As are all living organisms the human body is composed of cells. The cell is the structural and functional unit of all living organisms.

Each cell must obtain energy and nutrients to sustain it - to do its unique job within the organism. When each individual cell fails to do so it will die.

In humans (as in other multicellular organisms), cells are aggregated into tissues - with specific functions - such as:

- muscle
- nerve
- connective
- epithelial

Tissues are coordinated into organs that work cooperatively within the total organism. We tend to associate ourselves with these specific organs and organ systems. For example, we get stomach aches and head aches. We seldom say "The cells of my stomach lining are stretched too much by the dinner I just ate, and the stretch receptors of my stomach are sending nerve messages to my brain". We say "I ate too much and my stomach hurts." Yet it is each and every one of the cells of our body that must be fed and nourished, and from that we must remove waste products.

Each cell must interact with its surroundings to obtain needed materials for survival through its boundary, the cell membrane. Each cell requires its own energy and nutrient supply and synthesizes its own materials. Each cell also produces its own waste products that must be expelled into its surroundings. All of these materials enter and leave the cell through the membrane.

As multicellular organisms, we have systems to coordinate and integrate functions. Our circulatory system, for example, delivers nutrients to and removes waste products from cells. Our digestive system processes foodstuffs and extracts the nutrients we need for absorption. Kidneys help regulate fluid balance and remove metabolic wastes.

But back to the cell. What is a cell?
Cell Membrane
A cell is defined by its boundary, the cell or plasma membrane, that is composed of protein and phospholipid, a composition that allows membranes to regulate what enters and leaves the cell.

- Some materials move passively - in fact the cell has no control
- Some materials are actively moved across membrane using energy that comes from the foods we eat

Nucleus
Cell activities are ultimately controlled by the nucleus of the cell. The nucleus contains genetic information (DNA) that regulates the activities of its cell through directing the synthesis of enzymes, proteins that function as catalysts for all chemical reactions (metabolism) that occur in a cell. Each cell must synthesize its own enzymes from its own nucleus' directions. We will see the critical role enzymes play in digestion as we continue with this section.

- When genetic information malfunctions (a mutation) a cell can not function correctly
- Some metabolic disorders that are related to diet, result from genetic problems relating to the ability to synthesize and secrete enzymes needed for digestion.

Cytoplasm
The contents of a cell are known as the cytoplasm, a fluid matrix of water, carbohydrates, lipids, amino acids, salts (electrolytes), etc. and suspended organelles (that are not the subject of nutrition this term, but a vital part of how cells work) each of which does a specific function to keep cell operating.

What do cells need?
Each cell needs 40-50 things (molecules/chemicals -- or nutrients) to sustain it, and to maintain its proper cytoplasmic activities. These molecules pass into each cell from the surrounding medium. Few cells of multicellular organisms are in contact with the external environment, and cells cannot directly exchange nutrients, wastes, and gases to the external environment; our circulatory system transports needed materials to the body's cells and removes wastes from the cells.

What Are the Nutrients?
We briefly identified the nutrients during our introduction and we will have entire chapters on these as the course goes on; but it never hurts to review a bit:
**Bulk nutrients**

**Water**
Water is the single most-needed substance for all living organisms. It is literally the basis of life. Although we need more water than any other nutrient, water is usually discussed along with the functions of minerals.

Another substance needed for life is **oxygen**, but since oxygen is breathed in and absorbed through the lungs, it's not really considered a nutrient.

**Carbohydrates**
- **Needed:** About 60% of calories consumed but activity-dependent. Active people need more.
- **Function**
  - Fuel
  - Some fuel reserve
- Generally any carbohydrate we can digest (for example, humans can not digest cellulose) will be converted to glucose, so in one sense, we can eat any type, but some foods that contain carbohydrate also have other beneficial substances and make better food choices. This is particularly true of whole grains and vegetables!

**Lipids or fats**
- **Needed:** No more than 25-30% of calories
- **Functions**
  - Fuel reserve
  - Hormone precursors
  - Protection and insulation of body organs
- Need to have some awareness of saturated/unsaturated fats, and of omega-3 and omega-6 fatty acids. It's important to minimize the amount of saturated fat and trans-fat in the diet.

**Proteins**
- **Needed:** 10-15% of calories
- **Functions**
  - Tissue and membrane structure
  - Enzymes
  - Some hormone precursors
- Virtually all protein taken in must be digested into its component amino acids which are then rebuilt by individual cells into the proteins needed for each cell to function.
- Composition of protein (number and proportion of essential amino acids) eaten is somewhat important for its usefulness
- Excess protein consumed as well as protein lacking in amino acid balance will be metabolized for fuel or processed to reserve fuel (fat). The human body stores no protein and no amino acids.
Micronutrients: Vitamins and Minerals

Vitamins
• Variety of organic compounds that we can not manufacture that are essential for certain metabolic needs
• Some Functions:
  ▪ Co-enzymes
  ▪ Visual pigments (Vitamin A)
  ▪ Hormone precursors
  ▪ Clotting factor in blood (Vitamin K)
  ▪ Tissue structure (Vitamin C in collagen)
  ▪ Anti-oxidants (C and E)
• Vitamins may be water or fat soluble
• Amounts required are critical
  ▪ Too much or too little have negative consequences

Minerals
• Minerals are a group of inorganic substances used for variety of purposes
• In general the best dietary sources of minerals for humans are the darkly pigmented vegetables. Many of our vegetables are rich in phytochemicals, as well, as are some of our darkly pigmented fruits.
• Some Functions:
  Nerve and muscle function (Ca++, K+, Na+)
  Bone structure (Ca++)
  Red blood cell formation (Fe++)
  Thyroid function (I-)

Let's now turn to some of our systems that are involved with getting the needed nutrients to our cells: Digestion, Circulation and Regulatory systems.
Obtaining and Processing "Food" - The Digestive System
Animals, including humans, are incapable of manufacturing their own foodstuffs since they cannot photosynthesize. They must obtain prefabricated food from the environment, and pre-treat, digest or process these foods to obtain needed materials (nutrients) for the body.

