Antimicrobial Prophylaxis for Surgical Patients

Jon Jancik, PharmD, BCPS
Hennepin County Medical Center
jon.jancik@co.hennepin.mn.us

Why is the topic important?

- CDC
  - 500,000 Surgical Site Infections (SSIs) occur annually
    - 60% more likely to spend time in an ICU
    - 5x more likely to be readmitted to the hospital
    - 2x more likely to die
- Second most common nosocomial infection (most common is surgical patients)
  - 2-5% clean extra-abdominal operation
  - Up to 20% intraabdominal

Wound Classification Criteria

<table>
<thead>
<tr>
<th>Classification</th>
<th>Infection Rate</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>&lt;2%</td>
<td>Elective</td>
</tr>
<tr>
<td>Clean - Contaminated</td>
<td>&lt;10%</td>
<td>Urgent/Emergent</td>
</tr>
<tr>
<td>Contaminated</td>
<td>20%</td>
<td>Acute, trauma (&lt;4h), spillage</td>
</tr>
<tr>
<td>Dirty</td>
<td>40%</td>
<td>Purulence or abscess, trauma (&gt;4h), perf of GI tract</td>
</tr>
</tbody>
</table>
# Clean
- Uninfected operative wound
- No inflammation
- Nontraumatic
- Respiratory, GU, GI, Oropharyngeal tract not entered for surgery
- Closed drainage systems may be placed
- Examples
  - Splenectomy, mastectomy, CABG, Biopsy

# Clean - Contaminated
- Respiratory, GU, GI, Oropharyngeal tract entered for surgery under controlled conditions
- Absence of infection / inflamed tissue / trauma
- Minor break in technique
- Open drain may be placed in surgery
- Examples
  - Cholecystectomy, gastrectomy, appendectomy, Bowel resection

# Contaminated
- Fresh traumatic wound
- Gross spillage from GI tract
- Major break in technique
- Presence of inflamed, non-purulent tissue
- Examples
  - Repair of stab wound, inflamed appendix (non-ruptured), Clean/contaminated with significant spillage
Dirty - Infected

- Wounds that indicate existing infection
- Presence of acute purulent infection
- Wounds with retained devitalized tissue, foreign body, and/or delayed treatment
- Perforated viscus encountered
- Examples
  - Suppurative appendix, I&D abscess

Wound Classification Criteria

<table>
<thead>
<tr>
<th>Classification</th>
<th>Infection Rate</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean* ^</td>
<td>&lt;2%</td>
<td>Elective</td>
</tr>
<tr>
<td>Clean</td>
<td>&lt;10%</td>
<td>Urgent/</td>
</tr>
<tr>
<td>Contaminated</td>
<td></td>
<td>Emergent</td>
</tr>
<tr>
<td>Contaminated*</td>
<td>20%</td>
<td>Acute, trauma (&lt;4h), spillage</td>
</tr>
<tr>
<td>Dirty *</td>
<td>40%</td>
<td>Purulence or abscess,</td>
</tr>
</tbody>
</table>

*Prophylaxis not indicated
^maybe

Prophylaxis v Therapy

- Contaminated and dirty procedures require antibiotic therapy NOT prophylaxis
  - Prophylaxis is not to sterilize tissue
  - Used to reduce the microbial burden of the intraoperative contamination to a level that cannot overwhelm host defense
- Maybe
  - Any operation in which a SSI would pose a catastrophic risk
  - Cardiac, Neurosurgical, Prosthetic arterial grafts, ect
Risk factors for SSI

Wound

Host

Infection

Bacteria

Risk of SSI

Dose of bacterial contamination x virulence

Resistance of the host patient

=

Risk of Surgical Site Infection

Host Factors

- Age
- Nutritional status
- Smoking
- Obesity
- Coexistence of infection at a remote site
- Colonization with microorganism
- Altered immune response
- Length of preoperative stay
History Lesson

- 1950's
  - Confusing and heated debate concerning efficacy
  - Poor studies: small, nonrandomized, timing, blinding
  - Miles: SSIs suppressed with Abx in "decisive period"

- 1960's: Better Studies
  - Burke: timing and efficacy, after surgery
  - Bernard and Cole: demonstrated efficacy

- 1970's and 80's
  - Understanding of endogenous flora
  - Many well done studies showing benefit
  - Duration: 24 h v. longer
  - MN hospitals: 1979: 41% pts received abx within 4 hr

History Lesson - Today

- Still the same issues
  - We're getting better but not 100%
  - More studies

- JACHO
  - Used as an indicator
    - Right drug
    - Right time
    - Right duration

Current Standards:

- When to administer first dose
- Which agent to use
- What is the correct dose
- How long do we give it
It’s all in the timing….

- **Goal**
  - To achieve serum and tissue levels of the drug that exceed the MIC of the bugs to be encountered
  - To maintain that level throughout the case
    - Time of closure considered to be most important

---

Right spot at the right time

---

**What if my timing is off?**

- **Stone and colleagues**
  - Ann Surg 1976
    - Lowest rates of SSIs when antimicrobial dose administered 1 hr before incision
    - 1st dose post-op: similar results to no antibiotic

- **Classen and colleagues**
    - Looked at rates of surgical wound infections corresponding to the temporal association between administration and the start of surgery.
Infection Rate v Abx Timing

So What Are My Choices?

