دکتر مهران امیری زاده

متخصص فارماکوتراپی

فلوشیپ فارماکوتراپی مراقبت های ویژه(ICU)

عضو هیئت علمی دانشگاه علوم پزشکی لرستان

What is resistant—my body or the germ? Antibiotic resistance does not mean our body is resistant to antibiotics; it means that the bacteria or fungus are resistant to the antibiotics designed to kill them.

About Antibiotic Resistance

Antibiotic resistance happens when germs like bacteria and fungi develop the ability to defeat the drugs designed to kill them. That means the germs are not killed and continue to grow.

Infections caused by antibiotic-resistant germs are difficult, and sometimes impossible, to treat. In most cases, antibiotic-resistant infections require extended hospital stays, additional follow-up doctor visits, and costly and toxic alternatives.

Antibiotic resistance does not mean the body is becoming resistant to antibiotics; it is that bacteria have become resistant to the antibiotics designed to kill them.

Antibiotic Resistance Threatens Everyone

Antibiotic resistance has the potential to affect people at any stage of life, as well as the healthcare, veterinary, and agriculture industries, making it one of the world's most urgent public health problems.

Each year in the U.S., at least 2.8 million people are infected with antibiotic-resistant bacteria or fungi, and more than 35,000 people die as a result.

Terms

On CDC's website, antibiotic resistance is also referred to as antimicrobial resistance or drug resistance.

No one can completely avoid the risk of resistant infections, but some people are at greater risk than others (for example, people with chronic illnesses). If antibiotics lose their effectiveness, then we lose the ability to treat infections and control public health threats.

Many medical advances are dependent on the ability to fight infections using antibiotics, including joint replacements, organ transplants, cancer therapy, and treatment of chronic diseases like diabetes, asthma, and rheumatoid arthritis.

Brief History of Resistance and Antibiotics

Penicillin, the first commercialized antibiotic, was discovered in 1928 by Alexander Fleming. Ever since, there has been discovery and acknowledgement of resistance alongside the discovery of new antibiotics. In fact, germs will always look for ways to survive and resist new drugs. More and more, germs are sharing their resistance with one another, making it harder for us to keep up.

Learn how CDC is leading efforts to combat antibiotic resistance through the Antibiotic Resistance Solutions Initiative.

Select Germs Showing Resistance Over Time

Antibiotic Approved or Released	Year Released	Resistant Germ Identified	Year Identified
Penicillin	1941	Penicillin-resistant *Staphylococcus aureus*	1942
		Penicillin-resistant *Streptococcus pneumoniae*	1967
		Penicillinase-producing *Neisseria gonorrhoeae*	1976
Vancomycin	1958	Plasmid-mediated vancomycin-resistant *Enterococcus faecium*	1988
		Vancomycin-resistant *Staphylococcus aureus*	2002
Amphotericin B	1959	Amphotericin B-resistant *Candida*	2016

Methicillin	1960	Methicillin-resistant *Staphylococcus aureus*	1960
Extended-spectrum cephalosporins	1980 (Cefotaxime)	Extended-spectrum beta-lactamase-producing *Escherichia coli*	1983
Azithromycin	1980	Azithromycin-resistant *Neisseria gonorrhoeae*	2011
Imipenem	1985	*Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae*	1996
Ciprofloxacin	1987	Ciprofloxacin-resistant *Neisseria gonorrhoeae*	2007
Fluconazole	1990 (FDA approved)	Fluconazole-resistant *Candida*	1988
Caspofungin	2001	Caspofungin-resistant *Candida*	2004
Daptomycin	2003	Daptomycin-resistant methicillin-	2004

Antibiotics save lives but any time antibiotics are used, they can cause side effects and lead to antibiotic resistance.

Since the 1940s, antibiotics have greatly reduced illness and death from infectious diseases. However, as we use the drugs, germs develop defense strategies against them. This makes the drugs less effective.

What is misuse of antibiotics?

Misuse of antibiotics happens when a person is prescribed

- the wrong antibiotic,
- the wrong dose of an antibiotic, or
- an antibiotic for the wrong length of time.

Talk with your doctor about the best treatment for your illness.

