DIARRHEA 6/8/10

ACUTE Symptoms < 2 weeks

<12hours: Ciguatera: reef fish, Neurotoxic shellfish: Gulf of Mexico, Shellfish.
E Coli (beef, salad dressing); Bacillus cereus poisoning:1-6 hrs
Staph aureus (1-8 hrs pp) Ham, poultry, pastries, salads, potato salad.

8-36 hours: Clostridia perfringens: beef, gravy;. Fried rice pork. Clostridia: buffet pathogen; Vibrio parahaemolyticus: most common cause of sea-food (raw osysters).

> 24 hours

Non-inflammatory, high water volume diarrhea:

E. Coli---enterotoxigenic
Listeria: milk, icecream, poulching.
Vibrio cholerae; Vibrio fulnificus: Raw oysters in a person with liver failure.
Parasitic: Giardia (belching, abdominal pain, ELISA: S & S = 92% and 98%!!) Cryptosporidia (difficult to treat), microsporidia, Isospora (acid fast) via HIV
Viral: HIV, Norwalk virus & Rota virus

Inflammatory, smaller volume diarrhea:

Viral: CMV
Parasitic: Entamoeba histolytica, strongyloides, Trichuris Tricuria (Whipworm)
E. Coli (O157:H7>>Shiga Toxin) enterohemorrhagic or enterinvasive
Clostridium difficile
Salmonella – dairy, raw eggs, sickle cell anemia. Even if 2 wks, do NOT treat unless immunocompromised or elderly.
Campylobacter – 3 B's: Bloody diarrhea, mimics IBD, and is associated with Guillain Barre syndrome. 2-10 ds pp.
Shigella: egg salad
Yersinia – rash, joint pain, abdominal pain. 30% of appendicitis. Pork, tofu.
Franciscella tularensis (tick vector; South-Mid West: Arkansas, Missouri, Oklahoma)

CHRONIC Symptoms > 2 weeks

OSMOTIC Osmotic gap > 50: Osmotic gap = 290 - 2*(Na + K) 24 hours fast resolves the diarrhea. *

Laxatives: Magnesium, poylethylene glycol, sorbitol, lactulose

Carbohydrate malabsorption (lactose intolerance) (increased w/bacterial overgrowth, sprue, IBD): Dx= give lactose and measure H2 in breath.

Secretory: Osmotic gap < 50: Continues despite fasting.

CANCER & LYMPHOMA

Stimulant laxatives Bisacoydal (ducolax), cascara, senna (ex-lax), phenophtalein turns NaOH red in urine.

Short bowel (< 100 cm lost, Crohn's,surg) with malabsorbed bile acids stimulating the colon to secrete salt and water and also enhancing colonic oxalate absorption causing kidney stones. Rx=cholestyramine and vitamins (B12).*

bacterial toxins: C. Difficile
Diverticulitis
Dysmotility: Post vagotomy/ Irritable bowel
Endocrine
DM
Hyperthyroidism
Adrenal insufficiency
Gastrinoma – get serum gastrin level.
Vipoma – get vasoactive intestinal polypeptide in serum.
Carcinoid – flushing; Get 5 HO indole acetic acid in urine.
MCT-medullary ca Of thyroid
Mastocytosis

Inflammatory: WBCs with possibly RBCs. WBCs detected by lactoferrin assay of stool.

IBD: Cronh's or ulcerative colitis
Ischemic colitis
Microscopic colitis: either lymphocytic colitis or collagenous colitis(which is steroid responsive.)
Inflammatory infectious agents with acute diarrhea: campylobacter, gonorrhea (anal intercourse) Amebiasis, MTB.
Radiation colitis

Malabsorption with Fatty diarrhea: stool is greasy & foul smelling Low carotene, iron, Vit D, K Ca & ^INR.

Primary mucosal disease: Sprue;, Tropical Sprue, Crohn's disease, and Whipples:male(white)wt V(93%), steatorrhea(81%), arthralgias(73%), dementia. Dx:serum PCR or Bx:PAS macrophages.

Short bowel (> 100 cm lost, Crohn's,surgery) causes severe loss of bile absorption causing decreased bile salts, which are no longer able to absorb fats. Treat with low fat diet, medium chain triglyceride oil for calories, and vitamins. *

Biliary disease with inadequate bile acids: As above.

Pancreatic exocrine deficiency occurs in chronic pancreatitis. DM & B12 def. Normal D xylose test. R/o pancreatic CA.

Bacterial overgrowth: deconjugates bile acids causing decreased fat absorption; do hydrogen breath test with glucose or lactulose and look for rise in hydrogen in the breath; treat empirically with antibiotics.

Lymphatic obstruction
Lymphoma, strongyloides, schistosomiasis.

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*24 hour fast resolves the diarrhea.

TPN deficiencies

WEEKS	Vit's B & C, water soluble, except for B12	CHF, Nystagmus, ataxia, confabulation, memory loss (B1, B complex). Anemia (B2). Dermatitis & stomatitis (B2, B6, B Complex). Diarrhea (B complex). Petechial hemorrhages & echymoses (C)
	Mg	lethargy, anorexia, cramps, tetany
	Zinc	acrodermatitis, poor wound healing, and dysgeusia.
MONTHS	Copper	**B12-like deficiency** plus depigmented skin and kinky hair.
	Vit K	Increased INR
YEARS	Vit's A & D(fat soluble)	Night blindness; hypocalcemia
	Selenium	Myalgias, cardiomyopathy, anemia (hemolytic)
	Chromium	Hyperglycemia
	Iron, cobalt(?)	Anemia, microcytic
	B12	Anemia, macrocytic. Dementia, Smooth tongue, degeneration of dorsal & lateral spinal cord: ataxia, spasticity, loss of position & vibration sense.

VITAMINS: B and C are water soluble. A, D, E & K are lipid soluble. DEFICIENCIES

B1, Thiamine	**Wet beriberi**: heart failure, ascites, peripheral edema **Dry beriberi**: >**Wernicke's** encephalopathy: vomiting, **nystagmus, ophthalmoplegia**, **ataxia, disorientation.(fully reversible with B_1).** >**Korsakoff's** syndrome: **Retrograde amnesia, confabulation.(½ reversible with B_1)**
B2, Riboflavin	NC, NC anemia, ST, glossitis, cheilosis, angular stomatitis, seborrheic dermatitis of perineum & scrotum. (Occurs with phenothiazines & tricyclic antidepressants.). Prevents migraine.
B6, Pyridoxine	Glossitis, cheilosis, vomiting & seizures (rare. Relative B6 deficiency occurs in use of **INH**, cycloserine, penicillamine, & etoh'm.)
B complex, Niacin (part of NAD and NADP)	**Pellagra**: "**3 Ds: Dermatitis, Diarrhea, Dementia**". Dermatitis, glossitis, stomatitis, proctitis, diarrhea, depression, dementia, psychosis. Made from tryptophan so not actually a vitamin. Seen in **carcinoid in which tryptophan is consumed** and in **INH**.
B12 (develops in years)	Macrocytic anemia, **smooth tongue**, **decreased DTRs**, decreased vibratory & position sense, spasticity, ataxia, **memory loss**.
Vit C, Ascorbic Acid.	**Scurvy: Petechial hemorrhages & ecchymoses**. Then hyperkeratotic papules around hair folicles & Sjogren's syndrome.
Vit A	Night blindness
Vit D	hypocalcemia, increased PTH. Rickets in children.
Vit E	**Areflexia and decreased vibration & position sense** are due to spinal cord deterioration.

VITAMIN OVERDOSE

Vit A	Flaky skin, athralgias, alopecia, fever, HS megaly.
Vit B6	peripheral neuropathy: Absent position and vibration sense (NL motor & other sensory)
Vit D	Inc Ca, Hypercalcuria, renal stones(?) (Sarcoid & lymphomas have increased 1,25(OH)2 D
Vit E	Non toxic. Can reverse coagulation.
Vit C	Possible oxalate renal stones and interference with B12 absorption.
B complex, Niacin	Acanthosis nigricans, cholestatic jaundice.

Disease	Intestinal Angina = Chronic mesenteric ischemia	Diverticulitis
Setting	arteriosclerotic disease	elderly
CM's	Post prandial abdominal pain, fear of eating, weight loss, abdominal bruit	Abd pain, ^ T, LLQ mass, ^ WBC
Radiology	MR angio, duplex doppler US, CT with contrast, arteriogram	CT: Pericolic fat density (stranding), air in divertic, thickened bowel wall, soft tissue mass, ? Abscess. BE & colonoscopy contraindicated. (divertics in left colon, bleeding divertics in right colon.)
RX	If severe symptoms, angioplasty or surgical re-vascularization.	Mild: Liquid diet, cipro or metronidazole; Severe: NPO, IV fluids, broad spectrum ab'cs, surgery in 15%.
Other		Complications are perforation, obstruction ("Picket fence" or ?Ca), fistula into bladder or vagina

Tumor markers:
CEA in Pancreas & colon
CA19-9 and CA125 in pancreas and ovary.

