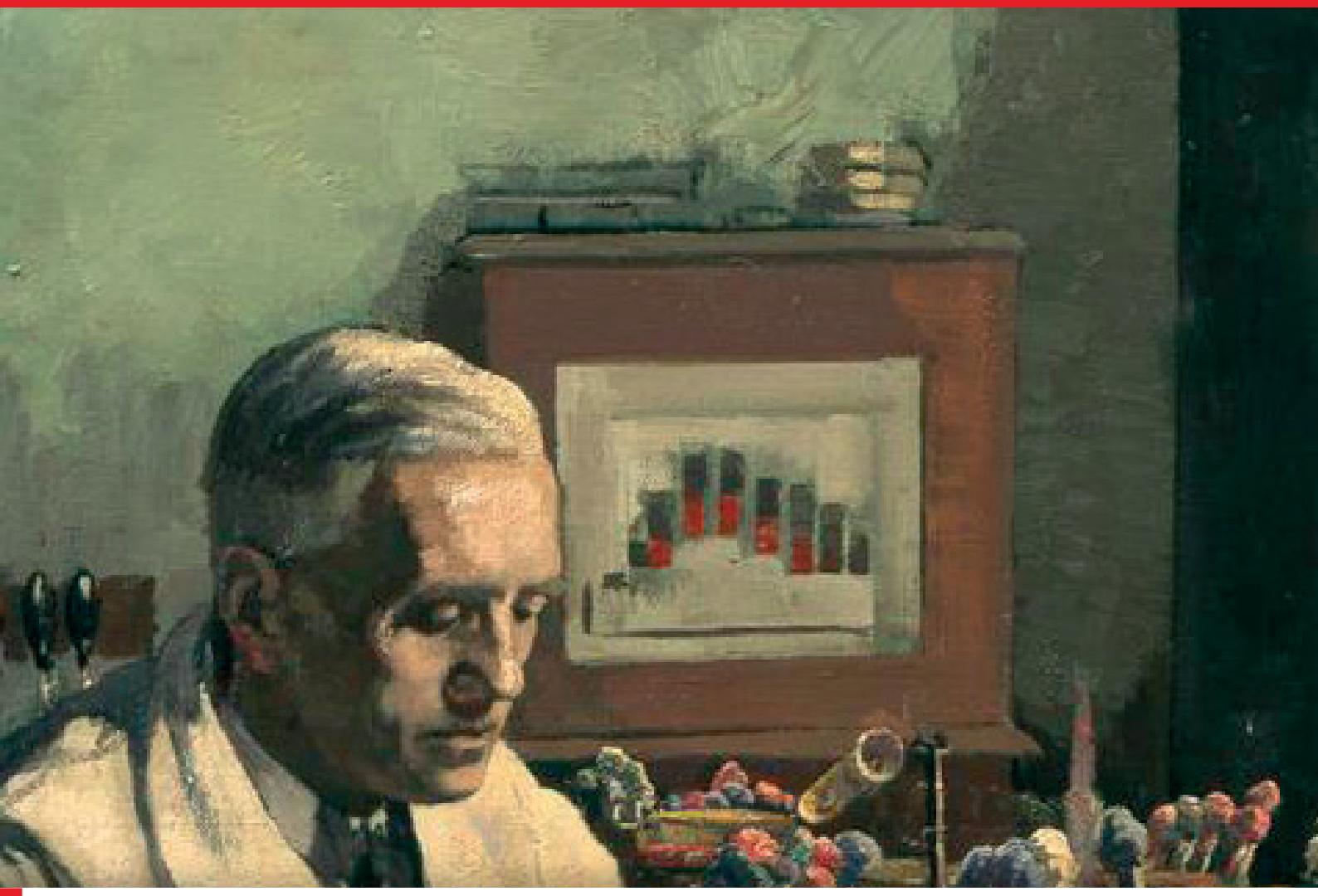
