Managing Dyspepsia for college health providers

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Objectives

- Review differential diagnosis for patients with upper abdominal sx, including dyspepsia
- Discuss a cost-effective evaluation of a dyspeptic patient in college health setting
- Review treatment strategies for the various etiologies of dyspepsia
Consider a case…

- 20 y/o college junior with burning pain in subxiphoid region off & on for a few months, particularly worse in last week or so with looming midterm exams.
Differential Dx: upper abd pain

- Peptic ulcer disease
- Nonulcer dyspepsia, aka functional dyspepsia (60%)
- GERD
- Biliary/hepatic
- Pancreatitis
- Gastroparesis
- GI malabsorptive d/o (lactose intol, celiac)
- Abd wall pain
- Meds, esp NSAIDs though many
- Ischemic, infiltrative, metabolic, malignancy...
Definition: Dyspepsia

Rome III criteria

- Post-prandial fullness &/or
- Early satiation &/or
- Epigastric pain or burning

(Rome II included heartburn)

AGA

- Chronic or recurrent pain or discomfort centered in the upper abdomen
- Does not include reflux if heartburn is ONLY symptom
- Does not include acute abdomen
Dyspepsia definition for today

Upper abdominal discomfort w/ or w/o reflux sx

Specifically will address evaluation of:
- GERD
- Undifferentiated dyspepsia

And management and treatment of:
- GERD
- PUD
- Functional dyspepsia
Epidemiology: Dyspepsia

- Prevalence in US of ~25% (weekly sx)
  - Rises to 40% if include heartburn
  - Fewer than half seek medical care
- Likely lower in college population
  - US householder survey: prevalence of 13%
    - When IBS sx and GERD excluded, 3%
  - Abdominal sx common in stress, eating d/o
Clinical approach: History

PQRST

- Provocation/Palliation
- Quality
- Region, Radiation
- Severity, associated Sx
- Timing

Red Flag Sx

- Age >55 (some say 45)
- Unintended wt loss
- Persistent vomiting
- Dysphagia, odynophagia
- Sx of GI bleeding: hematemesis, melana, BRBPR
Clinical approach: PE

VS, including wt
- Orthostatics only if ill

Pertinent system
- Abdominal exam

System above/system below
- Chest: heart/lungs
- Back: CVAs, M/S
- Consider u/a, esp female pt

Red Flag Signs
- GI bleed: heme+ stool or Fe Def anemia
- Orthostasis
- Peritoneal signs
- Abdominal mass
- Jaundice
Classic GERD

- Heartburn: substernal pain that may be associated with sense of acid regurgitation &/or sour taste
- Epigastric pain radiating to chest
- Sx worse w/ large meal, bending forward or lying down; sx better w/ antacids
- PE usually completely normal
Classic PUD/FD

- Burning pain in epigastric region
  - Possibly radiating to back
- Better w/ eating, antacids; perhaps worsened by spicy/acidic foods
- PE w/ mild subxyphoid or RUQ tenderness,
How helpful is H&P?

- Patients do not always present as textbook cases...
- *Individual s/sx* are not very helpful
  - Mostly b/c DDx so broad
  - Symptoms so nonspecific
Accuracy of individual sx to dx
GERD

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR +</th>
<th>LR -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>68</td>
<td>52</td>
<td>1.4</td>
<td>0.6</td>
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<tr>
<td>Pharyngeal pain</td>
<td>19</td>
<td>85</td>
<td>1.3</td>
<td>1.0</td>
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<tr>
<td>Acid regurgitation</td>
<td>60</td>
<td>52</td>
<td>1.3</td>
<td>0.8</td>
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<tr>
<td>Odonophagia</td>
<td>10</td>
<td>92</td>
<td>1.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Retrosternal burning</td>
<td>61</td>
<td>51</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Belching</td>
<td>49</td>
<td>60</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Nausea</td>
<td>38</td>
<td>68</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>54</td>
<td>47</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Retrosternal pain</td>
<td>57</td>
<td>39</td>
<td>0.9</td>
<td>1.1</td>
</tr>
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</table>
...But overall gestalt not too bad

