Name:	**Biology**
Period:	**Evolution Extra Credit**

Aim: Explain antibiotic resistance as an example of evolution in response to environmental change.

Article	This article argues that…	Brief Summary of Article	Do you agree or disagree with the article's premise? Why/why not?
Antibiotics: Misuse puts you and others at risk			
GPs 'over-prescribing' antibiotics, says Cardiff University study			
Physicians across US Prescribing Unnecessary Antibiotics for Sore Throat, Bronchitis			
Study shows overuse of antibiotics			
Antibiotic Resistance, Mutation Rates and MRSA			

After reading articles and completing the above chart, answer the questions below:

1. What is it about MRSA that makes it so dangerous?

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2. Daniel argues that antibiotics can be taken to prevent bacteria from growing. In what ways is he right? In what ways is he wrong?

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3. What’s wrong with the following statement: When bacteria are treated with antibiotics, they develop increased resistance to the antibiotic and pass on increased resistance to offspring.

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4. Mrs. Jones developed a sore throat the week after her daughter was sick and had taken antibiotics. She began to take her daughter’s antibiotic pills without going to the doctor to get diagnosed. Explain at least 3 reasons why this was a bad choice.

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5. Is it possible for an antibiotic to stop being effective altogether? Why/why not?

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Antibiotics: Misuse puts you and others at risk

Antibiotics can be lifesavers, but misuse has increased the number of drug-resistant germs. See how this affects you and what you can do to help prevent antibiotic resistance.

By Mayo Clinic staff http://www.mayoclinic.com/health/antibiotics/FL00075

If you think antibiotic resistance isn't a problem or doesn't affect you, think again. A prominent example of the dangers of antibiotic resistance is the spread of methicillin-resistant Staphylococcus aureus (MRSA). MRSA was once a concern only for people in the hospital, but a newer form of MRSA is causing infections in healthy people in the community.

Antibiotic resistance occurs when antibiotics no longer work against disease-causing bacteria. These infections are difficult to treat and can mean longer lasting illnesses, more doctor visits or extended hospital stays, and the need for more expensive and toxic medications. Some resistant infections can even cause death.

Although experts are working to develop new antibiotics and other treatments to keep pace with antibiotic-resistant strains of bacteria, infectious organisms can adapt quickly. Antibiotic-resistant bacteria will continue to be a global health concern — and using antibiotics wisely is important for preventing their spread.

When is it appropriate to use antibiotics?

Antibiotics are effective against bacterial infections, certain fungal infections and some kinds of parasites. Antibiotics don't work against viruses. The chart shows common illnesses and whether they're caused by bacteria or viruses. Taking an antibiotic when you have a viral infection won't make you feel better — and can contribute to antibiotic resistance.

Bacterial infections	Viral infections
Bladder infections Many wound and skin infections, such as staph infections Severe sinus infections that last longer than 2 weeks Some ear infections Strep throat	Bronchitis Colds Flu (influenza) Most coughs Most ear infections Most sore throats Stomach flu (viral gastroenteritis)

Consequences of antibiotic misuse

If antibiotics are used too often for things they can't treat — like colds, flu or other viral infections — not only are they of no benefit, they become less effective against the bacteria they're intended to treat.

Not taking antibiotics exactly as prescribed also leads to problems. For example, if you take an antibiotic for only a few days — instead of the full course — the antibiotic may wipe out some, but not all, of the bacteria. The surviving bacteria become more resistant and can be spread to other people. When bacteria become resistant to first line treatments, the risk of complications and death is increased.

The failure of first line antibiotics also means that doctors have to resort to less conventional medications, many of which are more costly and associated with more-serious side effects. For instance, the drugs needed to treat drug-resistant forms of tuberculosis (TB) are much more expensive than are the drugs used to treat nonresistant TB. The course of treatment is long — up to two years — and the side effects can be severe.

Other consequences are the increased costs associated with prolonged illnesses, including expenses for additional tests, treatments and hospitalization, and indirect costs, such as lost income.

