **Cancer**
   - risk of cancer increases with body fat
   - not sure why – may be correlated with greater levels of some hormones
   - eg. estrogen in women

**Total Body Fat**

variable

can be estimated in several ways:

1. **skinfold measurements**
2. **waist/hip ratios**
3. **Hydrodensitometry**
1. skinfold measurements

~ 1/2 the fat in body lies directly beneath the skin

the thickness of this subcutaneous fat is directly related to total body fat

fat fold measurements correlate directly with the risk of heart disease

they assess risk better than BMI

2. waist/hip ratios

is also a good indicator of fat distribution

waist circumference/hip circumference = WtoH Ratio

but may not be appropriate for women, older people or some ethnic groups

may also not be useful in assessing changes in body fat

3. Hydrodensitometry

take two weights: one on land, other in water

gives a measure of the body’s volume

can calculate the body density

from this can estimate % Body Fat

Fat Values

eg  normal wt male:  10-25% body fat
normal wt female:  18-32% body fat

athletes generally lower
  eg. males:  5-10%
  females:  15-20%

some need more fat than others
  eg. Alaskan fishermen
  eg. starting pregnancy
research has shown that health problems develop when fat exceeds:
  22% in men <40 yrs old
  25% in men >40 yrs old
  32% in women <40 yrs old
  35% in women >40 yrs old

if not enough body fat:
  1. reduced hormone synthesis
  2. infertility
  3. depression
  4. abnormal hunger regulation
  5. unable to keep warm

→ fashion models are generally unhealthy

**Fat Distribution**

may be more important than % fat alone

2 major kinds of fat distribution patterns:
  1. lower body fat
  2. upper body fat

1. **lower body fat**

  fat around hips and thighs

  is most common in women in reproductive years

  is not associated with any health risks
  (except children!)

2. **upper body fat**

  (=central obesity, = intra abdominal fat)

  stored around abdomen

  presents a greater risk than fat elsewhere in body

  increases risk of premature death due to:
  heart disease
  stroke
  diabetes
  hypertension
some cancers

abdominal fat is common in men and in women after menopause

also, people with central obesity smoke more and drink more than average
  → smoking may directly affect fat distribution

more exercise → less central obesity

upper body fat seems to go straight to liver
  → LDL’s

**Urinary System**

Urine production and eliminations are one of the most important mechanisms of body homeostasis
  → composition of blood is determined more by kidney function than by diet

all body systems are directly or indirectly affected by kidney function

kidney function is closely tied to circulatory system

typically referred to as “excretory system”

excretory wastes = metabolic wastes
  → chemicals & toxins produced by cells during metabolism

but we have several organs that serve an excretory function other than kidneys:

1. **kidneys**
2. **skin**
   sweat glands rid body of water, minerals, some nitrogenous wastes (ammonia)
3. **lungs**
   rid body of CO2 from energy metabolism of cells
4. **intestine**
   in addition to getting rid of undigested food residue
   feces also contains some metabolic wastes as well
bile pigments
salts
calcium
some toxins

**Functions of Urinary System:**
1. removal of metabolic wastes
2. elimination of toxins
3. elimination of excess nutrients
4. elimination of excess hormones
5. regulation of fluid volume
6. regulation of electrolytes
7. regulation of acid base balance
8. regulation of blood volume and pressure
9. erythropoiesis
10. calcium absorption

**Histology of Kidney**

nephron is basic functional unit of the urinary system
can find various parts of the nephron and its blood supply in the cortex and medulla of kidney

**Nephric Tubule**

the nephric tubule is organized into several discrete structures

**Bowman’s Capsule**
cup shaped mouth of nephron
usually in cortex

**Proximal Convoluted Tubule**
attached to Bowman’s Capsule
highly coiled (convoluted)
inner surface contains microvilli

**Loop of Henle**
large loop consisting of:
descending limb & ascending limb
extends down into medulla

**Distal Convoluted Tubule**
appears similar to PCT

**Collecting Tubule**
many DCT’s drain into one collecting tubule
bundles of collecting tubules = **pyramids**

**Pyramids** drain into **Calyces** (sing. = **calyx**)  
**Calyces** coalesce to form **pelvis**

**Blood Supply**

kidneys are highly vascularized

every minute, 1200 ml/min of blood flows through kidneys  
$\rightarrow = \frac{1}{5}$th of cardiac output  
45 gallons/day  
all blood $\sim 60x's/day$

