**Dabigatran: Unique Dosing Situations**

Jill Cwik, Pharm.D.
Advocate Lutheran General Hospital
Clinical Pharmacist, Cardiology/Critical Care
September 16, 2011

The speaker has no conflict of interest to disclose.

**Objectives**

- Identify appropriate patients for dabigatran therapy
- Outline a strategy to convert between dabigatran and warfarin therapy
- Identify appropriate strategies for initiation and cessation of dabigatran therapy

**Mechanism of Action and Indication**

- **Dabigatran** is an oral competitive and reversible direct thrombin inhibitor
  - Binds to both free and clot-bound thrombin
  - Inhibitory effect on tissue factor-induced platelet aggregation
- **FDA approved indication**: prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation (AF)

**RE-LY: Clinical Efficacy**

18,113 patients with AF documented on ECG screening or within 6 months before enrollment and at least 1 of the following:
- Previous stroke or TIA, or systemic embolism
- NYHA class II or higher, symptomatic heart failure
- 75 y/o or 65-74 y/o plus DM, HTN, or CAD

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Dabigatran 110mg</th>
<th>Dabigatran 150mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint: stroke or systemic embolism</td>
<td>1.53</td>
<td>1.11</td>
<td>1.57</td>
</tr>
<tr>
<td>Safety Endpoint: Major bleeding</td>
<td>0.34</td>
<td>0.34</td>
<td>0.41</td>
</tr>
</tbody>
</table>

**RE-LY: Main Findings**

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Dabigatran 110mg</th>
<th>Dabigatran 150mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual rate (%)</td>
<td>1.11</td>
<td>0.91</td>
<td>1.09</td>
</tr>
<tr>
<td>RR 95% CI</td>
<td>0.96-1.11</td>
<td>0.34-0.99</td>
<td>0.33-0.92</td>
</tr>
<tr>
<td>Annual rate (%)</td>
<td>1.57</td>
<td>0.52</td>
<td>0.76-1.13</td>
</tr>
<tr>
<td>RR 95% CI</td>
<td>0.41-1.57</td>
<td>0.51-0.81</td>
<td></td>
</tr>
</tbody>
</table>

**Dabigatran: Role in Stroke Prevention**

- **2011 ACCF/AHA/HRS Guideline Focused Update Recommendation**: Class I, LOE B
  - Dabigatran is a useful alternative to warfarin for prevention of stroke and systemic thromboembolism in patient with paroxysmal to permanent AF and risk factors for stroke or systemic embolization
  - Those with the following are excluded: prosthetic heart valve, hemodynamically significant valvular disease, severe renal dysfunction (CrCl<15 mL/min) or advanced liver disease (impaired baseline clotting function)

**Connolly SJ et al.** NEJM 2009;361:1139-51.

**Dabigatran (Pradaxa®)** Prescribing information. Ridgefield, CT: BI Pharm, Inc. 2011
Dabigatran: Use Criteria

• Patients taking warfarin therapy with excellent INR control may have little to gain by switching to dabigatran

• Considerations:
  – Twice-daily dosing
  – Greater risk of nonhemorrhagic side effects


Dabigatran: Patient Selection

• Patients who will benefit from dabigatran over warfarin:
  – AF and ≥1 additional risk factor for stroke
  – Ability to comply to twice daily dosing
  – Availability of an anticoagulation management program to sustain routine monitoring of INR
  – Patient preferences
  – Cost
  – Other factors


Dabigatran: Dosing

• Capsules cannot be crushed, chewed or broken
• Stability: 30 days once bottle is opened
  – Extended stability to 60 days currently under FDA review

<table>
<thead>
<tr>
<th>Creatinine Clearance (CrCl)</th>
<th>Recommended Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt; 30 mL/min</td>
<td>150 mg orally, twice daily</td>
</tr>
<tr>
<td>CrCl 15-30 mL/min</td>
<td>75 mg orally, twice daily</td>
</tr>
<tr>
<td>CrCl &lt; 15 or on dialysis</td>
<td>Dosing recommendations cannot be provided</td>
</tr>
</tbody>
</table>

Dabigatran (Pradaxa®) Prescribing information. Ridgefield, CT, BI Pharm, Inc. 2011

