

History of Sewage and Antibiotics

The history of anti-biotic success parallels the success of sewage treatment. They seem to occur in similar times in history. New research in many journals has questioned the effectiveness of antibiotics. Most studies show that placebo is as effective as and sometimes more effective than antibiotics. Could it be that the drug companies have claimed success with their anti-biotics that is actually more attributable to sewage reducing micro-orgasms levels than the antibiotics? If you read these articles maybe you will agree.

Map Stops Cholera

John Snow's Map of London

By [Matt Rosenberg](#),

[Washington Road Map](#) [European Geography](#) [The World Map](#) [Longest River in Europe](#)
[Water Resources Management](#)

In the mid-1850s, there were two major theories about the transmission of cholera. Dr. John Snow used techniques which would later be known as medical geography to confirm that the transmission of the disease occurred by swallowing contaminated water or food and not by inhaling infected air.

Dr. Snow knew that he had identified the transmission method for the "cholera poison." This "poison" was later identified as the bacterium VIBRIO CHOLERAE. Cholera leads to an infection of the small intestine which results in extreme diarrhea which may lead to massive dehydration and death. The disease can be treated by giving the victim a lot of fluids -- either by mouth or intravenously (directly into the blood stream).

As sanitation and more effective water treatment increases throughout the world, the number of cholera victims decreases. Cholera has existed in Northern India for centuries and it is from this region that regular outbreaks are spread. The disease diffuses as people travel from the source area. With modern transportation such as airplanes, diseases can be spread a great distance very rapidly.

In the nineteenth century, there were several outbreaks of cholera in London. In the 1849 outbreak, a large proportion of the victims received their water from two water companies. Both of these water companies had the source of their water on the Thames River, just downstream from a sewer outlet. In an 1854 outbreak, most of the deaths occurred within the area of the Southwark and Vauxhall Water Company. Fortunately, just before the outbreak, the Lambeth Water Company relocated their water source to a less polluted point so fewer deaths occurred among their customers. The distribution of deaths was one of the primary factors which proved that the deaths were caused by ingestion.

Dr. Snow plotted the distribution of deaths in London on a map. He determined that an unusually high number of deaths were taking place near a water pump on Broad Street. Snow's findings led him to petition the local authorities to remove the pump's handle. This was done and the number of cholera deaths was dramatically reduced.

The work of Doctor Snow stands out as one of the most famous and earliest cases of geography and maps being utilized to understand the spread of a disease. Today, specially trained medical geographers and medical practitioners routinely use mapping and advanced technology to understand the diffusion and spread of diseases such as AIDS and cancer. A map is not just an effective tool for finding the right place, it can also be a life saver.

George E. Waring: Modern Sewage Disposal (1891)

The life of man involves both the production of food, directly or indirectly by the growth of plants, and the consumption and destruction of the organized products of such growth. The production and the destruction are constant. Between consumption and renewed growth there intervenes a process which prepares what we reject for the use of plants.

It is this intervening process that we have to consider in applying the comparatively new art of sewage disposal. The process itself has gone on from the beginning of the world, but it has been left to unguided natural action, which takes no account of the needs and conditions of modern communities.

In the primitive life of sparse populations, it was comparatively safe to disregard it; but, as population became more dense, and, especially as men gathered into communities, it became increasingly important to bring it under control, for it then involved a serious menace to the safety of the people. So long as our offscourings could be scattered broadcast over the ground, their destruction was attended with little danger; but when it became necessary to concentrate them in underground receptacles, a capacity for real mischief was developed. As these receptacles increased, with the growth of communities, the menace increased, until, in the light of modern knowledge as to the conditions of healthful living, the need for radical measures of relief became obvious. It is the application of these measures that we are now to consider.

The sewerage of towns, and the drainage of important buildings, are now controlled by expert engineers, and they rarely fail to be reasonably well done. The economy of good plans is understood, and especially the vital necessity for good construction. In fact, it may be said that the adoption of excellent methods and appliances for removing liquid wastes from houses and towns is becoming general. It will in time

become universal.

This, however, is only the first step in sanitary improvement. It is only the step of removal. It gets our wastes out of our immediate neighborhoods; it does not destroy them. It is now recognized that quick and complete removal is only the beginning of the necessary service, and that proper ultimate disposal is no less important to health, to decency, and to public comfort. The organic wastes of human life must be finally and completely consumed. It is not enough to get them out of the house and out of the town; until they are resolved into their elements, their capacity for harm and for offense is not ended. It does not suffice to discharge them into a cesspool, nor does it always suffice to discharge them into a harbor, or into a water-course, leaving them there to the slow process of putrefaction.

The need for improving the conditions of sewage disposal has long been recognized, and, especially in connection with large foreign towns, efforts of the most costly character have been made to obviate accumulations due to the discharge of sewers. The floods made foul with the wastes of the huge population of London have been poured into the Thames, until, in spite of years of effort to relieve that river, its condition has become, in the language of Lord Bramwell, "a disgrace to the Metropolis and to civilization." The millions expended since 1850 on the still unsolved problem have not thus far effected more than a mitigation of the evil. London is today, apparently, as far as ever from its ultimate solution, though of course the former direct discharge of sewage all along the river front, and the resulting local stench, have been suppressed. The case grows in gravity with the growth of the population, and measures which promise success when adopted are not able to cope with the greater volumes produced later....

In our country, New York City and the towns on the Mississippi, and on other very large rivers, have such tidal and flood conditions as to secure satisfactory disposal by dilution and removal. At Boston, Philadelphia, and Chicago, the needed relief can, under the methods adopted, be secured only by works of the greatest magnitude and cost, while the smaller towns have, as a rule, yet to devise methods by which, unless they are exceptionally well placed, they can destroy their wastes at a practicable cost. The importance of relief is being more and more realized, but the means of relief are little understood by the people. A wider appreciation of the efficiency of these means is a necessary condition precedent to general improvement.

Systematic works, chiefly by removal through intercepting sewers, have, until recently, been confined to cities. Smaller towns are now perfecting their methods of removal, and there is a growing desire to find means for purifying the outflow which will not cost more than can be afforded. Interest is also growing among householders, who are becoming convinced of the dangers of cesspools, with their retention of putrefying wastes within contaminating reach of houses and of their sources of water supply.

In its progress thus far, the art of disposal has worked itself out mainly by

progressive practice. It began in the instinctive desire to get offensive matters out of sight. As new difficulties presented themselves, and as the requirements of a better civilization arose, new methods were devised for better concealment in the ground, or better removal by sewers.... It is hardly half a century since the dangers of incomplete sewage removal were appreciated and radical measures of relief were attempted. In London, large brick sewers, not only in the streets, but under and about houses, which had long existed as the seats of foul deposits, now had their condition pointed out, and a "Blue Book" of the British Parliament, published in 1852, set it forth in a manner to secure effective attention. It was shown that these sewers and drains were so large that they could not be kept clean by their natural flow. It was then that the movement for the use of pipes for sewerage and house drainage received its first general impetus.

In 1857 there was presented to Parliament a report by Henry Austin, C.E., on the means of deodorizing and utilizing the sewage of towns. There followed, not only an improvement of much of the local drainage on London, but the carrying out of a plan for keeping foul sewage out of the Thames, by collecting it in reservoirs some miles down the river, to be discharged at the beginning of the outgoing tide. As has already been intimated, this work was ineffective, so far as the main purpose of purifying the Thames was concerned, and the problem seems still to be overtaxing the capacity of English engineers.

