HORMONES, ENZYMES, REGULATORY SUBSTANCES AND STUFF

NEUROENDOCRINE HORMONES: All of below are either exclusively endocrine (glandular secretions into bloodstream), exclusively neural (neurotransmitter) or both. All of below serve regulatory (as opposed to digestive) functions.

- **GASTRIN**: Endocrine.
  - **STRUCTURE**: Active part of peptide is on carboxy-end. It shares the last four residues in common with CCK (Trp-Met-Asp-Phe), and it has a protective NH$_2$ on the carboxy end to help prevent degradation.
    - **PENTAGASTRIN** Drug that mimics Gastrin, containing the last four residues in gastrin, and therefore containing similar biological activity.
  - **Distribution**: Gastrin is made by G-CELLS in the ANTRUM of the Stomach.
  - **FNXNS**:
    - It stimulates release of HCl in Parietal Cells.
    - Also stimulates growth of gastric mucosa and proliferation of intestinal enterocytes.
      - Intestinal Resection: If you cut out part of the intestine, higher levels of Gastrin will result.
  - **REGULATION**:
    - Gastrin release is inhibited by acid in the stomach. Primary negative feedback mechanism.
    - Gastrin release is stimulated by digested proteins and by Acetylcholine.

- **CHOLECYSTOKININ (CCK)**: Endocrine and neural
  - **STRUCTURE**: Biological activity is contained in last seven residues on carboxy-end, with last four residues in common with Gastrin, and with a protective NH$_2$ on the carboxy terminus.
    - Activity on PARIETAL CELLS: CCK in the stomach can bind to Gastrin receptors to BLOCK the effects of Gastrin.
  - **Distribution**: CCK is made from I-CELLS.
  - **FNXNS**:
    - Stimulates contraction of the gall bladder
    - Stimulates secretion of pancreatic enzymes
    - Inhibits gastric emptying as part of the Entero-Gastric Reflex. The presence of CCK indicates that the duodenum is full and gastric emptying should be slowed.
  - **REGULATION**:
    - CCK-release is stimulated by the presence of peptides in the duodenum.

- **SECRETIN**: Endocrine and neural.
  - **Distribution**: Secretin comes from S-CELLS in the duodenum.
  - **FNXNS**:
    - It inhibits stomach motility when released in Duodenum via the Entero-Gastric Reflex.
  - **REGULATION**:
    - Secretin-release is stimulated by acid in the Duodenum.

- **SOMATOSTATIN**: The universal inhibitory substance. It acts in endocrine, neural, and paracrine fashion.
  - **Distribution**: Somatostatin is all over the place.

- **GASTRIC INHIBITORY PEPTIDE (GIP)**: Endocrine.
  - **FNXNS**:
    - Inhibits the release of Gastrin by a pharmacological mechanism. Thus the effect is dose-dependent, and a large (non-physiological) dose is required to elicit a response.
      - Dr. Greenwald thinks this effect is secondary importance because it is only pharmacological.
    - Major fnxn = GIP stimulates release of Insulin from Pancreas.
  - **DISTRIBUTION**: Antrum of stomach + duodenum.

- **VASOACTIVE INTESTINAL PEPTIDE (VIP)**: Primarily neural
- **MOTILIN**: Endocrine.
  - **FNXN**: It elicits the Migrating Motor Complex in the small intestine, to propel bacteria aborally.

- **GASTRIC RELEASING PEPTIDE (GRP)** (Bombesin): Neural. Involved in the release of Gastrin. Its release is Non-Adrenergic Non-Cholinergic.
  - **REGULATION**: Its release stimulated during the Cephalic Phase of gastric secretion.

- **ENKEPHALIN** (an Opioid):
  - **FNXN**: Decreases GI-motility by inhibiting the release of ACh.
- Inhibits Somatostatin release from enteroendocrine.
  - **Gastric Releasing Peptide** is also released in stomach. This release is Non-Adrenergic Non-Cholinergic. It also stimulates release of Gastrin.
    - **GASTRIC PHASE**: When food enters stomach, about 50% of secretion.
    - **INTESTINAL PHASE**: Post-gastric-emptying.
- **NEGATIVE FEEDBACK**: **ACID** is the primary inhibitor of Gastric secretions.
  - Acid stimulates the release of Somatostatin, which turns off Parietal Cells and G-Cells.
- **GASTRIC MUCOSAL ISCHEMIA**: Ischemia of mucosa causes increased permeability --> Gastric Ulcers
  - Etiology: Lots of things; shock, burns, sepsis, trauma.
  - Treatment: Use acid-reducers like H₂-Blockers
  - VICIOUS CYCLE: The excess acid can cause *conversion of pepsinogen to pepsin* which will stimulate further acid release. That normally only occurs in lumen but with a lesion it can occur in mucosa, and that is not good.
- **HELCOBACTER PYLORI**: Those little critters in the stomach that have been recently proven to cause ulcers.
  - **Urease**: These bacteria can survive in acid because they have high urease which can take urea and create HCO₃⁻ and NH₃ out of it, forming a good acid-buffer.
  - ULCER treatment should include antibiotics to fight these bacteria, but *H.Pylori is not always found in ulcer patients!* Criteria for determine presence of H-Pylori:
    - Do a biopsy and identify histologically
    - Grow cells in culture
    - Measure the amount of the enzyme urease.
- **INNISIFIC FACTOR (IF)**: Produces by parietal cells in stomach, it is necessary for Vit-B12 absorption.
  - Saliva: Vit-B12 combines with R-Protein.
  - Stomach: Secretes intrinsic factor into bolus.
  - Intestine: Vit-B12 lets go of R-Protein and binds to **Intrinsic Factor**
  - Ileum: The Vit-B12/IF Complex is absorbed through special transporters. Without the IF, only 20% of B12 is absorbed.
  - **PERNOCIOUS ANEMIA**: Autoimmune disease destroys parietal cells, thereby destroying intrinsic factor source and resulting in B12-deficient.
- **ACHLORHYDIA** is an overgrowth of bacteria in stomach resulting in low HCl secretion which will cause high Gastrin levels.
- **PEPSIN**: Released as pepsinogen in chief cells. Acid converts the proenzyme to pepsin. Pepsin is an endopeptidase.
  - Pepsin can continue to activate once active.
  - REGULATION: Following factors stimulate pepsinogen secretion, from most to least prominent.
    - Acetylcholine
    - H⁺
    - Secretin
    - CCK
  - **Pepsinogen I** found in Chief Cells.
  - **Pepsinogen II** found in duodenum and correlates with duodenal ulcers.
- **ZOLLINGER-ELLISON SYNDROME**:  
  - **ETIOLOGY**: Pancreatic tumor --> Under secretion of Pancreatic Enzymes --> Over secretion of GASTRIN due to no CCK.
  - **SYMPTOMS**:
    - Peptic Ulcer Disease
      - Increased Gastric Emptying.
    - **Diarrhea** from hypergastrinemia
    - Steatorrhea (fat in stool):
      - Denaturation of pancreatic lipase due to acidic environment in the duodenum.
      - Reduced Intrinsic Factor activity.
    - **GERD**