High-Yield Infectious Disease: A Review

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Topics Discussed

(in no particular order.....)

- Health Care Associated Infections, including Infection in Transplant Patients
- Bioterrorism
- New Topics in Antibiotics
- Frequently Tested Topics
LEARNING OBJECTIVES

• Diagnose disease states that are less common and confusing
• Improve management of comorbidities that may complicate care
• Improve familiarity with some of the new antibiotics
• Improve familiarity with identification and management strategies in bioterrorism
• Review frequently tested topics
Case #1

- 57 yo female status post liver transplantation 18 months ago presents with acute onset of dyspnea and dry cough. Pt’s current therapy consists of tacrolimus, Imuran, and inhaled pentamidine. She has an allergy to sulfa.
Case #1

- Physical Exam findings are as follows:

  Vitals-- 38.0C BP-140/78 pulse-114 RR-25 Pulse Ox-86% on RA
  Lungs- fine crackles bilaterally
  CBC, BMP, U/A all normal.

  CXR shows bilateral opacities
  CT shows bilateral fine alveolar and interstitial infiltrates.
  Sputum sample cannot be obtained.
What is the likely cause?

A. Aspergillus fumigatus
B. Candida glabrata
C. Candida kansasii
D. Pneumocystis jirovecii
E. Staphylococcus aureus
F. Streptococcus pneumoniae
Case #2

- 27 yo male with 2 day history of diarrhea (>10 BMs daily) with worsening abdominal pain and fever. Recently underwent dental surgery for which he received Unasyn and clindamycin.

- Physical exam and ancillary testing:
  - Tmax- 38.8C  Pulse-120 RR-22 BP-90/52
  - Abdomen is distended, and bowel sounds are absent.
  - WBC- 28  BUN/Cr—26/2.7  Albumin of 2.1
CASE #2

Which of the following is the most appropriate?

A. Intravenous metronidazole and oral vancomycin
B. Intravenous metronidazole and intravenous vancomycin
C. Oral metronidazole
D. Intravenous vancomycin
E. Oral metronidazole and oral vancomycin
F. Oral vancomycin
CASE # 2 CONTINUED

Patient spent a week in ICU. Subsequently transferred to the general medical floor to a two-bed hospital room. In addition to bleach, which of the following would be the most effective in preventing the spread of C. diff?

A. Barrier precautions and alcohol hand sanitizer
B. Aerosolized hydrogen peroxide “bomb”
C. Barrier precautions and soap and water for hand hygiene
D. Airborne precautions and alcohol hand sanitizer
E. Droplet precautions and soap and water for hand hygiene
F. Airborne precautions and soap and water for hand hygiene
Case #3

- A 19 yo male is hospitalized for fever, shaking chills, and worsening abdominal discomfort and pain for 1 week. Patient underwent cardiac transplantation 3 years ago due to congenital defect. His immunosuppressive regimen consists of cyclosporine, trimethoprim-sulfamethoxazole, and acyclovir.

- VS- Tmax 38.6, BP-110/72, RR- 16-18, HR-78
- Lungs-clear
- Heart- regular, rhythmic, Normal s1, s2
- Abdomen- absent bowel sounds; notable rebound diffusely; exquisite tenderness to palpation
- Abdominal X-ray shows free air and ileus—
- Surgery is consulted, exploratory laparotomy is performed and a jejunal perforation is found.
CASE #3

Infection with which of the following would explain the patient’s bowel perforation?

A. Herpes simplex virus  
B. *Strongyloides stercoralis*  
C. Cytomegalovirus  
D. *Escherichia coli* O127  
E. *Giardia lamblia*
Case #4

- 37 yo woman with history of Chronic Hepatitis C from a blood transfusion for which she has declined treatment. While vacationing in Aruba, she fell while swimming and cut her hand on an oyster shell.
Case #4

- Physical Exam:
  VS- 39.3 Pulse-107
  RR-22  BP-88/62

Hand is shown
Abdomen is distended with fluid wave. Liver and spleen not palpable.
CASE #4

Which of the following is the most likely cause?

