In the name of Allah

The most gracious

The most merciful

Malabsorption

By

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The small intestine

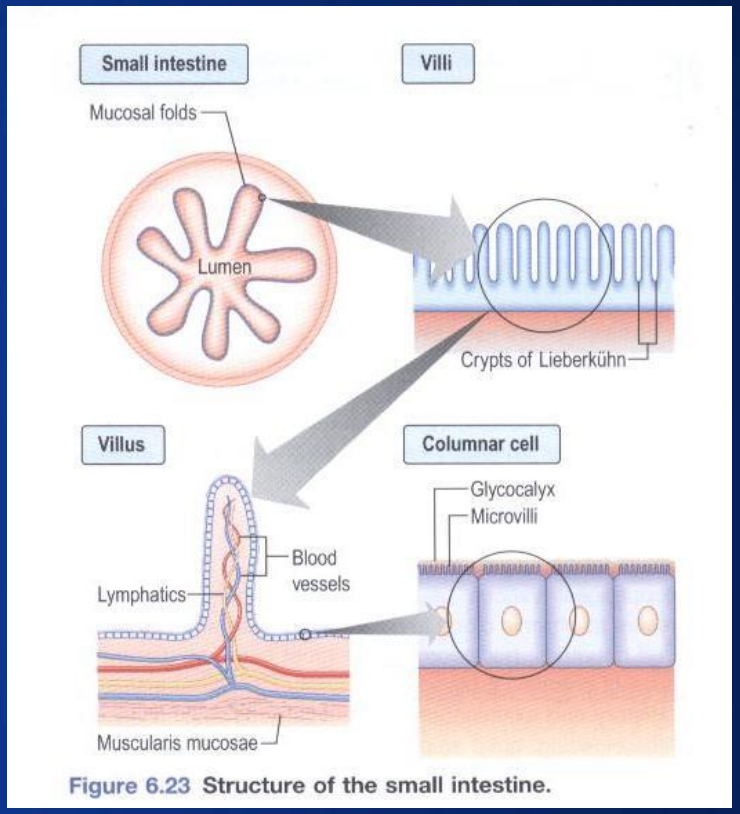

Figure 6.23 Structure of the small intestine.

- 3 -6 m in length
- 300m2 in surface area
- Upper 40% duodenum & Jejunum
- Folds → villi → micro villi

Enteric nervous system :

- 10^8 neurons
- Controls the functioning of the small intestine
- Autonomous
- Coordinate with C.N.S

Gut motility

- interstitial cells of Cajal.
- MMC

I. Quiescence period

II. irregular contractile activity

III. regular phasic contractions

Neuroendocrine peptide production :

