GASTROENTEROLOGY

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- ❏ muscle: upper 1/3 striated muscle, lower 2/3 smooth muscle; innervation: vagus nerve
- ❏ mucosa: stratified squamous epithelium; submucosa: connective tissue, lymphocytes, plasma cells, nerve cells; muscularis propria: inner circular, outer longitudinal muscle
- ❏ peristalsis - rhythmic contractions that propel contents onward
  - neuronal control via brainstem "swallowing centre" (cranial nerve nuclei)
  - primary = induced by swallowing
  - secondary = induced by esophageal distention (e.g. during reflux)
  - tertiary = spontaneous
- ❏ lower esophageal sphincter
  - internal muscles - intrinsic muscle of distal esophagus
    sling fibres of proximal stomach
  - external muscles - crural diaphragm
  - normal resting pressure = 15-30 mm Hg
  - starts to relax at onset of swallowing
  - contraction = cholinergic (via vagus nerve)
  - relaxation = non-adrenergic, non-cholinergic (nitric oxide and VIP)

MAJOR SYMPTOMS OF ESOPHAGEAL DISORDERS

Dysphagia

- ❏ difficulty in swallowing, with a sensation of food “sticking" after swallowing
- ❏ 2 distinct syndromes: oropharyngeal and esophageal dysphagia
- ❏ oropharyngeal
  - inability to transfer food from mouth to esophagus (i.e. difficulty in initiating swallowing)
  - food sticks immediately after swallowing
  - often with nasal regurgitation
  - neurologic
    - cortical: pseudobulbar palsy (UMN lesion), due to bilateral stroke
    - bulbar: ischemia (stroke); syringobulbia; tumour (LMN)
    - peripheral: polio; ALS
  - muscular
    - muscular dystrophy
    - cricopharyngeal incoordination (failure of UES to relax with swallowing), sometimes seen with gastroesophageal reflux
    - Zenker's diverticulum (pharyngeal diverticulum formed when cricopharyngeus muscle fails to relax)
- ❏ esophageal
  - see Figure 1

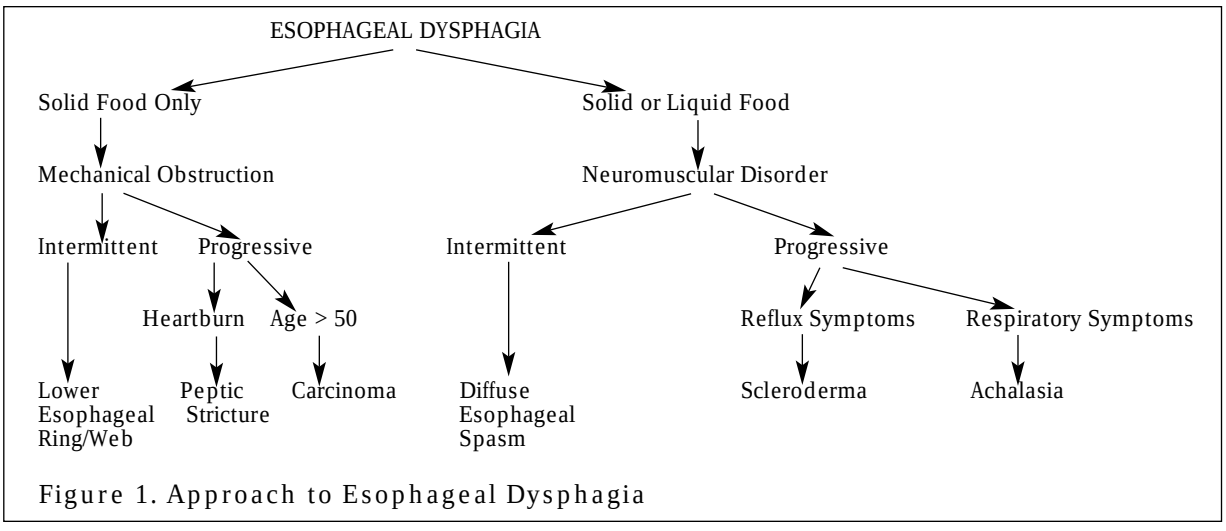


Figure 1. Approach to Esophageal Dysphagia

Heartburn (Pyrosis) (see Gastroesophageal Reflux Disease Section)
- ❑ most common

Chest Pain
- ❑ may be indistinguishable from angina pectoris, but not predictably elicited by exertion, and often occurs spontaneously
- ❑ most common esophageal cause of chest pain is GERD

Odynophagia
- ❑ pain on swallowing
- ❑ causes
  - infection - Candida, Herpes, Cytomegalovirus (common only in immunosuppressed, especially AIDS)
  - inflammation/ulceration (ex. caustic damage)
  - drugs: doxycycline, wax-matrix potassium chloride, quinidine
  - radiation

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

- ❑ definition = reflux of stomach/duodenal contents severe enough to produce symptoms and/or complications. The most common condition affecting the esophagus
- ❑ etiology
  - lower esophageal sphincter relaxes inappropriately: most common
  - low basal LES pressure
  - hypersecretion of gastric acid
  - delayed esophageal clearance
  - delayed gastric emptying from any cause
- ❑ presentation
  - heartburn (retrosternal burning radiating to mouth)
  - acid regurgitation, waterbrash
  - non-specific chest pain
  - dysphagia (abnormal motility or reflux-induced stricture)
  - pharyngitis, laryngitis (with hoarseness)
  - respiratory: chronic cough, asthma, aspiration pneumonia, wheezing
- ❑ symptoms aggravated by
  - position (lying or bending)
  - increase in intra-abdominal pressure (pregnancy or lifting)
  - foods or medications decreasing LES pressure (nitrates, calcium channel blockers, theophylline, peppermint, fatty foods)
  - foods decreasing gastric emptying (alcohol, coffee, chocolate)
- ❑ pathophysiology
  - acid regurgitation—>esophageal inflammation, ulceration and bleeding—>muscle spasm (DES) and/or stricture (scarring)—> increased risk of Barrett's esophagus (columnar metaplasia)—> increased risk of adenocarcinoma
- ❑ investigations
  - diagnosis best made from history, must answer: (1) is there reflux (2) are symptoms due to reflux (3) has reflux led to esophageal damage
  - 24 hour pH monitoring (gold standard for proving presence of GERD) (correlate symptoms with increased acid)
  - endoscopy for presence of esophagitis or other complications (e.g. Barrett's esophagitis)
  - barium swallow (presence of stricture)
  - acid perfusion (Berstein) test (attempt to reproduce symptoms with direct perfusion of acid)
- ❑ management
  - see Figure 2

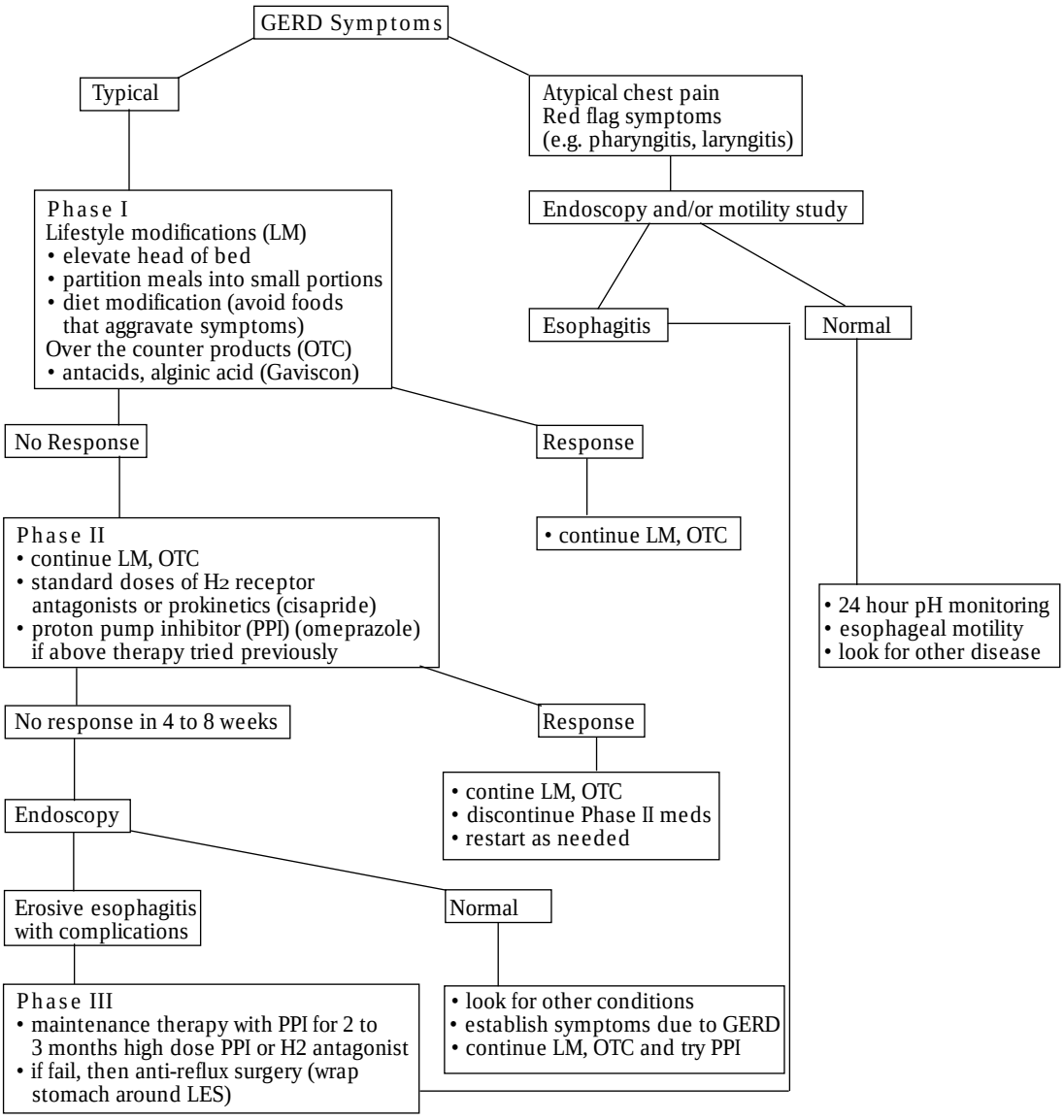


Figure 2. The Three-Phase Management of GERD

ESOPHAGEAL MOTOR DISORDERS

- ❑ symptoms
  - dysphagia with solids and liquids
  - chest pain
- ❑ diagnosis by esophageal motility study (see Figure 3)

Achalasia

- ❑ mechanism
  - incomplete relaxation of LES with swallowing: most important
  - high LES resting pressure (> 30 mm Hg)
- ❑ pathogenesis
  - unknown: thought to be abnormal inhibitory effect, possibly due to decreased release of nitric oxide
- ❑ etiology
  - idiopathic: most often
  - secondary to cancer (esophagus, stomach, elsewhere)
  - Chagas disease

- complications
  - respiratory - aspiration pneumonia, bronchiectasis, lung abscesses
  - gastrointestinal - malnutrition, increased risk of esophageal cancer
- diagnosis
  - chest x-ray - absent air in the stomach, with a dilated fluid filled esophagus
  - barium studies - prominent esophageal dilatation terminating in narrowing at the sphincter, giving a "bird's beak" appearance
  - endoscopic examination to exclude cancer, etc...
  - esophageal motility study required for definitive diagnosis
- treatment
  - dilatation of LES with balloon
    - > 50% good response and can repeat 1-3 times
    - 5% risk of perforation
    - may need lifelong GERD prophylaxis
  - surgery (Heller myotomy) if refractive to above treatment

Diffuse Esophageal Spasm (DES)

- normal peristalsis interspersed with frequent spontaneous abnormal waves which are high pressure, non peristaltic and repetitive
- etiology unknown
- barium x-ray: corkscrew pattern, tertiary waves
- treatment
  - reassurance
  - medical - nitrates, calcium channel blockers, anticholinergics
  - surgery (long esophageal myotomy) if unresponsive to above treatment

Scleroderma

- damage to small blood vessels —> intramural neuronal dysfunction —> progressive weakening of muscles in distal 2/3 of esophagus —> aperistalsis and loss of LES tone —> reflux —> stricture —> dysphagia
- treatment
  - aggressive GERD prophylaxis
  - anti-reflux surgery (gastroplasty included) only as a last resort since it carries significant morbidity

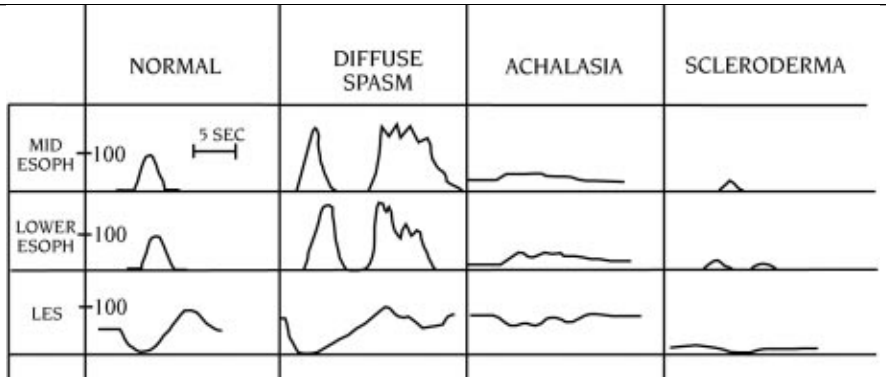


Figure 3. Manometry Tracings for Esophageal Motor Disorders

ESOPHAGEAL STRUCTURAL DISORDERS

Diverticula

- outpouchings of one or more layers of pharyngeal or esophageal wall
- commonly associated with motility disorders. Classified according to location
- pulsion type: associated with high intraluminal pressures or mural muscular defect

- ❑ traction type: esophageal wall pulled outward by inflamed and peribronchial mediastinal lymph nodes - not clinically significant
- ❑ diagnosis
  - barium swallow
  - manometric studies (pulsion diverticulum)
  - esophagoscopy - commonest cause of esophageal perforation

Types

- ❑ pharyngoesophageal (Zenker's) diverticulum
  - most frequent
  - posterior pharyngeal outpouching above cricopharyngeal muscle and below the inferior pharyngeal constrictor muscle
  - symptoms: dysphagia, regurgitation of undigested food, halitosis
  - treatment: myotomy of cricopharyngeus muscle +/– excise or suspend sac
- ❑ mid-esophageal diverticulum
  - secondary to mediastinal inflammation (traction type) or motor disorders
  - usually asymptomatic - no treatment required
- ❑ epiphrenic diverticulum
  - distal esophagus, large, associated with motility disturbances (pulsion type)
  - symptoms: asymptomatic or dysphagia, regurgitation, retrosternal pain, intermittent vomiting
  - complications: esophagitis, periesophagitis, hemorrhage secondary to ulceration
  - treatment
    - minor symptoms - no surgery
    - severe symptoms - diverticulotomy and anti-reflux operation (Nissen, Belsey)
    - 80-90% success rate

Benign Stricture

- ❑ presents as progressive dysphagia in face of reflux symptoms
- ❑ diagnose with barium study or endoscopy
- ❑ treatment
  - dilation and reflux medication
  - anti-reflux surgery if above unsuccessful

Esophageal Cancer (see General Surgery Notes)

Rings and Webs

- ❑ asymptomatic unless lumen diameter < 12 mm
- ❑ ring = circumferential narrowing (lower esoph) vs. web = partial occlusion (upper esoph)
- ❑ dysphagia occurs with large food bolus only
- ❑ Plummer-Vinson or Patterson-Kelly Syndrome
  - upper esophageal web with iron deficiency (+ cheilosis, koilonychia)
  - usually in middle aged females (>40 years)
  - increased risk of hypopharyngeal carcinoma
- ❑ Schatzki Ring (congenital ring)
  - mucosal ring at squamo-columnar junction above a hiatus hernia
  - causes intermittent dysphagia for solids
  - treatment involves shattering ring with bougie or use of peroral dilators

Barrett's Esophagus

- ❑ metaplasia of normal squamous epithelium to columnar epithelium for at least 3 cm above the gastroesophageal junction
- ❑ usually acquired (GERD, stricture)
- ❑ endoscopy shows fingers and islands of columnar epithelium in distal esophagus
- ❑ 50-fold increase in developing adenocarcinoma
- ❑ treat with aggressive anti-reflux regimen and esophagectomy for cancer (and perhaps for high grade dysplasia)

Notes

INFECTIOUS ESOPHAGITIS

- ❑ severe mucosal inflammation and ulceration (due to virus or fungus)
- ❑ seen in diabetes, malignancy, and immunocompromised patients
- ❑ symptoms: odynophagia, dysphagia
- ❑ diagnosis: endoscopic visualization and biopsy
- ❑ treatment
    - Candida (most common): nystatin swish and swallow, ketoconazole, fluconazole
    - Herpes (second most common): often self-limiting, acyclovir
    - CMV: IV gancyclovir