Antimicrobials Treat Infections Caused by Microbes

Microbes ,like bacteria , are very small living organisms,. Most microbes are harmless and even helpful to humans, but some can cause infections and disease.

Drugs used to treat these infections are called antimicrobials. The most commonly known antimicrobial is antibiotics, which kill or stop the growth of bacteria.

Two Types of Microbes

- Bacteria cause illnesses such as strep throat and food poisoning. Bacterial infections are treated with drugs called antibiotics (such as penicillin).
- Fungi cause illnesses like athlete's foot and yeast infections. Fungal infections are treated with drugs called antifungals.

How Germs Become Resistant and Spread

1. Germs (bacteria and fungi) are everywhere. Some help us. Some make people, crops, or animals sick. Some of those germs are resistant to antibiotics.
2. Antibiotics kill germs that cause infections. But antibiotic-resistant germs find ways to survive. Antibiotics also kill good bacteria that protect the body from infection.
3. Antibiotic-resistant germs can multiply. Some resistant germs can also give their resistance directly to other germs.
4. Once antibiotic resistance emerges, it can spread into new settings and between countries.

Germ Defense Strategies

Antibiotics fight germs (bacteria and fungi). But germs fight back and find new ways to survive. Their defense strategies are called resistance mechanisms. Bacteria develop resistance mechanisms by using instructions provided by their DNA. Often, resistance genes are found within plasmids, small pieces of DNA that carry genetic instructions from one germ to another. This means that some bacteria can share their DNA and make other germs become resistant.

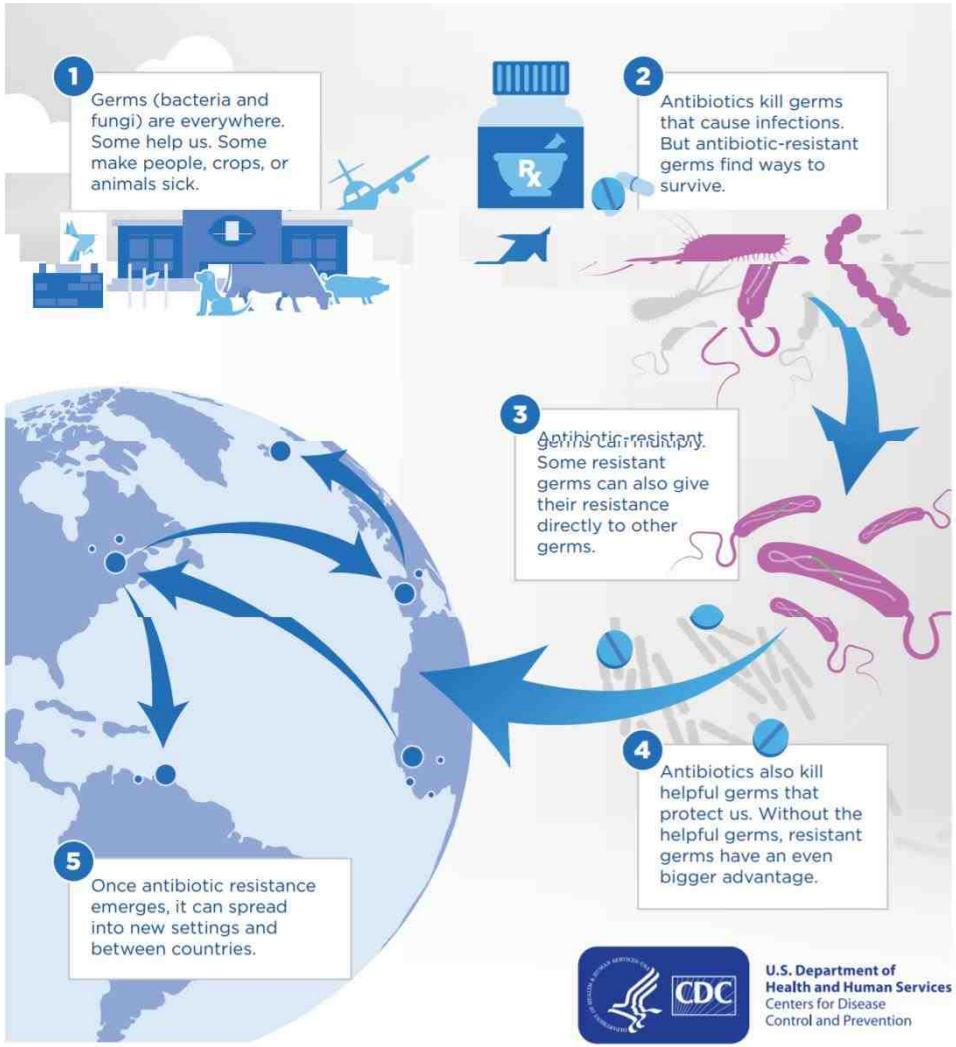
Examples of Defense Strategies for Germs