ACUTE CALCULOUS CHOLECYSTITIS: (NEJM 2008;358:2804. SM Strasberg

1. Imaging: U.S. has sensitivity of 98%. Biliary scintography hf gallbladder filling is more specific.

2. Diagnostic criteria for acute cholecystitis (3 (imaging) plus 1 of 1 and 1 of 2):
    1) imaging
    2) local signs: murphy's sign, tender RUQ; mass RUQ.
    3) Systemic signs: fever, ^ WBC, ^ CRP.

3. Tokyo guidelines for severity:
Grade 1. Acute cholecystitis that does not meet more severe grade.
Grade 2. One or more of: duration 3 days +/ WBC 18+/ palpable tender mass/ marked local inflammation" abscess, peritonitis, air, gangrenous cholecystitis.
Grade 3. Organ dysfunction.

Grade 1 can and should be operated immediately: I.E.: Operate if: fever or mildly elevated WBC (<18,000) and a positive Murphy's sign.

Treat with antibiotics if there is a Temp > 38.5 ($\geq$ 104), air in or around the gall bladder, WBC > 12.5.
Antibiotics: 2nd generation cephalosporin OR (quinolone + metronidazole): Cover enterobacter, E coli, salmonella, shigella, yersinia, and pseudomonas.

LOWER GI BLEEDING, INCLUDING VASCULAR ILLNESS PLUS DIVERTICULOSIS (1) September 27, 2005

Disease	Diverticulosis (2)	Angiodysplasia (AV malformation, vascular ectasia)	Intestinal angina= chronic mes-enteric ischemia	Ischemic Colitis= Colonic ischemia	Mesenteric vein thrombosis	Acute mesenteric ischemia **AN EMERGENCY**
Set-ting	Age 30 + Common in elderly	Usually older than 60. Predeliction in ESRD. ? relationship to aortic stenosis.	Atherosclerosis	90% over age 60. Vasculitides. DM AAA	Hypercoagulable state: OCPS, cirrhosis w/ portal HPT, abd surgery	Arrhythima, AF, valvular heartt dis, CHF, MI, hypotension, hyper-coagulable state
CM's	Hematochezia (maroon stool or bright red bleeding). Brisk! Diverticulosis causes 40% of massive rectal bleeding. **NO PAIN**	Bleeding may be chronic or sudden hematochezia (20-30% of acute lower GI bleed). NO PAIN	**PP abdominal pain. Fear of eating. Weight loss !!! USUALLY NO BLEEDING**	Patients not very ill; **mild abdominal pain**, tenderness. urge to defecate, usually hematochezia and/or bloody diarrhea	**Acute, subacute, or chronic abdominal pain,** Bleeding	**Sudden**,**very ill**,(Severe pain=small bowel), peri-umbilical pain, vomit, diarrhea, ileus, ^ WBC. Bleeding occurs later.
Patho gen-esis	Diverticulum causes vein to be draped over it, with only mucosa separating the vessel from the lumen.	Colon, stomach or small bowel. Ectatic, dilated thin walled vessel lined only with endothemlium or minimal smooth muscle colonic ischemia.	Atherosclerosis. May progress to Acute Mesenteric Ischemia.	Precipitants: v BP, Dehydration. Causes: DM, Dissection, vasculitides, coagulopathies. SMA supplies proximal and transverse colon, IMA supplies distal colon. Mostly in the distal colon. (3)	Hypercoagulable state	Embolic from heart or atheroembolic. Celiac artery>small bowel (gives severe pain), and SMA or IMA > large bowel.
Radi-ology etc	Diverticulosis occurs on the right. (Diverticulitis occurs on the left.) Colonocopy. Coagulate visible vessel. Radionuc imaging detects bleed of 0.1ml/min. Angiography: 0.5 ml/min. vassopressin & stabilize for srgry Helical CT may be useful.	Colonoscopy: 5 - 10 mm red, fernlike pattern. Sensitivity 80%. Helical CT angiography.	Duplex doppler US +/or angio	"Thumb-printing" & "cobble stoning" on KUB. Colonoscopy Pale mucosa, paucity of vessels, apthoid ulcers, sharply demarcated areas of inflammation.	Doppler US, CT scan, arteriography.	Angiography. Arteriography can also be avenue for thrombolysis.
RX	Above temporizing measures. Surgery.	Electrocoagulation Sclerotherapy with ethanolamine. Surgery if the site is clearly defined.	Angioplasty or surgical revascularization	Supportive, IV fluids, antibiotics. Surgery is rarely indicated (e.g., if bowel infarct). Tends to resolve in 2 - 4 weeks and usually does NOT recur.	Anti-coagulation if no bowel infarct. Otherwise, may require surgery.	**Emergency** angiography with thrombolysis or vasodilation (papaverine) OR emergency surgery.

(1) Etiology of lower GI bleeding overall is: diverticulosis 33%, **cancer & polyps 19%**, colitis and ulcers (IBD, infectious(salmonella, campylobacter, shigella, e coli 0157 h7, parasitic), ischemic, radiation induced) 18%, angiodysplasia 8%, hemorrhoids, fissures 4%, miscellaneous 8% (chronic & acute mesenteric ischemia, mesenteric vein thrombosis)

(2) **Diverticulitis** occurs in the elderly, has abdominal pain, LLQ mass, ^ WBCs. CT: Pericolic fat density with stranding, thickened bowel wall, soft tissue mass, and possible abscess. Colonoscopy **contraindicated**. Liquid diet, cipro or Flagyl. If severe: NPO, IV fluids, broad spectrum antibiotics, and surgery (in 15%). Complications: Perforation, obstruction, fistulae into bladder or vagina.

(3) **Ischemic colitis or colonic ischemia** occurs at the watershed of the middle colic and inferior mesenteric arteries.

ACUTE BILIARY DISEASE

Condition	Symptoms	Lab	Pathogenesis
Biliary colic			
Acute cholecystitis	persistent abdominal pain		Stone in GB neck or cystic duct leading to gallbladder wall inflammation.
Choledocholithiasis	Abdominal pain	Increase in bili, alk phos, AST. Pancreatitis	Stone in common duct
Cholangitis	Abdominal pain, fever, jaundice (Charcot's triad).	Increase in bili, alk phos, AST. Pancreatitis. Hi WBC.	Infection of hepatic ducts: Gm - bacilli, aerobic, anaerobic, enterococci. Give piperacillin & metronidazole.
Cholecysto-enteric fistula	Obstruction		Stone in duodenum causing "gallstone ileus" and obstruction.
Acalculous cholecystitis	In burn, trauma, immunosuppressed	Fever, increased amylase, negative Ultrasound	Salmonella, virus
Chronic acalculous cholecystitis	RUQ pain	Radio nucleotide ejection fraction of gall bladder is less than 35%.	GB dyskenesia.

AUTO-IMMUNE HEPATITIS AND RELATED ENTITIES

ALT	Alk Phos	ANA	Anti-smooth muscle AB	Anti-mito-chondrial AB	IgM	IgG	Liver Biopsy	
70	1,100	Pos (1)		Negative	Inc		lymphocytic destruction of bile ducts	Auto-immune cholangitis (1)(6)
50	500+	+ve in 70% (1)		Pos	Inc		lymphocytic destruction of bile ducts	Primary biliary cirrhosis(2)
230	120	Pos(3)	Pos(3)			Inc	piecemeal necrosis of hepatocytes	Autoimmune hepatitis
45	280						mild inflammation with concentric fibrosis around bile ducts (4)	primary sclerosing cholangitis (5)

(1) Some PBC is AMA negative and ANA positive and is called "auto-immune cholangitis"; it has the same outcome as AMA positive PBC.
(2) PBC: treat with chenodeoxycholic acid (ursodiol).
(3)Type II is rarer and has Anti-L/KM 1 Ab (Anti- liver/kidney microsomal type 1 antibody) and is more severe. This has increased P-ANCA (MKSAP 14).
(4) Diagnosis of primary sclerosing cholangitis is via ERCP: Diffuse strictures and beading of intrahepatic and extrahepatic ducts.
(5) PSC is diffuclt to treat; 10-15% get bile duct cancer.
(6) RX = Prednisone or prednisone and azathioprine.

Hypothyroidism causes elevation of liver enzymes and CK in about 25% to 40% of cases.
Primary biliary cirrhosis and hypothyroidism may co-exist via autoimmune pathogenesis.
The ALT may be elevated in hyperthyroidism.

EVALUATION FOR POSSIBLE B12 AND/OR FOLATE DEFICIENCY July 7, 2004

*Suspect if macrocytosis.

*Obtain blood before a meal (a single meal will correct folate deficiency). If both B12 and folate are normal (>300 pg/ml and >4 ng/ml, respectively), neither is deficiency is present.

*If either of the two tests is abnormal, test for methylmalonic acid (MMA) and homocysteine. B12 is required for metabolism of both MMA and homocysteine, whereas folate is only used in metabolism of homocysteine. Therefore:

If MMA & homocysteine are increased, deficiency is either a)B12 only or b) both B12 and folate.

