

## Digestion – Comparative Physiology: Table of Contents (3 lectures)

### Digestion 1: Transport

(32:59 min:sec)

0:00	Introduction: Trans-epithelial Transport
00:25	Definitions, Comparative Body Plans: single orifice / dual orifice digestive systems. Mouth / Anus. Intracellular Digestion – Endocytosis. Extracellular Digestion: two steps – reduce food to constitutive parts, transport small molecules into body.
03:28	Thermodynamics: (energy consumed, energy to do things with) First Law: Conservation of Energy (energy does not... disappear) Second Law: Matter goes from state of order to state of disorder (low entropy to high entropy). $\Delta G = \Delta H - T \cdot \Delta S$ (T=temperature) Free Energy (G); energy available for work. Enthalpy (H); heat of reaction, probability that a reaction will occur Entropy (S); state of order
06:07	First Law: Conservation of Energy – Energy balance; energy in = energy out Food in (E <sub>in</sub> ) = what that food is turned into (tissue, ATP, etc) plus heat loss plus non-digested food (E <sub>out</sub> )
07:31	Second Law: Order to Disorder. Diffusion – movement of molecules from area / space of high concentration to area of low concentration. Diffusion – random movement of a molecule, from ordered state (high density, low S) to disordered state (low density, high S)
08:35	Example of particles moving from low S to high S
09:38	Does life contradict the second law? Life is highly ordered (low S); death is highly disordered (high S). Life is sustained by a large input of energy. Biochemical energy (sun light > sugar via photosynthesis) = ATP produced by glycolysis, etc.
11:10	Properties of Cells 1. Resting State of a Cell 2. Transport of solute and of water across cell membrane; across epithelium
11:49	Resting State of a Cell: Electrochemical Gradient: unequal distribution of ions and of charge inside cell: high [K <sup>+</sup> ], low [Na <sup>+</sup> ], low [Cl <sup>-</sup> ] outside cell: low [K <sup>+</sup> ], high [Na <sup>+</sup> ], high [Cl <sup>-</sup> ] inside cell negative relative to outside
14:00	Mechanism for unequal distribution of ions 1. Cl <sup>-</sup> repelled from cell by negatively charged anions (proteins, other macromolecules) 2. Na <sup>+</sup> & K <sup>+</sup> distributed by Na/K Pump (a.k.a. Na/K ATPase) at the expense of energy (ATP)
16:05	Review: Resting State of Cell Next: Transport of Solute
16:25	Transport: Experiments of Ussing (experiments 1947-1958) salt transport across frog skin (across layers of cells) role of Na/K pumps (active transport), Na <sup>+</sup> and K <sup>+</sup> transporters (facilitated diffusion)

	<p>movement at the expense of energy (ATP)  pharmacological blockage – specific mechanisms</p>
20:07	<p>Definitions: Transport  Active Transport: movement of molecules across membrane at the expense of energy  Co-transport: two molecules move together driven by concentration gradient of one of the molecules.  Facilitated Diffusion: specific transport mechanism (protein) allows specific molecules across, driven by their concentration gradient  All are really "active transport", as all require energy, either directly or indirectly</p>
22:54	<p>Transport of water: osmosis</p>
23:11	<p>Water is moved by osmosis (exceptions: endocytosis) may be assisted by regulating membrane permeability (e.g. aquaporins – see kidneys)  Mechanism of Osmosis –  1. first transport salt at the expense of energy.  2. water follows to "dilute out the salts", water moves by osmosis from a region of low [salt] to a region of high [salt], consistent with the Second Law of Thermodynamics (low entropy to high entropy)  <b>WATER DOES NOT MOVE BY DIFFUSION, WATER MOVES BY OSMOSIS (tricky terminology stuff)</b></p>
25:08	<p>Review: so far discussing transport of water and water soluble stuff.  The cell membrane presents a barrier and thus transport mechanisms evolved to allow the selective movement of these substances across the membrane.  What about non-water soluble stuff (lipids / fat, steroid hormones)?  The cell membrane does NOT present a barrier to such molecules, yet there must nevertheless be some regulation of their movement.</p>
26:47	<p>Summary – cells use energy (ATP) to establish concentration gradients (creating states of low entropy).  Cells use these concentration gradients to drive subsequent reactions (and thus decaying to states of high entropy).  <math>E_{in} = E_{out}</math>  islands of low S maintained by input of energy; reactions become driven by entropy</p>
29:13	<p>Endocytosis: cell biology (cytoskeletal elements interacting with membrane to internalize "bubbles" of cell membrane that contain extracellular material (acted upon once inside cell).  Complex cellular processes</p>
30:39	<p>Exocytosis: release of substances stored within membrane vesicles  Secretory cells (endocrine – peptide hormones), (neurons – neurotransmitter), (gland cells – mucus, proteins, enzymes)  Complex cellular processes</p>

