

ACP Chapter Meeting November 2019: GI Update

Shan Cheng, MD

Indianapolis Gastroenterology and Hepatology



ACP GI Update

1. Ulcerative colitis/IBD
 - Diagnostics
 - Focus on therapy
2. Pancreatic cystic disease
3. Complementary/alternative medicine in functional GI disease (IBS/Functional dyspepsia)

Chapter I: Ulcerative Colitis/ Inflammatory Bowel Disease

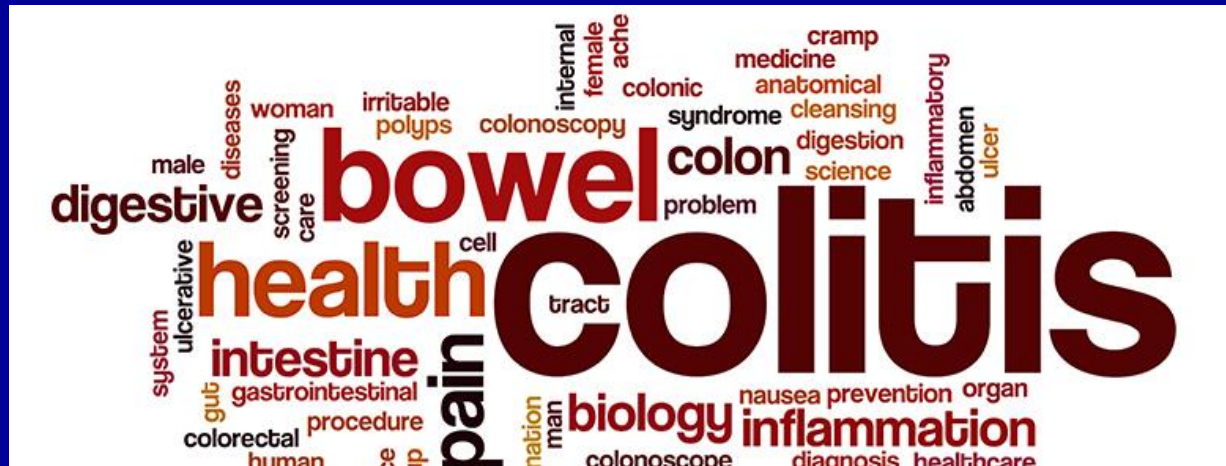
ACG Clinical Guidelines 2018
AGA Clinical Practice Guidelines 2019



Inflammatory Bowel Disease

- Two major diseases
 - Ulcerative colitis:
Mucosal inflammation in the colon
 - Crohn's disease:
Transmural inflammation throughout the GI tract
- Chronic inflammatory condition affecting the GI tract of variable severity, location, symptoms pattern
- Autoimmune pathways

The Clinical Presentation and Workup of Ulcerative Colitis



62 year old male presents to clinic with diarrhea and rectal bleeding....

HPI Points

- Duration
- Severity – Nocturnal, incontinence
- Fevers, sweats
- Prior workup
- Associated extraintestinal symptoms
 - Rash
 - Joint pain
 - Ocular disease
- Anorectal disease
- Associated autoimmune conditions
- Pain
- Family history – 10%

62 year old male p/w 10 weeks of recurrent diarrhea with multiple episodes of passing blood. Had some alteration in bowel habits in school years and prior colonoscopy at age 55 was normal except for hemorrhoids. Describes over 8 bm/day with occasional nocturnal symptoms

CBC notable for WBC 8, Hgb 8.1, MCV 68

Exam

- Pale
- Abdominal exam non-specific
- Severe disease – Hemodynamic instability, signs of malnutrition

Exam

Ask about skin changes

Erythema Nodosum



Exam

More skin changes

Pyoderma gangrenosum



Exam

Rectal and Peri-anal Exam



Labs

- CBC
- BMP
- LFTs
- ESR
- CRP
- Consider sprue serologies
- Stool studies more useful in acute phase disease

Imaging

- CT scan
- Abdominal plain films
- Small bowel imaging studies – evaluating for Crohn's
 - Small bowel follow through
 - CT or MR enterography
 - Capsule endoscopy



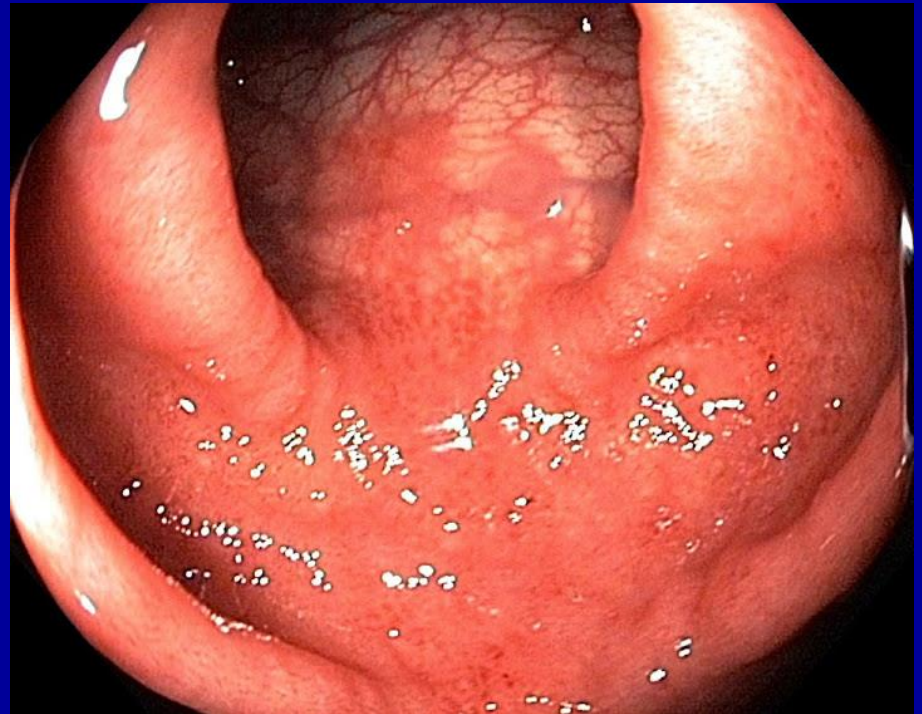
Differential Diagnosis

- Malignancy
- IBD – Ulcerative colitis vs Crohn's
- Functional GI – IBS et al
- Infectious colitis/STD
- Ischemia

- Diverticular colitis
- NSAIDs effects
- Radiation colitis

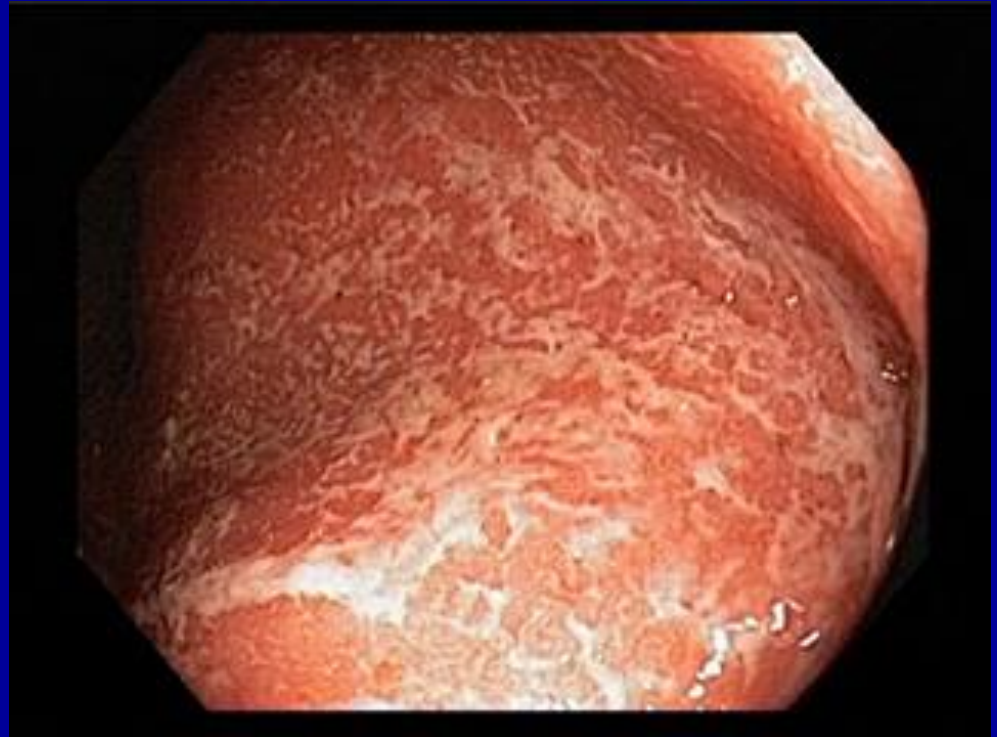
In this patient also consider workup for upper GI tract pathology