STOMACH AND DUODENUM

PEPTIC ULCER DISEASE

- ❑ erosion: superficial to the muscularis mucosa, thus no scarring
- ❑ ulcer: penetrates the muscularis mucosa and can result in scarring

Clinical Pearl

- ❑ Must always biopsy gastric ulcer to rule our cancer, but duodenal ulcers are almost never malignant

Etiology

- ❑ most common: Helicobacter pylori and NSAIDs
  Others: Zolliger-Ellison, idiopathic, physiological stress, cytomegalovirus, ischemic

Table 1. Etiologies of PUD

	Duodenal	Gastric
Helicobacter pylori	90%	60%
NSAIDs	7%	35%
stress-induced	< 3%	< 5%
Zollinger-Ellison syndrome	< 1%	< 1%

Helicobacter Pylori

- ❑ common infection (20-40% of Canadians, prevalence increases with age)
- ❑ Gram negative rod
- ❑ lies on the mucus layer adjacent to epithelial cell surface; does not invade
- ❑ primarily resides in stomach, especially antrum
- ❑ present in
    - 90% of duodenal ulcers
    - 60% of gastric ulcers
    - 50% of non-ulcerative dyspepsia
- ❑ high prevalence in
    - developing countries (crowding)
    - low socioeconomic status (poor sanitation)
- ❑ infection most commonly acquired in childhood, presumably by fecal-oral route

Table 2. Diagnosis of H. pylori

Test	Sensitivity	Specificity	Cost
Non Invasive: urea breath test	90-100%	89-100%	$$
serology	88-99%	89-95%	$ -but remains positive for variable period after treatment
Invasive (OGD): histology	93-99%	95-99%	$$$ - gold standard
microbiology culture	80%	95%	$$$
rapid urease test	89-98%	93-98%	$$ - rapid

Notes

Pathogenesis of PUD
- ❑ old rule: "no acid, no ulcer" still holds on most (but not all) occasions
- ❑ acid secreted by parietal cell (stimulated by vagal acetylcholine, gastrin, histamine) necssary for most ulcers
- ❑ mucosal defenses moderated by PGF2 and blood flow, mucus, etc...
- ❑ two theories of how Helicobacter causes ulcer
  - Helicobacter produces toxins, which cause gastric mucosal inflammation and necrosis
  - Helicobacter blocks gastrin G cells in antrum from sensing luminal acid—> increased serum gastrin—> increased gastric acid—> ulcer

Clinical Associations of PUD
- ❑ cigarette smoking: increases risk of ulcer, risk of complications, chance of death from ulcer and impairs healing rate

Clinical Pearl
Smoking and PUD
- ❑ 2x as often, 2x as long to heal, 2x more likely to recur

- ❑ alcohol: damages gastric mucosa but only rarely causes ulcers
- ❑ diet: causes dyspepsia in some patients poorly understood mechanisms but has little documented role in peptic ulceration
- ❑ physiological stress: causes ulcers and erosions, but only weak evidence linking psychological factors to ulcers
- ❑ ulcers associated with cirrhosis of liver, COPD, renal failure (uremia)

Presentation
- ❑ dyspepsia is commonest presentation (but only 20% of patients with dyspepsia have ulcers)
- ❑ in most studies, history not reliable in establishing diagnosis but duodenal ulcer is supposed to have 6 classical features:
  - epigastric
  - burning
  - develops 1-3 hours after meals
  - relieved by eating and antacids
  - interrupts sleep
  - rhythmicity (tends to occur in clusters over weeks with subsequent periods of remission)
- ❑ gastric ulcers have more atypical symptoms, always require biopsy to exclude malignancy
- ❑ may present with complications
  - bleeding 10% (especially severe if from gastroduodenal artery)
  - perforation 2% (usually anterior ulcers)
  - gastric outlet obstruction 2%
  - penetration (posterior) 2% - may also cause pancreatitis

Diagnosis
- ❑ history of previous ulcers, NSAID use, etc...
- ❑ investigations
  - endoscopy (most accurate) (see Colour Atlas C9)
  - upper GI series
- ❑ diagnosis of *H. pylori* (see Table 2)
- ❑ serum gastrin measurement if Zollinger-Ellison syndrome suspected
- ❑ differential diagnosis
  - functional dyspepsia
  - GERD
  - coronary artery disease
  - cancer of stomach
  - Crohn's disease
  - pancreatitis
  - cancer of liver, pancreas

Management
- ❑ 3 key modalities of management
  - stop NSAIDs
  - acid neutralization
  - *H. pylori* eradication

- ❑ stop NSAIDs
  - or continue NSAIDs but add either a proton pump inhibitor or misoprostol
- ❑ acid neutralization
  - antacids (magnesium hydroxide/Maalox and aluminum chloride/Mylanta)
    - weak bases react with gastric acid to form a salt and water
    - may also have role in mucosal protection
    - large doses required to heal ulcer
    - side effects include constipation (A1) and diarrhea (Mg)
  - anti-acid secretory drugs
    1. proton pump inhibitors
       - irreversibly inhibits parietal cell proton pump
       - omeprazole (Losec), lansoprazole (Prevacid), pantoprazole (Pantoloc)
       - almost 100% reduction of gastric acid secretion
    2. H2-receptor antagonists
       - ranitidine (Zantac), cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid)
       - 70% reduction in gastric acid secretion
  - mucosal protective agents
    1. sucralfate
       - increases mucosal defense mechanisms
       - as effective as H2-blocker
       - not absorbed systemically and therefore safe in pregnancy
       - side effect: constipation
    2. prostaglandin analogues (e.g. misoprostol)
       - used for prevention of NSAID-induced ulcers
- ❑ H. *pylori* eradiation (Canadian Concensus Guidelines)
  - eradication upon documentation of H. *pylori* infection controersial since most patients will not have peptic ulcer or cancer
  - however, empiric treatment suitable for younger patients with mild symptoms
  - 1st line triple therapy:
    - PPI + clarithromycin 500mg + amoxicillin 1000mg BID x 7 days
    - PPI + clarithromycin + metronidazole 500mg x 7 days

Clinical Pearl
Triple Therapy for eradication of H. pylori
❑ "Easy as 1-2-3" (one week, twice a day, 3 drugs)

    - success rate > 90% thus follow-up investigations are necessary only if poor patient compliance, presentation with ulcer complication
  - 2nd line quadruple therapy
    - PPI + bismuth + metronidazole + tetracycline (BMT) x 7 days
    - H_2 blocker + BMT x 14 days
  - treatment failure due to poor compliance or metronidazole-resistance

NSAID-Induced Ulceration

- ❑ cause gastric mucosal petechiae in virtually all users, erosions in most users, ulcers in some (25%) users
- ❑ only ulcers cause significant clinical problems
- ❑ most NSAID ulcers are clinically silent: in NSAID users, dyspepsia is as common in patients with ulcers as patients without ulcers
- ❑ more commonly causes gastric ulcers than duodenal ulcers
- ❑ may exacerbate underlying DU disease
- ❑ pathogenesis (direct vs. indirect)
  - direct: petechiae and erosions are due to local effect of drug on gastric mucosa: drug is non-ionized (HA) in acidic gastric lumen, therefore enters gastric epithelial cell where it becomes ionized (A–) at intracellular neutral pH, and damages cell
  - indirect: ulcers require systemic NSAID effect: NSAIDs inhibit mucosal cyclo-oxygenase, the rate-limiting step in the synthesis of prostaglandins, which are required for mucosal integrity

- ❑ risk factors
  - age
  - previous peptic ulcers/upper GI bleeding
  - high dose of NSAID/multiple NSAIDs being taken
  - concomitant corticosteroid use
  - concomitant cardiovascular disease/other significant diseases
- ❑ management
  - combine NSAID with PPI, or misoprostol (a PG analogue)
  - switch to cyclo-oxygenase (COX-2) specific drug-celecoxib
    Human prostaglandin synthesis is catalyzed by two isoforms of cylco-oxygenase (COX) - COX-1 is the isoenzyme found in the stomach, "strengthens" the gastric wall to prevent ulcers; COX-2 is the isoenzyme found in white blood cells, causes inflammation, thus COX-2 specific inhibitors reduce inflammation but do not cause ulceration in the upper GI tract

Stress-Induced Ulceration

- ❑ definition: ulceration or erosion in the upper GI tract of ill patients, usually in the ICU
- ❑ lesions most commonly in fundus of stomach
- ❑ only recognized symptom is upper GI tract bleeding
- ❑ risk factors
  - mechanical ventilation and coagulation are the two chief risk factors
  - multiorgan failure
  - septicemia
  - severe surgery/trauma
  - CNS injury ("Cushing's ulcers")
  - burns involving more than 35% of body surface
- ❑ pathogenesis unclear, probably involves ischemia, and, in CNS disease, hypersecretion of acid ("Cushing's ulcers")
- ❑ prophylaxis with gastric acid suppressants (H_2 antagonists) decreases risk of upper GI tract bleeding, but may increase risk of pneumonia; thus sucralfate is often used
- ❑ treatment same as for bleeding peptic ulcer but less often successful

Zollinger-Ellison Syndrome

- ❑ gastrinoma (most common in pancreas but 10-15% occur in duodenum)
- ❑ rare (< 1%)
- ❑ suspect if
  - strong family history or MEN
  - unusually severe symptoms of PUD
  - diarrhea and malabsorption
  - multiple ulcers in unusual sites
  - refratory to treatment
- ❑ diagnosis: serum gastrin measurement

ACUTE DIARRHEA

- ❑ defined physiology as > 200 g of stool/24 hours of < 14 days duration, but most patients complain of stools more frequent or more water than usual
- ❑ most commonly due to infections or drugs
- ❑ most infections are self-limited and resolve in less than 2 weeks
- ❑ diagnostic studies are not cost-effective in acute diarrhea without mucosol inflammation

Classification of Acute Diarrhea

- ❑ see Table 3

Table 3. Classification of Acute Diarrhea

	Inflammatory	Non-Inflammatory
Definition	• disruption of intestinal mucosa	• no disruption of intestinal mucosa
Mechanisms	• organisms or cytotoxins produced by the organisms directly invade mucosa, killing mucosal cells, but in both inflammatory and non-inflammatory diarrhea, the diarrhea is due to proteins stimulating intestinal water secretion/inhibiting water absorption	
Site	• usually colon	• small intestine
Sigmoidoscopy	• usually abnormal mucosa seen	• usually normal
Symptoms	• bloody (not always) • small volume, high frequency • often lower abdominal cramping with urgency +/– tenesmus • may have fever +/– shock	• watery, little or no blood • large volume • upper/periumbilical pain/cramp
Labs	• fecal WBC and RBC positive	• fecal WBC negative
Etiology	Infectious • Bacterial: • *Shigella*; • *Salmonella typhi*; • *Campylobacter*; • *Yersinia*; • E. *coli* (EHEC 0157:H7); • C. *difficile* • Protozoal: • E. *histolytica* (amebiasis); • Strongyloides	Infectious • Bacterial: • *Salmonella enteritidis*; • *Staph. aureus*; • B. *cereus*; • C. *perfringens*; • E. *coli* (ETEC, EPEC); • *Vibrio cholerae* • Protozoal: • *Giardia lamblia* • Viral: • Rotavirus; • Norwalk; • CMV Drugs: • antacids (Mg - Makes you Go); • antibiotics; • laxatives, lactulose; • colchicine
Differential	mesenteric ischemia radiation colitis chronic diarrheal illness (IBD)	chronic diarrheal illness (IBS, dietary intolerance)
Significance	• higher yield with stool C&S • can progress to life-threatening megacolon, perforation, hemorrhage	• lower yield with stool C&S • chief life-threatening problem is fluid and electrolyte depletion

Common Clinical Syndromes

- ❑ Food Poisoning
  - brief explosive diarrhea following exposure to food contaminated with bacteria or bacterial toxins
  - 90% due to 4 bacteria: *Salmonella* > *S. aureus* > *C. perfringens* > *B. cereus*
  - spontaneously resolves within 24-48 hours
- ❑ Traveler's Diarrhea
  - 3 unformed stools in 24 hours +/– nausea, vomiting, abdominal pain, tenesmus, blood/mucus in stool
  - up to 50% of travelers to developing countries affected in first 2 weeks and 10-20% after returning home

- cause - 80% bacterial
  - enterotoxigenic *E. coli*, other *E. coli*, *Campylobacter*, *Shigella*, *Salmonella*, *Vibrio* (non-cholera)
  - viral - Norwalk and Rotavirus accounting for about 10%
  - rarely protozoal (Giardiasis, Amebiasis)
- treatment and prophylaxis
  - can use bismuth subsalicylate (Pepto-Bismol), empiric quinolone such as ciprofloxacin or TMP/SMX prophylaxis for travelers who can't tolerate inactivity, have underlying medical condition (DM, AIDS, FBD, ESRD), or past history of traveler's diarrhea
  - if diarrhea persists after returning home, think of Giardia, Entamoebahistolytica, post-infections irritable bowel syndrome

Diagnosis

❑ see Table 4

Management

❑ Fluid and Electrolyte Replacement - note that exception extremes of age, and coma, it is electrolyte repletion which is most important, patient will drink water automatically

❑ Antidiarrheal Agents - if not inflammatory

❑ Antimotility agents - diphenoxylate, loperamide (Imodium) but contraindicated in mucosal inflammation
- Side effects - abdominal cramps, toxic megacolon

❑ Adsorbents - kaolin/pectin (Kaopectate), methylcellulose, activated attapulgite
- act by absorbing intestinal toxins/microorgansims, or by coating/protecting intestinal mucosa
- much less effective than antimotility agents

❑ Modifiers of fluid transport - may be helpful, bismuth subsalicylate (Pepto-Bismol)

❑ Antibiotics - Rarely indicated
- risks
  - prolonged excretion of enteric pathogen
  - drug side effects (including C. *difficile*)
  - develop resistant strains
- indications for antimicrobial agents in acute diarrhea
  - clearly indicated: *Shigella*, *Cholera*, *C. Difficle*, Traveler's Diarrhea (Enterotoxigenic *E. Coli*), *Giardia*, *Entamoeba histolytica*, Cyclospora
  - indicated in some situation: *Salmonella*, *Campylobacter*, *Yersinnia*, Non-enterotoxigenic, E. *Coli*
  - *Salmonella*: treat *Salmonella typhi* (typhoid or enteric fever) always, other salmonella only if, underlying immunodificiency, hemolytic anemia, extremes of age, aneurysms, prosthetic valves, grafts/joints

Table 4. Approach to Acute Diarrhea

A. History

1. *Search for Etiology*
   - Travel
   - Homosexual contacts
   - Outbreaks
   - Seafood ingestion
   - Extraintestinal manifestations of IBD
   - Family history
   - Antibiotics
   - Diet
   - Steatorrhea
   - Weight loss
   - Immunosuppressed
   - Laxative use
   - Tumour history
2. *Manifestations of Mucosal Inflammation*
   - Fever
   - Blood in stool
   - Abdominal pain between bowel movements
   - Tenesmus
3. *Severity of illness*
   - Frequency of bowel movements
   - Duration of illness

B. Physical Examination
- Overall appearance - toxic?
- Vitals - febrile? Hypotensive?
- Volume status - Dehydrated?
- Abdominal exam - Peritonitis?
- Rectal exam - tenderness?

