

Antimicrobial Prophylaxis for Surgery

Pharmacy 407

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First Line Treatment of Choice and Alternatives (Drug Dose and Duration):

Streptococcal Pharyngitis

Otitis Media

Sinusitis

Community Acquired Pneumonia in a young healthy person

Community Acquired Pneumonia in a person with a comorbid disease such as CHF, COPD, Diabetes etc

CAP Pneumonia – hospitalized

Simple Urinary Tract Infection Cystitis - young healthy woman

Urinary Tract Infection in a pregnant woman

Pyelonephritis

Bacterial Meningitis in a child (first line only)

Surgical Site Infections (SSIs)

- SSIs are the 2nd most frequently reported nosocomial infection
- Account for 14 - 16 % of nosocomial infections
- 2-5% undergoing clean extra-abdominal surgeries and 20% undergoing intra-abdominal surgeries develop SSIs

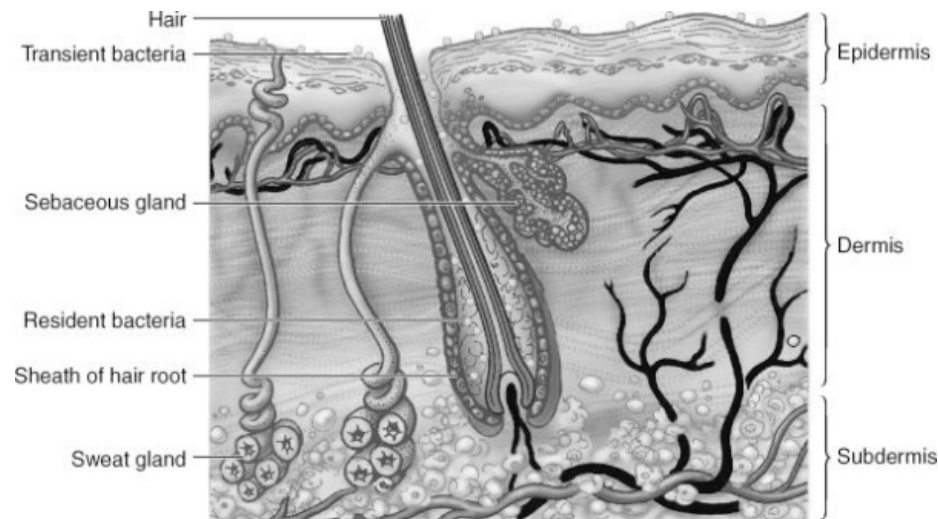
Post-Surgical Infections

- Result in increased hospital stay of 7- 10 days
- Patients with SSIs
 - 60% more likely to go to ICU,
 - 5 x more likely to be readmitted to hospital and
 - Twice as likely to die
- Incidence varies from surgeon to surgeon, procedure to procedure and patient to patient

Sources of Infection

- Environment
- Surgeon, surgical team
- Patient skin, mucous membranes
 - Usually gram positive cocci (staphylococci)
- Patient internal organs (if penetrated)
 - e.g. gram negative aerobes and anaerobic bacteria if incision in GI tract or GU tract or perineum

Transient and Resident Bacteria on the Skin



Skin layers with transient bacteria on the surface and resident bacteria in the deeper layers.

Transient bacteria more easily removed but resident bacteria difficult to remove .

Risk Factors

- Coincident remote site infections or colonization
- Diabetes
- cigarette smoking
- systemic steroid use
- obesity ($> 20\%$ $>$ IBW)
- Extremes of age
- Nutritional status
- Perioperative transfusion

Prevention

- Sterile ORs with positive pressure
- Surgeon preoperative hand/forearm asepsis
- Educated OR staff
- Policies and procedures
- Quality assurance

Prevention

- Patient preparation
 - Treatment of pre-existing infections
(e.g. UTI before prostate surgery)
 - Shower with antiseptic (chlorhexidine) at least night before surgery
 - Adequate skin-preparation
 - Hair clipping rather than shaving
 - Povidone-iodine (Betadine), alcohol, chlorhexidine gluconate (Hibitane)
 - Skin prepped in concentric circles (clean to dirty)
 - Antibiotic prophylaxis as indicated

Case 1

Mrs. Y.M. is a 24 year old woman who requires a caesarian section for failure to progress.