Colonoscopy



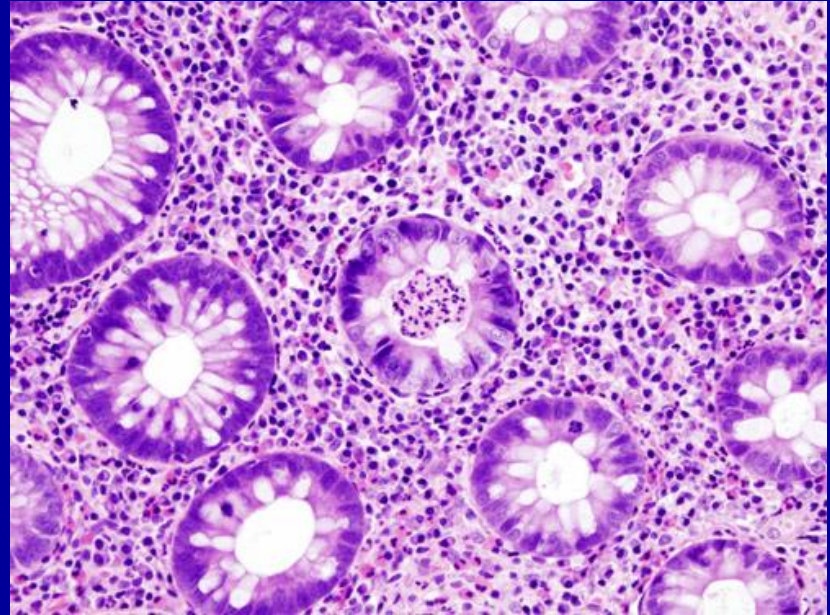
Colonoscopy

- Diagnosis
- Distribution
- Severity
- Complications
- Chronicity
- Bleeding



Pathology Findings

- Chronicity
- Crypt abscesses
- Lymphocytic and plasma cell infiltrates
- Absence/Presence of granulomas – reconsider Crohn's
- Rule out CMV

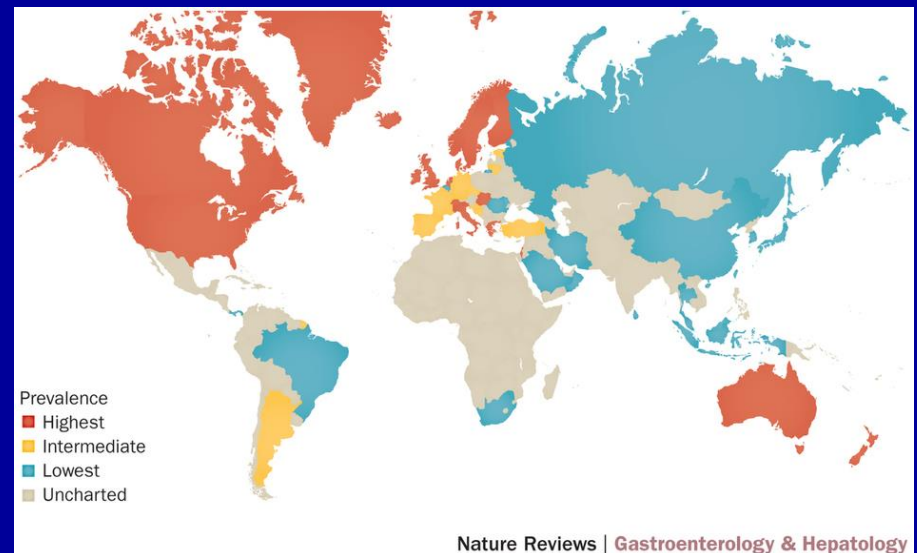


What is Ulcerative Colitis (UC)?

- Recurrent episodes of mucosal inflammation of the colon
- Rectum and extending proximal – typically continuous
- Imbalances between pro- and anti-inflammatory cytokines at the gut lumen
- Genetics/infectious/environmental theories

Epidemiology of UC

- Prevalence – 240 per 100,000
- M=F
- Slightly lower rates in non-whites
- Bimodal incidence
- Abx/Isotretinoin ?
- Smoking



Formal Definitions of Severity

- Mild disease - Majority
 - <4 bm/day with or without blood
 - Mild pain
 - No systemic toxicity
- Moderate disease
 - >4 loose/bloody stools
 - Mild anemia
 - Non-severe pain
- Severe disease
 - >6 bm/day
 - Severe pain, systemic toxicity, anemia, weight loss

Targeted Goals of Therapy

- Less than 2-3 bm/day
- No severe urgency
- No bleeding
- No significant pain/cramping



Worst Case Scenerios

- Fulminant colitis
- Toxic megacolon
- Perforation
- Severe bleeding
- Severe stricturing



Worst Case Scenario

- Colon cancer
 - Extent, duration, and severity
 - Increased risk after 8-10 years duration of disease
 - 1-2%/year after 10 years
 - Recommend 1-2 year surveillance after 10 years
 - Additional risk factors:
 - Family history of colon cancer doubles risk
 - Pseudopolyps
 - Primary sclerosing cholangitis

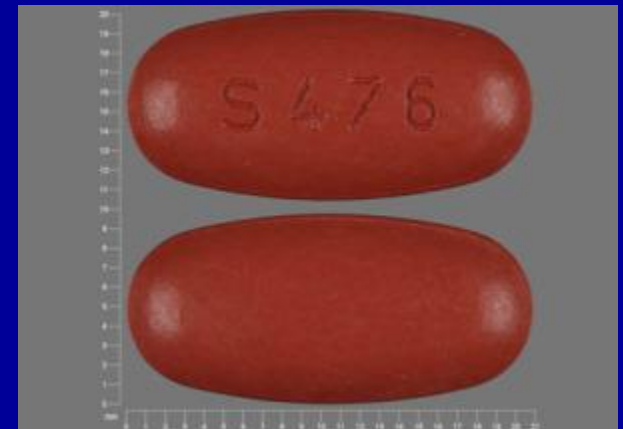
Treatment for Ulcerative Colitis

- Aminosalicylic acid (ASA) class
- Steroids
- Immunomodulators
- Biologics
- Surgery

Treatment – ASA Class

ASA (5-aminosalicylic acid)/Mesalamine Class

- Anti-inflammatory
- Good for mild and moderate disease
- Sulfasalazine is oldest and cheapest
- Modern agents composed of Mesalamine bound to carrier molecules with various timing/dosing of release
 - Rowasa
 - Asacol
 - Delzicol
 - Pentasa
 - Lialda
 - Apriso



Treatment – ASA Class

Multiple Routes

- Oral – Dosing generally 1.2-4.8 g/day
- Enema – Once to twice daily
 - Better response rates for left-sided disease
 - Reaches splenic flexure/sigmoid colon
- Suppository -
 - Once to twice daily for disease confined to distal 5-8 cm of rectum

Treatment – ASA Class

- Still controversial regarding colon cancer prevention
- Uncommon but multiple cases where exacerbates symptoms
- At least yearly BMP – Rare renal side effects
- No increased risk with higher dosing
- Poor compliance
- Dose daily or bid
- Ok in pregnancy and probably lactation

Treatment - Steroids

- Prednisone
 - Start high, slow taper
 - Significant side effects
 - Should not be afraid of acute toxicity, be very afraid of long-term effects
- Topical therapy with hydrocortisone enemas or foam
 - Not for maintenance
 - Quote 10-20% absorption



Treatment - Steroids

- Budesonide (Entocort, Uceris)
 - Few systemic side effects, less adrenal suppression
 - ? Role in disease management
 - Problematic insurance coverage

Treatment - Immunomodulator

6MP (6-Mercaptopurine) or
azathioprine (Imuran)

- Inhibit lymphocyte proliferation
- Considered for a long time, first-line for moderate severity, steroid sparing therapy
- Variable dosing
- Slow onset of activity
- Important to check regular labs



Treatment - Immunomodulators

- Complications of 6MP and Imuran
 - Marrow suppression
 - Hepatotoxicity
 - Pancreatitis
 - Constitutional symptoms/GI upset
 - Lymphoma

Treatment – Biologics

- Monoclonal antibodies directed against specific inflammatory pathway targets
- 60-70% response rates
- Well-tolerated
- Rapid onset

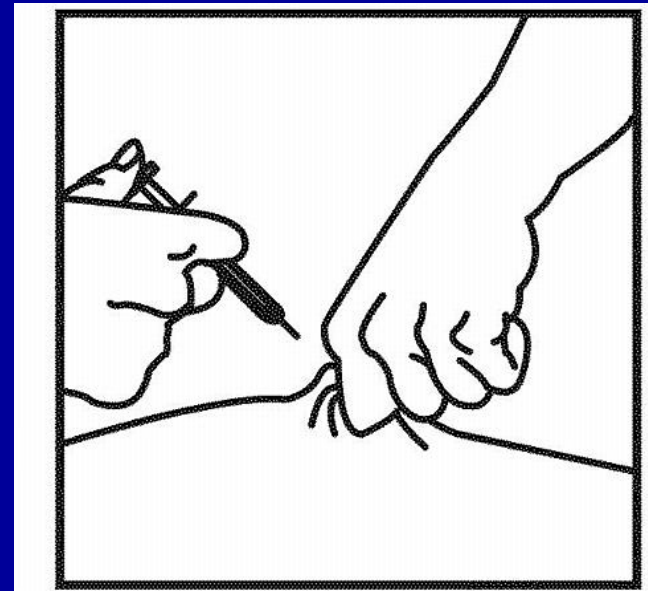


Treatment – Anti-TNF

- Remicade – Infusion (maintenance every 6-8 wks)
- Humira – SubQ every other week
- Cimzia – SubQ or infusions q 4 weeks