**Renal Artery**

brings blood to kidney  
branches into smaller and smaller arterioles

**Afferent Arteriole**

bring blood to individual nephrons

**Glomerulus**

dense capillary bed  
formed by afferent arteriole  
inside Bowman’s capsule  
**Bowman’s Capsule + Glomerulus = Renal Corpuscle**

**Efferent Arteriole**

blood leaves glomerulus via efferent arteriole  
$[\rightarrow$ artery$\rightarrow$capillary bed$\rightarrow$ artery$]$  

**Peritubular Capillaries**

efferent arteriole divides into another capillary bed  
surrounds the rest of the nephric tubule  
(PCT-LH-DCT-CT)

**Urinary Physiology**

urine formation in nephrons occurs by:  
1. filtration  
2. reabsorption
3. secretion

1. Filtration

occurs in renal corpuscle:

Glomerulus  \rightarrow  Bowmans Capsule

water, salts, small molecules and wastes are filtered out of blood capillaries of glomerulus:

fenestrated capillaries
\rightarrow  \text{act like sieve}

have \textbf{higher filtration pressure} than other capillaries of body

afferent arteriole is larger than efferent arteriole
\rightarrow  \text{increases pressure in glomerulus}
pressure \sim 45\text{mmHg}
\text{(vs 35 mmHg in most capillaries)}

not all water leaks out, some is retained since proteins and solutes that remain in blood attract water by osmosis (water follows salt)

if blood pressure is reduced
\rightarrow  \text{urine formation slows down}

kidneys can maintain a fairly constant filtration rate by:

1. renal autoregulation
   \text{kidney adjusts its own resistance to blood flow despite changes in systemic blood pressure by constricting and dilating local arterioles}
   = \text{autoregulation}

2. renin-angiotensin system
   \text{mainly controls systemic blood pressure in emergencies but will also increase pressure in glomerular capillaries}
   \text{renin is secreted by cells in walls of DCT (juxtaglomerular cells) in response to:}
   \text{decreased BP: below 80 mmHg}
   \text{eg. hemorrhage, dehydration}
   \text{direct sympathetic stimulation}
renin activates angiotensin (plasma protein)
angiotensin causes vasoconstriction of arterioles
throughout the body
→ raises blood pressure

3. local chemicals
some chemicals secreted by kidney have local effect on blood vessels

eg. prostaglandins (tissue hormones)
→ some vasodilators
→ some vasoconstrictors
eg. NO → vasodilator
eg. kallikrein (renal enzyme) → vasodilator
eg. adenosine
eg. endothelin

Sympathetic stimuli can override the above:

renal autoregulation can be overridden by emergency or stress

sympathetic fibers trigger strong constriction of afferent arterioles

shunts more blood to heart, brain, muscles

filtrate is essentially the same composition as plasma without formed elements or proteins

solute (filtrate) enter Bowmans capsule

2. **Tubular Reabsorption**

urine is not the same composition as this filtrate
needed nutrients are conserved
wastes and toxins are eliminated
blood levels of fluids, salts, acidity etc are actively regulated

reabsorption is more selective

occurs all along nephric tubule

overall, ~99% of glomerular filtrate gets reabsorbed
only ~1% of original filtrate actually leaves the body as urine

<table>
<thead>
<tr>
<th>Composition of Plasma, Filtrate &amp; Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>(solids in grams/24hrs; water in liters/24 hrs)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Filtrate</th>
<th>Reabsorbed</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amount</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteins</td>
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<td>15</td>
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<tr>
<td>Glucose</td>
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<tr>
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<tr>
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<td>1.4</td>
<td>1.4</td>
<td>0</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

different substances are reabsorbed back into blood from different parts of tubule:

**Proximal Convoluted Tubule**
- ~80% of materials to be reabsorbed are reabsorbed in PCT
- cells lining PCT have microvilli
- more mitochondria
- all small proteins, glucose, amino acids are reabsorbed
- most water, most salts are reabsorbed
- some wastes

