Update in Gastroenterology

&

other random evidence

Andrew Gentry
Gastroenterology
Bozeman Health Deaconess Hospital
Narcotic bowel syndrome

Diagnosis

Abdominal pain worsens with escalating doses of narcotics

Marked worsening when narcotic dose wanes

“Soar and Crash”

Progression of frequency duration and intensity of pain episodes

Pain not explained by current or previous GI diagnosis

Side effects

Sitophobia - fear of eating do to pain, weight loss

X-ray concerning for SBO
Breaking the Vicious Cycle

Vicious Cycle of Patient - Physician Interactions

- Pain
- Narcotics
- Maladaptive Therapeutic Interaction
- Physician frustration
- “Furor medicus”
- Healthcare / societal pressure
- Emergency room visits
- Increased healthcare utilization
- Narcotic Bowel Syndrome
- Patient frustration
- “Negative evaluations”
Treatment of Narcotic Bowel Syndrome

- Make diagnosis of Narcotic Bowel Syndrome
- Validate pain
- Discuss pathophysiology and willingness for Rx

Clonidine 0.1mg PO q 6hrs.

Lorazepam 1mg PO q 6hrs. with 1mg PO q 2hrs. prn

TCA or SNRI

PEG 3350 17g PO BID

Physician - Patient Relationship

Morphine equiv. dose (mg) 220 200 180 160 140 120 100 80 60 40 20 0

Day of taper -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 ... 21
Narcotic Side Effects

Newer Treatment Options
Pathophysiology

Decrease in lumen electrolytes
Increase in anal sphincter tone
Decreased motility

Ther Adv Gastroenterol 2015, Vol. 8(6) 360-372
Medications

Lubiprostone (Amitiza®)

Induces chloride channel secretion and soften stool

Tapentadol (Nucynta®)

Centrally activated so few peripheral receptors & lower side effects

Naloxone (Narcan®)

Oral reversal however large amounts enters blood stream and reverse opioid effect

Methylnaltrexone Bromide (Relistor®) - injection

Methly attached to naloxone so not centrally reversed
Breaking the Vicious Cycle
Intestinal Diet

https://en.wikipedia.org/wiki/John_Harvey_Kellogg
Alcoholic Hepatitis

Table 2. Mortality at 28 Days, 90 Days, and 1 Year.*

<table>
<thead>
<tr>
<th>End Point</th>
<th>Prednisolone</th>
<th>No Prednisolone</th>
<th>Pentoxifylline</th>
<th>No Pentoxifylline</th>
<th>Prednisolone Odds Ratio (95% CI)</th>
<th>P Value</th>
<th>Pentoxifylline Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-Day mortality — no./total no. (%)</td>
<td>73/526 (14)</td>
<td>95/527 (18)</td>
<td>85/518 (16)</td>
<td>83/535 (16)</td>
<td>0.72 (0.52–1.01)</td>
<td>0.06</td>
<td>1.07 (0.77–1.49)</td>
<td>0.69</td>
</tr>
<tr>
<td>90-Day mortality or liver transplantation — no./total no. (%)</td>
<td>144/484 (30)</td>
<td>141/484 (29)</td>
<td>139/473 (29)</td>
<td>146/490 (30)</td>
<td>1.02 (0.77–1.35)</td>
<td>0.87</td>
<td>0.97 (0.73–1.28)</td>
<td>0.81</td>
</tr>
<tr>
<td>1-Year mortality or liver transplantation — no./total no. (%)</td>
<td>210/371 (57)</td>
<td>211/376 (56)</td>
<td>205/365 (56)</td>
<td>216/382 (57)</td>
<td>1.01 (0.76–1.35)</td>
<td>0.94</td>
<td>0.99 (0.74–1.33)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

* The interaction between interventions was investigated as a secondary analysis.
Alcoholic Hepatitis

Conclusion

“Pentoxifylline did not improve survival in patients with alcoholic hepatitis. Prednisolone was associated with a reduction in 28-day mortality that did not reach significance and with no improvement in outcomes at 90 days or 1 year.”

