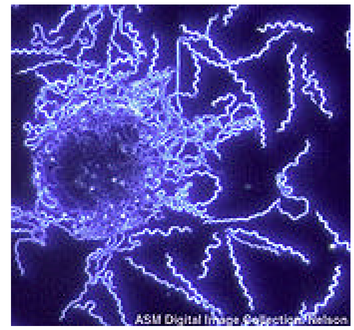
Super Bugs

An introduction to PBL through an exploration of antibiotic resistant bacteria and their impact on global health

October 13, 2004

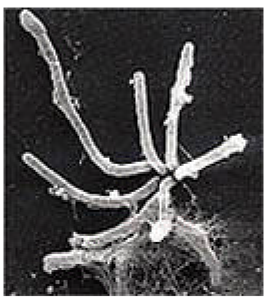
An Overview of Bacteria and Viruses

Bacteria


Borrelia burgdorferi
Nelson, ASM MicrobeLibrary

Bacteria consist of only a single cell, but don't let their small size and seeming simplicity fool you. They're an amazingly complex and fascinating group of creatures. Bacteria have been found that can live in temperatures above the boiling point and in cold that would freeze your blood. They "eat" everything from sugar and starch to sunlight, sulfur and iron. There's even a species of bacteria—*Deinococcus radiodurans*—that can withstand blasts of radiation 1,000 times greater than would kill a human being.

Classification


Leucothrix mucor
Appl. Environ. Microbiol. 55:1435-1446, 1989

Bacteria fall into a category of life called the Prokaryotes *(pro-carry-oats)*. Prokaryotes' genetic material, or DNA, is not enclosed in a cellular compartme nt called the nucleus.

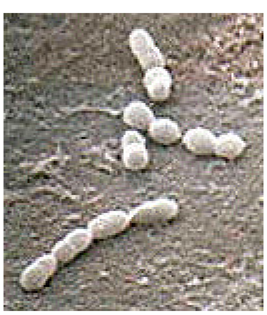
Bacteria and archaea are the only prokaryotes. All other life forms are Eukaryotes *(you-carry-oats)*, creatures whose cells have nuclei.

(Note: viruses are not considered true cells, so they don't fit into either of these categories.)

Early Origins

Bacteria are among the earliest forms of life that appeared on Earth billions of years ago. Scientists think that they helped shape and change the young planet's environment, eventually creating atmospheric oxygen that enabled other, more complex life forms to develop. Many believe that more complex cells developed as once free-living bacteria took up residence in other cells, eventually becoming the organelles in modern complex cells. The mitochondria *(mite-oh-con-dree-uh)* that make energy for your body cells is one example of such an organelle.

What They Look Like


Ball-shaped
Streptococci

Simonson, ASM MicrobeLibrary

There are thousands of species of bacteria, but all of them are basically one of three different shapes. Some are rod- or stick-shaped and called bacilli *(buh-sill-eye)*.

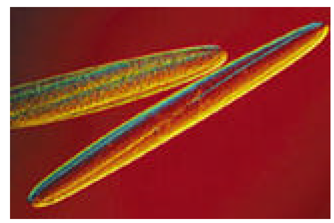
Others are shaped like little balls and called cocci *(cox-eye)*.

Others still are helical or spiral in shape, like the *Borrelia* pictured at the top of this page.

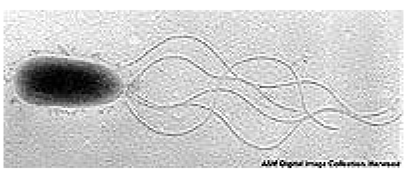
Some bacterial cells exist as individuals while others cluster together to form pairs, chains, squares or other groupings.

Where They're Found

Bacteria live on or in just about every material and environment on Earth from soil to water to air, and from your house to arctic ice to volcanic vents. Each square centimeter of your skin averages about 100,000 bacteria. A single teaspoon of topsoil contains more than a billion (1,000,000,000) bacteria.



Bacteria that live in guts of surgeon fish
Courtesy Norm Pace



Bacterium with flagella
Harwood, ASM MicrobeLibrary

How They Move

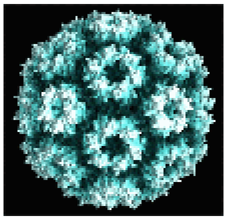
Some bacteria move about their environment by means of long, whip-like structures called flagella. They rotate their flagella like tiny outboard motors to propel themselves through liquid environments. They may also reverse the direction in which their flagella rotate so that they tumble about in one place.

Other bacteria secrete a slime layer and ooze over surfaces like slugs. Others are fairly stationary.

What They Eat

Some bacteria are photosynthetic *(foe-toe-sin-theh-tick)*—they can make their own food from sunlight, just like plants. Also like plants, they give off oxygen. Other bacteria absorb food from the material they live on or in. Some of these bacteria can live off unusual "foods" such as iron or sulfur. The microbes that live in your gut absorb nutrients from the digested food you've eaten.

Viruses



© Jean Yves-Sgro

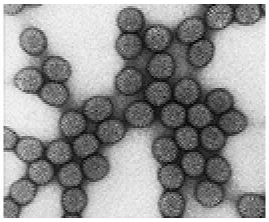
When is a life form not a life form? When it's a virus.

Viruses are strange things that straddle the fence between living and non-living. On the one hand, if they're floating around in the air or sitting on a doorknob, they're inert. They're about as alive as a rock. But if they come into contact with a suitable plant, animal or bacterial cell, they spring into action. They infect and take over the cell like pirates hijacking a ship.

What They Are

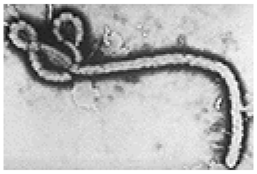
A virus is basically a tiny bundle of genetic material—either DNA or RNA—carried in a shell called the viral coat, or capsid, which is made up of bits of protein called capsomeres. Some viruses have an additional layer around this coat called an envelope. That's basically all there is to viruses.