**Loop of Henle**
- additional Cl\(^+\) and Na\(^+\) ions are reabsorbed by active transport
  - **countercurrent mechanism:**
    - high salt conc is maintained in medulla around loop
    - ascending limb is impermeable to water
    - creates high conc of salts

**Distal Convoluted Tubule & Collecting Tubule**
- high salt conc around nephric tubule causes water reabsorption in DCT and CT
- both salt and water reabsorption is partially controlled by hormones:
  - Na\(^+\) & K\(^+\) by aldosterone
  - H2O by ADH & aldosterone (indirectly)
**Aldosterone:**
- secretion controlled by $K^+$ & $Na^+$ ion concentrations in tissue fluids
- also affect reabsorption of water
- tied to renin secretion
- diuretics tend to
  - increase $Na^+$ reabsorption
  - and increase $K^+$ loss

**AntiDiuretic Hormone:**
- No ADH $\rightarrow$ tubules are practically impermeable to water
  - $\rightarrow$ release hypotonic urine
- with ADH $\rightarrow$ tubules are permeable to water
  - osmosis causes water reabsorption
  - $\rightarrow$ release hypertonic urine

3. **Tubular Secretion**
- cells of DCT and CT can secrete some substances
  - esp $K^+$ and $H^+$
  - also NH4 and
  - some drugs (eg. penecillin)

  can be active or passive processes

  usually urine is slightly acidic
  - $\rightarrow$ normal diet produces more acid than alkaline waste products

**Renal Clearance Rate**

the concentration of wastes in blood leaving kidneys (renal vein) is usually lower than their conc in blood entering kidneys (renal artery)
- $\rightarrow$ blood is cleared of wastes

  can estimate filtration rate of kidneys
  - need chemical that is filtered but not reabsorbed
    - eg. creatinine (but some is secreted too)
    - eg. inulin
  - measure how much of a known amount appears in urine then
Glomerular Filtration Rate = Renal Clearance Rate

Average Renal Clearance Rate
for most substances is ~20%
→~20% of materials in renal blood are
filtered and not reabsorbed/transit

requires many passes thru kidneys to completely rid blood of something

Reabsorption & Secretion
of Specific Nutrients

1. **Glucose**
easily filtered
requires energy to reabsorb
minimum amount of glucose in plasma to cause
- glucose to appear in urine
  = renal plasma threshold
  = 180-200 mg/100 ml

glycosuria/hyperglycemia
→ plasma glucose >200 mg/100ml

2. **Amino Acids**
all require carriers for active transport
presence in urine may be due to:
excess amounts in blood
missing or defective carriers

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Disease</th>
<th>Cause of Disease</th>
<th>Effects of Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>cystine</td>
<td>Cystinuria</td>
<td>defective cystine carriers</td>
<td>kidney stones</td>
</tr>
<tr>
<td>tryptophane</td>
<td>Hartnup disease</td>
<td>defective tryptophane carriers</td>
<td>cells deficient in NAD and NADP</td>
</tr>
<tr>
<td>methionine</td>
<td>Homocystinuria</td>
<td>enzyme defect causes buildup of this intermediate product</td>
<td>speech defects, mental retardation</td>
</tr>
<tr>
<td>phenylalanine</td>
<td>Phenylketonuria</td>
<td>enzyme defect causes buildup of this intermediate product</td>
<td>severe mental retardation</td>
</tr>
</tbody>
</table>

3. **Sodium**
90% of filtered sodium is reabsorbed in PCT
additional 10% may be absorbed in LH due to effects of Aldosterone:
without aldosterone
→8% of rest is reabsorbed
4. **Potassium**

90% of filtered potassium is reabsorbed in PCT

- high blood [K⁺]:
  - may occur in metabolic acidosis
  - can cause cardiac arrhythmias
- low blood [K⁺]:
  - can cause arrhythmias, muscle cramps

Additional 10% may be absorbed in LH due to effects of Aldosterone:

- without aldosterone
  - → all 10% is reabsorbed
- with aldosterone
  - → stimulates secretion of K⁺ into DCT
    - up to 50x’s more than was originally filtered

Diuretics cause

- greater reabsorption of sodium and increased loss of potassium
  - → may require KCl supplements