APUD cells → hormones

- Complex action
- Interact with each other & with ENS

Table 6.8 Gut regulatory peptides

Peptide	Localization	Main actions
Gastrin/cholecystokinin family		
Cholecystokinin (CCK) Multiple forms from CCK8 (8 amino acids) to CCK83; 8, 33 and 58 are predominant. Terminal 5 amino acids same as gastrin	Duodenum and jejunum (I cells) Enteric nerves CNS	Causes gall bladder contraction and sphincter of Oddi relaxation. Trophic effects on duodenum and pancreas. Pancreatic secretion (minor role). Role in satiety – acting in CNS
Gastrin	G cells in gastric antrum and duodenum	Stimulates acid secretion. Trophic to mucosa
Secretin-glucagon family		
Secretin	Duodenum and jejunum (S cells)	Stimulates pancreatic bicarbonate secretion
Glucagon	Alpha cells of pancreas	Opposes insulin in blood glucose control
Vasoactive polypeptide (VIP)	Enteric nerves	Intestinal secretion of water and electrolytes. Neurotransmitter. Splanchnic vasodilatation, stimulates insulin release
Glucose-dependent insulinotropic peptide (GIP)	Duodenum (K cells) Gastric antrum Ileum	Release by intraduodenal glucose causes greater insulin release by islets than i.v. glucose (incretin effect)
Glucagon-like peptide-1 (GLP-1)	Ileum and colon (L cells) Co-secreted with GLP1	Incretin. Stimulates insulin synthesis. Trophic to islet cells. Inhibits glucagon secretion and gastric emptying Stimulates growth of enterocytes
Glicentin	L cells	Stimulates insulin secretion and gut growth, inhibits gastric secretion
Growth hormone-releasing factor (GHRF)	Small intestine	Unclear
Pancreatic polypeptide family		
Pancreatic polypeptide (PP)	Pancreas (PP cells)	Inhibits pancreatic and biliary secretion
Peptide YY (PYY)	Ileum and colon (L cells)	Inhibits pancreatic exocrine secretion. Slows gastric and small bowel transit ('ileal brake'). Reduces food intake and appetite
Neuropeptide Y (NPY)	Enteric nerves	Stimulates feeding. Regulates intestinal blood flow
Other		
Motilin	Whole gut	Increases gastric emptying and small bowel contraction
Ghrelin	Stomach	Stimulates appetite, increases gastric emptying
Obestatin	Stomach and small intestine	Opposes ghrelin
Oxyntomodulin	Colon	Inhibits appetite
Gastrin releasing-polypeptide (bombesin)	Whole gut and pancreas	Stimulates pancreatic exocrine secretion and gastric acid secretion
Somatostatin	Stomach and pancreas (D cells) Small and large intestine	Inhibits secretion and action of most hormones
Substance P	Enteric nerves	Enhances gastric acid secretion, smooth muscle contraction
Neurotensin	Ileum	Affects gut motility. Increases jejunal and ileal fluid secretion
Insulin	Pancreatic β cells	Increases glucose utilization
Chromogranins	Neuroendocrine cells	Precursor for other regulatory peptides that inhibit neuroendocrine secretion

General principles of absorption

- simple diffusion
- facilitated diffusion
- active transport

Absorption of nutrients in the small intestine

(1) Carbohydrates

- starch $\xrightarrow{\text{amylase}}$ monosaccharide

(2) protein:

- dietary protein $\xrightarrow{\text{trypsin}}$ a.a. & peptides

(3) fat

- TGDcholesterol $\xrightarrow{\text{Bile \& P.lipase}}$ F.A. & M.G.
  fat soluble V .
  medium MCT $\longrightarrow$ portal Vein