Conversion from Dabigatran to or from Warfarin

<table>
<thead>
<tr>
<th>Renal Function (CrCl mL/min)</th>
<th>Conversion Instructions: Dabigatran to Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>Start warfarin 3 days before discontinuation of dabigatran</td>
</tr>
<tr>
<td>31-50</td>
<td>Start warfarin 2 days before discontinuation of dabigatran</td>
</tr>
<tr>
<td>15-30</td>
<td>Start warfarin 1 day before discontinuation of dabigatran</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>No recommendations can be made</td>
</tr>
</tbody>
</table>

Dabigatran (Pradaxa®) Prescribing information. Ridgefield, CT, BI Pharm, Inc. 2011

Converting Dabigatran to Parenteral Anticoagulants

<table>
<thead>
<tr>
<th>Agent</th>
<th>Conversion to Dabigatran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>Initiate dabigatran at the time heparin is discontinued</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Start dabigatran at the time of the next dose of enoxaparin was to be administered (may overlap by up to 2 hours)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal Function CrCl (mL/min)</th>
<th>Converting Dabigatran to Parenteral Anticoagulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 30</td>
<td>Start parenteral anticoagulation 12 hours after last dabigatran dose</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Start parenteral anticoagulation 24 hours after last dabigatran dose</td>
</tr>
</tbody>
</table>

Dabigatran (Pradaxa®) Prescribing information. Ridgefield, CT, BI Pharm, Inc. 2011

Discontinuation of Dabigatran Prior to Procedures

<table>
<thead>
<tr>
<th>Renal Function CrCl (mL/min)</th>
<th>Half-Life (hours) Mean (range)</th>
<th>Timing of discontinuation after last dose of dabigatran before surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 80</td>
<td>13 (11-22)</td>
<td>Standard Risk of Bleeding</td>
</tr>
<tr>
<td>50 to ≤ 80</td>
<td>15 (12-34)</td>
<td>High Risk of Bleeding</td>
</tr>
<tr>
<td>&gt; 30 to ≤ 50</td>
<td>18 (13-23)</td>
<td>≥ 48 hours 2-4 days</td>
</tr>
<tr>
<td>≤ 30</td>
<td>27 (22-25)</td>
<td>≥ 120 hours ≥ 5 days</td>
</tr>
</tbody>
</table>

- Standard risk of bleeding: electrophysiology procedures, cardiac catheterizations, no additional patient-specific risk factors.
- High risk of bleeding: surgery involving major organs, procedures requiring complete hemostasis or when additional patient risk factors are present.

Clinical Question

**HPI/CC:** 66 y/o M presents to the ED febrile and SOB resulting in hypoxic respiratory failure requiring intubation. Chest x-ray demonstrates a LLL infiltrate. The patient is transferred to the MICU with an oral-gastric tube placed.

**PMH:** Non-valvular atrial fibrillation

**Medications PTA:** Dabigatran 150mg po BID (last dose taken this morning)

**Pertinent Laboratories:**
- Weight: 80 kg
- Scr = 1
- CrCl = 60 mL/min
- INR = 1.2
- aPTT = 25

The medical team would like your recommendations to initiate therapeutic anticoagulation.

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**Dabigatran Monitoring**

- Dabigatran has the potential to prolong aPTT, TT, and ECT
  - aPTT targets the intrinsic pathway of the clotting cascade
    - 2-fold increase in patients treated with 150mg BID
    - Can increase to 1.5 x control 12 hours after dose/hover it becomes insensitive at higher concentrations
  - TT directly measures thrombin in plasma sample
    - Linear dose-response over therapeutic concentrations and provides direct measure of activity
    - Limitations: reagents are not standardized and cut-offs cannot be defined
  - ECT specific to thrombin generation
    - Available only in research setting
- Limited data on the use of ACT
- Dabigatran should be discontinued for at least 2 days for an accurate INR
- No guidelines for routine monitoring

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**Dabigatran and Cardioversion**

- **AF ≥ 48 hours or unknown duration:** therapeutic anticoagulation with warfarin for at least 3 weeks before and 4 weeks after cardioversion
- **RE-LY Data**
  - Incidence of stroke and major bleeding in within 30 days were similar in both dabigatran groups compared to warfarin with or without TEE
  - Study drug administration ≥ 3 weeks
  - Role of dabigatran unclear if in AF <48 hours
  - Reasonable alternative to warfarin