What you can do to safeguard antibiotic effectiveness

Repeated and improper use of antibiotics is the primary cause of the increase in the number of drug-resistant bacteria. Here's what you can do to promote proper use of antibiotics:

- **Understand when antibiotics should be used.** Don't expect to take antibiotics every time you're sick. Antibiotics are effective in treating most bacterial infections, but they're not useful against viral infections, such as colds, acute bronchitis or the flu. And even some common bacterial ailments, such as mild ear infections, don't benefit much from antibiotics.
- **Don't pressure your doctor for antibiotics if you have a viral illness.** Instead, talk with your doctor about ways to relieve your symptoms — for instance, a saline nasal spray to clear a stuffy nose or a mixture of warm water, lemon and honey to temporarily soothe a sore throat.
- **Take antibiotics exactly as prescribed.** Follow your doctor's instructions when taking medication. Don't stop treatment a few days early because you're feeling better. Taking the full course of antibiotics is the only way to kill all of the harmful bacteria. A shortened course of antibiotics, on the other hand, often wipes out only the most vulnerable bacteria while allowing relatively resistant bacteria to survive.
- **Never take antibiotics without a prescription.** If you didn't complete a full course of antibiotics, you might be tempted to use the leftover medication the next time you get sick or to pass it along to someone else. But this isn't a good idea. For one thing, the antibiotic might not be appropriate for another illness. And even if it is, you're not likely to have enough pills to combat the germs making you sick, which can lead to more resistant bacteria.
- **Prevent the spread of germs.** Good hygiene goes a long way in preventing infection. Wash your hands thoroughly with soap and water, especially after using the toilet, changing a diaper, or handling raw meat or poultry. Keep food preparation areas clean. Although special antibacterial cleaners and soap are widely available, they aren't necessary. Plain soap and water work fine to kill germs in most settings.

Protect yourself and others

Antibiotic resistance is a global health problem. Nearly all significant bacterial infections in the world are becoming resistant to commonly used antibiotics. When you misuse antibiotics, you help create resistant microorganisms that can cause new and hard-to-treat infections. That's why the decisions you make about using antibiotics — unlike almost any other medicine you take — have far-reaching consequences. Be responsible in how you use antibiotics to protect your health and that of your family, neighbors and community.

GPs 'over-prescribing' antibiotics, says Cardiff University study http://www.bbc.co.uk/news/uk-wales-24644191

GPs wrongly assume that patients want antibiotics resulting in too many being prescribed, according to a Europe-wide study by Cardiff University.

Research showed that for patients with an acute cough the drugs made little difference to their recovery time. Experts have voiced concern that over-prescribing antibiotics helps bacteria become increasingly resistant, making the drugs ineffective.

Since their arrival in the 1940s, antibiotics have been on the frontline of medicine's battle against disease. But experts are warning they are becoming increasingly ineffective at a rate that is alarming and irreversible because bacteria is becoming resistant to them.

Researchers at Cardiff and at Antwerp University in Belgium said an acute cough was one of the most common reasons for consulting and for prescribing antibiotics in primary care. Patients taking part in the study were asked if they expected, hoped for or asked for antibiotics when consulting their doctor for acute cough. Researchers found that the recovery time taken for patients remained largely the same, whether or not they expected, hoped for, asked for and/or received a prescription.

The study revealed that patient satisfaction with the consultation remained high, whether or not patients actually received antibiotics from their doctor. However, those who had hoped for antibiotic treatment, but did not receive it, were less satisfied.

Dr Nick Francis from the Cardiff University School of Medicine, who is also a GP in Ebbw Vale, said GPs prized their relationships with their patients, and may prescribe antibiotics because they feared "bad press" if patients did not get well.

'Safer approach'

"But we are saying you can maintain that relationship by equipping patients with good information about what they should be watching out for," added Dr Francis, who has been a GP for nearly 20 years.

"It's a safer approach and they can come back to the doctors once they know what to look out for."