If only homocysteine is increased, there is Folate deficiency only.

If MMA and homocysteine are both normal, this rules out B12 and folate deficiencies.

For folate deficiency, the causes are:

1) Nutritional: ETOH abuse, substance abuse, poor diet, overcooked foods, nursing homes, depressed patients.
2) Malabsorption: Sprue, Inflammatory Bowel disease, infiltrative bowel disease, short bowel disease.
3) Medications: trimethoprim, methotrexate, alcohol, phenytoin.
4) Other: pregnancy & lactation, chronic hemolysis, exfoliative dermatitis.

For B12 deficiency, the causes are:

1) Gastric: pernicious anemia, gastric resection, gastritis
2) Small bowel: Sprue, Crohn's disease, short bowel, blind loops
3) Pancreas: Pancreatic insufficiency.
4) Agents blocking absorption: Metformin, PPIs (omeprazole), neomycin
5) Diet: Strict vegans, vegetarian diet in pregnancy

For B12 deficiency, test for PA by **Antibodies to Instrinsic Factor**, which confirm PA. If these are absent, do the 1st part of the Schilling test (giving B12 without intrinsic factor):

1) If it is normal, there may be 1) partial ileal resection or ileal disease, 2) deficiency from diet, 3) agents blocking absorption.
2) If B12 excretion is low, the possible etiologies are PA (with false negative IF Ab assay), gastritis, sprue, bacterial overgrowth, ileal disease, or pancreatic disease.

In 2nd part of Schilling test, give 4 weeks of B12 I.M. to normalize the gut, and then give intrinsic factor with oral B12. If B12 excretion normalizes, this indicates pernicious anemia or gastritis. If excretion is still low, address sprue, Crohn's, bacterial overgrowth, or pancreatic insufficiency.

Sprue is diagnosed by detecting Anti-endomesial Abs, and Anti tissue transglutaminase IgA antibodies and then confirmed by small bowel biopsy. 1/4 of Celiac Sprue has dermatitis herpetiformis.

Crohn's disease is diagnosed radiologically, colonoscopy, and bowel biopsy.

Pancreatic insufficiency can be tested a) in special centers, by the secretin stimulation followed by collection of bicarbonate and pancreatic enzymes in the duodenum, or b) by testing for chymotrypsin and elastase in the stool.

Hemorrhoids can give iron deficiency.

Hepatitis A is no longer infective after 1 month of jaundice, even though jaundice may persist.

PORPHYRIAS

	Skin	Liver	Other Sx's	Precipitants	Urine	Serum	Other	Treatment
PCT: Porphyria Cutanea Tarda	Blisters on sun exposed areas	Increased AST, ALT. Increased risk of liver cancer. Increase in liver porphyrins.		Iron excess Sun exposure hemodialysis ETOH Smoking Estrogen use & pregnancy Hepatitis C infection.	Increase uroporphyrin	increase porphyrin (best diagnostic test) > 10 mcg/dL		Remove precipitants. Phlebotomy Low dose chloroquine
AIP: Acute Intermittent Porphyria		Increase risk of liver cancer	**GI** Abdominal pain 90% Vomiting 66% Constipation 66% **NEUROLOGIC** Trunk,limb,H,N pain 50% Paresis 50% (2) Psychiatric 50% (3) Convulsions 15% Respiratory paralysis 12% **AUTONOMIC** HPT 45% Tachycardia 66% Fever 20%	Alcohol abuse Smoking Pre-menstrual Infection Starvation Drugs Surgery	Increase ALA & PBG, aminolevulinic acid, and porphobi-linogen. (May be normal between attacks.		Lo serum Na. SIADH	Avoid certain drugs: ACEIs, CCBs, sulfa drugs and many others. IV heme preparations. IV carbohydrates

(1) There a four types of acute porphyria: acute IP, Hereditary coproporphia, variegate porphyria, ALA-dehydratase deficient porphyria. The last is the most rare and requires a special assay.

(2) Muscle weakness is usually symmetric and usually involves the proximal muscles of the upper limbs first.

(3) This ranges from minor behavioral changes to depression, agitation, psychosis, and hallucinations.

(Symptoms are from Ann Int Med 142:441 and from UpToDate.)

Consider the diagnosis of **cystic fibrosis** with bronchiectasis any of the following:
*recurrent idiopathic pancreatitis
*male infertility (congenital bilateral absence of the vas deferens)
*recurrent nasal polyps
*Steatorrhea
*Hepatomegaly or hepatic disease with cirrhosis
*Distal intestinal obstruction syndrome
*Nutritional problems with decreased protein, edema, and fat soluble vitamins

Liver enzymes in alcoholic hepatitis (from PIER):
AST/ALT ratio >2.0 Sensitivity 70% Specificity 92-100%

Based on liver biopsy as a gold standard. Useful for distinguishing alcoholic hepatitis from NASH.

GGTP is used as a measure of alcohol consumption, using 54 IU/L as a cutoff for abnormal test:

	men	women
Sensitivity	65	54
Specificity	89	97

Qualification for liver transplant is sobriety for > 6 months.

Ascitic fluid protein	SAAG $\geq$ 1.1	SAAG < 1.1
< 2.5 gm/dL	Cirrhosis	nephrotic syndrome
$\geq$ 2.5 gm/dL	Right sided heart failure, Budd-Chiari	Malignancy, TB

SAAG = "Serum-Ascites albumin gradient" (MKSAP 14; from Runyon BA Hepatology 2004.)

EXTRAINTESTINAL MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE*

Responsiveness to IBD Rx	Joints	Skin	Other
Responsive	polyartrhitis (knees, elbows)	erythema nodosum	iritis, uveitis
Not responsive	sacro-iliitis(in Crohn's dis)	poyderma gangrenosum	primary sclerosing cholangitis

*IBD is also associated with roughly a 3 x increase risk for DVT and PE. Also, there is an increased risk for amyloidosis.

CAUSES OF PANCREATITIS

1. Toxins, drugs: Alcohol, HCTZ, furosemide, salicilates, sulindac, metronidazole, pentamadine, didanosine, sulfasalazine, valproic acid.

2. Obstruction: Stones/ Tumor: cholangiocarcinoma, pancreatic cancer/ Pancreatic pseudocyst

3. Mechanical damage to the pancreas: Penetrating duodenal ulcer, ERCP, trauma

4. Infection: Mumps, Coxsackie, Hepatitis B, HIV, CMV. Bacteria: Legionella, Mycoplasma, Leptospira. Fungal: Aspergilla. Parasitic: Toxoplasmosis, ascariasis.

5. Connective tissue: SLE/ Sjogren's/ Primary biliary cirrhosis

6. Vascular: arterial embolism, polyarteritis nodosa

7. Metabolic: hypertriglyceridemia (may cause normal amylase); hyperparathyroidism

8. Inherited metabolic: cystic fibrosis, hereditary pancreatitis with 80% penetrance due to trypsinogen gene mutation.

9. Tropical pancreatitis: Childhood pancreatitis in India of unknown etiology.

10. Idiopathic

Amylase > 3x upper limit of normal is 98% specific for pancreatitis.

For predicting severe pancreatitis, IL6 has S & S of 100% and 86% but is not always available by hospital lab.

Cullen's sign: blue color around the umbilicus (hemoperitoneum).

Turner's sign: Blue to green color on the flank (catabolism of hemoglobin).

Hereditary GI syndromes:

FPPC: colonic polyps

Gardner Syndrome: Bone and soft tissue tumors. Do endoscopy and find multiple peri-ampulary carcinoma and colonic and duodenal polyps.

Peutz Jegher's syndrome: Melanotic spots on lips, buccal mucosa and skin. Hamartomas of small bowel, colon and stomach... occasionally malignant, in the small bowel (16 x normal).

Turcot's syndrome is defined as the presence of hereditary adenomatous polyposis and tumors of the central nervous system, including medulloblastoma.

Non-polyposis coli (Lynch syndrome)

Three 1st degree relatives with Colorectal cancer over 2 generations, at least 1 less than age 50. Also, increased risk for ovarian and endometrial cancer. For a relative, have colonoscopy every 3 years beginning 10 years prior to the youngest age of cancer.

For normal individuals, colonoscopy every 10 years if normal (including hyperplastic polyps) is one recommendation.

REVIEW

Differential diagnosis of peptic symptoms:

Heartburn suggestive of GERD

Dyspepsia suggestive of gastric ulcer or motility disorder

Peptic ulcer disease pain

Heartburn suggestive of GERD:

Medical: obesity, pregnancy, sleroderma, myositis, or hiatal hernia.

Large fatty meals, coffee, alcohol, chocolate, anti-cholinergics, smooth muscle relaxants (albuterol, CCBs, nitrates, sildenafil).

May be relieved by milk or antacids.

Retrosternal burning radiating to the neck most commonly ½ to 2 hours post prandially.

May be associated with radiation to arm, regurgitation, cough, wheezing, or dysphagia.

Worse when supine.

Acid or biliary taste.

May awaken patient from sleep.