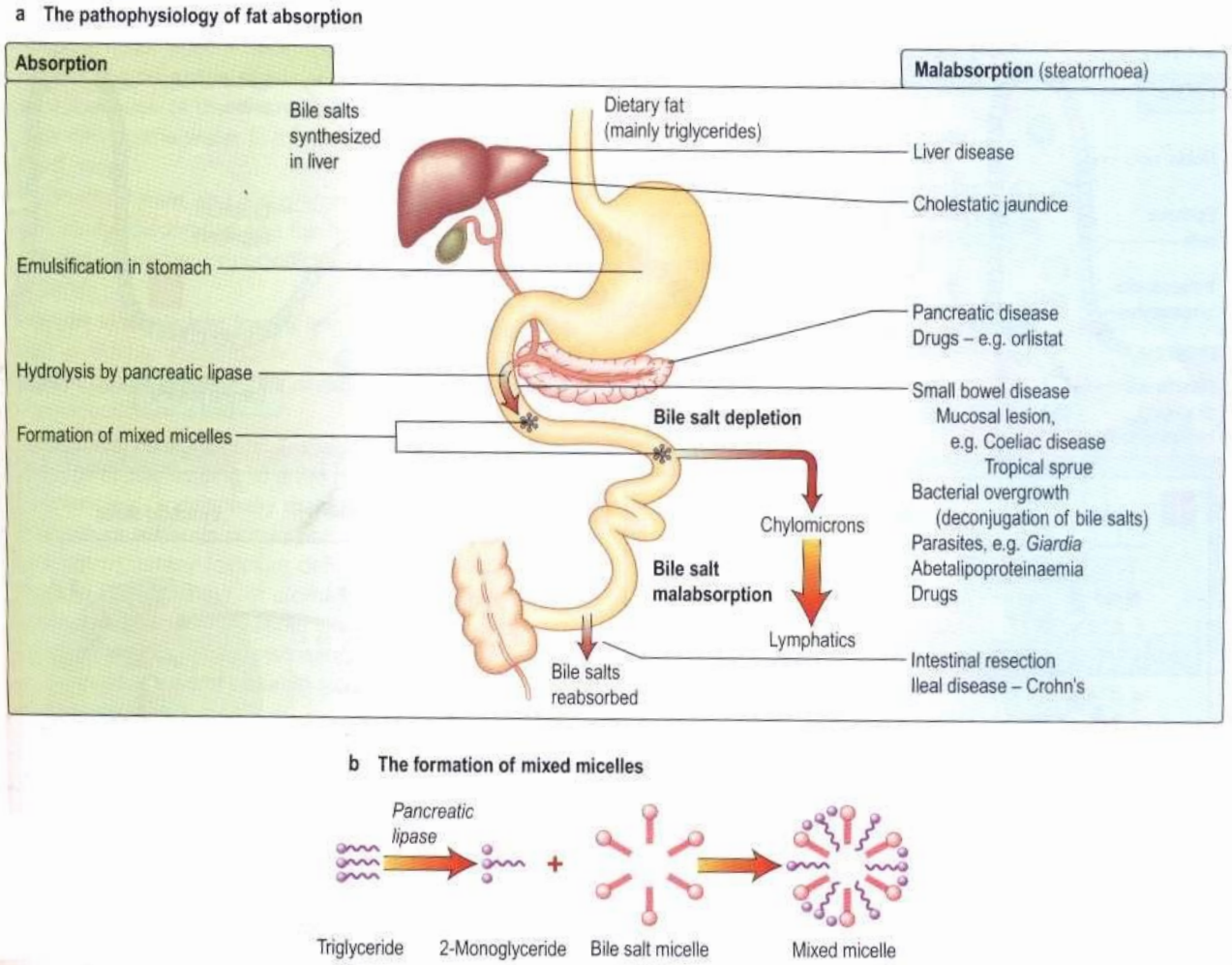

Figure 6.25 **(a)** The pathophysiology of fat absorption. **(b)** Diagram showing the formation of mixed micelles.

Water & electrolytes

Dietary & intestinal secretions absorbed coupled with absorption of monos. a.a. & bicarbonate in jejunum also ileum & colon

- water soluble vitamins
- metals & trace elements
- calcium absorption
- Iron absorption

Response of small bowel to antigens & pathogens

- physical defence
  - mucus layer
  - shedding of surface epithelial like cells
  - movement of luminal contents
  - colonization resistance

❖chemical defence

- **Enzymes = lysozymes**
  - **Antimicrobial peptides : defensins**
  - **Trefoil peptides : 3 factors , promotion of repair**

❖ Immunological defence

- **Humoral : Ig A**
  - **B cell sensitization**

B cell turn into plasma cell

Mesenteric L.N. → TD → blood →small bowel LP

– **Cellular defence T lymphocytes :**

- **GALT → peyer**
- **CD4 → lamina propria**
- **CD8 → Intraepithelial**

Commensal bacteria

- hundred thousand billion microbes
- activated immune system driven by the flora
- chemical signals recognized by toll like receptors that repair the epithelium.

