Hot Topics in Infectious Diseases

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Disclosures

• Dr. Bratzler has no financial relationships to disclose related to surgical site infection prevention.
How do you define a “hot topic?”

My topics........

- Surgical infections
- Antimicrobial stewardship
- Immunization
- Hepatitis C
- C. difficile
- A few other topics of contemporary interest
Current SSI Burden

Burden-US
- 160,000 - 300,000 SSIs per year
- 2%-5% of patients undergoing inpatient surgery
- Most common and most costly HAI

Surgical site infections are the most common hospital acquired infection!

Length of Hospital Stay
- ~7-11 additional postoperative hospital days

Cost
- Up to $3.5 to 10 billion annually

Factors Affecting Rates of Surgical Site Infections

- Host factors
  - age
  - morbid obesity
  - malnutrition
  - prolonged preoperative stay
  - infection at distal sites
  - cancer
  - diabetes
  - immunosuppression
  - ASA score
  - disease severity
  - prior operations, revision vs primary

- Surgical procedures
  - abdominal site
  - wound classification
  - procedure duration
  - poor hemostasis
  - drains/foreign bodies
  - dead space
  - urgency of surgery

- Endogenous flora/ Microbial factors
  - razor shaves
  - intraoperative contamination
  - prophylactic antibiotic timing, selection and duration
  - preoperative cleansing with chlorhexidine

- Surgical team and hospital practice factors
  - pre-operative screening for resistant organisms and decolonization
  - surgeon’s skill
  - surgical volume
Observations about SSIs

• All surgical wounds are contaminated by bacteria, but only a minority get infection.

• Different operations have different inoculums of contamination, and have different rates of infection.

• Similar operations performed by the same surgeon in different patient populations have different rates of infection.

• Wound infections have varying degrees of severity.

Antibiotics given after the wound is closed have little chance of getting to the wound space. Infected wounds almost always have to be opened to treat the infection.

Wound space
- Avascular
- Hypoxic
- Contents – interstitial fluid, glucose, blood.....

Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery

SHEA/IDSA Practice Recommendation

Strategies to Prevent Surgical Site Infections in Acute Care Hospitals: 2014 Update

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JAMA Surgery | Special Communication

Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017

Sandra I. Berrios-Torres, MD, Craig A. Umscheid, MD, MScCE; Dale W. Bratzler, DO, MPH; Brian Leas, MA, MS; Erin C. Stone, MA, Rachel R. Kite, MD, MScCE; Caroline E. Rankin, MD, MSHP; Sherry Morgan, RN, MLS, PhD; Joseph S. Solomkin, MD, John E. Mazuski, MD, PhD; E. Patchen Dellinger, MD; Kamal M. F. Rani, MD; Elie F. Berbari, MD, John Segreti, MD, Javad Parvizi, MD; Joan Blanchard, MSS, RSN, RN, CNOR, CIC; George Allen, PhD, CIC, CNOR; Ian A. J. W. Kuyattman, MD; Rodney Donlan, PhD; William F. Schuetz, MD, for the Healthcare Infection Control Practices Advisory Committee

Importance The human and financial costs of treating surgical site infections (SSIs) are increasing. The number of surgical procedures performed in the United States continues to rise, and surgical patients are initially seen with increasingly complex comorbidities. It is estimated that approximately half of SSIs are deemed preventable using evidence-based strategies.
GLOBAL GUIDELINES FOR THE PREVENTION OF SURGICAL SITE INFECTION


What do the guidelines say?

• For most operations, give an antibiotic dose before incision (right drug, big dose)
  – Stop antibiotics when the wound is closed
  – For elective colorectal surgery, also give oral non-absorbable antibiotics before surgery
• In orthopedic and cardiac surgery, consider nasal screening for S. aureus before surgery
  – If MSSA – decolonize the patient
  – If MRSA – decolonize the patient and add vancomycin
• Smoking cessation 4-6 weeks before operation

What do the guidelines say?

• Control blood sugar for at least two days after surgery for all operations
• Keep patients warm in the operating room
• High-flow oxygen for major operations
• Consider triclosan-coated sutures – particularly in colorectal surgery
Don't overuse non-beta lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.

While about 10 percent of the population reports a history of penicillin allergy, studies show that 90 percent on more of these patients are not allergic to penicillins and are able to take these antibiotics safely.

1. Appropriate selection of intravenous prophylactic antibiotics;
2. Postoperative normothermia (temperature of >98.6°F);
3. Oral antibiotics with mechanical bowel preparation;
4. Postoperative day 1 glucose 140 mg/dL;
5. Minimally invasive surgery; and
6. Short operative duration as defined by <100 or >100 minutes as a dichotomous outcome.
There was a strong stepwise inverse association between bundle score and incidence of SSI. Patients who received all 6 bundle elements had risk-adjusted SSI rates of 2.0% (95% confidence interval [CI], 7.9–0.5%), whereas patients who received only 1 bundle measure had SSI rates of 17.5% (95% CI, 27.1–10.8%).