Cefazolin 1 gm IV is ordered 1 hr pre-op.

Case #2

Case #2

Mrs. Jones is a 55 yr old woman having a vaginal hysterectomy for menorrhagia. She is quite healthy and takes only hydrochlorthiazide 25 mg daily for mild hypertension that has been well controlled.

Cefazolin 1 g I.V. is ordered to be given by the anaesthetist immediately before the surgery.

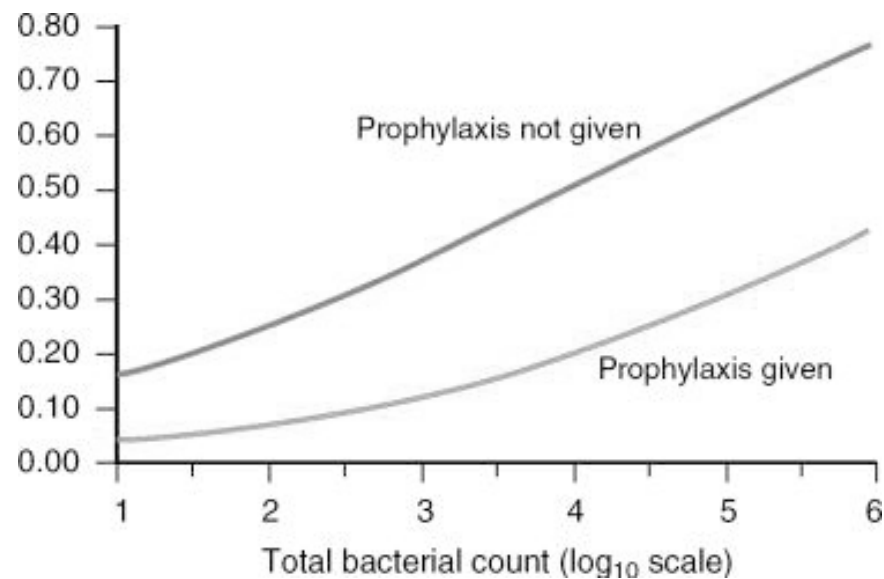
Antibiotic Prophylaxis

- Very brief course of antimicrobial agent just before surgery begins
- Timing important - important to have adequate drug concentrations at the time of surgery and throughout the surgery
- Goal not to sterilize tissues and not to cover all possible microorganisms but to reduce microbial burden to level that cannot overwhelm host defenses

Principles

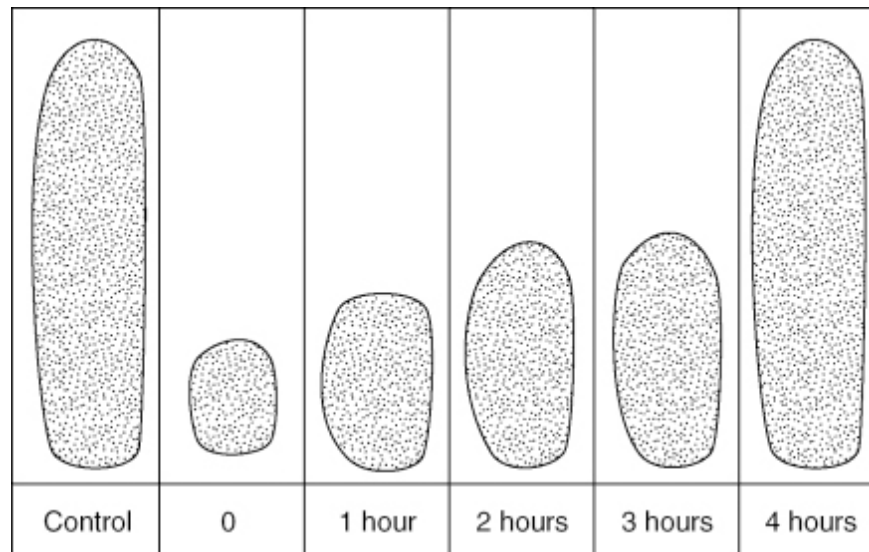
1. Use an agent shown to reduce SSIs for that type of surgery
2. Use an agent that is safe, inexpensive, and bactericidal with a spectrum that covers most probable contaminants
3. Time the infusion so that bactericidal concentration of drug is established in serum and tissues by the time skin incised
4. Maintain therapeutic levels in serum and tissues until at most a few hrs after incision closed

