Gastro-Intestinal Module

Session 4:

Lecture 4.1:

Function of The Stomach

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Objectives

- describe the functions of the stomach
- describe the components of gastric secretion and their cellular origins
- explain the mechanism of secretion of stomach acid
- explain the control of gastric acid secretion
- outline the ways in which gastric acid secretion may be reduced by drugs
  describe the function of the stomach defences
- describe the patterns of motility of the stomach, including receptive relaxation and peristalsis
- describe the process of gastric emptying and its control

Objective 1

Describe the functions of the stomach

The functions of the stomach

- **Stores Food**
- **Disinfects Food**
- **Breaks food down into Chyme**
- Chemical disruption (Acid and enzymes)
- Physical disruption (Motility)

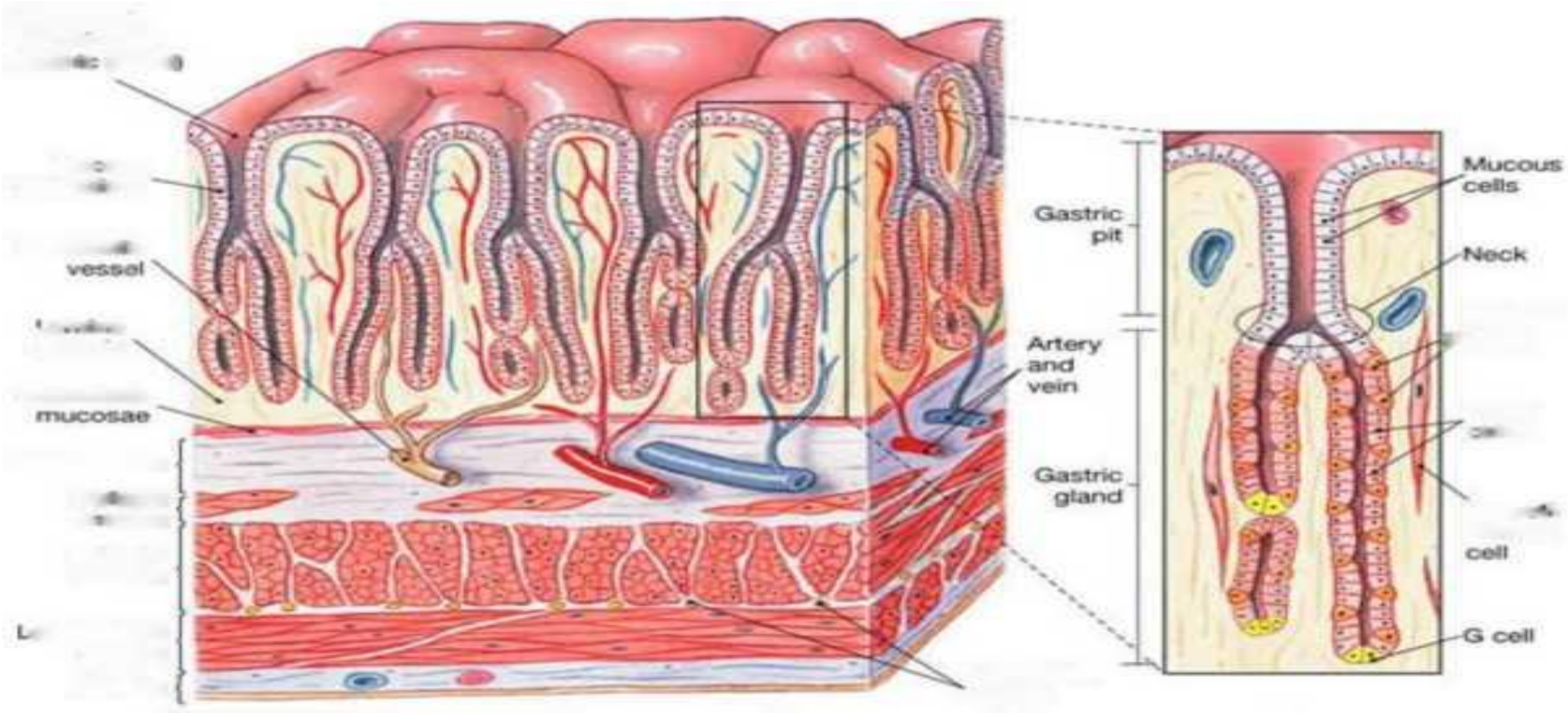
Objective 2