Oral tolerance

- barrier function to prevent excess Ag uptake
- active inhibition by T cells & dendritic cells
- excessive responce to gluten → Coeliac

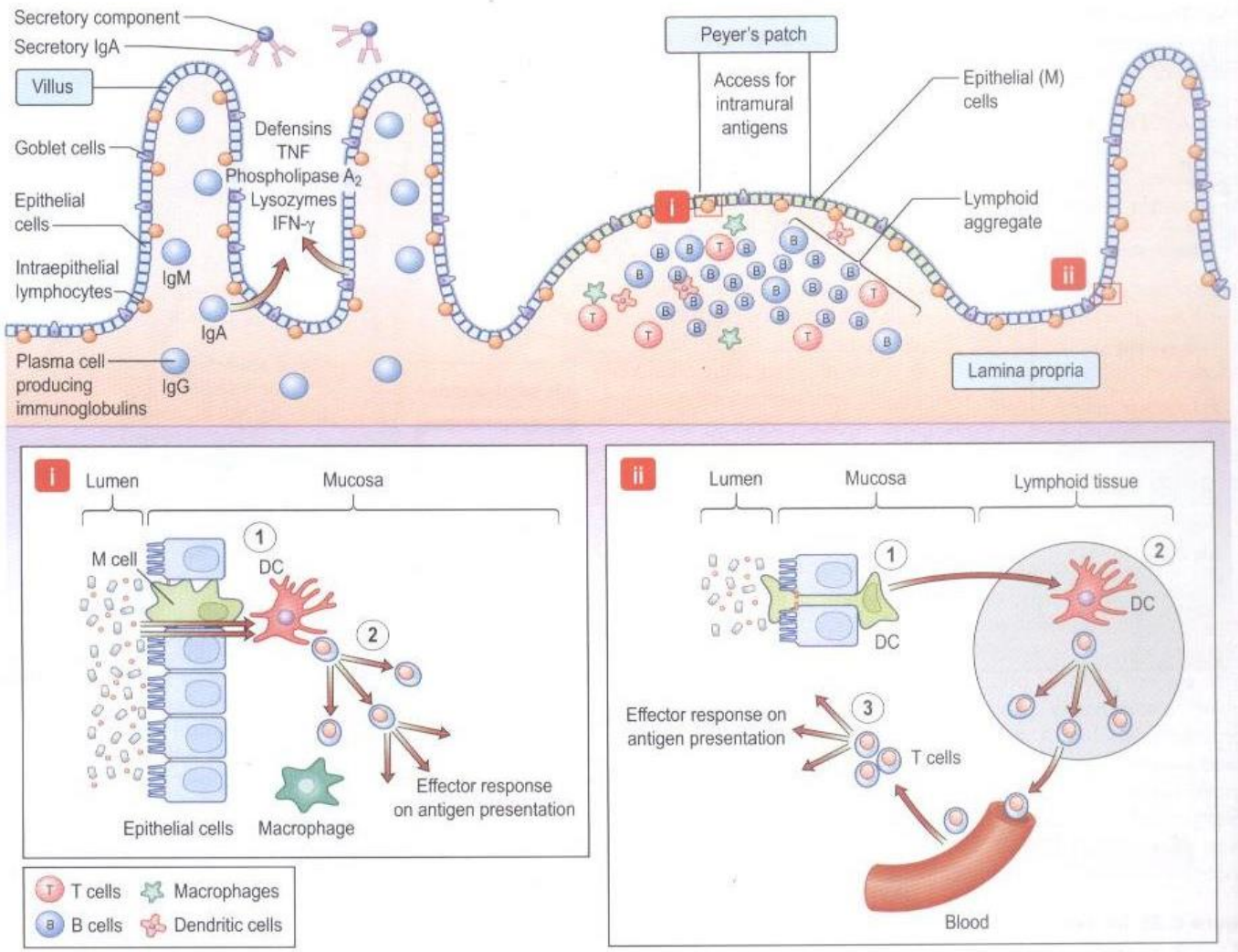

Figure 6.26 Small intestinal mucosa with a Peyer's patch, showing the gut-associated lymphoid tissue (GALT).

presenting features of small bowel disease :

→ 10 – 20% no symptoms !