Probability of Infection with Prophylactic Antibiotics



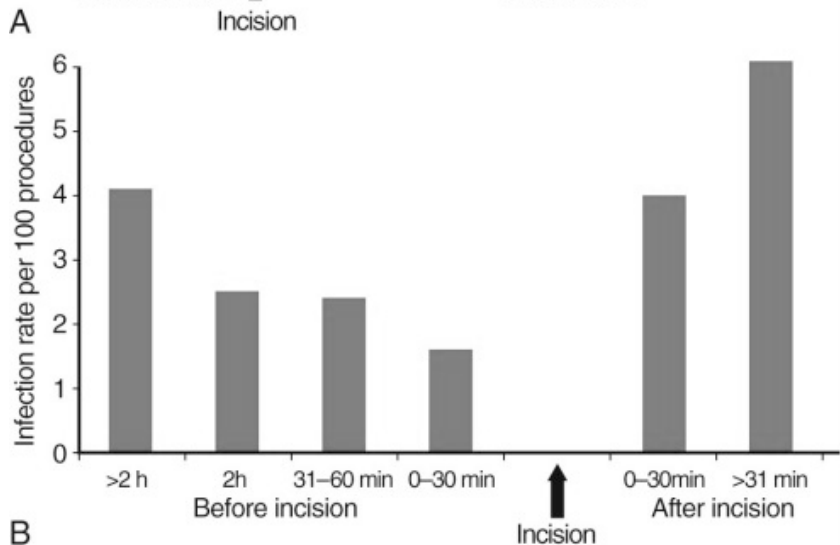
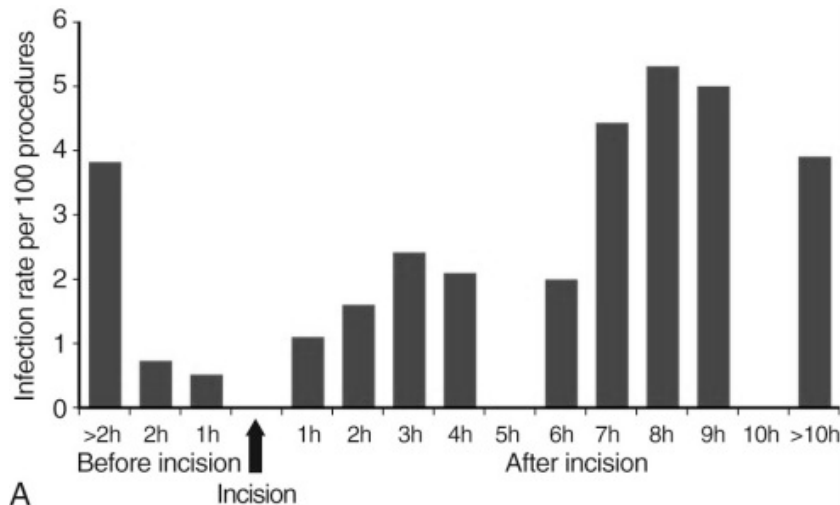
Reduction in risk of fever with prophylactic antibiotics for a given bacterial burden.

Timing of Prophylactic Antibiotics



Size of wound in animal model relative to timing of prophylactic antibiotic administration.

Timing of Prophylactic Antibiotics

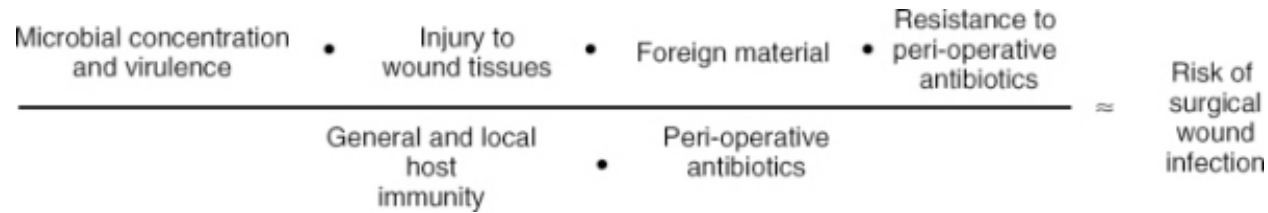


TRAPE study found SSI risk lowest if cephalosporins given within 30 minutes (Vancomycin or a fluoroquinolone within 1 hour.)