There was, at that time, little knowledge of the proper means of relief in such cases, and the enormous sums spent in works for the discharge of the sewage on the outgoing tide soon proved to have been a misdirected expenditure. The art of sewerage had, for many years, confined itself to an improvement of the means for distant removal, and the world accepted and still accepts, as a part of the policy of its great cities, the inevitable construction of majestic and costly engineering works for this service, carrying not only foul sewage, but floods of storm water as well. It is now demonstrated that, even at London, and in all but a few exceptional conditions, like those of New York, where the whole harbor is flushed twice a day by the great tides coming in through Long Island Sound and passing out at Sandy Hook, and of towns on great rivers, the effect of such works is, largely, to remove the point of deposit, not to prevent deposit, and that the great volume of their discharge has often added to the difficulty of final disposal.... Sooner or later, the provision of some means of purification, or, at least, of the removal of the grosser impurities of the sewerage, becomes imperative, and the question of sewage disposal is assuming greater importance year by year.

The tendency of legislation, here as well as abroad, is toward the prohibition of the fouling of rivers, thus far mainly for the protection of sources of water supply. This is doing much, and promises to do more, in the way of restricting the free discharge of sewage into streams. There is also a growing sentiment in favor of cleanliness, and causes of offence which have hitherto been disregarded are now attracting attention. Those who occupy lands past which streams flow are beginning to assert and to enforce their undoubted right to have them flow in their natural un-fouled

condition....

So, too, on the larger streams, villages are growing to towns, towns are growing to important cities, and conditions which were formerly tolerable are now becoming intolerable. The Schuylkill River, for example, which is the most important source of water supply for Philadelphia, is lined with populous and growing manufacturing towns, which have only this river for an outlet, and which also take their water supply from it. The same conditions exist along many of the rivers of New England, and throughout the older parts of the country generally, and they are extending westward. It is therefore clear that, in the case of towns not lying on the larger rivers, public sentiment and the rights of riparian owners will demand the increasing adoption of means for withholding crude sewage from them.

The following was written [by Waring] in 1888: "It is not likely that towns situated on great rivers or on the seacoast will, for a long time to come, give thought to any other disposal of their sewage than its discharge directly into the river or into the sea. As the country fills up, and as towns situated on small streams, or on no stream, increase in size and in wisdom, they must, perforce, seek for some means to get rid of the copious flow of water, made foul by its passage through the houses and shops of the people. The indications are clear that legislative control of this matter cannot long be delayed, and there is no more intricate or more interesting problem now presented to the sanitarian than the correct solution of this great question of the future...."

During the years that have since elapsed, the most important investigations of the Massachusetts State Board of Health . . . have confirmed the theories then held, and have thrown much light on the methods by which they may best be reduced to practice. It was only after this clear definition and demonstration of the processes involved, and of the methods of their application, that we were in a position to work with real knowledge. Then only could empiricism be made to give place to well Established theory.

Could we now set aside the influence of long years of practical work, the atmosphere would be greatly cleared; but practical work has a very persistent influence, and the art of purifying sewage will long feel the effect of experience with methods which would not have been devised in the light of what is now known. When the first attempts were made to get rid of the impurities of sewage by artificial means, great importance was universally attached to their manurial value, and promise was held forth of great profit to result from their development into a useful form. The obstacle of extreme dilution was not appreciated, and it was long before the discovery was made that, as with the gold said to exist in sea water, the attempt to separate these matters by artificial methods would cost more than they were worth.

The belief also prevailed that the chief source of offensiveness of sewage lay in the solid fecal matter that it contained, and this belief still finds much popular

acceptance. One of the most prominent sanitary exhibits at the World's Fair in Chicago, a Russian invention, has the separation of this matter for its chief end, and the description accompanying it urges such separation as the sine qua non and the chief need of hygiene improvement. Even in Paris, where the purification of sewage is being carried out on a very large scale, and where its requirements are well understood, the use of the tinette filtre, which holds back the solid parts of house drainage until they putrefy, and then allows them to flow to the sewer, in this worst possible form, has within recent years been allowed to come into extensive use. At Newport the old rule still prevails largely, that house drainage shall be retained in cesspools until it can, after decomposition, overflow as a foul liquid into the public sewers. The fact is, that fecal matter is of far less consequence than urine and the waste of the kitchen sink.

Then, too, it was long thought that if sewage could be purged of its suspended matter,--of that which clouds it and colors it,--purification would be effected. An imperfect clarification by mechanical or chemical processes is still applied in some cases where a high degree of purification is really needed, although it is now well known that such clarification does not and cannot remove from sewage its most putrescible matters, nor its minute living organisms. Imperfect results, which have satisfied legal requirements in Europe, are in such cases accepted as sufficient, in spite of a recognition of their incompleteness.

The purification of sewage is surely on the eve of great extension in this country, and it is necessary to its success that the importance of making it as thorough as possible be made known, as well as its conditions and requirements. If the work is to be done at all, it is worthwhile to do it well. Half-way measures, like chemical precipitants, may satisfy present legal demands, and they may, in exceptional cases, be advisable, but they will not meet the requirements of the better-informed public opinion that is now growing up. The means for entire purification are within reach, and imperfect results will not long be accepted as sufficient.

In practical work, two cardinal principles should be kept in view, and should control our actions:-

- (a) Organic wastes must be discharged at the sewer outlet in their fresh condition,--before putrefaction has set in; and
- (b) They must be reduced to a state of complete oxidation without the intervention of dangerous or offensive decomposition.

History of sewage management

Indoor plumbing in 8000 B.C.

Flush toilets first used circa 3000 B.C.

Evidence of indoor plumbing dates as far back as 8000 B.C.

The history of the toilet may not be everyone's idea of a good topic for a luncheon presentation, but then not everyone is a member of the Public Works Historical Society (PWHS).

During the PWHS annual meeting at the Public Works Congress, Jon Schladweiler, deputy director of Pima County (Arizona) Wastewater Management Department, told some fascinating tales about the early development of modern day toilets, sewer systems, and wastewater treatment methods.

Incredibly, the first signs of plumbing, he said, date back as far as 8000 B.C. in Scotland where evidence has been found of indoor plumbing pipes or troughs that carried water and wastes out to a nearby creek.

Approximately 4000 years later in Iraq, man was using the percolation system of drainage of waste as evidenced by what appeared to be round, vertical cesspits under the homes, 30 to 40 feet deep, lined with perforated brick.

By 3000 to 2000 B.C., the inhabitants of Mohenjo-Daro (in modern-day Pakistan) began assigning a separate room in the house to be a latrine room. Here drains were connected to a sewer in the street; ultimately the wastes went to either the Indus River or to large cesspits.

Flush toilets first used circa 3000 B.C.

About the same time on the Isle of Crete, flush toilets, with overhead reservoirs filled and flushed by servants or slaves, were used.

And if you think modern-day sewer projects take time, consider that in Rome work began on a sewer system - the Cloaca Maxima - in 735 B.C. and was not finished until 225 years later. But also consider, that same sewer is still being put to some beneficial use today, Schladweiler said.

Following the Middle Ages and the Fall of Rome, infrastructure building came to a near halt and was not resurrected for hundreds of years. People ceased the recreational bathing they once enjoyed, and it became popularly known that baptism was about the only total immersion many endured during their lifetimes.

Wastes were thrown into the streets, out doors, and from overhead windows. It was this habit, according to Schladweiler, that led to the Dejecti Efflusive Act in Rome, which allowed one to collect damages from being hit by wastes. It was also during this practice that, Schladweiler believed, it became polite for the gentleman to walk on the outside of a lady when walking down a street. This way, the gentleman would be more in the line of fire from wastes being thrown from overhead. "Many people think this custom was to protect a lady from being splashed by a passing carriage," he said, "but I believe that etiquette dates further back and actually derives from the waste throwing."

