Aspirin and Antibiotics:

Are They Needed Prior to an Endoscopy Procedure?

ASGE Guidelines

Dr. Haleh Pazwash
Antithrombotic Agents
(Antiplatelet Agents and Anticoagulants)

Reduce the risk of thromboembolic events in patients with conditions such as:

- atrial fibrillation (AF)
- acute coronary syndrome (ACS)
- deep vein thrombosis (DVT)
- hypercoagulable states
- endoprosthesis
Antiplatelet Agents

• ASA (aspirin)
  – Inhibit platelet aggregation
  – Prevent stroke or MI
  – Causes irreversible inhibition of the cyclooxygenase 1 and 2 enzyme system
  – 7 to 10 days after cessation required to regain full platelet function

• Dipyridamole (Persantine)
  – Used in combination with ASA in the secondary prevention of stroke
  – Duration of action of about 2 days after discontinuation
Aspirin and NSAIDS

• A study of 1174 patients who underwent polypectomy found **NO** difference in post polypectomy bleeding rates among those who received aspirin and/or an NSAID (3.2%) and those who did not (3.0%)
Anticoagulant Agents

Warfarin (Coumadin)

- Inhibits the vitamin K-dependent clotting factors II, VII, IX, and X and proteins C and S.
- Activity measured via the International Normalized Ratio (INR)
- The INR decreases to $\leq 1.5$ in approximately 93% of patients within 5 days of discontinuing therapy
Parental and Subcutaneously Administered Anticoagulants

• **Heparin IV**
  
  – Intravenously has a half-life of 60 to 90 minutes, and anticoagulant effects dissipate 3 to 4 hours after discontinuation

• **LMWH (enoxaparin [Lovenox])**
  
  – Last dose should be given 24 hours before the anticipated procedure

• **Desirudin (Iprivask)**
  
  – Approved for DVT prophylaxis after hip replacement and is administered subcutaneously
  
  – Discontinue this medication 10 hours before a high-risk procedure
Anticoagulant Agents

Novel Oral Anticoagulants (NOACs)

- Direct thrombin inhibitor, dabigatran [Pradaxa]
  - Prevents CVA and emboli in AF
- Direct factor Xa inhibitors (rivaroxaban [Xarelto], apixaban [Eliquis], edoxaban [Savaysa])
- Normal activated partial thromboplastin time rules out a clinically significant circulating drug level
- Creatinine clearance—stop Pradaxa 2 days prior
Anticoagulant Agents

Rivaroxaban (Xarelto)

- Prevention of VTE after orthopedic surgery, treatment of VTE, and prevention of CVA and embolism in patients with AF

Apixaban (Eliquis)

- Systemic embolism in AF patients, post orthopedic surgery prevention of VTE, and for treatment and reduction of recurrence of VTE
Antiplatelet Agents

- Classified based on their mechanisms of action
  - Aspirin (acetylsalicylic acid) and related compounds (nonsteroidal anti-inflammatory drugs and sulfinpyrazone) block cyclooxygenase, the enzyme that mediates the first step in prostaglandin and thromboxane biosynthesis from arachidonic acid
  - Dipyridamole inhibits phosphodiesterase-mediated breakdown of cyclic AMP, which prevents platelet activation by multiple mechanisms
  - P2Y₁₂ platelet receptor blockers (Ticlid, Plavix, Effient, Brilinta) achieve their antiplatelet effect by blocking the binding of ADP to a specific platelet receptor (P2Y₁₂), inhibiting adenylyl cyclase and platelet aggregation.
  - Glycoprotein IIb/IIIa antibodies and receptor antagonists (Aggrastat, Reopro, Integrillin) inhibit the final common pathway of platelet aggregation and may also prevent initial adhesion to the vessel wall.
  - Competitive and selective inhibitors of PAR-1 (the major thrombin receptor on platelets (Vorapaxar)
Risk of Antithrombotic

• Adverse events include GI bleeding
  – Important Factors:
    • urgency of the procedure
    • bleeding risk of the procedure
    • effect of the antithrombotic drug(s) on the bleeding risk
    • risk of a thromboembolic event related to peri-procedural interruption of antithrombotic agents
Procedure Risks