- Allergy Status?
  - β-lactam allergy?
    - History to uncover if allergy is real
    - History to discover the reaction
- Special circumstances with institution?
  - High MRSA rates
- Type of surgery
  - Encounter anaerobes v. just skin flora

Surgeries

- Covered in guidelines
  - Clinical Infectious Diseases 2004; 38:1706-15
  - Gynecological and Obstetrical
  - Orthopedic
  - Cardiothoracic and Vascular
  - Colorectal Surgery
Gynecological and Obstetrical

- Abdominal or vaginal hysterectomy
  - Cefotetan or cefoxitin
  - Metronidazole monotherapy
    - Less effective as a single agent for prophylaxis
  - β-lactam allergy
    - Clindamycin combined with gentamicin, aztreonam, ciprofloxacin or levofloxacin
    - Metronidazole combined with gentamicin, ciprofloxacin or levofloxacin
    - Clindamycin monotherapy

- Cesarean Section
  - Low risk for post operative infection
    - Low benefit but recommended
    - Similar agents to hysterectomy
  - High risk for post operative infection
    - C-section after rupture of membrane and/or onset of labor, emergency operation from which preoperative cleansing may have been inadequate
    - Similar agents to hysterectomy
  - Antimicrobials are not usually administered until after the cord is clamped

Orthopedic

- Total joint (hip and knee) arthroplasty
  - Cefazolin or Cefuroxime
  - β-lactam allergy
    - Vancomycin or Clindamycin
  - Proximal tourniquet use
    - Antimicrobial infusion should be complete prior to inflation
  - Antibiotic bone cement
    - No guidelines
Cardiothoracic and Vascular

- CABG, AAA, Valve replacement
  - Cefazolin or Cefuroxime
  - Beta-lactam allergy
    - Vancomycin or Clindamycin
  - Issue
    - Antimicrobials until all drains removed

Colorectal Surgery

- Oral bowel preparation
  - Neomycin plus erythromycin or neomycin plus metronidazole
    - Started no more than 18 to 24 hrs before surgery
      - 1 gm 19, 18 and 9 hours before surgery
  - Mechanical bowel preparation

Colorectal Surgery

- Parenteral prophylaxis
  - Cefotetan, cefoxitin, cefazolin + metronidazole
  - Allergy
    - Clindamycin + gentamicin or quinolone or aztreonam
  - Oral + parenteral prophylaxis is probably better than either alone
What is the right dose?

- Limited published data
- Dose should be based on:
  - Body weight
  - Adjusted dosing weight
  - BMI
    - (<80 kg use 1 gm, >80 kg use 2 gm)
- Repeat dose
  - case last > 2 x $t_{1/2}$ of drug being used
  - Major blood loss (>1.5 l)

Long Case

Dosing

- Obese pts undergoing gastric bypass
  - Cefazolin 1 gm
    - Blood and tissue levels below MIC for prophylaxis against gm + and gm-
  - Cefazolin 2 gm
    - Lower SSI than those receiving 1 gm
- Demonstrated in GI, Biliary and CV
  - Repeat dose in longer surgeries
    - Lower SSI rates
Redosing Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Redosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>3 – 5 hours</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>4 – 10 hours</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>3 – 6 hours</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>3 – 6 hours</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>6 – 8 hours</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>6 – 12 hours</td>
</tr>
</tbody>
</table>

The Correct Duration?

- Single dose v multiple dose
  - No benefit for additional doses
  - Prolonged use associated with resistant bacterial strains
- 24 hours at most
  - Exception is CV surgery (ASHP guidelines)
- Drains, Chest Tubes, etc
  - No need to cover until out

Benefits v Risk of Antibiotics

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease SSI, Pneumonia, Sepsis, Endocarditis, Urinary tract infections, Length of stay</td>
<td>Allergic reaction, Toxic effects of abx, C difficile, Adverse rxn of abx with other medication, Resistance, Increased MRSA, Cost</td>
</tr>
</tbody>
</table>
Nonantimicrobial Strategies

- Maintaining normal body temperature
  - Core temp of 34.7°C v 36.6°C
  - SSI 19% v 6% (p=0.009)
- Maintain normal blood sugars
  - CV surgery, ICU study
- Hyperoxygenation
  - Greif et al: colorectal pts
    - 30% v 80% inspired air during surg and 2 h after
      - SSI 11.2% v 5.2% (p=0.01)

No Magic Bullets……..

- Antimicrobial prophylaxis is an important adjunct to the prevention of surgical site infection
- BUT
  - You need to do it correctly!!!

Conclusion

- Proper agent selected for procedure
- Agent to be administered at correct time
  - Within the hour prior to surgery
- Agent to be given in the right dose
  - Larger doses for larger patients
  - Redose if long case
- Keep it to 24 hr or less (think single dose)
- Think about temp, sugar, and oxygen