Up until the 1500s, Schladweiler said, people were fairly careless and uncouth about where they deposited their bodily wastes. "Stairways, closets, corners were often fouled," he said. "People became accustomed to the stench." In Erasmus' writings on etiquette, he declared it was most rude to observe as

one relieved himself. Such was the commonness of public elimination that it was necessary to determine a protocol. Around the late 1596, Schladweiler continued, a gentleman seeking the queen's favor in England designed a toilet complete with a seal around the seat and cesspool into which it emptied. Still it did not become a popular notion.

Castle wastes channeled to moats and cesspits

Castles of the time did develop some form of discharge of wastes into surrounding moats or into large cesspools beneath the castle. It was particularly advantageous to build a portion of a castle out over water—the perennial solution to the ridding of wastes. Unfortunately, in some areas of the world, not a lot has changed.

Solid wastes began to become a problem along with the human wastes. In some of the larger cities where populations were dense, major health and aesthetic problems developed. In Berlin, a solution was sought with a law requiring every peasant that came into town to sell wares to carry a measure of garbage out with him when he left.

In Paris, landfills were developed for human wastes and remains and underground sewers began to be built. So accustomed to the stench and proud of their sewers were the French that they conducted weekend tours for the citizenry. Ladies and gentlemen in their Sunday best went for a cruise down the sewer pipe. The boats had wings that projected from each side which cleaned the sides as they went down the pipe. On weekends, these same boats carried the touring citizens.

Across the channel, in London, storm water and sewage were diverted into the Thames River to such an extent it became a dead river. In 1857 the stench from the river was so great that the English Parliament could not meet. Heavy curtains soaked in lime were hung over the windows to prevent the odor from permeating the building; often times, even that was not sufficient.

In Germany, a primitive flushing of the sanitary sewers was accomplished by the ebb and flow of the river tides. Wastes were literally flushed out with the tide.

When the immigrants journeyed to the New World, they tried to do things better by learning from the past. Progress was slow, but it continued as the larger cities devised systems to carry their wastes to the nearest body of water. In the mid-1800s, Boston was the site of the first "interceptor" system in the country. Early pipes, some of which still exist today, were made of clay, brick and hollowed logs. Washington, D.C. became the first city to use concrete for its sanitary sewers.

As the population began to link the spread of disease with their waste disposal methods, more and more innovative ideas were developed. Homes were located near creeks with privies linked by a foot bridge extending out over the water so that the wastes were dropped into the water and carried off. Schladweiler did not comment on what happened during dry season.

Excerpt from article, "1998 Congress Recap" by Joyce Everhart Jungclaus, published in the APWA Reporter. Used by permission. For more information call APWA, 816-472-6100.

Search Results

1800's

US population grew from 5 million to 75 million

PRIMARY DEVELOPMENT: COLLECTION SYSTEMS

PRIMARY PURPOSE: DISEASE PREVENTION

Pit privies and open ditches replaced by buried sewers: sewer population increased from 1 million in 1860 to 25 million by 1900.

"Treatment" was mostly dilution into receiving waters

EARLY MANAGEMENT PRACTICES

TRENDS: awareness and control of impacts of sewage discharge on receiving waters through standards, regulation, and simple treatment (probably now called "primary")

1887, first biological treatment, an intermittent sand filter, was installed in Medford, Mass.

1886, Standards for discharge loading and treatment developed at Lawrence, Mass experiment station and for Chicago, IL (Rudolph Hering)

1899, first federal regulation of sewage, Rivers and Harbors Appropriations ("Refuse Act") prohibited discharge of solids to navigational waters without permit from US Army Corps of Engineer

permit from US Army Corps of Engineers

1900's

Early 1900s, 1 million people served by 60 sewage treatment plants for removal of settling and floating solids.

TREND: population growth and sewer construction

1900-1930s, sewer population increased at ~ same rate as total population²

TREND: development of secondary (biological treatment)

1901: first trickling filter operated in Madison, WI

1909, first Imhoff tank (solids settling)

1914, first liquid chlorination process for effluent disinfection

1916, first activated sludge plant, San Marcos, T

1884 Nov 15, 1884 - The City Council in joint convention to-night listened to the report of the City Engineer, who was sent to Europe in the Spring to investigate the various plans in practical operation for the disposition and utilization of sewage, together with all matters relating thereto, ...
From [SEWAGE FOR PROVIDENCE](#). -

1887 May 4, 1887 - His Recommendations as to the Disposal of Sewage and Construction of System--Some Apparently Sound Suggestions. ... The most successful disposal of sewage is the disposal by irrigation, except where the sewage can readily be Into a large body of water, such as not to annoy people ...
From [CITY SEWERAGE](#). - Related web pages
pqasb.pqarchiver.com/latimes/access/318503852 ...

1889 Apr 1, 1889 - It is in this town, built upon land that two years ago was a wild prairie, that the system of sewerage which I wish to describe is in use. ... In the sewerage of certain towns the propriety of adopting the separate system is apparent. In other cases its superiority to the ...
From [The Pullman Sewerage](#) - Related web pages
cdl.library.cornell.edu/cgi-bin/moa/pageviewer ...

1899 Sep 21, 1899 - Lacoste said to-day that the question of the Dady con ession regarding Havana sewage would be by the Municipal Council to-morrow, but would probably not be settled then. Puerto Rican Relief Fund. The National Bank of North America, the depository for the Puerto Rican Relief Fund, ...
From [The Havana Sewage Concession](#). - Related web pages
select.nytimes.com/gst/abstract.html?res ...

- 1900 Jan 18, 1900 - The history of sanitary science furnishes proof that the fundamental theory of **sewage** in water, as Intended to be applied to the **Chicago** drainage canal, Is not correct or reliable, nor Is It a reasonable guarantee that Its application under conditions prevailing in the ...
From **INJUNCTION ASKED OF KOHLSAAT** - [Related web pages](#)
pqasb.pqarchiver.com/chicagotribune/access ...
- 1907 Jan 5, 1907 - Mr. **Hering** says that "the environment of **New York** does not offer '1,5 square miles of land suitable for **sewage** farming. ... History, however, so far as I am able to learn, does not record th disappearance of any railroad train or building Into this bottomless pit. ...
From **USE FOR JERSEY MEADOWS.; They Offer Site for [Sewage](#) Plants of That ...** - [Related web pages](#)
select.nytimes.com/gst/abstract.html?res ...
- 1912 Sep 20, 1912 - Forecast of the report of the Metropolitan Sewerage Commisison in New York, which is a board of engineers created to make plans for the protection of the waters of ... Dr. Soper, who is President of the Metropolitan Sewerage Comw,ston, was not present to present his paper personally. ...
From ... of **Experts Finds the Inner Harbor to be Polluted by [Sewage](#)**. - [Related web pages](#)
select.nytimes.com/gst/abstract.html?res ...
- 1913 Apr 21, 1913 - The necessity for prompt action in guarding New York against the disease-breeding waters contaminated by **sewage** in the Harlem, lower Hudson, and lower East Rivers and ... under Brooklyn to **Coney Island**, tile of all island **sewage** plant ..., miles off shore, and means to ...
From **[SEWAGE](#) PERIL HERE, SANITARIANS FIND; Englishmen Employed to Study ...** - [Related web pages](#)
select.nytimes.com/gst/abstract.html?res ...
- 1930 Major advances are just starting to make **sewage** control more viable
- 1988 Aug 7, 1988 - Given San Diego's history in **sewage** matters, the city does not appear to be in a very good bargaining position. Raw **sewage** was regularly

spilling into the bays and ocean before the city embarked on a program to renovate the current system. The city has repeatedly been fined for the ...
From [War Over City's Sewage System Not Worth Cost - Related web pages](#)
pqasb.pqarchiver.com/latimes/access/59852260 ...

