GI update

- Common conditions and concerns my patients frequently asked about

Specific conditions I'll try to cover today

1. Colon polyps, colorectal cancer and colonoscopy
2. Crohn's disease
3. Peptic ulcer disease
4. GERD (gastroesophageal reflux disease)

.

Colon cancer – causes/risk factors

- Old age – risk increases as we grow older (that is basis for beginning screening at age 50)
- Life-time average risk for colon cancer is about 1 in 22 (about 5%)
- Genetics – most colon cancer is sporadic and not hereditary, but having a parent or sibling with colon cancer doubles your risk (likely multiple abnormal genes). About 2% of colon cancers come from polyposis syndromes (which may be hereditary or sporadic) and markedly increase colon cancer risk
- Inflammatory bowel disease (ulcerative colitis and Crohn's) increases risk but only accounts for 2% of cases yearly (more discussion later)
- Life style
  - Diet – red meat, alcohol
  - Smoking, obesity, lack of physical exercise

Colon cancer pathogenesis

- Colon cancer arises in epithelial cells lining the colon thru a series of mutations
- Mutations arise in genes regulating cell growth (APC gene, TP 53 gene, K-RAS gene, MMR gene)
- Mutations typically lead to growth of polyps, which are potentially pre-cancerous and can gradually change from benign to malignant polyps to invasive cancer
- The sequence of polyp to cancer can take several years (typically about 10 years)

Colon polyps

- Colon polyps typically do not causes symptoms
- Incidence of colon polyps is about 15-20% over age 50
- Most polyps will not become malignant but we have no way to know which polyp will
- Multiple studies have shown that colonoscopy is the best way to detect (and remove) colon polyps
- Careful colonoscopy with removal of all polyps lowers the incidence of colon cancer by 80-85%

Colon cancer symptoms

- Blood in stool. Change in bowel habits. Weight loss. Fatigue.
- The most important message is that the prognosis of colon cancer is much better if detected BEFORE symptoms arises!
- There are about 180,000 new cases of colon cancer per year in US and about 50,000 deaths
- Globally colon cancer is the third most common cancer
- Colon cancer diagnosed prior to onset of symptoms has a 90% cure rate vs. 50% cure rate with symptoms prior to diagnosis

What if I don’t want a colonoscopy?

- Colonoscopy is a very safe test which is very comfortable with modern sedation
- The prep is much improved (no castor oil, no enemas) and primarily involves being on clear liquids the day before and drinking Miralax mixed in Gatorade to cleanse colon
- Risk of serious complication very small
- Major concern patients express is “hassle-factor” (time off from work, doing the prep, arranging a ride, etc) but benefits of colonoscopy have been demonstrated by years of experience
- If a patient still wants to forgo colonoscopy, the best option is Cologard

Cologard

- Cologard is a test for abnormal fecal DNA which is the product of a colon cancer or precancerous polyp
- Cologard detects 92% of colon cancers and 65% of pre-cancerous polyps
- All patients with abnormal Cologard test will need colonoscopy
- Patents using Cologard screening will need the test repeated every 3 years: colonoscopy > repeat in 10 years if exam negative; 3-5 years if benign polyp found; 1 year if colon cancer found (depending on surgical findings)
- Cologard is NOT suitable for patents with a past history of colon cancer or colon polyps, a family history of colon cancer or a history of inflammatory bowel disease

Other screening options which may be mentioned

- Fecal occult blood test > not nearly as accurate as colonoscopy or Cologard. Misses small polyps and about 50% of colon cancers
- CT colography > non-invasive imaging but requires prep much like colonoscopy and requires colonoscopy if possible polyp is seen. Not approved by Medicare.
- Sigmoidoscopy > widely used office procedure but typically done without sedation and only visualizes part of colon

Crohn's disease

- Type of inflammatory bowel disease (which also include ulcerative colitis)
- Typical symptoms include abdominal pain, diarrhea and weight loss
- Initial symptoms are often vague which can lead to a delay in diagnosis
- Causes: seems to be alterations in local intestinal immunity
  - Genetics – mutations in intestinal mucosal genes, especially the NOD2 gene, have been found. This seems to effect the "processing" of certain bacterial antigens which can trigger inflammation. Siblings of Crohn's patients are 30 times more likely to acquire the disease. Multiple genes are likely involved.
  - Colonization of the intestine with specific bacteria such as Mycobacterium avium is suspected to play a role (although a specific "Crohn's bacteria" has not been found)
  - Smoking doubles the risk of Crohn's disease
  - Diets with high animal protein and fats appear to play a role

Crohn’s disease - diagnosis

- Strong incidence of suspicion. Symptoms early-on are typically vague.
- Cases with small bowel disease can be more challenging
  - CT scan enterography is a non-invasive imaging study which can be very helpful
  - Capsule endoscopy (“pill-cam”) may pick up early Crohn’s and suggest further testing
  - Push-enteroscopy (with a long scope) can look at suspicious areas seen by CT or pill cam
  - Colonoscopy with biopsy will diagnose 70% of cases

Crohn’s disease - treatment

- No medications or surgery can cure Crohn’s disease
- Traditional medications (prednisone, mesalamine) help with inflammation during flare-ups but do not alter the course of the disease
- Half of patients with Crohn’s require surgery during the course of their disease
- A major advance has been the introduction of biologic agents

Biologic agents in Crohn's disease

- The pathogenesis of Crohn's is not fully known but alterations in immunity seem to turn on mediators of local inflammation
- Biologic agents target the pathways which cause local inflammation and tissue damage
- Biologics are typically "murine" (mouse) humanized monoclonal antibodies which are given by injection or infusion. They bind to and block local inflammatory mediators including TNF-alpha and integrin
- Biologics can block local inflammation and alter the course of active Crohn's