describe the components of gastric secretion

and their cellular origins

Stomach secretions come from **Gastric Pits**, indentations in the stomach mucosa that are the openings to gastric glands.

Gastric pits contain **Neck Cells**, and gastric glands contain **Parietal**, **Chief** and **G-Cells**, along with smooth muscle cells.



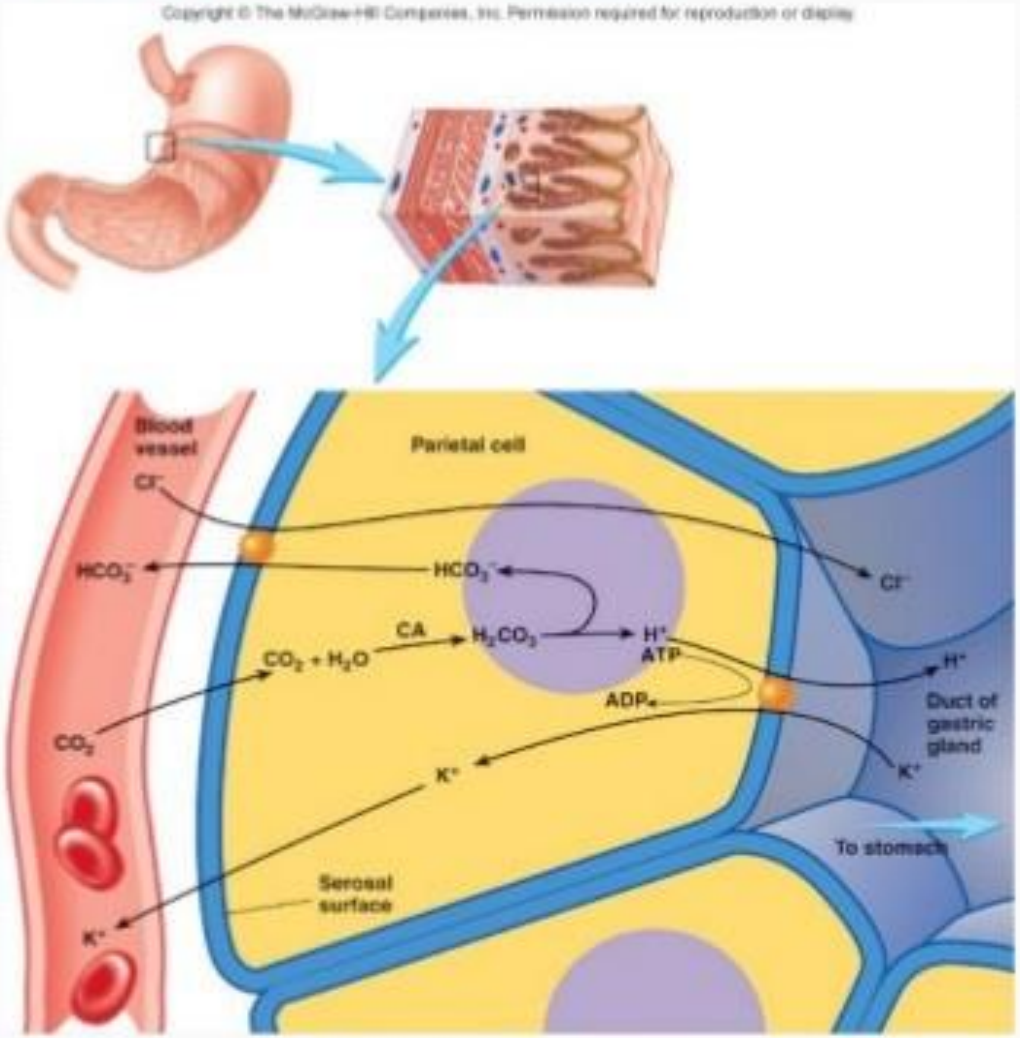
Secretion	Cellular Origin	Description
Hydrochloric Acid (HCl)	Parietal (Oxyntic) Cells	Acid keeps luminal pH < 2
Proteolytic Enzymes (Pepsin)	Chief Cells	Non-specifically breaks down proteins ^ peptides
Mucus	Neck Cells (Surface cells)	Sticky, so is not removed easily from the stomach lining and basic, due to amine groups on proteins
HCO_3^-	Neck Cells (Surface cells)	Secreted by surface cells into the mucus, provides a buffer for H+ ions
Gastrin	G-Cells	Binds to surface receptor on parietal cell, stimulating acid and intrinsic factor