2000 Mar 1, 2000 - Tuesday's Virginian-Pilot outlined a shameful 27-year history of sewage leaks at the trailer park. It told of children playing in raw sewage. Yet the place remains open for business. What does a business in [Chesapeake](#) have to do to be shut down? Then again, the park houses low-income ...

History of Antibiotics

Antibiotic Timeline

By [Mary Bellis](#), About.com

(Gr. anti, "against"; bios, "life") An antibiotic is a chemical substance produced by one organism that is destructive to another. The word antibiotic came from the word antibiosis a term coined in 1889 by Louis Pasteur's pupil Paul Vuillemin which means a process by which life could be used to destroy life.

Ancient History

The ancient Egyptians, the Chinese, and Indians of central America all used molds to treat infected wounds. However, they did not understand the connection of the antibacterial properties of mold and the treatment of diseases.

Late 1800s

The search for antibiotics began in the late 1800s, with the growing acceptance of the [germ theory of disease](#), a theory which linked bacteria and other microbes to the causation of a variety of ailments. As a result, scientists began to devote time to searching for drugs that would kill these disease-causing bacteria.

1871

The surgeon **Joseph Lister**, began researching the phenomenon that urine contaminated with mold would not allow the successful growth of bacteria.

1890s

German doctors, Rudolf Emmerich and Oscar Low were the first to make an effective medication that they called pyocyanase from microbes. It was the first antibiotic to be used in hospitals. However, the drug often did not work.

1928

Sir **Alexander Fleming** observed that colonies of the bacterium *Staphylococcus aureus* could be destroyed by the mold *Penicillium notatum*, demonstrating antibacterial properties.

1935

Prontosil, the first sulfa drug, was discovered in 1935 by German chemist Gerhard Domagk (1895–1964).

1942

The manufacturing process for **Penicillin G Procaine** was invented by Howard Florey (1898–1968) and Ernst Chain (1906–1979). Penicillin could now be sold as a drug. Fleming, Florey, and Chain shared the 1945 Nobel Prize for medicine for their work on penicillin.

1943

In 1943, American **microbiologist** Selman Waksman (1888–1973) made the drug streptomycin from soil bacteria, the first of a new class of drugs called aminoglycosides. Streptomycin could treat diseases like tuberculosis, however, the side effects were often too severe.

1955

Tetracycline was patented by Lloyd Conover, which became the most prescribed broad spectrum antibiotic in the United States.

1957

Nystatin was patented and used to cure many disfiguring and disabling fungal infections.

1981

SmithKline Beecham patented Amoxicillin or amoxicillin/clavulanate potassium tablets, and first sold the antibiotic in 1998 under the tradenames of Amoxicillin, Amoxil, and Trimox. Amoxicillin is a semisynthetic antibiotic.

History of antibiotics

Sulfa drugs. Sulfa drugs, originally developed for use in the dye industry, were the first effective drugs used to fight bacterial infection in humans. Prontosil, the first sulfa drug, was discovered in 1935 by German chemist Gerhard Domagk (1895–1964). Also called sulfonamides (pronounced sul-FOHN-uh-midze), these drugs are synthesized (made) in the laboratory from a crystalline compound called sulfanilamide (pronounced sul-fuh-NILL-uh-mide). They work by blocking the growth and multiplication of bacteria and were initially effective against a broad range of bacteria. However, many strains of bacteria have developed a resistance to sulfa drugs. Resistance occurs when some bacteria survive attack by the antibacterial drug and change in such a way that they are no longer affected by the drug's action.

Sulfa drugs are most commonly used today in the treatment of urinary tract infections. The drugs are usually taken by mouth, but other forms include creams that can be applied to burn wounds to prevent infection and ointments and drops used for eye infections.

Words to Know

Antibacterial: Working against bacteria either by destroying it or keeping it from multiplying.

Antibiotic resistance: The ability of bacteria to resist the actions of antibiotic drugs.

Soil bacteria: Bacteria found in the soil that destroy other bacteria.

Development of penicillin as an antibiotic. In 1928, British bacteriologist Alexander Fleming (1881–1955) discovered the bacteria-killing property of penicillin. Fleming noticed that a mold that had accidentally fallen into a bacterial culture in his laboratory had killed the bacteria. Having identified the mold as the fungus *Penicillium notatum*, Fleming made a juice with it that he named penicillin. After

giving it to laboratory mice, he discovered it killed bacteria in the mice without harming healthy body cells. Although Fleming had made an incredible discovery, he was unable to produce penicillin in a form useful to doctors.

It was not until 1941 that two English scientists, Howard Florey (1898–1968) and Ernst Chain (1906–1979), developed a form of penicillin that could be used to fight bacterial infections in humans. By 1945, penicillin was available for widespread use and was hailed as the new wonder drug. The antibiotic works by blocking the formation of the bacterial cell wall, thus killing the bacteria. It is still used successfully in the treatment of many bacterial diseases, including strep throat, syphilis (a sexually transmitted disease) and pneumonia. Fleming, Florey, and Chain shared the 1945 Nobel Prize for medicine for their work on penicillin.

The search for other antibiotics

Despite the effectiveness of penicillin, it was soon found that the drug worked against only certain types of bacteria. In 1943, American microbiologist Selman Waksman (1888–1973) developed the drug streptomycin from soil bacteria. It proved to be particularly effective against



A penicillin culture.

tuberculosis and was used in the treatment of many other bacterial infections. However, streptomycin caused harmful side effects, including hearing loss and vision problems that could lead to blindness.

The discovery of streptomycin led to the development of a new class of drugs called aminoglycosides (pronounced uh-MEE-noh-GLY-kuhzides) that include neomycin (pronounced ne-oh-MY-sin), kanamycin (pronounced kan-uh-MY-sin), and gentamicin (pronounced jen-tuh-MY-sin). These antibiotics work against bacteria that are resistant to penicillin, but they tend to have many of the same side effects as streptomycin and are used only for a short time in cases of serious infection.

Following World War II (1939–45), drug companies in the United States conducted worldwide searches to find molds and soil bacteria that could be synthesized (made in a lab) into antibiotics. Aureomycin (pronounced aw-ree-oh-MY-sin), the first of the class of antibiotics known as tetracyclines (pronounced teh-truh-SY-kleenz), was discovered in 1945. Another group, the cephalosporins (pronounced seff-uh-low-SPOR-inz), came from a bacteria group living in a drainage pipe on the Italian coast. The antibiotics in this group have effects similar to those of penicillin. Erythromycin (pronounced uh-ree-throw-MY-sin), made from soil bacteria found in the Philippines, is used in patients allergic to penicillin as well as to fight penicillin-resistant bacteria. Bacitracin (pronounced bass-uh-TRAY-sin), an antibiotic made from bacteria, was developed in 1945 and is used as an ointment that is applied directly to the skin.

Resistance to antibiotics

Resistance of bacteria to the effects of antibiotics has become a major problem in the treatment of disease. Bacteria that are not killed or stopped by antibacterial drugs may change in form so that they resist attack against their cell walls—or even produce enzymes that kill the antibiotics. Prescribing antibiotic drugs when they are not needed, not taking the drugs as prescribed, and using the drugs for long periods of time all contribute to the development of resistant strains of bacteria. The use of antibiotics in animal feed to promote animal growth has also led to the development of hardier strains of antibiotic-resistant bacteria. Since the first use of antibiotics in the 1940s, most known bacterial diseases have built up a resistance to one or more antibiotics.