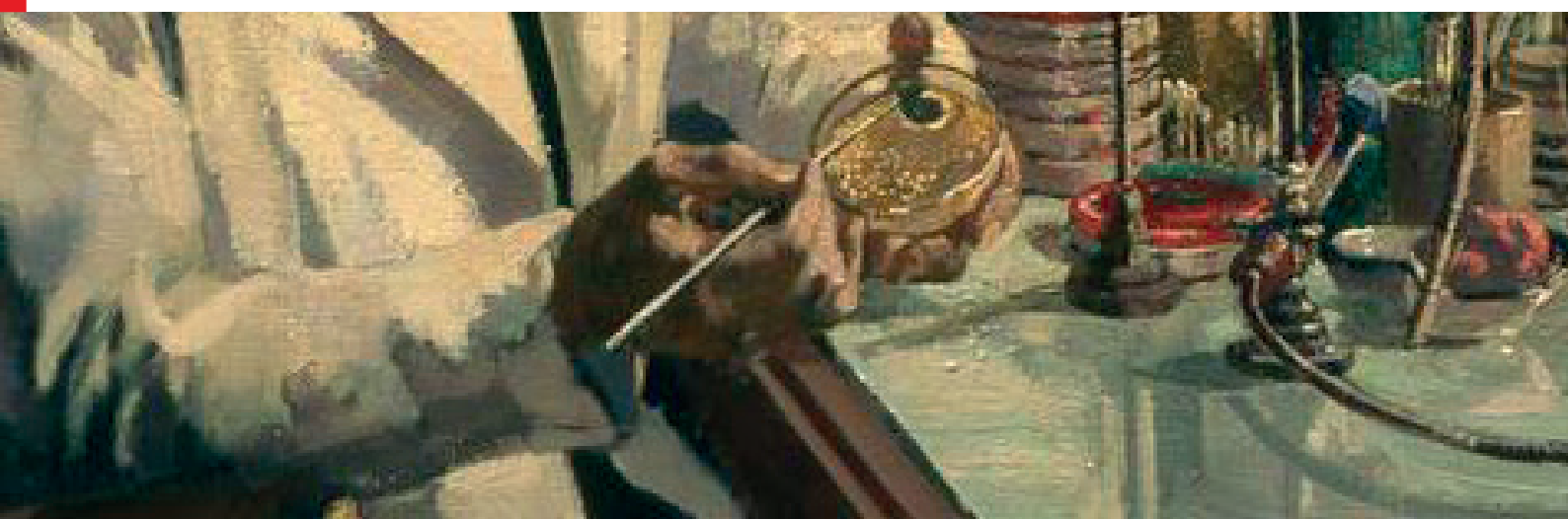
THIS DAY IN HISTORY