Deciding factors

- Insurance
- Patient preference
- Compliance
- Pregnancy



Treatment – Anti-TNF

Adverse effects

- Cost/Insurance
- Psoriasis (paradoxical response)
- Allergic response
- Lymphoma
- Infection/Sepsis

New(er) Biologics

- Entyvio (vedolizumab)
 - Monoclonal antibodies targeting gut-selective integrins
 - Good safety experience
- Stelara (ustekinumab) – Approved for Crohn's
 - Monoclonal antibodies targeting IL-12/23
 - Less frequent dosing
 - Good psoriasis data

Treatment – Maintenance for Moderate or Severe Disease

- Guided by steroid requirement
- Factor in distribution
- Proponents of top-down therapy
- Decisions often guided by acuity
- Good data for combined immunomodulator and biologic therapy in Crohn's
- Role for monitoring therapy (6MP metabolites, Humira/Remicade assays)

Treatment - Symptomatic

- Loperamide
- Anti-spasmodics
- Fiber/bulking agents
- Cholestyramine
- Probiotics

Just be careful...

Treatment - Other

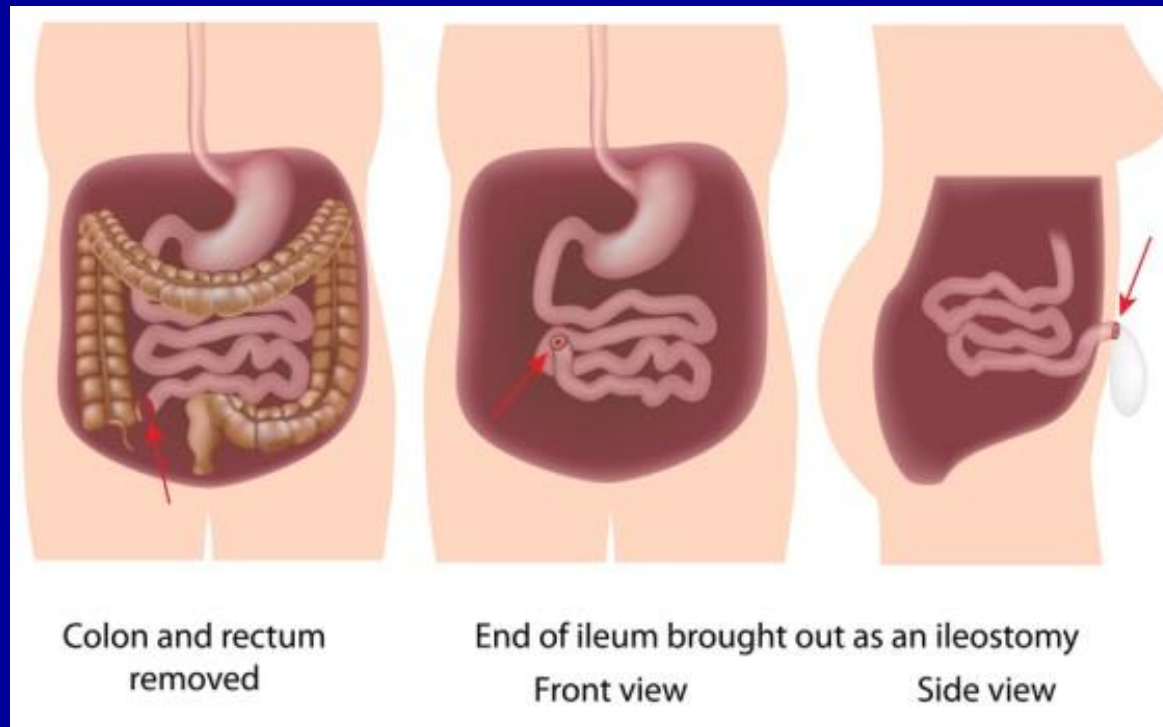
- Dietary
 - Bowel rest
 - Elemental diet
 - TPN
- Enteragam
 - Case reports

Treatment - Surgical

- Indications
 - Medically non-responsive
 - Cancer
 - Toxic megacolon
 - Refractory bleeding
 - Fulminant colitis not responding to medical therapy

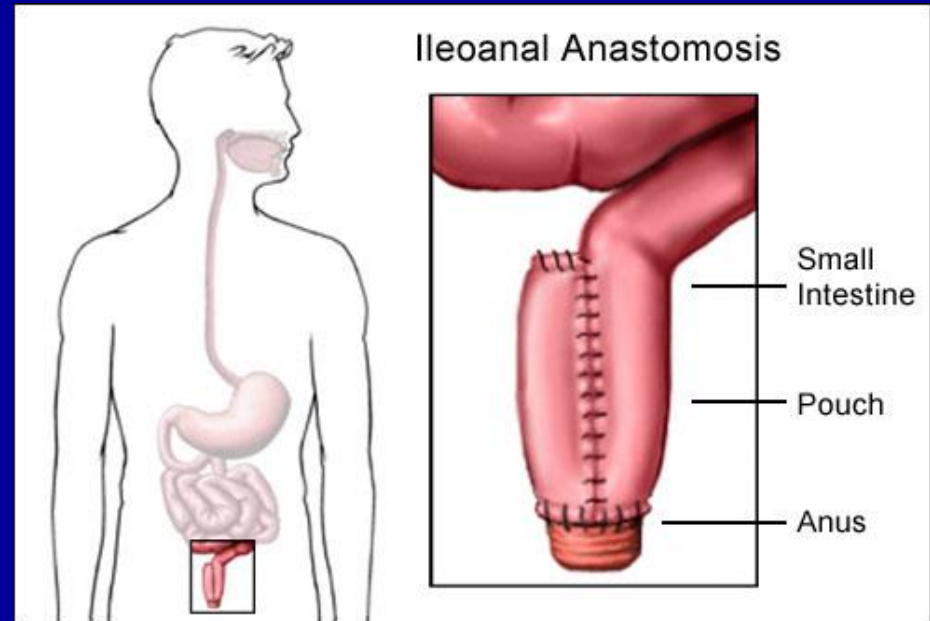
Treatment - Surgical

- Total proctocolectomy with end ileostomy



Treatment - Surgical

- Total proctocolectomy with ileal pouch anal anastomosis (IPAA, J-pouch)
 - 3-8 bm/day
 - Pouchitis in 7-33%
- Intermediate approaches in a staged fashion



Inpatient Points

- Acute infectious colitis vs. new UC is challenging
- IV steroids
- Antibiotics for systemic toxicity
- Colectomy in 5-10% of patients within the first year
 - Fulminant colitis failing medical therapy within 7d

Fulminant Colitis

- Severe colitis with systemic toxicity; ongoing bleeding, pain, diarrhea; often fever and anorexia
- Treatment
 - Antibiotics
 - NPO
 - Evaluate for colon dilation (generally $>6\text{cm}$ and cecum $>9\text{cm}$)
 - IV steroids
 - Consider for biologic therapy
 - Colectomy

Outpatient Points

- Major overlap with IBS
 - Objective measures with goal toward mucosal healing
- Caution with narcotics
- Proactive care
- Compliance can be hard

UC vs. Crohn's

- UC therapy principles apply to Crohn's colitis
- Differences
 - Discontinuous involvement
 - Surgery
 - Rate of escalating therapy
 - Proximal disease
 - Poor response to ASA
 - Earlier role for IM or Biologic therapy
 - Fistulizing disease
 - Smoking

Chapter II: Pancreatic Cystic Disease

Shan L. Cheng, MD
Indianapolis Gastroenterology and
Hepatology

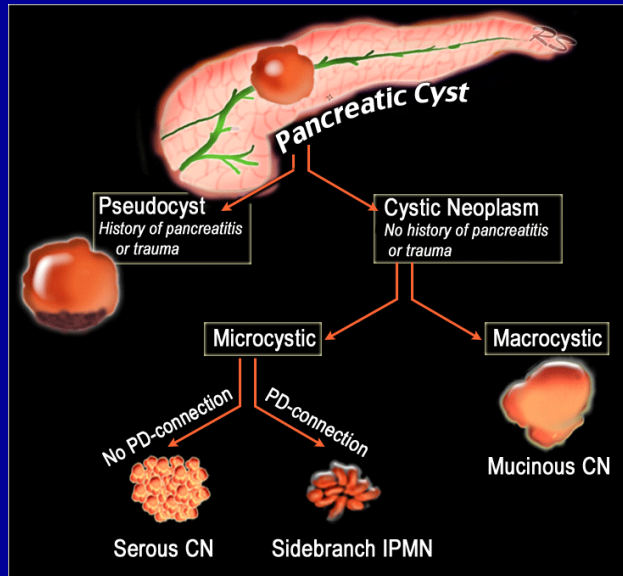
Pancreatic cysts

- Common!
 - 40% incidence in patients over 70 incidentally on MRI
- Overall risk of malignant transformation is quite low
 - Risk of cancer present at time of finding 0.25% with conversion rate 0.24%/year
- Mortality rate of pancreatic cyst surgery 2.1%. Morbidity rate 30%