Measures to control the spread of antibiotic-resistant diseases include prescribing the drugs only when necessary, prescribing the correct antibiotic for the disease being treated, and making sure the patient understands the importance of taking all of the prescribed medication. Research in newer types and

combinations of drugs is ongoing, as is research in the development of vaccines to prevent bacterial infections.

History of Quinolone Antibiotics

By Yury Bayarski ✨

The fluoroquinolone family is a relatively new group of antibiotics. They were first introduced in 1986, but they are really modified quinolones. The parent of the group is nalidixic acid. The majority of quinolones belong to a subgroup called fluoroquinolones, which have a fluoro group attached to the central ring system. Both terms are used to describe antibiotics in this class.

The fluoroquinolones have become an increasingly popular class of antibiotics for use in a variety of infections. These drugs are the only class of antimicrobial agents in clinical use that are direct inhibitors of bacterial DNA synthesis. Fluoroquinolones inhibit two bacterial enzymes, DNA gyrase and topoisomerase IV, which have essential and distinct roles in DNA replication.

The fluoroquinolones are classified into generations based on their antibacterial spectrum, with earlier generation quinolones more effective against Gram-negative bacteria and the spectrum of activity expanding to include more Gram-positive bacteria with the later generations.

The first-generation agents ("quinolones") had poor distribution into the body tissues and limited activity. They were used mainly for treatment of urinary tract infections. The early quinolones include: cinoxacin, nalidixic acid and oxolinic acid.

Second-generation fluoroquinolones have significantly increased antibacterial activity. These antibacterial agents have increased gram-negative activity, as well as some gram-positive and atypical pathogen activity. Compared with earlier quinolones, these drugs have broader clinical use in the treatment of complicated urinary tract infections and pyelonephritis, sexually transmitted diseases, pneumonias and skin infections.

Ciprofloxacin and ofloxacin are the most widely used second-generation fluoroquinolones because of their availability in oral and intravenous formulations and their broad set of FDA-approved indications.

The third-generation fluoroquinolones (levofloxacin, gatifloxacin, moxifloxacin, sparfloxacin, trovafloxacin) have expanded activity against gram-positive bacteria and atypical pathogens, such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Third-generation antibiotics are widely used in the treatment of community-acquired pneumonia, acute sinusitis and acute exacerbations of chronic bronchitis.

The fourth-generation fluoroquinolones (e.g. garenoxacin, gemifloxacin, trovafloxacin) add significant antimicrobial activity against anaerobes while maintaining the gram-positive and gram-negative activity of the third-generation antibiotics.

The quinolones have evolved from drugs used solely for the treatment of urinary tract infections to molecules with potent activity against a wide spectrum of bacterial pathogens and clinical utility in many indications throughout body tissues and fluids. Progressive modifications in molecular configuration have resulted in improved breadth and potency of activity and pharmacokinetics, which have identified those agents fit to survive in today's therapeutic environment.

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Antibiotic



Testing the susceptibility of *Staphylococcus aureus* to antibiotics by the Kirby-Bauer disk diffusion method. Antibiotics diffuse out from antibiotic-containing disks and inhibit growth of *S. aureus* resulting in a zone of inhibition.

In common usage, an antibiotic is a substance or compound (also called **chemotherapeutic agent**) that kills or inhibits the growth of **bacteria**.^[1] Antibiotics belong to the group of **antimicrobial** compounds used to treat infections caused by **micro-organisms**, including **fungi** and **protozoa**.

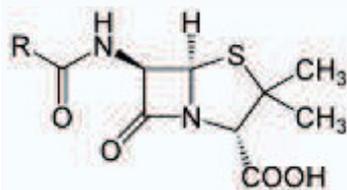
The term "antibiotic" (from the **Ancient Greek**: Ovri – anti, "against" and **Ancient Greek**: pio< – bios, "life") was coined by **Selman Waksman** in 1942 to describe any substance produced by a **micro-organism** that is antagonistic to the growth of other micro-organisms in high dilution.^[2] This original definition excluded naturally occurring substances, such as **gastric juice** and **hydrogen peroxide** (they kill bacteria but are not produced by micro-organisms), and also excluded synthetic compounds such as the **sulfonamides** (which are antimicrobial agents). Many antibiotics are relatively **small molecules** with a **molecular weight** less than 2000 Da.^[citations needed]

With advances in **medicinal chemistry**, most antibiotics are now modified chemically from original compounds found in nature,^[3] as is the case with **beta-lactams** (which include the

penicillins, produced by fungi in the genus *Penicillium*, the cephalosporins, and the carbapenems). Some antibiotics are still produced and isolated from living organisms, such as the aminoglycosides; in addition, many more have been created through purely synthetic means, such as the quinolones.^[citations needed]

History of antibiotics

See also: [Timeline of antibiotics](#)



Penicillin, the first natural antibiotic discovered by [Alexander Fleming](#) in 1928.

Many cures for infectious diseases prior to the beginning of the twentieth century were based on [medicinal folklore](#). Cures for infection in [ancient Chinese medicine](#) using plants with antibiotic-like properties began to be described over 2,500 years ago.^{[4][5]} Many other ancient cultures, including the [ancient Egyptians](#), [ancient Greeks](#) and [medieval Arabs](#) already used [molds](#) and plants to treat [infections](#).^{[6][7]} [Cinchona bark](#) was a widely effective treatment of [malaria](#) in the 17th century, the disease caused by protozoan parasites of the genus [Plasmodium](#).^[8] Scientific endeavours to understand the science behind what caused these diseases, the development of synthetic antibiotic chemotherapy, the isolation of the natural antibiotics marked milestones in antibiotic development.^[9]

Originally known as antiobiosis, antibiotics were drugs that had actions against bacteria. The term antiobiosis which means ‘against life’ was introduced by the French bacteriologist [Vuillemin](#) as a descriptive name of the phenomenon exhibited by these drugs.^[10] (Antiobiosis was first described in 1877 in bacteria when [Louis Pasteur](#) and [Robert Koch](#) observed that an airborne bacillus could inhibit the growth of [Bacillus anthracis](#).^[11]). These drugs were later renamed antibiotics by [Selman Wakeman](#), an American microbiologist in 1942.^{[12][10]}

