Practical Approaches to the Differential Diagnosis of IBD

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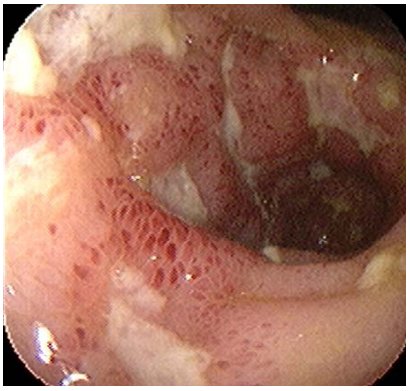
CROHN'S & COLITIS FOUNDATION OF AMERICA

The DDx of IBD

- Does this patient with suggestive symptoms actually have IBD?



- Concepts
  - Impractical approaches
  - Pearls from EBM
  - Pattern Recognition
  - Three Lenses
  - Cases
  - Improving your pattern recognition

Impractical Approaches

GUEST LAUNDRY & DRY CLEANING LIST

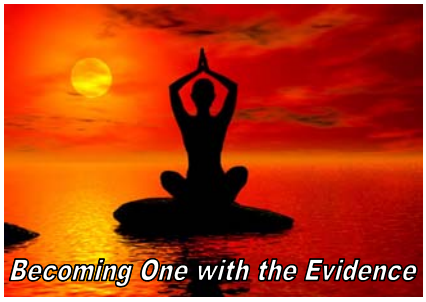
Name: _____ Date: _____

Room No. _____ Inv. No. _____

LAUNDRY			DRY CLEANING		
No.	ARTICLE	Price	No.	ARTICLE	Price
	Handkerchiefs			Blouses	
	Pajamas, Cotton			Coat, rain	
	Pajamas, silk/rayon			Coat, top or over	
	Shirts, dress			Dress	
	Shirts, silk/rayon, sport			Dress, formal	
	Shirts, Tuxedo			Jacket or sport coat	
	Slacks, wash			Suit, 2-pc.	
	Socks, press			Suit, 3-pc.	
	Underwear, shorts			Slacks	
	Underwear, tops			Shirts	
				Tie	
				Vest	

Special Instructions:

Your list must accompany you package. If incorrect, our count to be accepted as correct. We cannot be responsible for valuables left in clothing. In case of any claim against this order, you must notify the office/front desk within 72 hours. No claims to exceed ten times the laundry or cleaning charges.



Impractical Approaches

- Laundry List

GUEST LAUNDRY & DRY CLEANING LIST

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LAUNDRY			DRY CLEANING		
No.	ARTICLE	Price	No.	ARTICLE	Price
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- EBM Nirvana

The Laundry List

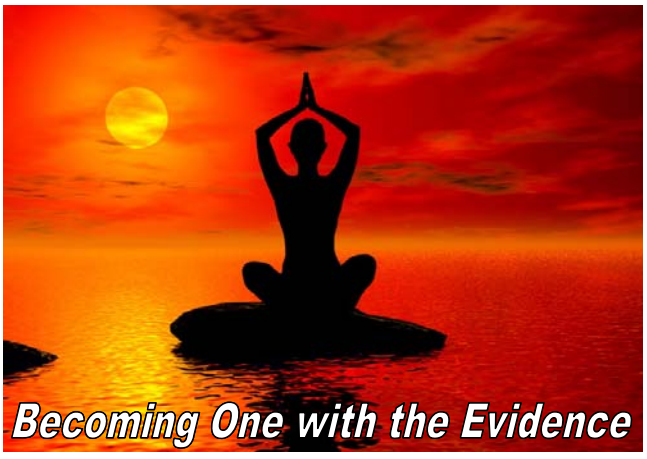
- Classic example
  - Patient: “I think I have all the symptoms of UC”
  - 3rd year med student in July:
    “We need to rule out ZE, VIPoma, Yersinia……”
- Laundry List PROs:
  - ☺ It does provide a complete differential
  - ☺It is safe → defensive medicine
- Laundry List CON:
  - ☹ It is inefficient, and does not prioritize diagnoses