Food processing involves a number of activities including:
- Obtaining (procurement of) food
- Ingestion (eating)
- Processing - or digesting food to nutrients
- Absorption of nutrients
- Assimilation of nutrients in cells and tissues

Needless to say we cannot discuss everything in a few lectures. We will not discuss much about obtaining or ingesting food. As a note, however, comparing strategies for obtaining food and methods of ingestion are fascinating biological and ecological subjects.

Humans are grouped with those organisms that have structures such as teeth, which mechanically reduce the size of large food objects. We search out whole foodstuffs, and use the teeth of the oral cavity to render the food into pieces small enough to process. (OK, we may use knives and forks or chopsticks before teeth in many cases.) Where we deviate from other animals is the search process. We use the grocery store, deli or restaurant for obtaining food.

Our digestive system is an extracellular digestive system, one that is outside of the individual cells. Once digested, nutrients are absorbed into the body and assimilated in individual cells.

In fact, our digestive system is a 25-foot tube (more or less) that passes through the interior of our body. As with most animals we have a one-way digestive tract that facilitates food processing. (Some primitive animals lack a complete digestive tract and must spit back out non-digested substances.)

Our one-way passage has a progressive series of activities that allows for the ingestion of larger food items, because more "treatment" is available as we progress through the digestive tract.

Our fairly long digestive tract is indicative of a plant-eating heritage. Herbivores usually have long digestive tracts since whole plant foods are hard to digest. In fact we are pretty versatile in our ability to digest a variety of foodstuffs, as mentioned in our introduction.

To best see how our digestive system works, let's take a tour of our digestive tract and follow the passage of food.
**Ingestion**

**Mouth:**
Chews and mixes food with saliva.

**Pharynx:**
Directs food from mouth to esophagus.

**Salivary glands:**
Secrete saliva (contains starch-digesting enzymes).

**Epiglottis:**
Protects airway during swallowing.

**Trachea:**
Allows air to pass to and from lungs.

**Esophagus:**
Passes food from the mouth to the stomach.

**Esophageal sphincter:**
Allow passage from mouth to esophagus and from esophagus to stomach.
Prevent backflow from stomach to esophagus and from esophagus to mouth.

**Stomach:**
Adds acid, enzymes, and fluid. Churns, mixes, and grinds food to a liquid mass.

**Pyloric sphincter:**
Allows passage from stomach to small intestine. Prevents backflow from small intestine.

**Liver:**
Manufactures bile salts, detergent-like substances, to help digest fats.

**Gallbladder:**
Stores bile until needed.

**Bile duct:**
Conducts bile from the gallbladder to the small intestine.

**Ileocecal valve (sphincter):**
Allows passage from small to large intestine. Prevents backflow from large intestine.

**Appendix:**
Stores lymph cells.

**Small intestine:**
Secrete enzymes that digest all energy-yielding nutrients to smaller nutrient particles. Cells of wall absorb nutrients into blood and lymph.

**Pancreas:**
Manufactures enzymes to digest all energy-yielding nutrients and releases bicarbonate to neutralize acid chyme that enters the small intestine.

**Pancreatic duct:**
Conducts pancreatic juice from the pancreas to the small intestine.

**Stomach**

**Pyloric sphincter**

**Bile duct**

**Ileocecal valve**

**Gallbladder**

**Liver**

**Appendix**

**Rectum**

**Anus:**
Holds rectum closed. Opens to allow elimination.

**Elimination**

**Large intestine (colon):**
Resorbs water and minerals. Passes waste fiber, bacteria, and unabsorbed nutrients along with water to the rectum.

**Anal canal**

**Anus**

**Rectum**

**Stoma**

**Appendix**

**Pancreas**

**Pyloric sphincter**

**Stomach**

**Esophagus**

**Trachea**

**Epiglottis**

**Salivary glands**

**Pharynx**

**Mouth**

**Esophageal sphincter**

**Eosophagus**

**Bile duct**

**Ileocecal valve**

**Gallbladder**

**Liver**

**Stomach**

**Pyloric sphincter**

**Bile duct**

**Ileocecal valve**

**Gallbladder**

**Liver**

**Appendix**

**Rectum**

**Anus**

**Elimination**

**Large intestine (colon):**
Resorbs water and minerals. Passes waste fiber, bacteria, and unabsorbed nutrients along with water to the rectum.

**Rectum**

**Anus:**
Holds rectum closed. Opens to allow elimination.
Oral Cavity
- Food is taken into oral cavity (more commonly called the mouth)
- There are three major parts to the oral cavity
  Teeth
  - Mechanically reduce size of food pieces (break up chunks of food)
    - Canines --- tear food
    - Molars --- crush food
    - Incisors --- bite food
  - Herbivores
    - More broad crushing teeth to grind plant foods
  - Carnivores
    - More piercing and sharp teeth to tear and bite
  - Alignment of teeth important (note overbite and inability to bite thin things (like lettuce))

Tongue
- Manipulates food "bolus" (term used to describe what chunk of food becomes after oral cavity processing)
- Pushes food bolus to rear of oral cavity for swallowing

Salivary Glands
- Secrete saliva
  - Slightly acid pH 6 ---\(\Rightarrow\) 6.5
  - Mixture of:
    - Lubricant material
    - Antimicrobial agents
      - Counter what we put in our mouths
    - Bicarbonate buffer
      - Maintain pH
    - Salivary amylase
      - Starts the digestion of starch to maltose

Recall our earlier reference to enzymes, proteins that catalyze chemical reactions. Much of digestion is chemical and requires many enzymes. We are now seeing the first of these digestive enzymes. We will see many more as we pass through the digestive tract. Recall, too, that enzymes are specific. To help us learn enzymes, their names are usually relative to their function and end in the suffix, "ase".

For example: salivary amylase:
A common form of starch is properly called amylose. Amylase helps to break down amylose into a disaccharide, maltose
**Pharynx**
- Cavity in back of oral cavity
- Co-functions as a respiratory passage
- Therefore you need to close the "naso-pharynx" ----> trachea route during food movement or, more specifically, during the process of swallowing.