C. Further Investigations if ≥ 2 of:
- Fever > 38.5 ºC
- Severe abdominal pain or peritonitis
- Positive test for fecal leukocytes
- Bloody diarrhea
- Severe volume depletion
- Duration > 7 days
- Extremely young or old, or immunocompromised

< 2
- Symptomatic Treatment
- Fluid Replacement
- Antidiarrheal agents

≥ 2 Go to D. (see next page)

D. Diagnostic Tests
- Stool WBC
- Culture
- O&P
- Flexible sigmoidoscopy
- C. *difficile* toxin

D. Diagnostic Tests

- ❑ stool WBC - stool smeared on slide and methylene blue drops added
  - > 3 PMNs in 4 HPFs = ++
  - usually positive for infectious but also IBD and radiation
- ❑ culture - routinely only for *Campylobacter, Salmonella, Shigella, E. Coli*
  - if you want others - order them specifically
- ❑ O&P - may need 3 stool samples because of sporadic passage
- ❑ flexible sigmoidoscopy - useful if inflammatory diarrhea suspected
  - biopsies can be taken; useful to rule out idiopathic inflammatory bowel disease (Crohn's diseae and ulcerative colitis)
- ❑ C. *difficile* toxin - indicated when recent/remote antibiotics use, hospitalization, nursing home or recent chemotherapy

Table 5. Pathogens in Infectious Diarrhea

Pathogen	Source	Treatment	Miscellaneous
Bacteria (invasive)			- Dx: stool WBC+, RBC+, C&S
Campylobacter jejuni	- uncooked meat - especially poultry	- usually none	- most common bacterial cause of diarrhea
Shigella dysenteriae	- fecal-oral	- amoxicillin or ciprofloxacin - TMP/SMX if resistant	- very small inoculum needed for infection
Salmonella typhi	- fecal-oral	- ciprofloxacin - TMP/SMX	- extremes of age, gallstones predispose to chronic carriage
Yersinia	- contaminated food - unpasteurized milk	- supportive - no antibiotics	- mimics appendicitis or Crohn's
EHEC 0157	- uncooked hamburger - swimming water	- supportive - monitor renal function - no antibiotics	- causes HUS in 10% especially in kids - Dx: special E. *coli* culture
Bacteria (non-invasive)			- Dx: clinically
Vibrio cholerae	- fecal-oral	- aggressive fluid and lytes resuscitation - tetracycline	- mortality < 1% if treated aggressively
Salmonella enteritidis	- uncooked eggs/poultry - low gastric acid, sickle cell, asplenia have increased nsk	- for immunocompromised children, cancer or hemoglobinopathy, use ciprofloxacin/ceftriaxone - others supportive	- #1 cause of food poisoning
S. *aureus*	- unrefrigerated meat and dairy products	- supportive - +/– antiemetics	
ETEC	- contaminated food/water	- supportive - empiric ciprofloxacin	- #1 cause of traveller's diarrhea
Parasites			- Dx: stool O&P
Entamoeba histolytica	- 10% prevalence worldwide - 80% endemic areas - fecal/oral	- metronidazole + iodoquinol if symptomatic - only iodoquinol for asymptomatic	- if untreated, can cause disseminated disease - sigmoidoscopy shows flat ulcers with yellow exudate
Entamoeba dispar			- non-pathogenic, indistinguishable from E. *hisolytica* by the usual microbiological (morphological) techniques, is over 100 fold more common in Ontario than B. *histolytica*
Giardia lamblia	- nursery school (#1) - travel - "beaver fever" - HIV+ - homosexual men - immunodificiency	- metronidazole	- Sudan Stain for fat in stool - duodenal aspiration
Viruses			
Rotavirus	- fecal/oral	- supportive	- can cause severe dehydration
Norwalk Agent	- fecal/oral	- supportive	- often causes epidemics

CHRONIC DIARRHEA

❑ passage of frequent unformed stools (> 200 mL of stool water/24 hours) of > 14 days duration

Classification of Chronic Diarrhea

❑ see Table 6

Table 6. Classification of Chronic Diarrhea

Type	Characteristics
Inflammatory • Ulcerative colitis • Crohn's disease • Malignancy: lymphoma, adenocarcinoma	Fever, hematochezia, abdominal pain; usually weight loss with carcinoma
Osmotic Ingestion • Lactose intolerance • medications, laxatives	 Stool volume decreases with fasting Increased stool osmotic gap: fecal [Na+] + [K+] < 1/2 serum osmolality – 25 mmol/L
Maldigestion and Malabsorption • Pancreatic insufficiency • Bile salt deficiency • celiac sprue • Whipple's disease • bowel resection	See Maldigestion and Malabsorption Weight loss, fecal fat > 7-10g/24h stool collection anemia, hypoalbuminemia
Secretory • bacterial enterotoxins • secretagogues - VIP, gastrin, carcinoid	Large volume (>1L/d); little change with fasting Normal stool osmotic gap: secretory: fecal [Na+] + [K+] = 1/2 serum osmolality
Functional • Irritable Bowel Syndrome	see Irritable Bowel Syndrome Section

MALDIGESTION AND MALABSORPTION

❑ definitions
- maldigestion - inability to break down large molecules in the lumen of the intestine into their component small molecules
- malabsorption - inability to transport molecules across the intestinal mucosa to the body fluids

❑ most definitively diagnosed by 72 hour stool collection (weight, fat content) but this is a cumbersome test, therefore diagnosis often made by combination of
- history: weight loss, diarrhea, steatorrhea, weakness, fatigue
- lab: stool fat globules on fecal smear, low serum carotene, folate, Ca^{2+}, Mg^{2+}, vitamin B_{12}, albumin, elevated INR/PTT

❑ treatment- problem specific

Classification of Diseases of Malabsorption and Maldigestion

❑ maldigestion
- pancreatic exocrine deficiency
  - primary diseases of the pancreas (e.g. cystic fibrosis, pancreatitis)
  - inactivation of lipase due to acidic environment
- bile salt deficiency
  - may be secondary to liver disease, terminal ileal disease (impaired recycling), bacterial overgrowth (deconjugation), drugs (e.g. cholestyramine)
- specific enzyme deficiencies
  - e.g. lactase

❑ malabsorption
- inadequate absorptive surface (e.g. bowel resection, extensive Crohn's)
- specific mucosal cell defects (e.g. abetalipoproteinemia)

- diffuse disease
  - immunologic or allergic injury (e.g. Celiac disease)
  - infections/ infestations (e.g. Whipple's disease, Giardiasis)
  - infiltration (e.g. lymphoma, amyloidosis)
  - fibrosis (e.g. systemic sclerosis, radiation enteritis)

❑ drug-induced
- cholestyramine, ethanol, neomycin, tetracycline

❑ endocrine
- diabetes

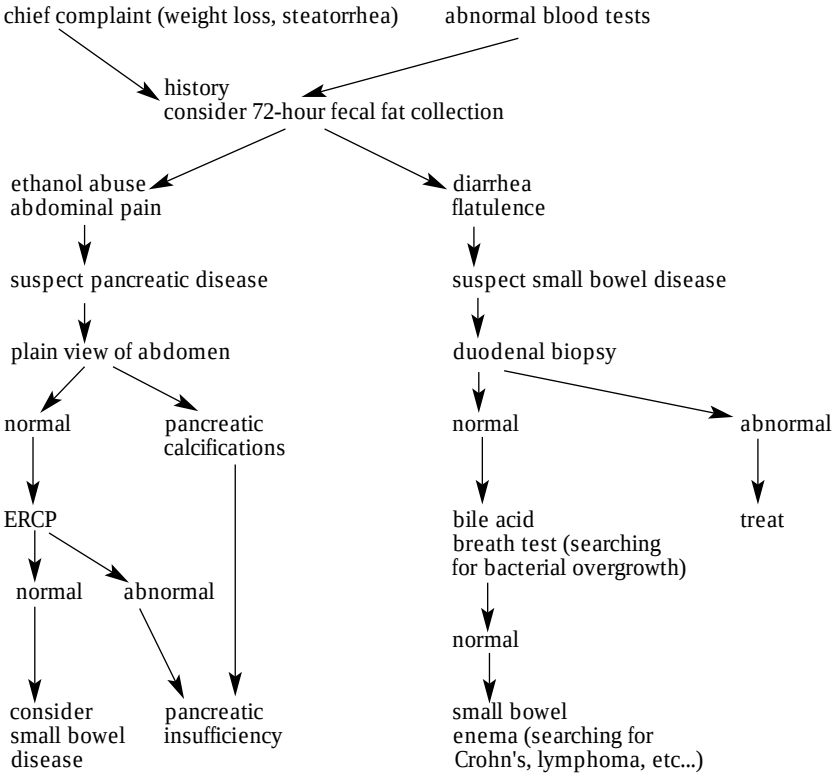


Figure 4. Approach to Malabsorption

Manifestations of Malabsorption

❑ fat soluble vitamin deficiency
- vitamin A
  - night blindness
  - dry skin
  - keratomalacia
- vitamin D
  - metabolic bone disease
- vitamin E
  - hemolytic anemia (in kids)
  - neurological problems
- vitamin K
  - bleeding disorder (II, VII, IX, X)
  - measure for ↓ serum carotene, ↓ vitamin A levels, ↑ INR

❑ other deficiencies
- iron
  - absorbed in duodenum, upper jejunum
  - anemia, glossitis, koilonychia (spoon nails)
  - measure for ↓ hemoglobin, ↓ serum iron, ↓ serum ferritin
- calcium
  - absorbed in duodenum, upper jejunum
  - binds to calcium binding protein in cell (levels increase by vitamin D)

- deficiency leads to hypocalcemia, metabolic bone disease, and may get tetany and paresthesias
- measure for ↓ serum calcium, serum magnesium, and ALP
- evaluate for ↓ bone mineralization radiographically

- folic acid
  - absorbed in jejunum
  - megaloblastic anemia, glossitis
  - decreased red cell folate
  - may see increased folic acid with bacterial overgrowth
- vitamin B12
  - absorption (see Figure 5)
  - terminal ileal disease, pernicious anemia
  - subacute combined degeneration of the spinal cord, peripheral neuropathy, dementia
  - differentiate cause by Schilling test (see Figure 6)
- carbohydrate
  - complex polysaccharides hydrolyzed to oligosaccharides and disaccharides by salivary and pancreatic enzymes
  - disaccharide hydrolysis by brush border enzymes
  - monosaccharides absorbed in duodenum/jejunum
  - patients have generalized malnutrition, weight loss, and flatus
  - measure by D-xylose test
- protein
  - digestion at stomach, brush border, and inside cell
  - absorption occurs primarily in the jejunum
  - patients have general malnutrition and weight loss
  - amenorrhea and decreased libido if severe
  - measure serum albumin
- fat
  - lipase, colipase, and bile salts needed for digestion
  - products of lipolysis form micelles which solubilize fat and aid in absorption
  - fatty acids diffuse into cell cytoplasm
  - generalized malnutrition, weight loss, and diarrhea
  - measure fecal fat excretion

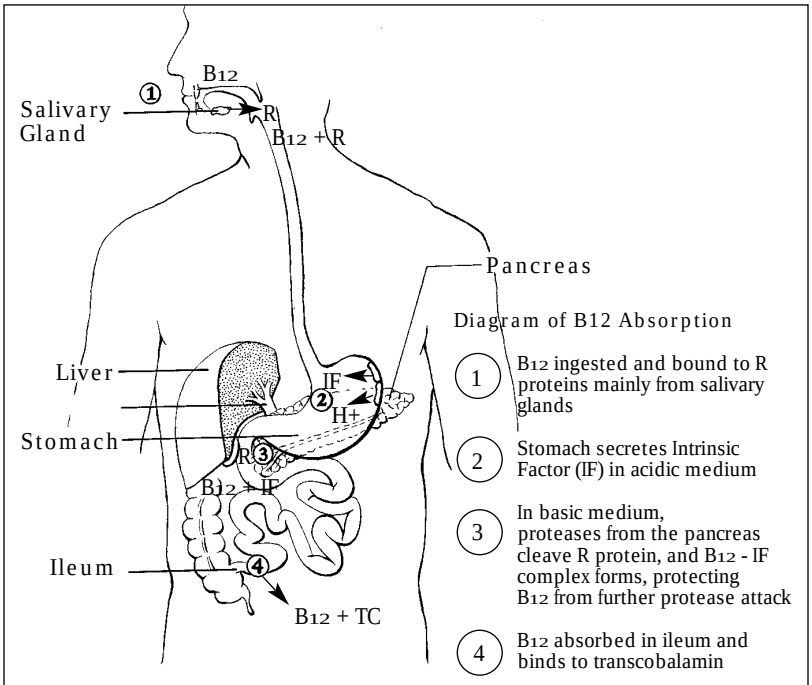


Figure 5. B12 Absorption

Drawing by Carin Cain

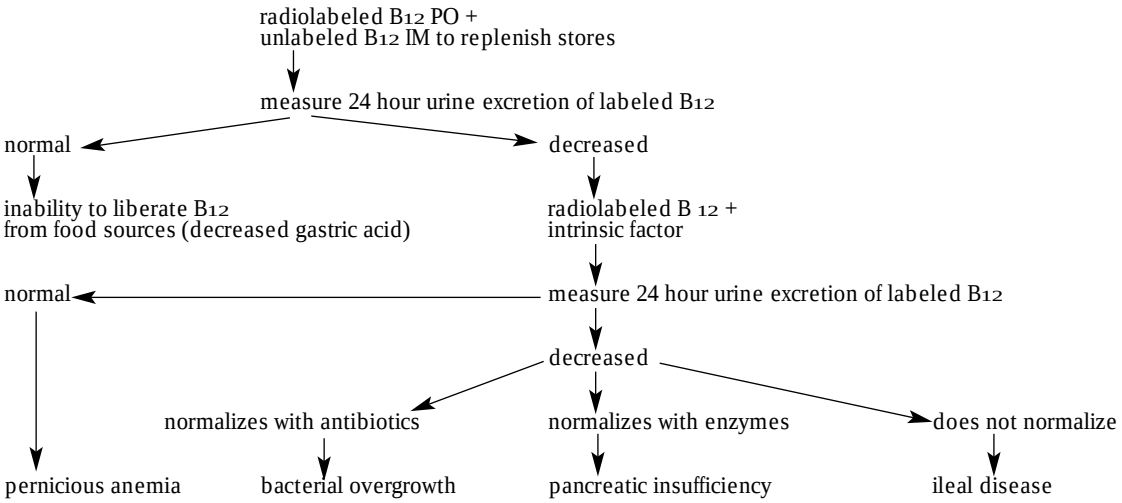


Figure 6. Schilling Test

CELIAC DISEASE

- ❑ also known as gluten enteropathy, sprue
- ❑ abnormal jejunal mucosa which improves with gluten-free diet and deteriorates when gluten reintroduced
- ❑ most severe in proximal bowel, therefore iron, calcium, and folic acid deficiency common
- ❑ more common in women
- ❑ family history – 10% of first degree relatives
- ❑ etiology
  - common with other autoimmune diseases
  - gluten, a protein in cereal grains, is toxic factor
  - HLA B8 (chromosome 6) found in 80-90% of patients compared with 20% in general population; also associated with HLA-Dw3
- ❑ pathology
  - villous atrophy and crypt hyperplasia
  - similar pathology in: small bowel overgrowth, Crohn's, lymphoma, Giardia
  - increased number of plasma cells and lymphocytes in lamina propria
- ❑ presentation
  - may present any time from infancy (when cereals introduced), to elderly, but peak presentation in infancy and old age
  - classically diarrhea, weight loss, anemia
- ❑ investigations
  - small bowel follow through to exclude lymphoma
  - jejunal biopsy confirms clinical suspicion
  - response to gluten withdrawal with full clinical and histological recovery is diagnostic
  - serum endomysial antibody is 95% sensitive and specific
- ❑ treatment
  - gluten restriction in diet: barley, rye, oats, wheat ("BROW")
  - eat rice and corn flour
  - watch for complicating intestinal lymphoma: abdominal pain, weight loss, palpable mass
  - associated with increased incidence of carcinoma of the esophagus and colon

BACTERIAL OVERGROWTH

- ❑ syndrome caused by proliferation of bacteria in small bowel to concentrations > 104 bacteria/mL of bowel tissue

- clinical features
  - steatorrhea: bacteria deconjugate bile salts impairing micellar lipid formation
  - diarrhea: bowel mucosa damaged by bacterial products, impairing absorption
  - megaloblastic anemia due to vitamin B12 malabsorption
  - may be asymptomatic
- underlying etiologies
  - anatomic factors
    - jejunal diverticulae
    - surgical blind loop
    - Crohn's
    - strictures
  - decreased motility
    - scleroderma
    - diabetes
  - achlorhydria
  - described in elderly patients without any known etiologic factors
- diagnosis
  - bacterial cultures of jejunum represents “gold standard"
  - bile acid breath test (misses 1/3 of cases)
  - Schilling test abnormal (see Figure 6)
  - serum B12 decreased
  - increased or normal serum folate (since synthesized by GI bacteria)
  - symptoms relieved by trial of antibiotics
  - small bowel follow through to look for underlying cause
- management
  - treat underlying etiology if possible
  - broad spectrum antibiotics, killing anaerobes and aerobes e.g. amoxicillin+clavulinic acid (Clavulin) or tetracycline+metronidazole

IRRITABLE BOWEL SYNDROME (IBS)

- 30% of North Americans
- onset of symptoms usually in young adulthood
- women > men
- considered a disease, not just a label for all GI symptoms that are unexplained after investigation (this can be termed functional bowel disease; IBS is one form of functional bowel disease)
- diagnosis ("Rome Criteria”) – emphasize positive features rather than negative features