Alcoholic Hepatitis
Alcoholic Hepatitis
Sphincter of Oddi Syndrome

![Box plot showing RAPID scores over time for Sphincterotomy and Sham groups.](image)

No. of participants:
- Baseline: 141
- 3 months: 73
- 6 months: 130
- 9 months: 67
- 12 months: 129

JAMA, May 28, 2014, Vol 311, No. 20
Mortality of ERCP and Cholecystectomy

Therapeutic ERCP

0.4-0.5% Mortality

Laparoscopic Cholecystectomy

Case series of 1220 mortality rate 0%

Case series of 2117 mortality rate 0.5% (one surgeon had all the mortality)

0.1% in surgical textbooks

Case series of 9542 mortality rate 0.1%

GASTROINTESTINAL ENDOSCOPY Volume 75, No. 3 : 2012

Principles and Practice of Geriatric Surgery

International Journal of Surgery Volume 9, Issue 42011, Pages 318–323

World J Gastroenterol. 2006 June 28;12(24): 3887-3890
Hepatitis C treatment
Cannabinoid hyperemesis syndrome

Gallatin County leads the state in medical marijuana cardholders, providers

Bozeman Chronical Sunday, October 5

1,711 cardholders in Gallatin County
46% are over 50 years old

86 providers in Gallatin County
19.89 patients per provider
32 YO Female

- Abdominal pain
- Nausea persistent interfering with caloric intake
- Lap Chole without change in symptoms
- History of Anorexia and Bulimia
- Prior Meth addict 7 years clean
- Symptoms improve with hot baths
  - “some days I feel like a fish”
Case Series

• 98 Patients
  – All less than 50 YO
  – 68% use more than 2 years
  – 95% use more than weekly
  – 58% hot water bathing
  – Follow up available on 10%
    • 7 stopped
    • 6 resolution of symptoms

http://www.mayoclinicproceedings.org/article/S0025-6196(11)00026-7/abstract
Diagnostic Criteria

- Long term cannabis use
- Severe cyclic nausea vomiting
- Resolution with cessation
- Relief of symptoms with hot showers
- Abdominal pain
- Weekly use of marijuana
- Age less than 50
- Weight loss of >5kg
- Worse in AM
- Normal bowel habits and negative labs

- Heavy marijuana use
- Recurrent episodes
  - Nausea, vomiting, abdominal pain
- Compulsive bathing - relief
  - 98% reported cases
- Resolution after cessation

My explanation

Cannabis leads to a down regulation on naturally occurring anti-nausea mechanisms with cannabis making up the difference.

When withdrawn or out of system the naturally occurring chemicals are below patient nausea threshold.
Chagas disease

http://www.cdc.gov/parasites/chagas/gen_info/vectors/
Chagas Disease

Romana’s Sign

Acute infection

Feces being rubbed into eye

200,000 cases per year

Acute phase

Non-specific

Romana’s sign

Chronic phase

http://www.cdc.gov/parasites/chagas/gen_info/vectors/
Chagas Disease - Diagnosis

Blood smear or tissue

Laboratory tests

http://www.cdc.gov/parasites/chagas/gen_info/vectors/
Diverticulosis
Prevention with fiber

<table>
<thead>
<tr>
<th>Organization</th>
<th>Statement</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACG</td>
<td>Latest autopsy series 1969</td>
<td>35%-50%</td>
</tr>
<tr>
<td>ASGE</td>
<td>Earliest series in 1930</td>
<td>5-10%</td>
</tr>
<tr>
<td>ACP</td>
<td>“...may help to prevent the development of diverticular disease is not conclusive”</td>
<td></td>
</tr>
<tr>
<td>AGA</td>
<td>Chronic inflammation with abnormal microflora</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>5ASA - mesalamine products</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Probiotics in addition to 5ASA products</td>
<td>Gastrointest Pharmacol Ther 2010; 1(1): 27-35.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aliment Pharmacol Ther 30, 532–546</td>
</tr>
</tbody>
</table>
Pathophysiology of treatment options

**Alterations in Colonic Micro-ecology**
- Leads to activation of inflammatory cascade

**Mesalazine**
- Inhibition of:
  - TNFα and IFNγ synthesis
  - COX, TBX, PAF activity
  - Phagocytic and lymphocytic activity
- "Scavenger" effect
- Inhibition of NO release
- Increasing: Diverticulitis inflammation
- Decreasing: Diverticulitis inflammation