• Risk for Cerebrovascular Accident (CVA)
  – This score ranges from 0 to 9 and considers thromboembolic risk factors of:
    • congestive heart failure (1 point),
    • hypertension (1 point),
    • age $\geq$ 75 years (2 points),
    • diabetes (1 point),
    • stroke (2 points),
    • vascular disease (prior myocardial infarction [MI], peripheral artery disease, or aortic plaque) (1 point),
    • age 65 to 74 years (1 point),
    • and sex category (female) (1 point).
  – The higher the score, the greater the thromboembolic risk, and patients with a score of $\geq$ 2 are considered to be at high risk of thromboembolism (>2.2%/year)
<table>
<thead>
<tr>
<th>High Risk Procedures</th>
<th>Procedure + Risk for Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypectomy (3-10%)</td>
<td>Biliary or pancreatic sphincterotomy</td>
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<tr>
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<td>Treatment of varices</td>
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<td>PEG</td>
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<td>Therapeutic balloon-enteroscopy</td>
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<td>EUS with FNA</td>
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<td>Endoscopic hemostasis</td>
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<td>Tumor ablation</td>
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<td>Cystgastrostomy</td>
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<td>Ampullary resection</td>
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<td>EMR</td>
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<tr>
<td></td>
<td>Endoscopic submucosal dissection</td>
</tr>
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<td></td>
<td>Pneumatic or bougie dilation</td>
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<td>PEJ</td>
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<td>PEJ</td>
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<td>POEM</td>
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<td>Endoscopic therapy of Zenker’s diverticulum</td>
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<td>Low Risk Procedures</td>
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<tr>
<td>Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including mucosal biopsy</td>
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<tr>
<td>ERCP with stent (biliary or pancreatic) placement or papillary balloon dilation without sphincterotomy</td>
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<tr>
<td>Push enteroscopy and diagnostic balloon-assisted enteroscopy</td>
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<tr>
<td>Capsule endoscopy</td>
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<tr>
<td>Enteral stent deployment (<em>Controversial, 5 %</em>)</td>
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<tr>
<td><em>EUS without FNA</em></td>
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<tr>
<td>Argon plasma coagulation</td>
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<tr>
<td>Barrett’s ablation</td>
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<tr>
<td>Nonachalasia esophageal dilation</td>
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</tbody>
</table>
High Risk of Thrombosis

• Include placement of drug-eluting coronary stents ≤ 12 months previous

• Or placement bare metal coronary stents ≤ 1 month
High Thrombosis Risk

• 1/5 patients who experience a first thrombosis will experience a second stent occlusion at a rate of .6% per year over the first 3 years, with a cumulative risk of cardiac death of 27.9%

• Patients with ACS or ST elevation MI, multivessel percutaneous coronary intervention, diabetes, renal failure, or diffuse coronary artery disease are also at higher risk of stent occlusion or ACS event with alteration of antithrombotic therapy
**APAs**

**Duration of Action and Approach to Reversal When Indicated**

<table>
<thead>
<tr>
<th>Specific agents</th>
<th>Duration of action</th>
<th>Urgent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>7-10 days</td>
<td>Hold, can give platelets</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Varies</td>
<td>Hold</td>
</tr>
</tbody>
</table>
Antithrombotic Drugs

Duration of Action and Approach to Reversal When Indicated

Specific agents

**Thienopyridines:**
- clopidogrel (Plavix)
- prasugrel (Effient)
- ticlodipine (Ticlid)
- ticagrelor (Brilinta)

Duration of action

- 5-7 days
- 3-5 days
- 5-7 days
- 5-7 days
Antithrombotic Drugs

Duration of Action and Approach to Reversal When Indicated

Specific agents

- GPIIb/IIIa inhibitors:
  - tirofiban (Aggrastat)
  - abciximab (ReoPro)
  - eptifibatide (Integrillin)