Table 7. Diagnosis of IBS

at least three months of continuous or recurrent symptoms of
- abdominal pain or discomfort which is relieved by defecation and/or associated with a change in stool frequency
- and/or associated with a change in stool consistency

plus two or more of the following, at least 25% of the time
- altered stool frequency
- altered stool form (lumpy/hard or loose/watery)
- altered stool passage (straining, urgency, or feeling of incomplete evacuation)
- passage of mucus
- bloating or feeling of abdominal distention

- negative features (absence of)
  - weight loss
  - nocturnal defecation
  - blood or pus in stool
  - fever
  - anemia
  - abnormal gross findings on flexible sigmoidoscopy
- pathogenesis
  - normal perception of abnormal gut motility
  - abnormal perception of normal gut motility
  - psychological: "socially acceptable vehicle for accepting care"

- behavioural: symptoms of IBS common in general population; the small percentage of these who see physicians differ from non-patients only in their physician seeking behavior, therefore they want reassurance, expect more from doctors

❑ diagnosis
- history
  - ask about “Rome Criteria”
  - exclude negative features
  - review dietary history, medications, patient’s mood
- physical exam
  - should be unremarkable
- labs (use discretion)
  - CBC, TSH, ESR
  - stool for C&S, O&P, fat excretion
  - sigmoidoscopy

❑ management
- no therapeutic agent effective
- over 50% improve with time
- reassurance, bran or psyllium for constipation, loperamide for diarrhea
- consider use of antidepressants

INFLAMMATORY BOWEL DISEASE

❑ Crohn's disease and Ulcerative Colitis

❑ pathogenesis
- less understood than most other diseases
- perhaps chronic infection by undetectable organism
- perhaps inappropriate immune attack on normal mucosal bowel flora
- transgenic mice in which selected genes (T-cell receptor, interleukin 2, interleukin 10) have been disabled (“knockout mice") develop mucosal inflammation even when kept in sterile conditions

Table 8. Inflammatory Bowel Disease

	Crohn’s Disease	Ulcerative Colitis
inflammation	• transmural, skip	• mucosal, continuous
location	• any part of GI tract	• rectum always involved • isolated to large bowel
after surgery	• recurs	• cured

Table 9. Complications of IBD

Extra-Intestinal Manifestations
Urinary calculi - especially oxalate
Liver - percholangitis, cirrhosis, sclerosing cholangitis, fatty liver
Cholelithiasis - decreased bile acid resorption
Epithelium - erythema nodosum, erythema multiforme, pyoderma gangrenosum
Retardation of growth and sexual maturation - especially in kids
Arthralgias - arthritis, ankylosing spondylitis ~independent of IBD activity
Thrombophlebitis - migratory
Iatrogenic - steroids, blood transfusions, surgery
Vitamin deficiencies
Eyes - uveitis, chorioretinitis, iridocyclitis

Intestinal Manifestations
Cancer - increased risk with severe first attack, pancolitis, chronic symptoms and early onset
Obstruction - rare with UC, common in Crohn’s especially after multiple surgeries
Leakage (perforation) - 3%, can form abscess especially in Crohn’s (20%)
Iron deficiency- hemorrhage
Toxic Megacolon - 3% - more in UC
Inanition - severe wasting due to malabsorption and decreased PO intake
Stricture, fistulas (40% of Crohn’s), perianal abscesses

ULCERATIVE COLITIS

Pathology
- ❑ always involves rectum
- ❑ inflammation diffuse and confined to mucosa
- ❑ disease can involve any portion of lower bowel from rectum only (proctitis) to entire colon (pancolitis)
- ❑ proctitis most common

Epidemiology
- ❑ 2/3 onset by age 30 (with second peak after 50)
- ❑ small hereditary contribution (15% of cases have 1st degree relatives with disease)

Clinical Features
- ❑ generally, the more extensive the disease, the more severe the symptoms
- ❑ diarrhea, rectal bleeding most frequent, but can also have abdominal pain
- ❑ tenesmus
- ❑ systemic symptoms: fever, anorexia, weight loss, fatigue
- ❑ extra-intestinal manifestations as above
- ❑ characteristic exacerbations and remissions; 5% of cases are fulminant

Complications
- ❑ like Crohn's except for following
- ❑ more liver problems (especially primary sclerosing cholangitis in men)
- ❑ increased risk of colorectal cancer
    - risk increases with duration and extent of disease (5% at 10 years, 15% at 20 years for pancolitis; overall relative risk is 8%)
    - therefore, yearly screening colonoscopy and biopsy in pancolitis of 10 years or more
- ❑ toxic megacolon (transverse colon diameter > 6 cm on abdominal x-ray) with immediate danger of perforation

Investigations (see Colour Atlas C5)
- ❑ sigmoidoscopy without bowel prep, to diagnose
- ❑ colonoscopy (contraindicated in severe exacerbation), barium enema (not during acute phase or relapse), both of which determine length of bowel involved
- ❑ stool cultures to exclude infection
- ❑ mucosal biopsy (to exclude acute self-limited colitis)

Management
- ❑ 5-ASA drugs
    - topical (enema, suppository) or oral (in a capsule to delay absorption)
    - block arachidonic acid metabolism to prostaglandins and leukotrienes
    - topical: very effective (equal to or better than steroid suppositories and enemas) but useful only if inflammation extends proximally no further than splenic flexure
    - e.g. sulfasalazine (Salazopyrin)
        - a compound composed of 5-ASA bound to sulfapyridine
        - hydrolysis by intestinal bacteria releases 5-ASA, the active component
        - some use in acute, non-severe disease (2x as effective as placebo)
        - more use in maintaining remission (decreases yearly relapse rate from 60% to 15%)
- ❑ steroids
    - best drugs to remit acute disease, especially if mild or first attack (i.e. prednisone 40 mg daily)

- use suppositories for proctitis, enemas for proctosigmoiditis
- less toxic topical steroids (i.e. tixocortol enemas) have been shown to be equally effective when used as enemas/suppositories
- complications
    - common early in therapy = insomnia, emotional lability, weight gain/enhanced appetite
    - common if underlying risk factors = hypertension, diabetes, peptic ulcer, acne
    - anticipate if prolonged use = Cushing's habitus, impaired wound healing, adrenal suppression, infection diathesis, osteonecrosis, myopathy
    - insidious = osteoporosis (recent evidence suggests this starts early, may be prevented with calcium, vitamin D or etidronate), skin atrophy, cataracts, atherosclerosis, growth retardation, fatty liver
    - unpredictable and rare = glaucoma, pseudotumour cerebri
- if severe UC is refractory to steroid therapy, add IV cyclosporine - rapidly effective

❑ immunosuppressants
- azathioprine use not well documented
- may be added to steroids when steroids fail

❑ surgical treatment
- early in fulminant cases and toxic megacolon
- aim for cure with colectomy
- indications: failure of adequate medical therapy, toxic megacolon, bleeding, pre-cancerous changes picked up with screening endoscopic biopsies (dysplasia)
- see General Surgery Notes

❑ prognosis: 10 year survival has gone from under 80% in 1950's to over 97% in the 1980's

CROHN'S DISEASE

Pathology

❑ transmural inflammation with "skip" lesions is hallmark
❑ associated with granulomas and deep fissuring/aphthous ulcerations, strictures
❑ linear ulcers leading to mucosal islands and "cobble-stoning"
❑ deep fissures with risk of perforation usually into contiguous viscera leading to fistulae and abscesses
❑ enteric fistulae may communicate with skin, bladder, vagina, and other parts of bowel
❑ granulomas are found in 50% of surgical specimens, 15% of mucosal biopsies

Epidemiology

❑ bimodal: onset before 30 years, second peak age 60
❑ incidence of Crohn's increasing (relative to UC) especially in young females
❑ more common in caucasians, Ashkenazi Jews

Clinical Features

❑ may affect any part of GI tract from mouth to anus
- 35% small bowel only (ileitis)
- 45% both small and large bowel (ileocolitis)
- 20% large bowel only (colitis)

❑ most often presents as recurrent episodes of mild diarrhea, (more common with involvement of colon) abdominal pain and fever with spontaneous improvement
❑ remissions and exacerbations
❑ extra-intestinal manifestations as above
❑ features of colitis
- diarrhea, pain
- rectal bleeding less common than UC

- fistulas, fissures, peri-rectal abscesses
- extra-intestinal manifestations more common with colonic involvement

❑ features of ileocolitis
- fistulas, abscesses, may present with sepsis

❑ features of ileitis
- young person with history of fatigue, post-prandial pain and vomiting
- mass in right lower quadrant due to adherent bowel
- acute ileitis may present similarly to acute appendicitis

Complications

❑ intestinal obstruction due to edema, fibrosis
❑ fistula formation
❑ intestinal perforation (uncommon in Crohn's)
❑ malignancy – increased risk, but risk not as high as ulcerative colitis

Diagnosis (see Colour Atlas C4)

❑ endoscopy with biopsy
❑ barium studies
❑ bacterial cultures, O & P, C. *difficile* toxin to exclude other causes of inflammatory diarrhea

Management

❑ most uncomplicated cases can be managed medically
- 5-ASA drugs (sulfasalazine), treatment for active disease

❑ steroids
- prednisone 20-40 mg OD for acute exacerbations (but use only if symptoms are severe)
- no proven role for steroids in maintaining remissions
- masks intra-abdominal sepsis

❑ immunosuppressives (6-mercaptopurine, azathioprine)
- used chiefly as steroid-sparing agents
- requires > 3 months to have beneficial effect
- probably help to heal fistulae, decreases disease activity
- have important side effects (pancreatitis, bone marrow suppression, increased risk of cancer)

❑ metronidazole (Flagyl)
- decreases disease activity and improves perianal disease
- side effects common (50% have peripheral neuropathy after 6 months of treatment, usually reversible)
- use of ciprofloxacin+metronidazole effective in colonic disease in uncontrolled studies

❑ diet
- elemental diets help remit acute Crohn's disease but are not palatable
- TPN and bowel rest only of transient benefit
- those with extensive small bowel involvement need electrolyte, mineral and vitamin supplements

❑ antidiarrheal agents
- loperamide (Imodium) > diphenoxylate (Lomotil) > codeine (cheap but addictive)
- all work by decreasing small bowel motility
- use with caution

❑ cholestyramine
- a bile salt binding resin
- for cholerrhea with less than 100 cm of terminal ileum diseased or resected (see below)

❑ surgical treatment
- surgery generally reserved for complications such as fistulae, obstruction, abscess, perforation, bleeding, and rarely for medically refractory disease
- at least 50% recurrence within 5 years
- 40% likelihood of second bowel resection

- 30% likelihood of third bowel resection
- complications of ileal resection
    - < 100 cm resected —> watery diarrhea (impaired bile salt absorption) —> treatment: cholestyramine
    - > 100 cm resected —> steatorrhea (bile salt deficiency) —> treatment: fat restriction, MCT

CONSTIPATION

❑ passage of infrequent, or hard stools with straining (stool water < 50 mL/day)

Etiology

❑ in the absence of other clinical problems, most commonly due to lack of fibre in diet, change of diet, or poorly understood gut motility changes

❑ organic causes
- medication side effect (antidepressants, codeine) most common
- left sided colon cancer (consider in older patients)
- metabolic
    - diabetes
    - hypothyroidism
    - hypercalcemia
- neurological
    - intestinal pseudo-obstruction
    - Parkinson's disease
    - multiple sclerosis
- collagen vascular disease
    - scleroderma
    - amyloid

Investigation

❑ swallow radio-opaque markers to quantitate colonic transit time (normal: 70 hours)
- normal = misperception of normal defecation
- prolonged ="colonic inertia"
- prolonged plus abnormal anal manometry = outlet obstruction

Treatment

❑ bulk (bran, psyllium seed)
❑ emollients (docusate salts, mineral oil)
❑ hyperosmolar agents (lactulose)
❑ saline cathartics (magnesium citrate)
❑ stimulant cathartics (cisapride, castor oil)
❑ anthraquinones (senna, cascara) and diphenylmathanes (phenolphthalein, bisacodyl) effective but damage myenteric plexus if used chronically

UPPER GI BLEEDING

- ❑ bleeding proximal to the ligament of Treitz
- ❑ presentation
  - in order of severity of the bleed: hematochezia > hematemesis > melena > occult blood in stool
  - most often stops spontaneously
  - differential diagnosis
    - Esophagus
      - esophageal varices (20%)
      - esophagitis
      - esophageal cancer
      - Mallory-Weiss tear (10%)
    - Stomach
      - gastric ulcer (20%)
      - gastritis (e.g. from alcohol, or post surgery) (20%)
      - gastric cancer
    - Duodenum
      - duodenal ulcer (most common - 25%)
      - aortoenteric fistula - usually only if previous aortic graft
    - Coagulopathy (drugs, renal disease, liver disease)
- ❑ mortality
  - approximately 10% in most series, 80% stop spontaneously
  - peptic ulcer bleeding - low mortality (2%) unless rebleeding occurs (25% of patients, 10% mortality)
  - endoscopic predictors of rebleeding - spurt or ooze, visible vessel, fibrin clot
  - H2 antagonists have little impact on rebleeding rates and need for surgery
  - esophageal varices have a high rebleeding rate (55%) and mortality (29%)
- ❑ initial management
  - stabilize patient (IV fluids, cross and type, 2 large bore IV, monitors)
  - send blood for CBC, platelets, PT, PTT, lytes, BUN, Cr, LFTs
  - keep NPO
  - NG tube to determine upper versus lower GI bleeding (except in variceal bleeding)
  - endoscopy (OGD) - establish bleeding site + coagulate lesion

BLEEDING PEPTIC ULCER

- ❑ presentation: see Peptic Ulcer Disease
- ❑ approach to treatment: see Figure 7

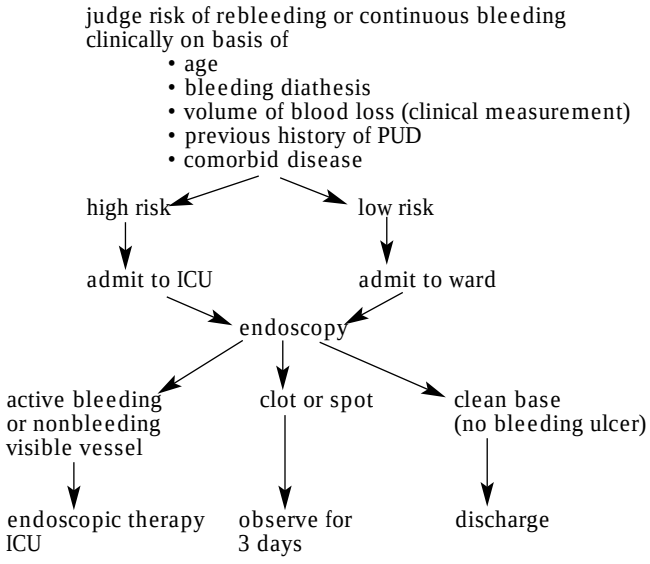


Figure 7. Approach to Management of Suspected Bleeding Peptic Ulcer

Notes

ESOPHAGEAL VARICES (see Colour Atlas C8)

- ❑ presentation: upper GI bleeding, characteristically massive
- ❑ almost always due to portal hypertension
- ❑ diagnosis best made by endoscopy
- ❑ often accompanied by varices in stomach

Clinical Pearl
- ❑ If varices only in stomach, think of splenic vein thrombosis

- ❑ if not bleeding, treat with beta-blocker
- ❑ management of bleeding varices
  - resuscitate
  - options to control acute bleeding
    - endoscopy - rubber band ligation; variceal injection less beneficial
    - intravenous octreotide (or somatostatin)
    - balloon tamponade
  - prevention of recurrent bleeding
    - endoscopy - variceal injection; rubber band ligation
    - beta-blocker and/or nitrates
    - surgery - esophageal transection (Sigura); portal-systemic shunt
    - transjugular intrahepatic portal-systemic shunt (TIPSS): radiological insertion of stent connecting portal and systemic circulations —> lowers portal pressure (high incidence of shunt occlusion and hepatic encephalopathy)

MALLORY WEISS TEAR

- ❑ 10% of massive upper GI bleeds
- ❑ tear in gastric mucosa on lesser curvature near gastroesophageal junction (20% straddle junction, 5% in distal esophagus)
- ❑ due to rapid increases in gastric pressure (i.e. retching)
- ❑ most patients alcoholics
- ❑ clinical presentation: retching followed by hematemesis +/– melena
- ❑ treatment
  - 90% stop spontaneously; NG (if needed) and replace lost volume
  - if persistent: require endoscopy with electrocautery or surgical repair

