Notebook of Medical Physiology: Gastrointestinal

WITH ASPECTS OF TOTAL PARENTERAL NUTRITION

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A revision text for candidates preparing for examinations in basic medical sciences; including multiple choice questions

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Ross Wilson Hawker

MD(Syd. & Q'ld), PhD(Q'ld), FRACP, FRACS(Hon), FFARACS(Hon).
Professor and Head, Department of Physiology, University of Queensland, Brisbane; Member of Board of Examiners, Royal Australasian College of Surgeons; Member of Board of Examiners, Faculty of Anaesthetists, Royal Australasian College of Surgeons; External Examiner in Physiology, University of Singapore; External Examiner in Physiology, University of Malaya, Kuala Lumpur.

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Preface

This is a revision text for students preparing for examinations in medical/surgical science. It is aimed primarily at postgraduates undertaking FRCS, FRACS, FFA, MRCP, FRACP and cognate professional examinations, and secondarily to medical students in both their preclinical and clinical years.

The style is unique and will not please everyone: it is deliberately cryptic and concise and attempts to compress large areas of physiology into readily assimilable facts and concepts with a minimum of description. This is illustrated by the many flow-diagrams and summaries. This didactic approach stems from over 25 years' experience on examination-orientated courses for the FRACS, FRCS, FFA and FRACP.

The self-assessment material in this book has several educational objectives. Firstly, many of the MCQ hopefully are of sufficient quality to merit their use by professional examining bodies, either directly or after further review. Secondly, a considerable number have been constructed to extend the material covered in the text or have some intrinsic teaching quality about them, which makes them unsuitable in their present form for examination purposes. Thirdly, some are intentionally provocative and are designed to prompt discussion by the reader with fellow students or tutors.

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Contents

1. Gastrointestinal hormones

The gastrointestinal tract has at least 13 different types of endocrine cells which secrete a number of hormones. While these hormones traditionally control gut functions their actions extend into diverse physiological (and pharmacological) processes. Their physiological significance is difficult to establish, and many of the functions ascribed to them are pharmacological and, hence, obfuscate their role in physiological control systems.

Gastrin is the most firmly established hormone, i.e. the administration of pure gastrin produces the physiological responses at plasma levels found to occur after the normal physiological stimulus (usually a meal) for that response. The other hormones are putative or candidate hormones.

Gut hormones can be detected in plasma by radioimmunoassay, and the cells secreting them can be localised by immunocytochemical techniques.

Gastrin (17 amino acids) and pancreozymin-cholecystokinin (PZ-CCK or CCK) (33 amino acids) have amino acid sequence similarities in their structure; and secretin (27 amino acids), glucagon (29 amino acids), gastric inhibitory peptide (GIP) (43 amino acids), and vasoactive intestinal peptide (VIP) (28 amino acids) are other structure/activity related hormones.

Other gut hormones include: motilin, chymodenin, bombesin, enteroxyntin and somatostatin.

In some hormones, fragments of the molecule produce responses e.g. for gastrin, the minimal active fragment is the C-terminal tetrapeptide; for PZ-CCK, the minimal active fragment for contraction of the gall bladder is the C-terminal heptapeptide, and for acid secretion is the C-terminal tetrapeptide. In other hormones e.g. secretin and glucagon, the whole molecule is required for activity.

Some hormones have been detected in a number of different forms. Variants of gastrin are G17 ('little gastrin'), G34 ('big gastrin'); and variants of cholecystokinin are CCK39 and CCK8.

Active analogues of hormones include pentagastrin, and OP-CCK (COOH-terminal octapeptide of CCK).

Hormone interactions have been reported e.g., CCK potentiates action of secretin on bicarbonate secretion by pancreas and reduces action of gastrin on acid secretion by parietal cells.

Trophic effects have been ascribed to some hormones e.g., gastrin

stimulates growth of parietal cells (gastrin-secreting tumours induce hyperplasia and hypertrophy of parietal cells, and antrectomy results in atrophy of these cells).

The distribution of gut hormones is summarised in Table 1.1; stimuli releasing hormones in Table 1.2; actions of hormones on secretion in Table 1.3; and actions of hormones on motility in Table 1.4. Further descriptions are included in the text where differences between physiological and pharmacological actions are not always stressed: hence, there is often apparent (and confusing) overlap of their functions.

Table 1.1 Distribution of hormones.

	Antrum	Duodenum	Jejunum	Ileum
Gastrin	+	+		
PZ-CCK		+	+	+
Secretin		+		
*Glucagon		+	+	+
VIP	+	+	+	+
GIP		+	+	+
Motilin		+	+	+
Chymodenin		+	+	

+ = main sites of origin
* = enteroglucagon which is structurally different from pancreatic glucagon

VIP is also found in oesophagus, rectum, pancreas and brain.

Table 1.2 Stimuli releasing hormones.

	*Protein	*Fat	#Carbohydrate	Acid	Distension
Gastrin	+	0	0	-	+
PZ-CCK	+	+	0	0	0
Glucagon		+	+		
Secretin	0	0	0	+	0
VIP				+	
GIP		+	+		

* = digestive products of protein (e.g. peptides and amino acids) and fat (e.g. monoglycerides and fatty acids)
# = released by hexoses
+ = stimulates release of hormones
0 = no effect
- = inhibits release

Alkali in duodenum increases secretion of motilin.