Two Types of Cysts

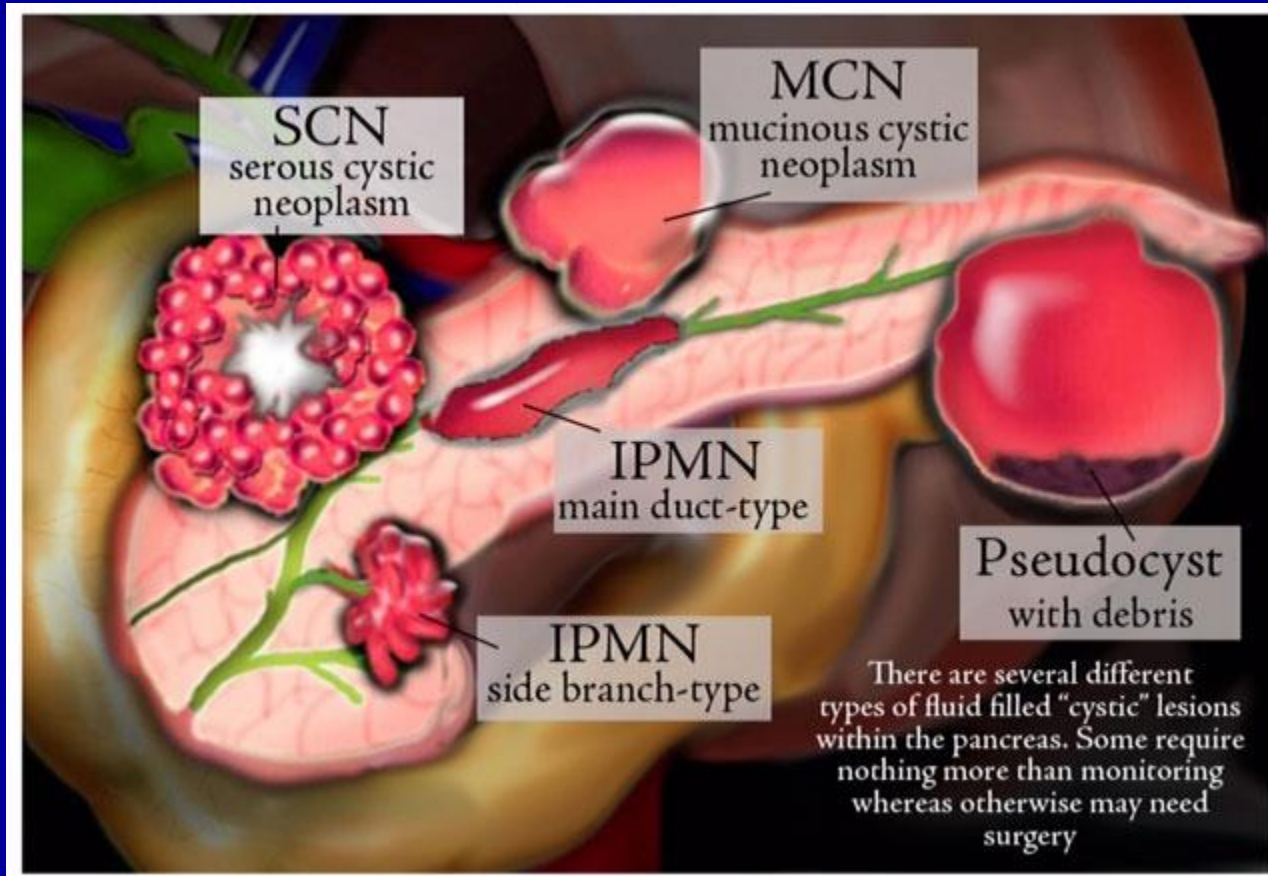
Non-Neoplastic

- Pseudocysts



Neoplastic

- IPMN - Intraductal papillary mucinous neoplasm
- MCN - Mucinous cystic neoplasm (no communication with duct)
- Serous cystadenoma (rare, honeycomb, central scar, very low risk)
- Solid pseudopapillary neoplasm (rare, young women, behaves like low grade pancreatic adenoca > surgery)
- Neuroendocrine tumor



Pseudocyst

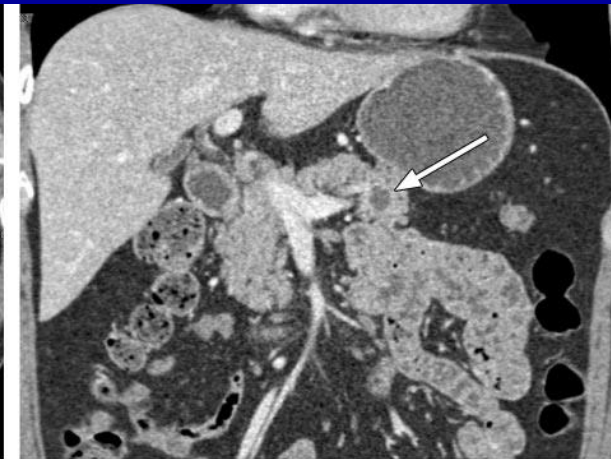
- Associated with acute and/or chronic pancreatitis
- Fluid +/- debris
- Less common than neoplastic cysts
- EUS can be useful to delineate chronic pancreatitis and if aspirated, high amylase, low CEA

IPMN – Intraductal Papillary Mucinous Neoplasm

- The most common type of pancreatic cysts
- 40% multifocal
- Men = Women
- 7th decade



a.



b.

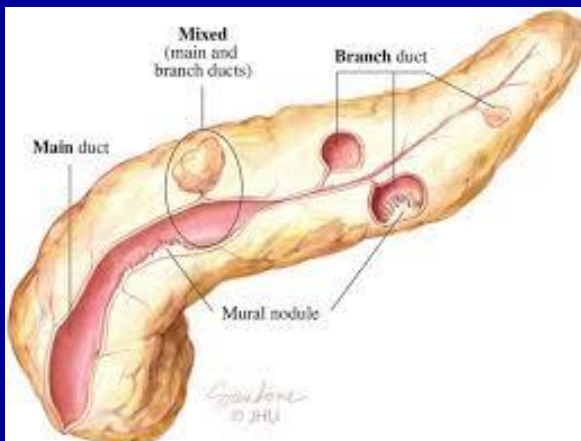
IPMN

Side Branch (Branch Duct)

- Most common cyst
- Low risk of progression

Main Duct

- High risk of malignancy with 38-68% risk of high grade dysplasia in specimens



High Risk Characteristics of IPMNs

Clinical

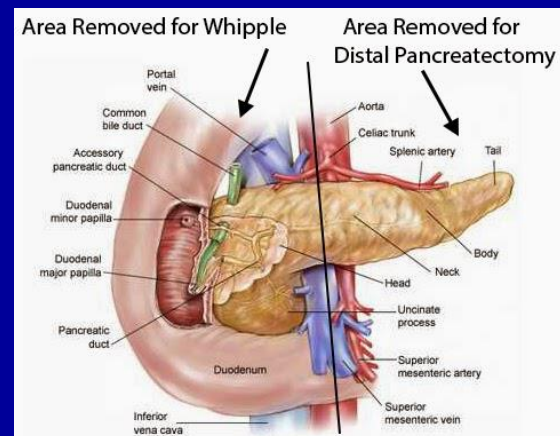
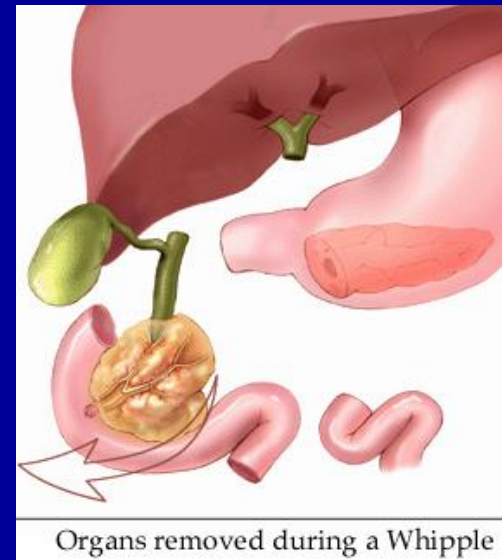
- Jaundice
- Acute pancreatitis related
- Elevated serum 19-9

Imaging:

- Mural nodule or solid component
- Main pancreatic duct diameter >5mm or change in upstream duct
- **Size > 3 cm or increase 3mm/yr**