LOWER GI BLEEDING

- ❑ bleed distal to ligament of Treitz
- ❑ presentation
  - hematochezia
  - anemia
  - occult blood in stool
  - rarely melena
- ❑ differential diagnosis
  - massive: diverticulosis, angiodysplasia, occasional UGI site (DU), aortoenteric fistula
  - intermittent: hemorrhoid, colitis, anorectal lesions
  - occult: neoplasms, colon CA
- ❑ systemic diseases (always consider in cases of UGI or LGI bleeding)
  - blood dyscrasias (e.g. thrombocytopenia)
  - coagulation disorders (e.g. DIC)
  - vascular malformations (e.g. Osler-Weber-Rendu syndrome)
  - vasculitides (e.g. HSP, PAN)

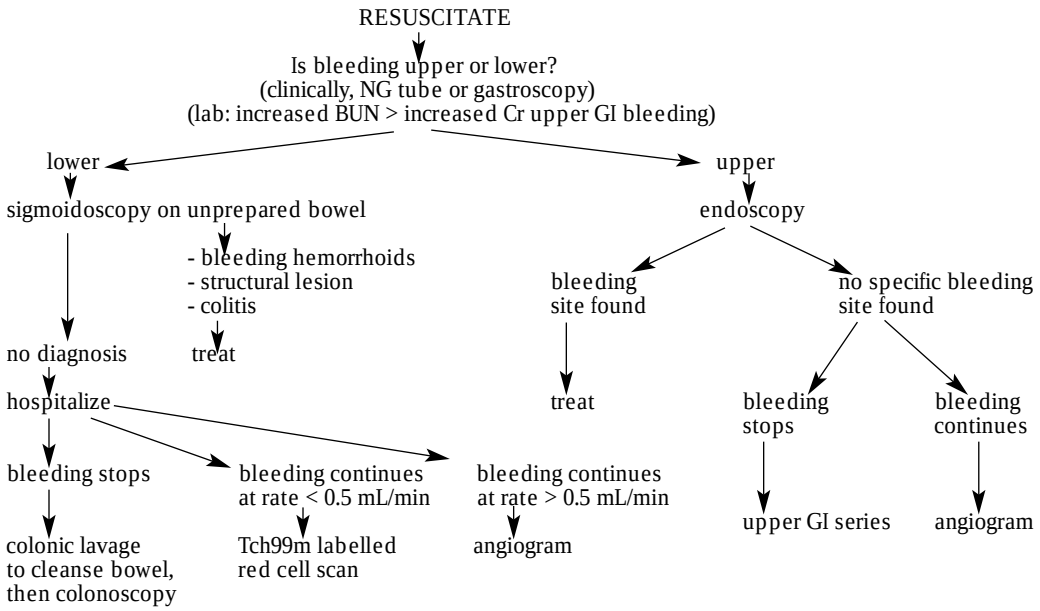


Figure 8. Approach to Hematochezia

COLON CANCER (see Colour Atlas C6, C10)

Pathophysiology

- ❑ environmental influences (presumed)
  - high dietary fat consumption
  - low dietary fiber consumption
- ❑ genetic influences
  - all colorectal cancers considered to have genetic component, inherited/acquired, to varying degrees
  - familial syndromes (see Risk Factors) inherit genetic alterations that make them these individuals susceptible to environmental factors in development of colon cancer
  - multiple "step-wise" somatic mutations, contributed by environment, have been implicated
  - genetic changes implicated are
    - activation of proto-oncogenes (K-ras)
    - loss of tumour-supressor gene activity (APC, DCC, p53)
    - abdnormalities in DNA repair genes (hMSH2, hMLH1) - especially HNPCC syndromes (see below)
- ❑ morphologic progression
  - normal colon —> hyperproliferative epithelium —> adenoma —> carcinoma

Risk Factors

- ❑ age
  - 90% of cancers in people > 50 years old
  - person 50 years old has 5% chance of developing colorectal cancer by 80 years old
- ❑ Adenomatous Polyps
  - large, villous, and moderate to severe dysplasia more likely to be cancer
  - number of adenomas present synchronously (at the same time) or metachronously (at different times) in the colon is proportional to cancer risk
- ❑ family history
  - sporadic cancer
    - risk 1.8 times higher for those with one affected relative, 2-6 times higher with two affected relatives
    - risk is greater if relative has cancer diagnosed < 45 years old

- familial adenomatous polyposis and Gardner's syndrome
  - autosomal dominant, inactivated APC gene on 5q
  - over 100 of adenomatous polyps develop in colon and rectum, starting at age 15-20 years old
  - if colon is not removed, risk of cancer is 100%
  - Gardner's syndrome is a variant, with polyposis plus extracolonic manifestations (osteomas, soft tissue tumours, congenital hypertrophy of retinal pigmented epithelium)
- hereditary nonpolyposis colorectal cancer (Lynch syndrome, or HNPCC)
  - autosomal dominant (hMSH2, hMLH1)
  - discrete adenomas (polyposis does not occur)
  - occurs earlier, age 40 -50 years, often proximal in location and multiple, more commonly mucinous or poorly differentiated becaues no preceeding polyp stage; cancer are often diagnosed late in disease
  - criteria
    - ≥ 3 relatives with colorectal cancer, where 1 is 1st degree relative of other 2
    - ≥ 2 generations of colorectal cancer
    - ≥ 1 colorectal cancer before age 50 years

❑ Inflammatory Bowel Disease
- ulcerative colitis
  - after 10 years with the disease, cancer risk rises by 1% for each additional year
- Crohn's disease
  - exact risk of cancer remains unclear

Management (see General Surgery Notes)

LIVER DISEASE

Lab Tests of Liver Function

❑ prothrombin time (PT)
- daily marker of hepatic protein synthesis
- must exclude co-existent vitamin K deficiency

❑ serum albumin level
- detects prolonged (weeks) hepatic dysfunction
- must exclude malnutrition and renal or GI losses

Lab Test of Hepatobiliary Disease

❑ elevated AST, ALT > 1000 = hepatocellular damage
- sensitive but not specific for liver damage
- implies hepatitis (inflammation) or vascular injury (ischemia)

Clinical Pearl
❑ AST > ALT = alcoholic liver disease
❑ ALT > AST = viral hepatitis

❑ elevated ALP = cholestatic disease
- intrinsic disease (toxic, infectious, inflammatory)
- systemic disease (sepsis, pregnancy)
- infiltrative disease (tumour, fat, lymphoma)
- mass lesions (stone, tumour, abscess)

ACUTE VIRAL HEPATITIS

Clinical Features

❑ most are subclinical
❑ prodrome (flu-like illness) may precede jaundice by 1-2 weeks
- nausea, vomiting, anorexia, taste/smell disturbance (aversion to cigarettes)
- headaches, fatigue, malaise, myalgias
- low grade fever may be present
- arthralgia and uticaria (especially hepatitis B)

❑ clinical jaundice (icteric) phase (50% of cases) lasting days to weeks
- pale stools and dark urine 1-5 days prior to icteric phase
- hepatomegaly plus RUQ pain
- splenomegaly and cervical lymphadenopathy (10-20% of cases)

- ❑ recovery
  - continued hepatomegaly and abnormal liver enzymes
- ❑ hepatic enzymes
  - hepatocellular necrosis which causes increased AST, ALT >10-20X normal
  - ALP and bilirubin minimally elevated
  - WBC normal or slightly depressed initially, followed by relative lymphocytosis with atypical lymphocytes (similar to mono)
- ❑ prognosis: resolves or progresses to chronic and/or fulminant disease
  - poor prognosticators
    - age
    - comorbidity
    - persistently high bilirubin (> 340 mmol/L), elevated INR, low albumin, hypoglycemia
- ❑ management
  - supportive (hydration, diet)
  - indications for hospitalization: encephalopathy, coagulopathy, severe vomiting, hypoglycemia

Complications

- ❑ fulminant hepatitis (<1% of acute viral hepatitis cases)
  - occurs in Hep B, B+D, E in pregnancy, A in adults (rare)
  - mortality rate varies with age and approaches 90-100% in patients >60 years of age
- ❑ chronic hepatitis: Hep B, B+D, or C (see below)
- ❑ cholestasis (most commonly during HAV infection)
  - prolonged but self-limited

Hepatitis A Virus (HAV)

- ❑ spread by fecal-oral route
- ❑ incubation period 2-6 weeks
- ❑ infectivity: late incubation to early clinical
- ❑ clinical acute hepatitis develops in most infected adults, but in only 10% of children
- ❑ serology: anti-HAV
  - IgM: current infection or convalescence
  - IgG: current or previous infection; confers immunity
- ❑ management
  - general hygiene
  - treat close contacts with anti-HAV immune globulin 0.02 mg/kg as soon after exposure as possible
  - prophylaxis for high risk groups (e.g. travelers) with immune globulin or HAV vaccine

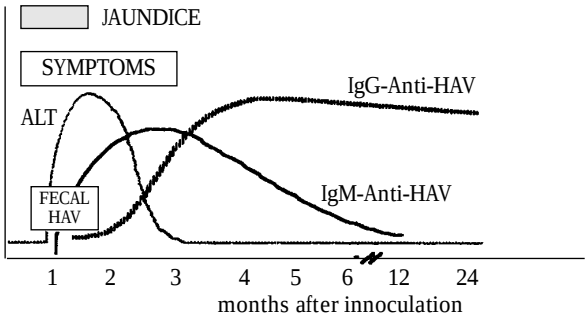


Figure 9. Time Course of Hepatitis A Infection

Hepatitis B Virus (HBV)

- ❑ transmission via parenteral route or equivalent
- ❑ incubation period 6 weeks-6 months
- ❑ infectivity: during HBsAg positivity
- ❑ high risk groups
  - neonates of carriers (“vertical transmission”)
  - partners of infected acutely and chronically infected individuals, with male homosexuals at particular risk
  - IV drug users
  - hospital employees
  - patients from endemic country

- ❑ serology (see Table 10)
  - HBsAg: surface antigen
  - HBeAg: e antigen (a component of HBV core); marker of viral replication
  - HBcAg: core antigen (cannot be measured in serum)
  - both HBsAg and HBeAg are present during acute hepatitis B
  - anti-HBc and anti-Hbe appear during the acute phase of the illness but do not provide immunity
  - anti-HBs follows HBsAg clearance and confers long-term immunity
- ❑ vertical transmission
  - occurs during 3rd trimester or early post-partum
  - HBsAg +ve, HBeAg +ve mothers —> 90% of infants infected
  - HBsAg +ve, anti-HBe +ve mothers —> 10-15% infected
  - give HBIG and full HBV vaccination to newborns of HBsAg +ve mothers (90% effective)
- ❑ prevention
  - HBV vaccine = recombinant HBsAg
    - given to high risk persons and Grade 7 students (in Ontario)
    - seroconversion rates about 94% after 3 injections
  - hepatitis B immune globulin (HBIG) = anti-HBs
    - for needle stick, sexual contact, and neonates born to mothers with acute or chronic infection
- ❑ complications
  - serum sickness-like prodrome
    - immune complex disease: urticaria, angioedema, fever, arthritis, hematuria and proteinuria which all precede onset of jaundice
  - glomerulonephritis

Table 10. Hepatitis B Serology

	HBsAg	Anti-HBs	HBeAg	Anti-HBe	Anti-HBc
Acute HBV	+	–	+	–	IgM
Chronic HBV (high infectivity)	+	–	+	–	IgG
Chronic HBV (low infectivity)	+	–	–	+	IgG
Recovery	–	+	–	+	IgG
Immunization	–	+	–	–	–

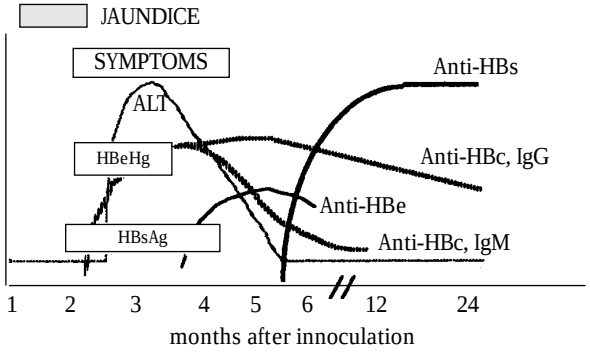


Figure 10. Time Course of Acute Hepatitis B Infection

Hepatitis C Virus (HCV)

- ❑ transmission is chiefly parenteral
  - transfusions (HCV is the most common cause of post-transfusion hepatitis)
  - IV drugs use
  - sexual transmission occurs but risk is less than with HVB
  - 40% of cases have no risk factors

- ❑ clinical incubation period 5-10 weeks
- ❑ AST and ALT levels fluctuate (unlike Hep A or B)
- ❑ more than half progress to chronic liver disease (see below)
- ❑ serology
  - HCV RNA (detected by PCR assay)
  - anti-HCV
  - develops in 6-8 weeks in 85% of patients
  - persists in chronic infection and does not confer immunity
- ❑ prevention: no accepted vaccine for HCV

Hepatitis D Virus (HDV)
- ❑ infectious only in the presence of HBV because HBV proteins are required for replication
- ❑ 2 patterns of transmission
  - nonparenteral transmission by close personal contact in endemic areas (Mediterranean)
  - transmission by blood products in non-endemic areas (IV drugs, blood transfusions)
- ❑ types of infection
  - coinfection: simultaneous HBV and HDV infection
  - superinfection: appears as clinical exacerbation in a chronic HBV patient
- ❑ predisposes to severe or fulminant course
- ❑ serology: HBsAg, anti-HDV IgM or anti-HDV IgG
- ❑ prevention: HBV vaccine

Hepatitis E Virus (HEV)
- ❑ fecal-oral transmission occurring in epidemics in Asia, Africa, Central America
- ❑ most have mild disease, but in 3rd trimester of pregnancy 10-20% have fulminant liver failure
- ❑ serology: anti-HEV
- ❑ prevention: no vaccine available

CHRONIC HEPATITIS
- ❑ defined as an elevation of serum transaminases for > 6 months
- ❑ requires a liver biopsy to determine severity/need of treatment

Etiology
- ❑ viral (B, B+D, C, not A or E)
- ❑ drugs (methyldopa, INH, nitrofurantoin, amiodarone)
- ❑ idiopathic
- ❑ genetic (Wilson's disease, α-1-antitrypsin deficiency)

Presentation
- ❑ most have constitutional symptoms such as fatigue, malaise, anorexia, weight loss
- ❑ signs of chronic liver disease
- ❑ hepatomegaly (firm) and splenomegaly
- ❑ increased AST, ALT

Chronic Hepatitis C
- ❑ accounts for 30-40% of chronic hepatitis in USA
- ❑ >50% of acute HCV infections go on to become chronic; of those 20-30% go on to cirrhosis; and of those 2-5% per year develop HCC
- ❑ slow progression from time of acute infection
  - clinical chronic hepatitis -10 years
  - cirrhosis -20 years
  - HCC - 30 years
- ❑ serology: anti-HCV, non-specific +ve autoantibodies
- ❑ interferon therapy
  - 50% respond but 70% relapse
  - must exclude autoimmune hepatitis because interferon detrimental
- ❑ liver transplant for end stage disease

Chronic Hepatitis B

- ❑ develops in 1-2% of immunocompetent adults with acute HBV hepatitis and 90% of those infected at birth
- ❑ accounts for approximately 10% of chronic hepatitis in North America
- ❑ risk groups
  - immunosuppression
  - chronic hemodialysis patients
- ❑ range of severity
  - asymptomatic carrier
  - chronic persistent hepatitis
    - histology shows inflammation confined to portal areas
    - mild symptoms such as fever, anorexia, and abdominal pain
  - chronic active hepatitis
    - histology shows inflammation extending beyond portal area in association with necrosis and fibrosis
    - more sever disease which may progress to cirrhosis
- ❑ 2 phases of viral replication
  - replicative phase (HbeAg +ve)
    - high infectivity; increased liver injury
    - associated with more severe hepatitis (e.g. chronic active hepatitis)
  - non-replicative phase (anti-Hbe +ve)
    - low infectivity and minimal liver injury
    - associated with milder disease (e.g. chronic persistent hepatitis)
  - distinctions in replicative phase and histological classification do not always coincide
- ❑ treatment of chronic replicative hepatitis with alpha-interferon
  - 4-month (16-week) course of 5 million units sc od or 10 million units sc 3x per week
  - increases annual rate of cessation of viral replication from 7% to 40%; loss of HBsAg less common
  - relapse after successful therapy is rare (1 to 2%)
- ❑ no treatment is indicated or available for asymptomatic, nonreplicative hepatitis B carriers
- ❑ end-stage treatment is transplant, although acute hepatitis may recur in the transplanted liver

Chronic Hepatitis B + D

- ❑ HDV increases severity of hepatitis but does not increase risk of progression to chronic hepatitis
- ❑ low-dose interferon has limited impact, high-dose under investigation
- ❑ liver transplant more effective than in HBV alone