Antimicrobial Stewardship

More is usually not better!
“……the idea that stopping antibiotic treatment early encourages antibiotic resistance is not supported by evidence, while taking antibiotics for longer than necessary increases the risk of resistance.”
Facts about Antibiotic Resistance

- 30-50% of antibiotic use in hospitals is unnecessary or inappropriate.
- Antibiotic overuse contributes to the growing problems of *Clostridium difficile* infection and antibiotic resistance.
- Reducing unnecessary antibiotic use can decrease antibiotic resistance, *Clostridium difficile* infections, and healthcare costs, and improve patient outcomes.
- Improving antibiotic use is a medication-safety and patient-safety issue.

https://www.cdc.gov/getsmart/healthcare/evidence.html
What about antibiotics in outpatient practices?

• At least 30% of antibiotic courses prescribed in the outpatient setting are unnecessary, meaning that no antibiotic is needed at all. Most of this unnecessary use is for acute respiratory conditions, such as colds, bronchitis, sore throats caused by viruses, and even some sinus and ear infections.
  – Total inappropriate antibiotic use, which includes unnecessary antibiotic use plus inappropriate antibiotic selection, dosing, and duration, may approach 50% of all outpatient antibiotic use.

• Antibiotics are the most common cause of adverse drug events (ADEs) in children, accounting for 7 of the top 10 drugs leading to pediatric ADE-related emergency room (ER) visits.
"Many new tests for infectious disease rely on detection of very small amounts of genetic material from many potential pathogens. There is significant potential for confusion between colonization and infection, with overdiagnosis leading to overtreatment of disease."

### Diagnostic Stewardship

**General principles**
- Test only if the clinical presentation is consistent with an infection
- Report results in a format that guides appropriate practice

**Urine cultures**
- Only if the patient has symptoms of UTI (or urologic surgery or pregnancy)
- Report likely contamination
  - No pyuria – no culture
  - Selective reporting of antibiotics you want used

**Blood cultures**
- Only if patient has symptoms – repeat only if worried about endovascular infection
- Use rapid tests such as PCR
  - Note likely skin contaminants
  - Selective reporting of antibiotic susceptibility

**C. difficile**
- Test only if patient has diarrhea (Abx exposure)
  - Continue use of toxin testing
- Toxin negative/PCR positive – likely colonization

**Automation**
- Use clinical decision support
  - Hard stops for contraindications (e.g., laxative use in a patient with diarrhea)
A few updates related to adult vaccination.

Background

- Annual influenza vaccination is recommended for all persons age 6 months and older unless contraindicated.

- During the 2014-2015 influenza season,
  - Fewer than 60% of adults were vaccinated
  - Fewer than 44% of children were vaccinated

Centers for Disease Control and Prevention. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015–16 Influenza Season. MMWR Morb Mort Wkly Rep. 2015; 64(30): 818-825. Available at: [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm)

Influenza Epidemiology

- Spread person-to-person through respiratory droplets

- Incubation period 1-4 days (average 2)

- Patients are infectious from 1 day before* symptoms and up to 5-7 days after becoming sick

*One of the important reasons that all healthcare workers should be required to receive the influenza vaccine
Influenza Epidemiology

- Uncomplicated influenza
  - fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis

- Complicated influenza
  - primary influenza viral pneumonia; exacerbate underlying medical conditions (e.g., pulmonary or cardiac disease); lead to secondary bacterial pneumonia, sinusitis, or otitis media
  - Young children with influenza virus infection might have initial symptoms mimicking bacterial sepsis with high fevers, and febrile seizures
  - Death

Influenza Vaccination

Reductions in Hospitalization and Death

Pneumococcal Disease
Case Presentation

• “Jane” was a 47-year-old female who presented to her local hospital ED with severe shortness of breath
  – Symptoms (shaking chill, fever, and productive cough) started 2 days earlier
  – Well known to local hospital personnel due to history of inpatient and outpatient treatment for alcoholism

Case Presentation

............the patient was hypoxic, hypotensive, and hypothermic at the time of the initial evaluation in the ED
Burden of Pneumococcal Disease

- Pneumococcus accounts for a spectrum of illness ranging from otitis media and sinusitis to pneumonia, bacteremia, and meningitis
  - In the United States, pneumococcal disease results in millions of ambulatory patient visits, hundreds of thousands of hospitalizations, tens of thousands of deaths, and billions of dollars in healthcare costs annually.