Resistance Mechanisms (Defense Strategies)	Description
Restrict access of the antibiotic	Germs restrict access by changing the entryways or limiting the number of entryways. **Example:** Gram-negative bacteria have an outer layer (membrane) that protects them from their environment. These bacteria can use this membrane to selectively keep antibiotic drugs from entering.
Get rid of the antibiotic	Germs get rid of antibiotics using pumps in their cell walls to remove antibiotic drugs that enter the cell. **Example:** Some *Pseudomonas aeruginosa* bacteria can produce pumps to get rid of several different important antibiotic drugs, including fluoroquinolones, beta-lactams, chloramphenicol, and trimethoprim.

Examples of Defense Strategies for Germs

Change or destroy the antibiotic	Germs change or destroy the antibiotics with enzymes, proteins that break down the drug. **Example:** *Klebsiella pneumoniae* bacteria produce enzymes called carbapenemases, which break down carbapenem drugs and most other beta-lactam drugs
Bypass the effects of the antibiotic	Germs develop new cell processes that avoid using the antibiotic's target. **Example:** Some *Staphylococcus aureus* bacteria can bypass the drug effects of trimethoprim
Change the targets for the antibiotic	Many antibiotic drugs are designed to single out and destroy specific parts (or targets) of a bacterium. Germs change the antibiotic's target so the drug can no longer fit and do its job. **Example:** *Escherichia coli* bacteria with the *mcr*-1 gene can add a compound to the outside of the cell wall so that the drug colistin cannot latch onto it.

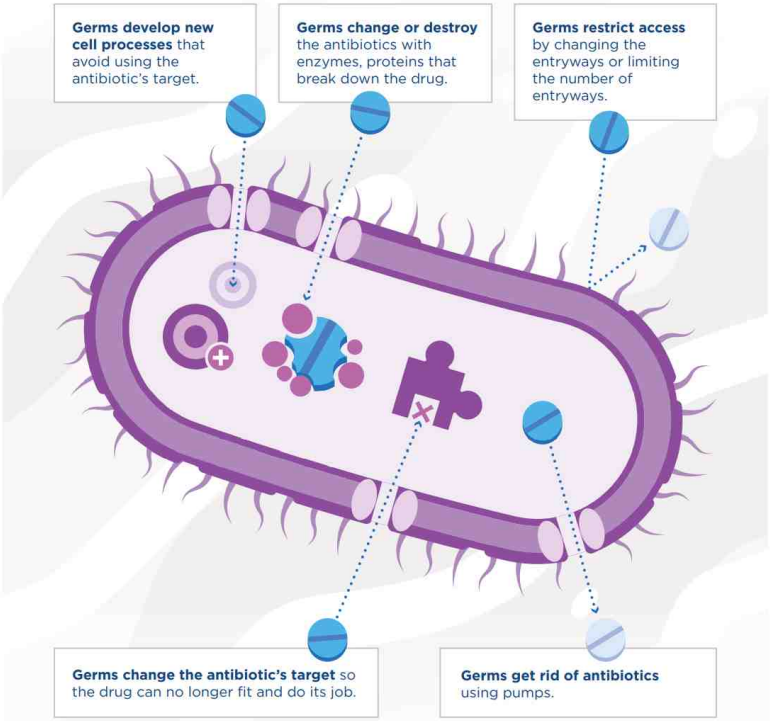
How Antibiotic Resistance Spreads



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

How Bacteria and Fungi Fight Back Against Antibiotics

Antibiotics fight germs (bacteria and fungi). But germs fight back and find new ways to survive. Their defense strategies are called **resistance mechanisms**. Only germs, not people, become resistant to antibiotics.