What They Look Like



Rotavirus
Courtesy CDC

There are thousands of different viruses that come in a variety of shapes. Many are polyhedral *<polly-hee-drul>*, or multi-sided. If you've ever looked closely at a cut gem, like the diamond in an engagement ring, you've seen an example of a polyhedral shape. (Unlike the diamond in a ring, however, a virus does not taper to a point, but is shaped similarly all around.) Other viruses are shaped like spiky ovals or bricks with rounded corners.



Ebola virus
Courtesy CDC

Some are like skinny sticks while others look like bits of looped string. Some are more complex and shaped like little lunar landing pods.

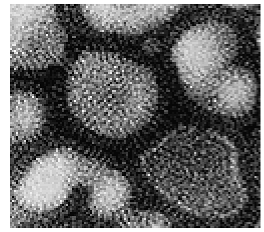
Where They're Found

Viruses are found on or in just about every material and environment on Earth from soil to water to air. They're basically found anywhere there are cells to infect. Viruses have evolved to infect every form of life, from animal to plant and from fungi to bacteria.

However, viruses tend to be somewhat picky about what type of cells they infect. Plant viruses are not equipped to infect animal cells, for example, though a certain plant virus could infect a number of related plants. Sometimes, a virus may infect one creature and do no harm, but cause havoc when it gets into a different but closely enough related creature. For example, the Hantavirus is carried by deer mice without much noticeable effect on the rodents. But if Hantavirus gets into a person, it causes a dramatic and frequently deadly disease marked by excessive bleeding.

Single-Minded Mission

Viruses exist for one purpose only: to reproduce. To do that, they have to take over the reproductive machinery of suitable host cells.



Type A flu virus
Courtesy CDC

Upon landing on an appropriate host cell, a virus gets its genetic material inside the cell either by tricking the host cell to pull it inside, like it would a nutrient molecule, or by fusing its viral coat with the host cell wall or membrane and releasing its genes inside. Some viruses inject their genes into the host cell, leaving their empty viral coats sitting outside.

If a virus is a DNA virus, its genetic material then inserts itself into the host cell's DNA. If the virus is an RNA virus, it must first turn its RNA into DNA using the host cell's machinery before inserting into the host DNA. The viral genes are then copied many, many times, using the machinery the host cell would normally use to reproduce its own DNA. The virus uses the host cell's enzymes to build new viral capsids and other viral proteins. The new viral genes and proteins then come together and assemble into whole new viruses. The new viruses are either released from the host cell without destroying the cell or eventually build up to a large enough number that they burst the host cell like an overfilled water balloon.

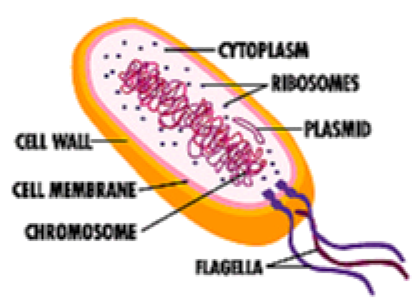
Virus Or Bacterium?

Because bacteria and viruses cause many of the diseases we're familiar with, people often confuse these two microbes. But viruses are as different from bacteria as goldfish are from giraffes.

For one thing, they differ greatly in size. The biggest viruses are only as large as the tiniest bacteria.

Another difference is their structure. Bacteria are complex compared to viruses.

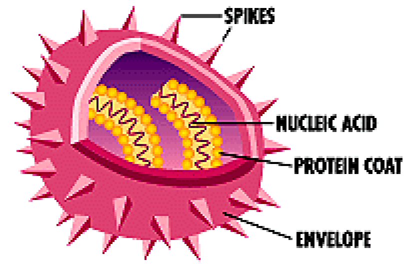
A typical bacterium has a rigid cell wall and a thin, rubbery cell membrane surrounding the fluid, or cytoplasm (*sigh-toe-plasm*), inside the cell. A bacterium contains all of the genetic information needed to make copies of itself—its DNA—in a structure called a chromosome (*crow-moe-soam*). In addition, it may have extra loose bits of DNA called plasmids floating in the cytoplasm. Bacteria also have ribosomes (*rye-bo-soams*), tools necessary for copying DNA so bacteria can reproduce. Some have threadlike structures called flagella that they use to move.



© Eric MacDicken

A virus may or may not have an outermost spiky layer called the envelope. All viruses have a protein coat and a core of genetic material, either DNA or RNA. And that's it. Period.

Which brings us to the main difference between viruses and bacteria—the way they reproduce.



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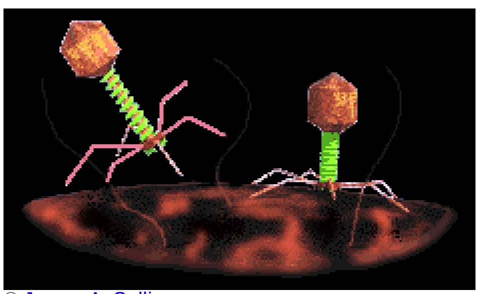
Viral vs. Bacterial Reproduction

Bacteria contain the genetic blueprint (DNA) and all the tools (ribosomes, proteins, etc.) they need to reproduce themselves.

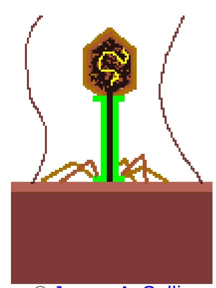
Viruses are moochers. They contain only a limited genetic blueprint and they don't have the necessary building tools. They have to invade other cells and hijack their cellular machinery to reproduce. Viruses invade by attaching to a cell and injecting their genes or by being swallowed up by the cell.