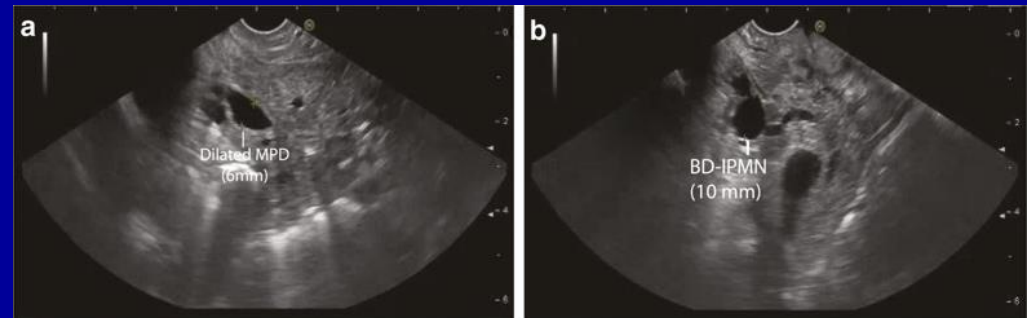
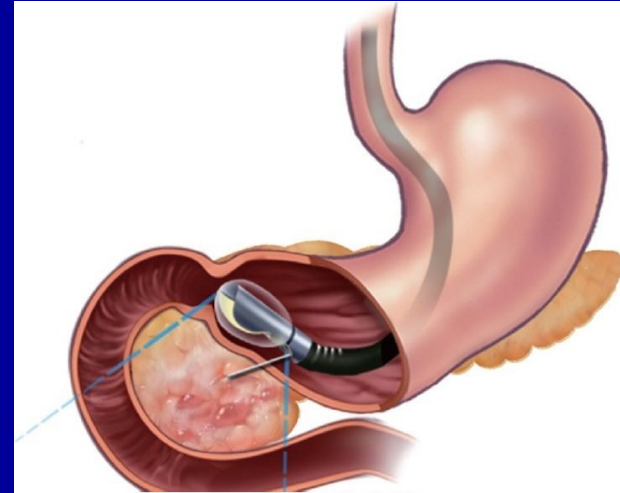
If High Risk Characteristics...

- Endoscopic ultrasound
- Referral to multidisciplinary HPB group
 - Advanced endoscopists
 - HPB surgery



EUS

1. Useful to identify cyst types
 - Appearance, CEA, Amylase
2. Evaluate for higher grade dysplasia and cancer



Imaging/Surveillance

- Goal of imaging is to assess type of cyst and risk of progression
- >3cm needs likely surgery input and close monitor
- Varying intervals of imaging monitor based upon cyst size. Stable size over 3-5 yrs means malignancy unlikely
- MRI/MRCP slightly superior but CT/EUS are still good alternatives



Final recommendations

- Patients who are not medically fit for surgery do not need further evaluation for incidentally found cystic disease
- MRI/MRCP is the preferred test for surveillance
- 3 cm size, main duct involvement/dilation or associated symptoms (jaundice, pancreatitis) are concerning features

Chapter III: Update on Complementary and Alternative Medicine for Functional Gastrointestinal Disease

Complementary and Alternative Medicine (CAM)

- Defined as medical practice not considered to be part of “traditional medicine”
- *Complementary* medical practice is taken in conjunction with conventional medicine
- *Alternative* medical practice is taken or used in place of conventional medical practice

Shifting Definitions of CAM

Influences of:

- Culture
- Ethnicity
- Religion
- Education
- Economic forces
- Attitudes of local medical practitioners



Hussain 2006

CAM Practices

- Biologic-based therapies
 - Herbal products and dietary constituents or additives found in nature
- Manipulative and body-based treatment
 - Acupuncture, massage, chiropractic or other body-based manipulation
- Mind-body interventions
 - Meditation, hypnosis, psychologic therapy
- Alternative medical systems
 - Homeopathy, traditional Chinese medicine

Complementary and Alternative Medicine (CAM) – U.S. Market

- 35% of U.S. population used some form of CAM between 1997-2002
- From 2012 NIH Survey data
 - Total of \$30 billion/year
 - \$14.7 billion on practitioners
 - \$12.8 billion on supplements



What is Driving These Trends?

Consumer Appeal for CAM

1. Perception that natural therapies may be safer and more effective
2. Sense of active participation in medical care through holistic approach
3. Utilization in the most difficult to treat chronic medical ailments

Functional GI Disease

- Disease from altered physiologic function instead of identifiable structural or biochemical cause
- Lack of structural target emphasizes symptom-based management
- Most patients and physicians are dissatisfied with current treatment options



van Tilburg 2008

Functional GI for the Purpose of This Talk

- **Irritable bowel syndrome**

- **Functional dyspepsia**

- Functional diarrhea
- Functional constipation
- Functional abdominal pain



Burden and Costs of Care of Functional GI Disease

- 41% of GI specialty practice
- IBS prevalence of 5-25%

Drossman 1997

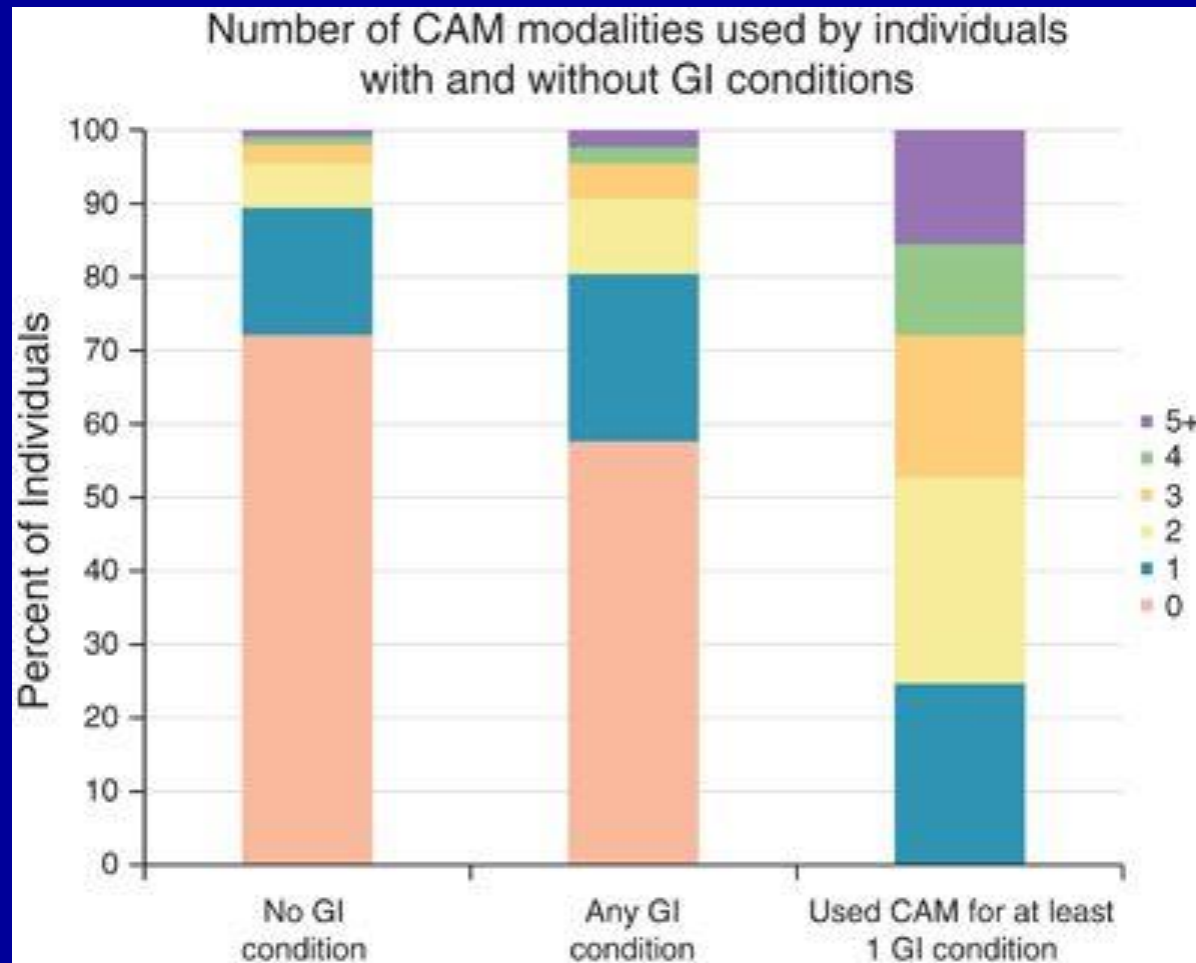
- Dyspepsia prevalence up to 25% (excluding GERD)