How Antibiotic Resistance Moves Directly Germ to Germ

Any antibiotic use can lead to antibiotic resistance. Antibiotics kill germs like bacteria and fungi, but the resistant survivors remain.

Resistance traits can be inherited generation to generation. They can also pass directly from germ to germ by way of **mobile genetic elements**.

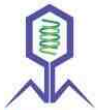
Mobile Genetic Elements

Plasmids

Circles of DNA that can move between cells.

Transposons

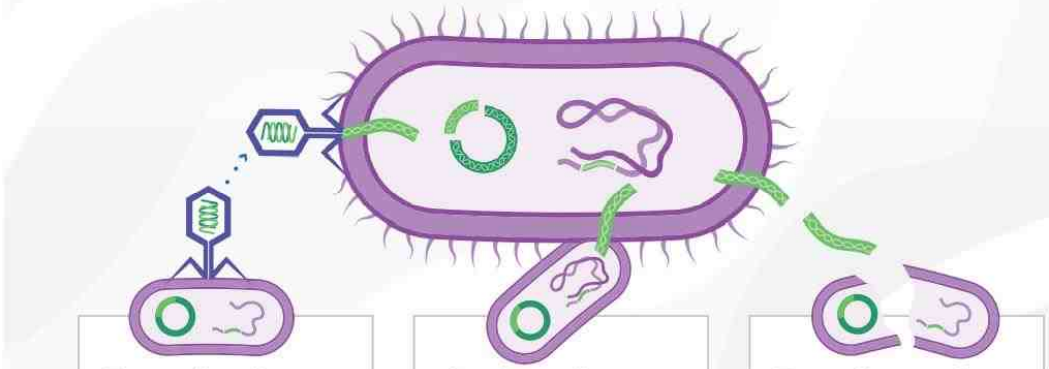
Small pieces of DNA that can go into and change the overall DNA of a cell. These can move from chromosomes (which carry all the genes essential for germ survival) to plasmids and back.



Phages

Viruses that attack germs and can carry DNA from germ to germ.

How Mobile Genetic Elements Work



Transduction

Resistance genes can be transferred from one germ to another via phages.

Conjugation

Resistance genes can be transferred between germs when they connect.

Transformation

Resistance genes released from nearby live or dead germs can be picked up directly by another germ.

Healthcare infection control is critical to fight antibiotic resistance and COVID-19.

Patients hospitalized with a viral infection, such as COVID-19 or influenza (flu), can also get infections caused by bacteria or fungi. These are sometimes referred to as "secondary" infections. during the pandemic in 2020 indicate that, overall, most hospitalized patients with COVID-19 are about as likely to have a secondary infection as hospitalized patients with influenza-like illness (influenza-like is used for flu surveillance worldwide, defined as fever and cough and/or sore throat).

Data show that hospitalized patients with COVID-19 were likely to get these secondary bacterial or fungal infections while in the hospital (called hospital-onset infections). In contrast, hospitalized patients with influenza-like illness more often got secondary bacterial or fungal infections while in the community (called community-onset infections) before hospitalization.

These data show that patients with COVID-19 may be more susceptible to getting a secondary infection while hospitalized. Infections that occur while in a hospital are more likely to be caused by resistant germs.

Also, during the pandemic in 2020, some germs—including methicillin-resistant *Staphylococcus aureus* (MRSA)—caused more hospital-onset blood infections overall (in all patients, not just those with COVID-19 infections).

Reports also describe hospital-onset COVID-19-associated pulmonary aspergillosis (infections caused by the fungus *Aspergillus*, which can be resistant with few treatment options). Scientists thought that aspergillosis occurred mostly in people with weakened immune systems or organ transplants. However, in recent years and during the pandemic, it has been increasingly reported as a co- or secondary respiratory infection among people with other respiratory infections, like COVID-19. Resistant *Aspergillus fumigatus* is emerging globally though only a few cases have been reported in the United States.

Reports describe sporadic antibiotic-resistant outbreaks in COVID-19 units and higher rates of hospital-onset infections.