Dr Francis said there were also fears that over-prescribing antibiotics could result in bacteria becoming more resistant to them. He added: "The study provides clear evidence that patient views are not associated with illness severity and is therefore unlikely to represent a rational reason for prescribing antibiotics. "Moreover, clinicians are not good at correctly assessing patient views on use of antibiotics. "We believe it is likely that satisfaction could have been increased through enhanced communication, as has been found in previous studies."

Last year, Dr Robin Howe of Public Health Wales said increasing resistance to antibiotics could lead to more illness and deaths. Dr Howe said clinicians and patients must accept they could only be used when they had most benefit.

Physicians across US Prescribing Unnecessary Antibiotics for Sore Throat, Bronchitis

http://www.nature.com/scitable/topicpage/antibiotic-resistance-mutation-rates-and-mrsa-28360

Most people don't need antibiotics for common illnesses such as a sore throat. Yet, a surprising number of physicians across the U.S. continue to prescribe antibiotics to patients with sore throat and acute bronchitis, a recent study reported. Inappropriate use of antibiotics makes microbes resistant to the medicines. For decades, the Centers for Disease Control and Prevention (CDC) has been trying to educate physicians and the public against the misuse of common antibiotics. But, a recent study conducted by researchers Brigham and Women's Hospital (BWH) found that people still use antibiotics for sore throat.

"We know that antibiotic prescribing, particularly to patients who are not likely to benefit from it, increases the prevalence of antibiotic-resistant bacteria, a growing concern both here in the United States and around the world," said Jeffrey Linder, , a physician and researcher in the Division of General Medicine and Primary Care at BWH and senior author of the study.

For the study, the scientists looked at data from national representative surveys from 1996 to 2010. They found that the rate of antibiotic prescription for adults in the U.S. was 60 percent. The survey had data on more than 39 million bronchitis and 92 million sore throat visits to primary health care centres.

Generally, sore throat and acute bronchitis can't be treated with antibiotics because in many cases a virus is responsible for the infection. Antibiotics are used to treat strep throat and in the study, just 10 percent had the condition.

"Our research shows that while only 10 percent of adults with sore throat have strep, the only common cause of sore throat requiring antibiotics, the national antibiotic prescribing rate for adults with sore throat has remained at 60 percent.

For acute bronchitis, the right antibiotic prescribing rate should be near zero percent and the national antibiotic prescribing rate was 73 percent," Linder said in a news release.

Centers for Disease Control and Prevention (CDC) says that the threat of microbes getting resistant to a drug isn't restricted to a country but is problem faced by the entire world. The U.S., for example, faces some real danger from methicillin-resistant Staphylococcus aureus (MRSA).

Study shows overuse of antibiotics

http://www.usatoday.com/story/news/nation/2013/04/10/medication-antibiotic-overuse/2071899/
Mike Stobbe, Associated Press *5:34 p.m. EDT April 10, 2013*

NEW YORK — U.S. doctors are prescribing enough antibiotics to give them to 4 out of 5 Americans every year, an alarming pace that suggests they are being overused, a new government study finds.

Overuse is one reason antibiotics are losing their punch, making infections harder to treat. The report released Wednesday gives the first detailed look at usage of these medicines in every state and finds it highest in the South and Appalachia.

"It sounds high," said Keith Rodvold, a professor of pharmacy practice at the University of Illinois at Chicago.

There is no scientific consensus on an appropriate level of antibiotic prescribing. But some experts said the new study's results are disturbing, and that rates are probably excessive even in the states with the lowest antibiotic prescription levels.

Antibiotics have been commonly available since the 1940s, and have done wonders at saving patients with infections ranging from pneumonia to sexually spread diseases. But bacteria have increasingly gained the power to shrug off antibiotics.

Experts say chances of resistance increase when antibiotics are not used long enough or are taken for the wrong reasons, allowing bacteria to survive and adapt. The Centers for Disease control and Prevention is tracking at least 20 strains of resistant bacteria.

CDC researchers conducted the new study, analyzing a national prescription drug database for 2010. The findings are being published in Thursday's *New England Journal of Medicine*.