The process of swallowing raises the larynx (region above trachea) that helps the glottis to seal so we do not inhale food (choking)

Assuming swallowing occurs properly, the food bolus moves to the:

**Esophagus**
- Tubular passageway for more or less rapid movement of bolus
- Movement by **peristalsis** (waves of circular muscle contraction)
- Facilitated by **ciliated epithelium**

**Stomach**
- Separated from esophagus by a **sphincter**, the esophageal or cardiac sphincter
- A sphincter is a ring of muscle tissue that seals one section of the digestive tract from another; a sphincter normally prevents backward movement of digesting substances. Sphincters are found at most digestive "junctions".
Human Body - 9

Stomach structure
- Reasonably large muscular sac
- Three-layered wall:
  - Inner mucus membrane layer of connective tissue. The stomach mucosa is composed of columnar epithelium and mucus glands
  - Middle layer of smooth muscle
  - Outer layer of connective tissue

Stomach functions
- The stomach is used for food storage.
- The stomach volume allows for discontinuous feeding.
- Mixing of food bolus and mechanical reduction of bolus via muscular churning and stomach movement occurs in the stomach.
- Secretions of gastric juices by stomach mucosa glands promote stomach function.

Gastric Juices
- Gastrin
  - Hormone that stimulates secretions of HCl and pepsinogen
- Hydrochloric acid (HCl)
  - Dissolves food particles (acid hydrolysis)
  - Destroys microorganisms
  - Makes stomach about pH 2
    - Optimum for functioning of pepsin
- Pepsinogen
  - Converted to the enzyme, pepsin, in presence of HCl. Pepsin breaks peptide bonds of proteins (at \( \text{NH}_2 \) group).
- Mucus
  - Lubricates stomach lining, protecting stomach. Mucus is secreted by goblet cells in the stomach lining.
  - A few other enzymes, such as alcohol dehydrogenase
The release of gastric juices is regulated by the endocrine and nervous systems:
- At the smell, taste or sight of food, the brain sends messages to "prepare" the stomach.
- The presence of food, which stretches the stomach, stimulates the release of gastrin, which stimulates more release of gastric juices.
- Certain "foods", such as partially digested proteins, caffeine and alcohol, stimulate gastrin release.

**Nutrient Absorption from the stomach**
- Some salts
- Some H₂O
- Some small lipid-soluble molecules such as alcohol
  This means that alcohol can rapidly reach target cells (especially when there is no competing food in stomach) bypassing the nutrient regulation of the liver (to be discussed later).

At the conclusion of stomach activities (as long as 4 hours after food enters) the food bolus is converted to **chyme**, which passes into the small intestine via the pyloric sphincter.

**Small Intestine**
At this point, we move into the small intestine for chemical digestion. Most digestion involves breaking down the larger carbohydrate, protein and lipid molecules into their smaller sub-units, or building blocks, a process catalyzed by specific **enzymes** and regulated by **hormones**. The mechanisms of nutrient digestion will be discussed with the chapters on nutrients, but a brief introduction is appropriate at this time while we discuss the processes of digestion.

The enzymes of digestion catalyze a type of chemical reaction called **hydrolysis**, in which water is added to split the larger nutrient molecules in food apart. When cells build up their structural and functional molecules, they use the chemical reaction called **condensation**, or dehydration synthesis, removing water to join smaller molecules into the larger macromolecules.
Structure of the Small Intestine
- The small intestine is where the majority of digestion and absorption of nutrients occurs.
- The small intestine is separated from the stomach by the pyloric sphincter.
  
  - Length = 20 feet
  - Surface area = 4500 sq ft (about size of tennis court)
  - Diameter = 1 1/2"

  Divided into 3 regions:
  - Duodenum = 9 inches
  - Jejunum = 3 feet
  - Ileum = remainder

Structure of the cells of the small intestine
The great surface area of the small intestine is achieved by internal convolutions called villi, that have more bumps called microvilli. This design is critical to the absorption of digested nutrients, to be discussed later.

- Each villus has blood capillaries and a lymph capillary to remove nutrients for absorption into the body for distribution and use by cells.
- Other cells of the lining of small intestine are glandular cells that secrete digestive juices into small intestine.
- The intestines are "anchored" by a membranous mesentery, which is also lined with capillary beds to carry absorbed nutrients from the small intestine.
Digestion Function of the Small Intestine

1. Duodenum
   Intestinal mucosa secrete "intestinal juices" comprised of:
   **Hormones**
   - Secretin
     - Promotes release of bicarbonate from pancreas to neutralize acid contents from stomach
     - Increases rate of bile secretion from liver
     - Stimulus is acid
   - Cholescystokinin
     - Promotes gall bladder contraction and emptying
     - Promotes pancreatic enzyme secretions
     - Stimulus is fatty acids and/or protein
   - Gastric inhibitory peptide
     - Slows stomach activity
     - Stimulus is lipid in intestine
     - Lipids need more time for enzymes to work

**Enzymes** secreted by intestinal mucosa
Recall that enzymes are specific proteins that function to catalyze the chemical reactions that occur in living organisms. The **hydrolytic enzymes** of digestion use the process of hydrolysis (adding a water molecule to break down larger molecules into their smaller sub-units).

**Protein Digestion:**
- Amino peptidases: peptides \(\rightarrow\) amino acids
- Dipeptidases: dipeptides \(\rightarrow\) amino acids
- Enterokinase: trypsinogen \(\rightarrow\) trypsin

**Nucleic Acid Digestion:**
- Nuclease: nucleic acids \(\rightarrow\) nucleotides

**Carbohydrate Digestion:**
- Maltase: maltose \(\rightarrow\) glucose
- Lactase: lactose \(\rightarrow\) glucose and galactose
- Sucrase: sucrose \(\rightarrow\) glucose and fructose
The pancreas and the liver produce and secrete intestinal juices via the pancreatic duct and common bile duct into the small intestine.

**Pancreas Products:**

**Pancreatic enzymes:**

- **Carbohydrate Digestion**
  - Pancreatic amylase: starch $\rightarrow$ maltose
- **Lipid Digestion**
  - Lipase: fats $\rightarrow$ fatty acids and glycerol
- **Nucleic Acid Digestion**
  - Nuclease: nucleic acids $\rightarrow$ nucleotides
- **Protein Digestion**
  - Trypsin*
  - Chymotrypsin*
  - Carboxypeptidase*
  
  *Secreted in non-active forms called zymogens, acted on by other enzymes to active forms in the small intestine so they won't harm the pancreas. These 3 all act on proteins.