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**Dabigatran and Ischemic Stroke**

- Considerations with monitoring dabigatran as compared to warfarin therapy
  - INR cannot be used reliably in dabigatran treated patients
  - Limitations with reliability of aPTT, TT or ECT
- Dabigatran treated patients who present with an ischemic stroke should not be considered for t-PA
  - Potentially high risk of hemorrhage

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**Dabigatran Related Bleeding and Reversal**

- Patient bleeding on dabigatran
  - Mild Bleeding
  - Delay next dose or discontinue
  - Symptomatic treatment
  - Mechanical compression
  - Surgical Intervention
  - IVF and hemodynamic support
  - Administration of blood products
  - Oral charcoal administration
  - Hemodialysis
  - Factor VII or prothrombin complex concentrates
  - Charcoal filtration

- Moderate-Severe Bleeding
  - Life-Threatening Bleeding

### Dabigatran: Special Populations

**Case 1**
- 84 y/o female, weight 40 kg
- Dabigatran 75mg po BID
- Treatment x 4 months
- Presents with rectal bleeding
  - CrCL=32 mL/min
  - TT= 5600 ng/mL (31-225 ng/mL)
- Expired from hemorrhagic shock

**Case 2**
- 89 y/o female, weight 45 kg
- Dabigatran 110mg po BID
- Treatment x 5 months
- Presents with recurrent epistaxis x 1 week and surgery for cochlear implant removal
  - CrCL= 29 mL/min
  - TT= 2670 ng/mL (31-225 ng/mL)
- Dabigatran discontinued

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**Considerations for Dabigatran Initiation**
- Appropriate monitoring
- Compliance
- Atherosclerotic arterial disease
- Bleeding risk / lack of reversal
- Alterations in renal function
- Obese or underweight patients
- Drug-interactions
- Available route of administration
- Insurance coverage/ cost

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**Dabigatran: Unique Dosing Situations**

Jill Cwik, Pharm.D.
Advocate Lutheran General Hospital
Clinical Pharmacist, Cardiology/Critical Care
September 16, 2011

The speaker has no conflict of interest to disclose.
ICHP Clinical Pearl
Dabigatran: Unique Dosing Situations
Jill Cwik, Pharm.D.

Reference List
1. Product Information. Pradaxa (Dabigatran etexilate mesylate). Ridgefield, CT ; Boehringer Ingelheim, March 2011.
Controversies surrounding creatinine clearance

Justin M. Schmidt, Pharm.D., BCPS
Assistant professor
Chicago College of Pharmacy-Midwestern University

Internal medicine clinical pharmacist
Edward Hines Jr. VA Hospital
The speaker has no conflicts to disclose.

Objectives

- Recognize new and traditional methods of estimating kidney function using creatinine measurement.
- Identify factors that confound creatinine-based estimation of kidney function.

What is your practice site?

1. Non-ICU hospital
2. Community
3. Long-term care
4. Nephrology service
5. ICU service
6. Student/resident
7. Other

Which method do you use to estimate kidney function for drug dosing?

1. C/G with IBW
2. C/G with Adj BW
3. MDRO
4. CKD-EPI

Timeline

C/G equation

CKD-EPI


MDRO

SC-standardized
Standardization of SCr

- Isotope dilution mass spectrometry (IDMS) – standardized
- 5-20% positive bias before standardization
- Affects all SCr based assessments of kidney function
  - No universal C/G "adjustment factor"

After standardization of SCr, dosing medications with C/G would be expected to result in which of the following?
1. Increased dose/frequency
2. No change in dose/frequency
3. Decreased dose/frequency

Cockcroft-Gault

\[ \text{Cr}_G = \frac{[(140-\text{age}) \times \text{weight}/(72 \times S_{\text{cr}})] \times 0.85}{\text{female}} \]

Variations on a theme

- SCr rounding in elderly
  - To 1 mg/dL:
    - Likely under doses medications
  - To 0.7 mg/dL
    - Some support

Variations on a theme

- Weight
  - IBW
  - Adjusted
  - Total

Recalibrated Creatinine

- Comparison points (cp)
- CR: Commercial
- IR: Reference
- SCr: Serum creatinine

Williams, Pharmatherapy 2011;31:656-69.
Williams, Pharmatherapy 2011;31:656-69.
MDRD

- Equations
  - 6 variable
    - eGFR = 170 x Scr^{-0.996} x age^{-0.179} x BLM{-0.170} x Alp^{-0.318} x (0.762 if female) x (1.180 if black)
  - 4 variable
    - eGFR = 186 x Scr^{-1.154} x age^{-0.203} x (0.742 if female) x (1.212 if African American)
    - eGFR = 175 x Scr^{-1.154} x age^{-0.203} x (0.742 if female) x (1.212 if African American)

Using MDRD to estimate GFR would be expected to result in which of the following (compared to C/G)?