Cognitive Problems

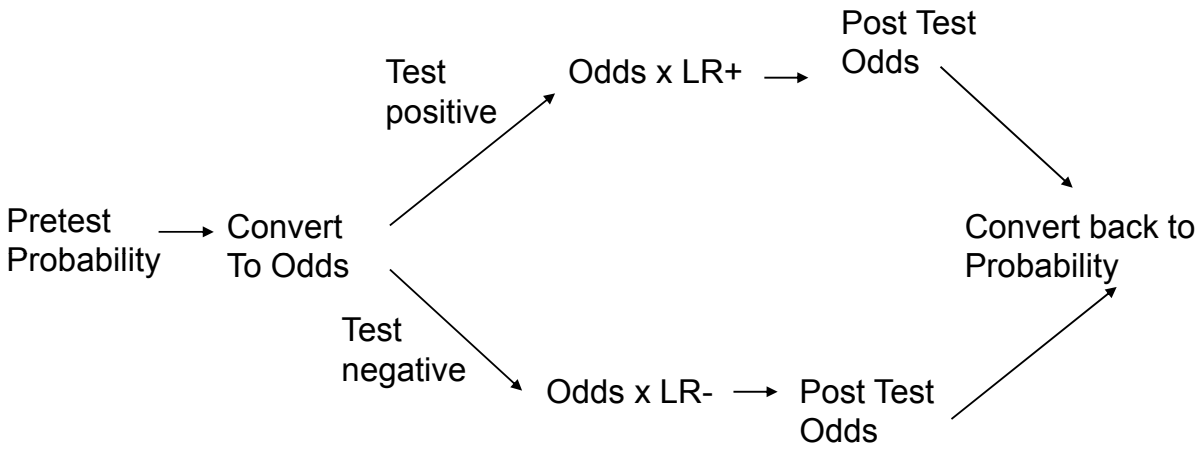
- Problems with too many choices
  - Harder to make a choice when options↑
  - Humans tend to make pairwise comparisons
    - Diagnosis A vs. Diagnosis B
  - If 30 possible diagnostic choices
    - 2^{30} = 1,073,741,824 diagnostic comparisons
- Human brains generally function better with a short list of likely diagnoses
- How to focus? Three lenses

Another Impractical Approach

- EBM Nirvana
  - Start with pretest probability
  - Engage in multiple calculations of odds and probabilities



How EBM DDx is supposed to work



Issues: Pretest probability rarely accurately known

Likelihood Ratios often not published for diagnostic tests

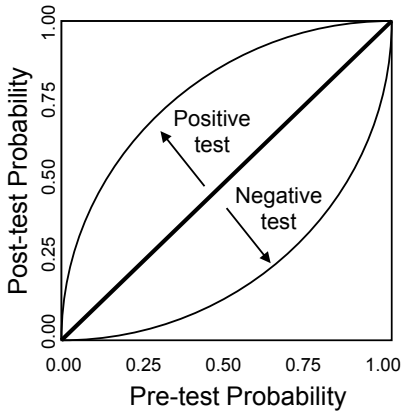
Way too much conversion

Only addresses **ONE** possible diagnosis at a time

Pearls from EBM

Useful Concepts from EBM

- Pretest probability
  - Some diseases ARE more common
  - Varies by practice, referral patterns
  - Can change over time (C. difficile)
- Test results shift the probability
  - Most useful near 50%
  - Less useful at extremes
    - Hard to be 100% certain of anything



What Does Work

Pattern Recognition

What Does Work

- Pattern recognition
  - Most common strategy used in practice
  - Time efficient
  - Remarkably accurate, with sufficient experience
- Integrates all available data
  - History of present illness
  - PMH / FHx / Social Hx / Medication Hx
  - Labs and Imaging
  - Endoscopy and Pathology

Problems with Pattern Recognition

- Premature closure
  - Patient: " I'm calling because I'm having a flare"
  - PCP: "I'll call in prednisone"
  - Not considering alternatives strongly enough
  - Ignoring warning flags if present
- Lack of knowledge/experience
  - Learners don't know, or fail to recognize warning flags of alternative diagnoses