- *Acinetobacter baumanii*
- *Streptococcus pyogenes*
- *Pasteurella multocida*
- *Rickettsia rickettsii*
- *Vibrio vulnificus*
- *Clostridium tetani*
Case #5

- 45 yo man with history of splenectomy following car accident is bitten by his dog on his leg. Immunizations are UTD, including *H. influenza* and pneumococcal.

- Multiple blood cultures reveal gram negative rods and x-ray of hand shows no gas nor foreign body.

- Leg is erythematous with no drainage

- LFTs: ALT- 556 AST- 390

- Peripheral smear shows Howell-Jolly bodies
CASE #5
Which of the following is the most likely cause of the patient’s presentation?

- *Capnocytophagia canimorsus*
- *Pasteurella multocida*
- *Salmonella typhi*
- *Streptococcus pyogenes*
- *Staphylococcus aureus*
- *Escherichia coli*
Case #6

- 37yo male TSA employee presents to the ED due to 2 day history of fever and dyspnea. No recent sick contacts or exposures. Patient is febrile, diaphoretic and toxic appearing
Case #6

- Tmax 38.0°C, BP-92/56  RR-32  Pulse-110
- Coarse bronchial breath sounds are heard
- Ancillary testing shows a WBC of 16 and CXR shows widened mediastinum and bilateral pleural effusions.
- Buffy coat gram stain shows “boxcar” shaped gram-positive bacilli.
CASE #6

Which of the following is the most appropriate treatment?

A. Cipro, rifampin, and vancomycin
B. Penicillin, rifampin, and vancomycin
C. Erythromycin, vancomycin, and rifampin
D. Erythromycin, clindamycin, and rifampin
BIOTERRORISM
Bioterrorism: An Overview

- Formerly taboo subject now out in the open
- Bioterrorism potentially a greater threat than conventional terrorist attack
- Fatality level likely greater than previous attacks

- Examples throughout history:
  1. Rome
  2. Siege of Kaffa
  3. French and Indian War
  4. American Revolution
  5. WWI and WWII
  6. 2001 Anthrax attacks
Working Group on Civilian Biodefense

**Category A organisms**
- Anthrax
- Botulinum toxin poisoning
- Smallpox
- Plague
- Tularemia
- “viral hemorrhagic fevers” (Lassa, Marburg, and Ebola)

-obtaining and producing biologic weapons is relatively easy
-Production is comparatively simple
-Dispersion is straightforward
Anthrax (Bacillus anthracis)

- Gram positive aerobic rod that forms extremely hardy spores
- Incubation period; 1-60 days
- Three types: cutaneous (woolsorter’s disease) inhalational (pulmonary) and gastrointestinal
- Appears as a Gram positive “boxcar” bacilli
- Inhalational anthrax presents as a nonspecific flu-like illness with cough, dyspnea, and chest pain that rapidly progresses to shock and death
- Initial findings may include mediastinal widening, pleural effusions, and less commonly, infiltrates.
- Cutaneous anthrax includes painless, pruritic, edematous papule with possible hemorrhagic and/or necrotic progression.
Anthrax (*Bacillus anthracis*)
Anthrax (Bacillus anthracis)

Treatment:
- Fluoroquinolone
  - or
  - Doxycycline
- One or two of the following gram positive covering (Penicillin, erythromycin, rifampin, vancomycin, or clindamycin)
- No isolation required
- Live vaccine targeting toxins, but limited availability
A 14 yo boy with chronic constipation is evaluated in the ER for blurred vision, diplopia, slurred speech, nasal regurgitation of fluid, and BL upper extremity weakness. Visual symptoms began first, followed by upper extremity findings several hours later. Began less than 24 hours ago. This ED has seen four similar patients in the last 24 hours. Pt’s only medication is a magnesium containing laxative that he uses infrequently. He did use it today.