Table 1.3 Actions of hormones on secretion.

	Gastric HCl	Pancreatic HCO_3^-	Pancreatic enzymes	Bile HCO_3^-	Pancreatic insulin
Gastrin	+ (P)	+	+	+	+
PZ-CCK	+	+ (P)	+ (P)	+ (P)	+
Secretin	–	+ (P)	+ (P)	+ (P)	+
Glucagon	–				+
VIP	–	+	+		+
GIP	–				+

(P) = physiological action

VIP (especially), glucagon, GIP and secretin stimulate secretion of intestinal juice.

Table 1.4 Actions of hormones on motility.

	Gastric motility	Gastric emptying	Intestinal motility	Gall bladder contraction
Gastrin	+	–	+	+
PZ-CCK	+	– (P)	+	+ (P)
Secretin	–	–	–	+
Glucagon	–	–	–	+
Motilin	+	–		

+ = stimulates
– = inhibits
(P) = physiological action

GIP inhibits motility of proximal stomach.

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Multiple choice questions

1. Gastrin:
   1 is secreted by G cells in the antrum and duodenum;
   2 release is stimulated by digestive products of protein in the stomach;
   3 stimulates acid secretion by the parietal cells;
   4 increases gastric motility;
   5 and PZ-CCK have similarities in structure and activity.

2. Pancreozymin-cholecystokinin (PZ-CCK):
   1 is secreted by cells in the duodenum;
   2 release is stimulated by digestive products of fat in the small intestine;
   3 stimulates enzyme secretion by the pancreas;
   4 inhibits gastric emptying;
   5 potentiates effect of gastrin on acid secretion by the parietal cells.

3. Secretin:
   1 is secreted by cells in the duodenum;
   2 release is stimulated by an acid medium (e.g. pH 6) in the duodenum;
   3 stimulates bicarbonate secretion by the ductular epithelial cells o the pancreas;
   4 increases intestinal motility;
   5 and motilin have structure/activity relationship.

4. Enteroglucagon:
   1 is secreted by cells in the jejunum and colon;
   2 release is stimulated by digestive products of fat and by hexoses in the small intestine;
   3 stimulates acid secretion by the parietal cells;
   4 decreases intestinal motility;
   5 secreted by the small intestine and by the pancreas are the same molecule.

5. With respect to gastrointestinal hormones which are correct:
   1 vasoactive intestinal peptide (VIP) is present in the stomach, small intestine and colon and causes vasodilatation;
   2 the terminal tetrapeptide of gastrin and PZ-CCK are identical;
   3 gastric inhibitory peptide (GIP) is abundant throughout the colon;
   4 secretin, glucagon, VIP and GIP are a structurally homologous family;

5 'little gastrin' (G17) is about half as abundant in serum as 'big gastrin' (G34), and is about 5 times more active than 'big gastrin' on acid secretion;
6 serum gastrin activity can be detected by immunoassay at times when there is no known stimulus for G17 release (e.g. during sleep): this activity is due to 'big big gastrin' which apparently is unable to cross capillary walls and thus to stimulate gastrin receptors;
7 'enterogastrones' inhibit gastric acid secretion and include secretin and VIP.

6. Gastrointestinal hormones influence many gastrointestinal functions. Which of the following statements are true?
1 the primary action of secretin in man is to stimulate pancreatic secretion of water and bicarbonate;
2 in healthy man, gastrin release is usually stimulated by administration of exogenous secretin;
3 cholecystokinin and pancreozymin have distinctly different modes of action and chemical structures;
4 cholecystokinin stimulates pancreatic enzyme secretion;
5 pancreatic glucagon (greatly) decreases volume flow and enzyme output of the stimulated pancreas;
6 gastric inhibitory polypeptide (GIP) occurs in cells in the duodenal mucosa;
7 vasoactive intestinal polypeptide (VIP) weakly stimulates electrolyte and water secretion by the pancreas, and stimulates secretion and muscle contraction in the small intestine.

7. The actions of gastrin include:
1 reduction in gastrointestinal motility;
2 increased output of pancreatic enzymes;
3 decreased output of bile;
4 increased output of pepsinogen;
5 decrease in tone of lower oesophageal sphincter;
6 increased output of hydrogen ion by the parietal cell.