5. **Hydrogen Ions (H⁺)**

Linked to potassium secretion

6. **Bicarbonate Ions (HCO₃⁻)**

Usually all is reabsorbed

**Urine Analysis**

The kidneys perform their homeostatic functions of controlling the composition of internal fluids of body

The by product of these activities is Urine

Urine contains a high concentration of solutes

In a healthy person, its volume, pH and solute concentration vary with the needs of body

During certain pathologies, the characteristics of urine may change dramatically
an analysis of urine volume, physical and chemical properties can provide valuable information on the internal conditions of the body

**Physical Characteristics**

1. **Volume**
   - normal = 1000 – 1800ml/day (2-3.5 pints)
   - influenced by:
     - blood pressure
     - blood volume
     - temperature
     - diuretics
     - mental state
     - general health

2. **Specific Gravity**
   - weight compared to water
   - water = 1.000
   - measures solute concentration
   - average range: 1.008 - 1.030

3. **Color**
   - normal = yellow-amber (from hemoglobin breakdown)
   - influenced by:
     - ratio of solutes
       - >solute conc. = darker yellow to brownish
       - <solute conc. = less color to colorless
     - diet (eg. beets)
     - blood in urine

4. **Transparency**
   - turbid indicates mucus, bacteria or cells

5. **Odor**
   - normal = musty
   - diabetics → sweet odor

6. **pH**
   - normal urine is slightly acidic: 5.0 - 7.8
   - influenced by:
     - diet
       - eg. high protein → acidic
       - vegetables → alkaline
metabolic disorders:
   eg. lungs, kidneys, digestive system, etc

7. **Cells and Castings**
   normally find epithelial cells and some bacterial cells and various cells casts
   Bacteria
   
   \[
   \begin{align*}
   < 100-1000/ml &= \text{contamination by normal flora} \\
   >100,000/ml &= \text{indicates active colonization of urinary system}
   \end{align*}
   \]
   RBC’s & WBC’s
   presence is almost always pathological inflammation of urinary organs
   pus from infections

**Chemical Characteristics**

1. **Water**
   normally is 95% of total urine volume
   remaining 5% consists of solutes

2. **Normal Solutes**
   mostly wastes or excess amounts of nutrients, hormones, etc
   
   **organic** – mainly ‘nitrogenous’ compounds:
   
   **urea** (95% of N wastes)
   from deamination of amino acids
   
   **creatinine**
   from breakdown of energy transferring molecule especially in muscle cells
   
   **uric acid**
   from breakdown of nucleic acids
   
   **inorganic** –
   
   **chlorides and salts**
   
   **ammonia** – N containing cmpd, not much produced, very toxic
   
   **phosphates**
   
   **sulfates**

3. **Abnormal Solutes**
   normal constituents of plasma
   usually do not appear in urine:
   too large to be filtered out
   all is reabsorbed
   
   a. albumin (protein)
normally too large to filter out
presence indicates increased permeability of glomerular membrane due to:
  injury
  high blood pressure
  irritation
  toxins

b. glucose
  normally, all is filtered and all reabsorbed
  body reabsorbs as much as is needed
  when it appears in urine indicates high blood sugar concentrations
  → symptom of diabetes mellitus

c. ketones
  produced when excessive quantities of fats are being catabolized
  high quantities may be caused by:
  diabetes
  starvation
  dieting
  → too little carbohydrates in diet
Other Functions of Kidneys

in addition to their primary role in removing metabolic wastes and excess nutrients and hormones from the body, kidneys also:

5. Control rate of erythropoiesis

kidneys produce hormone = **erythropoietin** that regulates erythropoiesis:
- hypoxic ➔ secretes more erythropoietin
- excessive O2 inhibits hormone production

    - testosterone enhances kidney production of erythropoietin
    - estrogen and progesterone have no effect

6. Affects the absorption of Calcium from intestine

activates Vitamin D circulating in blood

7. Help to regulate blood pressure & volume

    [more later]

renin-angiotensin mechanism

    lower BP:
    ➔ kidneys release enzyme = renin
    ➔ renin triggers production of angiotensin II
    ➔ angiotensin causes:
    ➔ vasoconstriction ➔ raises BP
    ➔ release of ADH ➔ conserves water to raise BP

helps maintain high filtration pressure in Renal corpuscles

blood pressure is directly affected by the volume of fluids retained or removed from body:

    greater volume ➔ increases BP
    ➔ eg. excessive salts promote water retention
    lower volume ➔ decreases BP
    ➔ eg. dehydration
    ➔ eg. internal bleeding
Kidneys can directly affect blood volume by altering salt and water reabsorption under influence of Aldosterone and ADH

eg. Aldosterone promotes salt retention and therefore water retention by kidneys
eg. ADH promotes water retention by kidneys