- diarrhoea
- streatorrhoea
- abdominal pain
- weight loss
- Nutritional deficiencies

Deficiency syndromes and the sites of nutrient absorption

Nutrient	Site of absorption	Deficiency syndrome
Vitamin		
A*	Small intestine	Xerophthalmia
B_1 (thiamine)	Small intestine	Beriberi ; Wernicke's encephalopathy
B_2 (riboflavin)	Proximal small intestine	Angular stomatis; cheilitis
B_6 (pyridoxine)	Small intestine	Polyneuropathy
B_{12}	Terminal ileum	Macrocytic anaemia neuropathy; glossitis
C	Proximal ileum	Scurvy
D*	Jejunum as free vitamin	Rickets ; osteomalacia
E*	Small intestine	Haemolysis, neurological deficit
K*	Small intestine	Bleeding disorders
Folic acid	Jejunum	Macrocytic anaemia
Nicotinamide	Jejunum	Pellagra
Mineral		
Calcium	Duodenum + jejunum	**Tetany**
Copper	Stomach + Jejunum	Menkes' kinky hair syndrome
Fluoride	Stomach	Dental caries
Iodide	Small intestine	Goitre (p622); cretinism
Iron	Duodenum + jejunum	Microcytic anaemia (p312)
Magnesium	Small intestine	**Tetany**
Phosphate	Small intestine	Osteoporosis; anorexia; weakness
Selenium	Small intestine	Cardiomyopathy
Zinc	Jejunum	Acrodermatitis enteropathica; poor wound healing

Investigation of small bowel disease

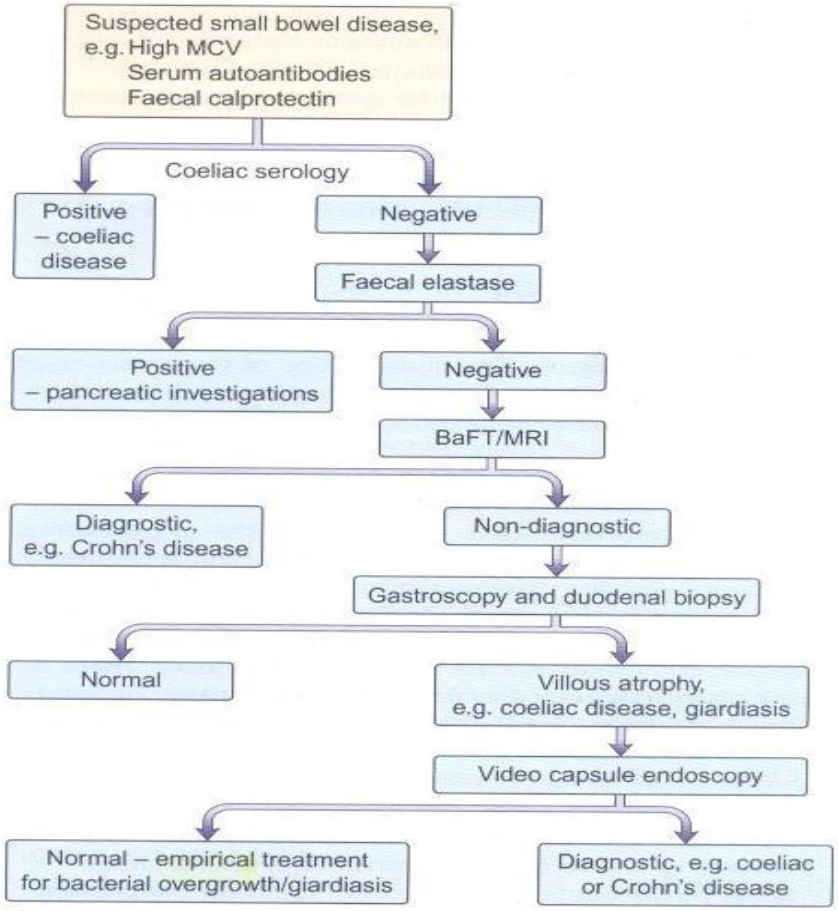

Figure 6.27 Flow diagram for investigation of patients with suspected small bowel disease. BaFT, barium follow-through; MRI, magnetic resonance imaging.