Chang 2004

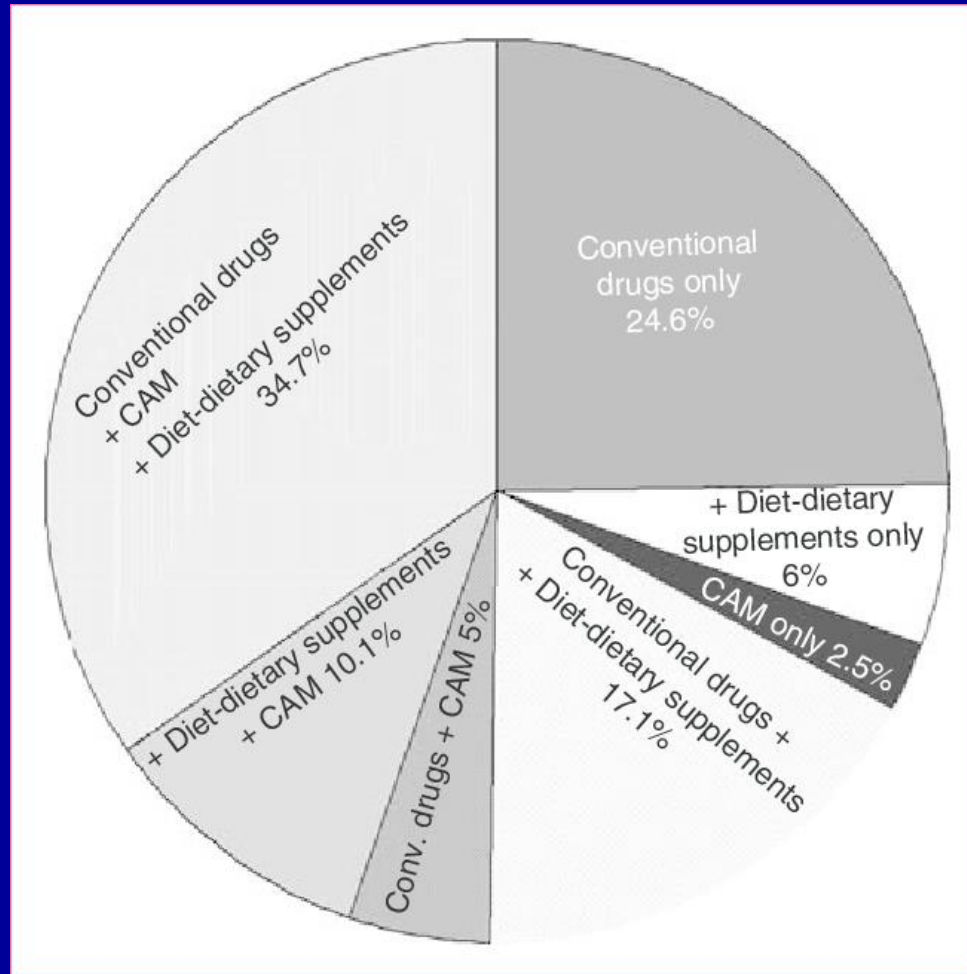
- 2.4-3.5 million physician visits annually for IBS symptoms in the U.S.
- \$1.6-\$10 billion in direct costs
- \$19.2 billion in indirect costs

AGA 2002

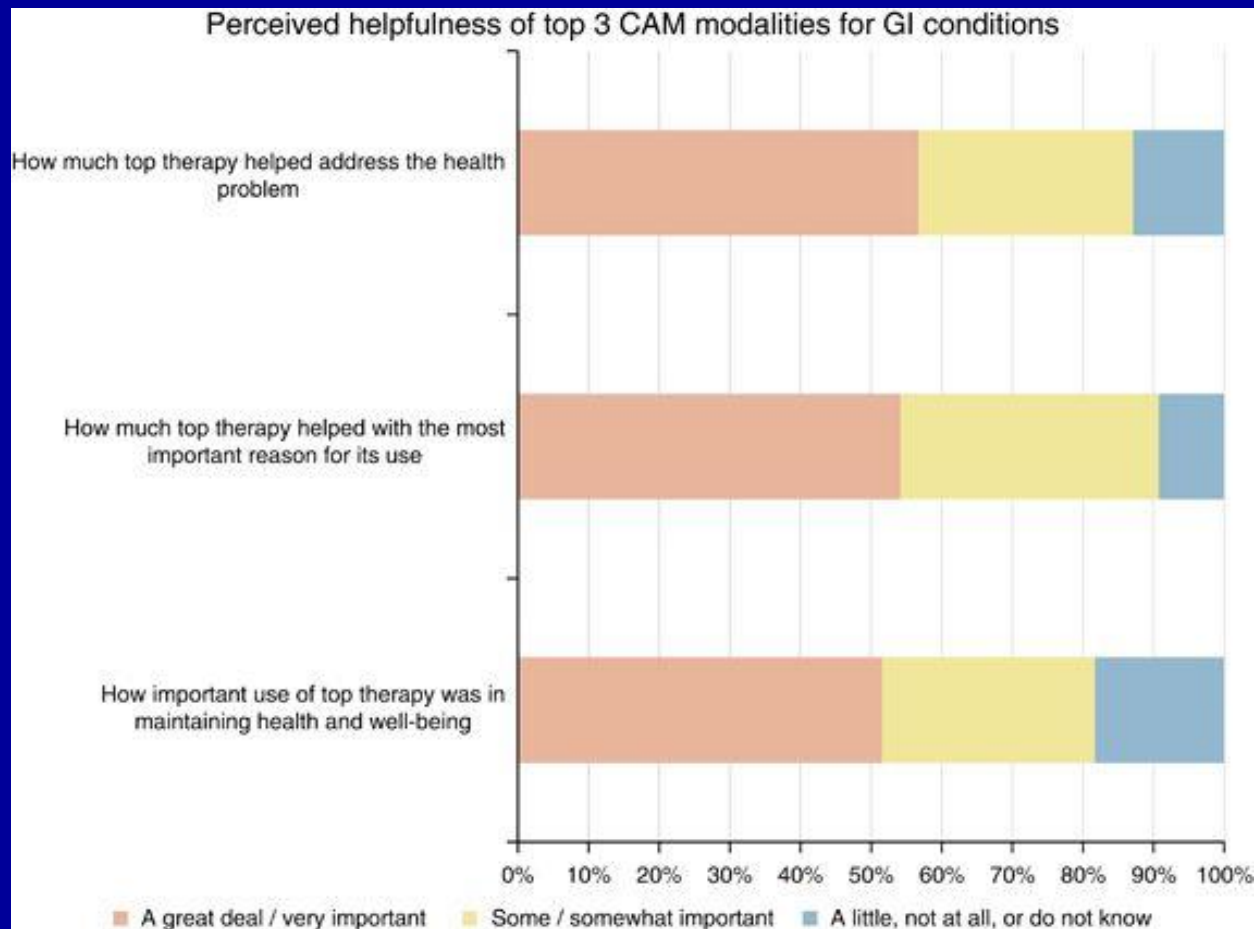
Use of CAM in Functional GI



Use of CAM in Functional GI



Use of CAM in Functional GI



Evidence Based Approach: Limitations of CAM Research and the Available Literature

Limitations of CAM Research

- Many controlled trials of CAM products are from primary non-English texts or published in journals not MEDLINE accessible
- Heterogeneous treatment products
 - Multiple manufacturers
 - Multi-component products
 - Different practitioners

Koretz 2004
Vickers 1998

Limitations of CAM Research in Functional GI Disease

- Studied endpoints related to symptoms or other subjective data
- Publication bias
 - From a systematic review of controlled trials by national origin, “published studies from Asia or Eastern Europe are almost always positive”

Koretz 2004
Vickers 1998

Placebo Effect in Functional GI Disease

- Wide range in published trials of placebo response rate for functional GI treatments:
 - Functional Dyspepsia (45 trials): 6-72%
 - IBS (50 RCTs): 3-84%
- Tremendous ability to skew data if study controls are not adequately established
- Factors determining placebo effect
 - Natural history
 - Placebo response – may have neurobiologic basis
 - Pavlovian conditioning
 - Suggestion

Placebo Effect in Functional GI Disease

- True significance of placebo effect may be determined by increased:
 - Study duration
 - Number of follow-up visits
 - Study size
- Effect stabilizes at 40% with increased duration (over 3 weeks) and sample size (500 patients)

Musial 2007

Herbal and Biologic Therapy



History and Controversy

- Plant-derived extracts are common resources for traditional pharmacologic therapies (ex. digoxin, antibiotics, morphine)
- Drug definition: A "drug" is any article (except devices) "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and [includes] "articles (other than food) intended to affect the structure or function of the body."