The pancreas also secretes a **bicarbonate** buffer to neutralize the pH of chyme.
**Liver Products:**
- Produces bicarbonate to help neutralize acid from stomach
- Synthesizes and secretes bile salts (a cholesterol derivative)
  - Bile salts emulsify fats for easier digestion by lipases
- Excretes bile wastes
  - Bile pigments
  - Red blood cell breakdown products
  - Cholesterol
  - Lecithin
  - $H_2O$ is also in bile
- Bile can be secreted through the bile duct from the liver to the duodenum or shunted to the gall bladder for storage until stimulated by CCK (cholecystokinin)
- Gall stones can form when cholesterol, a steroid not soluble in $H_2O$, precipitates out of bile.

**Absorption of digested nutrients - The jejunum and ileum**

About nine liters of fluid are absorbed daily (1.5 liters of ingested nutrients, plus mucus and digestive juices, including lots of water, which is absorbed mostly in the large intestine).

Although some nutrients can pass through the intestinal membranes via diffusion or facilitated diffusion, much of our nutrient absorption takes place by active transport, requiring protein carrier pumps in the membranes of the microvilli cells that line the intestine. The carrier molecules are nutrient specific (e.g., glucose, amino acids, etc.), and are distributed along the length of the jejunum and ileum, their distribution somewhat related to the time it takes to digest specific nutrient groups. (Substances that are harder to digest will have their carriers lower in the intestine providing longer periods of time for digestion to occur.) The motion of the villi of the intestine helps to draw nutrients to the carrier molecules in the membranes.
Soluble nutrients are then passed to the intestinal capillaries for transport through the hepatic portal vein to the liver.

Non-water soluble lipids cannot pass directly into the capillaries. Glycerol, fatty acids, cholesterol, and phospholipids are absorbed by the microvilli cells and modified with protein coats to form **chylomicrons**. The chylomicrons are then passed to the lymph vessel, called a lacteal, associated with each villus, and travel in lymph vessels to the circulatory system. They eventually do get to the liver where they are unpackaged, processed and repackaged for general circulation (more later), but can travel through much of the body's circulatory pathways first (as does the alcohol that is absorbed across the stomach).

**Absorption of Nutrients**

**Carbohydrates and Amino Acids**
- Lipids and Fat-Soluble Substances

*Rate of passage and absorption in the small intestine*
As stated, to be absorbed, a nutrient must contact a microvillus membrane surface. (That may be why there is so much microvilli surface area.)

We use the phrase "easily digested" for materials that pass easily across membrane surfaces and those that require little enzymatic digestion, such as the simple sugars (monosaccharides and disaccharides).

"Poorly digestible" materials require longer passage time and are absorbed more slowly; their carriers are concentrated lower in the small intestine. These include:
- All lipids ---> because hydrophobic in nature
- Proteins ---> large molecules that require many different enzymes
- Many plant foods ---> surrounded by cellulose, the non-digestible fiber
Ideally, we need a mix of food. A high concentration of sugar, that requires little digestion, may result in too rapid absorption, which can exceed liver regulatory property, and result in too much blood sugar (details later).

A diet too high protein and fat, while slowing the rate of movement in the stomach, may not have adequate time for total digestion/absorption.

A high fiber diet adds bulk to chyme and makes for more a more uniform passage. More fiber means an optimum time for absorption, and also keeps chyme moving thorough the intestine.

Most vitamins are better consumed with food stuffs because of timing. A supplement on an empty stomach may just move through the small intestine missing the needed carrier molecules, or it may not dissolve adequately in the digestive tract.

**Large Intestine**

About 9 hours after ingestion of food, the remainder of chyme passes through the ileoecal valve into the large intestine

**Structure of Large Intestine**

- **Ceacum**
  - About 3" with appendix at end.
  - Blind pouch where ileum enters large intestine.
  - No apparent function in human, although in many organisms caeca are used for assisted digestion.
- **Ascending - Transverse - Descending Colon**
  - Most activities of large intestine occur in the colon.

- **Rectum**
  - Separated from colon by sphincter
  - Storage of material to be eliminated, allowing for discontinuous elimination (combination of autonomic and conscious control)
- **Anus**
  - Sphincter of skeletal muscle under conscious control, seals digestive system from external world
Functions of large intestine, especially colon

- Reabsorption of sodium and water from chyme (Na⁺ from active transport and H₂O passively in response to Na⁺) This process solidifies chyme to feces.

- Elimination of wastes
  - Nondigested and nonabsorbed food
  - Cells of intestinal mucus layers
  - Bile pigments and bile salts excreted from the liver via the bile duct
  - Some toxic substances from liver via the bile duct
  - Some minerals when excess found in blood, especially iron and calcium

- Incubation and growth of bacteria using non-digested food
  - Types of bacteria in colon
    - Mutualistic bacteria that produce
      - Vitamin K
      - Thiamin
      - Riboflavin
      - Vitamin B₁₂
    - Commensal bacteria
      - Feed on our leftovers
      - Their growth and population density does inhibit establishment of pathogenic bacteria, however.

Some characteristics of our relationship with our "live-ins"

- Many bacteria have versatile respiratory pathways that produce gaseous waste products (e.g., H₂, CH₄, CO₂) depending on what they are fed, that is responsible for most of our intestinal gases
- Antibiotics may interfere with normal intestinal flora populations. May have pathogens established as a result. Some preservatives may also interfere (no good data)
- Cultivate *E. coli* as indicator of fecal contamination of H₂O
- Acidophilus milk that introduces a constant population of "good guys" into the intestine

Rate of movement in large intestine:
Substances move through the large intestine by peristalsis, and by muscle churning and mixing. The average time for materials to stay in the large intestine is 1-3 days. Usually things work pretty well in the large intestine, in spite of the number of commercials that would lead us to think that our intestines can't work properly without their products.

Problems that can arise are:
- Movement too rapid = diarrhea (much water loss) (more later)
- Movement too slow = constipation (too little water) (more later)
- Colon cancer
Regulating Absorbed Nutrients - The Liver

Although we haven't really discussed this, all cells and tissues need to maintain osmotic balance, the ratio of solutes to water inside and outside of the cells. Blood, which transports nutrients to cells, must have a proper osmotic balance to have the correct viscosity and pressure, and to prevent too much water from entering or leaving the blood (which is what having proper pressure and viscosity does).