STUDY GUIDE



FEB. 14, 1929: INVENTION OF PENICILLIN

Images, biographies, discussion questions and more



PENICILLIN

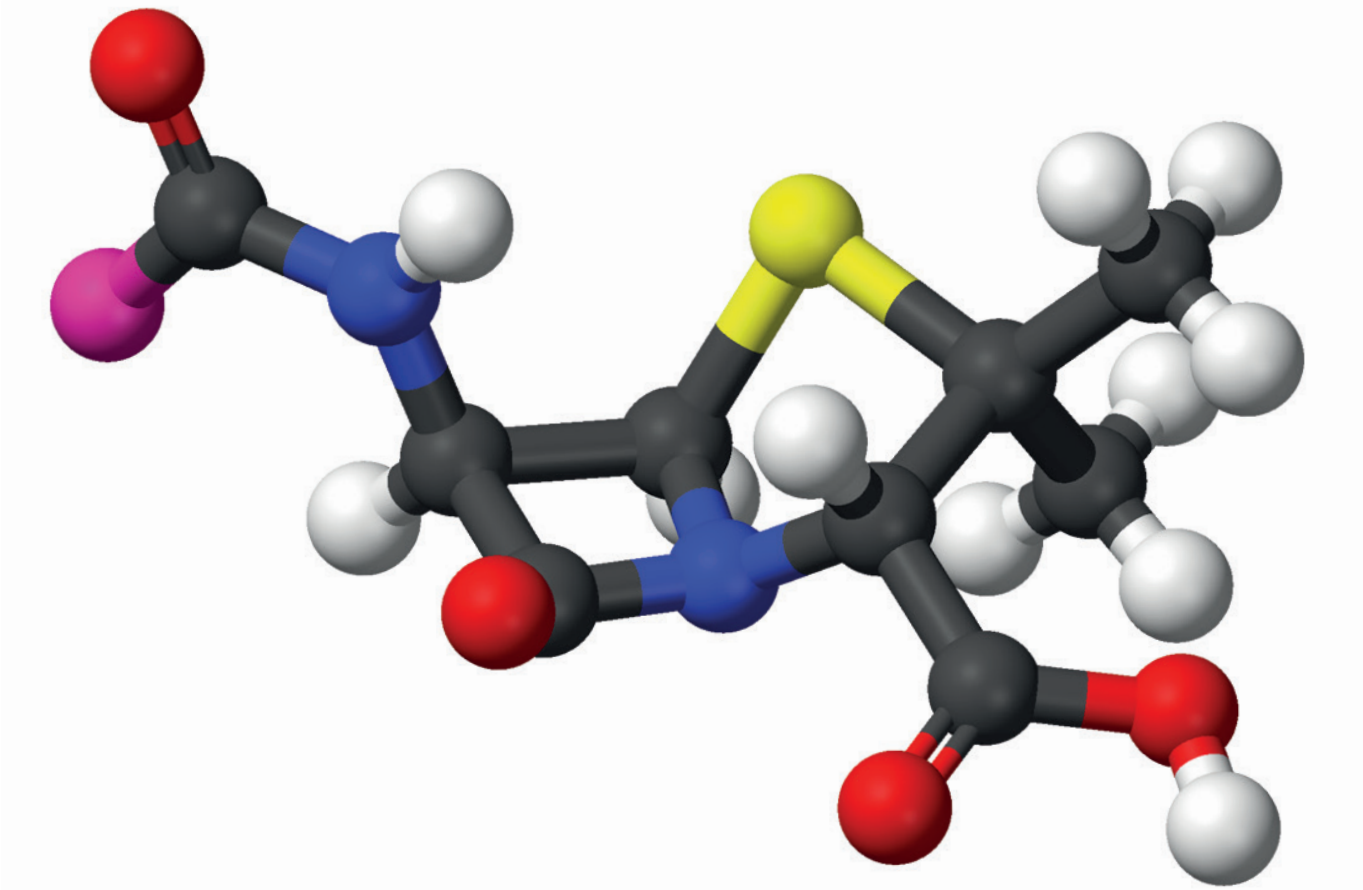
Setting the Stage

Before the invention of penicillin, minor injuries like cuts or scratches could lead to deadly infections. Even a paper cut could kill you. Surgeries and childbirth were much more dangerous than they are today and there was no cure for countless conditions considered treatable today, like tuberculosis, meningitis and rheumatic fever. Before penicillin, treatment for infections included a variety of remedies with varying degrees of effectiveness including fresh air, bloodletting and herbs. Infected wounds were often burned out with a hot iron or boiling oil.

Once its use became widespread in the 1940s, penicillin had an enormous impact, preventing countless deaths. Without penicillin, World War II would have resulted in far more fatalities, as infected wounds could not have been treated. In addition, modern medical breakthroughs like organ transplants and chemotherapy, which rely on antibiotics to be successful, would not be possible.

Cover photo: A portrait of Sir Alexander Fleming, the discoverer of Penicillin, 1944.

FEB. 14, 1929
INVENTION OF PENICILLIN



Penicillin

On September 28, 1928, British bacteriologist Sir Alexander Fleming made an accidental discovery that ushered in a new era for humanity, the age of antibiotics.