Here's an example of viral infection. This is virus version of the horror movie *Alien*.



© James A. Sullivan

These are T4 bacteriophages (*back-tear-e-oh-faj-es*). They are a kind of virus that infects bacteria. Here they are landing on the surface of an *E. coli* bacterium.



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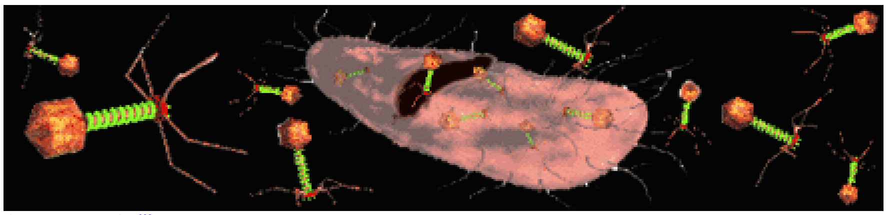
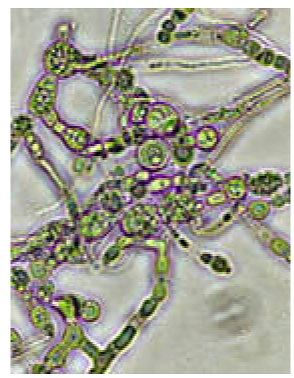
The bacteriophage cuts a hole in the *E. coli's* cell wall. It then injects its genetic material into the bacterium. By taking over the *E. coli's* genetic machinery, the viral genes tell the bacterium to begin making new virus parts. These parts come together to make whole new viruses inside the bacterium.

Eventually so many new viruses are made that the *E. coli* bursts open and dies, releasing all those new viruses to infect more cells!



Fungi

When you hear the word fungus, you probably think of mushrooms. Did you know bread mold is a kind of fungus, too? And that the itchy burning of athlete's foot is, yes, caused by another fungus? And that when you take penicillin, you're taking a medicine made by a fungus?



Fungal hyphae
Courtesy of Alex Hausler, Givaudan Roure

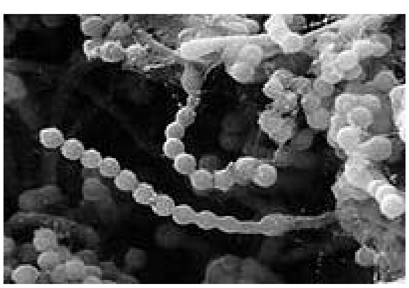
Fungi come in a variety of shapes and sizes and different types. They can range from individual cells to enormous chains of cells that can stretch for miles.

Classification

Fungi are eukaryotic *(you-carry-ah-tick)* organisms—their DNA is enclosed in a nucleus. Many of them may look plant-like, but fungi do not make their own food from sunlight like plants do.

What They Look Like

Fungi include single-celled creatures that exist individually—the yeasts—and multicellular bunches, such as molds or mushrooms. Yeast cells look like little round or oval blobs under a microscope. They're too tiny to see as individuals, but you can see large clusters of them as a white powdery coating on fruits and leaves.



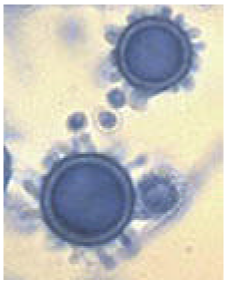
Paecilomyces variotii

Molds are described as filament-like, or filamentous, because they form long filament-like, or thread-like, strands of cells called hyphae *(high-fee)*. These hyphae are what give mold colonies their fuzzy appearance. They also form the fleshy body, or mushroom, that some species grow. It may seem odd to think of something as big as a mushroom as a microbe. But the cells of the hyphae making up that mushroom are connected in a closer way than the cells of other multicellular creatures, like you and me, are. The cell walls separating the cells in hyphae usually have openings that allow the protoplasm <*pro-toe-plazm*>, or fluid that fills cells, to flow between them. Essentially, a fungal hypha is like a tube. Your cells, on the other hand, are completely walled off from each other and the cell fluid, or cytoplasm <*sigh-toe-plazm*>, inside doesn't mingle between cells.

Where They're Found

Fungi usually grow best in environments that are slightly acidic (a pH measurement of 5 or so; a pH of 7 is neutral). They can grow on substances with very low moisture. Fungi live in the soil and on your body, in your house and on plants and animals, in freshwater and seawater. A single teaspoon of topsoil contains about 120,000 fungi.

How They Spread



Fungal spores

Fungi are basically static. But they can spread either by forming reproductive spores that are carried on wind and rain (see the page Microbial Reproduction for more details) or by growing and extending their hyphae. Remember that hyphae are chains of fungal cells. Hyphae grow as new cells form at the tips, creating ever longer and branching chains of cells. It takes a lot to stop them, too. Hyphae are tough enough to punch through plant cell walls and the hard exoskeletons of insects (see the Fire Ant Killer story in the News section for a photo of an ant killed by a fungus).

What They Eat

Fungi absorb nutrients from living or dead organic matter (plant or animal stuff) that they grow on. They absorb simple, easily dissolved nutrients, such as sugars, through their cell walls. They give off special digestive enzymes to break down complex nutrients into simpler forms that they can absorb.

Friendly Fungi

Some fungi are quite useful to us. We've tapped several kinds to make antibiotics to fight bacterial infections. These antibiotics are based on natural compounds the fungi produce to compete against bacteria for nutrients and space. We use *Saccharomyces cerevisiae*

Yeast cell (blue highlights scars where buds formed)
Microbiol. Rev. 54:381-431, 1990

What Is An Antibiotic?

