Why Do Some Antibiotics Fail?

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April 2010

Objective

- To outline common reasons why antibiotic therapy is not successful and how this can be avoided.

And to teach you a little bit about how to kill bugs.

Case

- A 55 yo female presents with urinary frequency and burning. She is placed on cephalexin (“Keflex”). Urine cultures grow Enterococcus. The doctor notes that the lab report does not mention sensitivity results for cipro (like they do for ampicillin and some other antibiotics), but decides not to change the patient’s antibiotics. The patient returns the next week with a kidney infection. Repeat urine cultures again grow Enterococcus.
Why did this patient’s infection worsen?

- 1. She did not take the antibiotics.
- 2. She needed to drink more fluids.
- 3. Cephalosporins, like cephalexin, do not treat *Enterococcus*.
- 4. Cranberry extract works better for UTI’s than antibiotics.

Why antibiotics fail…

- Some bacteria are intrinsically resistant to the certain antibiotics.
  - You can use a literal ton of cephalosporins to treat an *Enterococcus* infection, and they will never cure the infection.
  - One bug spray may work for fleas, but not wasps.

Case

- A 67 yo female develops pneumonia following admission for a MI. She is placed on piperacillin-tazobactam (“Zosyn”). Sputum cultures grow *Enterobacter*, sensitive to pip-tazo. By mistake, the patient is given pip-tazo 3.375gm every 8 hrs over 30 minutes instead of the recommended prolonged infusion over 4 hours. A few days later the patient becomes sicker and is found to have *Enterobacter*, resistant to pip-tazo, in her blood cultures.
Why did this patient’s infection spread to her blood?

- 1. Her heart disease made her more susceptible to infection.
- 2. The antibiotic levels were too low because of the incorrect infusion times.
- 3. A healthcare worker spread the infection to her from someone else in the unit.

Why antibiotics fail...

- Bacteria may develop resistance to certain antibiotics.
  - The proper dosing (including infusion time) of antibiotics is important to prevent the development of resistance.
  - Important decisions are made on the basis of drug levels (such as vancomycin troughs). It is very important that they are drawn correctly.

Why antibiotics fail...

- You might kill the first few ants with the toxic ant food, but the rest of them figure it out and won’t eat anymore.
  - This happens a lot faster if the ants only take a little nibble of the poison instead of a feast.
Case

- A 84 yo female develops right lower quadrant pain and fever. CT scan of the abdomen performed in the ED shows evidence of diverticulitis and a right lower quadrant abscess. She is placed on ciprofloxacin and metronidazole. Surgery is consulted, but declines to operate due to the patient's advanced age and multiple medical problems. She is treated with 4 wks of abx; however, a repeat scan shows persistence of the abscess.

Why is the abscess still there?

- 1. Those antibiotics don’t cover bowel bacteria.
- 2. The patient didn’t take her antibiotics after she was discharged.
- 3. The abscess needs to be drained.
- 4. The radiologists misread the CT.

Why antibiotics fail...

- Antibiotic may not be able to penetrate into the site of the infection.
  - Abscesses, infected joints, CNS infections, etc
  - Infections of prosthetic devices, like central lines and artificial heart valves, are very difficult to treat without removal.

- It doesn’t matter how much bug spray is outside, as long as the bees are safe inside the hive.
Case

- A 4 yo female presents with a cough which has been present for several months. Her mother reports that the cough is worse at night or after she exercises. She does not have any associated fevers. The patient has been treated with a variety of oral antibiotics without improvement.

Why didn’t the antibiotics make her better?

- 1. She doesn’t have an infection.
- 2. They did not give her the right type of antibiotics.
- 3. They didn’t treat her with antibiotics long enough.
- 4. The pharmacy accidentally gave her baby aspirin instead of antibiotics.

Why antibiotics fail…

- The patient does not actually have an infection.
  - Cancer, rheumatologic disorders, and unusual infections due to fungi or mycobacteria may masquerade as a bacterial infection.
  - You can spray the “termites” with all the bug spray you want, but if the damage to the wood was actually due to water, then the poison is not going to help.
Case

- A 43 yo patient with leukemia develops a very low WBC count and fever following chemotherapy. The patient is placed on multiple, broad-spectrum antibiotics (doripenem and vancomycin) without improvement in her fevers. Blood and urine cultures are without growth. Unfortunately, the patient becomes septic and dies. Repeat cultures taken in the ICU prior to death are also without growth.

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Why did this patient die?

- 1. The antibiotics weren’t strong enough.
- 2. The patient was too immunosuppressed to fight off the infection.
- 3. The micro lab messed up the cultures.
- 4. The ICU doctors should have gotten an Infectious Diseases consult.

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Why antibiotics fail...

- A functioning immune system is often more important than the antibiotics.
  - Multiple levels and types of immunodeficiency lead to various risks, i.e. BMT vs. AIDS vs. DM vs. pregnancy, etc.
  - *If you are staked to the ant hill with your hands tied behind your back, it really doesn’t matter how much bug spray you own.*
Case

- A 44 yo male with a h/o iv drug abuse is injured in a motor vehicle accident. He develops an infection of his right leg wound with MRSA. He is treated with iv vancomycin while hospitalized. Because of his history of drug abuse, the physician wants to avoid sending the patient home with an iv line, so he writes the patient a script for vancomycin 1000mg po Q12hrs. The patient returns with recurrent infection.

Why did this patient’s infection recur?

- 1. Vancomycin is not a good treatment for MRSA.
- 2. He has a different type of infection this time.
- 3. He didn’t take the antibiotic.
- 4. Oral vancomycin is not absorbed.

Why antibiotics fail...

- Some antibiotics have good oral bioavailability. Some don’t…or in the case of vancomycin, none.
  - Agents with good po bioavailability include:
    - Quinolones, linezolid, TMP/sulfa, metronidazole, doxycycline
  - If you are supposed to feed the bugs the poison, but you shake it on them instead, it’s probably not going to work.
Same Case...Different Drug

- A 44 yo male with a h/o iv drug abuse is injured in a motor vehicle accident. He develops an infection of his right leg wound with MRSA. He is treated with iv vancomycin while hospitalized. Because of his history of drug abuse, the physician wants to avoid sending the patient home with an iv line, so he writes the patient a script for linezolid 600mg Q12hrs. The patient returns with recurrent infection.

Why did this patient’s infection recur?

- 1. Linezolid is not a good treatment for MRSA.
- 2. He has a different type of infection this time.
- 3. He didn’t take the antibiotic.
- 4. Oral linezolid is not absorbed.

Why antibiotics fail...

- Patient non-adherence
  - Multiple potential causes of non-adherence:
    - Inability to afford meds (2 weeks of linezolid – $1900)
    - Drug abuse
    - Mental illness
    - Side effects
    - Difficult dosing regimen
  - The bug spray doesn’t work if the bugs are outside and the spray is under the kitchen sink.
Summary

- Antibiotics fail for a variety of reasons.
- Different antibiotics provide coverage for different bacteria.
- Proper antibiotic dose, duration, and route of administration are all important to prevent the development of resistance.
- Host factors, such as immunosuppression or barriers to adherence, are also important in the success of antibiotic therapy.

Questions