Timing of Administration and Infection Rate Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE) 2008

From Mandell, G, 7th ed. 2010

Risk Factors for Surgical Infection



- Microbial concentration and virulence
- Injury to wound tissues
- Foreign material
- Resistance to peri-operative antibiotics

- General and local host immunity
- Perioperative antibiotics

Surgical Wound Classification

Class I - Clean

- An uninfected wound with no inflammation and the respiratory, alimentary, genital or uninfected urinary tract is not entered
- Primary closure or closed drainage

Class II - Clean-Contaminated

- respiratory, alimentary, genital or uninfected urinary tract are entered under controlled circumstances without unusual contamination
- (e.g. biliary tract, appendix, vagina, oropharynx provided no infection or break in technique)

Surgical Wound Classification

Class III - Contaminated

- Open, fresh, accidental wounds
- Operations with major break in technique e.g. spillage from GI tract, open cardiac massage

Class IV - Dirty Infected

- Perforated viscera, existing clinical infection, or old traumatic wounds with retained devitalized tissue
- (organisms present in operative field before surgery)

Choice of Antibiotic

Cephalosporins best studied

- effective against many gram positive and gram negative organisms
- Safe
- Acceptable pharmacokinetics
- Reasonable cost

Choice of Agent

- Cefazolin 1- 2 g widely used - considered first choice for clean surgery
 - (clindamycin or vancomycin chosen if allergy)
- Surgery on distal GI tract requires agent that provides anaerobic coverage including *B. fragilis* (e.g. ceftiofur, or (cefazolin + metronidazole)
 - Alternative aminoglycoside + clindamycin or metronidazole)
- 3rd or 4th generation cephalosporins not routinely recommended

Choice of Agent

- Vancomycin is not routinely recommended
 - May be choice if high incidence of MRSA or MRSE post-operative infections
 - May be chosen in severe penicillin allergy

Choice of Agent

- Cephalosporins exhibit time-dependent PK
 - Ideal to maintain levels > MIC for target pathogens for duration of operation
 - When duration exceeds this time additional dose is given (3 - 4 hours for cefazolin)
 - Rule of thumb
 - A full dose of cefazolin 1 - 2 g should be given to adult no more than 30 - 60 minutes before the skin is incised (larger doses in obese patients)
 - With cesarean section dose given immediately before surgery
- If vancomycin, aminoglycoside or fluoroquinolone used 1-2 hr infusion time
- “on-call to O.R.” infusion not recommended due to time delays

Duration of Prophylaxis

- Majority of published evidence demonstrates prophylaxis after wound closure unnecessary
- Most studies comparing single dose to multiple dose prophylaxis show multiple doses not beneficial
- Prolonged use of prophylactic antibiotics associated with resistance
- For majority of operations a single dose is recommended
 - repeat dose if the operation is still in progress > 2 $t_{1/2}$ s after the first dose

	Recommended	Penicillin Allergy
Abdominal or Vaginal Hysterectomy (Enteric Gram negative, anaerobes, Grp B Strep, Enterococci)	Cefazolin or Cefoxitin (Cefazolin + metronidazole)	(clindamycin + Gentamicin, aztreonam or ciprofloxacin) (metronidazole + gentamicin or ciprofloxacin or levofloxacin) clindamycin
Cesarean Section	Cefazolin, or cefoxitin immediately before incision	

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Case #3

Mr. N. C. is a 75 year old 85 Kg man who is having a hip replacement.

Cefazolin 1gm I.V. q8h x 24 hours is ordered beginning in the O.R.

	Recommended	Penicillin Allergy
Orthopedic total hip or knee <i>(S. aureus, S. epidermidis)</i>	Cefazolin Cefuroxime ≤ 24 hours	Vancomycin or clindamycin
Cardiothoracic / Vascular surgery <i>(S.aureus, S. epidermidis, Gram neg bacilli)</i>	Cefazolin 1-2 g Cefuroxime 1.5g ≤24 hours (48h)	Vancomycin (possibly clindamycin)

Case #3

Mr. N. C. is a 75 year old 85 Kg man who is having a hip replacement.