Objective 3

Explain the mechanism of secretion of stomach acid

Hydrochloric Acid Production

1. CO_2 and Cl^- diffuse from the blood into the stomach cell.
2. CO_2 combines with H_2O to form H_2CO_3.
3. H_2CO_3 dissociates into bicarbonate ($HCO3^-$) and H^+.
4. H^+ combines with Cl^- in duct of gastric gland to form HCl^-.
5. An ATP pump is necessary to pump the HCl^- into the duct since the concentration of HCl^- is about a million times more concentrated in the duct than in the cytosol of the cell.



Objective 4

explain the control of gastric acid secretion

A complex of neural and endocrine systems controls acid secretion. Parietal cells are stimulated by **Acetylcholine**, **Gastrin** and **Histamine**, which act via separate receptors to promote acid secretion.

Acetylcholine

Ach is released from **postganglionic parasympathetic neurones**, stimulated by gastric distension as food arrives. It acts on **muscarinic receptors** on parietal cells.

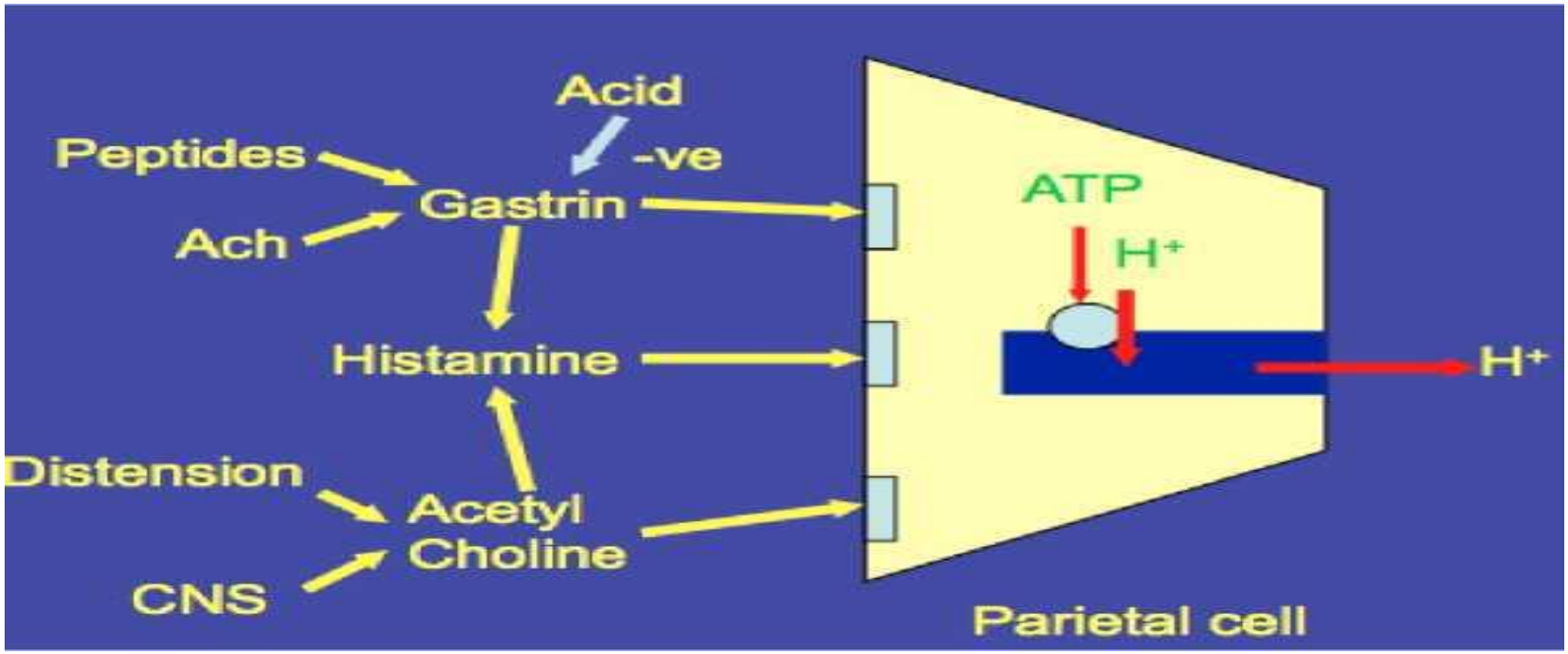
Gastrin

Gastrin is released from endocrine cells in the stomach, **G-Cells**. It is a 17-amino acid polypeptide, which binds to surface receptors on parietal cells. Gastrin secretion is stimulated by the presence of peptides and Ach from intrinsic neurones. It is inhibited by low pH in the stomach, which acts as a 'feedback' control.

Histamine

Histamine is released from **Mast Cells** and diffuses locally to bind **H_2** surface receptors on parietal cells. Acid secretion is then stimulated via c-AMP.