Answers

1. 1, 2, 3, 4, 5
2. 1, 2, 3, 4
3. 1, 3
4. 1, 4
5. 1, 2, 4, 5, 6, 7
6. 1, 4, 5, 6, 7
7. 2, 4, 6

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2. Motor function of alimentary tract

OESOPHAGEAL MOTILITY

- Oesophagus (in man)
  - upper 1/3 striated muscle
  - lower 2/3 smooth muscle

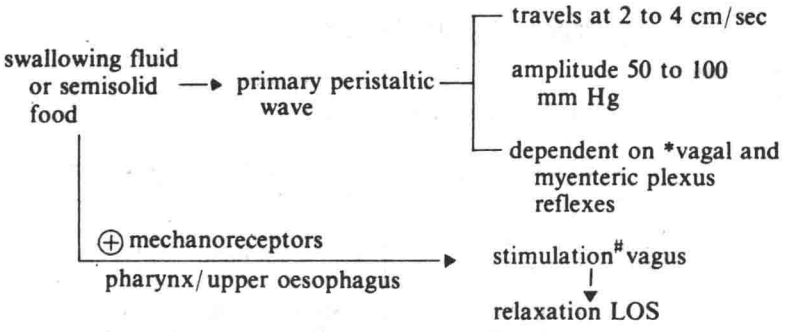
- Oesophagus
  - 25 cm long; passes through right crus of diaphragm; at rest is closed at both ends by sphincters
  - cricopharyngeal sphincter
    - 2 to 3 cm long
    - resting intraluminal pressure 50 to 100 mm Hg
    - initiates primary peristaltic wave (during swallowing) (pressure 50 to 100 mm Hg)
  - resting intra-oesophageal pressure reflects intrapleural pressure (pressure falling with inspiration, rising with expiration)
  - intra-oesophageal pressure (rest, supine) ~ 15 mm Hg < intragastric pressure
  - entry of food → secondary peristaltic wave (pressure 50 to 100 mm Hg)
  - lower oesophageal sphincter (LOS)
    - 2 to 5 cm long
    - resting intraluminal pressure 15 to 40 mm Hg above intragastric pressure
    - lies partly above and below diaphragm

Peristaltic waves in oesophagus

1. primary peristaltic waves
2. secondary peristaltic waves

1. *Primary peristaltic waves*

These are initiated in pharynx during swallowing and proceed over cricopharyngeal sphincter and down oesophagus.



* = main factor
\# = nonadrenergic inhibitory vagal mechanism (purinergic system) (vago-vagal reflexes)

Since the upper 1/3 of oesophagus consists of striated muscle, the primary peristaltic wave in this region is controlled almost exclusively by vagal reflexes. In the lower 2/3 of oesophagus both vagal (mainly) and myenteric plexus reflexes (intrinsic reflex arcs) are involved.

In upright position, liquids and semisolid foods fall by gravity to lower oesophagus well ahead of primary peristaltic wave.

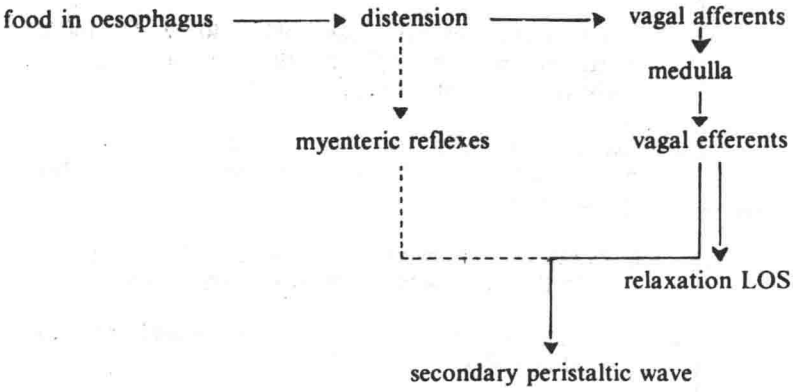
2. *Secondary peristaltic waves*

These are initiated by entry of bolus of food into the oesophagus and propel food downward. Any food not cleared from oesophagus by the primary peristaltic wave invokes vago-vagal (mainly) and myenteric plexus reflexes → secondary peristaltic waves → emptying of oesophagus.

Both primary and secondary peristaltic waves in oesophagus are controlled (mainly) by vagal reflexes and, less importantly, by local myenteric reflexes.

Vagotomy → weak peristaltic waves (via intrinsic reflex arcs). The intraluminal pressure is reduced although the frequency and amplitude of autonomous action potentials from the circular and longitudinal smooth muscles (induced by distension of intraluminal contents) persist, thus suggesting the weak peristaltic waves result from

incordinated (asynchronous) contraction of these muscles in the absence of vagal innervation.



Tertiary, non-peristaltic, high pressure waves are sometimes detected by radiology in distal oesophagus. They are associated with diffuse oesophageal spasm → retrosternal pain on swallowing (especially in the over 75 age group).

Oesophageal sphincters

1. cricopharyngeal (pharyngo-oesophageal) sphincter
2. lower oesophageal (gastro-oesophageal) sphincter

1. *Cricopharyngeal sphincter*

Cricopharyngeal sphincter
- anatomical sphincter (composed of fibres of cricopharyngeal muscle and circular smooth muscle; innervated by glossopharyngeal/vagus, and vagus, respectively)
- high resting intraluminal pressure (50 to 100 mm Hg)
- opens on swallowing and pressure falls briefly to atmospheric pressure; contracts ≈ 1 sec later and pressure rises above resting level as primary wave is initiated and spreads distally over it
- relaxes voluntarily in sword swallowers and beer swillers (where beer is poured down and not swallowed)