Gastrointestinal disorders and malabsorption

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Introduction

Source: http://www.austincc.edu/apreview/PhysText/Digestive.html
The stomach

- Divided in 3 major zones: cardiac zone, body and pyloric zone (antrum, pyloric canal and sphincter)
- Mix of food with acidic gastric juice
- Approx. 2.5L per 24h
The stomach

- HCl → acidic pH necessary for pepsin (from pepsinogens) to begin digestion of proteins and stimulates bile secretion
- Mucus → protection of the mucosal surface
- Intrinsic factor → binds to vit B12, allows its absorption in the terminal ileum
The stomach

Three phases for regulation of gastric secretion:

- Cephalic: neuronal (vagus nerve)

- Gastric: local response to food in stomach, hormonal (gastrin)

- Intestinal: inhibitory phase, response to entry of gastric contents into duodenum and jejunum, hormonal and neuronal
The stomach: gastrin secretion regulation

- Production by G cells of antrum

- Stimulated by antral distention (meals), protein digestion in stomach and vagal stimulation

- Transported by blood through liver to the parietal cells of the fundus of the stomach

- Stimulation of gastric acid secretion

- Gastrin also stimulates:
  - Secretion of gastric pepsinogens, intrinsic factor
  - Secretion of secretin (small intestin)
  - Secretion of bicarbonate, enzymes (pancreas)
  - Secretion of hepatic bile
  - Motility, mucosal growth, blood flow to stomach

- Inhibition of gastrin by the action of acid on the G cells
Disorders and investigations of gastric function

Limited use of biochemical tests
Use of endoscopy or contract radiography

- Peptic ulceration: most cases due to colonisation by *Helicobacter pylori*
  Diagnosis by serology

- Other cause: hypergastrinaemia

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Gastric secretion</th>
<th>Gastrin response to secretin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zollinger-Ellison syndrome</td>
<td>Greatly ↑</td>
<td>↑</td>
</tr>
<tr>
<td>Hypersecretion of gastrin by antral G-cells</td>
<td>Greatly ↑</td>
<td>None or ↓</td>
</tr>
<tr>
<td>Pernicious anaemia</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Post vagotomy</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>CKD</td>
<td>Variable</td>
<td>↓</td>
</tr>
</tbody>
</table>
Disorders and investigations of gastric function

**Intrinsic factor**
Intrinsic factor: glycoprotein, essential for absorption of vitamin B12 (cyancobalamin) in terminal ileum

**Pernicious anaemia**
Autoimmune destruction of parietal cells in stomach
Resulting in achlohydria and anaemia
Macrocytic, megaloblastic, heamolytic anaemia

Diagnosis: low serum B12, positive parietal cell autoantibodies, high plasma gastrin

B12 absorption restored by administration of intrinsic factor
The pancreas

Endocrine function
• Secretion in the blood stream
• Islets of Langerhans
• Production of insulin, glucagon, somatostatin, pancreatic polypeptide

Exocrine function
• Secretion out of the body (gut lumen)
• Alkaline, bicarbonate-rich solution (pH 8.0)
• Approx. 1.5 L per day
• Proenzyme forms of proteases, trypsin, chymotrypsin, carboxypeptidase
• Lipase, colipase, amylase

Secretion under the control of 2 hormones secreted by the small intestine:
➢ Secretin: stimulation of secretion of an alkaline fluid
➢ Cholecystokinin (CCK): stimulation of secretion of pancreatic enzymes and contraction of the gallbladder

Secretin and CCK secretion in response to presence of acid, AA, partly digested proteins in the duodenum
Disorders of the exocrine pancreas

Major disorders of exocrine pancreas
- Acute pancreatitis: biochemistry essential in diagnosis and management
- Chronic pancreatitis: biochemistry of limited used
- Pancreatic cancer: biochemistry of little use
- Cystic fibrosis: inherited metabolic disease

Acute pancreatitis
- Acute abdomen with severe pain
- Most frequent causes: excessive alcohol ingestion, gallstones
- Less common causes: infection, hypertriglycaemia, hypercalcaemia
- Severe acute pancreatitis → mortality up to 25%

Biochemistry
- High serum amylase activity (>10 ULN)
- Serum lipase activity: more specific, but less used in UK
- Plasma may be lipaemic
- Mild increase bilirubin and ALP
- Early increase AST: characteristic of pancreatitis caused by gallstones

<table>
<thead>
<tr>
<th>Causes of increased plasma amylase</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 ULN: acute pancreatitis</td>
</tr>
<tr>
<td>&gt;5 ULN: perforated duodenal ulcer, intestinal obstruction, other acute abdominal disorders, acute oliguric renal failure, DKA, ruptured Fallopian tube</td>
</tr>
<tr>
<td>Usually &lt;5 ULN: salivary gland disorders, CKD, macroamylasaemia</td>
</tr>
</tbody>
</table>
Disorders of the exocrine pancreas