Gastrin and Ach stimulate mast cells, so Histamine works as an **amplifier**.



Phases of Control

There are three phases of gastric secretion.

Cephalic Phase

The 'brain led' phase. The **sight and smell of food**, and the act of **swallowing**, activates the **parasympathetic nervous system**, which stimulates the **release of Ach**. This stimulates parietal cells directly and via histamine **(^ Acid)**.

Gastric Phase

Once food reaches the stomach, it causes **distension**, further stimulating Ach release, and subsequently parietal cells .

The arrival of food will also **buffer** the small amount of stomach acid in the stomach in between meals, causing **luminal pH to rise**. This **disinhibits Gastrin (^ Acid)**.

Acid and enzymes will then act on proteins to **produce peptides**, **further stimulating Gastrin** release as the pH falls and the initial disinhibition is removed **(^ Acid)**.

Intestinal Phase

Once chyme leaves the stomach in significant quantities, it stimulates the release of the hormones **Cholecystokinin** and **Gastric Inhibitory Polypeptide** from the intestines that antagonise Gastrin **(* Acid).** Coupled with this, the small amount of acid left in the stomach is no longer being buffered by food, and the **low pH inhibits Gastrin (* Acid)**.

The low pH of the stomach between meals can aggravate ulcers. Because of this, pain from ulcers is particularly bad at night.