Tests of absorption

- fat malabsorption
  - lactose tolerance test
  - hydrogen breath test
  - tests for pancreatic insufficiency
  - other blood tests
  - tests for PLE
  - antitrypsin clearance
  - Bile salt loss
  - Stool tests

Table 6.9 Disorders of the small intestine causing malabsorption

Coeliac disease
Dermatitis herpetiformis
Tropical sprue
Bacterial overgrowth
Intestinal resection
Whipple's disease
Radiation enteropathy
Parasite infestation (e.g. *Giardia intestinalis*)

Coeliac disease

Inflammation of mucosa of upper small bowel

1% population

Prolamins → gliadin wheat

→ hordeins barley

→ secalins rye

Resist digestion & remain in the intestine triggering immune response

Bind to APC $\xrightarrow[CD_4\ T]{HLAII}$ **interferon gamma**

B cell → endomysial & tissue glutaminase a.b.

→ villous atrophy mainly proximal small bowel

10 – 15% of 1st – degree relative 90% of pts has HLADQ2

C/P

- **any age more ♀**
- **silent or ? IBS**
- **routine ex ↑ MCV or ↓ Fe**
- **tiredness , malaise & anaemia**
- **neuropsychiatric : anxiety or depression**
- **osteoporosis**

Diagnosis

- small bowel biopsy (2nd part)
- endoscopy
- subtotal villous atrophy

endomysial & anti tissue glutaminase a.b. 90% sensitivity

HLA DQ2 in 90%

- ↓ Ca , Fe &folate ↑ P ↓ Albumin & Hb
- Howell – Jolly bodies
- S.B. follow through → Dilatation
- DXA
- Capsule endoscopy

ttt

Replace iron folic acid , Ca , vits , gluten free diet for life

Oats are tolerated

Meat dairy products & fruits are all safe

EMA , t TG for monitoring

pneumococcal vaccine every 5 ys

Complications

- refractory C.D.
- enteropathy associated Tcell lymphoma
- small bowel adenocarcinoma
- ulcerative jejunitis
- carcinoma of the oesophagus

Dermatitis herpetiformis

uncommon blistening subepidermal eruption of the skin associated with gluten sensitive enteropathy

morph.abn. not as severe as in C.D.

skin condition responds to dapsone

gluten free diet improves both enteropathy & skin lesion

Tropical sprue

chronic diarrhoea in residents or visitors of tropical areas

T.sprue : severe malabs

T. malabsorption : mild asymptomatic

Aet : unknown ? infective

Clinical features :

Diarrhoea , anorexia abd. distension & wt loss (of variable intensity)

Epidemics → thousands

Diagnosis &ttt

Acute infective causes must be excluded esp. giardia

Partial villous atrophy

- Leave the sprue area + f. A, 5 mg/d
- tetracycline lg daily /6m
- B12 in acute cases

Bacterial over growth

Anaerobic bacteria more than aerobic

Ileum & colon mainly

❖ major functions :

- ferment non digestible residue
- vit K production
- protect gut mucosa of colonization

B.O. found in

- structural abnormality as stricture or div.
- Elderly
- It deconj. B. salts so can be found in small bowel aspirates

C/P & ttt

- diarrhoea & steatorrhoea
- steatorrhoea dto conj. Bile salt deficiency
- ↓ B12
- ↑↑ serum folate