The definition most of us use for an antibiotic is: any substance produced by a microorganism which harms or kills another microorganism. However, **antibiotics DO NOT** harm viruses. The reason that physicians sometimes prescribe antibiotics when you may have a viral infection, is because of the possibility that you may also acquire a bacterial infection because you are so ill with a virus - being ill places a person at risk for certain bacterial infections that are normally handled without any problem.

The overwhelming majority of antibiotic substances are natural products that certain bacteria and fungi (molds) produce and send outside of their cells. About 90% of the antibiotics in use today, are isolated from bacteria. There are a few antibiotics, however, which are completely synthetic... that is, are made from scratch in the laboratory. These particular antibiotics are designed to inhibit some process previously identified to be completely unique to bacteria, and necessary for the bacterium to remain alive.

For a bacterium or a fungus living out in the wild, if they can make something that removes or drastically "slows-down" the competition for the available nutrients, then they'll have an advantage. So, even though these microorganisms don't have the ability to decide what to make... through mutations and other events, it is possible for them to acquire such an ability to compete.. then, it is these organisms which survive more readily within the environment. We use antibiotics for a different reason, of course, that is, to help us kill harmful bacteria that cause infection and disease. To determine which antibiotic works best against a given bacterium, tests are done in the laboratory, just like the one below:

My special thanks to Raymond Lin for his permission to use the antibiotic sensitivity-plate image you see to the left of this text. A drop of liquid is removed from a culture of the bacterial cells in suspension, and the drop is placed on a Petri dish containing agar and nutrients. A sterile glass rod, bent at a 90-degree angle, is then used to spread the drop all over the surface of the agar (a spread plate). Then small, circular, sterile discs, each saturated with a different antibiotic are dropped on the plate, equidistant from one another. The plate is then incubated at an appropriate temperature e, and one looks for zones around each disc where no growth is occurring (bacteria sensitive). If the bacterium is resistant to a given antibiotic, growth will occur all around the disc.

When taking an antibiotic, **it is very important to follow all instructions from your physician and pharmacist, to the letter.** While at the proper dosage most antibiotics will not hurt us, there can sometimes be harmful side-effects. Some people are allergic to a given antibiotic - allergies to penicillin or its derivatives, are relatively more common. In this case, there are other antibiotics - like cephalosporin, for example, which may be used as a substitute. And, sometimes certain types of antibiotics, like streptomycin, can cause damage to the nerves involved with balance and hearing (8th cranial nerve - vestibular and auditory branches, respectively). Therefore, after taking an antibiotic, if you experience **any one of** the following symptoms: feel sick to your stomach, acquire a rash, feel dizzy, or hear "ringing" in your ears, call your physician right away. Any children taking an antibiotic, should therefore be carefully monitored for any of the above symptoms.

One of the **major** problems we now face, is that many of the disease-causing bacteria that we know of (like *staphylococcus* - "staph"), have become resistant to the effects of different antibiotics. This resistance appears when a member of the bacterial population (need be only a single cell) genetically acquires the ability to destroy the antibiotic. Then, although all other members of the bacterial population may be killed, this one resistant cell will divide (as often as every 20 minutes in some cases) and produce a population that is now no longer harmed. This concern is great, because certain strains of disease-causing bacteria now have only one antibiotic remaining which will kill them. Because of this concern, there are significant efforts to find new natural sources of antibiotics, or to make completely synthetic ones in the laboratory. It is for this reason that physicians may hesitate to prescribe a certain antibiotic until it is clear that it is absolutely necessary. One of the reasons this problem now exists, is because of our prior, indiscriminate use of antibiotics in human and domestic animal health (particularly cattle and pigs). In some countries of the world, one still does not need a prescription to use an antibiotic - one may purchase them just as one may purchase aspirin.

Sometimes, we can determine exactly what an antibiotic looks like, and we can chemically add or remove some things from the original structure, and produce an altered form of the original material. This new, altered, substance is called a semi-synthetic antibiotic. These chemical changes are sometimes made to make the antibiotic last longer in our bodies. I'm sure that you are familiar with the antibiotic, penicillin, and the semi-synthetic form called Ampicillin. Penicillin is produced by a particular kind of fungus (*Penicillium* - a kind of fungus that can grow on bread). However, penicillin is very sensitive to stomach acid, and will be broken-down before it can do any good. It is for this reason that penicillin is given with a shot. A semi-synthetic derivative, called Ampicillin, has therefore been made, because this form is resistant to stomach acid - is why one can take Ampicillin in tablet form (better, huh?).

Back in 1929, penicillin was re-discovered by a Scottish researcher named Alexander Fleming (penicillin was originally discovered by a French medical student by the name of Duchesne). It wasn't until 1941 in England, that an Australian (Howard Florey) and an Englishman (Ernst Chain) developed commercial methods to produce penicillin for human use. The TOTAL amount of penicillin available for use in the clinical trial on humans at that time, was LESS THAN the amount one would receive in a single shot, today! At that time, of course, World-War II was in progress, and there was a major effort to try to make penicillin available to all of the British, U.S., and other allies involved with fighting Germany, Japan, and Italy. Because England did not have the industrial capacity necessary for large-scale production, nor protection from bombing raids, the entire process was moved to the United States. It is for this reason primarily, that the pharmaceutical industry became so well-established in the U.S. Initially, only military personnel were allowed access to this life-saving material. Eventually, prior to the end of World-War II, penicillin was made available to the general public.

(from science.howstuffworks.com)

How Antibiotics Function:

Antibiotics are low molecular weight substances that interfere with specific activities in certain types of organisms. These effects could be cidal (killing) and/or static (inhibitory). If an antibiotic has a widespread effect on Gram-positive and Gram-negative bacteria it is said to be a broad spectrum antibiotic. A narrow spectrum antibiotic will only affect either Gram-positive or Gram-negative bacterial strains. Antibiotics are found throughout nature and are used by organisms like molds and soil inhabitants to gain advantages over their competitors. The early antibiotics were isolated from these natural sources, however today many are genetically engineered to be even more effective than their natural counterparts. For an antibiotic to be useful to humans it must have the ability to destroy pathogens while being relatively non-toxic to the host organism. It should be chemically stable and be able to reach the part of the host organism in which the infection persists.

