Answers to Question Box Items

Q1. 02/14/03
Can you explain PAE?

A1. The post-antibiotic effect (PAE) refers to the suppression of bacterial growth that persists after the removal an antibiotic exposure. In other words, it is a persistent effect on the bacteria during a drug-free period. This is often confused with the sub-MIC effect (SME), which refers to the effects of sub-inhibitory antibiotic concentrations on bacterial growth.

Q2. 02/14/03
How does treating infections in AIDS patients affect resistance rates overall? (realizing that it is not ethical to not treat these patients)

A2. This is a very interesting question. In antimicrobial research, the ability of an antibiotic to produce a three-log kill (decrease the bacterial load by three logs) is an important characteristic. In theory, if an antibiotic is able to produce a three-log kill, the host’s immune system can usually kill the remaining bacterial population. However, with an immunocompromised host, such as an HIV patient, little to no immune function exists to fight infection. Furthermore, it is believed that the remaining bacterial population (after a three-log kill) is less susceptible to the antimicrobial (assuming a fairly normal distribution of MICs among the population). Therefore, in theory, an immunocompromised host would be more likely to develop a resistant infection because their immune system is unable to “take over,” and the less susceptible population is allowed to grow. This idea supports the common practice of discontinuing prophylaxis for opportunistic infections in HIV patients once their CD4 count is above a certain level.

I am not aware of any studies that have been done to establish the effect of HIV on antimicrobial resistance overall. It would be difficult to elucidate whether the increase in overall resistance rates is due to the propensity of HIV patients to become infected because of immunosuppression or to the actual HIV virus itself. However, it is important to remember that increased antibiotic use has been directly linked to increased resistance. Thus, HIV is causing increased antibiotic use, which in theory, should cause increased antibiotic resistance.

Q3. 02/26/03
Can you post the information that was given for slide 8 in the Diabetic Foot Ulcer lecture?

A3. I believe this is referring to the slide that listed the treatment options for mild or moderate/severe diabetic foot ulcer infections. Notice that for the mild infections the drugs have mainly Gram-positive coverage, which makes sense because mild infections are typically caused by staphylococci and streptococci. On the other hand, the moderate-severe treatment regimens have broader coverage, to include
Gram-positives, Gram-negatives, and anaerobes. Ciprofloxacin has been used as monotherapy, but due to increasing resistance among *S. aureus* and poor streptococcal and anaerobic coverage, a combination of clindamycin plus levofloxacin is typically recommended over ciprofloxacin monotherapy. Ampicillin/sulbactam is usually preferred in more acute infections when you suspect enterococcal involvement. Piperacillin/tazobactam is preferred in recurring infections when you have an increased suspicion of Gram-negative/pseudomonal involvement.

Q4. 03/26/03
We have an infant in our pharmacy, born to an HIV infected mother (prenatally on Combivir and Viramune, with 2 other drugs added during pregnancy). After birth, the infant is taking Retrovir prophylactically. Knowing that HIV can be transmitted vertically, is the prophylaxis to prevent HIV infection or progression to AIDS syndrome in the infant?

A4. The zidovudine for the baby is prophylaxis to prevent HIV infection. Zidovudine is commonly given to infants for six weeks after birth to prevent transmission. The use of zidovudine in the mother during pregnancy and in the infant, after birth, has reduced the rate of vertical transmission by approximately two thirds, in the absence of breastfeeding. Shorter regimens in the infant have reduced the transmission by ~50% in a non-breastfeeding population and by ~37% in breastfeeding populations. (Bhana N, Ormrod D, Perry CM, and Figgitt DP. Zidovudine: a review of its use in the management of vertically-acquired pediatric HIV infection. *Paediatr Drugs* 2002;4(8):515-53.)

Q5. 03/26/03
We know that resistance can be chromosomally- or plasmid-mediated, and plasmids are sometimes lost. If the bacteria is not exposed to an antibiotic for a long period of time, can the chromosomally-mediated resistance ever be lost? Or is the resistance just turned off only to be turned on when antimicrobial pressure is initiated?

A5. This is a fairly complicated question, but I will try to answer it on a basic level. Plasmids can be “lost” because plasmids are typically not passed down from generation to generation like chromosomal mutations. For some organisms, such as *Pseudomonas aeruginosa* with Type-I beta-lactamases, the chromosomal change remains whether or not an antibiotic is present. However, the expression of the resistance is induced (derepressed) in the presence of certain antibiotics. So, even though the resistance may not always be “expressed”, the chromosomal change is still present.

Regarding chromosomal mutations, rather than thinking of this on the basis of an individual microorganism, think of encompassing an entire bacterial population. Within that bacterial population, there is usually a (somewhat) normal distribution of MICs to a particular antimicrobial, meaning that a small subset of bacteria is
highly susceptible to the antimicrobial, most are susceptible at a moderate level, and another small subset is resistant. In order for the resistant population to proliferate and dominate, the environment must favor the production of the resistant microorganisms (e.g. in the presence of an antibiotic). Without favorable environmental conditions, the small subset of resistant organisms may diminish due to natural selection, but the actual chromosomal change is not lost…just the bacteria containing the chromosomal mutation. Please remember that there are many substances in the environment that we don’t recognize as antibiotics that can also cause chromosomal mutations in microorganisms, leading to antimicrobial resistance.

Q6. 03/26/03
I heard you shouldn’t go to the dentist if you are pregnant because bacterial infections in the mouth can cause fetal problems. Is this true?

A6. Dental procedures should be avoided during the first trimester because you want to avoid the possibility of any systemic infection during the major organ development of the baby. The second trimester is considered safe, so pregnant patients should schedule dental appointments during the second trimester. The third trimester is avoided due to discomfort for the patient in the dental chair.