There have been outbreaks of antibiotic-resistant *Acinetobacter* and *Candida*, including *C. auris*, in COVID-19 units. Scientists suspect that infection control lapses caused by pressures of the pandemic (e.g., increased hospitalizations, PPE shortages) may have influenced the spread of these germs in hospitals. CDC and public health partners responded to more than 20 outbreaks caused by resistant

Antibiotic use varies across healthcare settings.

Antibiotics are not effective against COVID-19 because antibiotics do not treat infections caused by viruses. Antibiotics save lives but any time antibiotics are used, they can cause side effects and lead to antibiotic resistance.

- In hospitals, antibiotic use increased for some specific antibiotics like azithromycin and ceftriaxone, which are often used to treat community-onset respiratory infections. This use likely reflects difficulties in distinguishing COVID-19 from community-acquired pneumonia caused by bacteria when patients first arrive for inpatient healthcare.

- In outpatient settings, such as doctor's offices, antibiotic use has dropped significantly. This is likely because outpatient healthcare use declined during the pandemic. Azithromycin prescribing was higher than expected, especially in geographic areas with high numbers of COVID-19 cases. This might be a reflection of its early promotion as a potential therapy, despite its ineffectiveness against viruses.

Experts are concerned that the pandemic could undo much of the nation's progress on antibiotic resistance, especially in hospitals.

Data show that COVID-19 can create a perfect storm for antibiotic-resistant infections in healthcare settings. For example, some patients with COVID-19 might stay in hospitals for a long time. Hospitals have also experienced staffing shortages, a higher number of sick patients to care for, and difficulties implementing infection control practices. Unfortunately, these burdens on some healthcare systems could have made it harder to track hospital-onset infections early in the pandemic.

In the community, public health personnel experienced difficulty monitoring antibiotic-resistant germs like drug-resistant gonorrhea and foodborne germs.

Public health personnel have been diverted to the pandemic response, and people had reduced access to care and testing services. For example, fewer people received regular screening for gonorrhea, according to data presented during a 2020 STD Prevention Conference panel discussion and a National Coalition of STD Directors . This means many cases were not identified, leading to the possible spread of more infections—including potentially antibiotic-resistant ones

- In nursing homes, antibiotic use spiked with changes in the pandemic, but remains lower overall compared to pre-pandemic measurements. In nursing home settings, azithromycin prescribing remained elevated through October 2020.

Some testing for antibiotic resistance slowed during the pandemic.

The number of bacterial and fungal specimens and isolates received/tested in 2020 by CDC's AR Lab Network was about 23% less than 2019 levels. This may be because healthcare facility and public health staff had to shift focus to COVID-19. The AR Lab Network's seven regional labs supported each other during the COVID-19 pandemic to maintain critical national testing for antibiotic resistance. For example, some labs offered tests outside of their typical regions when others were challenged by supply shortages or staff and equipment were diverted to COVID-19 testing.

Biggest Threats and Data

According to the report, **more than 2.8 million antibiotic-resistant infections occur in the U.S. each year, and more than 35,000 people die** as a result. In addition, 223,900 cases of *Clostridioides difficile* occurred in 2017 and at least 12,800 people died.

Additionally, the estimated national cost to treat infections caused by six multidrug-resistant germs identified in the report and frequently found in health care can be substantial—more than $4.6 billion annually.

Dedicated prevention and infection control efforts in the U.S. reduced deaths from antibiotic-resistant infections by 18% overall and by nearly 30% in hospitals. However, the number of people facing antibiotic resistance is still too high. More action is needed to fully protect people.

Biggest Threats and Data

CDC is concerned about rising resistant infections in the community, which can put more people at risk, make spread more difficult to identify and contain, and threaten the progress made to protect patients in healthcare. The emergence and spread of new forms of resistance remains a concern.