Other studies have focused on antibiotic prescriptions for specific groups like Medicare patients. This is the first to look at it for all Americans. Doctors and other health care providers prescribed 258 million courses of antibiotics in 2010, for a population just shy of 309 million, the researchers found. That translates to 833 antibiotic prescriptions for every 1,000 people, on average.

But rates were much higher in West Virginia, Kentucky and Tennessee, where about 1,200 were written for every 1,000 people. On the low end were Alaska, Oregon and California, where prescriptions were at or below 600. Earlier studies found similar geographic trends.

Why the difference? One possibility: Southerners suffer more infections than people in other parts of the country. Southern states have the highest rates of obesity and diabetes, and diabetics tend to have more infections than other people, noted the CDC's Dr. Lauri Hicks, one of the study's authors. "So some of that prescribing may be warranted," she said.

During the swine flu pandemic of 2009 and 2010, the South saw more reports of illness than other parts of the country. Experts at the time said patients with flu-related pneumonia should be treated with both antiviral medicines and antibiotics to prevent all forms of deadly complications, Rodvold noted.

The South also has higher rates of certain other respiratory infections, including bronchitis, according to a study last year by University of Pittsburgh researchers.

And the CDC study found the most frequently prescribed antibiotic was azithromycin, which is commonly used for bronchitis symptoms. But that's a problem. Bronchitis is usually caused by a virus, and antibiotics like azithromycin don't work against viruses. "Some of the prescribing may not be warranted," Hicks said.

Antibiotic Resistance, Mutation Rates and MRSA

http://www.nature.com/scitable/topicpage/antibiotic-resistance-mutation-rates-and-mrsa-28360

By: Leslie Pray, Ph.D.

In bacteria, mutations in plasmids can accumulate surprisingly fast. What does this mean for us humans, who have to fight with these new antibiotic resistant strains?

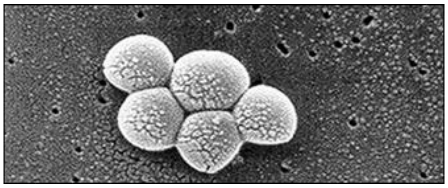

Figure 1: *Staphylococcus aureus* bacteria.

"Staph" skin infections are caused by a bacterium that can divide every half hour in optimal conditions. Theoretically, a single cell can form a colony of more than a million cells in ten hours.

Suppose that one morning, on your way to class, you were to touch a surface, like a doorknob, that was contaminated with some lingering *Staphylococcus aureus* (Figure 1). The bacterium *S. aureus*, known by health care workers as "staph," is the most common cause of skin infections in humans. Suppose another student who had walked into the building just minutes beforehand had left the organism there, after grabbing hold of the same doorknob. Now imagine that you have an open cut on your finger, and some of the bacteria that are on that doorknob get into your wound. Although this seems like a minor event, it could actually have great repercussions for your overall health.

Mutation Rates and Bacterial Growth

Even if only a single *S. aureus* cell were to make its way into your wound, it would take only 10 generations for that single cell to grow into a colony of more than 1,000 (2^{10} = 1,024), and just 10 more generations for it to erupt into a colony of more than 1 million (2^{20} = 1,048,576). For a bacterium that divides about every half hour (which is how quickly *S. aureus* can grow in optimal conditions), that is a lot of bacteria in less than 12 hours. *S. aureus* has about 2.8 million nucleotide base pairs in its genome. At a rate of, say, 10^{-10} mutations per nucleotide base, that amounts to nearly 300 mutations in that population of bacteria within 10 hours!

To better understand the impact of this situation, think of it this way: With a genome size of 2.8×10^6 and a mutation rate of 1 mutation per 10^{10} base pairs, it would take a single bacterium 30 hours to grow into a population in which every single base pair in the genome will have mutated not once, but 30 times! Thus, any individual mutation that could theoretically occur in the bacteria will have occurred somewhere in that population—in just over a day.