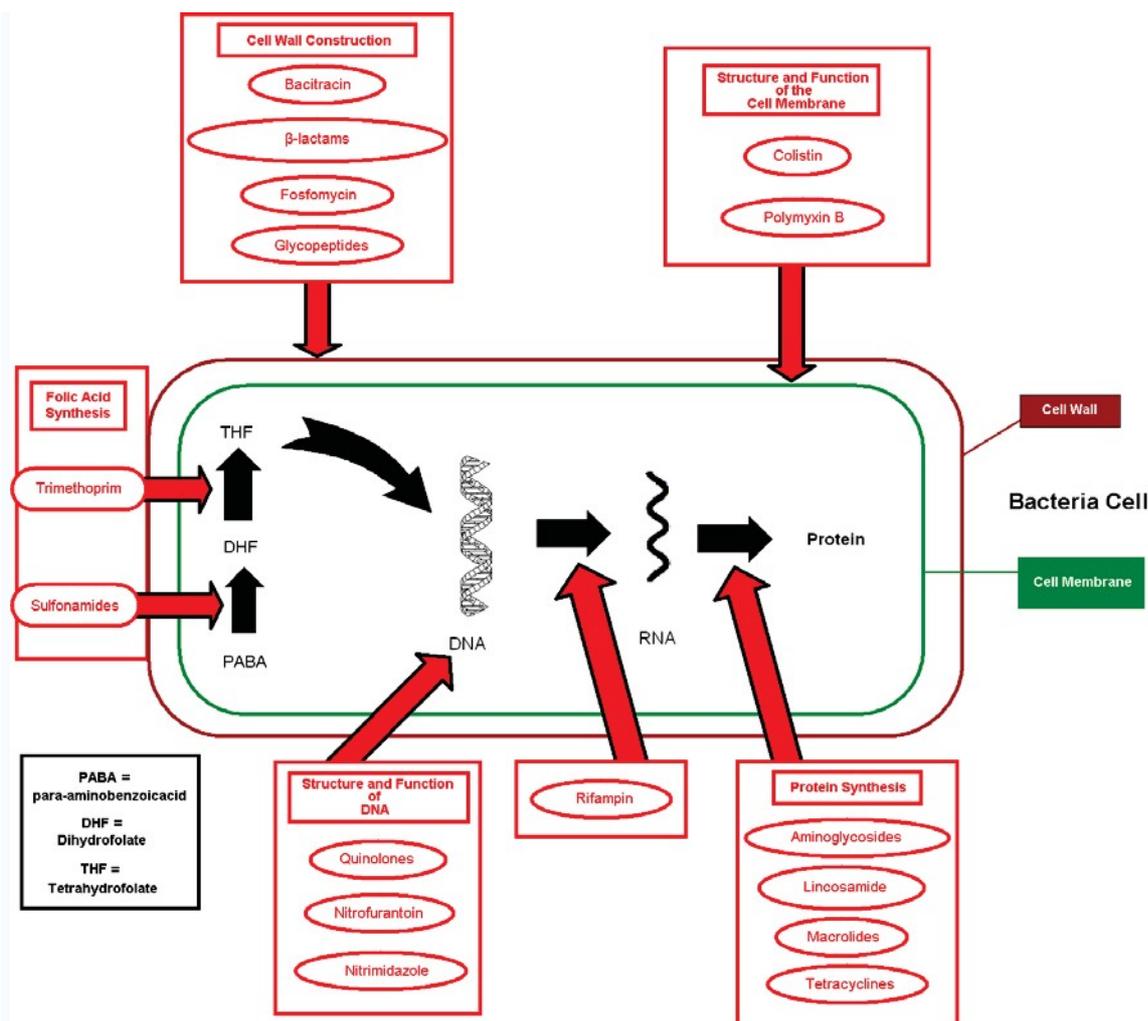
Synthetic antibiotic chemotherapy as a science and the story of antibiotic development began in Germany with [Paul Ehrlich](#), a German medical scientist in the late 1880s. Dr. Ehrlich noted that certain dyes would bind to and color human, animal or bacterial cells, while others did not. He then extended the idea that it might be possible to make certain dyes or chemicals that would act as a magic bullet or selective drug that would bind to and kill bacteria while not harming the human host. After much experimentation, screening hundreds of dyes against various organisms, he discovered the first medicinally useful drug, the man-made antibiotic, [Salvarsan](#).^{[10][12][13]} However, the adverse side-effect profile of salvarsan, coupled with the later discovery of the antibiotic penicillin, superseded its use as an antibiotic. The work of Ehrlich, which marked the

birth of the antibiotic revolution, was followed by the discovery of Prontosil by Domagk in 1932.^[13] **Prontosil**, the first commercially available antibacterial antibiotic was developed by a research team led by **Gerhard Domagk** (who received the 1939 **Nobel Prize for Medicine** for his efforts) at the **Bayer** Laboratories of the **IG Farben** conglomerate in Germany. Prontosil had a relatively broad effect against **Gram-positive cocci** but not against **enterobacteria**. The discovery and development of this first **sulfonamide** drug opened the era of antibiotics.

The discovery of natural antibiotics produced by microorganisms stemmed from earlier work on the observation of antibiosis between micro-organisms. Pasteur observed that "if we could intervene in the antagonism observed between some bacteria, it would offer 'perhaps the greatest hopes for therapeutics'".^[14] Bacterial antagonism of *Penicillium* sp. were first described in **England** by **John Tyndall** in 1875.^[14] However, his work went by without much notice from the scientific community until **Alexander Fleming's** discovery of **Penicillin** in 1928. Even then the therapeutic potential of penicillin was not pursued. More than ten years later, Ernst Chain and Howard Florey became interested in Flemming's work, and came up with the purified form of penicillin. The purified antibiotic displayed antibacterial activity against a wide range of bacteria. It also had low toxicity and could be taken without causing adverse effects. Furthermore its activity was not inhibited by biological constituents such as pus, unlike the sulfonamides. At the time, no-one had discovered a compound equalling this activity. The discovery of penicillin led to renewed interest in the search for antibiotic compounds with similar capabilities.^[15] Because of their discovery of penicillin Ernst Chain, Howard Florey and Alexander Fleming shared the 1945 Nobel Prize in Medicine. In 1939, **Rene Dubos** isolated **gramicidin**, one of the first commercially manufactured antibiotics in use during World War II to prove highly effective in treating wounds and ulcers.^[16] Florey credited Dubos for reviving his research in penicillin.^[16]

Antimicrobial pharmacodynamics

Main article: [Antimicrobial pharmacodynamics](#)



Points of attack on bacteria by antibiotics

The environment of individual antibiotics varies with the location of an infection, the ability of the antibiotic to reach the infection site, and the ability of the microbe to inactivate or excrete the antibiotic. At the highest level, antibiotics can be classified as either **bactericidal** or **bacteriostatic**. Bactericidals kill bacteria directly where bacteriostatics prevent **cell division**. However, these classifications are based on laboratory behavior; in practice, both of these are capable of ending a bacterial infection.^[17] The bactericidal activity of antibiotics may be **growth phase** dependent and in most but not all cases the action of many bactericidal antibiotics requires ongoing cell activity and cell division for the drugs' killing activity.^[18] The **minimum inhibitory concentration** and **minimum bactericidal concentration** are used to measure in vitro activity of an antimicrobial and are excellent indicators of antimicrobial potency. However, in clinical practice, these measurements alone are insufficient to predict clinical outcome. By combining the **pharmacokinetic** profile of an antibiotic with the antimicrobial activity, several pharmacological parameters appear to be significant markers of drug efficacy.^{[19][20]} The activity

of antibiotics may be concentration-dependent and their characteristic antimicrobial activity increases with progressively higher antibiotic concentrations.^[21] They may also be time-dependent, where their antimicrobial activity does not increase with increasing antibiotic concentrations; however, it is critical that a minimum inhibitory serum concentration is maintained for a certain length of time.^[21]

Administration

Oral antibiotics are simply ingested, while **intravenous** antibiotics are used in more serious cases, such as deep-seated **systemic infections**. Antibiotics may also sometimes be administered **topically**, as with **eye drops** or **ointments**.

Antibiotic classes

Main article: [List of antibiotics](#)

Unlike many previous treatments for infections, which often consisted of administering chemical compounds such as **strychnine** and **arsenic**, which also have high **toxicity** against **mammals**, most antibiotics from microbes have fewer side-effects and high effective target activity. Most anti-bacterial antibiotics do not have activity against viruses, fungi, or other **microbes**. Anti-bacterial antibiotics can be categorized based on their target specificity: "narrow-spectrum" antibiotics target particular types of bacteria, such as **Gram-negative** or **Gram-positive** bacteria, while **broad-spectrum antibiotics** affect a wide range of bacteria.

