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 carboy 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 adequately 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 bia 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 H_2-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.
- **HELICOBACTER 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 HCO_3^- and NH_3 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.
- **INTRINSIC 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.
    - **PERNICIOUS ANEMIA:** Autoimmune disease destroys parietal cells, thereby destroying intrinsic factor source and resulting in B12-deficiency.
- **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 itself* 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**