**Faecal Stasis within Diverticula**
- Causes altered colonic micro-ecology and activation of inflammatory cascade

**Probiotics**
- Increasing of:
  - IgA production
  - IL-10 synthesis
  - Phagocytic and lymphocytic activity
- "Metabolic competition" with pathogens
- Anti-bacterial effect
- Increasing: Diverticulitis inflammation
- Decreasing: Diverticulitis inflammation

**References**
- Aliment Pharmacol Ther 30, 532–546
Diet and inflammatory conditions of colon

Colon cancer rate African Americans

65:100,000

Colon cancer rate of rural South Africans

<5:100,000

Two week food exchange

Colonoscopy with biopsy

Reciprocal mucosal biomarkers

Microbiota known for cancer

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4415091/
Bile acid synthesis for cancer
Diet and inflammatory conditions of colon

Animal protein and fat intake

2-3 times higher in American population

Fiber higher in African diet

World Health Organization

“Consumption of red [and processed] meat as probably carcinogenic to humans”
Law of unintended consequences

Folic Acid and Neural Tube Defects
7391 hundred women
Reduction in NTD
RR 0.31 with CI (0.17-0.58)
1995 changed folate supplementation

Folic Acid and Advanced Colon Polyps
1mg of folic acid vs placebo
Advanced lesion
11.6% for folic acid
6.9% for placebo

Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD007950
JAMA. 2007 Jun 6;297(21):2351-9
Aspirin use to prevent colon cancer

Aspirin use over 75mg

Reduction in all cause mortality in first 10 years

Relative Risk 0.94

Reduction in Colorectal cancer in over 20 years

Risk reduction of 33% (relative risk reduction)

Recommendation add for colon cancer prevention
Anticoagulation - know thy enemy
# New Anticoagulation

Table 1—[Section 1.0] Comparison of the Pharmacologic Properties of the New Oral Anticoagulants That Are Approved or in the Most Advanced Stages of Clinical Development

<table>
<thead>
<tr>
<th>Property</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target</td>
<td>Thrombin</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>628</td>
<td>436</td>
<td>460</td>
<td>548</td>
</tr>
<tr>
<td>Bioavailability, %</td>
<td>6</td>
<td>80</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Dose frequency</td>
<td>od/bid</td>
<td>od/bid</td>
<td>bid</td>
<td>od</td>
</tr>
<tr>
<td>Tmax, h</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1-2</td>
</tr>
<tr>
<td>Half-life, h</td>
<td>12-17</td>
<td>7-11</td>
<td>9-14</td>
<td>9-11</td>
</tr>
<tr>
<td>Protein binding, %</td>
<td>35</td>
<td>95</td>
<td>87</td>
<td>54</td>
</tr>
<tr>
<td>CYP metabolism, %</td>
<td>None</td>
<td>32</td>
<td>15</td>
<td>&lt;4</td>
</tr>
<tr>
<td>P-gp transport</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Renal excretion, %</td>
<td>80</td>
<td>66</td>
<td>25</td>
<td>35</td>
</tr>
<tr>
<td>Extrarenal excretion, %</td>
<td>20</td>
<td>34</td>
<td>75</td>
<td>65</td>
</tr>
</tbody>
</table>

CYP = cytochrome P450; od = once daily; P-gp = p-glycoprotein efflux transporter; Tmax = time to maximum concentration.
Dabigatran or Pradaxa®

- Non valvular A-fib, DVT/PE
- Direct thrombin inhibitor
- Less bleeding risk compared to warfarin
- Renally cleared
- Reversal agent Praxbind® recently approved
- May see in increase in PTT
- May be removed with Dialysis
Rivaroxaban or Xarelto®

- Binds to factor Xa (oral LMWH)
- Non valvular A-fib, joint replacements, DVT/PE
- No significant change in bleeding compared to warfarin
- Renally cleared
- No reversal agents in trials
- Half life of 7-11 hours
- Not expected to be removed with dialysis
Apixaban or Eliquis®