Antibiotics which target the bacterial cell wall (**penicillins**, **cephalosporins**), or cell membrane (**polymixins**), or interfere with essential bacterial enzymes (**quinolones**, **sulfonamides**) usually are **bactericidal** in nature. Those which target protein synthesis, such as the **aminoglycosides**, **macrolides** and **tetracyclines**, are usually **bacteriostatic**.^[22]

In the last few years three new classes of antibiotics have been brought into clinical use. This follows a 40-year hiatus in discovering new classes of antibiotic compounds. These new antibiotics are of the following three classes: cyclic lipopeptides (**daptomycin**), glycylcyclines (**tigecycline**), and oxazolidinones (**linezolid**). Tigecycline is a broad-spectrum antibiotic, while the two others are used for Gram-positive infections. These developments show promise as a means to counteract the bacterial resistance to existing antibiotics.

Production

Main article: [Production of antibiotics](#)

Since the first pioneering efforts of **Florey** and **Chain** in 1939, the importance of antibiotics to **medicine** has led to much research into discovering and producing them. The process of production usually involves the screening of wide ranges of microorganisms, and their testing and modification. Production is carried out using **fermentation**, usually in strongly aerobic form.

Side effects

Although antibiotics are generally considered safe and well tolerated, they have been associated with a wide range of adverse effects.^[23] Side effects are many, varied and can be very serious depending on the antibiotics used and the microbial organisms targeted. The safety profiles of newer medications may not be as well established as those that have been in use for many years.^[23] Adverse effects can range from fever and nausea to major allergic reactions including **photodermatitis**.^[citation needed] One of the more common side effects is **diarrhoea**, sometimes caused by the anaerobic bacterium **Clostridium difficile**, which results from the antibiotic disrupting the normal balance of the **intestinal flora**,^[24] Such overgrowth of pathogenic bacteria may be alleviated by ingesting **probiotics** during a course of antibiotics.^[citation needed] An antibiotic-induced disruption of the population of the bacteria normally present as constituents of the normal vaginal flora may also occur, and may lead to overgrowth of yeast species of the genus **Candida** in the vulvo-vaginal area.^[25] Other side effects can result from interaction with other drugs, such as elevated risk of **tendon** damage from administration of a **quinolone** antibiotic with a systemic **corticosteroid**.

Drug-Drug interactions

Contraceptive pill

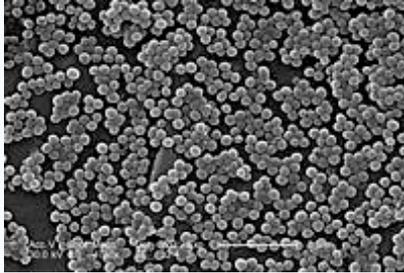
Hypothetically, interference of some antibiotics with the efficiency of birth control pills is thought to occur in two ways. Modification of the intestinal gut flora resulting in the reduced absorption of the estrogens and induction of hepatic liver enzymes which metabolise the pills active ingredients faster may affect the pill's usefulness.^[26] However, the majority of studies indicate that antibiotics do not interfere with contraception,^[26] even though a small percentage of women may experience decreased effectiveness of birth control pills while taking an antibiotic the failure rate is comparable to those taking the pill.^[27] Moreover, there have been no studies that have conclusively demonstrated that disruption of the gut flora affects contraception.^{[28][29]} Interaction with the combined oral contraceptive pill through induction of hepatic enzymes by the antifungal medication **griseofulvin** and the broad-spectrum antibiotic **rifampicin** has been shown to occur. It is recommended that extra contraceptive measures are applied during antimicrobial therapy using these antimicrobials.^[26]

Alcohol

Alcohol can interfere with the activity or metabolism of antibiotics.^[30] It may affect the activity of liver enzymes, which break down the antibiotics.^[31] Moreover, certain antibiotics, including **metronidazole**, **tinidazole**, **co-trimoxazole**, **cephamandole**, **ketoconazole**, **latamoxef**, **cefoperazone**, **amoxicillin**, **cefmenoxime**, and **furazolidone**, chemically react with alcohol, leading to serious **side effects**, which include severe vomiting, nausea, and shortness of breath. Alcohol consumption while taking such antibiotics is therefore not recommended.^[32] Additionally, serum levels of doxycycline and **erythromycin** succinate may, in certain circumstances, be significantly reduced by alcohol consumption.^[33]

Antibiotic resistance

Main article: [Antibiotic resistance](#)



SEM depicting [methicillin-resistant Staphylococcus aureus](#) bacteria.

The emergence of antibiotic resistance is an evolutionary process that is based on selection for organisms that have enhanced ability to survive doses of antibiotics that would have previously been lethal.^[34] Antibiotics like Penicillin and Erythromycin which used to be one-time miracle cures are now less effective because bacteria have become more resistant.^[35] Antibiotics themselves act as a selective pressure which allows the growth of resistant bacteria within a population and inhibits susceptible bacteria.^[36] Antibiotic selection of pre-existing antibiotic resistant mutants within bacterial populations was demonstrated in 1943 by the [Luria-Delbrück experiment](#).^[37] Survival of bacteria often results from an inheritable resistance.^[38] Any antibiotic resistance may impose a biological cost and the spread of antibiotic resistant bacteria may be hampered by the reduced [fitness](#) associated with the resistance which proves disadvantageous for survival of the bacteria when antibiotic is not present. Additional mutations, however, may compensate for this fitness cost and aids the survival of these bacteria.^[39]

The underlying molecular mechanisms leading to antibiotic resistance can vary. Intrinsic resistance may naturally occur as a result of the bacteria's genetic makeup.^[40] The bacterial chromosome may fail to encode a protein which the antibiotic targets. Acquired resistance results from a mutation in the bacterial chromosome or the acquisition of extra-chromosomal DNA.^[40] Antibiotic-producing bacteria have evolved resistance mechanisms which have been shown to be similar to and may have been transferred to antibiotic resistant strains.^{[41][42]} The spread of antibiotic resistance mechanisms occurs through vertical transmission of inherited mutations from previous generations and genetic recombination of DNA by horizontal genetic exchange.^[38] Antibiotic resistance exchanged between different bacteria by [plasmids](#) that carry genes which encode antibiotic resistance which may result in co-resistance to multiple antibiotics.^{[38][43]} These plasmids can carry different genes with diverse resistance mechanisms to unrelated antibiotics but because they are located on the same plasmid multiple antibiotic resistance to more than one antibiotic is transferred.^[43] Alternatively, cross-resistance to other antibiotics within the bacteria results when the same resistance mechanism is responsible for resistance to more than one antibiotic is selected for.^[43]

Antibiotic misuse



WARNING: Antibiotics don't work for viruses like colds and the flu. Using them for viruses will **NOT** make you feel better or get back to work faster.

Antibiotics are strong medicines. Keep them that way. Prevent antibiotic resistance. Antibiotics don't fight viruses—they fight bacteria. Using antibiotics for viruses can put you at risk of getting a bacterial infection that is resistant to antibiotic treatment. Talk to your healthcare provider about antibiotics, visit www.cdc.gov/getsmart, or call **1-800-CDC-INFO** to learn more.



Taking antibiotics for viral infections such as a cold, a cough, or the flu will **NOT**:

- Cure the infection
- Keep other people from catching it
- Help you feel better



This poster from the U.S. Centers for Disease Control and Prevention "Get Smart" campaign, intended for use in doctor's offices and other healthcare facilities, warns that antibiotics do not work for viral illnesses such as the common cold.