Antibiotics work in a variety of ways, most of which attack the cells natural working processes and cause the cell to die without replicating. Some broad-spectrum antibiotics use several of the following modes of cellular attack:

1. Cell Wall Synthesis Inhibitors
2. Cell Membrane Inhibitors
3. Protein Synthesis Inhibitors
4. Nucleic Acid Effectors
5. Competitive Inhibitors

Cell Wall Synthesis Inhibitors: These types of antibiotics are particularly selective because they typically target the formation of peptidoglycan cell walls which are only found in prokaryotic cells. These do not affect eukaryotic cells of humans due to the lack of cell walls. These types of antibiotics are referred to as Beta lactam antibiotics. They interfere with the cell wall component D-alanyl-D-alanine, which is a dipeptide that is required for normal synthesis of peptidogylcan cell walls. For these antibiotics to be effective, the cell must be in active growth, which involves formation of new cell walls. D-alanyl-D-alanine serves as one of the last steps in the cross-linking of the cell wall peptide side chains, and its incorporation is known as transglycosylation.

They can do this in a number of ways. The well-known penicillin antibiotic binds and inhibits two types of enzymes (carboxypeptidases and transpeptidases) that are involved in the cross-linking. Polypeptide antibiotics prevent cell wall formation by inhibiting cell wall peptides from interacting with the lipid carrier molecule that transports them to the outside of the cell membrane. An example of this type is bacitracin and it is referred to as a transpeptidation blocker. Other antibiotics that prevent cell wall formation can mimic the structure of D-alanyl-D-alanine, one such antibiotic is cycloserine. Once it enters the chain "pretending" to be D-alanyl-D-alanine, cell wall synthesis is obstructed. Blocking of cell wall biosynthesis prevents the cell from growing, replicating, and many other functions. It may die immediately or eventually die off as part of its natural life without the opportunity to replicate.

Cell Membrane Inhibitors: These are less common than the other types of antibiotic inhibiting mechanisms. Cell membrane inhibitors attack the integrity of the bacterial membranes. An example of these is polymyxin, which binds to the membrane phospholipids. Once the antibiotic has disrupted the membrane, the cell loses its integrity and will die off. However a problem arises in that there is a similarity between the phospholipids in eubacterial and eukaryotic cell membranes. These drugs can therefore be very dangerous to the patient due to the lack of selectivity in target cells.

Protein Synthesis Inhibitors: These types of antibiotics have numerous ways of attacking protein synthesis in bacterial cells and will usually target activities occurring at the ribosome. These drugs affect the ribosome and do not bind to any other components of the protein synthesis process.

Aminoglycosides, like kanamycin, bind to the 50S subunit of the ribosome and prevent translation from beginning by distorting the ribosome so it can no longer carry out its main functions. Although most of the protein synthesis inhibitors are lethal due to the inability to make essential proteins, in this particular instance this can be lethal when the multitude of 30S tRNA subunits begin to collect. Kanamycin is actually a combination of three antibiotics that work together. Another group of antibiotics, called the tetracyclines, also target ribosomes. They differ from the aminoglycosides in that they bind to a different site on the ribosome (70S and 80S). Chloramphenicol inhibits a class of enzymes that aid in growing the polypeptide chain during protein synthesis. It binds to the 70S subunit of the ribosome. Macrolide antibiotics prevent elongation of the growing protein, translocation of the ribosome along the mRNA, or both. An example is erythromycin, which binds to a specific site on the ribosome (50S). Other types of protein synthesis inhibitors serve similar functions as the Macrolide family but bind to different sites on the ribosome. It is important to note which site on the ribosome the antibiotics interact with because it can determine how effective the antibiotics are and what function they serve.

Nucleic Acid Effectors: Some antibiotics attack the DNA or RNA of a cell. These can affect the synthesis of the DNA (in some case RNA) or could effect if the specific genetic "messages" can be read. This serves to block the natural growth of the cell and will lead to a death without replication.

One group is called quinolones, and an example of this type is nalidixic acid. Nalidixic acid binds itself to an enzyme responsible for DNA replication. The enzyme topoisomerase, which uncoils the supercoiled DNA before replication, becomes ineffective. The drug can also inhibit the enzyme gyrase, which returns the DNA to its supercoiled state after replication. However this class of drugs is not specific to the bacterial world and has been known to affect animal cells. A new class of drugs, called rifamycins, solves the specificity problem of the quinolones. These only attack the eubacterial RNA polymerase, which is essential to mRNA synthesis. It is inactive toward RNA polymerase found in eukaryotic cells.

Noncompetitive and Competitive Inhibitors: Many of the previous types of antibiotics that inhibit specific enzymes are competitive or noncompetitive inhibitors. The noncompetative inhibitors block the enzyme for performing its normal "tasks" by mimicing the substrate of the enzyme and blocking adn then altering the enzyme structure, which makes the enzyme inactive.

The competitive inhibitors do not alter the enzyme itself, but instead occupy the enzymes so that they have less chance of interacting with the normal substrates. The Sulfonamides are a class of competitive inhibitors. These inhibit enzymes like DHF reductase that are required in a series of reactions to synthesize a folic acid necessary in 1-carbon transfer. Without this the cells will die. A class of drugs that include ethambutol and isoniazid serve to inhibit mycolic acid synthesis and incorporation into cell walls. These have the same effect on bacterial cells as the other cell wall inhibitors discussed earlier. One interesting fact is that they are actually activated by a bacterial enzyme called peroxidase and thus will only be active in bacterial cells.