<table>
<thead>
<tr>
<th>Overall Clinical impression</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR +</th>
<th>LR -</th>
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<tbody>
<tr>
<td>GERD</td>
<td>0.59</td>
<td>0.83</td>
<td>3.5</td>
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<td>PUD</td>
<td>0.37</td>
<td>0.83</td>
<td>2.2</td>
<td>0.7</td>
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<tr>
<td>FD</td>
<td>0.43</td>
<td>0.69</td>
<td>1.4</td>
<td>0.8</td>
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<tr>
<td>Malignancy</td>
<td>0.13</td>
<td>0.97</td>
<td>4.3</td>
<td>0.9</td>
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</table>
Diagnostic tests

- Esophageal manometry
- Bernstein test
- Ba swallow
- Endoscopy: EGD
- pH monitoring
- Upper GI
- Omeprazole challenge
Useful tests Dx GERD

<table>
<thead>
<tr>
<th>Test</th>
<th>SN</th>
<th>SP</th>
<th>LR+</th>
<th>LR-</th>
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<tbody>
<tr>
<td>Omeprazole challenge</td>
<td>0.78</td>
<td>0.85</td>
<td>5</td>
<td>0.3</td>
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<tr>
<td>Endoscopy</td>
<td>0.22</td>
<td>0.74</td>
<td>0.9</td>
<td>1.1</td>
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<tr>
<td>24hr pH monitoring</td>
<td>0.80</td>
<td>0.73</td>
<td>3</td>
<td>0.3</td>
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</table>
Diagnosing GERD

- Clinical gestalt usually suffices
  - Omeprazole test (~ treatment trial) wins gold star!
  - More cost effective than pH or EGD

- Consider additional testing if:
  - Red flag symptoms present: EGD or Ba swallow/UGI
  - Considering GERD as etiology of atypical sx presentation
    - chronic cough or laryngitis: pH probe
    - chest pain: omeprazole challenge
  - Lack of response to acid suppression therapy
Dx Tests: dyspepsia

- Two categories of nonGERD dyspepsia
  - Those w/ identifiable cause: ulcer, malignancy
  - Those w/o identifiable cause: functional dyspepsia (FD)
    - aka nonulcer dyspepsia (NUD) or idiopathic dyspepsia

- FD is dx of exclusion
Useful tests to dx PUD

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
<th>SN</th>
<th>SP</th>
<th>LR+</th>
<th>LR-</th>
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</thead>
<tbody>
<tr>
<td><strong>PUD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGD</td>
<td>0.92</td>
<td>0.99</td>
<td>92</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>UGI</td>
<td>0.54</td>
<td>0.91</td>
<td>6</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td><strong>Gastric ulcer</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGD</td>
<td>0.85</td>
<td>0.98</td>
<td>42</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>UGI</td>
<td>0.91</td>
<td>0.99</td>
<td>91</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td><strong>Duodenal ulcer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGD</td>
<td>0.99</td>
<td>1.00</td>
<td>99</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>UGI</td>
<td>0.50</td>
<td>0.99</td>
<td>50</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>
Weighing pros & cons

EGD more accurate
EGD allows for add’l testing

UGI less expensive
UGI has fewer complications
The elephant in the room…
Etiology of ulcers

- Most PUD caused by H. pylori &/or NSAIDs
  - Other factors are synergistic: tobacco, ETOH, other meds
  - 75% of pt w/ DU, GU have H.pylori
  - Only 15% w/ H.pylori will develop ulcer
- Eradicating H.pylori cures ulcer
Diagnosing H. Pylori

Invasive tests
(ie req’s GI involvement, EGD)