Biologic agents in Crohn's disease

- Biologics may lower resistance to various infections such as TB and may increase the risk of certain cancers such as lymphoma. My experience was that biologic agents are remarkably well tolerated
- Experience is growing about the long term use of biologics. Likely further research will lead to more targeted biologics.
- There is an incidence of loss of responsiveness to a certain biologic agent but this is often managed by switching to a different class of biologic
- Biologics are a very fertile area of research by pharmaceutical companies (as illustrated by ads on TV) and will likely ultimately help us find the underlying causes of Crohn's
- If you look at biologics ads on TV (such as for Crohn's, psoriasis or ulcerative colitis) they typically end in "-mab"

Peptic ulcer disease

- Break (or “ulceration”) in the lining of the stomach or duodenum
- Common causes
  - Helicobacter pylori
  - Non-steroidal anti-inflammatory drugs
  - Smoking and alcohol consumption
  - Stress due to serious illness (“stress ulcer”)
- Symptoms
  - Upper abdominal pain
  - Vomiting, poor appetite
  - Weight loss

Peptic ulcer disease

- Complications
  - Dyspepsia with weight loss
  - Bleeding - may be chronic and occult or acute with vomiting blood or passing black stools (melena)
  - Perforation
  - Obstruction (from scar tissue around the ulcer)

  * 1/3 of older patients have no symptoms and present with complications

H pylori

- A major causative factor in peptic ulcer disease
- Acquired by oral route and causes chronic inflammation of the stomach lining
- In under-developed countries often acquired at an early age
- Long-standing infection causes chronic gastritis and increases the risk of stomach cancer as well as ulcer disease
- H pylori secretes urease enzyme which creates a favorable alkaline environment for the bacteria (and basis for a diagnostic test)

H pylori – diagnosis

- H pylori can be diagnosed by:
  - Urea breath test
  - Testing blood for antibodies
  - Biopsies at the time of endoscopy
  - Testing stool sample for H pylori bacterial products (“fecal antigens”)

H pylori treatment

- H pylori can be stubborn to treat
- Typically treatment is a two week course of two antibiotics often combined with oral bismuth (Pepto-Bismol) which inhibits the bacteria plus an acid blocker such as Prilosec
- Compliance with this complicated regimen is an issue and treatment can fail if medications are not taken properly

NSAID’s and ulcers

- Gastric mucosa is protected by a layer of mucus which is stimulated locally by certain hormone-like chemicals called prostaglandins, which are produced by enzymes called “COX-1” or cyclo-oxygenase-1
- NSAID’s block prostaglandin synthesis which can lead to mucosal damage
- Prostaglandins have many other functions and can cause problems such as joint inflammation

*This can lead to the problem that NSAID’s are <u>good</u> for joint inflammation but <u>bad</u> for gastric mucosa (“ulcerogenic”)

Ulcer management

- Stop NSAID's if possible
- Test for H pylori > eradicate with mentioned regimens; document cure by urea breath test or fecal antigen
- Acid suppression with a PPI (proton pump inhibitor) like Prilosec
- Avoid smoking and alcohol
- To scope or not to scope
  - "Test and treat" for H pylori in absence of warning signs
  - Scope with warning signs (weight loss, anemia, new onset of symptoms over age 45-50, lack of response to therapy)

GERD (gastroesophageal reflux disease)

- Symptoms:
  - Heartburn
  - Acid taste in throat
  - Wearing away of dental enamel
  - Chest pain
  - Breathing problems
  - Strong association with sleep disturbances and sleep apnea

GERD: Causes

- Incompetent lower esophageal sphincter
- Hiatal hernia
- Obesity
- Pregnancy
- Smoking
- Certain medications

* 10-20% of US population report some GERD symptoms

GERD: complications

- Esophagitis (damage to lower esophageal mucosa)
- Esophageal stricture (scarring and narrowing)
- Barrett’s esophagus and esophageal cancer

GERD: Barrett's esophagus

- Pre-malignant change in esophageal mucosa due to chronic acid irritation (" intestinal metaplasia")
- Found in 5-10% of patients seeking attention for heartburn, but many patients with Barrett's have no symptoms
- Caucasian males over age 50 with chronic GERD symptoms are at highest risk
- A major reason for gastroscopy in chronic GERD is to check for Barrett's
- A percentage of Barrett's metaplasia changes to dysplasia over time so patients with Barrett's undergo endoscopic surveillance with biopsies
- Barrett's with dysplasia can be treated by ablation with laser or radio-frequency, endoscopic excision or surgery in more extensive cases

GERD: diagnostic measures

- Gastroscopy (check for esophagitis, stricture and Barrett's)
- Esophageal manometry
  - Swallowing problems
  - Pre-operative evaluation
- Esophageal pH monitoring (Bravo capsule)
  - Evaluate persistent symptoms despite appropriate therapy
  - Atypical symptoms (such as "non-cardiac chest pain")
  - Pre-operative evaluation
  - Recurrent symptoms after surgery

GERD: Treatment

Life-style changes

- Weight-loss
- Dietary modification (avoiding certain foods such as fatty or fried foods)
- Avoid eating for 3 hours prior to retiring
- Elevation of head of bed
- Avoiding alcohol and smoking

Medications: antacids, acid blockers (especially PPI's)

Surgery (failure to respond to medical therapy or intolerance to medications)

GERD: Surgery

Most patients with reflux symptoms are well managed medically and don't need surgery

- Most chronic reflux candidates have hiatal hernia with weak LES (lower esophageal sphincter)
- Operation typically done by laparoscopy with improved results and faster recovery
- Concept is to repair hiatal hernia and create new sphincter with "fundoplication" or wrap around GE junction

* 80-90% of patients are happy with results of "lap Nissen"; a major interest is long-term results since this is a fairly new operation