On physical exam, Patient is afebrile, RR-12, BP 100/50, HR 50-60, Pupils are dilated, Extraocular movements show bilateral deficits in cranial nerve IV. He cannot abduct his arms against resistance. CBC, BMP, CT, and LP are performed; all results are normal.
What is the most likely diagnosis?

A. Multiple sclerosis
B. Guillain-Barre syndrome
C. Myasthenia gravis
D. Poliomyelitis
E. Botulism

**Hint:** note the ophthalmoplegia and ptosis in the left picture and the fixed, dilated pupils in the right. Child was fully conscious at time of photo.
Botulism

- Caused by toxin from anaerobic gram positive bacillus Clostridium botulinum
- Naturally occurring botulism develops from contaminated food, particularly canning or pickling
- Use as a bioweapon would involve intentional contamination of food or aerosolized toxin
- **Classical clinical triad is bulbar palsy, afebrile with clear sensorium, flaccid descending paralysis**
- **Five D’s: diplopia, dysphonia, dysarthria, dysphagia, descending, symmetric flaccid paralysis that develops 12-72 hours after exposure**
- No fever and preservation of mental status
- Treatment is antibotulinum immune globulin and supportive care
Case #8

- 59yo man comes to ED with a 2 day history of fever, headache, diffuse myalgia, abdominal pain, malaise, and mouth sores, followed by a painful papular rash that began on face and trunk and extended to arms and legs. Patient had chickenpox as a child.

- Physical exam shows a toxic appearing man febrile to 39.1C HR-110 RR-22 and normal BP

- Patient’s appearance is as shown
Case #8

- Which of the following is the most appropriate management for close contacts of the patient?
  A. Prophylaxis with acyclovir
  B. Prophylaxis with Cidofovir
  C. Vaccinia vaccination
  D. Hyperimmune globulin injection
Smallpox
Smallpox

- Caused by a DNA virus
- Last wild-type case eliminated in 1977, but still exists in laboratories around the world.
- Most of the world’s population is not immune because routine immunization was discontinued.
- Presents with high fever and malaise followed by vesicular/papular/pustular rash which begins on face and extremities and spreads to trunk
- Skin lesions, unlike chickenpox, are in synchronous stages of development (e.g. All papules, all vesicles)
- **No. Treatment.** (other than supportive)
- Vaccine if exposure within 7 days
- Respiratory and contact isolation
Case #9

- 42 yo man is hospitalized with cough, fever (38.8°C) and pleuritic chest pain immediately after attending a soccer game. Seven people who also attended the game with patient have been hospitalized with pneumonia. One has died.

- Physical exam and ancillary testing show HR of 114 and RR of 28 with 88% RA Pulse ox. Lungs show egophony on the right.
- WBC-18.8 with 20% bandemia
- CXR shows dense infiltrate in the right middle and right lower lobes with air bronchograms. Blood cultures NGTD
Which of the following is the most likely diagnosis?

A. Inhalational anthrax
B. Mycoplasma pneumonia
C. Methicillin resistant *staphylococcus aureus*
D. Tularemia
Tularemia (Francisella tularensis)

- Natural occurring zoonosis with features similar to Yersinia
- Caused by a gram negative coccobacillus
- Typically transmitted through ingestion of food (oropharyngeal tularemia) or through insect vector bites (oculoglandular fever)
- In a bioterrorism attack, an unexplained pneumonia like syndrome would be the most likely presentation of tularemia.
- There is no person to person transmission
- Recommended treatment is streptomycin (preferred), or gentamicin, doxycycline, or ciprofloxacin. Vaccine has limited efficacy.
Case #10

- 21 yo female is brought to ED with one day history of delirium and fever
- Physical exam Tmax 39.5C, BP- 84/44 HR- 132 RR-34. Oriented only to person. Significantly labored breathing. No lymphadenitis. Abdomen-unremarkable.
- WBC-32 CXR- diffuse bilateral alveolar infiltrates
- WBC-32 CXR- diffuse bilateral alveolar infiltrates
- Peripheral blood smear shows gram negative coccobacilli with bacteria that look like safety pins.