The first rule of antibiotics is try not to use them, and the second rule is try not to use too many of them.^[44]

—Paul L. Marino, The ICU Book

Inappropriate antibiotic treatment and **overuse of antibiotics** have been a contributing factor to the emergence of resistant bacteria. The problem is further exacerbated by **self-prescribing** of antibiotics by individuals without the guidelines of a qualified clinician and the non-therapeutic use of antibiotics as growth promoters in agriculture.^[45] Antibiotics are frequently prescribed for indications in which their use is not warranted, an incorrect or sub-optimal antibiotic is prescribed or in some cases for infections likely to resolve without treatment.^{[23][45]}

Several organizations concerned with antimicrobial resistance are lobbying to improve the regulatory climate.^[45] Approaches to tackling the issues of misuse and overuse of antibiotics by the establishment of the U.S. Interagency Task Force on Antimicrobial Resistance which aims actively address the problem antimicrobial resistance are being organised and coordinated by the **US Centers for Disease Control and Prevention**, the **Food and Drug Administration (FDA)**, and the **National Institutes of Health (NIH)** and also includes several other federal agencies.^[46] An NGO campaign group is Keep Antibiotics Working.^[47] In France, an "Antibiotics are not automatic" government campaign starting in 2002 led to a marked reduction of unnecessary antibiotic prescriptions, especially in children.^[48]

The overuse of antibiotics like penicillin and erythromycin which used to be one-time miracle cures were associated with emerging resistance since the 1950s.^{[35][49]} Therapeutic usage of antibiotics in hospitals has been seen to be associated with increases in multi-antibiotic resistant bacteria.^[49]

Common forms of antibiotic misuse include failure to take into account the patient's weight and history of prior antibiotic use when prescribing, since both can strongly affect the efficacy of an antibiotic prescription, failure to take the entire prescribed course of the antibiotic, failure to prescribe or take the course of treatment at fairly precise correct daily intervals (e.g. "every 8 hours" rather than merely "3x per day"), or failure to rest for sufficient recovery to allow clearance of the infecting organism. These practices may facilitate the development of bacterial populations with **antibiotic resistance**. Inappropriate antibiotic treatment is another common form of antibiotic misuse. A common example is the prescription and use of antibiotics to treat viral infections such as the **common cold** that have no effect.

In agriculture, associated antibiotic resistance with the non-therapeutic use of antibiotics as growth promoters in animals resulted in their restricted use in the UK in the 1970 (Swann report 1969). Currently there is a EU wide ban on the non-therapeutic use of antibiotics as growth promoters. It is estimated that greater than 70% of the antibiotics used in U.S. are given to feed animals (e.g. chickens, pigs and cattle) in the absence of disease.^[50] Antibiotic use in food animal production has been associated with the emergence of antibiotic-resistant strains of bacteria including *Salmonella* spp., *Campylobacter* spp., *Escherichia coli*, and *Enterococcus* spp.^{[51][52]} Evidence from some US and European studies suggest that these resistant bacteria cause infections in humans that do not respond to commonly prescribed antibiotics. In response to these practices and attendant problems, several organizations (e.g. The American Society for

Microbiology (ASM), American Public Health Association (APHA) and the American Medical Association (AMA) have called for restrictions on antibiotic use in food animal production and an end to all non-therapeutic uses.^[citation needed] However, delays in regulatory and legislative actions to limit the use of antibiotics are common, and may include resistance to these changes by industries using or selling antibiotics, as well as time spent on research to establish causal links between antibiotic use and emergence of untreatable bacterial diseases. Two federal bills (S.742^[53] and H.R. 2562^[54]) aimed at phasing out non-therapeutic antibiotics in US food animal production were proposed but not passed.^{[53][54]} These bills were endorsed by public health and medical organizations including the American Holistic Nurses' Association, the American Medical Association, and the American Public Health Association (APHA).^[55] The EU has banned the use of antibiotics as growth promotional agents since 2003.^[56]

One study on **respiratory tract infections** found "physicians were more likely to prescribe antibiotics to patients who they believed expected them, although they correctly identified only about 1 in 4 of those patients".^[57] Multifactorial interventions aimed at both physicians and patients can reduce inappropriate prescribing of antibiotics.^[58] Delaying antibiotics for 48 hours while observing for spontaneous resolution of respiratory tract infections may reduce antibiotic usage; however, this strategy may reduce patient satisfaction.^[59]

Excessive use of **prophylactic** antibiotics in travelers may also be classified as misuse.

In the **United Kingdom**, there are **NHS** posters in many doctors surgeries indicating that 'unfortunately, no amount of antibiotics will get rid of your cold', following on from many patients specifically requesting antibiotics from their doctor inappropriately, believing they will help treat viral infections.

Resistance modifying agents

One solution to combat resistance currently being researched is the development of pharmaceutical compounds that would revert multiple antibiotic resistance. These so called resistance modifying agents may target and inhibit MDR mechanisms, rendering the bacteria susceptible to antibiotics to which they were previously resistant. These compounds targets include among others

- **Efflux inhibition**(Phe-Arg- ϕ -naphthylamide)^[60]
- Beta Lactamase inhibitors - Including **Clavulanic acid** and **Sulbactam**

Beyond antibiotics

The comparative ease of identifying compounds which safely cured bacterial infections was more difficult to duplicate in treatments of fungal and viral infections. Antibiotic research led to great strides in the knowledge of **biochemistry**, establishing large differences between the cellular and molecular physiology of the bacterial cell and that of the mammalian cell. This explained the observation that many compounds that are toxic to bacteria are non-toxic to human cells. In contrast, the basic biochemistries of the fungal cell and the **mammalian** cell are much more similar. This restricts the development and use of therapeutic compounds that attack a

fungal cell, while not harming mammalian cells. Similar problems exist in antibiotic treatments of **viral** diseases. Human viral metabolic biochemistry is very closely similar to human biochemistry, and the possible targets of antiviral compounds are restricted to very few components unique to a mammalian virus.

Research into **bacteriophages** for use as antibiotics is presently ongoing. Several types of bacteriophage appear to exist that are specific for each bacterial taxonomic group or species.^[citation needed] Research into bacteriophages for medicinal use is just beginning, but has led to advances in microscopic imaging.^[61] While bacteriophages provide a possible solution to the problem of antibiotic resistance, there is no clinical evidence yet that they can be deployed as therapeutic agents to cure disease.^[citation needed]

Phage therapy, the use of particular viruses to attack bacteria, has been used in the past on humans in the US and Europe during the 1920s and 1930s, but these treatments had mixed results. With the discovery of penicillin in the 1940s, Europe and the US changed therapeutic strategies to using antibiotics. However, in the former Soviet Union phage therapies continued to be studied. In the Republic of Georgia, the Eliava Institute of Bacteriophage, Microbiology & Virology continues to research the use of phage therapy. Various companies and foundations in North America and Europe are currently researching phage therapies.^[citation needed] However, phage are living and reproducing; concerns about genetic engineering in freely released viruses currently limit certain aspects of phage therapy.

Bacteriocins are also a growing alternative to the classic small-molecule antibiotics^[62]. Different classes of bacteriocins have different potential as therapeutic agents. Small molecule bacteriocins (**microcins**, for example, and **lantibiotics**) may be similar to the classic antibiotics; **colicin**-like bacteriocins are more likely to be narrow-spectrum, demanding new molecular diagnostics prior to therapy but also not raising the spectre of resistance to the same degree. One drawback to the large molecule antibiotics is that they will have relative difficulty crossing membranes and travelling systemically throughout the body. For this reason, they are most often proposed for application topically or gastrointestinally^[63]. Because bacteriocins are peptides, they are more readily engineered than small molecules^[64]. This may permit the generation of cocktails and dynamically improved antibiotics that are modified to overcome resistance.

Probiotics are another alternative that goes beyond traditional antibiotics by employing a live culture which may in theory establish itself as a symbiont, competing, inhibiting, or simply interfering with colonization by pathogens.

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