SN EDUCATOR GUIDE

June 10, 2017

New 'Rules' for Finding Antibiotics

Cross-Curricular Discussion

After students have had a chance to review the article "New 'rules' for finding antibiotics," lead a classroom discussion based on the questions that follow. You can copy and paste only the questions that apply to your classroom into a different document for your students.

Biological and Chemical Sciences
Discussion Questions:

1. **What are some important differences between bacteria and other microorganisms?**
   - [*Bacteria are prokaryotic cells, which lack a membrane-bound nucleus and organelles. Some bacteria live independently in the environment. Other bacteria hang out in our bodies, in the space outside of our cells, where they may cause disease or even help us (as with the bacteria that aid digestion in our intestines). Some of the nastier bacteria actually invade our cells and replicate inside our cells, for example in tuberculosis lung infections.*
   - *Fungi are eukaryotic (complex) cells. Fungal cells are surrounded by a thick cell wall and can cause athlete's foot, for example. The mushrooms on pizza are fungi.*
   - *Protozoa are eukaryotic cells that are similar to our own — they are basically single-celled animals. However, some of the more vicious ones (like malaria) can invade our cells. Other protozoa just spend their whole lives harmlessly floating around in ponds.*
   - *Viruses are rogue genes that invade host cells, command cells to make more copies of the viral genes and usually (but not always) kill the host cells before spreading to infect more host cells. Viruses include the common cold, for example, and Ebola.*]

2. **What is the difference between gram-positive and gram-negative bacteria?**
   [*Different categories of bacteria have different types of cell walls. Gram-positive bacteria have a thick peptidoglycan (linked protein + sugar) cell wall. Gram-negative bacteria have a thinner peptidoglycan cell wall, then another membrane, then an outer layer of lipopolysaccharide. Thus gram-negative bacteria are protected by more walls made of more materials than are gram-positive bacteria.*
   The Gram's staining procedure, which was invented by the Danish bacteriologist Hans Christian Gram, makes gram-positive bacteria appear purple and gram-negative bacteria appear pink to red under the microscope.]

3. **How do antibiotics kill bacterial cells but not human cells?**
   [*The trick to developing antibiotics is to find a structural difference between the bacterial cells and human cells, and then create drugs that target the feature that bacteria but not human cells possess. For example, one major difference between bacterial and human cells is that bacteria have a cell wall around their plasma*

membrane, whereas human cells have only a plasma membrane. Antibiotics often attack the thick cell walls of bacteria. If a drug interferes with bacterial cell walls, the bacterial cells can be killed but the drug won't affect human cells.
Another major difference between bacterial and human cells is their ribosomes. Both cell types use ribosomes to produce proteins, but there are important differences between bacterial (prokaryotic) and animal (eukaryotic) ribosomes. Thus, it is possible to develop drugs that bind to bacterial ribosomes and stop their protein production, yet don't affect ribosomes or protein production in human cells.]

4. **What is an amine functional group? Explain the chemical and physical properties of an amine group based on its molecular structure. If a molecule without an amine functional group were synthesized to contain an amine, how might the properties of the molecule change?**
[*An amine is a nitrogen- and hydrogen-containing functional group with a trigonal pyramidal shape. Amines fall into different categories depending on how many hydrogens are bonded to a nitrogen atom. A primary amine is a nitrogen atom bonded to two hydrogen atoms and one hydrocarbon (RNH2 structure). A secondary amine is a nitrogen bonded to one hydrogen and two hydrocarbons (R2NH). Finally, a tertiary amine is a nitrogen bonded to three hydrocarbons and no hydrogen atoms (R3N). Because of the extreme polarity of the nitrogen to hydrogen bond, the trigonal pyramidal molecular shape of the functional group and the small size of the nitrogen and hydrogen atoms, both primary and secondary amines will interact through hydrogen bonding with other molecules. If primary or secondary amine groups were synthesized onto molecules that did not originally contain them, the new molecules would likely have a higher boiling point because of their newly created region for hydrogen bonding and stronger intermolecular attraction. The new molecules would also probably have a greater attraction to other polar or partially charged molecules.*]

Extension Prompts:

5. **What are the major categories of existing antibiotics? Pick an antibiotic and research how it works.**
[*Antibiotics can be divided into groups based on what targets they attack in bacterial cells:*
- *Many antibiotics attack the bacterial cell wall and are called broad-spectrum antibiotics. The structures of these drugs generally mimic part of the bacterial cell wall, such as peptidoglycan. That mimicry allows the drugs to get taken up by enzymes that synthesize the cell wall (such as transpeptidases), bind irreversibly to the enzymes or to the incomplete cell wall, and prevent the cell wall from being finished. These antibiotics cause osmotic lysis for actively growing, new bacteria. Some major types of antibiotics that target the cell wall include ß-lactams, or molecules that contain a beta-lactam ring in their chemical structure. ß-lactams include penicillins (such as penicillin and amoxicillin), cephalosporins, carbapenems, monobactams, glycopeptides and bacitracin (which specifically blocks transport of peptidoglycan components).*
- *ß-lactamase inhibitors block bacterial ß-lactamase enzymes that would otherwise destroy ß-lactam antibiotics, so they are often mixed in with ß-lactam antibiotics.*

- *Antibiotics that target unique features in bacterial versus animal cell plasma membranes include: polymyxins and cyclic lipopeptides.*
- *The large ribosomal subunit is made up of 31 proteins and two ribosomal RNAs (rRNAs) in prokaryotes, but 50 proteins and three rRNAs in eukaryotes. Many antibiotics attack these key features that make the prokaryotic large (50S) ribosomal subunit different from the eukaryotic large ribosomal subunit, thereby inhibiting bacterial protein synthesis: macrolides (such as erythromycin and azithromycin), chloramphenicol, lincosamides, oxazolidinones and streptogramins.*
- *Likewise, the small ribosomal subunit is composed of 21 proteins and one rRNA in prokaryotes, but 33 proteins and a larger rRNA in eukaryotes. A number of antibiotics attack these key differences in the prokaryotic small (30S) ribosomal subunit, again inhibiting bacterial protein synthesis: tetracyclines (such as tetracycline and doxycycline), aminoglycosides and nitrofurans.*
- *In a similar fashion, some antibiotics selectively inhibit prokaryotic but not eukaryotic transfer RNAs (tRNAs), including mupirocin and furanomycin.*
- *Some antibiotics selectively target prokaryotic DNA synthesis enzymes, such as metronidazole.*
- *Similarly, antibiotics that inhibit prokaryotic but not eukaryotic DNA gyrases include quinolones (such as ciprofloxacin and levofloxacin).*
- *Some antibiotics inhibit prokaryotic RNA polymerases but not eukaryotic RNA polymerases: rifampin, streptovaricins and actinomycin.*
- *Finally, some antibiotics inhibit prokaryotic enzymes involved in essential folic acid synthesis: trimethoprim and sulfonamides.*]

6. **How do bacteria become resistant to antibiotics?**
   - [*In some cases, bacteria decrease the permeability of their cell wall or their channels, and antibiotics can no longer penetrate the bacteria. Some bacteria have used that method against vancomycin and ß-lactams.*
   - *In other cases, bacteria actually use pumps to spit out any antibiotic that gets in. Some bacteria have used that method against tetracyclines, quinolones, aminoglycosides, ß-lactams and macrolides.*
   - *A variety of bacterial enzymes can interfere with or destroy antibiotics. Some bacteria have used that method against ß-lactams, aminoglycosides, macrolides, rifamycins, chloramphenicol, tetracyclines and vancomycin.*
   - *Finally, bacteria mutate so that the shape of an antibiotic target changes and the antibiotic will no longer attack that target. Some bacteria have used that method against macrolides, quinolones, aminoglycosides, penicillins, vancomycin and rifamycins.*]

7. **What are plasmids and why are they important for antibiotic resistance in bacteria?**
   [*Plasmids are typically small circular pieces of DNA that replicate independently from the host's chromosomal DNA. They are infectious from one bacterium to others. If an antibiotic-resistance gene is in the main bacterial chromosome, it gets passed down to the direct descendants of that bacterium. But if an antibiotic-resistance gene is in a plasmid, it can rapidly spread to other bacteria.*]

Biological and Chemical Sciences Question Bank

What are some important differences between bacteria and other microorganisms?

What is the difference between gram-positive and gram-negative bacteria?

How do antibiotics kill bacterial cells but not human cells?

What is an amine functional group? Explain the chemical and physical properties of an amine group based on its molecular structure. If a molecule without an amine functional group were synthesized to contain an amine, how might the properties of the molecule change?

What are the major categories of existing antibiotics? Pick an antibiotic and research how it works.

How do bacteria become resistant to antibiotics?

What are plasmids and why are they important for antibiotic resistance in bacteria?