Risk factors are obesity, pregnancy, scleroderma, myositis, and hiatal hernia.

Dyspepsia suggestive of gastric or motility disorder (non-ulcer dyspepsia):

Epigastric fullness, Belching, Bloating, nausea, food intolerance.

Antacids give partial or no relief.

Management of GERD:

Weight loss,

Avoidance tight clothing,

Elevation of the head of the bed with wooden blocks by 6 in (pillows can make things worse by abdominal compression!)

D/C smoking

No large meals before lying down,

None of the following

- cigarettes
- chocolate,
- alcohol,
- coffee,
- mint,
- fatty foods,
- orange juice,
- beta blockers,
- nitrates, and
- anticholinergics

PUD pain is suggested by

Similar to non-ulcer dyspepsia except

Relieved by food and ant-acids: Duodenal ucler.

Worse with food: Gastric ulcer.

Less likely to have bloating.

Pain awakens patient from sleep.

May be relieved by antacids.

Differential diagnosis includes angina, DES, biliary disease, pancreatic disease, cancer.

Alarm symptoms are:

Onset after age 50.

Anorexia

Weight loss

Dysphagia

GI bleeding – either gross or occult>> This implies stool guiacs in GERD or dyspepsia.

Anemia >> This implies you obtain a CBC in GERD or dyspepsia.

Vomiting

90% of PUD patients are either infected with H pylori or are taking NSAIDS or both.

If a patient has Dyspepsia without classic GERD symptoms and there are no alarm features present, stop NSAIDs, stop PPIs and anti-H2 agents for 2+ weeks and do stool antigen test.

If positive, treat for H pylori. If negative treat symptoms. If symptoms persist, do endoscopy.

Results of treatment of H. Pylori with O-CLAM: Omeprazole 20mg, Amoxycillin 1gm, Clarithromycin 500 BID x 7 days. (Gut 2002:50:26.)

Symptoms	OAC	Placebo
Reflux	24%	12% (significant)*
Ulcer	27%	17% (significant)
Dysmotility	21%	16% (not significant)

*Others indicated no effect on GERD but positive impact on dyspepsia.

With eradication of H. pylori infection, H. pylori ulcers are cured and ulcer recurrence is decreased to less than 5% in developing countries.

In patients with uncomplicated H. pylori-related peptic ulcer disease, it is not necessary to maintain the patient on long-term antisecretory therapy after uncomplicated H. pylori eradication therapy.

Helicobacter pylori occurs in 95% of duodenal ulcers and 75 to 85% of gastric ulcers.

Only 15% of infected individuals develop peptic ulcer disease.

H. pylori colonization produces urease, which hydrolyzes urea to ammonium ion and carbon dioxide, which increases the gastric pH and helps the organism avoid the harmful effects of gastric acid.

For stomach ulcers, H. pylori promotes inflammation by generating inflammatory cytokines, increased hydrogen ions by breakdown of ammonium ion, and proteases and phospholipases that cause degradation of the mucus gel layer that protects the gastric mucosa from the stomach acid.

For causing duodenal uclers, H. pylori infection may cause gastric metaplasia in the duodenum and thus create an environment for infection or it may cause increase stomach acid and decreased duodenal pH, causing duodenal ulceration.

The 1-year relapse rate of duodenal ulcers after eradication of H. pylori is less than 15%.

Causes of acid secretion: acetylcholine, caffeine, histamine, and gastrin.

Sucralfate, a complex polyaluminum hydroxide salt, binds tightly to the ulcer bed

at acid pH to promote healing. (Does not effect pH.)

Sucralfate stops diffusion of hydrogen ion to the base of the ulcer and binds bile salts and pepsins.

Typhlitis or necrotizing enterocolitis, is a poorly understood phenomenon that occurs primarily in immunocompromised patients. It probably involves a combination of mucosal injury to the bowel wall from cytotoxic chemotherapy, neutropenia, and impaired host defense against microorganisms. The cecum is almost always involved, but other parts of the ascending colon and terminal ileum also may be involved. Blood, stool, and C. difficile cultures should always be performed. A surgical consult is mandatory, and patients with evidence of bowel perforation or infarction should receive an exploratory laparotomy. Others may be treated conservatively with broad-spectrum antibiotics, serial examinations, and periodic CT scans.

MedStudy:

Esophogram in solid dysphagia is still the 1st test because if there is a diverticulum, there is increased risk of perforation, and also, because there may be an extrinsic mass as a cause of the dysphagia.

Enterocyclis is a small bowel barium study using an NG tube to place the barium and is useful to diagnosis Crohn's disease.

Treat SBP with cefotaxime 2gm q6hr (3rd generation; not optimal for pseudomonas, which requires ceftazidime or cefepime.

INFLAMMATORY BOWEL DISEASE October 20, 2005

	age onset	Smok-ing	Oral cont's	appen-dectomy	mono-zygotes	skip areas	deep	crypt absce sses	aph-thous ulcers	AB@
Regional enteritis (Crohn's)	15-30, 60-80	induces	rr 1.9	No effect	67% concord	yes	yes	no	yes	ASCA $
Ulcerative colitis	15-30, 60-80	protects	rr 1.0	Pro-tects	8% concord	no	no	yes	no	P-ANCA (70%)

*Both have incidence around 10/100,000, have ages of onset 15-30 and 60-80, are most common in Jewish, then whites, then African Americans.

@ Anti-Saccharomyces Cervisiae antibody; P-ANCA: Anti-myeloperoxidase antibody.

$In Crohn's disease, there is a major new genetic susceptibility gene locus with mutations designated NOD2 and CARD15. (These are also markers for Blau syndrome: Autosomal dominant, early onset granulomatous inflammation of joints, skin, and uveal tract.)

HARRISON'S ACCESS MEDICINE

Is cholelithiasis of rf for cholangiocarcinoma? Is rubber industry?

AST, ALT up to 400-500

*hepatitis C

*alcoholic hepatitis.

AST, ALT above 500 excludes these, but would be consistent with:

*Hep A and B

*Severe CHF with hypotension

*Hepatic vein thrombosis (Budd-Chiari syndrome)

Case:

51 y.o. man

Fever, RUQ pain and tenderness, nausea

WBC 13,000

Bilirubin 2.4 mg/dL

US: poor quality; mild intra-hepatic duct dilation, thickened gallbladder, but no obvious stones.

The doctor starts anti biotics.

What is the next test:

a) technicium HIDA scan or b) ERCP.

Answer is HIDA. In patients with cholecystitis, either calculous or acalculous, the cystic duct will not be patent and the gallbladder will not be visualized. There is no evidence of choledocholithiasis, and so ERCP is not indicated.

Table on ucler findings:

Endoscopic finding	**Risk of re-bleed**	**mortality rate**	**action**
Active bleed	55%	11%	3 day observation
Nonbleeding visible vessel	43	11	"
Adherent clot	22	7	" ? days*
Flat pigmented spot	10	3	" ? days*
Clean ulcer base	<5	2	discharge

_____

*Harrison's says "non clean ulcer base" lesions are observed for 3 days.

NEJM 1994;331:717.

The majority of episodes of acute diarrhea are self-limited and require no evaluation or treatment.

Indications for evaluation of acute diarrhea are:

*profuse diarrhea with dehydration,

*grossly bloody stools,

*fever above 38.5øC (101.3øF),

*prolonged-duration severe abdominal pain, and

*extensive co-morbidities.

	Amylase	Lipase
pancreatitis	^	^
gallstones	^	^
gut mucosal lesions	^	^
renal failure	^	^
parotitis	^	nl
macro-amylasemia	^	nl
tub-ovarian disease	^	nl
chronic alcoholism	^	nl

Most useful facters adversely affecting survival in acute pancreatitis:

1) **Organ Failure**

2) **Pancreatic necrosis**

3) **BMI >29**

4) **HCT > 44%**

5) hyperglycemia, hypocalcemia, hypoalbuminemia.

(Not often cited:

CRP > 150 mg/L

Typsinogen activation peptice)

RANSON CRITERIA: (GO TO CALCULATOR)

0 hours	48 hours
Age > 55	HCT drop 10%
WBC>16,000	BUN increase > 5.
Glucose > 200mg/dL	CA < 8
LDH>350	PO2 < 60
AST>250	Base deficit > 4
	Fluid needs > 6 liters

Apache II score > 8 (cumbersome)

What's true about cardiac cirrhosis?

*Severe right-sided heart failure may lead to chronic liver injury and cardiac cirrhosis.

*Elevated venacava increases hepatic central vein pressure so pathology extends outward from central vein rather than from the portal triads (portal venule, hepatic arteriole, bile ductule).

Gross examination of the liver shows a pattern of "nutmeg liver."

*AST & ALT mildly increased, except with severe CHF & hypotension.

*Budd Chiari can cause the same LFTs and pathology but is differentiated clinically.

*Constrictive pericarditis can cause a similar picture. It is suspected on eccho and confirmed by right heart cath showing a square root sign due to limited right heart filling diastole.

Gastric outlet obstruction ----- enlarged gastric bubble with decompressed small intestinal loops..