1. Increased dose/frequency
2. No change in dose/frequency
3. Decreased dose/frequency

MDRD

- Ccr < 60 mL/min
- Elderly
- BSA adjustments
- For dosing?
  - Generally MDRD results in higher estimates of GFR compared with C/G

CKD-EPI

- GFR = 141 x min(Scr/κ, 1)^α x max(Scr/κ, 1)^{-1.209}
  × 0.993^{45} x 1.018 [if female] x 1.159 [if black]
  - κ is 0.7 for females, 0.9 for males
  - α is -0.329 for females, -0.411 for males
  - min indicates the minimum of Scr/κ or 1
  - max indicates the maximum of Scr/κ or 1
- Better than MDRD for GFR > 60 mL/min
CKD-EPI

- In one study
  - ~5 mL/min greater estimates vs C/G overall
  - ~8 mL/min greater in African Americans
- This resulted in...
  - 15-25% discordance
- MDRD resulted in...
  - 20-36% discordance

What do the pharmacy experts use?

- What equation do you use to adjust meds?
  - Nephrology pharmacists 96.4%
  - Critical care pharmacists 94.6%

Who are Cockcroft & Gault?

What do organizations recommend?

- NIDDK/NKDEP (Jan 2010 recommendation)
  - Use either C/G or MDRD
- FDA guidance to industry (Mar 2010 draft)
  - Use either C/G or MDRD

Labeling

- A review of NME’s from 1998-2007 revealed:

```
57%

25%

14%

7%
```

- General guidance
- Our method not specified
- Ideal/lean body weight
- Weight not specified

Limitations of SCr

- Changing renal function
- Can reflect changes in diet/muscle mass

Which of the following is recommended in the setting of acute kidney injury?

1. C/G
2. MDRD
3. CKI-EPI
4. 24 hr urine collection
Hey, where are my pearls???

- For now
  - C/G to estimate Clcr for drug dosing
  - IBW/adjusted (unless actual used in FDA PK studies)
  - Scr: rounded to 0.7 mg/dL as opposed to 1 mg/dL
  - MDRD/ckd-epi for most accurate assessment of renal function
  - For acutely changing Scr or narrow therapeutic index
    - Consider 24 hr urine collection
  - Watch for revisions to guidance!

Which of the following methods of measuring kidney function is most accurate when GFR is > 60 mL/min?

1. Cockcroft/Gault
2. 4-variable standardized MDRD
3. 6-variable MDRD
4. CKD-epi

Which of the following is currently a limitation of creatinine-based measures of kidney function?

1. Inter-laboratory variability in creatinine measurement
2. Fluctuation with muscle mass
3. Inconvenient sample collection
4. Expense

Team Scores:

- [ ]
- [ ]
- [ ]
- [ ]

References:

- Based on references from the provided text.

References:

- Based on references from the provided text.

5
References


Probiotics: The Helpful or Harmful Fungus among us?

September 16, 2011

Sarah M. Wieszczkiewicz, Pharm.D., BCPS
Clinical Pharmacist, Infectious Diseases
Advocate Lutheran General Hospital

Speaker has no conflict of interest to disclose.

World Health Organization

Definition

Probiotics are: “live microorganisms which when administered in adequate amounts confer a health benefit on the host.”

Drug versus Dietary Supplement

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dietary Supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>• An article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease</td>
<td>• A product taken by mouth that contains a “dietary ingredient” intended to supplement the diet</td>
</tr>
<tr>
<td>• Regulated by the FDA</td>
<td>• Regulated by the FDA’s Center for Food Safety and Applied Nutrition</td>
</tr>
<tr>
<td>• Requires FDA approval prior to marketing</td>
<td>• Does NOT require FDA approval prior to marketing</td>
</tr>
</tbody>
</table>

Required to record and forward to FDA any reports of serious adverse effects.