Many nutrients are osmotically active solutes (that means they affect water movement) and would have a potential negative impact on blood volume/viscosity/pressure (not to mention fluid balance). Therefore it is critical to regulate nutrient levels in blood.

As we have become aware, discontinuous eating is followed by discontinuous digestion and absorption of nutrients so that what enters the blood may have variable concentrations of nutrients. This can be especially so when you have consumed a lot of concentrated sugar, or alcohol.

To minimize nutrient overload in the blood, water-soluble materials absorbed via the intestine pass from the intestinal capillaries to the hepatic portal vein then to the liver before entering general circulation. While lipids enter circulation through the lymph system, they, too, eventually get to the liver. In the liver a variety of regulations occurs that we shall now discuss. The liver plays a major role in monitoring blood nutrient levels. The liver also converts nutrients absorbed into the best forms for cells to utilize (when it can do so).
Some Liver Functions
1. Regulates Blood Glucose Levels
   Too much glucose in blood
   - Liver removes glucose from blood
   - Converts glucose to insoluble glycogen
   - Stores excess glycogen as reserve in liver (24 hours worth)
   - When glycogen reserve's full, converts surplus to adipose
   Too little glucose in blood
   - Liver converts glycogen reserve back to glucose
   - No glycogen reserve?
      - Liver converts whatever else is available to glucose, because brain most have glucose
      - What's available for conversion?
        - Amino acids
        - Fatty acids (That must be aerobically used)

The liver's role is but a part of the blood glucose picture. **Hormones** are super important too, especially two from the **pancreas**:
- Insulin
  Promotes absorption of glucose from blood to cells
- Glucagon
  Promotes glycogen conversion to glucose

Additional Liver Functions
2. General nutrient metabolism
   - Glycogen ---&gt; Adipose
   - Fats ---&gt; Fat inter conversion
   - Amino acids ---&gt; Fats
   - Amino acids ---&gt; Carbohydrates
   - Amino acids ---&gt; Amino acid inter conversion
   - Lactic acid ---&gt; Glycogen (Lactic acid accumulates during muscle activity)

3. Deamination of amino acids for conversion
   - Product ammonia complexed to urea for disposal
   - Removal of NH₃ from blood ---&gt; urea for disposal

4. Helps regulate osmotic balance of blood by removal of excess amounts of osmotically active nutrients

5. Manufactures blood proteins (that also maintain osmotic balance of blood)
   - Fibrinogen
   - Albumins
   - Gamma globulin
6. Manufactures blood lipids such as cholesterol

7. Manufactures bile salts to aid in fat digestion in intestines

8. Detoxifies and removes some injurious chemicals (poisons)
   - Heavy metals
   - Some hormones inactivated and prepared for excretion
   - Some particulates
   - Alcohol

9. Short-term storage of some vitamins and minerals

10. Red blood cell involvement
    - Manufactures rbc in embryo
    - Maturation factors stored for rbc
    - Destroys rbc (along with spleen)
    - Produces bile pigments (rbc breakdown products) for removal through digestive tract.
Human Circulatory System
Our circulatory system has three basic components

Heart
Series of vessels

- Arteries
  - Take blood from the heart
  - Arteries control flow of blood with elastic recoil property
  - Structure 3-layered
    - Thick outer elastic fibers-collagen
    - Muscle layer (circular muscles)
    - Endothelium (connective tissue)

- Capillaries
  - Very small vessels
  - Intricate network throughout body tissue
  - Connect to individual cells
  - Single endothelium layer thick

- Veins
  - Return blood to the heart
  - Veins less rigid than arteries, serve as volume reserve
  - Veins also have a set of valves to prevent back flow
  - Structure 3-layered
    - Thin outer elastic fibers
    - Muscle layer
    - Thin endothelium

Circulating fluids
- Blood
- Lymph

Let's now look at the components of the human circulatory system with some detail.
Blood
Blood is a connective tissue in a liquid matrix called plasma. Plasma comprises about 50-60% of the blood. Suspended within the plasma are the living cells of blood, called formed elements. There are three types of "formed elements". All are manufactured in bone marrow.

- **Erythrocytes**
  - Coated with hemoglobin to carry oxygen
- **Leukocytes**
  - Many types
  - Made in bone marrow or in lymph system, and matured in lymph
  - Function in body defense
- **Platelets**
  - Cell fragments
  - Function in blood clotting
  - Play a role in plaque formation in blood vessels

Plasma components
- **Water** (90%)
- **Solute**
  - Salts and inorganic ions
    - Regulate pH
    - Regulate some osmotic pressure
  - Plasma proteins (All made in liver)
    - Albumins
    - Fibrinogens
    - Globulins
  - Organic nutrients
    - Glucose
    - Lipids, phospholipids
    - Amino acids
    - Lactic acid, other organic acids
    - Vitamins
  - Nitrogen waste products
  - Hormones
  - Dissolved gases
    - Nitrogen
    - Oxygen
    - Carbon dioxide
The Heart and the Human Circulatory Pathway
The heart, our circulatory system pump, consists of four chambers: two atria (right and left) and two ventricles (right and left). The right atrium receives blood from the body, and the right ventricle pumps blood to the lungs (pulmonary circulation) for oxygenation. Blood returns from the lungs to the left atrium, and is then pumped from the left ventricle to circulate to the cells and tissues of the body (our systemic circulation).

We can trace the pathway of blood to, through, and from the heart in the following way:

1. Cardiac and Pulmonary Circulation
   Anterior (superior) and posterior (inferior) vena cavae
   \[\text{Right atrium}\]
   Tricuspid valve (connected by ligaments) (right atrio-ventricular valve)
   \[\text{Right ventricle}\]
   Pulmonary semilunar valve
   Pulmonary artery branches to 2 then to 4
   Lungs - rich capillary bed surrounding alveoli
   Pulmonary veins (4) (note carry O₂-rich blood)
   \[\text{Left atrium}\]
   Bicuspid valve (left atrio-ventricular valve) (mitral valve)
   \[\text{Left ventricle}\]
   Aortic semilunar valve
   Aorta branches over the heart and down the mid-dorsal area of thorax and abdomen
2. **Systemic Circulation**

Major vessels from the aorta to body - often in pairs
- Coronary (left and right)
- Carotids to head
- Brachial to arms
- Hepatic - liver
- Splenic - spleen
- Renal - kidney
- Iliac - lower abdomen
- Femoral - legs

From arteries to arterioles to capillary beds in target organs and tissue with comparable veins return to starting point!!!
How does all this work?
As we have all experienced, a circulatory system needs some type of "pumping" device, our heart, which uses muscular activity, to facilitate circulation of blood to the body’s cells. In addition, the pump must also carry adequate O₂ from lungs prior to general circulation. Since the lungs exchange oxygen to capillaries, however, the force of blood flow drops dramatically as it leaves the lungs. To solve the problem of reduced force, oxygenated blood is returned to the heart for a second "pumping".