Mutations, Antibiotic Resistance, and Staph Infections

Now, say that a few days after your initial infection with *S. aureus*, you decide to go to the local health center to have your wound examined. Maybe your finger is not healing as quickly as you had expected. Maybe its red color is a bit worrisome. Maybe the wound is starting to ooze a bit. Maybe you vaguely recall hearing or reading something about some kind of bacterial infection that is popping up on college campuses across the country and landing some students in the hospital. Concerned that your wound might be infected, the physician at the health center decides to prescribe an antibiotic.

Under a best-case scenario, the prescribed antibiotic would kill all of the replicating *S. aureus* cells in your body, mutant or otherwise, and your wound would quickly heal. After all, the potency of antibiotic treatment is why, when penicillin entered medical care in the 1940s, it was deemed a "miracledrug." Penicillin and other antibiotics have saved countless lives for more than half a century. Under a different scenario, however, any one of those mutations could give your *S. aureus* infection the ability to resist the particular drug you are being treated with. Luckily, in the real world, usually more than one mutation is required to generate drug resistance, and bacteria cannot double quite so quickly inside a person with a functioning immune system. But the problem still remains: The rapid division of bacterial cells causes them to evolve resistance to most treatments rather quickly.

Thus, although you are on antibiotics and you are otherwise healthy, a total of 600 mutations have accumulated by the time you go to bed that night. Any one of those mutations could give your staph infection the capacity to continue replicating, even in the presence of the antibiotic. All it takes is a single mutated *S. aureus*—one that, through one of a number of innovative biochemical means, does not die in the presence of whatever antibiotic the physician decided to prescribe—to render that antibiotic useless (at least for this particular infection). Moreover, when that mutant cell replicates, it will pass on its resistant phenotype to its daughter cells, and they to theirs. Thus, a rapidly growing proportion of the replicating bacteria still present in your body will be drug resistant. This is because the drug will kill only those cells that do not have the newly evolved drug-resistance capacity. Thus, the entire bacterial population will eventually become resistant to the prescribed antibiotic. When that happens, your infection will be said to be antibiotic resistant, and your physician will have to prescribe a different drug to combat it.

MRSA: The Spread of Drug Resistance

In fact, there is a good chance that the staph infection you picked up from that contaminated doorknob is already antibiotic resistant. Most staph infections in humans are caused by methicillin-resistant *Staphylococcus aureus*, or MRSA, a drug-resistant phenotype that has been circulating for more than 45 years, almost as long as methicillin has been on the market. According to the U.S. Centers for Disease Control (CDC), in 2004, 63% of all reported staph infections in the United States were caused by MRSA (CDC, 2007). That figure represents a remarkable 300% increase in just 10 years' time. (In 1995, about 22% of all reported staph infections were MRSA, compared with only 2% in 1974.) The irony is that methicillin, a chemically modified version of penicillin, was developed in the 1950s as an alternative treatment for the growing proportion of staph infections already resistant to penicillin. At that time, about 60% of all staph infections were resistant to penicillin.

Needless to say, physicians no longer prescribe traditional antibiotics for methicillin-resistant staph infections (Micet, 2007). Instead, they usually administer "last-resort" intravenous vancomycin, although a growing number of doctors are now prescribing other newer antibiotics. Even with these options, scientists estimate that about 19,000 people in the United States die every year from MRSA (Klevens *et al.*, 2007)—that's more than the number of U.S. residents and citizens that die from HIV/AIDS (about 17,000 every year). Of course, not all staph infections are deadly. In fact, about 30% to 40% of us have both methicillin-resistant and non-methicillin-resistant *S. aureus* living on the surface of our skin yet suffer no symptoms at all. Most deaths from *S. aureus* occur when what is normally "just" a skin infection enters the bloodstream and becomes invasive, affecting a person's internal anatomy. Moreover, most MRSA deaths occur in the hospital among patients being treated for other reasons and whose immune systems are too weak to fight off the infection, even when vancomycin is administered. In fact, MRSA used to occur only in hospitals. Also, as little as twenty years ago, MRSA did not spread via contaminated doorknobs (except in hospitals). The first so-called "community-acquired" MRSA infection—an infection occurring in a person neither hospitalized nor having had any recent contact with someone who was hospitalized—wasn't reported until the early 1990s. Since then, a growing number of MRSA cases and deaths have occurred outside of hospitals.