- Biopsy urease test
- Histology
- Bacterial culture

Noninvasive tests

- Urea breath test
- Serology
- Stool antigen
Urea breath test

- Carbon labeled urea is hydrolyzed by H. Pylori: $\text{CO}_2 + \text{NH}_3$
- Sn ~ 88-95% ; Sp ~ 95-100%
- False neg if on abx, acid suppression, bismuth
- Costs $50-100
- Check on local availability (ie not available at SU)
Serology

- Detection of IgG antibodies
- Sn 90-100%; Sp 76-96%
- Serology can remain + even after eradication
  - 40% still + after 18 months
  - Thus, not so useful for f/u testing
  - Useful if low probability and never tested
- Cost: ~$30
Stool antigen test

- Enzyme immunoassay of fecal sample
- Sn ~94%; Sp 86-92
- Newer rapid stool Ag tests developed but lower sn
- Cost ~$80
Diagnosing H. Pylori?

Serology is appropriate 1st line H. Pylori test in college pop
- Lower prevalence of H. Pylori in younger people
- Lower cost as first line test
- Likely better compliance vs stool Ag collection

Bottom line:
- If testing for HP, order serology unless known past +
- If testing for eradication (after treatment, or recurrent sx) then use stool Ag test, or breath test
Undifferentiated dyspepsia
(ie no alarm sx & r/o GERD dominant clinically)

Possible approaches:

1. Empirical acid suppression
2. Noninvasive HP test, scope positives
3. Noninvasive HP test, treat positives
4. Empirical HP eradication w/o testing
5. Endoscopy directly
And the cost effective winner is…

1. Empirical acid suppression
2. Noninvasive HP test, scope positives
3. Noninvasive HP test, treat positives
4. Empirical HP eradication w/o testing
5. Endoscopy directly
Why?

The thinking:
- Prevalence of PUD (~15%) is much lower than FD (50-70%) in primary care pop
  - Likely even lower in college pop
- Proven benefit of H Pylori eradication eliminating sx & curing ulcer (level 1a) AND preventing relapse

The evidence:
- Multiple cost-effective analyses support
- Few RCTs do
  - Metaanalysis of 5 trials shows equivalent cure, more cost
- AGA guidelines concur
- No studies specifically in college health
- If no funding for HP testing, empiric acid suppression not unreasonable
Dyspepsia

Suspect other causes (ie, biliary)?

- Yes → Work-up/Treat condition found
- No → NSAID/Cox-2 inhibitor use?
  - Yes → Stop/change med or add PPI
  - No → Red flag signs or symptoms age>45 (55)
    - Yes → Send to ER immediately
    - No → Clinicians gestalt supports GERD?
      - Yes → GERD therapy
      - No → H. pylori test
        - positive → Eradication therapy
        - negative → Empiric FD therapy

Send to ER immediately

Refer to GI for endoscopy

positive → Treat condition found

negative → Empiric FD therapy
Pulling it all together…

- **Upper abdominal sx**
  - H&P to direct what is highest on DDx list

- **If left w/ Dyspepsia**
  - On NSAIDs? If so, stop; if not…
  - Red flag sx? If so, refer; if not…
  - Does clinical gestalt suggest GERD? If so, tx GERD; if not, test for H. Pylori
  - If pos for H. Pylori, eradicate; if negative, treat as functional dyspepsia
Treatment

- GERD
- H. Pylori
- Functional dyspepsia

Discuss recurrent sx, lack of response
Treatment: GERD

Goal:
- symptom relief
- healing of esophageal erosions
- prevent complications
GERD: Nonpharm Tx

- **Lifestyle modification**
  - Elevated head of bed, esp if nocturnal sx*
  - Avoid tight fitting clothes
  - Don’t eat before bed; remain elevated after eating
  - Decrease/quit smoking
  - Lose weight*

- **Dietary modification**
  - Limit ETOH
  - Chew gum/use lozenges to promote salivation
  - Avoid triggering foods
    - Some specific triggers: fatty foods, chocolate, peppermint, acid beverages (OJ, soda)

* Only * has evidence to demo benefit
Med Tx: GERD

- Antacids (B)