Cefazolin 1gm I.V. q8h x 24 hours is ordered beginning in the O.R.

Case #4

Case #1

Mrs. H. G. is a 38 year old 60 kg woman who is 5'5". She is booked for a laparoscopic cholecystectomy. She is otherwise quite healthy. She has 2 children. She does not take any prescription medication regularly except a BCP and only takes occasional ibuprofen for headaches and Claritin extra in the fall for hay fever.

Cefazolin 1 g I.V. is ordered on call to the O.R.

	Risk Factors	Recommended
Esophageal, gastroduodenal (Gram + cocci, Gram - bacilli)	High risk <ul style="list-style-type: none"> ➤ Obese ➤ esophageal obstruction, ➤ decreased gastric acidity or G I motility 	High risk only Cefazolin 1- 2gm
Biliary Tract (gram - bacilli, Enterococci, clostridia)	High risk <ul style="list-style-type: none"> ➤ Age> 70 yrs ➤ acute cholecystitis, ➤ non-functioning gallbladder, ➤ obstructive jaundice, ➤ Common duct stones 	High risk only Cefazolin 1 - 2 gm

Case #4

Case #1

Mrs. H. G. is a 38 year old 60 kg woman who is booked for a laparoscopic cholecystectomy. She had an episode of acute cholecystitis approximately two months ago. Cholelithiasis was diagnosed on ultrasound. She was booked for an elective cholecystectomy.

She is otherwise quite healthy. She has 2 children. She does not take any prescription medication regularly except a BCP and only takes occasional ibuprofen for headaches and Claritin extra in the fall for hay fever.

Cefazolin 1 g I.V. is ordered on call to the O.R.

Case #5

T. R. is an 18 yr old male who has acute appendicitis which does not appear to have ruptured. He is booked for emergency surgery.

Cefoxitin 1 g IV q8h x 24 hours is ordered beginning on call.

Case #6

Mr. T. K. is a 67 year old 78 Kg gentleman who presented with a ruptured appendix. He had felt some pain for 4 days now, but put off having it looked at.

Surgery is booked and Cefoxitin 1 gm stat and q6h x 24 hr beginning in the OR.

	Recommended	Penicillin Allergy
<p>Colorectal Surgery</p> <p>(Gram negative enteric bacilli, anaerobes, enterococci)</p>	<p>Oral bowel prep (neomycin + erythromycin or neomycin + metronidazole) preoperative</p> <p>Cefoxitin 1- 2g or (cefazolin 1- 2g plus metronidazole 0.5g)</p>	<p>(Clindamycin + gentamicin, or ciprofloxacin)</p> <p>Or</p> <p>(Metronidazole + gentamicin or ciprofloxacin)</p> <p>Levofloxacin may be substituted for ciprofloxacin</p>
<p>Appendectomy (Non-perforated)</p>	<p>Cefoxitin or Cefazolin + metronidazole</p>	

Case #5

T. R. is an 18 yr old male who has acute appendicitis which does not appear to have ruptured. He is booked for emergency surgery.

Cefoxitin 1 g IV q8h x 24 hours is ordered beginning on call.

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Ruptured Abdominal Viscus

- Enteric gram-negative organisms suspected as pathogens
- Cefoxitin 1-2 g q 6h ± gentamicin 1.5 mg/kg q8h
- β -lactam allergy - clindamycin + gentamicin, ciprofloxacin, levofloxacin (750mg)
- Therapy is considered treatment and continued for 5 days or as the patient progresses

Case #6

Mr. T. K. is a 67 year old 78 Kg gentleman who presented with a ruptured appendix. He had felt some pain for 4 days now, but put off having going to the doctor.

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Prosthetic Device Infections

Risk of infections may be increased in patients with

- Vascular grafts
- Orthopedic prostheses
- (no good human controlled trials re: antibiotic prophylaxis)
- Risk of hematogenous joint infection thought to be increased in 1st 2yrs after total joint replacement
- Most wouldn't recommend prophylaxis with implanted dialysis catheters, ventriculoperitoneal shunts, cardiac pacemaker or defibrillators

References

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Principles and Practices of Infectious Diseases. Mandel G. et al.
7th edition 2010

(IDSA Guidelines - Surgical Prophylaxis 1997)