How DDx can actually work

- Find middle ground between
  - Premature closure
  - Laundry list
- Two stage workup
  - Start with a short lineup – focused list
  - Reserve the laundry list for diagnostic failures

Three Lenses

Focus your Differential

Pretest Probability

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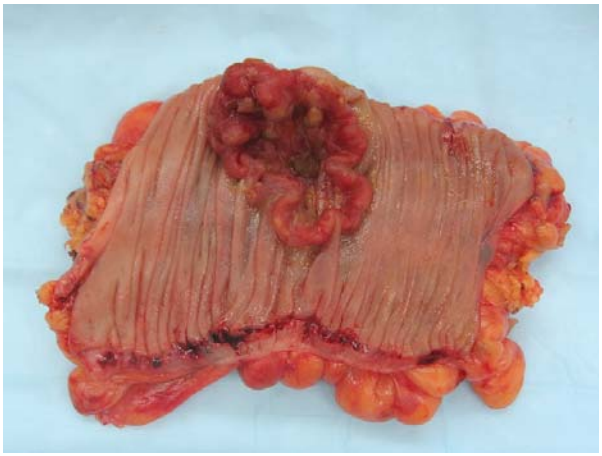
Diagnoses Not to Be Missed



CRC

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IBS

Suggestive History

- Clues

First Stage: Lineup of Likely Suspects

- IBD
- IBS
- Acute colitis
- C diff
- CRC
- History-based Dx 1
- History-based Dx 2

Filling the Lineup - Pick 2

- Strategy to prevent Premature Closure
- Warning Flags from History
  - Cancer – radiation? Cancer syndrome?
  - Surgery - post chole? Vagotomy?
  - Pain history – NSAID enteropathy?
  - Older – atherosclerotic Hx? Microscopic colitis?
  - Autoimmune disease – vasculitis?
  - MGUS – intestinal amyloidosis?
  - Antibiotics – C diff?

Gathering Data

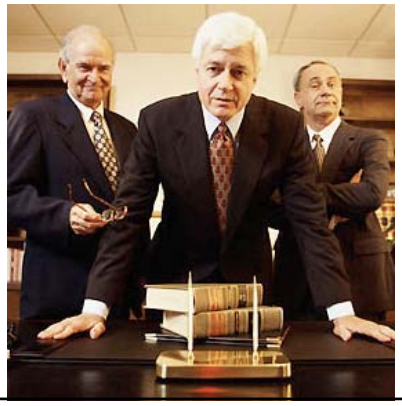
- With a lineup in place, characterize symptoms
- Get labs
  - Inflammation (ESR, CRP, fecal marker)
  - SB function (iron, vit D, B12, Alb)
- Consider imaging
  - CTE
    - Find, localize inflammation
      - If small bowel, consider whether DBE needed

Gathering Data

- Ileocolonoscopy
  - Define severity
  - Define extent
  - Biopsy for histopathology
- Additional scoping
  - EGD, DBE if Sx and imaging suggest proximal dz and no Dx from ileocolonoscopy

Scope Everybody for Dx?

- Expensive, invasive
- Practical considerations
  - Expectation is to scope
    - Referring doc and patient
  - Get disease extent, distribution *before* Rx
  - Difficult to justify cost, risks of therapy without histopathology
  - If diagnosis missed without scope, made later by others –
    you will meet lawyers
  - You need a good reason **not** to scope



Illustrative Fictional Cases

Case 1

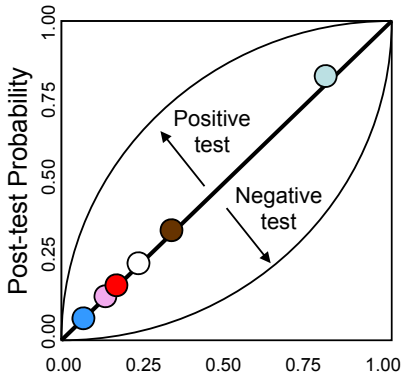
- 18 year old female, college freshman
- Bloating, gas, diarrhea 4-10x/d for past 4 weeks
  - No blood or mucus
  - LLQ cramping before BMs
- Midterms start next week
- Cousin has Crohn's
  - Sure she has Crohn's
  - Referred from student health
- WBC 8, Hgb 12, Plt 289
- Alb 4.2, iron sat 22%
- ESR 17, CRP 0.2