Infection with which is most likely?

a) Francisella tularensis
b) Salmonella enterica
c) Staphylococcus aureus
d) Aeromonas
e) Yersinia pestis
f) Streptococcus pneumoniae
Black Death
European Tour
1347 - 1351

European Tour
1347 - 1351

Crimea
Rhine Valley
Calais
Dorset
Bristol
London
Yorkshire
Milan
Flanders

Tuscany
Aragon
Catalonia
Languedoc
Barcelona
Castile
Canterbury
Bordeaux
East Anglia
Plague (Yersinia Pestis)

THE ‘BLACK DEATH’ ENTERED ENGLAND IN 1348 THROUGH THIS PORT.
IT KILLED 30-50% OF THE COUNTRY’S TOTAL POPULATION
Plague (Yersinia Pestis)

- Systemic infection caused by gram-negative bacillus (or coccobacillus)
- Spread by aerosolization of the bacteria or by inoculation from flea bites
- Consists of three clinical syndromes: bubonic, pneumonic, and septicemic
- Person-to-person spread is possible
Plague (Yersinia Pestis)

- Systemic infection may induce overwhelming sepsis in an otherwise healthy person.
- Antibiotics and patient isolation for the first 48 hours of therapy to prevent secondary spread of pneumonic plague.
- Mortality rate approaches 100% if not treated with antibiotics within 24 hours of developing symptoms.
Plague (Yersinia Pestis)

- Gram stain shows small gram negative coccobacilli. Wayson stain shows pathognomonic bipolar “closed safety-pin” appearance.
- Reduced the world population from 450 million to 350-375 million in the 14th century.
New Topics in Antibiotics
New Topics in Antibiotics

- New Antimicrobial Agents
- New Uses for older drugs
- Antibiotic dosing
- Antibiotic stewardship and rational use
New Antibiotics

- Ceftaroline
- Daptomycin
- Tigecycline
- Fidaxomicin
- Telavancin
- Fosfomycin
Ceftaroline

- (Saravolatz, et al “Ceftaroline: A Novel Cephalosporin with Activity against Methicillin-resistant Staphylococcus Aureus” CID 2011:52 (1 May)
- New parenteral broad-spectrum cephalosporin
- Broad activity against MDR gram-positive bacteria, including Streptococcus Pneumoniae and Staphylococcus Aureus, including methicillin resistant, vancomycin-resistant, linezolid resistant, and daptomycin-nonsusceptible strains
- Antibiotic activity similar to those of other B-lactams; binding to pencillin-binding proteins and inhibiting cell wall synthesis.
Ceftaroline

- In vitro activity suggests activity vs. VRE, but no clinical data yet to support in vivo efficacy.
- Variable activity vs. enterobacteriaceae
- No activity against nonfermentative gram-negative bacilli, including *Pseudomonas aeruginosa*
- Side effect profile similar to comparator drugs
- Possible synergy with tobramycin vs. MRSA
- Twice daily IV dosing (600mg)
Daptomycin

- **Daptomycin** is a novel lipopeptide used in the treatment of certain infections caused by Gram-positive organisms. It is a naturally occurring compound found in the soil saprotroph *Streptomyces roseosporus*.