That morning, Fleming returned to his laboratory at St. Mary's Hospital in London after a two-week vacation with his family in Scotland. As a member of the hospital's inoculation department, Fleming had been studying the influenza virus. By most accounts, Fleming had rather untidy personal habits and had left his lab table something of a mess. Upon his return to work, he noticed that some petri dishes containing staphylococcus cultures had been contaminated and grown mold. Fleming examined the dishes under a microscope and made a startling discovery: The mold had disrupted the normal growth of the cultures. Fleming identified the mold as penicillium notatum, a mold similar to the kind found on bread, and immediately set about growing more of the mold. Within a few weeks he was able to confirm his

findings. The penicillium mold prevented the growth of the staphylococci, and Fleming believed it also could be used to treat infectious disease. Fleming later wrote of the discovery, "When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine...but I guess that was exactly what I did."

Fleming had discovered the world's first antibiotic, a type of drug that destroys or limits the growth of harmful bacteria. Today, antibiotics are used to treat everything from ear infections to strep throat to pneumonia. But the impact of penicillin was not immediate--in fact, Fleming's discovery initially attracted little notice. Then, in 1938, an Australian pathologist working at Oxford University named Dr. Howard Florey stumbled upon Fleming's paper on penicillium and decided to try to isolate the active ingredient in what Fleming called his "mould juice." However, even after Florey's team, including biochemist Dr. Ernst Chain, had created effective penicillin injections, they struggled to produce enough penicillin to make treatment with it viable--it could take thousands of liters of penicillin to treat just one infection.

Finally, in the summer of 1941, Florey and Chain teamed up with a group of American scientists in Peoria, Illinois, to find a way to mass-produce penicillin. Together they discovered a method to enhance a different species of the penicillium bacteria that allowed them to create much greater quantities of the drug. In the first five months of 1942 alone, 400 million units of pure penicillin were produced. That March, 14 years after Fleming's discovery, a Connecticut woman named Anne Miller became the first person to be successfully treated by penicillin. The most immediate impact of penicillin was felt in World War II, when it was used to prevent gangrene in wounds, saving lives and reducing the need for limb amputation.

At war's end, in 1945, Fleming, Florey and Chain were awarded the Nobel Prize for medicine. In his acceptance speech, Fleming presciently warned of the dangers of antibiotic resistance.

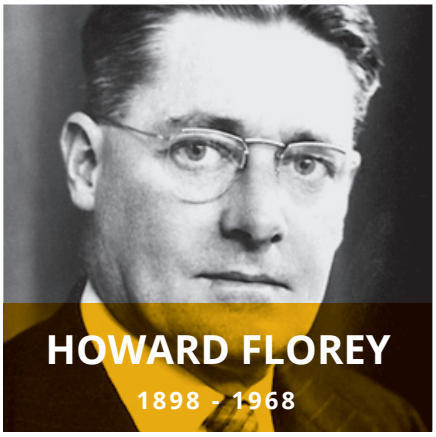
Today, penicillin is the most widely used antibiotic in the world; it has saved hundreds of millions of lives. □

DID YOU KNOW?

In the early days of penicillin use, producing it from mold was difficult, expensive and time-consuming. In an attempt to meet demand, doctors discovered they could reuse it by extracting it from previous patients' urine.