Burden of Pneumococcal Disease

- 400,000 cases of pneumococcal pneumonia annually
- 12,000 cases of pneumococcal bacteremia annually
- 3,000 cases of pneumococcal meningitis annually


Risk Factors for Pneumococcal Disease

- Demographic factors
- Substance abuse
- Comorbid medical conditions
  - Heart disease
  - Chronic lung disease (including asthma)
  - Diabetes mellitus
  - Chronic liver or kidney disease
  - Recent influenza infection
  - Cochlear implant or CSF leak
Pneumococcal polysaccharide vaccine (PPSV23; Pneumovax 23)

- Purified pneumococcal polysaccharide (23 types)
- Not effective in children younger than 2 years
- 60%–70% against invasive disease
  - Less effective in preventing pneumococcal pneumonia
- Vaccine induces humoral immunity with poor stimulation of immunologic memory

Summary – PPSV23

- Clearly reduced the incidence of invasive pneumococcal disease
  - Failure to vaccinate source of medical malpractice cases
- A number of observational studies showed reductions in complications for those patients who did get pneumonia
- Unclear if actual hospitalizations for pneumonia reduced
Pneumococcal Conjugate Vaccine (PCV13; Prevnar 13)

- More than 90% effective against invasive disease caused by vaccine serotypes in children
- 45% effective against vaccine-type non-bacteremic pneumococcal pneumonia in adults older than 65 years
- 75% effective against vaccine-type invasive disease in adults older than 65 year

PCV13

- Capsular polysaccharides for 13 serotypes of S. pneumoniae are conjugated to a carrier protein (diphtheria CRM197)
- Elicits a T-cell response resulting in immunologic priming and an immunologic memory response
PCV13 was effective in preventing vaccine-type pneumococcal, bacteremic, and nonbacteremic community-acquired pneumonia and vaccine-type invasive pneumococcal disease

FDA New Indication for PCV 13

- Prevnar 13 (pneumococcal 13-valent conjugate vaccine [diphtheria CRM197 protein], Pfizer) has received FDA approval for an expanded age indication to include adults 18 through 49 years of age, in addition to the already approved indication for adults 50 years and older, for active immunization for the prevention of pneumonia and invasive disease
Missed Opportunities Persist

• Despite the burden of pneumococcal disease, the availability of two vaccines to prevent the disease, and widely disseminated guidelines for use of pneumococcal vaccines, vaccination rates – particularly for adults – are woefully low.

Where is the liability risk?

• Liability cases in three states
  – Very consistent theme
    • Young males who have previously had a splenectomy (no documentation of PPV)
      – Subsequently hospitalized (in some, multiple times)
        – not given PPV
      – At least one case had visits to primary care physicians and an emergency department – not given PPV
    • All three developed purpura fulminans (two with significant amputations, one with menigitis and renal failure, one death)
Pneumococcal Vaccination of High-risk Adults

How old is the patient?

- 19-64 years
- 65 years or older

Immunocompromised, CSF Leak, or Cochlear implant?

- Yes
- No

PCV13 (Prevnar 13) AND PPSV23 (Pneumovax)*

- Sickle cell disease/other hemoglobinopathy
- Congenital or acquired asplenia
- Congenital or acquired immunodeficiency
- HIV infection
- Chronic renal failure
- Nephrotic syndrome
- Leukemia
- Lymphoma
- Hodgkin disease
- Generalized malignancy
- Iatrogenic immunosuppression
- Solid organ transplant
- Multiple myeloma

PPSV23 (Pneumovax only)

For patients with:
- Chronic heart disease†
- Chronic lung disease‡
- Diabetes mellitus
- Alcoholism
- Chronic liver disease, cirrhosis
- Cigarette smoking

* Including congenital heart failure and cardiac syndromes (excluding hypertension).
† Including chronic obstructive pulmonary disease, emphysema, and asthma.
‡ Including chronic obstructive pulmonary disease, emphysema, and asthma.

PCV13 (Prevnar 13) AND PPSV23 (Pneumovax)

PCV13 first, followed by a dose of PPSV23, at least 12 months later.

If the patient has received any doses of PPSV23, the dose of PCV13 should be given at least 1 year after receipt of the most recent PPSV23 dose.

If the patient has received a dose of PCV13 at a younger age, another dose of PCV13 is not recommended. The patient should receive PPSV23.

* All patients ages 19 through 64 years who are immunocompromised or who have functional asplenia should receive PCV13 followed by PPSV23 at least 8 weeks after their PCV13 dose. These patients should also be reimmunized with PPSV23 five years after their first PPSV23 dose.
† Includes B- (humoral) or T- (lymphocyte) deficiencies, complement deficiencies (particularly C1, C2, C3 and C4 deficiencies), and phagocytic disorders.
‡ Diseases requiring treatment with immunosuppressive drugs, including long-term corticosteroids and radiation therapy.
Prevalence of HPV in the U.S. in the pre-vaccine era....