Lineup

- IBS
- Acute colitis – norovirus?
- C diff
- Crohn's
- History-based Dx 1 – Caffeine?
- History-based Dx 2 – Lactose intolerance
- CRC

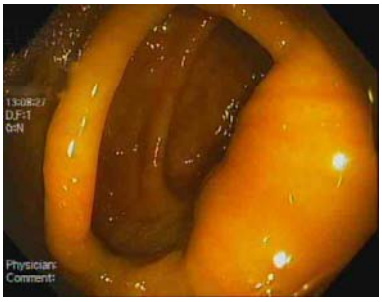
Probabilities

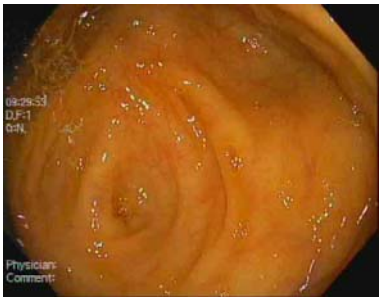
- IBS – new stressor, Sx roughly compatible
- Acute colitis – crowded environment
- C diff – no Abx, maybe
- Crohn's – atypical
- Caffeine – lots
- Lactose – more than parents
  - possible

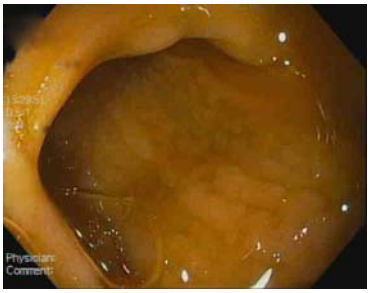


Evaluation

- Stop caffeine and lactose
- C diff toxin testing
- Schedule endoscopy for next week
  - Can cancel if resolves after midterms over
  - Or if C diff positive
- If continues, can consider viral testing

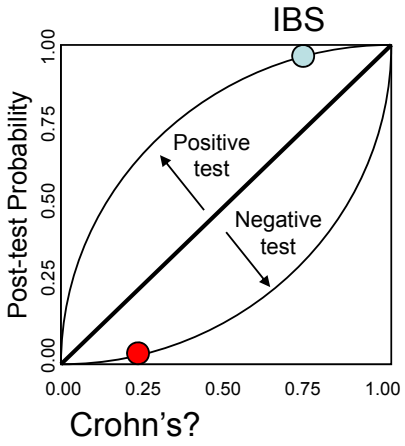






Outcome

- IBS – 90% better after midterms
  - Complicated by caffeine overindulgence
  - Complicated by unrecognized lactose intolerance
- Diagnostic Certainty?



Is this good enough?

If not,
CTE vs. Capsule?

Case 2

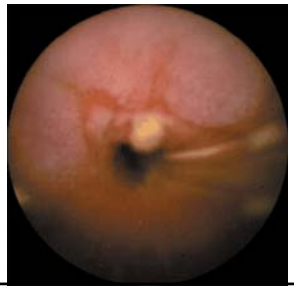
- 25 yo weekend warrior – hockey player
- Recent loose stools 2-4/d x 2m with blood, RLQ abd pain, episodes n/v in past 2 weeks, , some fatigue
- No FHx IBD, uncle with CRC
- WBC 6.7, Hgb 10.8, Plt 307
- Alb 3.8, iron sat 15%
- ESR 19, CRP 0.4

Lineup

- Acute colitis – Shigella, EHEC?
- IBS ↓
- IBD?
- CRC?
- History-based Dx – NSAIDs
  - Uses “some”

Data Gathered

- Stool cultures negative
- Scope unrevealing, including TI
  - ***Not*** striking visceral hypersensitivity
- Admits to remarkable NSAID consumption
  - While on midazolam – *and* driver confirms
  - In bottles of naprosyn/week, not pills
- CTE suggests multiple ileal narrowings
- Maybe capsule endoscopy?
- DBE biopsies – nonspecific injury
  multiple weblike strictures dilated.