8. Regulate pH of body fluids

[more later]

able to actively secrete excess hydrogen ions

**Fluid & Electrolyte Balance**

body is ~2/3rd water (males=63%; women=52%)

this water occupies three “compartments”:

- **intracellular** → 63% (or 40% of body wt) → 25L
  
  facilitates chemical reactions, solvent

- **extracellular** → 37% (or 20% of body wt) - [15L]
  
  provides internal environment for cells and transport, protection, etc

- **transcellular** (CSF, eye, synovial joints, bursae)

- **interstitial** 30% → 12L

- **lymph**

- **plasma** (=intravascular) 7% → 3L

Total: 40L*

*based on 70kg (154lb) person

Total amount of water & water in each compartment remain relatively constant

water content and movement is tied to electrolytes and solute concentrations and movement

eg. if solutes leave a compartment by diffusion;
  
  water also leaves by osmosis
  
  → water follows salt

can’t talk about fluid balance without talking about electrolyte balance

balance means: **input = output**
**Inputs**
1. digestive tract: food and drink
2. metabolism: each cell produces water in catabolism of glucose

**Outputs**
1. urine (kidneys)
2. lungs: water vapor expired with air
3. sweat (skin)
4. feces (intestines)

Output is crucial element in control of fluids and electrolytes.

Most important output organ is kidney.

Urine volume is controlled by:
- glomerular filtration rate
- reabsorption by tubules

Glomerular filtration rate remains fairly constant → not a strong controlling influence on urine volume.

Major control of urine volume is reabsorption of water.

Reabsorption can be controlled to make output match input.

Controlled by two major hormones:
- ADH
  - Decrease in ECF volume stimulates release of ADH
  - Osmoreceptors in hypothalamus?
  - Makes distal & collecting tubes permeable to water → increases water reabsorption → decreases urine volume

- Aldosterone
  - Increases tubular reabsorption of sodium and other ions → increases water reabsorption by osmosis → decreases urine volume

Additional factors that can affect fluid loss
1. Urine volume can also be affected by amount of solutes in urine → the more solutes the more urine
Diabetes mellitus
excess glucose spills over into urine
causes excess water to enter nephric tubule by osmosis
results in excessive water loss & dehydration

2. hyperventilation
over extended time can lose significant water from lungs
may result in dehydration

3. prolonged vomiting or diarrhea

fluid input can also be regulated to some degree to help maintain fluid balance:

dehydration → salivary secretions decrease
→ dry mouth → thirst

provides a stimulus for “behavioral modification”

but still requires voluntary act

if fluid intake is stopped completely a balance cannot be maintained
→ even if kidneys shut down
still lose water through lungs and skin

Composition of Fluids

these fluid compartments contain critical electrolytes and solutes:

cations: Na⁺; Ca²⁺; K⁺; Mg²⁺
anions: Cl⁻; CHO₃⁻; HPO₄⁻²; Proteins

These electrolytes function:
1. essential nutrients or building blocks
2. serve critical role in regulation of various metabolic pathways
3. affecting membrane potentials of muscle and nerve cells
4. control water movement between compartments by affecting osmotic pressures

Ions in Extracellular Fluids differ greatly from those in Intracellular Fluids:

<table>
<thead>
<tr>
<th>most abundant cations</th>
<th>ECF</th>
<th>ICF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td></td>
<td>K⁺; Mg⁺</td>
</tr>
</tbody>
</table>
While the electrolyte content of the **Extracellular Fluid Compartments** (mainly Interstitial Fluids & Plasma) they do differ significantly in the amount of **protein** anions:

→ plasma has much more protein than interstitial fluids

proteins generally cannot cross capillary walls or cell walls so they are less common in tissue spaces

the chemical content of these compartments helps to control movement of water between them

**Water Movement Between Compartments**

2 major factors control the movement of water between compartments:

- **osmotic pressure (OP)**
  (electrolytes and solutes)
  osmotic pressure develops in compartment with higher concentration of solutes
  *tends to pull water into compartment*

- **hydrostatic pressure (HP)**
  (water pressure, blood pressure)
  *tends to push water out of compartment*

the force that moves water between adjacent compartments

= the **effective filtration pressure (EFP)**

If these four forces balance out

→ **EFP = 0**

there is no net movement of water between compartments

If:  
**HPA + OPB > HPB + OPA**
fluid leaves A and enters B

If: \( HPA + OPB < HPB + OPA \)

\( \rightarrow \) fluid leaves B and enters A

eg: if \( B = \text{blood} \)
    IF = interstitial fluid
    HP and OP measured as mmHg

arterial end of capillary bed:

\[
\begin{array}{ccc}
\text{A} & \text{B} \\
(BHP + ISFOP) & (ISFHP + BOP) \\
(37 + 0) & (1 + 25) \\
(37) & (26)
\end{array}
\]

venous end of capillary bed

\[
\begin{array}{ccc}
\text{A} & \text{B} \\
(BHP + ISFOP) & (ISFHP + BOP) \\
(17 + 0) & (1 + 25) \\
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main factor that controls exchange of fluid between blood and tissue spaces is **hydrostatic pressure**

the mechanism that regulates water movement between capillaries and tissue spaces is essentially the same as that which regulates movement of water from cells to tissue spaces

in this case hydrostatic pressure in both “compartments” is almost 0 therefore major controlling factor is changes in **osmotic pressure**

changes in solutes is controlled by active transport across the cell membrane esp. sodium/potassium pump
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**effective filtration pressure (EFP)** = the force that moves water between adjacent compartments

\[
\begin{align*}
\text{A} & \quad \text{B} \\
\text{fluid compartment} & \quad \text{fluid compartment} \\
\text{HPA} & \quad \text{OPA} \\
\text{HPB} & \quad \text{OPB} \\
\end{align*}
\]

If: these four forces balance out then \( \text{EFP} = 0 \)
- there is no net movement of water between compartments

If: \( \text{HPA} + \text{OPB} > \text{HPB} + \text{OPA} \)
- fluid leaves A and enters B

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- fluid leaves B and enters A

eg:

**arterial end of capillary bed:**

\[
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changes in solutes is controlled by active transport across the cell membrane
- esp. sodium/potassium pump
Water Balance Disorders

eg. dehydration

output > input

caused by:
  excessive sweating
  water deprivation
  chronic diarrhea
  excessive vomiting

Blood loses water → ECF loses water → cells lose water

infants & elderly more likely to suffer dehydration
  since their kidneys are less able to conserve water

Treatment: replace water and lost electrolytes

eg. water intoxication

input > output

often happens after dehydration
  → water is taken in too quickly without electrolytes

input → to blood → to tissue spaces → to cells

can cause edema as water collects in ISF

causes cells to swell as it moves from tissue spaces into cells

especially affects cells sensitive to ion concentrations: muscle and nerve cells

can result in:
  heat cramps
  convulsions
  confusion
  coma
**eg. edema**

= abnormal accumulation of water in ECF

caused by:
- decreases in plasma proteins due to
  - liver disease
  - kidney disease
  - starvation
- obstruction of lymphatic vessels
- increased venous pressure
- increased capillary permeability
  - eg. inflammation
  - sunburn

**Acid/Base Balance**

some of most critical ions in body fluids are H⁺ (hydrogen) and OH⁻ (hydroxyl) ions

the concentrations of these two ions affect the acidity or alkalinity of body fluids

acidity/alkalinity is measured on pH scale
1 pH unit = 10 fold change in [H⁺]
pH of 7 is neutral
- pH < 7: more H⁺, fewer OH⁻
- pH > 7: fewer H⁺, more OH⁻

large organic molecules, especially proteins, are extremely sensitive to changes in pH
→ easily denatured

since proteins serve a wide variety of roles in the body
(enzymes, fibers, carriers, hormones, oxygen transport, immunity, etc)
variations in pH affect almost every aspect of physiology and cell metabolism

even slight changes in pH can be fatal
- blood = 7.35 – 7.45
- ≤7 or ≥7.8 is fatal

various acids and bases continually enter and leave body:
- in foods and drink
- gastric secretions
- bicarbonates from pancreas
- etc

need some mechanism to neutralize them:
body is protected against large changes in pH in two step process:

1. **buffers** – absorb excess hydrogen or hydroxyl ions to prevent drastic changes in pH

2. **elimination** – acids (or bases) are removed from body by:
   - **kidneys** - can secrete H⁺ and HCO₃⁻
   - **lungs** – as CO₂ is eliminated H⁺ are converted to water
   - **skin** – can excrete some acids in sweat

**Buffers**

a buffer is a substance that prevents marked changes in pH of a solution when acids or bases are added

eg. 1 drop of HCl in pure water

\[ \text{pH} = 7 \rightarrow 3.5 \]

1 drop of HCl in plasma

\[ \text{pH} = 7.41 \rightarrow 7.27 \]

→ blood is buffered

buffers act by combining with strong acids or basis and taking them out of solution
→ “absorbs” the H or OH ions

buffers consist of weak acid and its salt

major buffers in body fluids:
- bicarbonate
- phosphate
- hemoglobin
- plasma proteins

all buffers have limited capacity

buffering alone cannot maintain homeostasis indefinitely

at some point the acids and bases must actually be removed from the body

two main removal systems:
1. Respiratory Mechanisms
2. Excretory Mechanisms
**Respiratory Mechanisms**

respiration plays vital role in removing excess acids

with each expiration, CO2 and therefore H⁺ are removed

\[
\text{carbonic anhydrase} \quad \text{CO}_2 + \text{H}_2\text{O} \quad \text{H}_2\text{CO}_3 \quad \text{H}^+ + \text{HCO}_3^-
\]

pH receptors in arteries can increase or decrease respiratory rate based on buildup of acids in blood

acidosis $\rightarrow$ stimulates hyperventilation

**Excretory Mechanisms**

cells of DCT and CT can secrete H⁺ & HCO₃⁻

if blood pH decreases below normal levels tubules will increase secretion of H⁺

more efficient mechanism than respiratory system

usually urine is slightly acidic

$\rightarrow$ normal diet produces more acid than alkaline waste products

**Acid/Base Imbalances**

1. **Acidosis**

   $\rightarrow$ accumulation of excess acids

   $\rightarrow$ excessive loss of bases

   a. **Respiratory Acidosis**

      factors that cause buildup of CO₂ in blood

      generally due to factors that hinder pulmonary ventilation

      **symptoms:**

      labored breathing

      cyanosis

      depression of CNS $\rightarrow$ drowsiness, disorientation

      coma $\rightarrow$ death

      can be compensated for by kidneys

   b. **Metabolic Acidosis**
accumulation of non-respiratory acids or excessive loss of bases
e.g. poor kidney function
prolonged diarrhea
severe vomiting → loss of duodenal fluids
diabetes mellitus → ketone bodies are acidic

2. Alkalosis
   → accumulation of excess bases
   → excessive loss of acids

a. Respiratory Alkalosis
   caused by hyperventilation
   anxiety
   fever
   some poisonings

   symptoms:
   light headedness
   agitation
   tingling
   dizziness

b. Metabolic Alkalosis
   caused by:
   gastric drainage (lavage)
   prolonged vomiting of stomach contents
   too many antacids
Summary of Acid-Base Homeostasis

Acids produced by Metabolism

Acids produced by respiration

Acids in foods and drinks

Excessive loss or gain of acids or bases

Buffers
[bicarbonates; phosphates; proteins]

Acids and Bases combine with chemical buffers to prevent harmful changes in pH and allow time for lungs and kidneys to remove them

Breathing Rate
stimulated by CO2 & H⁺ ions

regulates CO2 in plasma

Tubular Secretion
secrete excess H⁺ or HCO₃⁻ into urine

regulates pH of blood

Acid/Base Homeostasis
Reproductive System

Function: producing offspring

propagation of the species
→ in terms of evolution
   - the only reason all the other systems exist

only major system that doesn’t work continuously
→ only activated at puberty

unlike most other organisms on planet
→ mammals only reproduce sexually

humans are dieocious
→ separate sexed (many animals are monoecious or hermaphrodites)

in 7th week of embryonic development genes are activated that trigger differentiation of gonads