Gastroparesis ----- no radiologic changes.

For acute pancreatitis, commonly associated drugs are sulfonamides, estrogens, 6-mercaptopurine, azathiaprine, anti-HIV medications, and valproic acid, HCTZ, furosemide, ASA, and sulindac.

Pancreatic insufficiency >> decreased fat digestion >> decreased fat absorption >> decreased absorption of A, D (osteopenia), E (areflexia), decreased vibration & position sense), and K (increased PT).

Pancreatic insufficiency >> decreased enzymatic digestion of B12 binding proteins >> decreased B12 and macrocytic anemia.

UC: continuous areas, superficial inflammation, crypt abscesses.

Crohn's: skip areas, cobble-stoning, deep penetration of inflammation to submucosa.

Antibiotic-associated colitis: pseudomembranes.

Herpes proctitis: similar to IBD in immunocompromised and immune-competent patients macroscopically but is limited to the anorectum.

Cirrhosis:

Synthetic problems:

*edema (v albumin)

*bruisability (v vitamin K, v platelets)

*gynecomastia, testicular atrophy, decreased body hair, palmar erythema (increased androstenedione from decreased liver clearance)

*asterixis and encephalopathy (ammonia)

*parotid gland and lacrimal gland hypertrophy

*Dupuytren's contractures

Portal systemic pressure:

*varices and GI bleeding

*Thrombocytopenia (splenomegaly)

*spider angiomata

*caput medusa

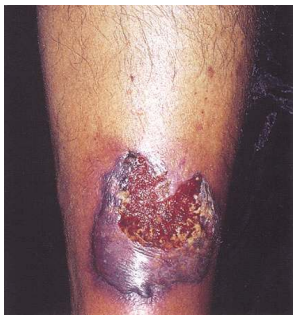
Alcoholic cirrhosis has a micronodular appearance on biopsy.

Viral Hepatitic cirrhosis has a coarsely nodular appearance on biopsy.

Pyoderma gangrenosum (PG).

10% of cases of UC.

Severe disease.



Begins as a pustule, eventually ulcerates.

Tender with necrotic tissue and exudate.

Dorsum of feet and legs (but anywhere).

Rx=Intravenous glucocorticoids (antibiotics if secondary infection).

Ddx: deep fungal infections, ecthyma gangrenosum (which is typically painless) as a result of disseminated Pseudomonas infection, sporotrichosis, and Mycobacterium marinum (treated with clarithromycin plus rifampin). Other extracolonic dermatologic manifestations of inflammatory bowel disease include erythema nodosum and neutrophilic dermatosis (Sweet's syndrome).

Gamma glutamyltransferae (GGT) indicates liver disease: cirrhosis, hepatitis, etc.

Case:

17 y.o. Asian (less commonly Blacks, and even less commonly Northern Europeans)

Abd. Bloating, diarrhea, post dairy.

Dx=lactase deficiency. Lactose, the disaccharide present in milk, requires digestion by brush border lactase into glucose and galactose. Lactase is present in the intestinal brush border in all species during the postnatal period but disappears except in humans.

Ddx: irritable bowel syndrome.

Rx= Avoidance of hi lactose (milk, ice cream)

Oral galactosidase ("lactase") enzyme replacement.

Case:

62-year-old woman.

>crampy abdominal pain

>watery diarrhea

>weight loss

>Colonoscopy: gross: normal colonic mucosa.

>Colonoscopy: Biopsy: inflammation with extensive subepithelial collagen deposition and lymphocytic infiltration of the epithelium.

Dx=Collagenous colitis.

Rx=Bismuth subsalicylate.

(CCBs and nitrates can treat achalasia!!)

CMV esogphagitis and colitis are treated with gancicyclovir. CMV that is resistant is treated with Foscarnet.

Barrett's esophagus: metaplasia of the squamous epithelium of the distal esophagus to columnar epithelium.

Treatment with acid suppression does not cause regression of metaplasia.

Longa segment (> 2 cm) present in 0.5% of population.

Short segment (<2 cm) is present in 20% of population.

The risk of adenocarcinoma is 0.5% per year.

Patients with short-segment disease are not routinely followed with repeated esophagoscopy,

whereas those with long-segment disease require surveillance at 1-year intervals for the first 2

years. If no progression is detected, surveillance can be done every 2 to 3 years.

The treatment of choice for high-grade dysplasia is esophagectomy of the diseased segment. Photodynamic laser therapy and thermocoagulation are being developed as alternatives to esophagectomy in patients with established high-grade dysplasia.

In those with longer sections of metaplasia (longer than 3 cm), the risk of adenocarcinoma is 30 to 125 times that of the general population. The mean annual incidence is 1 in 200 patient years.

Pill-induced esophagitis is usually caused by antibiotics (tetracyclines, penicillin, and clindamycin). Less commonly: NSAIDS, bisphosphonates, vitamin C and ferrous sulfate.

Case

25-60 y.o. man or woman (equal frequency)

chest pain

dysphagia

regurgitation

abscence of gastric air bubble on CXR.

Esophogram: bird’s beak.

Dx=Achalasia.

Case:

Painless GI bleeding.

Tagged red blood cell scan localized the bleeding source.

No colonsocopy.

Procedure of choice: mesenteric angiography with selective embolization or coiling of the culprit artery. (Low complication rate–colonic ischemia in 10%.)

There is an approximately 25% risk of acute rebleeding.

Indications to proceed with surgical intervention include unstable vital signs or a requirement of more than 6 units of packed red blood cells in 24 h.

Risk factors for diverticular bleeding are hypertension, atherscl erosis, and NSAIDs.

Constipation, a low-fiber diet, laxatives, and diverticulitis are not risk factors for bleeding.

Case:

Vomiting, fever, severe retrosternal chest pain, subcutaneous emphysema, mediastinal crunch with inspiration.

Left pleural effusion.

Elevated amylase.

Dx=Esophogeal rupture (Boerhaave's syndrome).

Diagnostic confirmation: PO water-soluble gastrograffin leaks into the mediastinum on CXR.

Treatment includes broad-spectrum antibiotics and surgical repair of the laceration.

Case

Severe anal pain, worse with defecation.

Mild bleeding, staining toilet paper or coating the stool.

Associated constipation, trauma, Crohn's disease, tuberculosis and syphilis.

Exam: Fissure is in the posterior midline with a skin tag at the distal end. There is hypertrophied anal papilae at the proximal end.

Dx: Chronic anal fissure.

Ddx: Rule out Crohn’s disease, STD, or anal cancer, particularly if there is a lateral location.

Rx: Decrease sphincter tone by topical nitroglycerin or botulinum toxin. Surgery with lateral internal sphincterotomy and dilation.

Acute anal fissures appear like a linear laceration

Rx is conservative with increased dietary fiber intake, topical anesthetics or glucocorticoids, and sitz baths.

Indications for ERCP:

Unexplained jaundice

Evaluation of periampullary masses.

Unexplained recurrent pancreatitis (examine sphincter of Oddi manometry

Retrieve impacted common bile stones and relieve strictures, both pancreatic and biliary.

Relieve pseudocysts when there is a pancreatic duct stricture preventing adequate drainage.

ERCP is contra-indicated in acute pancreatitis if there is no evidence of a complicating

common bile duct stone.

Case:Woman age 55.

NSAID use.

Watery diarrhea, abdominal pain, and GI bleeding.

Dx: Collagenous and NSAID colitis.

Complications of NSAID colitis may include stricture, obstruction, perforation, and fistulization.

Case: Over age 40, white male or female (later age), Depression, fatigue, impotence, & arthralgias.

Fe/TIBC > 45% has sensitivity of 98%. If positive, repeat it with an overnight fast. Fe/TIB>60%:hi spec. If positive, genetic testing confirms hemochromatosis: C282Y and H63D genotypes. C282Y homozygosity is most common.

C282Y homozygosity with indirect iron store indices (i.e., increased ferritin or Fe/TIBC) can be treated.

C282Y/H63D patients should have indirect blood studies, and if these are positive, liver biopsy, which, if positive, would lead to treatment.

Case

23-year-old Turkish, Arab, Armenian, or Sefardic Jewish female

Multiple episodes of severe abdominal pain since age 15.

The pain lasts 2 to 3 days and then spontaneously resolves.

Normal radiologic studies and exploratory laparatomy and/or appendectomy.

Migratory arthritis of knees and ankles.

Positive family history for same complaints.

PE 39.8øC (103.6øF). Heart rate is 130.

Chest exam: ? pleural effusion with decreased breath sounds and dullness to

percussion of half the lung field.

Moderate diffuse abdominal tenderness with mild rebound, but no guarding.

Swollen left knee erythematous with an effusion.

Rash (erysipeloid) of lower extremities

WBC: 15,000.

ESR 110 s.

CT: Intra-pleural and intra-peritoneal fluid.

Arthrocentesis: white blood cell count of 68,000 with 98% neutrophils.

Culture is negative at 1 week.

The patient's symptoms resolve over the course of 72 h.