Case 3

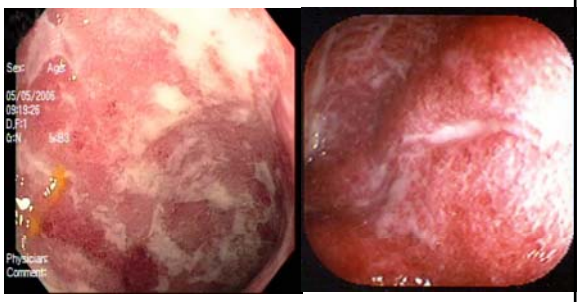
- 28 y/o female with 3 m of BLQ pain, 4-7 loose BM/d, 3-5/d with blood, ++ urgency, stiffness in knees, 7 lb wt loss, and worsening fatigue
- Aunt with Crohn's (2 surgeries)
- Well water, camping this summer
- 4 oral ulcers, RLQ> LLQ tenderness
- WBC 10.2, Hgb 10.5, Plt 512 from PCP
- Alb 3.3, iron sat 7%, 25-OH vitD: 7
- ESR 44, CRP 3.7

Lineup

- Crohn's ↑
- UC
- Infectious
- NSAIDs for knee pain
- CRC, FAP? ↓
- IBS↓

Workup

- Stool studies negative
- Scope – active pancolitis
  - Less active in transverse
  - Linear, deeper ulcers in R
  - 2 tiny ulcers in TI



- Denies NSAIDs
- Biopsies: chronic inflammation throughout, basal plasmacytosis, crypt distortion, no granulomas. Distribution c/w UC. TI inflammation nonspecific, could represent backwash ileitis.

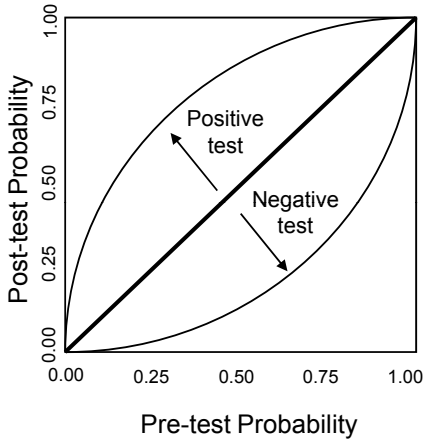
Chronic colitis, but…

- Sure it is UC > Crohn's?

UC	Crohn's
Continuous	? Transverse skip
Blood in stools	SB function ↓
Urgency	Family History CD
	Ulcers with depth

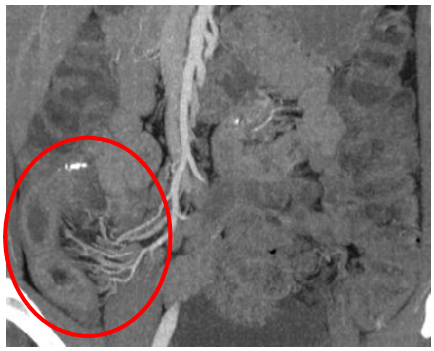
What next?

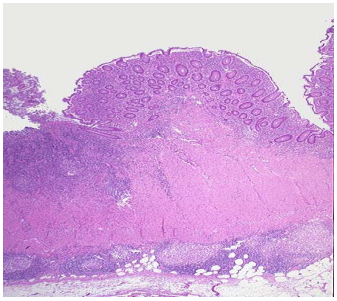
- Is there real SB disease?
  - CTE, capsule, DBE, serologies
  - Need tissue
- Imaging-guided endoscopy
  - CTE first
    - DBE if clear target
    - Capsule if not
- When serologies for Dx?
  - When all endoscopes are broken.