PEOPLE TO KNOW

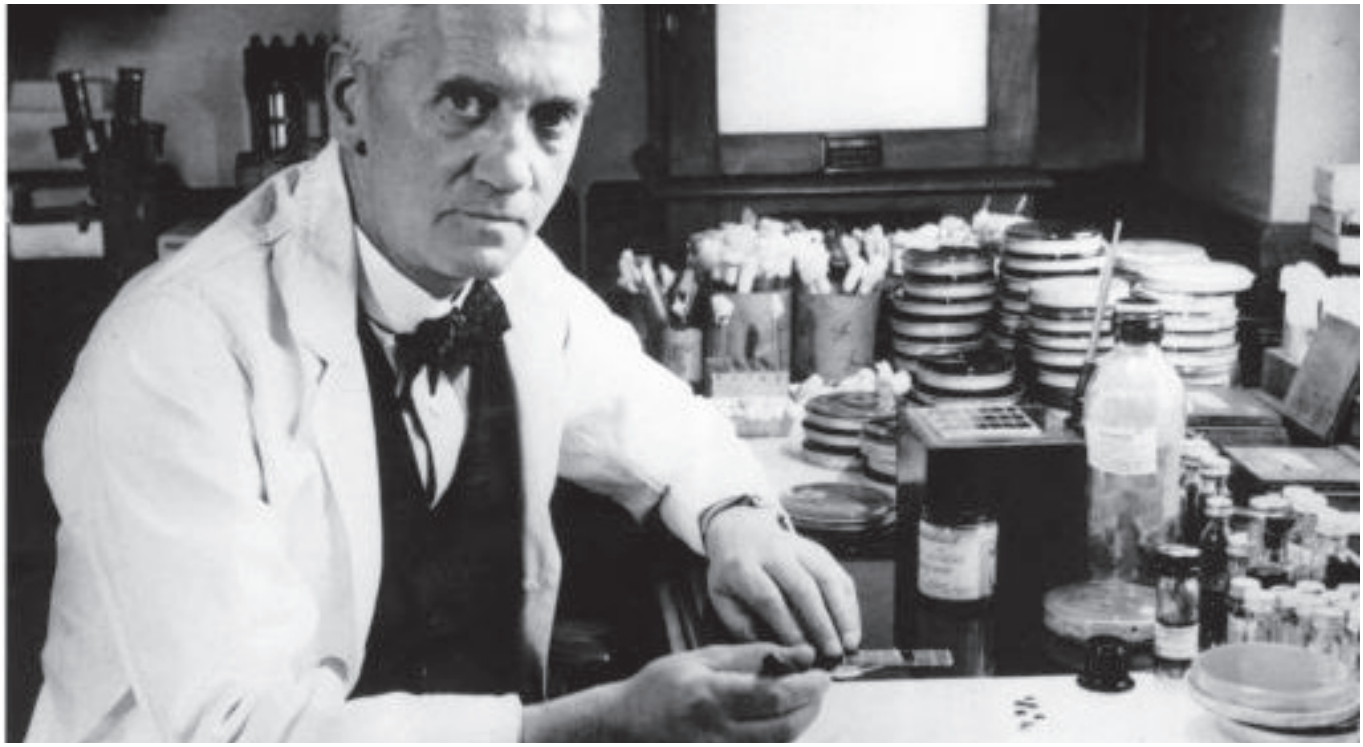
Fleming, a Scottish doctor and bacteriologist, studied medicine at St. Mary's Hospital Medical School in London. He abandoned his original plan of becoming a surgeon when he was given an opportunity to join the inoculation department at St. Mary's Hospital to work in the then-burgeoning field of bacteriology. Fleming served as a doctor during World War I, during which he studied infected wounds. Fleming observed that antiseptics used on wounds were actually harming the body's own immune response to the infection, causing more health issues than they helped. He instead recommended that wounds be kept clean and dry to promote healing. After the war, Fleming returned to St. Mary's, where he eventually discovered penicillin. In 1945, Fleming was awarded the Nobel prize for medicine for his work on penicillin. In 1946, he became head of St. Mary's inoculation department, which was renamed the Wright-Fleming Institute, in honor of Fleming and his former mentor Almroth Edward Wright, a pioneer in vaccine therapy research.