Structure/Function versus Health Claims

<table>
<thead>
<tr>
<th>Structure/Function</th>
<th>Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FDA requires that manufacturers’ substantiations of claims are to be supported/accepted by experts in the field</td>
<td>• Describe “a relationship between a food, food component, or dietary supplement ingredient, and reducing risk of a disease or health-related condition”</td>
</tr>
<tr>
<td>• Claim is truthful and not misleading</td>
<td>• Requires a petition containing the scientific evidence supporting the claim to be submitted to the FDA</td>
</tr>
<tr>
<td>• Data do not have to be made publicly available and do not need to be disclosed</td>
<td>• Only data from studies in healthy populations are evaluated</td>
</tr>
<tr>
<td>• Manufacturers must state, “The FDA has not evaluated the claim and the product is not intended to diagnose, treat, cure, or prevent any disease”</td>
<td>• Data must be published</td>
</tr>
</tbody>
</table>

Probiotic Evaluation Standards

Guideline Recommendations

• Identification of the genus and species of the probiotic strain
• In vitro testing to validate the mechanism of effect
• Substantiation of clinical health benefit with human trials
• Safety assessment
• Manufacturers responsibility to ensure that an independent third party reviews and evaluates all scientific evidence
Probiotic Claims

- Marketed as dietary supplements
  - *Saccharomyces boulardii*
  - *Lactobacillus species*
  - *Bifidobacterium species*

- Structure/function claims on packaging
  - Promotes intestinal health
  - Keeps intestines functioning well
  - Maintains balance of intestinal flora and protects intestinal tract

Helpful?

- Proposed mechanisms
  - Lower intestinal pH
  - Modifying the host immune response
  - Decrease colonization and invasion by pathogenic organisms
  - Protease production that decreases toxicity of *C. difficile* toxins

- Many disease states studied
  - e.g., prevention of antibiotic-associated diarrhea (AAD) and treatment of *Clostridium difficile* infection (CDI)

Meta-analysis (11 of studies included)

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccharomyces boulardii is well described and may be effective for immune modulation in specific patient populations with particular patient-related characteristics. Primary prevention (with further study) may improve clinical outcomes in subsets of patients, as demonstrated in a recent study.</td>
<td>Small sample sizes and lack of control for clinical outcomes of pathologically significant differences in pathogenic organisms with different study designs of probiotics.</td>
</tr>
</tbody>
</table>

Helpful Yogurt?

- Randomized, double-blind, placebo-controlled study (N = 135)
- Objective: To determine the efficacy of a *Lactobacillus* drink for the prevention of AAD and CDI
- 97ml yogurt drink Q12h during antimicrobial treatment and for one week after cessation of antimicrobial; placebo group received sterile milkshake
- Exclusion criteria: diarrhea on admission, bowel pathology that may result in diarrhea, antimicrobial use in previous 4 weeks, severe illness, immunosuppression, bowel surgery, artificial heart valves, history of rheumatic disease or endocarditis

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>AAD N (%)</th>
<th>Absolute Risk Reduction (95% CI)</th>
<th>Number Needed to Treat</th>
<th>CDI N (%)</th>
<th>Absolute Risk Reduction (95% CI)</th>
<th>Number Needed to Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probiotic (N = 57)</td>
<td>7 (12%)</td>
<td>21.6% (6.6-34%)</td>
<td>5 (3.15)</td>
<td>0</td>
<td>17% (7-27)</td>
<td>6 (4-14)</td>
</tr>
<tr>
<td>Placebo (N = 56)</td>
<td>19 (34%)</td>
<td>0</td>
<td>0</td>
<td>9 (17%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>p = 0.007</strong></td>
<td><strong>p = 0.001</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Conclusion: Probiotics may reduce the incidence of AAD and CDI.

*Potential to decrease morbidity, healthcare costs, and mortality if used routinely in patients aged over 50.*

Helpful Yogurt?

- Limitations:
  - Patients taking high risk or more than 2 recent courses of antimicrobials were excluded
  - Products were in different containers (thus, not blinded)
  - Placebo group received milk product which may have contributed to diarrhea (may have led to CDI testing)
  - Not clear if subjects in each group were screened equally when diarrhea occurred
Or Harmful?