Duration of action

- 1-2 seconds
- 24 hours
- 4 hours
## Antithrombotic Drugs

### Duration of Action and Approach to Reversal When Indicated

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<tr>
<th>Specific agents</th>
<th>Duration of action</th>
<th>Urgent</th>
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</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin)</td>
<td>5 days</td>
<td>Vitamin K, PCC</td>
</tr>
<tr>
<td>Heparin</td>
<td>IV 2-6 hours, SQ 12-24 hours</td>
<td></td>
</tr>
<tr>
<td>LMWH: enoxaparin (Lovenox)</td>
<td>24 hours</td>
<td></td>
</tr>
</tbody>
</table>
Antithrombotic Drugs

Duration of Action and Approach to Reversal When Indicated

Specific agents

- Direct factor Xa Inhibitor:
  - rivaroxaban (Xarelto)
  - apixaban (Eliquis)
  - edoxaban (Savaysa)

Duration of action

- 48 hours

Urgent

- Charcoal (if last intake within 2-3 hours);
- nonactivated PCC or activated PCC;
- HD
Antithrombotic Drugs

Duration of Action and Approach to Reversal When Indicated

**Specific agents**
- Direct thrombin inhibitor, oral: dabigatran (Pradaxa)
- IV: desirudin (Iprivask)

**Duration of action**: 48 hours

**Urgent**
- Charcoal (if last intake within 2-3 hours); nonactivated PCC or activated PCC; HD
Praxbind

• An antidote for Pradaxa is Praxbind
• Use in cases of life-threatening, uncontrolled bleeding or prior to emergency surgery
Vorapaxar (Zontivity)

• First-in-class antiplatelet medication approved by the FDA in January 2014

• Competitive and selective inhibitor of PAR-1, the major thrombin receptor on human platelets

• Associated with risk of severe bleeding - 4.2%

• Black box warning
Risk of Stopping Antithrombotic Therapy Before Elective Endoscopy

• When antithrombotic therapy is required for a short period of time (ie, after VTE or bare metal stent insertion), elective procedures should be **delayed** until such therapy is no longer indicated.

• Decisions about discontinuing or temporary cessation of these agents should be **individualized**.
Risk of Stopping Antithrombotic Therapy Before Elective Endoscopy

Role of Bridge Therapy

- Evidence for the use of Heparin IV and lovenox as bridge therapies for endoscopic procedures in patients on warfarin (Coumadin) is limited

Cessation of APA

- Hold the thienopyridine (plavix, effient, ticlid, brilinta) for procedure BUT continue the aspirin
## Summary of Available Evidence for Bleeding Risk

*with common endoscopic procedures on antithrombotic agents*

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Therapeutic warfarin/heparin</th>
<th>Thienopyridine</th>
<th>ASA/NSAID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td>Low risk</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>EGD/colonoscopy +/- biopsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colonoscopy/polypectomy</td>
<td>High risk</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>High</td>
<td>Unknown</td>
<td>Low</td>
</tr>
<tr>
<td>EUS/FNA</td>
<td>High</td>
<td>Unknown</td>
<td>Low</td>
</tr>
<tr>
<td>PEG</td>
<td>Unknown</td>
<td>Low for plavix only</td>
<td>Low</td>
</tr>
</tbody>
</table>
Reinitiation of Antithrombotic Agents After Elective Endoscopy

- 2014 AHA/ACC guideline recommends that warfarin (Coumadin) be restarted within 24 hours of the procedure in patients with valvular heart disease and a low-risk for thromboembolism.

- In patients at high risk for thromboembolism, Heparin or LMWH should be restarted and continue until the INR reaches an appropriate therapeutic level.
Reinitiation of Antithrombotic Agents After Elective Endoscopy

• Heparin may be restarted 2 to 6 hours after a therapeutic procedure

• Delay reinitiation of Lovenox for 48 to 72 hours after surgery in patients believed to be at high risk for bleeding
Endoscopic Procedures in Acutely Bleeding Patient on Antithrombotic Therapy

- Endoscopic evaluation and therapy in patients using antithrombotics with active GI bleeding is both warranted and safe.

- The most common etiologies for upper GI blood loss in these patients are PUD; erosive diseases of the esophagus, stomach, and duodenum.