(from www.esb.utexas.edu)

Facts About Antibiotic Resistance

Frequently Asked Questions about Antibiotic Resistance

What are bacteria and viruses?

Bacteria are single-celled organisms usually found all over the inside and outside of our bodies, except in the blood and spinal fluid. Many bacteria are not harmful. In fact, some are actually beneficial. However, disease-causing bacteria trigger illnesses, such as strep throat and some ear infections. Viruses are even smaller than bacteria. A virus cannot survive outside the body's cells. It causes illnesses by invading healthy cells and reproducing.

What kinds of infections are caused by viruses and should not be treated with antibiotics?

- Colds
- Flu
- Most coughs and bronchitis
- Sore throats (except for those resulting from strep throat)

How do I know when an illness is caused by a viral or bacterial infection?

Sometimes it is very hard to tell. Consult with your doctor to be sure.

When do I need to take antibiotics?

Antibiotics are very powerful medications. They should only be used when prescribed by a doctor to treat bacterial infections.

Do I need an antibiotic when mucus from the nose changes to yellow or green?

Yellow or green mucus does not indicate a bacterial infection. It is normal for the mucus to get thick and change color during a viral cold.

Should I ask my doctor to prescribe antibiotics?

Talk to your doctor about the best treatment. You should not expect to get a prescription for antibiotics. If you have a viral infection, antibiotics will not cure it, help you feel better, or prevent someone else from getting your virus.

What is antibiotic resistance and why should I be concerned?

Antibiotic resistance occurs when bacteria change in a way that reduces or eliminates the effectiveness of antibiotics. These resistant bacteria survive and multiply - causing more harm, such as a longer illness, more doctor visits, and a need for more expensive and toxic antibiotics. Resistant bacteria may even cause death.

What can I do to avoid antibiotic-resistant infections?

Start by talking with your health care provider about antibiotic resistance.

- Ask whether an antibiotic is likely to be effective in treating your illness.

- Do not demand an antibiotic when your health care provider determines one is not appropriate.
- Ask what else you can do to help relieve your symptoms.

What can I do to protect my child from antibiotic-resistant bacteria?
Use antibiotics only when your doctor has determined that they are likely to be effective. Antibiotics will not cure most colds, coughs, sore throats, or runny noses. Children fight off colds on their own.

If mucus from the nose changes from clear to yellow or green, does this mean that my child needs an antibiotic?
Yellow or green mucus does not mean that your child has a bacterial infection. It is normal for the mucus to get thick and change color during a viral cold.

Does this mean that I should never give my child antibiotics?
Antibiotics are very powerful medicines and should only be used to treat bacterial infections. If an antibiotic is prescribed, make sure you take the entire course and never save the medication for later use.

How do I know if my child has a viral or bacterial infection?
Ask your doctor. If you think that your child might need treatment, you should contact your doctor. But remember, colds are caused by viruses and should not be treated with antibiotics.

Facts About Antibiotic Resistance

- Antibiotic resistance has been called one of the world's most pressing public health problems.
- The number of bacteria resistant to antibiotics has increased in the last decade. Nearly all significant bacterial infections in the world are becoming resistant to the most commonly prescribed antibiotic treatments.
- Every time a person takes antibiotics, sensitive bacteria are killed, but resistant germs may be left to grow and multiply. Repeated and improper uses of antibiotics are primary causes of the increase in drug-resistant bacteria.
- Misuse of antibiotics jeopardizes the usefulness of essential drugs. Decreasing inappropriate antibiotic use is the best way to control resistance.
- Children are of particular concern because they have the highest rates of antibiotic use. They also have the highest rate of infections caused by antibiotic-resistant pathogens.
- Parent pressure makes a difference. For pediatric care, a recent study showed that doctors prescribe antibiotics 65% of the time if they perceive parents expect them; and 12% of the time if they feel parents do not expect them.
- Antibiotic resistance can cause significant danger and suffering for people who have common infections that once were easily treatable with antibiotics. When antibiotics fail to work, the consequences are longer-lasting illnesses; more doctor visits or extended hospital stays; and the need for more expensive and toxic medications. Some resistant infections can cause death.

How You Can Help Prevent Antibiotic Resistance

- Do not take an antibiotic for a viral infection like a cold, a cough or the flu.
- Take an antibiotic exactly as the doctor tells you. Do not skip doses. Complete the prescribed course of treatment, even if you are feeling better.
- Do not save any antibiotics for the next time you get sick. Discard any leftover medication once you have completed your prescribed course of treatment.
- Do not take antibiotics prescribed for someone else. The antibiotic may not be appropriate for your illness. Taking the wrong medicine may delay correct treatment and allow bacteria to multiply.
- Antibiotic prescriptions in outpatient settings can be reduced dramatically - without adversely affecting patient health - by not prescribing antibiotics for viral illnesses, such as colds, most sore throats, coughs, bronchitis, and the flu.
- Parents should not demand antibiotics when a health care provider has determined they are not needed.
- Parents should talk with their health care provider about antibiotic resistance.
- Parents should not give their children antibiotics for a viral infection like a cold, a cough, or the flu. Antibiotics should be used only to treat bacterial infections.
- Parents should ensure that their children take all medication as prescribed, even if symptoms disappear. If treatment stops too soon, some bacteria may survive and re-infect.

Cold and Flu Season: No Reason for Antibiotics

Colds, flu, and most sore throats and bronchitis are caused by viruses. Antibiotics do not help fight viruses. And they may do more harm than good: taking antibiotics when they are not needed - and cannot treat the illness - increases the risk of a resistant infection later.