**Digestion 2: Secretion / Absorption in the mammalian digestive system**

(36:47 min:sec)

0:00	Introduction
00:21	Digestive system is a tube running through the body – mouth to anus Ingestion, sequential breakdown to small molecules, absorption into body, feces (non-absorbed material) Two steps: secretion of enzymes, fluids to breakdown food; absorption of materials
01:18	Anatomy of mammalian (human?) digestive system. mouth, stomach, small intestine (3 sections), colon pancreas, liver, gall bladder most of digestion occurs in the duodenum of the small intestine (most enzymes secreted here) one enzyme secreted in mouth (amylase), one enzyme secreted in stomach (protease), host of enzymes secreted into duodenum mouth – mechanical breakdown, saliva stomach – mechanical breakdown small intestine – digestion (enzymatic digestion) and absorption colon – water and salt recovery
03:42	Mouth: properties (sensory, behavior, secretory) & Saliva
05:34	Salivary Gland (exocrine gland): Glandular Secretion water, mucus, enzyme (protein) mucus, enzymes – vesicles, released by exocytosis water – osmosis, flushes mucus and enzymes from gland regulation? signal >> (neural) Definitions: exocrine glands v. endocrine glands
07:53	Stomach: properties (movement, muscles), secretory gastric juice: mucus, HCl, pepsinogen (converted to pepsin by HCl) highly regulated! sensory inputs (neural), food, hormones (+/-)
10:02	Stomach as an exocrine gland Glandular secretion of gastric juice: gastric pits and gastric glands Goblet Cells (gastric pit): mucus secretion (vesicles) Chief Cell (gastric gland): protease pepsinogen (vesicles) Parietal Cell (gastric gland): secretes H <sup>+</sup> and Cl <sup>-</sup> which form HCl in stomach
11:49	Electron micrograph of goblet cell
12:05	Electron micrograph of 2 parietal cells and a chief cell, and proximity of two gland ducts.
12:49	HCl functions relaxes cellulose, converts inactive pepsinogen to pepsin (specific acid sensitive site), denatures proteins (low pH), proteolytic – acid hydrolysis, inhibits micro-organisms
14:47	HCl production & secretion H <sub>2</sub> O + CO <sub>2</sub> >> HCO <sub>3</sub> <sup>-</sup> + H <sup>+</sup> , accelerated by carbonic anhydrase (reversible and conc. dependent) HCO <sub>3</sub> <sup>-</sup> exchanged for Cl <sup>-</sup> (Cl <sup>-</sup> is thus effectively pumped into cell from body, which further drives production of HCO <sub>3</sub> <sup>-</sup> and H <sup>+</sup> ) H <sup>+</sup> /K <sup>+</sup> pump (ATPase).