Idiopathic Chronic Active Hepatitis

- ❑ can be severe - 6 month mortality of 40%
- ❑ diagnosis of exclusion: rule out viruses, drugs, metabolic or genetic derangements
- ❑ extrahepatic manifestations
  - amenorrhea, rashes, acne, thyroiditis, Sjögren's
  - immune complex disease: arthritis, GN, vasculitis
- ❑ antibodies
  - hypergammaglobulinemia
  - ANA (homogenous), RF, Anti-smooth muscle, Anti-LKM (liver kidney microsome)
  - can have false positive viral serology (especially anti-HCV)
- ❑ management: steroids (80% respond) ± azathioprine

DRUG-INDUCED LIVER DISEASE

Table11. Classification of Hepatotoxins

	Direct	Indirect
example	CCl_4 acetaminophen	isoniazid phenytoin
dose-dependence	usual	unusual
latent period	hours-days	weeks-months
host factors	not important	very important
predictable	yes	no

Specific Drugs

- ❑ acetaminophen
  - can cause fulminant hepatic failure (transaminases > 1000 U/L)
    - requires 10-15g in normals, 4-6g in alcoholics
  - mechanism: high acetaminophen dose saturates glucuronidation and sulfation elimination pathways, therefore a reactive metabolite is formed which covalently binds to hepatocyte membrane
  - nausea and vomiting within 4-12 hours followed by clinical evidence of hepatic dysfunction and lab evidence of hepatocellular necrosis in 12-24 hours
  - blood levels of acetaminophen correlate with the severity of hepatic injury
  - therapy
    - gastric lavage and oral charcoal
    - N-acetylcysteine within 16 hours of ingestion
- ❑ chlorpromazine
  - cholestasis in 1% after 4 weeks; often with fever, rash and eosinophilia
- ❑ isoniazid
  - 20% develop elevated transaminases but < 1% develop clinically significant disease
  - susceptibility to injury increases with age
- ❑ methotrexate
  - may rarely cause cirrhosis, especially in the presence of obesity, diabetes, alcoholism
  - scarring develops without symptoms or changes in liver enzymes, therefore biopsy may be needed
- ❑ amiodarone
  - can cause same histology and clinical outcome as alcoholic hepatitis

WILSON'S DISEASE

- ❑ autosomal recessive defect in copper metabolism
- ❑ slow accumulation of copper with deposition in tissues
- ❑ clinical manifestations
  - liver: cirrhosis, chronic active hepatitis, acute hepatitis, fulminant liver failure, no increased HCC
  - eyes: Kayser-Fleischer rings (copper in Descemet's membranes) - in all patients with CNS involvement
  - CNS: basal ganglia (wing flapping tremor, Parkinsonism), cerebellum (dysarthria, dysphagia, incoordination, ataxia), cerebrum (psychosis, affective disorder)
  - kidneys: Fanconi's syndrome (proximal tubule transport defects) and stones
  - blood: intravascular hemolysis - may be initial presentation
  - joints: arthritis, bone demineralization, calcifications
- ❑ diagnosis
  - suspect if elevated LFT's with clinical manifestations
  - requires 2 of 3
    - reduced total serum copper (ceruloplasmin)
    - high liver copper on biopsy
    - Kayser-Fleischer rings
- ❑ other tests
  - radiocopper incorporation study - diagnostic
  - urine copper elevated - non-specific
- ❑ treatment
  - chelators (penicillamine, trientine), zinc acetate
  - screen relatives
  - liver transplant in severe cases

HEMOCHROMATOSIS

- ❑ excessive iron storage which causes multi-organ system dysfunction
- ❑ total body stores of iron increased to 20-40g (normal 1g)
- ❑ Primary
  - common recessive gene (5%), 1:400 adults are homozygotes
  - increased gut absorption of iron

- ❑ Secondary
  - parenteral iron overload – transfusions
  - chronic hemolytic anemia - thalassemia, pyruvate kinase deficiency
  - excessive iron intake
- ❑ iron deposition manifestations
  - liver: cirrhosis —> 30% get HCC (200x risk); most common cause of death (1/3 of patients) even if excess iron removed
  - pancreas: diabetes (chronic pancreatitis)
  - skin: bronze or grey colour (melanin, not iron)
  - heart: dilated cardiomyopathy
  - pituitary: hypogonadotropic hypogonadism (impotence, decreased libido, amenorrhea)
  - joints: arthralgias (especially hands), chondrocalcinosis
- ❑ screen if patient has any clinical features or family history
  - % transferrin saturation (free Fe/TIBC) > 50%
  - serum ferritin > 1000
- ❑ diagnosis (after positive screen)
  - liver biopsy (increased iron deposits)
  - MRI - to measure iron deposition
- ❑ treatment
  - phlebotomy (once or twice weekly until anemia develops or serum iron and ferritin normalizes, then lifelong maintenance phlebotomies every 2-6 months)
  - desferrioxamine if phlebotomy contraindicated (e.g. cardiomyopathy, anemia)
  - normal life expectancy if treated before cirrhosis or diabetes

ALCOHOLIC LIVER DISEASE

Types of lesions

- ❑ fatty liver (all alcoholics) - reversible
- ❑ alcoholic hepatitis (35% of alcoholics) - reversible
- ❑ cirrhosis (10-15% of alcoholics)

Pathophysiology

- ❑ several mechanisms that are incompletely understood
- ❑ fatty liver related to increased NADPH —> fatty acid and triglyceride formation
  - EtOH impairs release of triglycerides causing accumulation in the liver
- ❑ acetaldehyde probably a direct toxin
  - combines with hapten —> immunological damage
- ❑ alcohol metabolism causes
  - relative hypoxia in liver zone III > zone I
  - necrosis and hepatic vein sclerosis
- ❑ alcohol causes liver cells to swell
  - turbulence in sinusoids
  - deposition of collagen in the space of Disse
  - portal hypertension

Clinical Features

- ❑ 13 g ethanol = 1 beer = 4 oz. wine = 1.5 oz. liquor
- ❑ alcohol abuse: 40 g/day in females or > 80 g/day in males x 10-20 years is the threshold for liver disease
- ❑ clinical findings do not predict type of liver involvement
- ❑ fatty liver
  - mildly tender hepatomegaly; jaundice rare
  - mildly elevated transaminases < 5X
- ❑ alcoholic hepatitis
  - variable severity: mild to fatal liver failure
  - clinically similar to viral or toxic injury
  - constitutional symptoms ± fever; abdominal distress; jaundice; tender hepatomegaly; splenomegaly (1/3)
- ❑ blood tests are non-specific, but in general
  - AST:ALT > 2:1 (transaminases never > 600, usually < 300)
  - increased GGT
  - increased triglycerides
  - increased INR, decreased albumin
  - increased MCV, decreased platelets

Biopsy
- ❑ histology of alcoholic hepatitis (triad)
  - hepatocyte necrosis with surrounding inflammation in zone III
  - alcoholic hyaline (Mallory bodies)
  - spider fibrosis (surrounding hepatocytes and central vein)
  - ± fat

Prognosis
- ❑ fatty liver: rapid and complete resolution with cessation of EtOH intake
- ❑ alcoholic hepatitis: mortality
  - immediate: 5%
  - with continued alcohol: 70% in 5 years
  - with cessation: 30% in 5 years

Treatment
- ❑ stop alcohol
  - Alcoholics Anonymous, disulfiram, lithium, naltrexone
- ❑ multivitamin supplements (with extra thiamine)
- ❑ caution giving drugs metabolized by the liver
- ❑ propylthiouracil (PTU) - equivocal efficacy
  - reduces hypercatabolism
- ❑ prednisone
  - has been shown to decrease mortality in a severely ill subgroup with alcoholic hepatitis
- ❑ colchicine (0.6 mg BID)
  - may slow disease progression

FATTY LIVER
- ❑ distinguish between microvesicular (early) and macrovesicular (late)

Etiology
- ❑ alcohol
- ❑ diabetes
- ❑ obesity
- ❑ jejuno-ileal bypass
- ❑ hyperlipidemic states
- ❑ drugs (methotrexate, tetracycline, amiodarone, valproic acid)
- ❑ Reye's syndrome
- ❑ fatty liver of pregnancy

CIRRHOSIS

Definition
- ❑ diffuse fibrosis plus nodular regeneration
- ❑ irreversible, although colchicine may be of some benefit

Etiology
- ❑ alcohol (85%)
- ❑ viral (B, B+D, C but not A nor E)
- ❑ autoimmune
- ❑ genetic
  - Wilson's disease
  - hemochromatosis
  - glycogen storage diseases
  - galactosemia
  - Gaucher's disease
  - a-1-antitrypsin deficiency
- ❑ drugs and toxins
  - methyldopa, INH, MTX, BCP
- ❑ biliary cirrhosis
  - primary
  - secondary
- ❑ chronic hepatic congestion
  - cardiac cirrhosis (chronic right heart failure, constrictive pericarditis)
  - hepatic vein thrombosis (Budd-Chiari)
- ❑ idiopathic

Management
- ❑ treat underlying disorder
- ❑ alcohol cessation
- ❑ follow patient for complications (see below)
- ❑ prognostic factors include
  - nutrition
  - ascites
  - encephalopathy
  - labs: albumin, INR, bilirubin
- ❑ liver transplantation for end-stage disease

Table 11. Clinical Features of Liver Disease

	Hepatocellular Dysfunction	Portal Hypertension
constitutional symptoms:	• anorexia • fatigue • fever / chills	
muscle and skin:	• jaundice • bruising (petechiae, ecchymosis) • muscle wasting • xanthomas and xanthelasmas	
head and neck:	• parotid hypertrophy • fetor hepaticus	• hepatic encephalopathy
chest:	• spider nevi (distribution of SVC) • gynecomastia • pectoral alopecia	
abdomen:	• hepatomegaly (RUQ pain) • ascites	• splenomegaly • ascites • varices • caput medusae
genitals:	• testicular atrophy • altered hair distribution	
extremities:	• palmar erythema • ankle edema • pale nails • clubbing • Dupuytren's contracture	• asterixis • ankle edema

HEPATIC ENCEPHALOPATHY

- ❑ acute neuropsychiatric syndrome secondary to liver disease
  - distinguish from non-liver-related neuropsychiatric disease in a patient with liver problems (e.g. alcohol withdrawal or intoxication, sedatives, subdural hematoma, metabolic encephalopathy)
- ❑ mechanism
  - porto-systemic shunt around hepatocytes —> toxins (believed to be ammonia from gut, mercaptans, fatty acids, amino acids) affect brain

Table 13. Hepatic Failure vs. Hepatic Encephalopathy

	Fulminant Hepatic Failure	Portosystemic Encephalopathy
symptoms at onset	agitation, delirium	somnolence
precipitating factors	rarely found	commonly found
pathology	cerebral edema	astroglial cell proliferation
prognosis	usually death	usually responds to treatment

- ❑ diagnosis
  - chiefly clinical, supported by laboratory findings, exclusion of other neuropsychiatric diseases
  - only pathognomonic finding is fetor hepaticus (musty odour of breath due to sulphur-containing compounds)
  - asterixis (also seen in renal failure, respiratory failure, drug overdose, hypoglycemia)
  - characteristic EEG findings: diffuse (non-focal), slow, high amplitude waves
- ❑ precipitating factors
  - nitrogen load (GI bleed, protein load from food intake, renal failure, constipation)
  - drugs (narcotics + CNS depressants)
  - electrolyte imbalance (hypokalemia, alkalosis, hypoxia, hypovolemia)
  - infection
  - deterioration in hepatic function or superimposed liver disease
- ❑ management
  - treat underlying liver disease and treat precipitating factors
  - decrease the generation of nitrogenous coumpounds (see below)
- ❑ decreasing nitrogenous coumpounds
  - decrease dietary protein to 50g/day; vegetable protein better tolerated than animal protein
  - lactulose
    - prevents diffusion of NH_3 from the colon into blood by lowering pH and forming non-diffusable NH^{4+}
    - serves as a substrate for incorporation of ammonia by bacteria, promotes growth in bowel lumen of bacteria which produce minimal ammonia
    - also acts as a laxative
  - neomycin eliminates ammonia-producing bacteria from bowel lumen
    - less effective than lactulose plus more side-effects (ototoxicity, nephrotoxicity))
    - combination of the two may be most effective

PORTAL HYPERTENSION

- ❑ pathophysiology
  - pressure = flow x resistance
  - unlikely that increased flow alone can cause portal hypertension (can occur in AV-fistulae or massive splenomegaly)
  - 3 sites of increased resistance
    - pre-sinusoidal (e.g. portal vein thrombosis, schistosomiasis, sarcoidosis)
    - sinusoidal (e.g. cirrhosis, alcoholic hepatitis)
    - post-sinusoidal (e.g. right-sided heart failure, hepatic vein thrombosis, veno-occlusive disease, constrictive pericarditis)
- ❑ signs of portal hypertension - see clinical features of liver disease
- ❑ management (see General Surgery Notes)
  - ß-adrenergic blockers (propanolol, nadolol) and nitrates
    - reduce the risk of bleeding from varices

ASCITES

- ❑ free fluid in the peritoneal cavity
- ❑ ultrasound is gold standard
- ❑ clinically detectable when > 500 mL (bulging flanks, shifting dullness, fluid wave)

Causes of Ascites	
serum [alb] – ascitic [alb] > 11 g/L	serum [alb] – ascitic [alb] < 11 g/L
cirrhosis/severe hepatitis chronic hepatic congestion (right heart failure, Budd-Chiari) nephrotic syndrome massive liver metastases myxedema	peritoneal carcinomatosis TB pancreatic disease nephrotic syndrome (can be both)

- ❑ diagnostic paracentesis: send for ascitic fluid for
  - cells and differential
  - chemistry albumin, protein, amylase, tryglyclides)
  - culture and sensitivity and gram stain
  - cytology for malignancy

Pathogenesis in Cirrhosis

- ❑ underfill theory
  - portal hypertension and hypoalbuminemia lead to transudation of Na^+ and water into peritoneum
    - causes decreases intravascular volume and secondary renal Na^+ and water retention
- ❑ overflow theory
  - liver disease primarily causes renal retention of Na^+ and water which then "overflows" into peritoneal cavity
- ❑ combined theory
  - liver disease causes vasodilation
  - decreased effective intravascular volume (i.e. volume to capacitance ratio low, but absolute volume is high)
  - therefore secondary urinary Na^+ and water retention

Treatment

- ❑ paracentesis safe
- ❑ medical
  - Na^+ restriction
  - diuretics (spironolactone, furosemide)
  - aim for 0.5 kg loss per day (rate of ascitic fluid absorption)
- ❑ surgical
  - peritoneal-systemic (LeVeen) shunts, TIPSS, liver transplantation
  - reserved for medically unresponsive cases

Bacterial Peritonitis

- ❑ primary (spontaneous) vs. secondary (usually results from perforated viscus)

Spontaneous Bacterial Peritonitis

- ❑ complicates ascites, does not cause it (occurs in 10% of cirrhotic ascites)
- ❑ fever, chills, abdominal pain, ileus, hypotension, encephalopathy
- ❑ E. *coli* is most common pathogen, *Strep.*, *Klebsiella*
- ❑ diagnosis: absolute neutrophil count in peritoneal fluid $> 0.25 \times 10^9$ cells/L or WBC count $> 0.5 \times 10^9$ cells/L ± positive culture
- ❑ treatment
  - IV antibiotics (ceftriaxone a good choice until C&S is available)

RENAL FAILURE IN CIRRHOSIS

- ❑ classify as
  - pre-renal
  - acute tubular necrosis (ATN)
  - hepatorenal syndrome
- ❑ hepatorenal syndrome is secondary to
  - overaggressive diuresis or large volume paracentesis
  - GI bleeding
  - sepsis
- ❑ differentiate hepatorenal syndrome from pre-renal failure
  - clinical (very difficult)
  - intravenous fluid challenge (improves prerenal failure)
  - pulmonary capillary wedge measurements (preferable)
- ❑ differentiate hepatorenal syndrome from ATN (see Table 14)
- ❑ treatment for hepatorenal syndrome is generally unsuccessful
  - vasopressin, octreotide, or norepinepherine may help (increased renal blood flow)
  - liver transplant definitive

Table 14. Differential Diagnosis of Acute Azotemia in Liver Disease		
Laboratory Findings	Prerenal Azotemia or Hepatorenal Syndrome	Acute Renal Failure (ATN)
urine [Na+] (mEq/L)	< 10	> 30
urine:plasma creatinine ratio	> 30:1	< 20:1
urine osmolality	at least 100 mOsm greater than plasma osmolality	equal to plasma osmolality
urine sediment	normal	casts and cellular debris

HEPATOPULMONARY SYNDROME
- ❑ intrapulmonary vasodilation leading to hypoxia from V/Q abnormalities
- ❑ improves with supplemental oxygen
- ❑ no proven medical therapy