Pancreatic insufficiency
- Reduced exocrine function: fat malabsorption, clinically significant when 90% of function lost
- Symptoms: weight loss, malaise, diarrhoea, steatorrhoea

Causes
- Chronic pancreatitis
- Pancreatic surgery
- Acute pancreatitis
- Cystic fibrosis
- Diabetes

Assessing pancreatic function
- Gold standard: faecal elastase, single stool sample
- Pancreatic specific
- Not degraded in the intestine
- Normally high concentration in faeces
### Pancreatic cancer

- Incidence 9/100,000 per year
- 3-5% 5 year survival
- Symptoms: weight loss, constant pain/back pain, jaundice, new onset diabetes

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>anaemia</td>
</tr>
<tr>
<td>LFTs</td>
<td>Obstructive picture: ↑↑↑ Bilirubin, ↑↑↑ ALP</td>
</tr>
<tr>
<td>Deranged clotting</td>
<td>Reduced Vit K absorption</td>
</tr>
<tr>
<td>Tumour marker</td>
<td>Ca19-9 (↑ in other cancers)</td>
</tr>
<tr>
<td>Imaging</td>
<td>CT scan</td>
</tr>
</tbody>
</table>
The small intestine

- Divided into 3 sections: duodenum, jejunum and ileum
- Approx. 7m long (adult)
- Intestinal villus: increased surface area
Colon

- Approx. 1.5 m (adult) from the ileum to anus
- Divided into: cecum, appendix, colon, rectum and anal canal
## Digestion and absorption

<table>
<thead>
<tr>
<th>Major Digestive Enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enzyme</strong></td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td><strong>Carbohydrate Digestion:</strong></td>
</tr>
<tr>
<td>Salivary amylase</td>
</tr>
<tr>
<td>Pancreatic amylase</td>
</tr>
<tr>
<td>Maltase</td>
</tr>
<tr>
<td><strong>Protein Digestion:</strong></td>
</tr>
<tr>
<td>Pepsin</td>
</tr>
<tr>
<td>Trypsin</td>
</tr>
<tr>
<td>Peptidases</td>
</tr>
<tr>
<td><strong>Nucleic Acid Digestion:</strong></td>
</tr>
<tr>
<td>Nuclease</td>
</tr>
<tr>
<td>Nucleosidases</td>
</tr>
<tr>
<td><strong>Fat Digestion:</strong></td>
</tr>
<tr>
<td>Lipase</td>
</tr>
</tbody>
</table>
Digestion and absorption

- Most of it in duodenum and jejunum
- B12 and bile salts in the terminal ileum
- Reabsorption of Na and water

<table>
<thead>
<tr>
<th>Fluid, vitamins and minerals</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat soluble vitamins (A, D, E, K)</td>
<td>Jejunum</td>
</tr>
<tr>
<td>Iron, zinc, calcium</td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td></td>
</tr>
<tr>
<td>Vit B12</td>
<td>Ileum</td>
</tr>
<tr>
<td>Magnesium, calcium</td>
<td></td>
</tr>
<tr>
<td>Fluids and electrolytes</td>
<td></td>
</tr>
<tr>
<td>Fluids and electrolytes</td>
<td>Colon</td>
</tr>
</tbody>
</table>
Digestion and absorption

Peptides
- Pancreatic enzymes, e.g. trypsinogen, activated in the small intestine
- Absorbed as amino acids, dipeptides and tripeptides
- Hydrolysed in enterocytes to free amino acids

Lipids
- Emulsification with bile and bile acids
- Pancreatic lipase and co-lipase
- Triglycerides hydrolysed on brush border to monoglycerides and fatty acids
- Re-esterified in enterocytes to triglycerides
- Incorporated into chylomicrons with apo-lipoprotein B48
- Transported via lymph to thoracic duct and superior vena cava (in contrast to amino acids and sugars – transported via portal vein to liver)
Digestion and absorption

Carbohydrates
- Diet: polysaccharides (starch and glycogen), disaccharides and monosaccharides
- Salivary and pancreatic amylase for hydrolysis
- In brush border: disaccharideases → glucose, galactose, fructose
- Disaccharidease deficiency:
  - Fermentation in colon (flatulence and diarrhoea)
  - Often acquired following gut infection
  - Lactase activity lost after weaning (abdominal discomfort and explosive diarrhoea)

Others
- Calcium: active transport, controlled by 1,25-dihydroxyvitamin D
- Iron: rate of absorption determined by saturation of circulating transferrin
  When saturated, iron is not absorbed
Malabsorption

*Malabsorption: impaired absorption of products of digestion*

**Mucosal defects**

Biochemical or genetic abnormalities
- Coeliac disease (gluten-sensitive enteropathy)
- Other protein sensitivities: cows’ mil (infants), soya protein
- Disaccharidase deficiencies: inherited (lactase) or acquired (post-infection)
- Cystinuria, etc…