- 100% of sexually active men and women acquire genital HPV at some point in their lives.

- An estimated 79 million females aged 14–59 years are infected with HPV infection.

### HPV-associated cancers  United States, 2004-2008

<table>
<thead>
<tr>
<th>Anatomic Area</th>
<th>Average annual number of cases*</th>
<th>HPV attributable</th>
<th>HPV 16/18 attributable</th>
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<tbody>
<tr>
<td>Cervix</td>
<td>11,967</td>
<td>11,500</td>
<td>9,100</td>
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<td>Vagina</td>
<td>729</td>
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<td>400</td>
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<td>Vulva</td>
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<td>Anus (F)</td>
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<td>Oropharynx (F)</td>
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<tr>
<td>Total (Females)</td>
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<td>Anus (M)</td>
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<tr>
<td>Total (Males)</td>
<td>12,080</td>
<td>7,900</td>
<td>7,400</td>
</tr>
</tbody>
</table>

Current Recommendations for HPV Vaccine

• CDC now recommends 2 doses of HPV vaccine for people starting the vaccination series before the 15th birthday. Three doses of HPV vaccine are recommended for people starting the vaccination series on or after the 15th birthday and for people with certain immunocompromising conditions.

• CDC continues to recommend routine vaccination for girls and boys at age 11 or 12 years. The vaccination series can be started at age 9 years.
  – CDC also recommends vaccination through age 26 years for females and through age 21 years for males. Males age 22–26 years may be vaccinated.

Hepatitis C – a curable disease!
Who should get tested for hepatitis C?

• While anyone can get hepatitis C, 3 in 4 people with hepatitis C were born from 1945–1965.

• Obviously patients with persistent elevation of their hepatic transaminases, blood donors, etc.

http://www.hcvguidelines.org/
C. difficile Disease

Antibiotic prophylaxis for surgical site infections as a risk factor for infection with Clostridium difficile

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Abstract

C. difficile infection

- Older Americans are especially vulnerable to this deadly diarrheal infection.
  - Two out of every three healthcare-associated *C. difficile* infections occur in patients aged 65 years or older.
  - More than 80% of the deaths associated with *C. difficile* infection occurred among Americans aged 65 years or older;
  - and one out of every nine older adults with a healthcare-associated *C. difficile* infection died within 30 days of diagnosis
**C. difficile infection and Nursing Homes**

- More than 100,000 *C. difficile* infections develop among residents of US nursing homes each year, making *C. difficile* infections among the most serious healthcare complications that affect the nursing home population.

**CDI Disease Severity**

Does that patient have any of the following:
1. WBC ≥ 15,000
2. Hypoalbuminemia (serum albumin <3 g/dl)
3. Creatinine ≥1.5 times the premorbid level

Mild / Moderate Disease  
No  Yes  
Severe Disease
Treatment Guidelines
European Society of Clinical Microbiology

- Antibiotic treatment is recommended for all except very mild cases actually triggered by antibiotic use; suitable treatments include metronidazole, vancomycin, and fidaxomicin
  - For mild/moderate disease, oral metronidazole (500 mg 3 times daily for 10 days) is recommended as initial treatment
  - In patients for whom oral treatment is inappropriate, fidaxomicin may be used
  - For patients with severe CDI, suitable antibiotic regimens include vancomycin (125 mg 4 times daily for 10 days; may be increased to 500 mg 4 times daily) or fidaxomicin (200 mg twice daily for 10 days)
  - Use of oral metronidazole in severe or life-threatening CDI is discouraged
- Fecal transplantation is recommended for multiple recurrent CDI
- For patients with colonic perforation and/or systemic inflammation and deteriorating clinical condition despite antibiotic treatment, total abdominal colectomy or diverting loop ileostomy combined with colonic lavage is recommended

Recurrent C. difficile disease

- 1st recurrence can be treated with the same class stratification regimen used for the initial episode
- 2nd recurrence should be treated with tapering and pulsed oral vancomycin (below), with or without probiotics (i.e. *Saccharomyces boulardii* 500 mg orally twice daily)
  - 125 mg orally QID daily for 7 to 14 days, then BID for 7 days, then QD for 7 days, then q48H for 7 days, Q72h for 14 days
- 3rd recurrence after a pulsed vancomycin regimen
  - Fidaxomicin 200 mg orally twice daily for 10 days if not used previously
  - Fecal microbiota transplant

Bezlotoxumab is a monoclonal antibody against *Clostridium difficile* toxin B that received US Food and Drug Administration approval in 2016 for secondary prevention of *C. difficile* infection in patients at high risk for recurrence
Other topics of note.....

• Zika virus
• Healthcare-associated *Candida auris* infections in the United States
• HIV transmission in sero-discordant couples when the infected partner is on effective HAART

Zika Virus Distribution