- Binds to factor Xa (oral LMWH)
- Non valvular A-fib, joint replacements, DVT/PE
- No significant change in bleeding compared to warfarin
- No reversal agents - in trials
- Half life of 9-14 hours
- Not expected to be removed with dialysis
Edoxaban or Savaysa®

• Binds to factor Xa (oral LMWH)
• Non valvular A-fib, DVT/PE
• No significant change in bleeding compared to warfarin
• Renally cleared
• No reversal agents - one in trials and promising
• Half life of 9-11 hours
• Not expected to be removed with dialysis
TABLE 2

How long to delay elective surgery or procedures after last anticoagulant dose

<table>
<thead>
<tr>
<th>Anticoagulant drug</th>
<th>Creatinine clearance (mL/min)</th>
<th>Low-risk surgery&lt;sup&gt;a&lt;/sup&gt;</th>
<th>High-risk surgery&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>&gt; 50</td>
<td>24 hours</td>
<td>2 days</td>
</tr>
<tr>
<td></td>
<td>31–50</td>
<td>2 days</td>
<td>4 days</td>
</tr>
<tr>
<td></td>
<td>≤ 30</td>
<td>4 days</td>
<td>6 days</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>&gt; 30</td>
<td>24 hours</td>
<td>2 days</td>
</tr>
<tr>
<td></td>
<td>≤ 30</td>
<td>2 days</td>
<td>4 days</td>
</tr>
<tr>
<td>Apixaban</td>
<td>&gt; 30</td>
<td>24 hours</td>
<td>2 days</td>
</tr>
<tr>
<td></td>
<td>≤ 30</td>
<td>2 days</td>
<td>4 days</td>
</tr>
</tbody>
</table>

<sup>a</sup>Examples include cardiac catheterization, diagnostic endoscopy, breast biopsy, and minor orthopedic procedures

<sup>b</sup>Examples include cardiac surgery, vascular surgery, spinal or neurosurgery, and abdominal surgery
# Aspirin

**Table 1—Vascular Disorders for Which Aspirin Has Been Shown to Be Effective and Lowest Effective Dose**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Lowest Effective Daily Dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient ischemic attack and ischemic stroke&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50</td>
</tr>
<tr>
<td>Men at high cardiovascular risk</td>
<td>75</td>
</tr>
<tr>
<td>Hypertension</td>
<td>75</td>
</tr>
<tr>
<td>Stable angina</td>
<td>75</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>75</td>
</tr>
<tr>
<td>Severe carotid artery stenosis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>75</td>
</tr>
<tr>
<td>Polycythemia vera</td>
<td>100</td>
</tr>
<tr>
<td>Acute myocardial infarction&lt;sup&gt;a&lt;/sup&gt;</td>
<td>160</td>
</tr>
<tr>
<td>Acute ischemic stroke&lt;sup&gt;a&lt;/sup&gt;</td>
<td>160</td>
</tr>
</tbody>
</table>

<sup>a</sup>Higher doses have been tested in other trials and not found to confer any greater risk reduction.
## Aspirin

**Table 5—Benefit and Harm of Antiplatelet Prophylaxis With Aspirin in Different Settings**

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Benefits, No. of Patients in Whom a Major Vascular Event Is Avoided per 1,000/y(^a)</th>
<th>Harm, No. of Patients in Whom a Major GI Bleeding Event Is Caused per 1,000/y(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at low to high cardiovascular risk</td>
<td>1-2</td>
<td>1-2</td>
</tr>
<tr>
<td>Essential hypertension</td>
<td>1-2</td>
<td>1-2</td>
</tr>
<tr>
<td>Chronic stable angina</td>
<td>10</td>
<td>1-2</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>20</td>
<td>1-2</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>50</td>
<td>1-2</td>
</tr>
</tbody>
</table>
Aspirin Dosing

• Risk of Peptic ulcer bleeding
  – 75 mg, 2.3 (1.2 to 4.4)
  – 150 mg, 3.2 (1.7 to 6.5)
  – 300 mg, 3.9 (2.5 to 6.3)
DVT and cirrhosis
Endoscopic therapy in PPI erra
PPI use of This puri es