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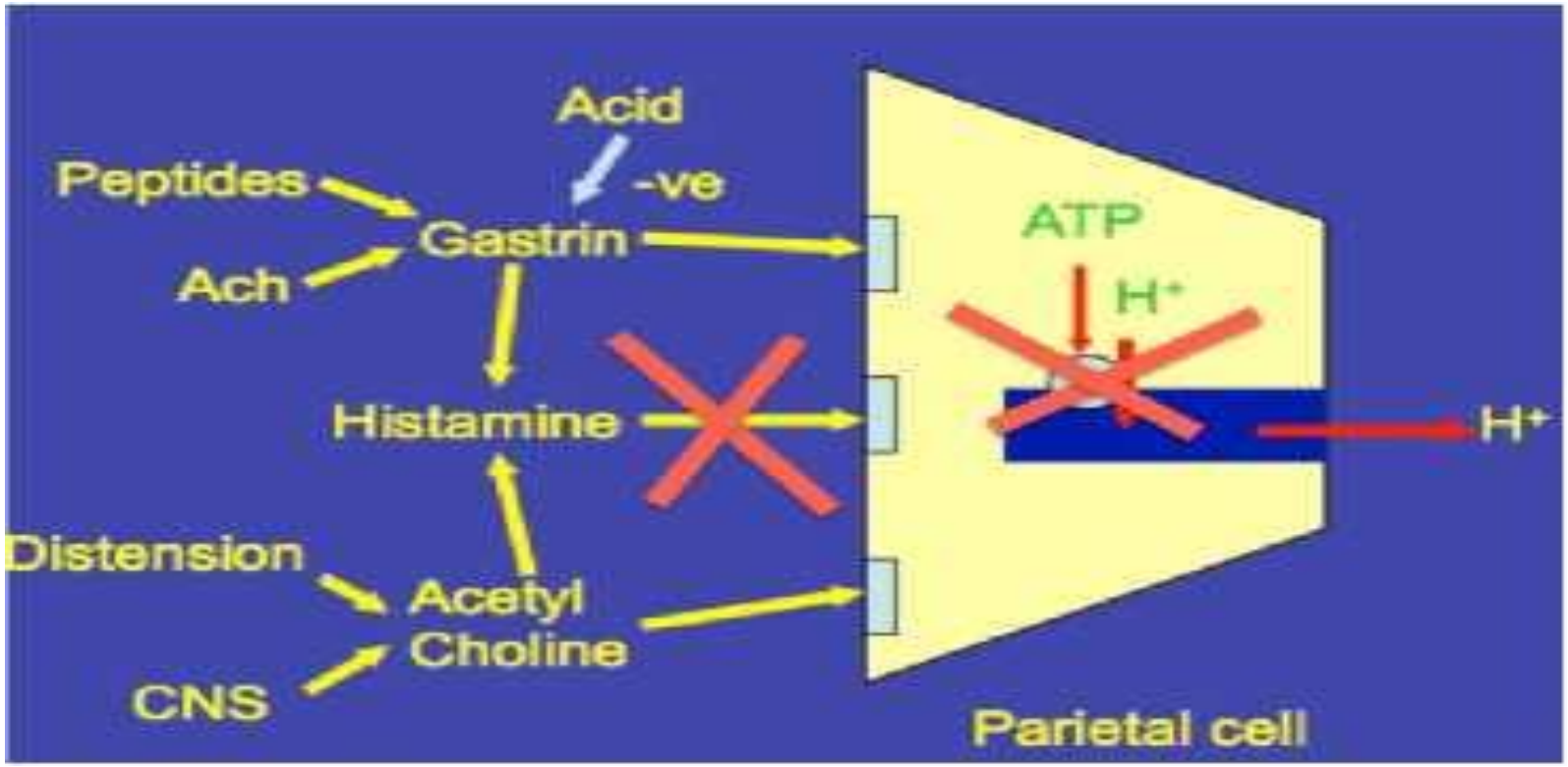
Objective 5

Outline the ways in which gastric acid secretion may be reduced by drugs

Acid secretion may be reduced by inhibition of:

- **Histamine at H2 Receptors** o E.g. Cimetidine o Removes the amplification of Gastrin/Ach signal
- **Proton Pump Inhibitors (PPIs)** o E.g. Omeprazole
  - o Prevents H+ ions being pumped into parietal cell canaliculi



Objective 6

describe the function of the stomach defences

Stomach Defences

The surface cells of the stomach mucosa secrete a thick layer of alkaline mucus, which offers some mechanical protection, and traps H+ ions diffusing into it from the stomach lumen, by reacting with HCO3- ions also produced from the surface cells. This prevents the pH of the surface of the mucosa cells from falling too low. The production of defences is stimulated by prostaglandins.