Florey was an Australian-born doctor, pathologist and pharmacologist who is credited with helping to transform Fleming's discovery of penicillin into a viable treatment. Florey was working at England's Lincoln College, Oxford, where in 1939, he and a team, including Ernst Chain, began working to identify and extract the active ingredient in Fleming's mold, as well as a way to mass-produce it. In 1940, the team performed a successful experiment with bacteria-infected mice that proved penicillin was effective. Human testing, including on wounded World War II troops in North Africa, began in 1941 and from there, Florey worked, along with a group of American scientists, on developing a way to mass-produce penicillin so it could be used for treatment on a large scale. Robert Menzies, the 12th prime minister of Australia, said of Florey, "...in terms of well-being, Florey was the most important man ever born in Australia."

Chain was born in Germany, but emigrated to Great Britain in 1933, after the Nazis came to power. A biochemist, Chain joined the pathology department at the University of Oxford and eventually began working alongside Florey and other scientists on the potential of naturally occurring substances produced by microorganisms to fight infection. Along with Florey, he discovered the chemical makeup of penicillin, helping to isolate and then mass-produce it, in order to develop it into a practical cure.

SEE IT



Alexander Fleming in his lab.

Equipment used for making early forms of penicillin, Wellcome Images.

SEE IT

Reprinted from
The British Journal of Experimental Pathology,
1929, Vol. X, p. 226.

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM, WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZAE*.

ALEXANDER FLEMING, F.R.C.S.
From the Laboratories of the Inoculation Department, St. Mary's Hospital, London.

Received for publication May 10, 1929.

WHILE working with staphylococcus variants a number of culture-plates were set aside on the laboratory bench and examined from time to time. In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro-organisms. It was noticed that around a large colony of a contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis (see Fig. 1).

Subcultures of this mould were made and experiments conducted with a view to ascertaining something of the properties of the bacteriolytic substance which had evidently been formed in the mould culture and which had diffused into the surrounding medium. It was found that broth in which the mould had been grown at room temperature for one or two weeks had acquired marked inhibitory, bactericidal and bacteriolytic properties to many of the more common pathogenic bacteria.

CHARACTERS OF THE MOULD.

The colony appears as a white fluffy mass which rapidly increases in size and after a few days sporulates, the centre becoming dark green and later in old cultures darkens to almost black. In four or five days a bright yellow colour is produced which diffuses into the medium. In certain conditions a reddish colour can be observed in the growth.

In broth the mould grows on the surface as a white fluffy growth, changing in a few days to a dark green felted mass. The broth becomes bright yellow and this yellow pigment is not extracted by $CHCl_3$. The reaction of the broth becomes markedly alkaline. the pH varying from 8·5 to 9. Acid is produced in three or four days in glucose and saccharose broth. There is no acid production in 7 days in lactose, mannite or dulcite broth.

Growth is slow at 37°C. and is most rapid about 20°C. No growth is observed under anaerobic conditions.

In its morphology this organism is a penicillium and in all its characters it most closely resembles *P. rubrum*. Biourge (1923) states that he has never found *P. rubrum* in nature and that it is an "animal de laboratoire." This penicillium is not uncommon in the air of the laboratory.

IS THE ANTIBACTERIAL BODY ELABORATED IN CULTURE BY ALL MOULDS?

A number of other moulds were grown in broth at room temperature and the culture fluids were tested for antibacterial substances at various intervals up to one month. The species examined were: *Eidamia viridiscens*, *Botrytis cineria*, *Aspergillus fumigatus*, *Sporotrichum*, *Cladosporium*, *Penicillium*, 8 strains. Of these it was found

First page of Alexander Fleming's paper on penicillin, Wellcome Images.

CONCURRENT EVENTS

THE GREAT DEPRESSION

The Great Depression, which lasted from 1929 to 1939, was the worst economic downturn in the history of the industrialized world. It began after the stock market crash of October 1929, which sent Wall Street into a panic and wiped out the accounts of millions of investors. Over the next several years, consumer spending and investment dropped, causing steep declines in industrial output and employment as failing companies laid off workers. By 1933, when the Great Depression reached its lowest point, some 15 million Americans were unemployed and nearly half the country's banks had failed.