Let's look now at the human heart (essentially 2 pumps) at work.
1. Blood needs to be pumped at a rate that provides optimal exchange of materials
2. Blood must be pumped with adequate force (pressure) to carry to all cells

Pressure (force) of heart beat
- Alternation of contraction and relaxation of muscles
- Systole = Contraction and pump
- Diastole = Relaxation
- Average pump rate = 5 liters/min. @ about 70 beats

The rate and pressure are important because the heart regulates the rate at that O₂, CO₂, wastes and nutrients get to and are removed from cells

Role of blood vessels (mostly arteries) in all this
We must maintain optimal pressure in arteries to assure delivery to all cells and tissues, even though the heart beat (systole) exerts much pressure on arteries.

The elastic recoil property (stretch) of arteries moderates the uneven pressure of the heart beat, so that a reasonably uniform pressure is maintained even when relaxed (diastole). This is especially true as arteries branch throughout the body into capillary beds.

As blood moves through body the rate and pressure decline with an increase in the total area of blood vessels. Blood pressure declines most in the capillary beds, promoting capillary exchange to individual cells.

The rate may increase a little in veins because the total area decreases from that of capillaries. In most cases, however, venous pressure is very low, so much so that movement of blood back to the heart requires the aid of muscles and the one-way valves in the veins to prevent backflow.

The exchange function of circulation
Recall that the purpose of a circulatory system is delivery and removal. This exchange occurs between capillaries and individual using pressure and solute gradients to promote movement of materials into and out of cells.
Capillary Exchange

Maintaining the pressure gradient between capillaries and cells

The pressure gradient is maintained by two forces:

- Hydrostatic pressure (the pumping force)
- Osmotic pressure (solutions/water) within cells and blood

Maintaining osmotic balance is one of jobs of blood proteins

If either (or both) blood pressure or osmotic pressure is affected, the rate of exchange will be affected. Increased pressure means more force into cells; decreased, less so. Neither is beneficial.

Variables affecting capillary exchange

- Rate of heart beat
- Strength of heart beat
- Volume of blood
- Elasticity of arteries
- Dilation or constriction of capillaries
- Proteins in blood for osmotic balance, as well as some solutes

Some blood pressure controls

- Spleen stores excess blood volume, as do veins
- Vasoconstriction temporarily increases blood pressure
- Diet for some people controls blood pressure
  - Some people are very sensitive to sodium, an osmotically active solute
- Stress levels play a role in blood pressure
The Lymph Vascular System
Although we seldom think about it, recall that in our introduction to the circulatory system, two circulatory pathways were mentioned. The second of these is the lymph system, a system that has many functions for the human.

Functions of the Lymph System
- Maintenance of fluid balance (sort of), especially excess tissue fluid (including blood proteins) leaked from capillaries
- Transport of lipids from digestive tract to liver for processing
- Body defense or Immune System - An independent function for the manufacture and storage of white blood cells for the Immune system

Why do we need a separate system to maintain fluid balance in the circulatory system?
- Some fluids and blood proteins will always "leak" from tissues and capillaries and we need to get them back into circulation...
- Many lipids are large for capillary transport from the digestive tract
- Foreign particles and cellular debris needs to be transported to disposal centers (lymph nodes)

Characteristics of Lymph transport
- No pump
- A system of vessels comprised of dead-end capillaries in the tissues that branch into lymph vessels (lymph veins) that have associated nodes or collecting ducts such as the thymus, tonsils, and spleen
- One-way movement by muscle contraction
- Dumps into the venous system near heart
  Thoracic duct
  Right lymphatic duct
Excretion and Fluid Regulation - The Kidney
You will recall that in the discussion of the liver we saw that much of what it did was process nutrients for reorganization and, when in excess, removal. We saw too, that the liver is limited in its ability to regulate; the liver can be overwhelmed at times (especially by sugar junkies)

Fortunately we also have systems that regulate fluid balance (osmoregulation) and remove metabolic wastes (excretion) from the body.

Fluid (Osmotic) Balance in the body
Systems to maintain proper fluid balance (ratio of water to solutes, or osmotic balance) must:

- Adequately distribute nutrients, (that are osmotically active)
- Remove wastes - especially nitrogen/ammonia
- Maintain osmotic balance of cells and tissues with both the internal environment and the external environment

Human Excretory System
The primary excretory and fluid balancing organ of the human is the kidney, an aggregate of functional units called nephrons that

- Filter
- Reabsorb
- Secrete
- Excrete

Prior to our kidney discussion, however - we do have other excretory methods that deserve listing...

- Lungs CO₂
- Bile pigments Hemoglobin and cholesterol from liver via colon
- Colon Some metals, salts and excess minerals
- Sweat glands Essentially a dilute urine

Kidney, Bladder and Associated Structures:
- Kidney
  - Cortex
  - Medulla
  - Pelvis
- Ureter
- Bladder
- Urethra
- Renal Arteries and Veins
Nephron Structure
The kidney is composed of a series of nephrons, each of which passes from the cortex to the medulla. Each nephron consists of:
- Glomerulus
- Renal Tubule
  - Bowman's Capsule
  - Proximal Convoluted Tubule
  - Loop of Henle
  - Distal Convoluted Tubule
  - Collecting Duct
- Peritubular capillaries

Functions of the Nephron

Filtration
- Blood enters glomerulus and filtered into Bowman's capsule
  - Blood fluid
  - Nitrogen wastes and other wastes
  - Salts
  - Solutes
  - Not filtered:
    - blood proteins (normally)
    - formed elements

We filter about 1200 ml blood/min. through kidneys
- About 125 ml of filtrate/min. = 180 liters/day (45-50 gallons)
- An arterial pressure at the kidney of 70 mm Hg promotes optimum filtration
  - If pressure increased ---> more filtrate
  - If pressure decreased ---> less filtrate
Reabsorption
Obviously we do not excrete 180 liters/day of fluid rich in plasma, nutrients and salts. It is very important to reabsorb filtrate.