Dx: FMF. Ddx: Acute intermittent porphyria (but this would not give serositis and joint effusions.)

Diagnosis usually can be made with clinical criteria alone, although there is gene testing available for the most common mutations that cause the disease.

Treatment is colchicine, which can prevent pain and amyloidosis.

The recommended screening test for acute pancreatitis is both serum amylase and lipase.

The sensitivity of the serum lipase level for acute pancreatitis may be as low as 70%. Hypertriglyceridemia can falsely lower levels of both amylase and lipase.

Serum amylase level may be elevated in renal insufficiency, salivary gland lesions, tumors, burns, and diabetic ketoacidosis, intestinal obstruction and peritonitis.

The pancreatic isoenzyme level diagnoses acute pancreatitis in confounding conditions.

Purtscher's retinopathy is a relatively rare but devastating complication of acute pancreatitis. It is characterized by sudden loss of vision and the presence of cotton-wool spots and hemorrhages in the area of the optic disc and macula. The cause is thought to be occlusion of the posterior retinal artery by aggregated granulocytes.

Both CAH and CPH may be associated with serologic evidence of hepatitis B infection.

Only liver biopsy distinguishes chronic active hepatitis (CAH) and chronic persistent hepatitis.

Chronic active hepatitis has piecemeal necrosis (erosion of the limiting plate of hepatocytes surrounding the portal triads), hepatocellular regeneration, and extension of inflammation into the liver lobule, features are not seen in chronic persistent hepatitis.

Case

21 y.o. woman begins daily isoniazid therapy for a positive tuberculin skin test.

She feels well, and the physical examination is unremarkable.

LFTs show ALT of 150 and total bilirubin of 1.o mg/dL.

Management:

Continue INH and monitor for symptoms.

If the patient is elderly, there is a higher risk of developing hepatic failure.

INH occurs in 10% of persons treated with isoniazid.

The risk of mortality among these is 1/100,000.

Relative contra-indication to INH in those with active liver disease.

Approach to INH monitoring in those receiving INH for latent TB:

Obtain baseline LFTs in

*Pregnant

*HIV positive

*Liver disease

*Older patients taking potentially hepatotoxic drugs

Monitor monthly for symptoms of hepatitis: fever, jaundice, n, v, abdominal pain.

Monitor LFTs “routinely” in patients with abnormal baseline LFTs, HIV positive, pregnant patients, those developing symptoms while taking INH.

The approach to INH monitoring in those being treated for TB is the same as above, except that LFTs are obtained in all patients.

Patients most appropriate for the approach of gallstone dissolution include those with a radiolucent, solitary stone less than 2 cm in diameter in a well-contracted gallbladder.

In this patient's case the stone is radiopaque.

Moreover, gallstones will recur in about 30% of patients treated with a nonsurgical therapy.

GERD with reflux esophagitis can cause heme positive stool.... per Harrison's question.

Laxative use is consistent with an osmotic gap: 2([Na] + [K]) <290 mosmol/kg. However, certain anionic laxatives containing sulfates or phosphates produce diarrhea without an osmotic gap, since sodium secretion occurs in response. In these cases direct measurement of the laxative in the stool is required to confirm the suspicion of laxative abuse.

A pungent stool odor with the presence of undigested meat in the stool may be suggestive of pancreatic insufficiency.

Case

57-year-old man

PUD improves after H. Pylori eradication, but symptoms recur in 3 months.

Stool analysis for H. pylori antigen is negative.

Upper GI endoscopy reveals esophagitis and multiple ulcers of the duodenum.

There is a history of kidney stones and chronic diarrhea.

There is a positive family history of pituitary adenoma and parathyroid hyperplasia.

Fasting gastrin levels are elevated and basal acid secretion is 15 meq/h.

Dx: r/o gastrinoma (ZE syndrome).

The best test is the secretin stimulation test. An increase in gastrin levels >200 pg within 15 min of administering 2 g/kg of secretin by intravenous bolus represents a paradoxical reponse (normally secretin inhibits gastrin secretion by the G cells) and has a sensitivity and specificity of >90% for ZES.

If positive, endoscopic ultrasonography can locate the gastrin-secreting tumor.

Genetic testing is done for mutations Multiple Endocrine Neoplasia type I (Pituitary adenoma, parathyroid hyperplasia, and either pancreatic or duodenal gastrinoma or insulinoma.

Use the secretin test for chronic pancreatitis, to detect the failure to secrete adequate amounts of bicarbonate-containing fluid and/or pancreatic enzymes.

Bicarbonate output declines first, then enzyme secretion.

Steatorrhea occurs only in the setting of markedly low intraluminal levels of pancreatic lipase.

HbsAg status relates to infection (which may be acute or chronic), while HbeAg status relates to infectivity.

HbsAg status	HbeAg status*	
infection status	infectivity status	Clinical state
Ag+,Ab-	Ag+, Ab-	Chronic infection, high infectivity
Ag+,Ab-	Ag-,Ab+	Chronic infection, low infectivity

*HbeAg positivity is a marker of viral replication and correlates with high HBV DNA.

RR for Duodenal ulcer:

NSAID use 10- 20x

H. Pylori infection 5-7x

Cigarette smoking 2x

Gastrinoma (ZES) Extremely high

Emotional stress 1x

HEPATITIS B MANAGEMENT

Indications for treatment:

HbeAg positive OR HbeAg negative +HBV DNA positive.

ALT above 2x normal after 3 to 6 months of observation

ALT below 2x normal but with recurrent flares of hepatitis

Co-existent polyarteritis nodosa

Drugs:

Interferon alpha. I.V. Most efficacious. Shortest duration of treatment.

Lamivudine. Oral

Adefovir (nephrotoxic in high doses). Oral

Entecavir (carcinogenic in rodents at high doses). Oral

Noncaseating granulomas, when present, are pathognomonic of Crohn's disease.

Other features do not distinguish: oral ulcers, continuous colonic involvement, crypt abscesses.

Nifedipine can control symptoms of achalasia in some patients.

Ddx of acute appendicitis:

Crohn's of terminal ileum.

Yersinia enterocolitica gastroenteritis

Mesenteric lymphadenitis

Ovarian torsion

Ovarian infection.

Dermatologic correlates of GI conditions

Skin lesion	Description	GI Correlate
Acanthosis nigricans	verrucous, hyperpigmented, elevated skin lesion in axilla or flexor surfaces	cancer of stomach, pancreas, colon
Pyoderma gangrenosum	round to oval, ulcerated center, covered with yellow exudate or crust	IBD
Erythema nodosum	raised red lesions over shins	IBD, TB, histoplasmosis, leprosy
Dermatitis herpetiformis	Red, papular, pruritic eruption on extensor surfaces of elbows, knees, buttocks. (85% of patients with DH have celiac sprue!!)	celiac sprue (24% of patients with sprue have DH. !)

Diagnosis of chronic pancreatitis requires positive documentation of two of the following:

*symptoms (abdominal pain radiating to the back).

* radiologic studies (Typical CT or calcifications on flat plate).

*abnormal test(s) of pancreatic function (bentiromide test, secretin test, 13 C-breath test),

Prophylaxis of acute hepatitis B infection: Passive immunization with HBIG (0.6 mL/kg), plus

Active immunization using HBV vaccine, administered at a separate site, as early as possible.

Case

65 y.o. man with left lower quadrant abdominal pain and fever.

Do you do endoscopy?

No: Endoscopy is contraindicated in the presence of diverticulitis because of the possibility of

perforation.

(Diverticulitis is usually left sided (distal colon), whereas diverticulosis (I believe) is usually right sided.)

Case

A 65-year-old man

N,V,D, abdominal pain.

(No Fever: toxic megacolon.)

Recent narcotics, CCBs, abdominal surgery, pneumonia, MI, CHF, or retroperitoneal pathology (e.g., pancreatic cancer)

Hypokalemia

Flat plate: Air for rectum to splenic flexure of the colon, no air-fluid levels (true mechanical obstruction).

Dx: acute colonic pseudo-obstruction (Ogilvie's syndrome)

Ddx: true mechanical obstruction OR toxic megacolon.

Rx: Remove drugs; Do colonoscopy to decompress the colon.

Causes of Colonic obstruction: 1) Ca, 2) Sigmoid diverticulities, 3) Volvulus. (90% of cases)

Causes of Small Intestinal obstruction: 1) Adhesions, 2) Hernias (75%)

Case

25-year-old man

Lower abdominal pain, chronic diarrhea, and weight loss.

Also, joint pain.

PE: oral aphthous ulcers and a genital ulcer. Uveitis. Erythema nodosum.

Colonoscopy: Discrete ulcers of terminal ileum, cecum, and ascending colon.

Pathergy: 2 mm papule 48 hours after insertion of a needle.

Dx: Beh‡et's disease

Ddx: conditions with oral aphthous ulcerations include pemphigus, celiac disease, vitamin deficiencies, malabsorptive states associated with macrocytic anemias, HSV, and HIV.

Case

28 yo man with pharyngitis, sore throat, fever and anorexia for 3 days.