- Risk Associated with Probiotic Use
  - "Well tolerated, minimal adverse effects"
  - Package insert lists gas, constipation, and thirst

“[If you have a central venous catheter, please speak with your health care professional before you start takingSaccharomyces boulardii. Very rare cases of fungemia have been observed in patients with a central venous catheter. In all cases the course was favorable after antifungal treatment.]”

Harmful?

- Saccharomyces fungemia is the most severe complication
- *S. cerevisiae* and *boulardii* used interchangeably as they are genetically similar and share metabolic properties

Harmful?

- 91 documented cases of invasive *Saccharomyces* infections
  - 54 *S. cerevisiae* invasive infections
  - 37 cases of *S. boulardii* fungemia

<table>
<thead>
<tr>
<th></th>
<th><em>S. boulardii</em></th>
<th><em>S. cerevisiae</em></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive tract disease</td>
<td>58%</td>
<td>6%</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Intravenous catheters</td>
<td>83%</td>
<td>29%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Intensive care unit admission</td>
<td>32%</td>
<td>0.05%</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

40% of all cases were associated with *S. boulardii* use

Harmful?

- Air and surface contamination evaluated before, during, and after opening a *Saccharomyces* capsule
  - Massive air contamination that persisted for 30 minutes
  - Persisted up to 2 hours on the table surfaces
  - Remained on the arm of a simulated patient for 30 minutes

Harmful?

- 60 cases of *S. cerevisiae* fungemia

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received <em>S. boulardii</em> probiotic preparation</td>
<td>48</td>
</tr>
<tr>
<td>Housed near patients receiving <em>S. boulardii</em></td>
<td>9</td>
</tr>
<tr>
<td>Admission in the Intensive Care Unit</td>
<td>60</td>
</tr>
<tr>
<td>Receiving enteral or parenteral nutrition</td>
<td>71</td>
</tr>
<tr>
<td>Central venous catheter present</td>
<td>93</td>
</tr>
<tr>
<td>Received broad spectrum antimicrobials</td>
<td>88</td>
</tr>
<tr>
<td>Fungemia detected a median of 10 ± 62.3 days (range 4-300) after probiotic administration</td>
<td></td>
</tr>
</tbody>
</table>

28% Mortality Rate

Harmful?

- Hand contamination on the technician who prepared the dose was evaluated
  - Gloves were not worn
  - Hands tested prior to preparation and after vigorous hand washing
  - Hands remained highly and persistently contaminated despite vigorous handwashing
2010 CDI Guidelines

“Administration of currently available probiotics is not recommended to prevent primary CDI, as there are limited data to support this approach and there is a potential risk of bloodstream infection.”


Patient Populations to Avoid Probiotics

- Immunocompromised patients
- Critically ill patients located in an intensive care unit
- Patients with central venous access or other lines/ports, etc.

Other Considerations

- Discrepancies in content
  - Doron and Gorbach evaluated 18 commercially-available probiotic products
    - 39% had discrepancies between actual concentrations and what the label claimed
  - Sargent et al. evaluated Brewer’s Yeast tablets
    - No viable yeast identified
  - Masco and colleagues evaluated 58 bifidobacteria-containing products
    - 29% contained no bifidobacteria

In Summary...

- Probiotics are dietary supplements
  - Only eligible for health claims versus drug claims
- Fungemia is a serious risk associated with probiotic use
- Avoid probiotics in immunocompromised or critically ill patients, patients with IV access

Post-Test Assessment

- Which one of the following claims is appropriate for probiotics?
  A. Prevents *Clostridium difficile* infection
  B. May be used as an adjunct to CDI treatment
  C. Treats *Clostridium difficile* infection
  D. Maintains balance of intestinal flora

Post-Test Assessment

- Which one of the following patients would probiotics be considered a possible option to prevent AAD and CDI?
  A. 89 yo F from a nursing home admitted to the ICU who is receiving cefepime for urosepsis
  B. 47 yo M admitted to the general medicine floor who is receiving moxifloxacin for CAP
  C. 60 yo F with no known health problems and a history of AAD who is initiated on antimicrobials for sinusitis in the outpatient setting
  D. 72 yo F on immunosuppressants s/p liver transplant who is initiated on ciprofloxacin for a UTI in the outpatient setting