Reabsorption is a combination of osmotic activity (movement of water in response to salt (a solute) gradients maintained in the kidney cortex and medulla, and active transport of solutes.

Our concern here will be reabsorption of nutrients from the filtrate back into the blood.

Nutrient Reabsorption
The proximal convoluted tubule has carrier molecules for active transport of most nutrients back into the blood capillaries that surround the nephron, such as:
- Glucose
- Amino acids
- Lactic, ascorbic, citric acids
- Mineral ions: calcium, phosphate, sulfate, K⁺, Na⁺

If the concentration of a substance is too high (e.g. abnormal glucose levels) the amount above threshold level will stay in the filtrate and be excreted in urine. This is especially true for elevated glucose and excess water-soluble vitamins.

Water Reabsorption
Water is reabsorbed in the both the proximal convoluted tubule and especially the descending Loop of Henle and the collecting duct tubules of the nephrons by osmosis, pretty much relative to body needs. If more water is in plasma, more is filtered and not reabsorbed. If there is too little water in the plasma, then more water is reabsorbed. In addition, hormones regulate the permeability of the distal convoluted tubule and the collecting duct for additional water reabsorption.

The Loop of Henle descends from the cortex of the kidney down into the medulla, and then ascends back through the medulla to the cortex.

The medulla of the kidney has a salt gradient (NaCl) that increases from a low concentration in the cortex end to a high concentration towards the pelvis region of the kidney. This salt gradient promotes the diffusion of water (in response to the salt solute concentration) from the descending Loop of Henle, and from the collecting duct, both of which pass through the medulla of the kidney. It's very clever, since the concentration of water is highest at the top of the tubules, and as water moves out while descending the tubules, the salt concentration increases, maintaining an osmotic gradient. This maximizes water reabsorption.
**Role of the Loop of Henle in Water Reabsorption**

The Loop of Henle, as it moves from the cortex to the medulla and back to the cortex, plays a major role in maintaining the salt gradient, and therefore reabsorption of water.

- The Loop of Henle establishes and maintains a salt gradient with Na⁺ pumps.
- Salts can be actively moved from the ascending Loop of Henle as filtrate moves up the tubule, which helps maintain a high salt concentration in the lower region of the kidney medulla.
- The ascending Loop of Henle is impermeable to water to ensure that water will not move back into the tubule, since salt is being pumped in.
- Some salts just pumped out of the ascending Loop of Henle passively move back into the descending Loop of Henle and recycle, that ensures that the lower end of the medulla always has a higher salt concentration than the upper end, for better water reabsorption. This mechanism is called the **counter current exchange**, a term that refers to any system when fluids moving in opposite directions exchange something.

**Secretions into the Kidney**

Many antibiotics, histamines, and acid [H⁺] ions, that were not filtered in the glomerulus, can be secreted from the peritubular capillaries into the distal tubules of the nephrons for excretion in the collecting duct as well.

**Excretion**

As the filtrate enters the kidney pelvis from the collecting ducts, all materials not reabsorbed will be excreted

- Wastes (especially Nitrogen)
- Excess (beyond threshold) nutrients
- Secretions
- Water

About 1-2 liters of filtrate are produced daily forming urine.
Some Excretory Controls

**Hormone Controls**

**ADH (Anti diuretic Hormone)**
- Produced in hypothalamus and secreted by the pituitary
- Promotes water reabsorption by increasing the permeability of the collecting ducts when fluid intake is low and blood osmotic pressure increases.
- Alcohol suppresses ADH so we excrete more water when we consume alcohol.
- High intake of water will increase blood volume and also suppress ADH, so that more water is excreted.
Aldosterone and Angiotensin
Low blood sodium content and/or low blood volume or pressure promote the release of rennin, an enzyme secreted by kidney. Rennin released into the blood activates angiotensin (a derivative of a plasma protein). Angiotensin stimulates the release of aldosterone, a hormone produced by the adrenal glands located next to the kidneys. Aldosterone promotes Na\(^+\) reabsorption in the Loop of Henle. This increases blood volume because the increasing level of Na\(^+\) attracts water, increasing blood volume. Angiotensin can also promote vasoconstriction that increases blood pressure.

The increase in blood volume caused by increasing the level of Na\(^+\) in the blood also increases blood pressure, that is sometimes a problem. Some hypertension is caused by salt sensitivity. These individuals need to control their intake of salt, since they are at greater risk of sodium imbalance.

Other Controls
- High urea or glucose concentrations in blood will increase osmotic blood pressure. This results in more filtrate concentration so less water is reabsorbed (because water follows osmotic gradients) Dilute urine is excreted.

Frequent dilute urination is a symptom of diabetes caused by the excretion of glucose above threshold levels.

- Caffeine dilates vessels and affects pressure in the glomerulus so reabsorption is decreased. Caffeine also lowers sodium reabsorption in the Loop of Henle Again, a more dilute urine is excreted.

- Some poisons block Na\(^+\) balance in the Loop of Henle. This affects the gradient for water reabsorption, so more urine
Throughout our discussion on the body we have seen how activities of circulation, digestion, and excretion are carefully regulated by actions of the nervous system and more frequently by **hormones**, the regulatory chemicals of the endocrine system. Hormones are produced in specialized areas of the body, secreted and circulated to the target cells and tissues.

Most hormones work on a stimulus/feedback system the result of which is the optimum functioning of appropriate organs and tissues. At times in our discussions of nutrition further mention will be made of hormone activity and hormone functioning.
To conclude our discussion of how our body works, let's turn more fully to some of the digestive problems associated with nutrition - a few of that have been mentioned already while traveling the digestive tract.