Antibiotics Are Not for Colds and Flu

- Most infections are caused by two main types of germs - bacteria and viruses.
    - Bacteria are organisms found almost anywhere, except normally sterile sites,
      such as the blood stream and spinal fluid. A few bacteria, known as pathogens,
      can cause diseases in humans, animals, and plants.
    - Viruses are organisms that cause disease by invading healthy host cells. As
      virus particles multiply, the host cells burst, allowing the viruses to infect other
      cells.
- Antibiotics kill bacteria, not viruses.
- Antibiotics will not cure upper respiratory viral illnesses, such as:
    - Colds or flu
    - Most coughs and bronchitis
    - Sore throats not caused by strep
    - Runny noses

- Tens of millions of antibiotics prescribed in doctor's offices each year are for viral infections, which cannot effectively be treated with antibiotics. Doctors cite diagnostic uncertainty, time pressure on physicians, and patient demand as the primary reasons why antibiotics are over-prescribed.
- Taking antibiotics for viral infections - such as a cold, cough, the flu and most bronchitis - will not:
    - Cure the infections
    - Keep other individuals from catching the illness
    - Help a person fell better
- Taking antibiotics for viral infections will increase the risk of antibiotic resistance.
- The spread of viral infections can be reduced through frequent hand washing and by avoiding close contact with others.

What To Do For Colds and Flu

- Children and adults with viral infections recover when the illness has run its course. Colds caused by viruses last for two weeks or longer.
- Measures that can help a person with a cold or flu feel better:
    - Increase fluid intake
    - Use a cool mist vaporizer or saline nasal spray to relieve congestion
    - Soothe throat with ice chips, sore throat spray, or lozenges (do not give lozenges
      to young children)
- Viral infections sometimes lead to bacterial infections. Patients should keep their doctor informed if their illness gets worse or lasts a long time.

(from www.cdc.gov)

Miracle Drugs vs. Superbugs

Preserving The Usefulness Of Antibiotics

by Tamar Nordenberg

The historical scourge known as the bubonic plague killed up to one-third of Europe's population in the 1300s. But in modern times, it has been controlled handily with the help of antibiotic drugs such as streptomycin, gentamicin and chloramphenical.

That is, until 1995, when a plague infection in a 16-year-old boy from Madagascar failed to respond to the usual antibiotic treatments. This first documented case of an antibiotic-resistant plague, reported in the September 1997 New England Journal of Medicine, eventually succumbed to another antibiotic.

In the United States and globally, many other infectious germs, including those that cause pneumonia, ear infections, acne, gonorrhea, urinary tract infections, meningitis, and tuberculosis, can now outwit some of the most commonly used antibiotics and their synthetic counterparts, antimicrobials. According to the Mayo Clinic in Rochester, Minn., drug resistance may have contributed to the 58 percent rise in infectious disease deaths among Americans between 1980 and 1992.

Antibiotic resistance isn't a new problem; resistant disease strains began emerging not long after the discovery of antibiotics more than 50 years ago. Penicillin and other antibiotics, which were initially viewed as miracle drugs for their ability to cure such serious and often life-threatening diseases as bacterial meningitis, typhoid fever, and rheumatic fever, soon were challenged by some defiant strains.

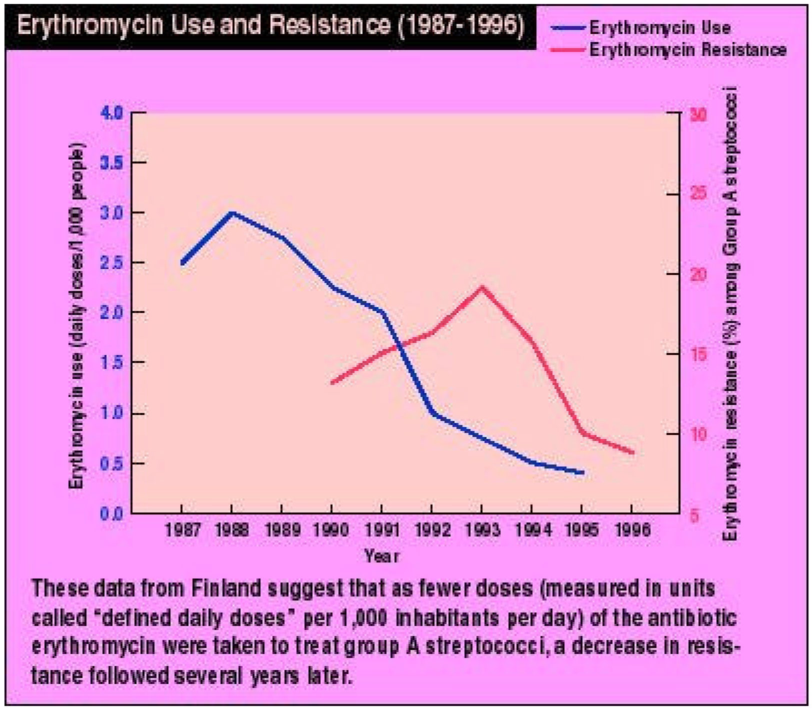
"What's different now," explains David Bell, M.D., an expert on antimicrobial resistance with the national Centers for Disease Control and Prevention, "is that we've reached a situation where it's no longer an isolated problem of this bug or that bug; virtually all important human pathogens treatable with antibiotics have developed some resistance."

Despite the frightening trend, most people aren't likely to encounter a "superbug" that can outsmart all antibiotics, says Mark Goldberger, M.D., director of the Food and Drug Administration's division of special pathogen and immunologic drug products. "For the average person walking around on the street, the risk at the moment remains low."