Inadequate absorptive surface
- Small intestinal resection
- Small bowel fistulae

Inflammatory, infiltrative or infective disorders
- Crohn’s disease
- Tropical and non-tropical sprue
- Infective enteritis
- Parasites, etc…

Others
- Malnutrition: mucosal/gut atrophy
- Lymphatic obstruction
Malabsorption

Defective luminal digestion
Pancreatic insufficiency
- Chronic pancreatitis
- Pancreatic carcinoma
- Cystic fibrosis
- Pancreatectomy

Biliary insufficiency
- Liver disease
- Bacterial overgrowth
- Terminal ileal disease/resection
- Drugs

Others
- Postgastrectomy steatorrhoea
- Endocrine disease
Coeliac disease

- Autoimmune mediated jejunal mucosal inflammation
- Proximal small bowel affected
- Symptoms: diarrhoea, weight loss, failure to thrive, stomatitis, bloating and pain
- Patient history: trigger by food
- Investigations: tissue transglutaminase antibodies
duodenal biopsy → gold standard
Inflammatory bowel diseases

**Crohn’s disease**
- Affects any part of the GI tract
- Skip lesions
- Usually small bowel
- Transmural inflammation
- Crypt abscesses

**Ulcerative colitis**
- Proximal from rectum
- Continuous involvement
- Always rectum
- Inflamed mucosa
- Superficial inflammation
- No crypt abscesses

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**Figure 4.** Gross (top), histological (center), and endoscopic (bottom) appearance of normal colon, Crohn’s disease, and ulcerative colitis.
Investigations

- Colonoscopy

- Faecal calprotectin: distinguish between IBD and non-inflammatory bowel conditions (IBS), to monitor IBD activity
- IBD and IBS can cause similar symptoms
- Released into the intestines in excess when inflammation
- NICE diagnostics guidance DG11
Clinical consequences of malabsorption

- Generalised malnutrition and weight loss (failure to thrive in children)
- Fat and carbohydrates calorie malabsorption
- Decreased absorption/reabsorption of fluid and electrolytes
- Fermentation of unabsorbed carbohydrates (and fat) in colon
- Gross fluid loss: hypotension and pre-renal failure
- Vitamin and mineral deficiencies

<table>
<thead>
<tr>
<th>Vitamin and mineral</th>
<th>Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron, B12, folate</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Vit D, Ca</td>
<td>Rickets - osteomalacia</td>
</tr>
<tr>
<td>Vit K</td>
<td>Bruising and bleeding</td>
</tr>
<tr>
<td>Iron, B12, B vitamins</td>
<td>Glossitis and stomatitis</td>
</tr>
<tr>
<td>K</td>
<td>Muscular weakness</td>
</tr>
<tr>
<td>Ca and Mg</td>
<td>Tetany, paraesthesiae</td>
</tr>
</tbody>
</table>
Cases
Case 1

Man, 53
Presents with severe abdominal pain. Radiates through to the back
No previous H/O of GI disease
Heavy alcohol intake over many years

Examination: tender epigastric region, midly shocked

<table>
<thead>
<tr>
<th>Test</th>
<th>result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>10 mmol/L</td>
<td>3.3-6.7 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>90 µmol/L</td>
<td>60-120 µmol/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.10 mmol/L</td>
<td>2.2-2.6 mmol/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>30 g/L</td>
<td>35-50 g/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>12 mmol/L</td>
<td>2.8-6.0 mmol/L (fasting)</td>
</tr>
<tr>
<td>Amylase</td>
<td>5000 U/L</td>
<td>&lt;300 U/L</td>
</tr>
</tbody>
</table>

↑↑ amylase = suggestive of acute pancreatitis

Slightly ↑ urea + N creatinine = renal hypoperfusion due to shock

Hypocalcaemia: protein-rich exudate in the peritoneal cavity, formation of insoluble calcium salts of fatty acids
Case 2

3 year old baby boy
Failure to thrive: below the 3rd centile for height, 10th centile for weight
Frequent diarrhoea
Did not enjoy his food

Examination: anaemia, abdominal distension, wasting of the muscles of the limbs, buttocks and shoulder girdle

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<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>30 g/L</td>
<td>34-42 g/L</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>97 g/L</td>
<td>105-127 g/L</td>
</tr>
<tr>
<td>Tissue transglutaminase antibody</td>
<td>Strongly positive</td>
<td></td>
</tr>
<tr>
<td>Duodenal biopsy</td>
<td>Total villous atrophy</td>
<td></td>
</tr>
</tbody>
</table>

History and findings on examination suggestive of GI disorder

Positive serology for tissue transglutaminase antibody suggestive of coeliac disease
Supported by biopsy appearance