- Acid suppression medications (A)
  - H2Blockers are consistently effective
  - All H2Bs are equivalent

  - Proton pump inhibitors consistently better than H2Bs
  - All PPIs are also equivalent
Med Tx: GERD

- Acid suppression meds lower acidity
  - Lessen sx; allow esophageal healing
  - Do NOT prevent actual refluxing

- Pro-motility agents (C)
  - ie bethanechol, metoclopramide
  - No longer used/recommended b/c of significant adverse effects, drug interactions with very limited efficacy
Other considerations

- Step up vs step down approach as initial mng
- Managing chronic sx
  - Intermittent—sx resolved; resume last effective dose when sx recur
  - Chronic—maintain on acid suppressive that manages sx if relapse within 3 months of stopping meds
- When to refer
  - Double to triple std dosing of PPI, and failure to respond
  - Surgery for recalictrant, chronic, severe GERD (A)

See GERD algorithm in handout
## Costs of Acid Suppression Meds

<table>
<thead>
<tr>
<th>H2-receptor blockers</th>
<th>Proton Pump Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranitidine 150mg bid ($12/ month)</td>
<td>Omeprazole 20mg QD ($13 generic; &gt;$200 if brand)</td>
</tr>
<tr>
<td>Famotidine 20 mg QD ($20)</td>
<td>Lansoprazole 30mg QD ($15 generic; $80+ if brand)</td>
</tr>
<tr>
<td>Cimetidine 800mg bid ($36)</td>
<td>Pantoprazole 40mg QD (~$100 not generic yet)</td>
</tr>
</tbody>
</table>
Treatment: PUD

Goal of treatment
- Sx relief
- Eradication of H. Pylori infection to heal ulcer, prevent relapse
- Manage sx following HP cure (equiv to functional dyspepsia tx)
Treatment: HP+ dyspepsia

- H pylori eradication requires abx + acid suppression
  - 10-14 day better efficacy vs 7 d or shorter
  - Complicated strategies, numerous RCTs, drug resistance
  - Changes frequently, so worthwhile to update at least annually: AGA or Sanford guide

- Specific factors affecting choice:
  - Efficacy of eradication
  - Cost
  - Compliance: ease of regimen and side effects
Categories of HP eradication Tx

- **Dual therapy** = PPI + one abx
  - Not recommended now b/c of low efficacy rates

- *Triple therapy* = PPI + 2 abx
  - Usually preferred for efficacy + compliance

- Quadruple therapy = PPI + 2 abx + bismuth

- **Sequential therapy** = PPI + 1 abx x 5 days followed by PPI + 2 new abx for next 5 days
  - Newer, proven effective; newly used to address resistance

*AGA rec’d 1st line; **Sanford rec’d 1st line
1st line in HP eradication

Triple therapy x 10-14d

1. PPI (doesn’t matter which one, just std dosing bid)
   - Omeprazole 20mg bid or ($26 generic)
   
2. Amoxicillin 1g bid ($15)
   
3. Clarithromycin 500mg bid ($100)

Note: prevpac = prevacid + amox + clarithro; convenient ordering but cost is $360

If allergic to PCN or macrolide, substitute metronidazole 500mg bid
Sequential therapy option

- PPI std dose bid x 10 days
- Amoxicillin 1g bid x 5 days (day 1-5)
  
  followed by
  
- Clarithromycin 500mg bid + tinidazole 500mg bid x 5 days (day 6-10)

- Rec’d by Sanford due to higher rates of cure
- Not 1st line rec’d in US; used for failed eradication
Test of cure?

- Upwards of 20% HP not successfully eradicated
  - Drug resistance, noncompliance
- Insufficient evidence to warrant routine test of cure
  - Cost effective analyses suggesting not valuable
When/how should I retest for HP?