PE: T 101. pharyngeal erythema. Mild jaundice.

Hgb 14.0 WBC 12,000. AST, ALT, & alk phos are normal. Total bilirubin is 3.6.

Dx: Gilbert’s syndrome. Most of the bilirubin is unconjugated bilirubin. Induction of hyperbilirubinemia can be caused by infection, exertion, surgery, alcohol, fasting, or rifampin. This patient had both infection and fasting (anorexia).

Causes of indirect hyperbilirubinemia: Cirrhosis. Hemolysis. Gilbert's syndrome.

Causes of direct hyperbilirubinemia: Hepatitis. Extrahepatic obstruction: e.g., Gallstones or pancreatic cancer.

Direct hyperbilirubinemia is unbound to albumin (indirect is bound) and leads to bilirubinuria. (i.e., in hepatitis, gallstones, pancreatic cancer).

Increased ALT is more sensitive and specific for liver disease than AST.

GGTP (Gamma glutamyl transferase) is sensitive but not specific for liver disease.

Acute biliary obstruction can cause AST & ALT elevations of 1,000 or more.

Hyperplastic polyps are totally benign colonic polyps.

Sessile polyps are usually villous adenomas and have high malignant potential.

90% of pancreatic cancers are of ductal origin and 5% are of islet cell origin.

DRUGS AND LIVER SYNDROMES:

Diffuse hepatocellular degeneration and necrosis (similar to viral hepatitis): halothane, isoniazid (INH), ketoconazole, methyldopa, and phenytoin, and acetaminophen is one of the most important causes of massive liver injury

hepatic failure.

Cholestatic picture: estrogens, amoxicillinclavulanate, piroxicam, and trimethoprim-sulfamethoxazole

Fatty liver: Steroids

Microvesicular steatosis (accompanied by profound lactic acidosis): tetracycline, valproic acid, and ddI.

Esophagitis biopsy: large multinucleated cells with Cowdry type A bodies HSV.

"Refractory candidiasis": think aspergillosis.

Mid esophogeal injury: Pills.

Adverse effects of IBD drugs:

Sulfasalazine: folate deficiency; reversible oligospermia

Olsalazine: diarrhea in 6% of patients

Azathioprine: allergic pancreatitis (in 15%).

Metronidazole: peripheral neuropathy

Polyarteritis nodosa:

GI: Abgdominal pain, GI bleed, ischemia, infarctions of bowel, liver or pancreas. 44%

Rash, purpura, livido reticularis, Raynaud's (43%)

HPT and/or renal insufficiency: 60%

Arthritis, arthralgia, myalgias: 64%

Peripheral neuropathy: 51%

CHF, MI, pericarditis 36%

CVA or seizures 23%

Hepatitis B is strongly associated with polyarteritis nodosa.

False positives in FOB testing:

NSAIDs

IRON

Red meat

Cauliflower or other peroxidase vegetables: raddish, turnip

False negatives: Vitamin C.

After an acute upper GI bleed, a gastric ulcer requires follow up and biopsy to rule out malignancy. This is not so with Duodenal ulcer.

Benign post operative cholestasis is a conjugated hyperbilirubinemia.

Pancreatic insufficiency >> decreased fat digestion >> decreased fat absorption >> decreased absorption of A, D (osteopenia), E (areflexia), decreased vibration & position sense), and K (increased PT). Harrison's e medicine, question 9 for med students says not D or K.

??????

Patients with celiac disease should stay on gluten free diet indefinitely because a) there may be subclinical deficiencies, and b) there may be some increase in GI malignancies.

Case

23 y.o. woman

Weight gain.

Rotavirus in community.

Ankle swelling.

Bilateral pedal edema.

Decreased breath sounds at bases bilaterally.

Abdominal fluid wave.

Lab: Hypoalbuminemia

Dx: Protein losing enteropathy.

Confirm: Alpha 1 anti-trypsin clearance in a 24 hour stool

Causes: Viral, rheumatoid arthritis, collagenous colitis, amyloidosis

Rx: Low fat diet with medium chain triglycerides.

Causes of hypoalbuminemia:

nephrotic syndrome; cirrhosis; CHF; malnutrition; acute & chronic inflammatory responses (this last causes and increase in TNF and IL-6 causing increased vascular permeability (albumin extravates); increase albumin degradation, and decreases synthesis of albumin.

Hepatitis C spread:

For monogomous relationships, they may not want to bother with condoms (only for multiple sex partners).

The risk of transmission among monogamous partners is estimated to be 0.1% annually.

Do not share razors or nail clippers.

Hep C is not spread via drinking glasses, utensils, hugging, sneezing, etc.

Parental exposure to blood is major source of infection.

Progression of Hepatitis C to cirrhosis is increased in men, heavy alcohol use, and infection after age 40.

In those with chronic infection, serious liver disease develops in 20%.

Genotype and viral load are NOT predictors of progression to fibrosis!!

Combination therapy with interferon and ribavirin is the standard treatment of HCV.

Genotype 1 is more difficult to clear than genotypes 2 and 3, but this does NOT determine likelihood of progression to end-stage liver disease.

Higher baseline viral levels also tend to predict poorer response to treatment but, again, do not predict progression to fibrosis.

Patients with stages 3 and 4 (bridging fibrosis and cirrhosis) are less likely to achieve SVR.

Decreases in viral levels of < 2-log10 after 12 weeks of treatment are predictive of lack of response to therapy.

The major concerns with ribavirin are hemolytic anemia and teratogenicity, while the interferons (standard or the long-acting pegylated forms) have a long list of potential side effects, of which neuropsychiatric problems such as depression and irritability are often the most troublesome.

Although patients with higher levels of HBV DNA are more infectious than those with lower levels of viral DNA, the risk of transmission in the latter case is not zero. (Even when there is Anti-HepBe antibody present.)

In the case of this patient, having "undetectable" HBV DNA simply indicates a level of HBV DNA that falls below the limit of detection of an unamplified assay (on the order of 105 copies/ml).

Thus, precautions should be taken to prevent sexual or household transmission to her fiancé (use of condoms, immunization if required, etc.) and to her future children (HBIG and HBV vaccination).

Case:

60 y.o. man

Pruritis, headache, symptoms of PUD.

Splenomegaly

97% on room air

HCT 60, platelets 400,000, WBC 12,000

LAP score 110.

EPOser is low.

BM: ^ cellularity, no iron stores.

Dx: PV

Timing of etoh withdrawal

6hr 1.5 days: tremulous, anxiety, GI upset, diaphoresis, palpitations.

6hr 2 days: seizures

12hr 2days hallucinosis, auditory, visual & tactile

2 ds 4 ds DTs: agitation, ^T, ^HR. Rule of 5s: 5% get DTs, 5% die of DTs.

ALCOHOL POISONING

Blood etoh: mg/dL	Sx's
20 - 50 *	fine motor coordination
50 - 100	judgment, coordination
100 - 150	ataxia
150 - 250	lethargy, stupor, falling from chair
300	coma in non-habituated
400	death

*Legal limit in most states is 0.02%

Diagnosis of IBS

(Manning criteria – probability increases with increasing number present):

*Bowel movement relieves pian.

*More frequent stools with pain onset.

*Looser stools with pain onset.

*Visible abdominal distension.

*Mucous in stools.

*Sensation of incomplete evacuation.

(BLOATING occurs in either diarrhea or constipation predominant – MKSAP 13 update.)

RX:

Diarrhea predominant:

(1) Trial of Lactose free diet. D/C caffeine

(2) Rice, banana, cactus pear.

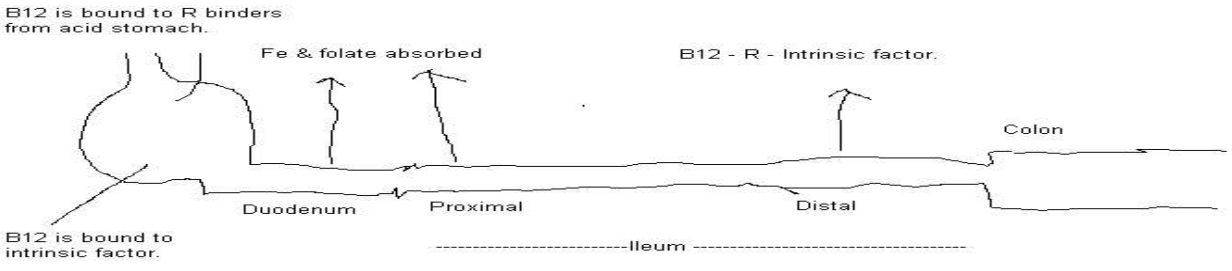
(3) Psyllium (Metamucil) 1 heaping TSP plus applesauce TID;

(4) Loperamide (Immodium) 2 mg after each unformed stool to a max of 8x daily, PRN

(5) Alosteron (Lotronex) can be given by GI specialists for unresponsive cases.

(6) Clonidine 0.1 mg bid improves diarrhea predominant (Camilleri, 2003).