Still, as one antibiotic's effectiveness wanes, doctors are forced in many cases to rely on more expensive and toxic drugs. Resistance is "a big problem and growing," says Linda Tollefson, director of surveillance and compliance in FDA's Center for Veterinary Medicine. "You're dealing with living microbes that have shown an incredible ability to accommodate antibiotics and come out winning. We have no idea what they are going to do next. Our fear is that we're seeing the tip of the iceberg."

To stop infectious germs from gaining ground, experts the world over, including doctors and scientists from FDA, CDC, and the World Health Organization, have been focusing since 1995 on finding ways to prolong the lives of antibiotics and to encourage drug companies to develop new "miracle drugs."

Survival of the Fittest



These data from Finland suggest that as fewer doses (measured in units called "defined daily doses" per 1,000 inhabitants per day) of the antibiotic erythromycin were taken to treat group A streptococci, a decrease in resistance followed several years later.

Every time a patient takes penicillin or another antibiotic for a bacterial infection, the drug may kill most of the bacteria. But a few tenacious germs may survive by mutating or acquiring resistance genes from other bacteria. These surviving genes can multiply quickly, creating drug-resistant strains. The presence of these strains may mean that the patient's next infection will not respond to the first-choice antibiotic therapy. Also, the resistant bacteria may be transmitted to others in the patient's community.

Experts say the risk is greatest, but still not high, for those in hospitals, nursing homes, and other settings where people tend to be sick often. In these environments, people may be taking an array of antibiotics (one researcher estimates that 25 to 40 percent of hospital patients get intravenous antibiotics), increasing the chance of a resistant germ originating within their own bodies. Also, hospitalized patients are surrounded by others whose infectious diseases may spread, and their immune systems may be weakened and incapable of beating the infectious bugs.

Organisms that have already developed defenses against antibiotic attack include:

- Staphylococcus aureus. This bacterium, which is the biggest cause of infections in patients in U.S. hospitals, can infect burns, skin, and surgical wounds. Since 1996, at least four patients--three in the United States and one in Japan--reportedly were infected with a strain that was partially resistant to normal doses of the powerful, last-resort antibiotic vancomycin. Some strains of S. aureus have already shown resistance to all antibiotics other than vancomycin, raising the fear that an invincible strain is near at hand.
- Enterococcus. This organism can cause everything from urinary tract to heart valve infections. Some strains can outmatch many previously effective antibiotics.

- Streptococcus pneumoniae. Up to 30 percent of the strains of this bacterium, which can cause pneumonia, meningitis, and ear infections, are at least partially resistant to antibiotics in the penicillin family, according to the Mayo Clinic.

Other germs that have grown resistant to formerly reliable antibiotics include Neisseria gonorrhoeae, the cause of the sexually transmitted disease gonorrhea; the food poisoners Salmonella, Escherichia coli (E. coli) and other Enterobacteriaceae; and Mycobacterium tuberculosis, which causes TB. Data from Finland shown in the chart above (source: Centers for Disease Control and Prevention CAUSE newsletter, October 1997) suggest that as fewer doses (measured in units called "defined daily doses" per 1,000 inhabitants per day) of the antibiotic erythromycin were taken to treat group A streptococci, a decrease in resistance followed several years later.

Luckily, Goldberger says, there is a renewed interest among U.S. drug companies in developing new antibiotics to target organisms that are developing resistance. Earlier this year, an FDA advisory panel recommended approval for the antibiotic Synercid. If approved, it could be used to treat such hospital-acquired infections as pneumonia and some vancomycin-resistant infections of the bloodstream.

Too Much of a Good Thing

Experts say that doctors are sometimes quick to prescribe antibiotics for all sorts of symptoms, even though antibiotics work only against bacterial infections, not viruses such as the flu or the common cold. More than 50 million of the 150 million antibiotic prescriptions written each year for patients outside of hospitals are unnecessary, according to a recent CDC study. (See chart.)

Sometimes, doctors lack knowledge about the symptoms and natural course of respiratory illnesses, which contributes to overuse, according to a CDC editorial in the Sept. 17, 1997, Journal of the American Medical Association. Also, many doctors have told CDC they sometimes write prescriptions simply to meet patient demands.

Patients therefore must take some of the responsibility for the overprescribing problem, according to Stuart Levy, M.D., director of Tufts University's Center for Adaptation Genetics and Drug Resistance. "Patients have been left out of the formula. Overuse of antibiotics was felt to be a physicians' problem when it is really as much a patient problem."

Patients can do their part to help curb resistance:

- Don't demand an antibiotic when the health-care provider determines one isn't appropriate.
- Finish each prescription. Even when the symptoms of an illness have disappeared, some bacteria may still survive and reproduce if the patient doesn't complete the course of treatment.
- Don't take leftover antibiotics or antibiotics prescribed for someone else. These antibiotics may not be appropriate for the current symptoms, and taking the wrong medicine could delay getting appropriate treatment and allow bacteria to multiply.

For more tips on proper antibiotic use, visit the Website of the Alliance for the Prudent Use of Antibiotics (www.healthsci.tufts.edu/apua/patient.htm).

Even when used carefully, all organisms can develop some resistance to antibiotics over time. "It is a perfectly natural phenomenon for a living organism to develop the means of survival in a hostile environment," wrote French microbiologist Jacques Acar in a 1997 article in World Health.

Preventing infection in the first place may therefore be the best defense against an antibiotic-resistant infection.

Frequent and thorough hand washing is one key to preventing the spread of infection. Good kitchen habits, such as storing foods at the proper temperature, washing fruits and vegetables thoroughly, and cooking foods completely, can also reduce the chance of getting a food-borne illness. (See "Can Your Kitchen Pass the Food Safety Test?" in the October 1995 FDA Consumer.)

"Take your basic precautions," Bell advises. "That means practicing common hygiene, as well as food safety in your kitchen."

Tamar Nordenberg is a staff writer for FDA Consumer.

(from www.fda.gov/fdac/)