Findings

- CTE – distal ileum, not in TI
  - Mucosal enhancement
  - Increased vascularity
- DBE Biopsies
  - Confirm CD in small bowel

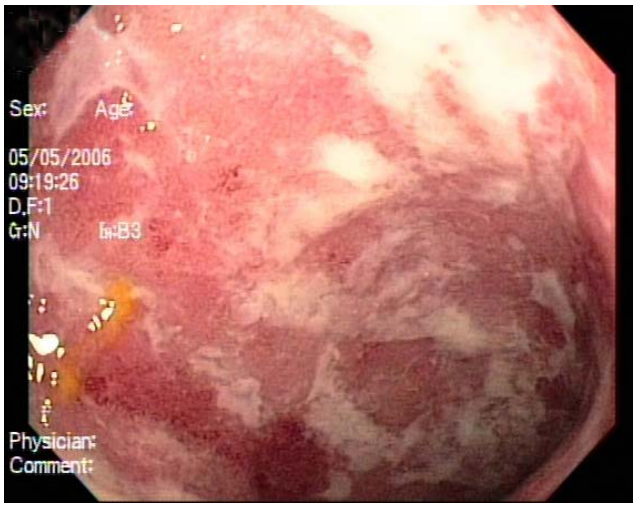




When it Is IBD

When it is IBD

- Don’t stop at diagnosis
- Gather data for future use
- Document extent of disease before therapy



A Public Service Announcement

- Vaccinate!
  - *Before immunosuppressed if possible*

Mahedevan and Kane handout from Friday breakout

Sands and Siegel handout from Saturday breakout

Melmed, *et al.* Am J Gastroenterol. 2006;101(8):1834-1840

More Problems with Pattern Recognition in IBD

- 'Pattern' of IBD varies – no one pattern!
  - Type: Crohn's vs. UC
  - Location: ileal vs. colonic vs. rectal
  - Variation in patients
    - Some never get voluminous diarrhea
    - Some rarely see blood
    - Some rarely have ↑ CRP

Improve Your Pattern Recognition

- Characterize this patient's pattern of flare
  - Detailed symptoms
  - Inflammatory markers
  - Imaging, endoscopy

Improve Your Pattern Recognition

- Measure the baseline when the patient is well
  - ESR, CRP, fecal markers, baseline bowel pattern
- Compare new flares to this pattern
  - Does everything – symptoms, history, noninvasive markers, fit?
  - If not, strongly consider alternative diagnoses, further diagnostic testing

Case 4

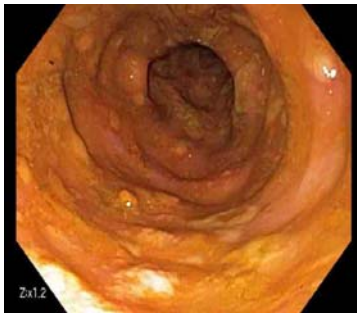
- 25 y/o male with pan-UC x 7 years
- Doing well x 5y on Aza 150 mg daily
- New flare
  - 12 bm/d, blood in about 25% of BMs
  - Large volume stools, aching abdominal pain
  - *Start a biologic?*
- Lineup
  - UC flare, infectious colitis, CMV
  - C diff, CRC, NSAID-induced

Does the Pattern Match?

Marker	Index UC flare	Baseline	New Flare
BMs	18/d, most AM	2-3/d	12/d
Blood	Most BMs, large amounts	Rare traces ~ monthly	1-2/d, small amount
Stool Volume	Small frequent	normal	Large frequent
Abd Pain	Cramp before BM	None	Aching constantly
WBC	12	7	19
CRP	4	0.3	6
FLA	400	18	1300

Outcome

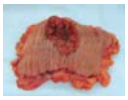
- Stool Cx, C diff toxin negative
- Flex sig – erythema, loss of vascularity, few shiny ulcers
- Biopsies + for C diff
- Responds to flagyl + prednisone
- No test is perfect….



A Few Bad Zebras to Keep in Mind

- Nonhealing firm fistula → adenoCa?
- Food right through me – bypass fistula?
  - Terminal ileum to sigmoid
- Obstruction – SB adenoCa or lymphoma?
- Bad headache in IBD – cerebral sinus thrombosis?
- Intractable steady bleeding out of proportion to diarrhea – CRC?

Summary

- Efficient diagnosis uses pattern recognition 
- Focus your differential with 3 lenses 
  - Likely 
  - Ones you would not want to miss 
  - Pick 2 – force yourself to avoid premature closure 
- Measure and document individual disease patterns in ***your patients*** to improve your pattern recognition 

Thank you

When Serologies?