**Digestive Problems and Nutrition**

1. **Choking**

   - Choking occurs when food is lodged in the trachea preventing breathing.
   - When someone is choking he/she cannot produce speech. This is an important clue!
   - Remedy:
     - Heimlich maneuver  See discussion and diagrams in text and take courses in CPR
   - Prevention:
     - Chew food thoroughly
     - Small pieces of food ingested
     - Reduced alcohol consumption while eating
       - (Do not eat while drinking excessively)
     - Reduce laughing while chewing/ingesting

2. **Gas**

   **Burping/belching**

   - Typical Causes
     - Swallowing air (often from tension/habit)
     - Drinking carbonated beverages
   - Remedy:
     - Change what is often an unconscious behavior
     - Don't drink carbonated beverages. They are empty calories anyway.
   - Other causes
     - Gall bladder problems
     - Colon problems
     - Obstruction of coronary vessels
Intestinal gas
- Usually Diet related
- By-products of intestinal bacteria
- Sometimes swallowed air gets that far
- Common inducers of intestinal gases are carbohydrates not digested by us but digested by our intestinal bacteria

3. Indigestion
- Gastric distress usually caused by excess acid content in the stomach.
- (Also called heartburn)
- Causes
  - Sometimes active ulcer
  - Overeating
  - Stress
- "Treatment":
  - For ulcers, see later
  - In general, avoid overeating!

A few words on antacids for the "treatment" of indigestion
- All antacids use the same mechanism --- they contain substances that neutralize the acidity of the stomach juices or suppress the production of stomach acid, but the ingredients are not all the same
- Some features
  - Strength - the ability to neutralize acid in a test tube
  - Form - Liquids generally act faster and can be more effective than tablets
  - Calcium carbonate - Although relief is rapid, the calcium can trigger a stomach acid surge a few hours after ingestion
  - Sodium content - Many antacids have high sodium content. These should be avoided by those who have hypertension or other sodium restricted diets. (The amount of sodium per dose varies considerably by brand --- from 0 mg/teaspoon to 15 mg)
  - Effect on bowel habits:
    - Magnesium hydroxide may cause diarrhea
    - Aluminum hydroxide may cause constipation
- Long term use of antacids may affect the natural bicarbonate buffer system, causing dependency.

Gastroesophageal Reflux is a chronic and frequent problem that can cause severe damage to the esophagus and requires medical attention.
4. **Vomiting**  
- Reverse peristalsis of stomach contents (sometimes duodenum)

- Causes:
  - Upset equilibrium (motion sickness)
  - Irritating substance in stomach
  - Pathogens (viral/bacterial)

- Problems:
  - Prolonged vomiting serious fluid loss and electrolytes loss because fluid replaced by capillary water loss (remember osmosis) (especially with children)
  - May be indication of serious illness

5. **Diarrhea**  
- Too rapid movement of intestinal contents for proper fluid reabsorption water withdrawn from surrounding cells of the intestine into intestine and added to digesting food ---> result: feces too liquid

- Some causes:
  - Stress and tension
  - Overeating
  - Some drugs
  - Certain foods and spices - especially unaccustomed ones
  - Spoiled foods
  - Too many intestinal bacteria

- Organic Causes of diarrhea
  - Irritable bowel syndrome
  - Colitis

- Chronic diarrhea
  - Serious fluid loss from body (water and electrolytes)
  - Some causes:
    - Medical treatments esp. radiation
    - Protein malnutrition
    - Malabsorption (causes ?)

- Treatment:
  - Short term - usually cures itself
  - Can use binders
    - kaolin - clay (attracts water)
    - pectin - (attracts water)
6. **Constipation**

Normal digestive cycle is 1-3 days in colon. Most individuals have a pattern dependent on physical makeup, environment, dietary habits. Failure to defecate is not constipation unless **irritating** (discomfort or difficult) or when muscles of colon are too loose to move contents.

- Minor constipation results when nervous system messages cannot be acted upon (then fecal material will continue to be dehydrated)

- Organic causes of constipation
  - Intestinal obstruction
  - Diverticulitis
  - Tumors
    - (Prevent colon peristalsis)

- Behavior/dietary causes of constipation
  - Too busy to respond to signals?
    - Routine eating/sleeping improves
  - Lack of physical activity
    Peristalsis is improved with physical activity
    (Better muscle tone)
  - Too little **fiber** or **fluid** in diet
    Fiber absorbs water / softens fecal substances
    Fiber also adds bulk in intestine that aids in movement
    Cereal fiber (esp. wheat) better for fecal weight

**Use of Laxatives**

Laxatives are not recommended because the intestine lining becomes irritated, and may lose muscle flexibility.

However, if you do have an occasional need:
- Prunes do contain a laxative (works about 8 hours after ingestion)
- Psilium - natural fiber material
- Magnesium - irritates colon
7. Ulcers

- Gastric ulcers (peptic ulcers)
- Duodenal ulcers (peptic ulcers)
- Esophageal ulcers

What is an ulcer?
Erosion of mucosa layer leaving sublayers exposed to gastric juices. Loss of fluid from exposed layers and/or eroded areas is painful (when touched). Erosion may progress to capillaries. Bleeding may actually perforate the stomach that can be fatal.

How can ulcers form?
- Pre-existing weakness in lining of digestive tract
- Secretion of gastric acid to cause erosion

Note: Most stomach pain is not stomach. Most ulcer pain (like fire/burning) is right under ribs.

Origin of most ulcers
- Some indication that the original weakness or irritation of the digestive tract is caused by a bacterium, *Helicobacter pylori*, common in unpasteurized milk, and a few other bacteria.
- The use of ibuprofen or naproxen can induce ulcers.
- Disorders that cause excess gastric secretions may induce ulcers.

Stress (as stated earlier), anxiety, and tension maintain the secretion of gastric juices that prevents healing, but stress is not generally the cause of ulcers.

Treating ulcers
The treatment of ulcers depends largely on the cause. Those caused by infection can be treated first to destroy the bacteria, and then with substances that promote healing of the stomach and intestinal linings. If caused by medications, stopping the medication is the first step. In any case, healing is promoted by:
- Fundamental change in lifestyle
  - Relax
  - Sleep
  - Stop smoking. Smoking seems to exacerbate ulcers.
- Diet:
  - It seems that only a few things aggravate the irritation
    - Caffeine
    - Alcohol
    - Meat extracts eg. bouillon, or partially digested proteins
  - Other than that:
    - Foods that please you probably help relax! So eat anything.