- Diverticular bleeding is the most common cause of lower GI bleeding.
Anticoagulants

• Correction of the INR to between 1.5 and 2.5 allowed successful endoscopic diagnosis and therapy

• INR level before endoscopy was not a predictor of rebleeding

• Performing endoscopic therapy in bleeding patients with INRs < 2.5 is reasonable
Endoscopic Procedures in Acutely Bleeding Patient on Antithrombotic Therapy

- Risk of bleeding vs. embolism
- Hold Coumadin, FFP, Factor Prothrombin Complex
- Using Vitamin K (5-10 mg by slow IV)
Endoscopic Procedures in Acutely Bleeding Patient on Antithrombotic Therapy

**Anticoagulants**

- Massive hemorrhage, hemodialysis can be used in patients receiving Pradaxa but **not** for Xarelto, Savaysa, and Eliquis
  - because of their decreased renal excretion and because they are highly protein bound

**Antiplatelet agents**

- Options include stopping these agents and/or administration of platelets
Urgent Endoscopy in the Patient with ACS or Recently Placed Vascular Stent

- 1% to 3% of patients with an ACS will present with or develop GI bleeding

- Patients who develop GI bleeding in setting of ACS have an almost 4- to 7-fold increased risk of in-hospital mortality over patients with ACS and no GI bleeding

*Intervention needed: Endoscope*

- Endoscopy was not found to be beneficial in patients who presented with occult GI bleeding and acute MI
“Heads, you get a quadruple bypass. Tails, you take a baby aspirin.”
Antibiotics

the question is to give or not to give…
Bacteremia

• Bacterial translocation occur during endoscopy because of mucosal (or deeper) trauma related to procedure

• Carries small risk of localization of infection (infective endocarditis)
Bacteremia Associated with Endoscopic Procedures

2015 ASGE evaluated

- Over 14.2 million colonoscopies, endoscopies and 2.8 mil flex sig
- Only 25 cases of IE
Procedures Associated with High Risk of Bacteremia

- Highest reported rates
  - Esophageal dilation
  - Sclerotherapy of varices
  - Obstructed bile ducts

- Streptococcus viridians
High Risk Procedures

• Esophageal bougie
  – Rate of 12% to 22%
  – Dilation of malignant strictures than benign strictures
  – Passage of multiple dilators than a single dilation

• Variceal Sclerotherapy
  – Rate as high as 52%
  – Mean of 14.6%

• Endoscopic Variceal Ligation
  – Rates of 1% to 25%
  – Mean of 8.8%
Procedures Associated with Low Risk of Bacteremia

- **EGD (with/without biopsy)**
  - Rates up to 8%
  - Mean of 4.4%

- **Bacteremia usually lasts less than 30 minutes**

- **Colonoscopy**
  - Rates as high as 25%
  - Mean of 4.4%

- **Colonic stent insertion (uncommon)**
  - Rate of 6.3%

- **Flexible sigmoidoscopy**
  - Less than 1%
Low Risk of Bacteremia

- No data associated with device-assisted enteroscopy
  - single-balloon and double-balloon enteroscopy, spiral enteroscopy)

- EUS (without FNA)
  - Rate of 2%
Bacteremia Associated with Routine Daily Activity

- Brushing and flossing teeth
  - Rates of 20% to 68%

- Use of toothpicks
  - Rates of 20% to 40%

- Chewing food
  - Rates of 7% to 51%
Infectious Endocarditis

Prevention of IE

• AHA 2007 Guidelines stated the administration of prophylactic antibiotics was no longer recommended

*Exceptions

– History of IE
– Cardiac Transplant
– Prosthetic Cardiac Valve
– CHD

Coverage should include PCN, or Vancomycin to cover Enterococcus*
EUS-FNA

- Clinical infection infrequent
- Prophylactic antibiotics not recommended in solid lesions
- Antibiotics IS recommended for 3-5 days following EUS-FNA of cystic lesions (to prevent cyst infection)
Role of Prophylactic Antibiotics Interventional EUS

- Interventional EUS procedures have not been studied
  - Pseudocyst drainage
  - Biliary drainage
  - Fine-needle injection of cysts and/or tumors
PEG or PEJ

• Vulnerable to infections:
  – Age
  – Compromised nutritional intake
  – Immunosuppression
  – Underlying medical comorbidities

• Antibiotics, such as Cefazolin 1 gm IV should be administered 30 minutes prior to procedure