- Daptomycin has a distinct mechanism of action, disrupting multiple aspects of bacterial cell membrane function. It appears to bind to the membrane and cause rapid depolarization resulting in a loss of membrane potential leading to inhibition of protein, DNA, and RNA synthesis, which results in bacterial cell death.
Daptomycin

- Daptomycin is active against Gram-positive bacteria only. It has proven *in vitro* activity against enterococci (including glycopeptide-resistant enterococci (GRE)), staphylococci (including MRSA), streptococci and corynebacteria.
- Daptomycin is approved in the United States for skin and skin structure infections caused by Gram-positive infections, *Staphylococcus aureus* bacteremia and right-sided *S. aureus* endocarditis. It binds avidly to *pulmonary surfactant*, and therefore cannot be used in the treatment of pneumonia.
Tigecycline

- **Tigecycline** is a glyciyclcline marketed by Wyeth under the brand name Tygacil. It was developed in response to the growing prevalence of antibiotic resistance in bacteria such as *Staphylococcus aureus* and *Acinetobacter baumannii*. The New Delhi metallo B-lactamase multidrug-resistant Enterobacteriaceae has also shown susceptibility to tigecycline.

- This antibiotic is the first clinically-available drug in a new class of antibiotics called the glyciyclclines. It is structurally similar to the tetracyclines and is actually a derivative of minocycline. Tigecycline has a substitution at the D-9 position which is believed to confer broad spectrum activity.
Tigecycline

- Tigecycline is bacteriostatic and is a protein synthesis inhibitor which occurs by binding to the 30S ribosomal subunit of bacteria.
- Tigecycline is given intravenously was at least equal to intravenous vancomycin and aztreonam to treat complicated skin and skin structure infections (cSSSI), and to intravenous imipenem and cilastatin to treat complicated intrabdominal infections (cIAIs) in phase III FDA trials.
Tigecycline

- Tigecycline is active against many Gram-positive bacteria, Gram-negative bacteria and anaerobes – including activity against MRSA, *Stenotrophomonas maltophilia, Haemophilus influenzae*, and *Neisseria gonorrhoea* and multi-drug resistant strains of *Acinetobacter baumannii*.

- It has no activity against *Pseudomonas* or *Proteus* species.

- New information suggests that use of tigecycline is associated with a significant increase in mortality and noncure rates in 13 RCTs (Prasad, et al CID June 15, 2012:54) for both non-FDA approved and approved clinical uses, suggesting the possibility of inadequate antimicrobial activity.
Fidaxomicin

- **Fidaxomicin** (trade name *Dificid*) is the first in a new class of **narrow spectrum** macrocyclic antibiotics.

- Fidaxomicin is non-systemic, meaning it is minimally absorbed into the bloodstream, it is bactericidal, and it has demonstrated **selective eradication of** pathogenic *Clostridium difficile* with minimal disruption to the multiple species of bacteria that make up the normal, healthy intestinal flora.
Fidaxomicin

- Works by inhibiting the bacterial enzyme RNA polymerase, resulting in the death of *Clostridium difficile*. It is active against gram positive bacteria especially clostridia.

- 13.3% of the subjects in phase III trials had a *Clostridium difficile* recurrence with fidaxomicin vs. 24.0% with oral vancomycin.
Telavancin

- **Telavancin** (trade name **Vibativ**) is a bactericidal lipoglycopeptide for use in MRSA or other Gram-positive infections. Telavancin is a synthetic derivative of vancomycin.
- Telavancin has a dual mechanism of action: like vancomycin, telavancin inhibits bacterial cell wall synthesis. In addition, it disrupts bacterial membranes by depolarization through inhibition of peptidoglycan synthesis.
- 10-fold greater activity than vancomycin in inhibiting syntheses of peptidoglycan in intact MRSA cells.
Telavancin

- The FDA approved the drug in September 2009 for complicated skin and skin structure infections (cSSSI), as well as gram-positive pneumonia.
- Consistently active against *Staphylococcus aureus*, (including MRSA, linezolid-resistant, daptomycin non-susceptible and vancomycin-intermediate strains), Clostridium species, Enterococcus, Streptococcus species, as well as *Bacillus anthracis*.
- Telavancin associated with higher rates of renal events, altered taste, and nausea and vomiting, but lower rates of pruritus and infusion-related events, compared with
Fosfomycin

- What’s old is new again: originally described and isolated on 1969 from cultures of *Streptomyces* species.
- Now used for the treatment of uncomplicated UTIs caused by E. coli and *Enterococcus faecalis*.
- Broad-spectrum activity against gram-positive and gram-negative bacteria.
Fosfomycin

- Form of the medication for intravenous use is *fosfomycin disodium*, which could limit its usefulness in patients with heart failure or whom are on hemodialysis.