HAEMATOLOGIC CHANGES IN CIRRHOSIS
- ❑ pancytopenia from hypersplenism
- ❑ decreased clotting factors
  - fibrin, thrombin, I, II, V, VII, IX, X

BILIARY TRACT

JAUNDICE
- ❑ history
  - dark urine, pale stools
  - pruritis
  - symptoms of biliary colic (obstructive jaundice)
  - history of drug and EtOH use, hepatitis
  - travel history
  - sexual history
  - family history
- ❑ physical exam
  - may be unremarkable
- ❑ investigations
  - bilirubin (conjugated and unconjugated)
  - AST, ALT, GGT, ALP
  - serologic tests for hepatitis
  - ultrasound for evidence of obstructive jaundice, CT
  - direct duct visualization (ERCP, PTC)
    (note: PTC only if obstruction suspected to be periportal rather than near sphincter or if previous gastric surgery)
  - liver biopsy

Classification of Jaundice

I. Predominantly Unconjugated Hyperbilirubinemia
1. Overproduction
   - Hemolysis
   - Ineffective erythropoiesis
2. Decreased hepatic uptake
   - Gilbert's syndrome
   - Drugs (e.g. rifampin)
3. Decreased conjugation
   - Hepatocellular disease
   - Drug inhibition (e.g. chloramphenicol)
   - Crigler-Najjar
   - Neonatal jaundice

II. Predominantly Conjugated Hyperbilirubinemia
1. Impaired hepatic secretion
   - Familial disorders
   - Hepatocellular disease
   - Drug-induced cholestasis (e.g. oral contraceptives, chlorpromazine)

- Primary biliary cirrhosis
- Sepsis

2. Extrahepatic biliary obstruction
   - Intraductal obstruction
     - Gallstones
     - biliary stricture
     - infection
     - malignancy
     - sclerosing cholangitis
   - Extraductal obstruction
     - Malignancy (e.g. pancreatic cancer, lymphoma)
     - Inflammation (e.g. pancreatitis)

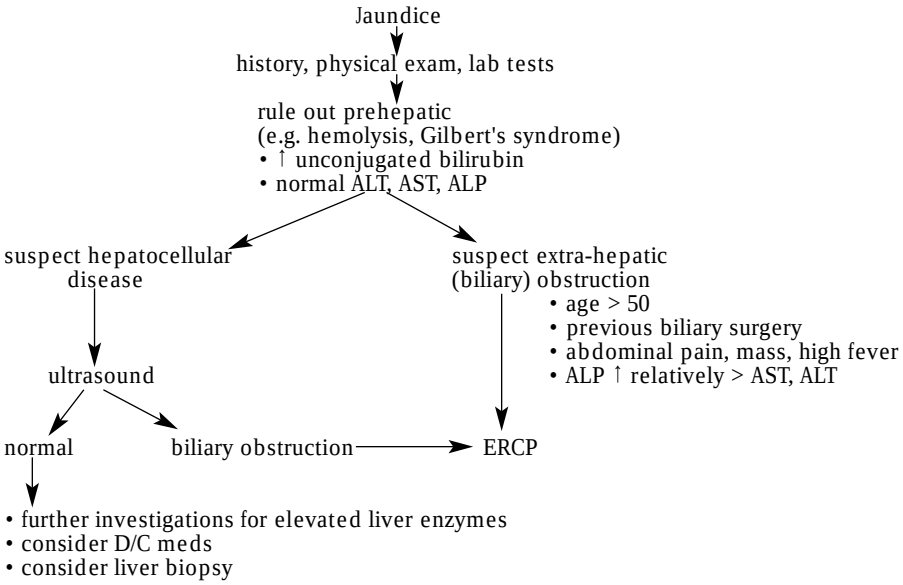


Figure 11. Approach to Jaundice

GILBERT'S SYNDROME

- ❑ mild reduction in glucuronyl transferase activity leading to defective conjugation of bilirubin
- ❑ affects 7% of population, especially males
- ❑ autosomal dominant
- ❑ presentation
  - presents in 20s-30s, often as an incidental lab finding
  - only manifestation is intermittent jaundice with incresed serum unconjugated bilirubin developing most characteristically while fasting
- ❑ no treatment indicated (entirely benign)

PRIMARY BILIARY CIRRHOSIS

- ❑ chronic inflammation and fibrous obliteration of intrahepatic bile ductules
- ❑ probably autoimmune (associated with rheumatoid arthritis, thyroiditis, CREST syndrome, vasculitis)
- ❑ affects mainly middle-aged women
- ❑ presentation
  - often asymptomatic
  - earliest symptoms: pruritus, fatigue
  - after several months-years: jaundice and melanosis (darkening skin) and other signs of cholestasis
  - eventually: hepatocellular failure, portal hypertension, ascites
  - physical examination
    - hepatomegaly with smooth surface in early stages, later on becomes nodular and cirrhotic
    - hypersplenism in late stages
    - xanthelasmas, xanthomas

- ❑ abnormal blood tests
  - increased ALP, GGT
  - anti-mitochondrial antibodies (98% specificity)
  - increased cholesterol —> xanthelasmas, xanthomas (mild increase in LDL, larger increase in HDL)
  - increased IgM
- ❑ diagnosis based on liver biopsy and normal ERCP (i.e. rule out CBD stones and sclerosing cholangitis)
- ❑ ultimately fatal although not all asymptomatic patients progress
- ❑ management
  - may treat with ursodiol, colchicine, methotrexate, cyclosporine cholestyramine (for pruritus and hypercholesterolemia), parenteral fat soluble vitamins, Vit D/calcium supplements
  - only proven treatment is transplant

SECONDARY BILIARY CIRRHOSIS

- ❑ results from prolonged partial or total obstruction of major bile ducts
- ❑ etiology
  - acquired: post-op strictures, gallstones, chronic pancreatitis, sclerosing cholangitis
  - congenital: CF, congenital biliary atresia, choledochal cysts
- ❑ clinical features
  - like primary, ± fever (bouts of cholangitis), ± RUQ pain (biliary colic)
  - portal hypertension only in advanced cases
- ❑ diagnosed by cholangiography
- ❑ treatment
  - release obstruction
  - if contraindicated, give antibiotics for cholangitis prophylaxis

SCLEROSING CHOLANGITIS

- ❑ inflammation of entire biliary tree (intra and extrahepatic bile ducts) leading to scarring and obliteration
- ❑ repeated bouts of cholangitis may lead to complete biliary obstruction with resultant secondary biliary cirrhosis and hepatic failure
- ❑ etiology
  - primary/idiopathic
    - most common
    - associated with ulcerative colitis in up to 70% (usually male); associated with AIDS
    - one of the most common indications for transplant
  - secondary
    - long term choledocholithiasis
    - cholangiocarcinoma
    - surgical/traumatic injury (iatrogenic)
    - contiguous inflammatory process
    - post ERCP
- ❑ presentation
  - similar to acute suppurative cholangitis
  - Charcot's Triad: RUQ pain, jaundice, fever/chills
  - Reynold's Pentad: add hypotension and delirium (more severe)
- ❑ diagnosis
  - increased ALP, bilirubin
  - minor increased in AST
  - ERCP shows narrowing of bile ducts, both intrahepatic and extrahepatic
- ❑ treatment
  - percutaneous or endoscopic dilatation of strictures
  - suppurative cholangitis requires emergency drainage of pus in CBD
  - surgical stent or biliary-enteric anastomosis
  - liver transplantation appears the best treatment for advanced sclerosing cholangitis (nearly 90% survive 1 year; mean follow-up from time of diagnosis to need for transplant is 5 years)
- ❑ prognosis
  - unfavourable regardless of treatment
  - mean survival after diagnosis remains 4-10 years

- ❑ physiology
  - acid in duodenum —> secretin —> water and bicarbonate from ductular cells
  - fat and protein in duodenum —> CCK —> enzymes from acinar cells (lipase, proteases) from acinar cells
  - secretin test
    - measure volume, HCO_3 and enzymes in pancreatic juice in response to IV injection of secretin
    - gold standard to diagnose chronic pancreatic insufficiency
- ❑ causes of increased serum amylase
  - pancreatic disease
    - acute pancreatitis, chronic pancreatitis with ductal obstruction, pseudocyst, abscess, ascites, trauma, cancer
  - non-pancreatic abdominal disease
    - biliary tract disease, bowel obstruction/ischemia, perforated or penetrating ulcer, ruptured ectopic pregnancy, aneurysm, chronic liver disease, peritonitis
  - non-abdominal disease
    - cancer (lung, esophagus, etc...), salivary gland lesions, bulimia, renal transplant/insufficiency, burns, ketoacidosis
  - macroamylasemia
  - when serum amylase > 5 times normal, the cause is almost always pancreatitis or renal disease

ACUTE PANCREATITIS

Causes

Gallstones (45%)
Ethanol (35%)
Tumors: pancreas, ampulla, choledochocele

Microbiological
- bacterial: mycoplasma, *Campylobacter*, TB, MAI, legionella, leptospirosis
- viral: mumps, rubella, varicella, viral hepatitis, CMV, EBV, HIV, Coxsackievirus, echo virus, adenovirus
- parasites: *Ascariasis, Clonorchiasis, Echinococcosis*

Autoimmune: lupus, PAN, Crohn's
Surgery/trauma
- manipulation of sphincter of Oddi (e.g. ERCP), post-cardiac surgery, blunt trauma to abdomen, penetrating peptic ulcer

Hyperlipidemia (TG >11.3 mmol/L), hypercalcemia, hypothermia
Emboli or ischemia
Drugs/toxins: azathioprine, mercaptopurine, ddI, furosemide, estrogens, methyldopa, H_2 blockers, valproic acid, antibiotics, acetaminophen, salicylates, ethanol, methanol, organophosphates
Idiopathic: 3rd most common - thought to be hypertensive sphincter or microlithiasis

Pathology
- ❑ mild
  - peripancreatic fat necrosis
  - interstitial edema
- ❑ severe
  - extensive peripancreatic and intrapancreatic fat necrosis
  - parenchymal necrosis and hemorrhage —> infection in 60%
  - release of toxic factors into systemic circulation and peritoneal space
- ❑ severity of clinical features may not always correlate with pathology

Presentation

- ❑ clinical: patient can look well or pre-morbid!
  - pain: epigastric, noncolicky, constant, can radiate to back, may improve when leaning forward (Inglefinger's sign); tender rigid abdomen; guarding
  - nausea and vomiting
  - abdominal distension from paralytic ileus
  - fever: chemical, not due to infection
  - jaundice: compression or obstruction of bile duct
  - tetany: transient hypocalcemia
  - hypovolemic shock: can lead to renal failure
  - adult respiratory distress syndrome
    - breakdown of phospholipase A_2
  - coma
- ❑ laboratory
  - increased pancreatic enzymes in blood
    - increased amylase: sensitive but not specific
    - increased lipase: > sensitivity and specificity - and stays elevated longer
  - increased WBC
  - imaging (see Colour Atlas C7)
    - x-ray: "sentinel loop" (dilated proximal jejunem), calcification and "colon cut-off sign" (colonic spasm)
    - U/S: best for evaluating biliary tree (67% SENS, 100% SPEC)
    - C/T scan with IV contrast: useful prognostic indicator because contrast seen only in viable pancreatic tissue. Non-viable areas can be biopsied percutaneously to diagnose infected pancreatic necrosis
    - ERCP + manometry: if no cause found
- ❑ course
  - usually a benign, self-limiting course, single or recurrent
  - occasionally severe leading to
    - shock
    - renal and pulmonary insufficiency
    - pancreatic abscess
    - coagulopathy
    - hyperglycemia and hypoglycemia
    - GI ulceration due to stress
    - death
  - functional restitution to normal occurs if primary cause and complications are eliminated (exception: alcohol)
  - occasional persistence of scarring and pseudocysts
  - rarely does chronic pancreatitis ever develop

Severity

- ❑ not proportional to the level of amylase
- ❑ Ranson's Criteria- pancreatitis not due to gallstones (criteria slightly different for gallstone-induced pancreatitis)
  - at admission
    - age> 55
    - WBC > 16x 10^9/L
    - blood glucose > 11 mmol/L (with no history of hyperglycemia)
    - serum LDH > 350 IU/L
    - AST > 250 IU/L
  - during first 48 hours
    - hematocrit drop > 10%
    - BUN rise > 1.8 mmol/L
    - arterial PO_2 < 60 mm Hg
    - base deficit > 4 mmol/L
    - serum calcium < 2 mmol/L
    - estimated fluid sequestration > 6 L
- ❑ difficult course if 2+ present
- ❑ high mortality if 3+ present

Notes

Differential Diagnosis
- ❑ perforated peptic ulcer
- ❑ biliary colic
- ❑ acute cholangitis, acute cholecystitis
- ❑ fatty infiltration of the liver (alcohol)
- ❑ small bowel obstruction
- ❑ mesenteric infarction
- ❑ dissecting aneurysm
- ❑ nephrolithiasis
- ❑ acute coronary occlusion

Treatment of Acute Pancreatitis
- ❑ Goals: (1) hemodynamic stability (2) alleviate pain (3) stop progression of damage (4) treat local and systemic complications
- ❑ IV crystalloid and NG suction (rests pancreas) if stomach dilated or inflammation severe or patient vomiting
- ❑ analgesics to control pain
- ❑ nutritional support (IV), NPO
- ❑ no benefit: antibiotics, glucagon, atropine, trasylol, H_2 blockers, peritoneal lavage
- ❑ follow clinically, and with CT/ultrasound to exclude complications
- ❑ debride abscesses
- ❑ drain pseudocysts if large or persisting or infected
- ❑ embolize hemorrhagic vessels

Complications
- ❑ pseudocyst (cyst-like structure encapsulated with fibrous material, not epithelium)
- ❑ abscess
- ❑ lungs: pleural effusion, atelectasis, pneumonia, ARDS
- ❑ acute renal failure (ATN)
- ❑ CVS: pericardial effusion, pericarditis, shock

CHRONIC PANCREATITIS

- ❑ a continuing inflammatory disease of the pancreas characterized by
  - irreversible morphological changes
  - typically causing pain
  - permanent loss of function (eg malabsorption syndrome, diabetes)

Causes
- ❑ nearly always alcoholic
  - alcohol increases viscosity of pancreatic juice
  - decreases pancreatic secretion of pancreatic stone protein (lithostatin) which normally solubilizes calcium salts precipitation of calcium within pancreatic duct
  - result is duct obstruction and subsequent gland destruction
- ❑ cystic fibrosis
- ❑ severe protein-calorie malnutrition
- ❑ hereditary pancreatitis
- ❑ primary hyperparathyroidism
- ❑ hyperlipidemia
- ❑ idiopathic
- ❑ never gallstones

Pathology
- ❑ irregular sclerosis
- ❑ destruction of exocrine parenchyma
- ❑ varying degrees of ductular dilatation and associated ductal strictures
- ❑ protein plugs
- ❑ calcification
- ❑ edema
- ❑ focal necrosis
- ❑ inflammatory cells
- ❑ cysts and pseudocysts
- ❑ infection

Notes

Presentation
- ❑ early stages
  - recurrent attacks of severe abdominal pain (upper abdomen and back)
  - chronic painless pancreatitis - 10%
- ❑ late stages – occurs in 15% of patients
  - malabsorption syndrome when > 90% of function is lost
  - diabetes, calcification, jaundice, weight loss, pseudocyst, ascites, GI bleed
- ❑ laboratory
  - increased serum glucose
  - increased ALP (portion of common bile duct within pancreas is narrowed by pancreatic inflammation)

Investigation
- ❑ flat plate (looking for pancreatic calcifications)
- ❑ ultrasound (calcification, dilated pancreatic ducts, pseudocyst)
- ❑ CT (calcification, dilated pancreatic ducts, pseudocyst)
- ❑ ERCP (abnormalities of pancreatic ducts-narrowing and dilatation)
- ❑ p-aminobenzoic acid (PABA) test (exocrine function-reflects duodenal chymotrypsin activity)
- ❑ 72 hour fecal fat test (exocrine function)
- ❑ secretin test, CCK test (exocrine function)

Treatment
- ❑ general management
  - total abstinence from alcohol
  - enzyme replacement may help pain by resting pancreas via negative feedback
  - pain relief
  - analgesics
  - celiac ganglion blocks
  - pain decreases with time as gland burns out
- ❑ steatorrhea
  - diet: restricted fat and protein (may also decrease pain)
- ❑ diabetes
  - insulin or oral hypoglycemic agents
- ❑ surgery
  - pancreatic resection if ductular obstruction
  - no surgical procedure can improve pancreatic function