The report lists 18 antibiotic-resistant bacteria and fungi into three categories based on level of concern to human health—urgent, serious, and concerning—and highlights:

Urgent Threats

- Carbapenem - resistant *Acinetobacter*
- *Candida auris*
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacterales
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- ESBL-producing Enterobacterales
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)

Concerning Threats

- Erythromycin-Resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

Watch List

- Azole-resistant *Aspergillus fumigatus*
- Drug-resistant *Mycoplasma genitalium*
- Drug-resistant *Bordetella pertussis*

Urgent Threats

Carbapenem-resistant *Acinetobacter*

Type: Bacteria

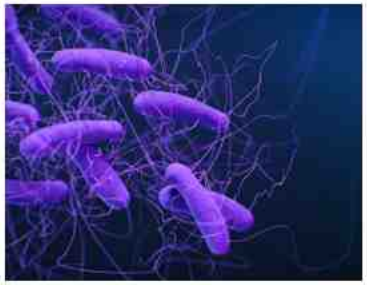
About: Carbapenem-resistant *Acinetobacter* cause pneumonia and wound, bloodstream, and urinary tract infections. Nearly all these infections happen in patients who recently received care in a healthcare facility.

Drug-resistant *Candida auris* (*C. auris*)

Type: Fungus

About: *C. auris* is an emerging multidrug-resistant yeast. It can cause severe infections and spreads easily between hospitalized patients and nursing home residents.

Clostridioides difficile (C. difficile)



Type: Bacteria

Also known as: *C. difficile* or *C. diff*, previously *Clostridium* difficile

About: *C. difficile* causes life-threatening diarrhea and colitis (an inflammation of the colon), mostly in people who have had both recent medical care and antibiotics.

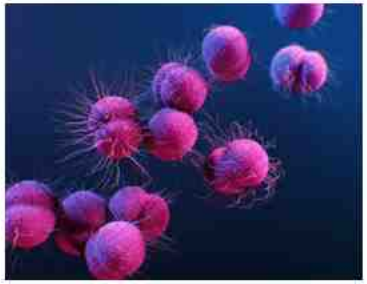
Carbapenem-resistant Enterobacterales (CRE)

Type: Bacteria

Also known as: Nightmare bacteria

About: CRE are a major concern for patients in healthcare facilities. Some Enterobacterales are resistant to nearly all antibiotics, leaving more toxic or less effective treatment options.

Drug-resistant *Neisseria gonorrhoeae (N. gonorrhoeae)*



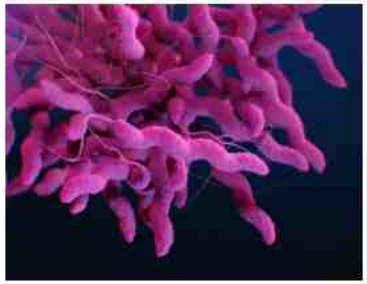
Type: Bacteria

Also known as: Drug-resistant gonorrhea

About: *N. gonorrhoeae* causes the sexually transmitted disease gonorrhea that can result in life-threatening ectopic pregnancy and infertility, and can increase the risk of getting and giving HIV.

Serious Threats

Drug-resistant *Campylobacter*

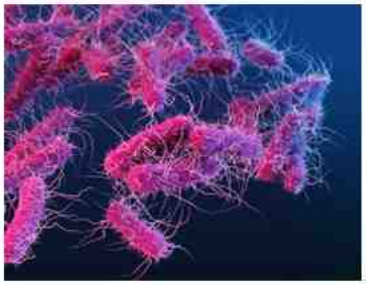


Type: Bacteria

Also known as: Campy

About: *Campylobacter* usually causes diarrhea (often bloody), fever, and abdominal cramps, and can spread from animals to people through contaminated food, especially raw or undercooked chicken.

ESBL-producing Enterobacterales



Type: Bacteria

Also known as: Extended-spectrum β-lactamase

About: ESBL-producing Enterobacterales are a concern in healthcare settings and the community. They can spread rapidly and cause or complicate infections in healthy people.

- ESBL stands for extended-spectrum beta-lactamase. ESBLs are enzymes that break down commonly used antibiotics, such as penicillins and cephalosporins, making them ineffective.

Vancomycin-resistant *Enterococcus* (VRE)

Type: Bacteria

About: Enterococci can cause serious infections for patients in healthcare settings, including bloodstream, surgical site, and urinary tract infections.