Constipation predominant:



Hydration Ex

ercise

Fiber and mild laxative or stool softener:

>Psyllium (Metamucil) (fiber)

>Docusate calcium (Surfak) 240 mg QD, Docusate sodium (Colace) (stool softener) 50 mg tabs, 1 to 4 times/day OR OSMOTICS: polyethylene glycol (Miralax) OR sorbitol.

>Do NOT use Senna (May cause melanosis coli and changes in GI motility.)

>Hyoscyamine or Tegaserod (Zelnorm) (Tegasoerod is evidenced based).

With hemolysis, the liver conjugating system is overwhelmed and indirect bilirubin is increased.

Likewise with hepatic dysfunction.With post hepatic obstruction, direct bilirubin is increased.

HEPATIC ENCEPHALOPATHY

STAGES:

1. Behavioral Changes, handwriting and tremor.

2. SSAD: Slowing mentation, somnolence, asterixis, and disorientation to time.

3. Sleeping most of the time, incoherent, disorientation to place, asterixis, hyper-reflexia, Babinski +ve.

4. Coma.

HEPATHIC ENCEPHALOPATHY: PRECIPITANTS. Mnemonic is "CAT BICEPS":

CA of the liver

Thrombosis of the hepatic and portal veins

Bleeding & dehydration

Infection, particularly SBP

Constipation

Electrolyte abnormalities including alkalosis, hypokalemia, hypoglycemia & hypoxemia

Protein excess

Sedative medications

PHYSIOLOGY:

The Ammonia hypothesis (There are other hypothetical causes of HE involving adverse effects of liver failure on brain neurotransmitters, but the Ammonia hypothesis is the main paradigm.)

NH3 is possibly toxic to the brain by at least two mechanisms: 1) effecting the transport into the brain by other ammino acids, such as tyrosine, phenylalanine and tryptophan, which effect neurotransmitter synthesis of dopamine, norepinephrine, and serotonin. 2) Increased production of glutamine which is hyperosmolar and leads to cellular edema.

Key reactions are:

NH4+ <> H+ + NH3 (lipid soluble)

Glutamine < > Glutamate + NH4+

Glutamate <> alpha ketoglutarate + NH4+

NH4 + + ornithine >> urea cycle >> NH2-CO-NH2 (urea)

*NH3 is lipid soluble and diffuses across cell membranes, whereas NH4+ does not. This is particularly relevant in the gut, kidney, and brain.

*In the liver and brain, the reaction, glutamate + NH4+ >> glutamine, is favored.

*In the kidney, the reaction, glutamine >> glutamate + NH4+ , is favored.

*In the liver, NH3 is removed from the blood via the urea cycle (excreted in the urine) and via the synthesis of glutamine, which is taken up by renal tubular cells, converted back to glutamate, a ketoglutarate, and NH3, which traverses the tubular cell membrane into the urine, is acidified to ammonium, NH4+, and excreted.

*In the brain, NH3 is converted to glutamine and removed from the brain and thence to the kidneys.

PATHOPHYSIOLOGY:

*Cirrhosis decreases urea and glutamine synthesis and also leads to shunting of NH3 away from the liver.

*GI bleeding, constipation and high protein increase ammonia in the gut.

*Alkalosis acts in 2 ways: 1) In the NH3 <> NH4+ balance, alkalosis favors NH3 and hence causes increased uptake of NH3 by the brain. 2) In the kidney, alkalosis reduces the breakdown of glutamine to NH4+ and hence reduces NH3 excretion in the urine.

*Hypokalemia effects the reactions in the kidney and inhibits this process via the production of intracellular acidosis. (Not sure exactly how but it does.)

*Lactulose works by a) creating an osmotic stooling and enhancing the passage of protein, b) being metabolized to acetic acid by gut bacteria leading to NH3 being converted to NH4+ and being excreted.

*IV ornithine aspartate and PO Sodium benzoate consume NH4+ by formation of glutamine and hippurate respectively.

HEPATIC ENCEPHALOPATHY: TREATMENT

Identify the precipitating causes.

Correct the above, particularly infection, dehydration, hypokalemia, alkalosis, bleeding.

*Nasogastric tube lavage to clear blood in bleeding patient.

*Protein restriction is not recommended.

*Lactulose 45 to 90 gm/day titrated to 2 to 3 soft stools / day.

*Give lactualose enemas if it can not be taken orally.

*75% of patients will improve within 2 days. For those not improving give either i.v. ornithine aspartate 20 gm over 24 hours which increases glutamine synthesis from NH3 or PO sodium benzoate 5 gm BID which increases formation of hipurate from NH3.

*Give rifaximin rather than neomycin but it is not shown to work.

*Give flumazenil only if the patient has been given benzodiazepines.

ALCOHOLIC HEPATITIS: Fever, hepatomegaly, jaundice, anorexia and leukocytosis.

AST/ALT is greater 2 in most cases. AST level is less than 500 IU/L GGT is elevated..

For treatment, determine whether there is need for steroids with either hepatic encephalopathy or by using the discriminant function = 4.6 x (PT in excess of control) + bilirubin.(mg/dL)

A score greater than 32 indicates a 50% mortality and indicates need for steroids:

Prednisolone (not prednisone which can not be metabolized by the liver) 40mg/day x 4 weeks with taper.

Give PO nutritional support.

CAUSES OF INCREASED AMYLASE & LIPASE

Cause	Amylase	Lipase
Pancreatitis	UP	UP
Biliary lesions	UP	UP
Gut mucosal inflammation	UP	UP
Renal Insufficiency	UP	UP
Macroamylasemia	UP	nl
Parotid inflammation	UP	nl
Chronic alcoholism	UP	nl
Tubo-ovarian inflammation	UP	nl

NAFLD: If there is suggestion of cirrhosis (low albumin, hi INR), do a liver biopsy to distinguish steatosis from cirrhosis; this is important in order to screen for esophogeal varices and hepatocellular ca.

In short bowel syndrome, gastric fluid is increased and this can be decreased by a PPI.

Small bowel bacterial overgrowth cases inflammation of mucosa and decreased lactase; give lactose free diet.

Gastric outlet obstruction causes elevated serum gastrin.

For esophogeal candidiasis, give systemic fluconazol 400 mg/day; do not give topical antifungal.

Ascending cholangitis versus acute cholecystitis:

In the former there is pain, fever, and jaundice (charcot's triad) and hypotension and mental confusion (Reynold's pentad). The white count is elevated. Imaging shows a dilated duct.

In the latter, there is no elevation of the bilirubin and the duct is not dilated.

The former is treated with antibiotics and ERCP;

The latter is treated with antibiotics and pain medication.

Pregnancy has physiologically palmar erythema, spider angiomata, and increased alkaline phosphatase.

Pancreas divisum is a cuase of recurrent pancreatitis. Do ERCP.

Sarcoid can give mild liver enlargement and elevated alkaline phosphatase.

Cameron's erosions are linear erosions at the GE junction when there is a large hiatal hernia.

For dx of microscopic colitis, sigmoidoscopy with biopsies may be sufficient.

Case

72 yo man with dizziness, black stools, and bruising.

Postural hypotension, a large tongue, pedal edema

4+ proteinuria.

Dx=amyloidosis.

Three causes of transient transanimitis: shock liver (>5,000), toxic insults, choledocholithiasis (enzymes to 1,000).

For hep C, interferon can not be used if there is decompensated liver disease.

Entecavir is now the treatment for hepatitis B (MKSAP 14).

Fundi gland polyp is not malignant.

	SAAG >1.1	SAAG < 1.1
Ascites protein <2.5	Cirrhosis*	nephrotic syndrome*
Ascites protein >2.5	Right heart failure; hepatic vein thrombosis*	TB or CA

*Albumin is low.

Case

32 yo man with anorexia, nausea, vomiting and slight epidgastric tenderness.

Dx: Gastroparesis. R/o DM, hypothyroidism, and electrolyte disorders; if negative this isidiopathic gastroparesis. IV treatment of choice = erythromycin lactobionate 3mg/kg Q8Hrs; altrnative=metoclopramide 5 - 10 mg sc TID.

PO Rx: Frequent small low fat low fiber meals.

Risk for transplacental hepatitis C infection in the neonate is 5%.

Familial pancreatitis: 40 % risk of pancreatic cancer by age 70.

Get a HIDA scan in acalculous cholecystitis and for a gall bladder ejection fraction for biliary dyskinesia (no inflammation, no increased LFTs).

McBurney's sign: point tenderness 1 inch from the anterior superior iliac crest towards the umbilicus indicating an appendicitis that is inflaming the peritoneum (early stage of appendicitis does not localize.

Rovsing's sign is pain over the appendix in the RLQ when palpating the LLQ.

Kehr's sign: pain in the left shoulder due to peritonitis or ruptured spleen.

Hepatopulmonary syndrome=Triad of hypoxemia (PaO21<80), portal HTN, and pulmonary vascular dilation documented by either microbubble migration or Tech 99 albumen injection with increased brain uptake. Other features are: 1) Orthodeoxia (v PaO2 from supine to upright), clubbing and v CO diffusion. Treatment is liver transplantation.