Physiology of Male Reproductive System

male hormone (=androgens) are secreted mainly by interstitial cells of testes

additional testosterone is secreted by Adrenal Cortex

at puberty Ant Pituitary secretes FSH & large amounts of LH (ICSH)
   FSH & LH cause testes to increase in size and begin sperm production
   LH → also triggers testes to produce testosterone

main male hormone is Testosterone
   There are two male hormones:
      testosterone
      androstenedione

testosterone functions:
   1. development and maintenance of secondary sexual characteristics
      hair pattern
      muscular development
      skeletal changes
      voice pitch
   2. behavioral changes (~sex drive, aggression, courtship)
behavior)
2. stimulates protein synthesis
3. promotes growth of skeletal muscles

Androgens are also produced in women
ovary & adrenal cortex
relatively weak
promotes protein synthesis, growth
not masculinizing

Negative feedback loop maintains constant level of testosterone in blood:
→ high testosterone levels inhibit LH

**Hypogonadism**
- is present in 0.13% of males
due to pituitary malfunction
symptoms:
  - retains juvenile physique
  - no secondary sex characteristics
  - voice remains high pitched
  - some feminizing traits
    - e.g. arrangement of fat deposits characteristic of women
malfunction usually occurs before puberty
but can be caused later by mumps or other inflammation

**Hypergonadism**
leads to excessive development of genitalia and secondary sex characteristics

**Male Menopause**
- age related, gradual reduction in testosterone and its effects
testosterone production decreases
FSH production increases

**spermatogenesis**
sperm are produced in seminiferous tubules
develop from **spermatogonia**

**Physiology of Female Reproductive System**
- maturation of egg
- development of uterine lining
- hormone secretion by ovary


are cyclic events

not continuous as in males

complex combination of several interdependent hormonal cycles

Ant Pituitary begins secreting FSH and LH ~7-8 yrs old

FSH & LH production increases until ~11-13 yrs old

→ triggers menstrual cycle & development of secondary sex characteristics

FSH & LH stimulate follicle cells in ovary to begin secreting estrogen & progesterone

Estrogen function:
1. development and maturation of reproductive tract
2. development and maintenance of secondary sexual characteristics
   change in fat distribution
   enlargement of mammary glands
   inhibits growth of extremities

estrogen concentration in women peaks at puberty

→ this tends to inhibit GH
→ growth slows
male androgens don’t have this inhibitory effect on growth

3. behavioral changes (~sex drive, courtship behaviors)

Progesterone function:
1. has its greatest effect on estrogen primed tissues
2. changes that favor pregnancy and lactation
   endometrial thickening
   development of mammary glands

Menstrual Cycle
~28 day cycle
4 phases:

menstrual phase (days 1-6)
shedding of uterine lining if no fertilization

proliferative (follicular) phase (days 6-12)
as follicle develops it secretes increasing amounts of estrogen
endometrium cells proliferate
ovulatory phase (days 12-16)
  ovulation→ release of mature egg from ovary
secretory (luteal) phase (days 16-28)
  follicle cells left behind after ovulation develop into
  corpus luteum
  corpus luteum secretes increasing amounts of progesterone
  continued increase in development of endometrium

This cycle is tied to variations in several hormones

Oogenesis

the eggs develop within follicles under influence of FSH & LH from Ant. Pituitary

egg → antrum → Graafian → Corpus Corpus nest → follicle → develops → follicle → ovulation → Luteum → Albicans
corpus albicans I= scar tissue

as follicle cells develop egg develops within

mature (Graafian) follicle contains egg surrounded by fluid filled antrum

egg undergoes meiosis but stops as secondary oocyte (metaphase II) until fertilization

Mammary Glands

during pregnancy breast development is stimulated by estrogen and progesterone secreted by placenta

at birth shedding of placenta
  → cuts off source of these hormones
  → stimulates Ant. Pit. to secrete prolactin

Prolactin stimulates lactation (devel of milk in glands)
  usually takes several days for full milk production

Suckling of infant further stimulates secretion of prolactin oxytocin (from Post. Pituitary)
  → promotes ejection of milk into ducts
  + feedback: more suckling → more milk released