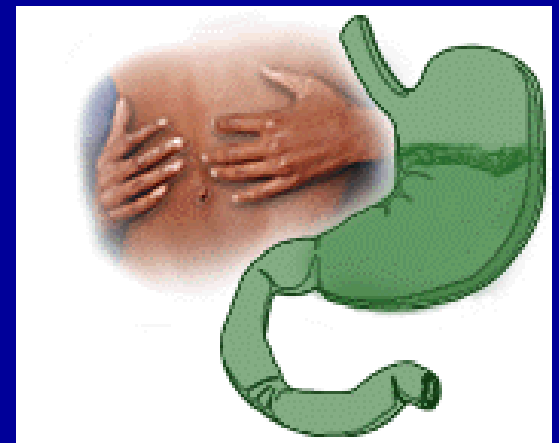


History and Controversy

- US Dietary Supplement Health and Education Act (DSHEA) 1994
 - Congress expanded the meaning of the term "dietary supplements" beyond essential nutrients to include such substances as ginseng, garlic, fish oils, psyllium, enzymes, glandulars, and mixtures of these.
- Herbal medicines and other alternative therapies are regulated as natural supplements, not drugs
- These may be marketed and sold without efficacy or safety testing

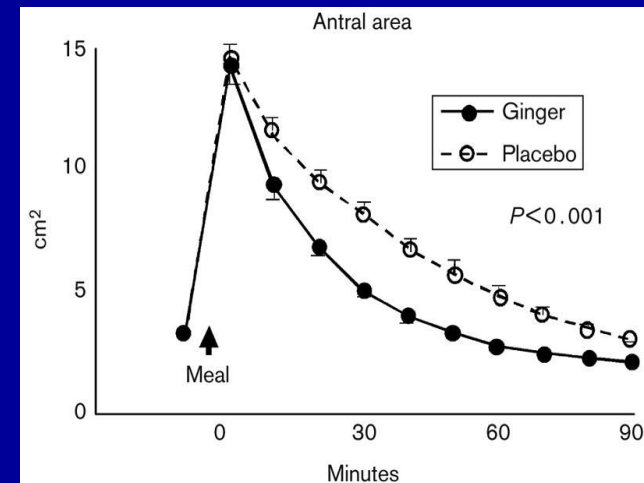
Functional Dyspepsia (FD)

- Herbal/Biologic
Complementary
Therapies
- Not comprehensive



Ginger (*Zingiber officinale*)

- Probably the most commonly used herbal remedy for GI disease often for nausea
- Utilized as a household treatment around the world for many GI complaints including dyspepsia
- Promotility effects documented in multiple studies
- Efficacy of symptom relief in dyspepsia is poorly established vs placebo



Wu 2008
Ernst 2000

Peppermint/Caraway Oil

(*Mentha piperita*/Carum carvi)

- Spasmolytic properties
- Dosage: 0.2-0.4 ml oil tid
- Cost: \$24-32/month
- Limited placebo-controlled RCTs show improvement
 - May *Aliment Pharm Ther* 2000:
96 patients w/ reduction in abdominal pain by symptom scoring (40% vs 22% (placebo), $p < 0.0001$)
 - Multiple studies where peppermint given in combination therapy vs placebo with overall efficacy



Peppermint/Caraway Oil (*Mentha piperita*/*Carum carvi*)

- Multiple non-placebo controlled trials show improvement
- Adverse effects
 - Heartburn
 - Interstitial nephritis and renal failure at excess dosages
 - Allergy, perianal burning
 - May increase serum levels of simvastatin

Iberogast (STW 5)



- European commercial combination product containing 9 herbs
- Main component is *Iberis amara*
- Cost \$30-35/month
- Utilized extensively for dyspepsia and IBS in Europe

Melzer 2004
Von Armin 2007

Table 1. Composition of STW 5

Drugs extracted (ethanolic 30%, DER 1:3)	Amount of extract (in 100 mL)
<i>Angelicae radix</i> (Garden angelica root)	10 mL
<i>Cardui mariae fructus</i> (Milk thistle fruits)	10 mL
<i>Carvi fructus</i> (Caraway fruits)	10 mL
<i>Chelidonii herba</i> (Greater celandine)	10 mL
<i>Iberis amara</i> * (Bitter candy tuft)	15 mL
<i>Liquiritiae radix</i> (Liquorice root)	10 mL
<i>Matricariae flos</i> (Chamomile flowers)	20 mL
<i>Melissae folium</i> (Balm leaves)	10 mL
<i>Menthae piperitae folium</i> (Peppermint leaves)	5 mL

DER, drug extract ratio.

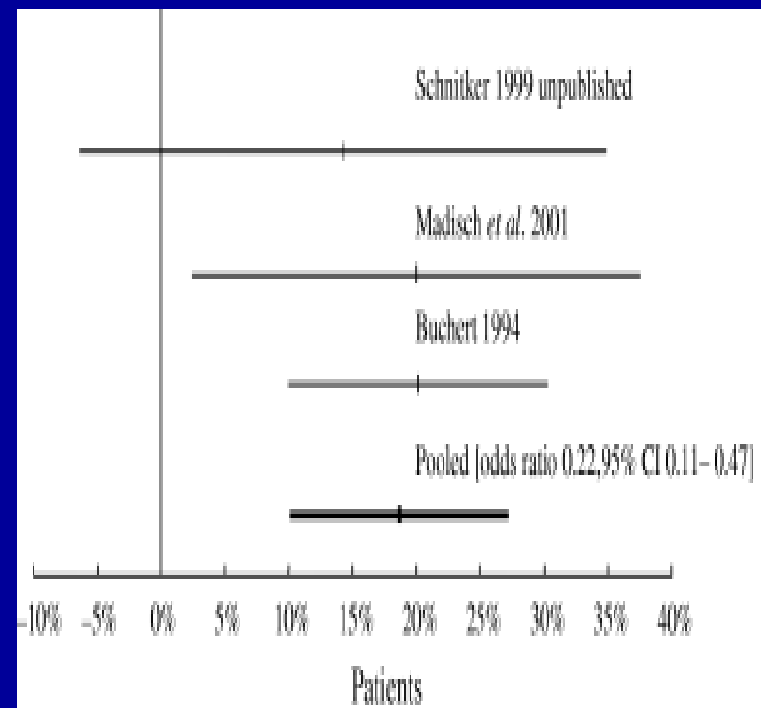
* Ethanolic extract (50%) of fresh plant, DER 1:2.

Iberogast (STW 5)

Multiple studies available

- 2004 Meta-analysis
 - Three randomized placebo controlled trials
 - 19% (CI 0.11-0.44) pooled rate difference between STW-5 and placebo for effect on most bothersome GI symptom
- Head-to-head versus metoclopramide shows no difference in effect
- No adverse events reported

Melzer 2004



Artichoke Leaf Extract (ALE)

- Holtmann et al Aliment Pharmacol Ther 2003
 - 247 patients randomized to ALE vs placebo.
 - Modest improvement in symptom scores esp. sensation of fullness; change in pain was not significant
 - Modest improvement in quality of life
 - No adverse events relative to placebo



Chili Pepper/Capsaicin

- Multiple physiologic studies show GI hypersensitivity followed by analgesia
- Bortolotti et al *Aliment Pharmacol Ther* 2002
30 patients in double-blind RCT versus placebo showed small improvement



Turmeric (*Curcuma longa*)

- Evidence of improved bile formation, secretion; antispasmodic activity
- Thamlikitkul *J Med Assoc Thai* 1989
116 patients w/ dyspepsia randomized to turmeric, *flatulence* (combination cascara, ginger, capsicum), or placebo
Significant improvement in turmeric group (33 improved) relative to placebo (20 improved) though no change significant improvement relative to *flatulence*



IBS

- Herbal Therapies
 - Big picture
 - Single agent evidence
- Other supplementary and biologic therapies



Cochrane Analysis Herbal Therapy for IBS

- Quality not quantity is the problem
 - Number of randomized trials for complementary medicine has doubled every five years
 - Nearly 50 systematic reviews
- Study controls largely compared to conventional medicine (usually antispasmodics)
 - Placebo in 6 trials



Cochrane Analysis

Limitations Identified

- No more than one trial compared the same herbal treatment and control
- No long-term follow-up
- Small sample sizes (average size 105)
- Few trials utilized double-blinding
 - Investigator assessment largely unblinded

Cochrane Analysis Conclusions

- Some herbal medicines improve GI symptoms of IBS
- Evaluated treatments appear generally safe but adverse effects not adequately reported
- Majority of included trials rated as poor methodologic quality
- ***Premature to recommend herbal medicines for routine use in IBS***



Peppermint Oil for IBS

- Common component of prescription and over-the-counter remedies
- Numerous small trials indicate peppermint superior to placebo for abdominal discomfort, bloating, global IBS symptoms
- Reviewing available trials, peppermint oil not proven beyond reasonable doubt



Aloe

- Considered “safe, natural” remedy
- Targeted for constipation predominant IBS
- Active ingredients are anthraquinones
- 35 patients randomized to combination aloe/celandin/psyllium versus placebo had improved bowel movement quality with drug but no change in abdominal pain



Odes 1991

Enzyme Supplements for Functional GI Disease

- Includes:
 - Pancreatic enzymes/extracts
 - Ox bile extract
- Developed for pancreatic insufficiency but also utilized for functional GI complaints
- Utility unproven in clinical trials



Probiotics

- Promoting beneficial alteration in gut flora and anti-inflammatory effects
- Selection criteria:
 - Human origin
 - Non-pathogenic species
 - Resistant to intestinal acid and bile
 - Ability to adhere to human epithelial cells and temporarily colonize
- Evidence is inconsistent and difficult to compare but shows overall trend of symptom improvement
- Seems more effective in IBS-D