Engineering and Experimental Design

Discussion Questions:

1. **Why is it important to take a full course of antibiotics and not just stop as soon as you start to feel better?**
   [*Not finishing the full course of antibiotics can promote antibiotic resistance. The first few doses of an antibiotic will wipe out most of the bacteria, but any mutant bacteria that are slightly resistant to the antibiotic will survive. If you stop taking the antibiotic then, those slightly resistant bacteria will reproduce, and all of the resulting bacteria will be slightly resistant to that antibiotic. After a few more rounds of taking a little of the antibiotic, but not enough, other mutated bacteria may be highly resistant to the antibiotic. In contrast, if you take the complete course of antibiotic without a break, eventually even the slightly resistant bacteria will likely die before they can reproduce.*]

2. **How can you deal with bacteria that are antibiotic resistant, or can easily mutate to become antibiotic resistant?**
   [*For bacteria that can mutate very easily (such as tuberculosis), doctors usually prescribe a cocktail, or mixture, of several antibiotics. That way even if the bacteria mutate to become resistant to one of the antibiotics, another antibiotic in the cocktail will likely kill them.*]

Extension Prompts:

3. **What are the advantages and disadvantages of routinely keeping farm animals on antibiotics?**
   [*Antibiotics can prevent bacterial infections in the animals, making it cheaper and easier to raise them, even in poor conditions where bacterial infections could easily spread. On the other hand, farms that use a lot of antibiotics are a training ground for bacteria to develop resistance, and antibiotic-resistant bacteria can be passed to humans who handle meat from the animals before it is fully cooked.*]

4. **Many antibiotics are naturally produced by certain microorganisms, and were discovered in these organisms in nature. Why would microorganisms produce antibiotics?**
   [*If a microorganism can kill off other types of microorganisms that might consume the same nutrients, it gives that microorganism a resource advantage.*]

5. **What are some ways that bacteria can be useful?**
   - [*Normal human microbiota. Your body actually contains as many bacterial cells as human cells, many on your skin and in your gastrointestinal tract. The relationship is mutually beneficial, since people provide the bacteria with an environment to live in and the good bacteria keep harmful bacteria away. Bacteria in the gastrointestinal tract aid with digestion, and they may aid (or in some cases hinder) the immune and endocrine systems.*
   - *Nitrogen fixation. Bacteria in the soil or water absorb nitrogen gas (N_2) from the air and convert it into ammonia (NH_3) or other nitrogen-containing molecules that can be readily taken up by plants and used to build larger biomolecules. Without this nitrogen fixation, there would be no plants and so no animals that eat plants.*
   - *Making yogurt and cheese. Milk can be turned into yogurt, a variety of different cheeses and other products by adding specific types of bacteria and treating the mixture under the right sorts of conditions. In general, the bacteria convert lactose (milk sugar) to glucose (simple sugar), then use fermentation to convert that glucose to lactic acid or lactate. Some bacteria can also ferment sugar to ethanol or ethyl alcohol plus carbon dioxide.*
   - *DNA and protein production. Bacteria are great at making lots of copies of themselves, which requires copying their DNA and proteins. If you are a biology researcher in need of lots of copies of a new gene or new protein, a simple solution is to stick the gene into a harmless strain of* E. coli*, let them reproduce for a while, then extract the copies of the gene or the protein made by the gene from all of the reproduced* E. coli.
   - *Bacterial degradation and remediation involves finding natural bacteria or genetically engineering bacteria to eat, or at least to surround and hide, substances we don't want in the environment. This includes oil spills, for example, and uranium ions.*
   - *Bacterial pesticides can be used instead of chemicals as a sometimes more environmentally benign method to kill certain insects. For example,* Bacillus thuringiensis *spores or their components (often sold as gardening supplies) can kill insect larvae before they develop into adult insects.*]

6. **How might antibiotic-resistant plasmids be useful for genetically engineering bacteria?**
   [*If a plasmid contains an antibiotic-resistance gene and also some new gene of interest, you can introduce it into a herd of bacteria, then add that antibiotic to eliminate any bacteria that did not take up the plasmid. Thus all of the surviving bacteria should have the gene of interest. You have to be sure you are using an antibiotic that wouldn't treat bacterial infections in humans, because you are making more bacteria resistant to that antibiotic.*]

Engineering and Experimental Design Question Bank

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What are the advantages and disadvantages of routinely keeping farm animals on antibiotics?

Many antibiotics are naturally produced by certain microorganisms, and were discovered in these organisms in nature. Why would microorganisms produce antibiotics?

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How can antibiotic-resistant plasmids be useful for genetically engineering bacteria?