• MRSA (Vancomycin)

• PEJ : Not studied
Cirrhosis with GI Bleeding

• Antibiotic prophylaxis associated with significantly lower overall mortality

• Outcomes
  – Reduce rebleeding and length of hospital stay

• Antibiotic therapy instituted at *admission*

• Oral norfloxacin is common

• Intravenous ceftriaxone
  – superior to norfloxacin in cases of variceal/nonvariceal GI tract bleeding in patients with cirrhosis

• Intravenous antibiotics
  – preferable in patients with active vomiting or hematemesis
Endoscopy in Patients with Synthetic Vascular Grafts

- Antibiotic prophylaxis **not** recommended after vascular graft or other nonvalvular cardiovascular device placement

  Pacemakers/ Defibrillators
Endoscopy in Patients with Orthopedic Prostheses

- Extremely Rare
- Uncertainty; Colonic Polypectomy within 6 months of prosthesis insertions
- 2009; American Association of Orthopedic Surgeons recommended Abx for all total joint replacement patients before any invasive procedure that may cause bacteremia
  - This statement later withdrawn due to lack of supporting clinical evidence
Immunocompromised Patients and Patients with Neutropenia

- Increased risk for patients with
  - Severe neutropenia (<500 cells/uL)
  - Advanced hematologic malignancies
  - Transplant recipients
  - Patients with HIV
  - Bone marrow transplantation
Peritoneal Dialysis

• International Society of Peritoneal Dialysis issued a position statement indicating that antibiotics may lower risk of peritonitis
  – Amp/Gent/Flagyl

• Administration of prophylactic antibiotics intraperitoneally
## Antibiotic Prophylaxis

<table>
<thead>
<tr>
<th>Patient Condition</th>
<th>Procedure Contemplated</th>
<th>Goal of Prophylaxis</th>
<th>Periprocedural Antibiotic Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile duct obstruction in absence of cholangitis</td>
<td>ERCP with complete drainage</td>
<td>Prevention of cholangitis</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Bile duct obstruction in absence of cholangitis</td>
<td>ERCP with incomplete drainage</td>
<td>Prevention of cholangitis</td>
<td>Recommended; continue antibiotics after procedure</td>
</tr>
</tbody>
</table>
## Antibiotic Prophylaxis

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</tr>
</thead>
<tbody>
<tr>
<td>Solid lesion in upper GI Tract</td>
<td>EUS-FNA</td>
<td>Prevention of local infection</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Solid lesion in lower GI Tract</td>
<td>EUS-FNA</td>
<td>Prevention of local infection</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Mediastinal cysts</td>
<td>EUS-FNA</td>
<td>Prevention of cyst infection</td>
<td>Suggested</td>
</tr>
<tr>
<td>Pancreatic cysts</td>
<td>EUS-FNA</td>
<td>Prevention of cyst infection</td>
<td>Suggested</td>
</tr>
<tr>
<td>Patient Condition</td>
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<td>------------------------------------------</td>
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<tr>
<td>All patients</td>
<td>PEG</td>
<td>Prevention of peristomal infection</td>
<td>Recommended</td>
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<tr>
<td>Cirrhosis with acute GI bleeding</td>
<td>Required for all patients</td>
<td>Prevention of infection and reduction of</td>
<td>On admission</td>
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<td>regardless of endoscopic</td>
<td>mortality</td>
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<td></td>
<td>procedures</td>
<td>Prevention of</td>
<td>Not recommended</td>
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<td>graft and device infection</td>
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<td></td>
<td>Prevention of septic arthritis</td>
<td>Not recommended</td>
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<td></td>
<td></td>
<td>Prevention of peritonitis</td>
<td>Suggested</td>
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<tr>
<td>Synthetic vascular graft and PPM/Defibrillator</td>
<td>Any endoscopic procedure</td>
<td>Prevention of</td>
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<td>Prosthetic joints</td>
<td>Any endoscopic procedure</td>
<td>Prevention of</td>
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<td>Peritoneal dialysis</td>
<td>Colonoscopy/py</td>
<td>graft and device infection</td>
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**Antibiotic Prophylaxis**
Happy Holidays