Lactobacillus species



- Sources: Fortified yogurt and milk, freeze-dried granules/powders
- Nobaek *Am J Gastro* 2000
60 patients had significant reduction in flatulence and pain after 4 weeks of therapy versus placebo
At one year still had a significant reduction in flatulence

Bifidobacterium infantis



O'Mahony *Gastroenterology* 2005

- 77 Irish patients meeting IBS Rome II criteria underwent 8 weeks of randomization to:
 - *B. infantis*
 - Lactobacillus
 - Placebo
- *B. infantis* had greater reduction in abdominal pain/discomfort, bloating/distention, and bowel movement discomfort
- No significant benefit for those randomized to lactobacillus
- No statistically significant difference for quality of life measures

Enteragam

- Serum-derived bovine immunoglobulin/protein isolate
- Strong safety record
- Mechanism of improving gut barrier integrity
- Multiple studies
 - Wilson 2013: RCT of 66 patients with IBS-D showed improvement vs placebo
- Safe



CBD Oil

- Evidence for THC exists with positive effects in functional GI
- CBD oil has not been demonstrated to be effective
- Preliminary studies with animal models show some decreased bowel inflammation and reduced hypermobility



Medical/ Biologic Summary

- Data is suboptimal for many reasons including
 - Heterogeneous products
 - Methodologic flaws of available studies
 - High placebo response requires adequate controls
- Promising agents include:
 - Peppermint oil
 - Iberogast (STW 5)
 - Ginger for nausea
 - Probiotics
 - Enteragum
- Significant toxicity is unlikely from studied drugs

Manipulative and Body- Based Treatment

Acupuncture

- Mainstay of Eastern medicine for over 2500 years
- The challenge of sham or placebo acupuncture is a problem for studies
- Strongest evidence for acupuncture to date exists in pain and post-operative nausea and vomiting

Koretz 2004

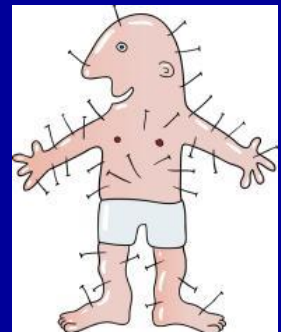
Schneider 2006



How Do You Placebo Control Acupuncture?

The Streitberger Needle

- A blunted telescopic placebo needle which simulates acupuncture without penetrating the skin
- Schneider *Gut* 2006
 - 43 patients with IBS randomized to traditional acupuncture versus sham acupuncture
 - Both groups were significantly improved in a global quality of life measure
- Studies utilizing sham acupuncture do not achieve double blinding



Cochrane Analysis 2008

Acupuncture for IBS

- Six studies met inclusion criteria with a total of 464 patients
 - Studies rated as “generally poor quality”
 - Primary outcome of global improvement
- Available evidence shows no significant difference between acupuncture and sham though data is limited



Other Possible GI Indications for Acupuncture

- Nausea and Vomiting
 - 21 non-randomized and 12 randomized studies showed acupuncture superior to control in 27/33 studies (11/12 RCT's)

Vickers 1996

Koretz 2004

- Pain
 - Multiple meta-analyses for pain have shown some effect inversely proportional to study quality
 - Individual RCTs for gastrointestinal pain are insufficient to draw conclusions

Koretz 2004

Adverse Complications of Acupuncture

- Serious side effects are extremely rare (less than 0.01%) but include:
 - Hep B/Hep C/HIV
 - Pneumothorax
 - Cardiac tamponade
 - Interference with pacing devices
- Typical adverse reactions are benign but documented

Koretz 2004
Ernst 2001
Melchart 2004

Adverse outcome	Estimated	Survey
Pain at needle site	0.2 - 0.13%	3.28%
Fatigue or exhaustion	2 - 41%	0.03%
Local bleeding	0.03 - 8%	1.38%
Faintness	0.01% - 7%	0.46%
Nausea	<1%	
Failure to remove needle	0.1%	0.25%
Headache		0.04%

Massage/Chiropractic

- Little available research regarding efficacy
- Data for infant massage and weight gain
- Small studies in spinal injury and constipation
- Case report of utility in cecal fecal bezoar

Diego 2005

Ayas 2006

Di Lorenzo 1993



Mind-Body Interventions

Hypnotherapy

- Induction of a state of consciousness with decreased voluntary action and susceptibility to suggestion
- Downsides:
 - Limited availability
 - Time-intensive
 - Expensive
- Safe



Hypnotherapy for IBS

- Multiple trials and reviews published over the years with clear data showing symptom improvement
 - 2005 Review: 14 published studies (6 controlled, 8 non-controlled); n=644
 - Consistently significant results with improvement in cardinal symptoms of IBS
 - Also improves non-colonic symptoms of IBS
- Meets American Psychologic Association efficacy guidelines for highest level of acceptance

Kearney 2008
Tan 2005

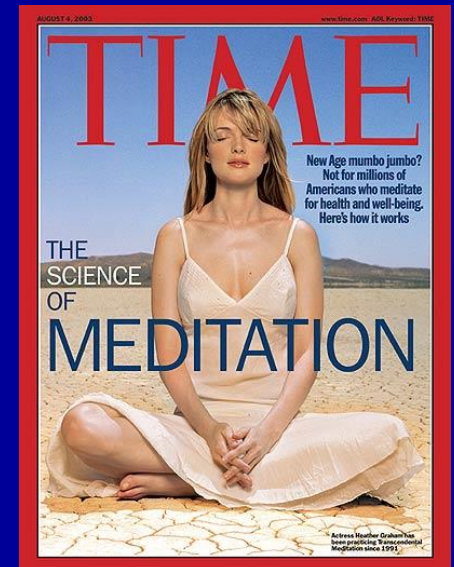
Hypnotherapy for IBS

- The most evidence-based mind-body intervention for functional GI disease
- Marked improvements in anxiety
- Early intervention may be better

Meditation

- The training of a person's attention which may alter perception of pain and stressors
- Mindfulness based stress reduction (MSBR) is increasing available
- Prior studies of MSBR for chronic pain, anxiety, cancer, psoriasis show improvement in symptoms or quality of life
- Gaylord *AJG* 2011 – 75 patients RCT to MM vs just support group: 38% vs 11%

Kearney 2008



Relaxation/Stress Management

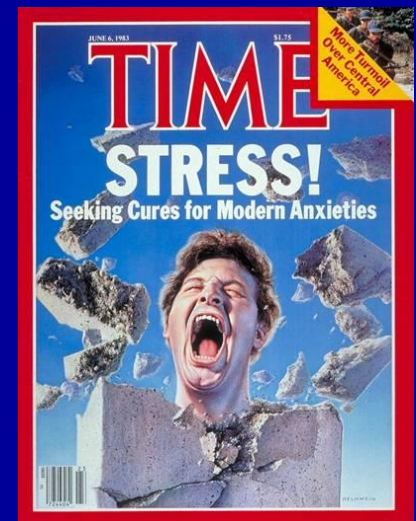
- Two small studies (n=16 and n=11) comparing relaxation therapy to control groups greater symptom reduction scores

Blanchard 1993

Lynch 1989

- Bowel sound biofeedback with a stethoscope
 - Patients trained to increase or decrease bowel sounds
 - Small case series (n=5) with suggestion of efficacy

Radnitz 1989



Psychologic Interventions for IBS

- Some consider this standard of care
- Psychotherapy
 - Includes psychodynamic therapy, cognitive behavioral therapy, and group therapy
 - Studies for IBS demonstrate superiority to supportive listening
- Cognitive behavioral therapy
 - Multiple clinical trials for IBS both with encouraging data for effect

Soo 2008
Spanier 2003

Alternative Medical Systems

Homeopathy

Traditional Chinese Medicine

Homeopathy

- Practice of formulating solutions of substances that duplicate symptoms of particular diseases then diluting the solutions
- No adverse effects (except lost time and money)

Homeopathy

- No known biologic feasibility
- Many RCTs suggest efficacy in medical disease
 - Homeopathy is much easier to blind
- No reportable evidence specifically in functional GI disease

Traditional Chinese Medicine

- Combination treatment with multiple modalities such as herbal treatment and acupuncture
- TCM herbal remedy efficacy remains in question



Summary

- Patients are using these therapies at rates of at least 35%
- Available research has marked limitations related to
 - Heterogeneity in treatment and study design
 - Methodologic flaws
 - Placebo effect seen in functional GI disease

Summary

- The Best Of List

- Peppermint oil for dyspepsia
- STW 5 (Iberogast) for dyspepsia
- Cognitive behavioral therapy
- Hypnotherapy
- Probiotics and Enteragum for IBS-D

Summary

- The above-mentioned herbal remedies are generally safe
- Acupuncture studies cannot be taken at face value but significant efficacy is repeatedly identified
- Psychotherapy shows encouraging results

Angell and Kassirer Say:

“There cannot be two kinds of medicine... There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously it no longer matters whether it was considered alternative at the outset.”

N Eng J Med 1998

Thanks much