- Treat w/ full course of eradication tx and sx have not responded
  - Question compliance w/ regimen
  - Check stool antigen to ensure HP infx resolved
- Known h/o +HP, responded to treatment with sx resolution &/or healing via EGD
  - If sx recur, check stool antigen for re-infection.
If HP+, treat again, perhaps w/ sequential or quadruple tx

If HP-, treat with PPIs x 4 wk more

If no response, refer to GI for EGD

Refer to algorithms in handout for dyspepsia
Treatment: Functional Dyspepsia

Goal:
1. Decrease sx

Delayed goal…
1. Accept/cope with sx if not resolving and become more chronic
FD: pharm approach

Following the original algorithm...

- Actually 1st stage: treating H. Pylori negative dyspepsia
- FD is a dx of exclusion and we have not yet fully excluded other causes.

1st line HP negative dyspepsia:

4 wk trial of PPIs
If no response…

- Reassess diagnosis
  - Are there new sx to suggest different dx or raise concern?
  - Address stress/functioning issues
- Consider trial of higher dosing PPI
  - Not proven to aid, but at this point, EGD still most likely neg
  - Double dose (ie 20 bid omeprazole)
- If sx particularly troubling, refer to GI for scope to r/o other etiology

Refer to algorithms in handout for dyspepsia
Options to manage *documented* FD

1. Cont’n GI treatments
2. Cont’n exploring other dx
3. other “nonGI” treatments
1. GI treatments

- Mild benefit noted in RCTs of FD for:
  - H2Bs (B)
  - PPIs (A-)
  - Prokinetic agents (C)
  - Antispasmodics (B)

- Most short term studies, heterogeneous population

- Benefit found relative small; more apt to reduce, not resolve sx
2. Other dx options?

- Always re-evaluate
  - Delayed gastric emptying? IBS? Celiac?
  - Panic/anxiety/other psychological issues

- May be more helpful to introduce this concept before referral to GI for scope
  - Introduce mind-body connection
  - Sx diary to help id personal triggers
3. Other “non-GI” options

- **Lifestyle modification**
  - Dietary changes to limit triggers
  - Nutrition consult

- **Psychotherapy**
  - Important to *not* convey message “this is in pt’s head”
  - Useful to id/manage triggers, aid in coping with chronic physical sx
3. “non-GI” options cont’n

- Antidepressants
  - Limited RCT data, some negative
  - May help if associated sx such as insomnia
  - Taking approach of “chronic pain management”
  - Low dose tricyclics (10mg amitriptyline QHS), or trazadone (25mg QHS)
Summary: key points

- H&P to sort dyspepsia from other etiologies
- Follow algorithm
  - Clinical dx of GERD dominant
  - If not GERD, test/treat HPylori
  - Refer to GI if significant alarm s/sx or failure to respond
- Most dyspepsia in college students will not require GI involvement/referral
Case discussions
Case 1

a 20 y/o college junior with burning pain in subxyphoid region off & on for a few months, particularly worse in last week or so with looming midterm exams. Eats lots of junk food; binge ETOH on weekends

a PMHx: no GI problems; recurrent knee injury uses rx naprosyn prn

a Exam basically negative
Case 2

- 26 yo female grad student w/ mid upper abd pain, radiates upwards; occ wakes her from sleep. Nausea, no vomiting; no alarm sx
- PMHx: neg
- SHx: no tob, ETOH social, max of 3 drinks; is sexually active w/ same partner of 2 years
- Exam benign
Case 3

- 20 y/o pledging a sorority notes worsening upper abdominal pain, nausea but no vomiting. Worse when eats so has decreased intake; tolerates low fat food better. Lost ~5# in last month but is happy w/ that
- PMHx: past abd sx but never evaluated
- Exam: pt thin, mild epigastric tenderness, no mass; noted to have Fe Def anemia
Case 4

- 47y/o veteran returning to grad work noting new onset RUQ pain, occ feeling like food sticks with swallowing. OK w/ liquids. No bleeding, no change in weight.
- PMHx: mild HTN controlled behaviorally
- SHx: former smoker; ETOH usually beers w/ dinner
- Exam negative