Estimated cases in hospitalized patients in 2017: 54,500

Estimated deaths in 2017: 5,400

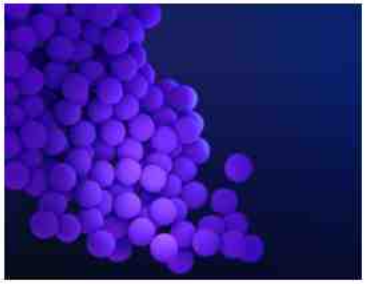
Multidrug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*)

Type: Bacteria

About: *P. aeruginosa* infections usually occur in people with weakened immune systems, and can be particularly dangerous for patients with chronic lung diseases.

Estimated cases in hospitalized patients in 2017: 32,600

Methicillin-resistant *Staphylococcus aureus (S. aureus)* (MRSA)

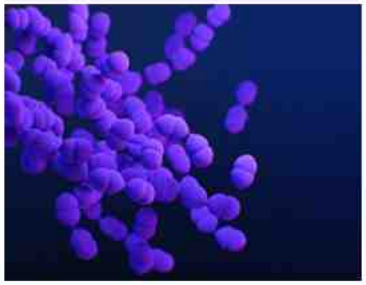


Type: Bacteria

Also known as: Resistant staph (short for *Staphylococcus*)

About: *S. aureus* are common bacteria that spread in healthcare facilities and the community. MRSA can cause difficult-to-treat staph infections because of resistance to some antibiotics.

Drug-resistant *Streptococcus pneumoniae (S. pneumoniae)*



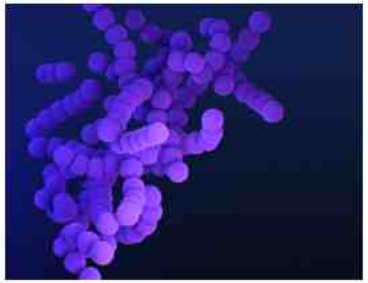
Type: Bacteria

Also known as: Pneumococcus

About: *S. pneumoniae* causes pneumococcal disease, which can range from ear and sinus infections to pneumonia and bloodstream infections.

Concerning Threats

Erythromycin-resistant Group A *Streptococcus*

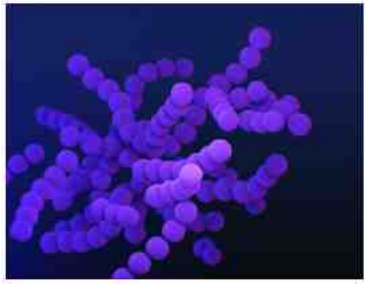


Type: Bacteria

Also known as: Resistant group A strep, GAS

About: GAS can cause many different infections that range from minor illnesses to serious and deadly diseases, including strep throat, pneumonia, flesh-eating infections, and sepsis.

Clindamycin-resistant Group B *Streptococcus*



Type: Bacteria

Also known as: Resistant group B strep, GBS

About: GBS can cause severe illness in people of all ages.

Estimated drug-resistant infections in 2016: 13,000

Watch List

Azole-resistant *Aspergillus fumigatus*

Aspergillus is a fungus that can cause life-threatening infections in people with weakened immune systems. These infections are treated with antifungals called azoles. Azoles are also increasingly used in agriculture to prevent and treat fungal diseases in crops. Azole use in human medicine and agriculture can contribute to resistance to antifungal medicines.

Antibiotic Resistance: 5 Things To Know

1 Antibiotic resistance occurs when germs defeat the drugs designed to kill them.

It does **NOT** mean the body is resistant to antibiotics.

2 Antibiotic resistance can affect people at any stage of life.

Infections caused by resistant germs are difficult—sometimes impossible—to treat. In many cases, these infections require extended hospital stays, additional follow-up doctor visits, and the use of treatments that may be costly and potentially toxic to the patient.

3 Healthy habits can protect you from infections and help stop germs from spreading.

Get recommended vaccines, keep hands and wounds clean, and take good care of chronic conditions, like diabetes.

4 Antibiotics save human and animal lives. Any time antibiotics are used, they can lead to side effects and resistance.

Antibiotics do not work on viruses, such as colds and the flu. Talk to your healthcare provider or veterinarian about whether antibiotics are needed.

5 Antibiotic resistance has been found in all regions of the world.

Modern trade and travel mean AR can move easily across borders. It can spread in places like hospitals, farms, the community, and the environment. Tell your healthcare provider if you recently traveled to or received care in another country.