- Current conventional wisdom suggests using fosfomycin in combination, rather than as monotherapy.
New Uses for Older Antimicrobials

- **Linezolid and ertapenem**: have been shown to be effective for treating diabetic foot infections without osteomyelitis. (Treatment should be limited to 10-14 days for each due to cost and potential risks of long-term therapy.

- **Colistin and polymyxins**: unique spectrum for multidrug-resistant *A. Baumannii, Pseudomonas* species, ESBL-producing *E.coli* and *Klebsiella pneumoniae*
Case #11

- 45 yo woman with DMII presents with fever, chills and hyperglycemia. Medications include Lantus, Novolog sliding scale, and aspirin.
- Physical exam shows temp of 39.0C, BP 82/48, HR-112 RR-24. Substantial area of necrosis on the plantar aspect of the left foot, with warmth and surrounding erythema. Probe between one of the many fissures between the patient’s toes do not demonstrate tracking. MRI is pending.
- WBC-29.3 H/H—9.4/30.1 BUN/Cr- 36/1.9 ESR-112
- Rest of the lab work is unremarkable.
- Which of the following is the best empiric treatment option?
  A. Vancomycin plus metronidazole
  B. Colistin
  C. Ciprofloxacin
  D. Ceftazidime
  E. Vancomycin plus imipenem
CASE #11 CONTINUED

The aforementioned patient is found to have osteomyelitis. After debridement, ID recommends 6 weeks of vancomycin and imipenem, which the patient elects to do at home. After 3 days of inpatient vancomycin, patient is discharged. Her serum creatinine at discharge is 1.1 mg/dL. 5 days later, the home health infusion nurse reports that the patient's serum creatinine is 0.9 mg/dL and her vancomycin trough is 18.

Given that her weight is 61kg, which of the following is the most appropriate management of the patient’s therapy?

A. Adjust vancomycin dose for a peak level of greater than 40.
B. Adjust vancomycin to a dose of 20 or greater
C. Reduce vancomycin level dose by 50%
D. Recheck serum creatinine and change vancomycin to linezolid
E. Complete vancomycin therapy without drug-level monitoring
Antibiotic Stewardship

- Programs aim to reduce unnecessary use of antibiotics, with particular attention to those drugs that are most likely to change the hospital environment to favor more resistant bacteria.

- 63yo homeless woman is found unconscious in a snowdrift
- Tmax 33.0°C, BP- 70/30, HR- 42, RR-10
- Numerous draining skin lesions are noted.
- Pt successfully resuscitated and started on Cefepime and Vancomycin, but blood cultures grow MRSA, all 4 bottles.
- At hospital day #3, patient improves, and pharmacy recommends changing antibiotic regimen to nafcillin alone.
Why???????????

A. Need for fewer daily infusions
B. Cost-saving
C. Reduced risk of nephrotoxicity
D. Reduction of selection for resistant colonizing organisms
CASE #12

40 yo missionary traveling to Guinea in Western Africa seeks disease prevention advice. He will be camping in tents and is otherwise healthy with no medical problems or allergies.

Which of the following is inappropriate advice for the patient?

A. Carbonated water (soda) is safe to drink
B. Hot tea is safe to drink
C. Do not use citronella based insect repellents
D. Sleep under bed netting
E. Locally made ice is safe to consume.
What other advice would you offer?

- Immunizations: which include hepatitis A, typhoid, and yellow fever.
- Prescription for traveler’s diarrhea
- Malaria prophylaxis
- Information about careful contact with local dogs
- Travel related automobile injury
Thank you and enjoy the resort!!