	<p>H<sup>+</sup> pumped out of cell into gland lumen at expense of ATP  Cl<sup>-</sup> diffuses out (Cl<sup>-</sup> channel) into gland lumen  gland lumen pH 2, intracellular pH "normal"  regulation? hormones? hormone action?</p>
18:34	<p>Small intestine:  Duodenum: secretory, plus input from pancreas and liver (via gall bladder); also absorptive  Jejunum, Ileum: primarily absorptive</p>
19:28	<p>Secretion in Duodenum  Intestinal Epithelium: diverse cells secreting "host of enzymes"  Liver: bile, a solution secreted into gall bladder, contraction of gall bladder releases bile into small intestine  bile = bile salts (emulsify lipids); bicarbonate to neutralize HCl based acidity; excretion products cleaned from blood (pigments, toxins, cholesterol, etc)  Pancreas: many enzymes, bicarbonate (principal source) to neutralize acidity from stomach</p>
22:25	<p>Intestinal Absorption: anatomy  enormous surface area: folds, villi (collections of cells), microvilli (membranes of single cells)  Anatomy of a villous (epithelium, lacteal, blood capillaries): transport across villous epithelium (amino acids and sugars via blood, fats via lacteal to lymph to blood).</p>
25:12	<p>Villous epithelium – schematic  overview of transport route for amino acids, sugars, lipids/fats</p>
26:02	<p>Micrograph of cat duodenum, showing folds and villi</p>
26:12	<p>Micrograph of villous showing anatomy of epithelium and location of lacteals and blood capillaries</p>
26:35	<p>Micrograph of several epithelial cells, showing "brush border" (microvilli)</p>
26:57	<p>Electron micrograph of microvilli – sites of transport</p>
27:25	<p>Biochemical Mechanisms: transport of amino acids, sugars, nucleotides (water soluble)  3 steps: active transport (Na/K pump), co-transport, facilitated diffusion  diversity &amp; specificity of co-transporters / transporters</p>
30:00	<p>Biochemical Mechanisms: transport of fats (membrane soluble)  emulsification (bile salts): micelles to cytoplasm to ER (to triglycerides) to golgi (vesicles) to body (by exocytosis) to lacteal, lymph, blood, liver etc...</p>
31:52	<p>Colon  water and salt recovery (major products of secretion – recycle)  Formation of feces</p>
32:40	<p>Zymogens: proenzymes: converted from inactive to active form  why? protection?  stomach: pepsinogen to pepsin via acid hydrolysis of specific site (HCl)  intestine: trypsinogen to trypsin by removal of 6 amino acids (autocleaved)  chymotrypsinogen to chymotrypsin also by proteolytic cleavage, but by trypsin</p>
34:42	<p>Summary: partitioning  successive breakdown of food  secretions (enzymes, HCl, HCO<sub>3</sub><sup>-</sup>, bile, mucus, water)  small intestine: enzymatic digestion, absorption</p>

	Colon: water, salt recovery All is highly regulated - hormones
--	---

### Digestion 3: Regulation

(14:44 min:sec)

0:00	Introduction; Coordination of digestion
00:10	3 levels of control: (1)input from mouth; (2)events of stomach; (3)events in duodenum, re. pancreas and gall bladder sensory input activates mouth and stomach food in stomach activates stomach food in duodenum stimulates events in duodenum and inhibits events in stomach
01:08	Mouth events, summary
01:45	Stomach events, summary: homeostasis
05:34	Gastrin (stomach). Gastrin (peptide hormone) released from cells of stomach wall, act on gastric gland cells to release/produce gastric juice Stimulus? 1. neural (vagus nerve); 2. food in stomach (mechanical and chemosensory)
05:22	Endocrine v. Exocrine glands – working definitions (release in v. release out) Liver, Pancreas, Stomach have both endocrine and exocrine functions
06:42	Duodenum: stomach contents enter duodenum, stimulate pancreas and gall bladder, inhibit stomach Secretin, GIP, VIP, CCK, bulbogastron (act on stomach: muscle relaxation or inhibit gastric juice production signals: acid, fat, carbohydrates, proteins (multiple signals) hormones have dual function: opposite effects on different tissues
9:15	Duodenum: more regulatory examples 1. no more food from stomach: enkephalins released (triggered by increase pH (no HCl)), activates gastric juice, inhibits intestine events 2. too much carbohydrate in blood, enteroglucagon released to inhibit pancreas and gall bladder activities (resulting in decreased digestion of carbs. and less absorption).
10:40	Hormone Release: Peptides signal binds to cell surface receptor activating intracellular transduction pathway which triggers the exocytotic release of membrane vesicles containing the peptide hormone
12:00	Hormone Action: Peptides (can not pass through cell membrane) activates cell surface receptor, activating an intracellular transduction process which activates the cellular response Transduction via G-proteins and second messengers
13:17	Summary (Big Picture) Energy in = work + heat + feces etc. governed by internal regulatory processes governed by individual life histories (interaction between physiology/behavior and environment)