AIDS AND THE G.I. TRACT

Odynophagia
- ❑ Candida (most common cause)
  - treatment= nystatin swish and swallow, ketoconazole, fluconazole
  - if oral thrush concomitantly present, diagnosis of Candida esophagitis established by history of odynophagia; otherwise need gastroscopy and biopsy
- ❑ ulcers from CMV
  - treatment = IV ganciclovir
- ❑ herpes
  - treatment = acyclovir
- ❑ idiopathic HIV-related
  - treatment = prednisone, thalidomide

Chronic Diarrhea
- ❑ commonly idiopathic
- ❑ associated with weight loss
- ❑ common causes: *Cryptosporidium, Mycobacterium avium complex,* CMV (causes mucosal ulcers), C. *difficile, Salmonella, Campylobacter*
- ❑ most useful test is stool examination: O&P, C&S, modified acid-fast stain for *Cryptosporidium* + *Isospora, C. difficile* toxin
- ❑ colonoscopy and small bowel biopsy only if loperamide not helpful and other tests normal

Abdominal Pain

- ❑ "HIV cholangiopathy" = sclerosing cholangitis due to CMV, *Cryptosporidium*, *Microsporidium* infection of bile ducts
  - increased ALP
  - diagnosis established by ERCP (biliary strictures)
  - endoscopic sphincterotomy helps in 1/3 of cases
- ❑ bowel obstruction from lymphoma, Kaposi's sarcoma, CMV
- ❑ peptic ulcer rare in AIDS because gastric acid levels low
- ❑ peritonitis
  - perforated bowel from CMV ulcer
  - acalculous cholecystitis
  - lymphoma

Liver Disease

- ❑ most common
  - fatty liver (presumably from malnutrition)
  - drugs (especially TMP/SMX, anti-TB drugs)
  - co-morbid chronic Hep B or C
- ❑ Mycobacterium avium complex and CMV cause elevated serum alkaline phosphatase

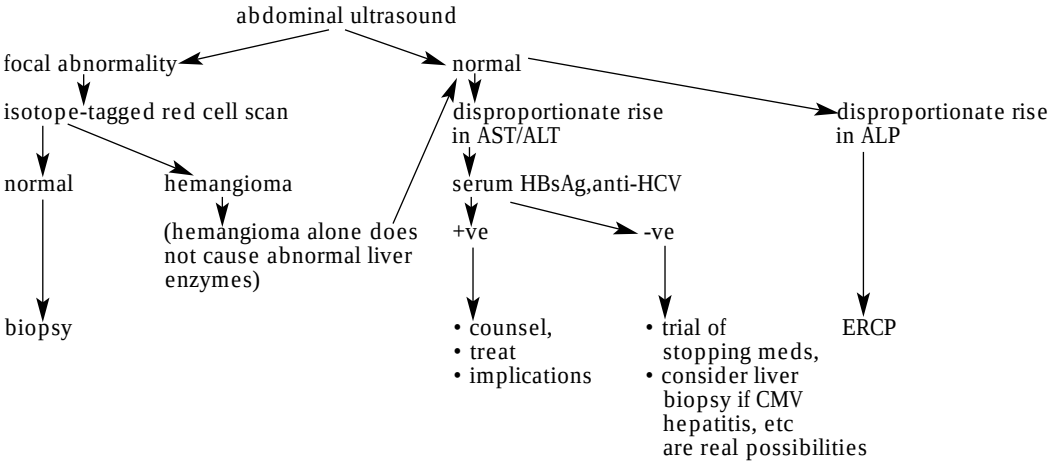


Figure 12. Evaluation of Abnormal Liver Enzymes in HIV Infection

RECOMMENDED NUTRIENT INTAKE (RNI)

- ❑ definition
  - RNI is the minimal intake of a nutrient that will be sufficient to meet the requirements of 97.5% of a healthy population
  - RNI will vary for different sub-populations, depending on: age, sex, pregnancy, lactation, etc...
- ❑ setting the RNI
  - assume a normal distribution of nutrient requirements
    - this is usually found in the experimental studies
  - for calorie requirement, RNI = mean population requirement
  - for others, RNI = mean population requirement + 2 x standard deviation
  - a correction factor for the average digestibility of the nutrient is also added into the final recommendation

CARBOHYDRATES

Simple Sugars

- ❑ monosaccharides (glucose, fructose, galactose, etc...)
- ❑ disaccharides (sucrose, lactose, etc...)

Complex Carbohydrates

- ❑ starch
- ❑ fibre (indigestible complex carbohydrates)
  - insoluble fibre acts mainly to increase stool bulk
  - soluble fibre "flattens" absorption curves for glucose and may reduce cholesterol absorption
- ❑ recommended intakes: 50+% as CHO (mostly complex CHO) and 32 g/day fibre

LIPIDS

- ❑ note difference between saturated (S) and polyunsaturated (P)
- ❑ essential fatty acids = linoleic, linolenic, and arachidonic
- ❑ deficiency leads to abnormal cell membrane and capillary structure, eczematous skin lesions, thrombocytopenia, poor wound healing, and abnormal metabolism of prostaglandins, thromboxanes, and leukotrienes
- ❑ recommended intakes: < 30% of diet; P/S ratio about 2.0

PROTEIN

- ❑ essential amino acids: Arginine, Histidine, Isoleucine, Leucine, Threonine, Lysine, Methionine, Phenylalanine, Tryptophan, Valine
- ❑ mnemonic: Any Help In Learning These Little Molecules Proves Truly Valuable
- ❑ Arg and His are “semi-essential" amino acids (they can be synthesized by the body, but not fast enough to keep up with the demand)
- ❑ sources of protein must be mixed to ensure a balanced intake of the essential amino acids
- ❑ this can be done on a vegetarian diet
- ❑ recommended intake: about 15% but reduce red meats (high saturated fats and cholesterol)

KWASHIORKOR AND MARASMUS

- ❑ kwashiorkor = disease syndrome produced by severe protein deficiency in face of adequate total calorie ingestion (usually complex carbohydrates)
- ❑ marasmus = severe deficiency of both protein and calories leading to wasting (low weight per height)
- ❑ response to starvation
  - first 24 hours: depletion of liver glycogen stores
  - after 24 hours: skeletal muscle breakdown (mobilize amino acids for gluconeogenesis and protein synthesis in liver)
  - in critical illness, serum tumour necrosis factor (TNF) is associated with movement of amino acids from periphery (muscle) to viscera (heart, etc...); nutrition is probably unable to prevent this process

DETERMINATION OF NUTRITIONAL STATUS

History

- ❑ weight gain or loss
- ❑ diet history; often unreliable, even when "food diaries" are kept
- ❑ GI functional inquiry (appetite, weight changes, nausea, vomiting, diarrhea, constipation)
- ❑ global clinical evaluation shown to be useful

Physical Examination

- ❑ hydration status
- ❑ weight and height (compare to standard tables)
- ❑ body mass index (BMI): weight (kg)/height2 (m2)
- ❑ muscle bulk, including forearm circumference
- ❑ subcutaneous fat (triceps skinfolds, etc...)
- ❑ cheilosis, glossitis, jaundice
- ❑ signs of specific nutrient deficiency

Laboratory Investigations

- ❑ plasma proteins (albumin, pre-albumin, transferrin)
  - decreases may indicate depressed nutritional status (not very specific)
- ❑ thyroid-binding pre-albumin, retinol-binding protein
  - too sensitive
- ❑ small changes in nutritional status can result in large changes in the following indices
  - hemoglobin levels
  - total lymphocyte count
  - cell-mediated immunity
  - muscle strength (hand-grip dynanometer; electrical stimulation of adductor pollicis)
  - INR: a measure of vitamin K status
  - creatinine-height index, compare to standard tables
  - other methods are available but mainly for research (underwater weighing, total body water, total body potassium, total body nitrogen, etc...)

ENTERAL NUTRITION

Diets Taken by Mouth

- ❑ normal diet ("diet as tolerated")
- ❑ puréed diet
- ❑ soft diet: for difficulty chewing
- ❑ full fluids: inadequate in vitamins and minerals
- ❑ clear fluids: inadequate in most nutrients, for short-term use (e.g. post-operative)

Special Diets

- ❑ taken normally
- ❑ stricture diet (low fibre)
- ❑ post-gastrectomy (anti-dumping) diet
  - liquids separated from solids
- ❑ weight-reduction diet
- ❑ weight-gain diet
- ❑ diabetic diet: low fat, low simple sugars
- ❑ diet for irritable bowel syndrome: high fibre
- ❑ low protein diet (renal disease)
- ❑ low sodium diet: hypertension, CHF, liver disease ("healthy heart")

Approaches

- ❑ nasogastric, nasoduodenal, or nasojejunal tube
- ❑ enterostomy feeding (e.g. gastrostomy tube)
- ❑ jejunostomy feeding

Indications
- ❑ oral consumption inadequate or contraindicated
- ❑ appropriate enteral feeding formula is available

Relative Contraindications
- ❑ vomiting and aspiration
- ❑ intestinal obstruction
- ❑ small bowel ileus
- ❑ enteroenteral or enterocutaneous fistulae
- ❑ uncontrolled diarrhea
- ❑ UGI bleeding

Feed Types for Enteral Nutrition
- ❑ blenderized
- ❑ milk-based
- ❑ semi-elemental (e.g. Isocal, Ensure)
- ❑ elemental: simple sugars or oligosaccharides, amino acids or short peptides, etc... (e.g. Vital)

Advantages
- ❑ avoids risks of parenteral nutrition
- ❑ no need for sterilized solutions or tubes
- ❑ relatively cheap

Complications
- ❑ aspiration
- ❑ diarrhea

Enteral Nutrition: Advantages Over Parenteral Nutrition
- ❑ fewer serious complications (especially sepsis)
- ❑ nutritional requirements for enterally administered nutrition better understood
- ❑ can supply gut-specific fuels such as glutamine and short chain fatty acids
- ❑ nutrients in the intestinal lumen prevent atrophy of the gut and pancreas
- ❑ prevents gallstones by stimulating gallbladder motility
- ❑ less expensive

PARENTERAL NUTRITION

Approaches
- ❑ parenteral nutrition to supplement enteral nutrition
- ❑ total parenteral nutrition (TPN)
    - when it is the only source of nutrition
- ❑ long-term TPN ("home TPN")

Indications for TPN
- ❑ not well understood; only situations where TPN has been well shown to increase survival are after bone marrow transplant and in short bowel syndrome
- ❑ preoperative: only useful in severely malnourished (i.e. lost more than 15% of premorbid weight, serum albumin < 28 g/L)
- ❑ renal failure: TPN shown to increase rate of recovery from acute renal failure, but not to increase survival
- ❑ liver disease: branched chain amino acids may shorten duration of encephalopathy, but do not increase survival
- ❑ inflammatory bowel disease: TPN closes fistulae, and heals acute exacerbations of mucosal inflammation, but effect is transient
- ❑ some evidence for efficacy, but convincing data not available
    - radiation/chemotherapy-induced enteritis
    - AIDS
    - severe acute pancreatitis

Clinical Setting where TPN is Often a Part of Routine Care

- ❑ patients with inability to absorb nutrients via the GI tract
  - small bowel resection (70% resected)
  - diseases of the small intestine (e.g. scleroderma, SLE, sprue, pseudo-obstruction, multiple enterocutaneous fistulae and Crohn's disease) not responding to other treatments
  - radiation enteritis
  - chronic severe diarrhea (e.g. primary GI disease, viral or bacterial enteritis)
  - intractable and protracted vomiting
- ❑ patients undergoing high-dose chemotherapy, radiation and bone marrow transplantation with impaired gut function
- ❑ moderate to severe acute pancreatitis with GI symptoms associated with oral ingestion of food
- ❑ severe malnutrition in the face of a non-functioning GI tract
- ❑ severely catabolic patients with or without malnutrition when GI tract is not usable within 5 days; examples include
  - > 50% body surface area burn
  - multisystem trauma
  - extensive surgery
  - sepsis
  - severe inflammatory disease

Relative Contraindications

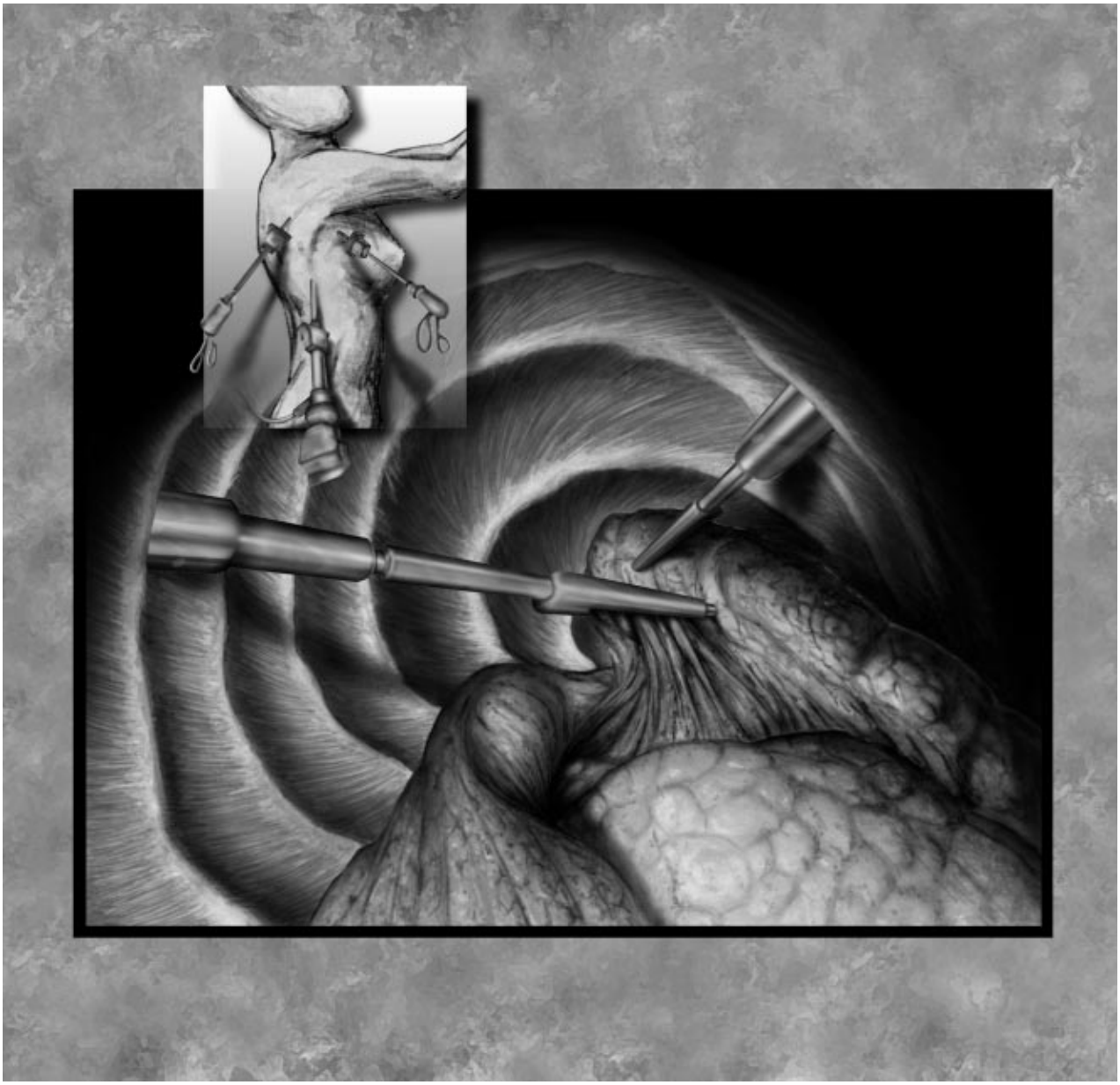
- ❑ GI tract functioning and can be used for enteral nutrition
- ❑ active infection; at least until appropriate antibiotic coverage
- ❑ inadequate venous access; triple-lumen central venous lines usually prevent this problem
- ❑ unreliable patient or clinical setting

TPN Prescription

- ❑ energy 30 calories/kg ideal weight/day in nonstressed patient increase by 50% in severe illness
- ❑ optimal ratio of carbohydrate to fat unknown, but usually 30% of energy is given as fat
- ❑ protein: 1 g/kg/day; increase by 50% in catabolic patients
- ❑ Na^+: 150 mmol/day plus abnormal losses, less if edema, ascites, heart failure
- ❑ K^+: 60 mmol/day plus abnormal losses
- ❑ fluid: 35 ml/kg/day plus abnormal losses

Complications of TPN

- ❑ sepsis: most serious of the common complications
- ❑ mechanical pneumothorax, etc... from insertion of central line catheter migration and thrombosis, air embolus
- ❑ metabolic: heart failure, hyperglycemia, gallstones, cholestasis
- ❑ TPN burn



Drawing by Jason Guerrero