- Trying to prognosticate risk of CD prior to colectomy
  - FHx CD and ASCA IgA best predictors (Melmed)
- Truly high risk scope
  - Trying to find reasons not to pursue scope
- Diagnostics
  - If no endoscopy available
- Prognostic
  - Maybe, but is it better than clinical history?

Melmed, *et al*. Dis Colon Rectum. 2008 Jan;51(1):100-8.

Characterizing Flares

- Stool – number, form, blood content, mucus content
- Rectal Sx – urgency – time to BM, number urgent episodes, # awaken from sleep, unproductive urges
- Pain – where, when, in assoc with BM or not, intensity
- Systemic Sx – fatigue, napping, fevers
- Extraintestinal Sx – joints, eyes, mouth, skin

Using Fecal Markers

- Noninvasive approach
- Imperfect Sens/Spec – better in colonic dz
- Tracks well with endoscopic activity
- Pick one – available, cheapest for you
  - See if it is helpful in tracking individual patients

Vaccinations

- Killed
  - Injected **influenza**
  - Human Papilloma Virus
- Component
  - **Pneumococcus** (PPV23)
  - **HBV**, HAV
  - H flu (Hib)
- Toxoid
  - **Tetanus** (Td, DTaP)

- Live (***avoid*** within 3m of immunosuppression!)
  - **Varicella** – chickenpox and shingles
  - Typhoid
  - Vaccinia – smallpox
  - Nasal spray: Flumist
  - Yellow fever, MMR

Appendix

The Laundry List

A Laundry List

- Osmotic Diarrheas
  - Magnesium, phosphate, sulfate
  - Intolerance of lactose, fructose

A Laundry List

- Fatty diarrheas
  - Pancreatic insufficiency
  - Small intestinal bacterial overgrowth

A Laundry List

- Other inflammatory diarrheas
  - Ulcerative jejunoileitis
  - Diverticulitis
  - Ischemic colitis
  - Radiation colitis

A Laundry List

- Abnormal motility
  - Post-vagotomy
  - Diabetes
  - Hyperthyroid
  - Post-sympathectomy syndrome

A Laundry List

- Infections
  - Clostridium difficile, CMV, Campylobacter, Salmonella, Shigella, E coli 0157:H7, Aeromonas, Plesiomonas
  - Entamoeba, tuberculosis, Yersinia, Chlamydia, Giardia, HSV, HIV

A Laundry List

- Neuroendocrine tumors
  - Gastrinoma
  - VIPoma
  - Somatostatinoma
  - Mastocytosis
  - Carcinoid syndrome
  - Medullary carcinoma of thyroid

A Laundry List

- Neoplasia
  - Colon carcinoma
  - Lymphoma
  - Small bowel adenocarcinoma
  - Villous adenoma

Impractical Approaches

- Premature Closure
  - Patient: “I have UC and I’m having a flare”
  - PCP: “I’ll call in the prednisone”
- Zebra Hunting
  - Patient: “I think I have all the symptoms of UC”
  - 3rd year med student:
    “We need to work you up for ZE and VIPoma”

A Laundry List

- Ileal bile acid diarrhea, post-cholecystectomy
- Pancreatic insufficiency
- SIBO
- Microscopic, lymphocytic, collagenous colitis
- Post-vagotomy, diabetes, hyperthyroid

A Laundry List

- Appendicitis, Lymphoma, SB adenocarcinoma, vasculitis, eosinophilic gastroenteritis, sarcoidosis
- ischemic colitis, radiation colitis or enteritis, diverticular colitis
- NSAID enteropathy
- CRC
- Endometriosis
- Carcinoid
- Medication induced colitis – nsaids, retinoids, gold, penicillins, mesalamine allergy

A Methodology of Pattern Recognition

- Know your practice
  - What is the pretest probability in your setting?
- Know your individual patients
  - What does a typical flare look like?
  - Stools, blood, mucus
  - Urgency, tenesmus
  - Abdominal pain, fatigue
  - ESR, CRP, fecal markers, flex sig, imaging?
  - Measure, record, and document what that patients bad flare looks like