The Tip of the Antibiotic-Resistance Iceberg

As worrisome as MRSA is, it is just the tip of the iceberg, so to speak. In fact, there are a number of far more threatening drug-resistant bacteria in existence, such as *Pseudomonas aeruginosa*. *P. aeruginosa* poses a greater threat because it has certain biological features that make it more readily resistant to antibiotics than MRSA. For example, *P. aeruginosa* has a highly impermeable outer membrane, whereas MRSA does not. This outer membrane makes it more difficult for antibiotic chemical compounds to actually get inside the bacterial cell so that they can inflict damage. Moreover, once the antibiotic compounds are inside it, *P. aeruginosa* has what are known as efflux pumps, which can very quickly pump foreign compounds like antibiotics back out of the cell before they have a chance to do damage. MRSA does not have efflux pumps. Because of these biological features, *P. aeruginosa* infections either quickly evolve multidrug resistance or are drug-resistant from the start. Unlike with MRSA, however, the likelihood of picking up a *P. aeruginosa* infection from a doorknob in a school building is practically nil. *P. aeruginosa* infections occur mostly among hospital patients—at least for now.

In both the hospital and the community, antibiotic resistance has emerged as a major public health problem. In fact, some scientists consider it the most important public health problem of the twenty-first century. The problem exists not just because bacterial mutation rates lead to a rapid accumulation of mutations (including drug-resistant mutations), but also because of the selective pressures that antibiotics impose. If a drug-resistant phenotype were to evolve and there were no antibiotic present, then that phenotype would fare no better than any other bacterial phenotype. In other words, it wouldn't flourish, and it might even die out. It is only when antibiotics are used that drug-resistant phenotypes have a selective advantage and survive.

Of course, not all mutations confer resistance, and most probably have nothing at all to do with resistance. That said, bacterial populations with especially high mutation rates (so-called "hypermutable" strains) often have higher antibiotic resistance rates. For example, in a study of cystic fibrosis (CF) patients infected with *P. aeruginosa* (which is a major cause of sickness and death among CF patients), where more than a third of all CF patients had hypermutable *P.*

aeruginosa infections, the hypermutable populations had higher resistance rates than isolates with "normal" mutation rates (Oliver *et al.*, 2000). Plus, there are other ways that bacteria evolve resistance, in addition to spontaneous nucleotide base mutations. For instance, bacteria can acquire resistance genes through conjugation (i.e., from plasmid DNA) and from recombination with other bacterial DNA following transformation.

The emergence and spread of antibiotic resistance has become such an important public health problem that many federal and state public health agencies now distribute educational posters to encourage "good hygiene" practices—practices that prevent the spread of antibiotic-resistant bacteria from one person to another and help keep those mutant *S. aureus* bacteria off doorknobs. Maybe you have seen one of these posters in a school hallway, in a locker room, or in a public bathroom, imploring you to wash your hands with soap and water to help prevent disease.
To make MRSA matters even worse, in 2002, health care workers reported the first cases of vancomycin-resistant MRSA. In other words, even "last-resort" vancomycin doesn't always work. Therein lies the crisis: People are dying from "simple" bacterial infections, all because of a very low mutation rate.

Beyond *Staphylococcus aureus*
Bacterial resistance to antibiotics and other drugs is inevitable, and MRSA is just one example of why scientists must be so concerned about mutation rates. For instance, the inevitability of mutation and the development of resistance is one of the reasons why tuberculosis, thought to be essentially eradicated in the 1940s, is again on the rise in many countries. Multidrug-resistant strains of microorganisms will continue to be a major world health concern, keeping many scientists across disciplines occupied with the development and testing of novel therapies.