The luminal pH of the stomach is usually below 2. Without any protection, this would dissolve mucosa. Neck cells secrete **mucus** to protect the mucosa.

Mucus

The mucus forms **a 'unstirred layer' that ions cannot move through easily**. H^+ ions slowly diffuse in and react with the **basic groups** on mucus and with **$HCO3^-$ that is secreted by surface epithelial cells**.

Mucus is **Sticky,** so is not easily removed from the stomach lining. It is also **Basic,** due to Amine groups on the proteins

Because of the unstirred layer, HCO_3- stays close to the surface cells. This means the pH at the surface cells **is well above 6**.

Mucus and HCO_3- secretion from neck cells and surface cells respectively is stimulated by **prostaglandins**, which are promoted by most factors that stimulate acid secretion.

Breaching the Stomach's Defences

- **Alcohol**
  - Dissolves the mucus, allowing the acid to attack the stomach

H. Pylori

- Surface cells become infected, inhibiting mucus/HCO_3^- production

NSAIDS

- **Inhibit prostaglandins**, therefore reducing defences
- Some, like aspirin are converted to a non-ionised form by stomach acid, allowing them to pass through the mucus layer into cells before they reionise.

If the stomach's defences are breached it results in **peptic ulcers**.

Treatment involves reducing acid secretion (see above) and, if present, eliminating *H. Pylori* with antibiotics.

Objective 6

describe the patterns of motility of the stomach, including receptive relaxation and peristalsis

Receptive Relaxation

As food travels down the oesophagus, a neural reflex carried out by the **vagus nerve** triggers the relaxation of the muscle in the stomach's wall, so pressure does not increase. This means that pressure in the stomach does not increase as it fills **limiting reflux** and allowing us to consume large meals (but not if there is damage to the vagus nerve).

Rhythmic Contractions

The stomach has longitudinal and circular muscle that is driven by a **pacemaker** in the **cardiac region**. The pacemaker fires **~3 times a minute**, causing regular**, accelerating peristaltic contractions** from the **Cardia ^ Pylorus.**

The full stomach begins regular peristaltic contractions, triggered by a pacemaker, in the cardiac region about three times a minute. These sweep over the stomach from cardia to pylorus, accelerating as they move. This combined with the funnel shape of the stomach both mixes the contents and decants liquid chyme into the pyloric region. A small squirt of chyme leaves the pylorus with each peristaltic wave before the pylorus shuts.

Gastric emptying rate is controlled by feedback from the duodenum via chemical signals, so that the rate of emptying of the stomach is appropriate for further digestion and absorption. Fats greatly slow gastric emptying as they take more time to digest and absorb.

Objective 7

describe the process of gastric emptying and its control

The accelerating, rhythmic, peristaltic contraction moves solid lumps backwards into the fundus of the stomach whilst letting liquid chyme move forwards.

As the chyme enters the pyloric region, a small squirt is ejected before the peristaltic wave reaches the pylorus and shuts it, so the rest of the chyme returns to the stomach.

Control of Gastric Emptying

o Three peristaltic waves ^ three ejected squirts of chyme a minute. o Squirt volume affected by the rate of acceleration of peristaltic wave and hormones from the intestine.

o Gastric Emptying is slowed by **fat, low pH and Hypertonicity in the duodenum**.

Sphincters exist at the entry and exit parts of the stomach. Although there is no distinct specialization of stomach muscle fibres at the cardia, several mechanisms have been implicated in preventing reflux of stomach contents into the oesophagus; these mechanisms will be outlined. At the pyloric end, the circular muscle coat is thickened to produce the pyloric sphincter which controls the flow of stomach contents into the duodenum.

How does the Stomach Function.mp4