Diagnosis : hydrogen breath test

ttt : correct underlying lesion

- Metronidazole , teracycline or ciprofloxacin

Intestinal resection

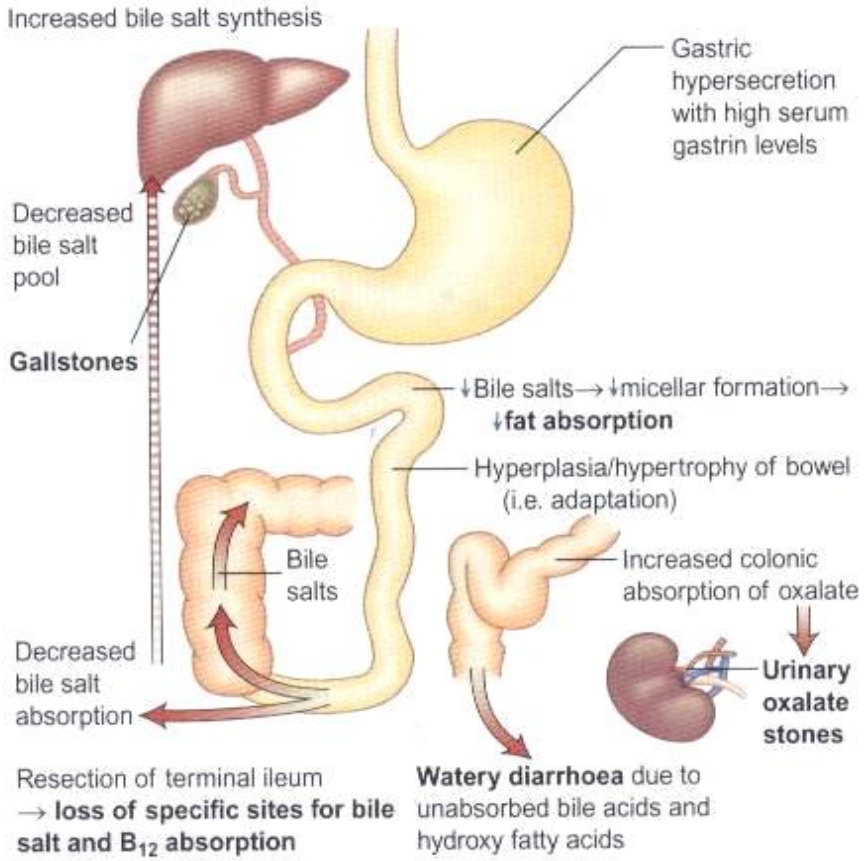

Figure 6.29 The effects of resection of distal small bowel.

If massive leaving < 1m.of small intestine

J.R. better tolerated than I.R.

Ileal resection :

- Bile salt induced diarrhoea.
- Steatorrhoea and gallstone formation.
- Oxaluria & oxalate stones.
- B12 deficiency
- Diagnosis:
- SBFT , SeHCAT, B12
- ttt : B12 & Cholestyramine.

Jejunal resection:

- Ileum compensate for absorption.
- Gastrin hypersecretion.

Massive intestinal resection (Short bowel syndrome)

(1) Shortened S.I ending at a terminal S.B. stoma : sodium & fluid depletion.

ttt : Octreotide, PPI, loperamide cholestyramine & Bile acids.

(2) Shortend S.I continuity with colon:

ttt: low fat high CHO diet.

Whipple's disease

- Rare bact. Dse , Tropheryma whipplei
- 1000 cases 87% male , Arthritis, wt loss, diarrhoea
- Fever, heart, lung, joint & Brain.

Endoscope: Pale shaggy duod mucosa ẻ eroded red friable patches.

Diagnosis

- Trilaminar cell wall of T. whipplei inside macrophages
- PCR & T. antibodies.

ttt

2wks streptomycin & penicillin or ceftriaxone then cotrimoxazole dialy for a year

Radiation enteritis:

> 40 Gy will damage the intestine

fibrotic stricture→ ischaemia & obstruction→ ms atrophy & ulcerative changes

- Nausea, vomiting , diarrhea that improve in 6wks

If > 3m. → chronic radiation enteritis

Malabs. dto bact. over growth

ttt

Symptomatic

Surgery only if obst. or perf.

Local steroids for proctitis.

Parasite infestation

- Giardia
- Cryptosporidiosis
- HIV patients.

Other causes of malabsorption:

- Bile salt binders & some antibiotics
- Orlistat (↓ lipase)
- Thyrotoxicosis.
- Zollinger Ellison S.
- Int.lymphangiectasia.
- Lymphoma.
- D.M.
- Hypogammaglobulinaemia.

Thank you