ST. VALENTINE'S DAY MASSACRE

Gang warfare ruled the streets of Chicago during the late 1920s, as chief gangster Al Capone sought to consolidate control by eliminating his rivals in the illegal trades of bootlegging, gambling and prostitution. This rash of gang violence reached its bloody climax in a garage on the city's North Side on February 14, 1929, when seven men associated with the Irish gangster George "Bugs" Moran, one of Capone's longtime enemies, were shot to death by several men dressed as policemen. The St. Valentine's Day Massacre, as it was known, was never officially linked to Capone, but he was generally considered to have been responsible for the murders.

PLUTO DISCOVERED

In February 1930, Pluto, once believed to be the ninth planet, is discovered over Flagstaff, Arizona, by astronomer Clyde W. Tombaugh. The existence of an unknown ninth planet was first proposed by Percival Lowell, who theorized that wobbles in the orbits of Uranus and Neptune were caused by the gravitational pull of an unknown planetary body. Lowell calculated the approximate location of the hypothesized ninth planet and searched for more than a decade without success. In 1929, the search for Pluto was resumed at the Lowell Observatory in Arizona. On February 18, 1930, Tombaugh discovered the tiny, distant planet by use of a new astronomic technique of photographic plates combined with a blink microscope. His finding was confirmed by several other astronomers, and on March 13, 1930--the anniversary of Lowell's birth and of William Herschel's discovery of Uranus--the discovery of Pluto was publicly announced. After its discovery, some astronomers questioned whether Pluto had sufficient mass to affect the orbits of Uranus and Neptune. In 1978, James Christy and Robert Harrington discovered Pluto's only known moon, Charon, which was determined to have a diameter of 737 miles to Pluto's 1,428 miles. Together, it was thought that Pluto and Charon formed a double-planet system, which was of ample enough mass to cause wobbles in Uranus' and Neptune's orbits. In August 2006, however, the International Astronomical Union announced that Pluto would no longer be considered a planet, due to new rules that said planets must "clear the neighborhood around its orbit." Since Pluto's oblong orbit overlaps that of Neptune, it was disqualified.

DISCUSSION QUESTIONS

1 How do you think life was different before the invention of penicillin?

2 Why do you think penicillin is often called a wonder drug?

3 Can you think of any modern-day medical innovations that have had a similar impact?

SUGGESTED ACTIVITIES

Ernst Chain in his lab during World War II.

MASS PRODUCTION

Divide the class into three groups. Assign one group to be the "producers" and give them a somewhat time-consuming task to complete, for example, stringing 10 small paper clips together to form one dose of "penicillin." Before beginning a string, the producer should have to wait in line to get the paper clips from the teacher, who has to count them out. Assign the second group of students to be doctors or nurses and the third group to be patients. Use a timer so that every 30 seconds or so a patient asks for a dose of penicillin and the doctors/nurses are asking (and cajoling) the producers for more. When a patient has to wait more than a minute for a dose, he is forced to leave the game. When the patients have all been forced out, ask the students to unpack the activity. Why was it difficult to make enough medicine? What would happen to patients if they were forced to wait too long? Why was it important to find ways to mass produce penicillin? Why would this be especially important in wartime?

TEAMWORK

Alexander Fleming is traditionally given most of the credit for developing penicillin, but further investigation reveals that a number of other scientists played important roles. In groups or individually, ask students to research and create a list of the many scientists who contributed to penicillin's development, along with their contribution. Then, have them create a visual representation of how penicillin became a drug, noting the many contributors along the way. See sample infographic here: https://www.kidsdiscover.com/infographics/how-a-bill-becomes-a-law-for-kids/

HISTORY TALKS

Ask students to imagine a conversation between Alexander Fleming and Howard Florey or Ernst Chain after Florey and Chain came across Fleming's work on penicillin and began to work on developing it as a practical treatment for infection. The conversation should include details from the scientists' lives and could cover Fleming's story of discovery, his speculations about its potential, and Florey's or Chain's plans for developing it, as well as both of their hopes for its future uses.

RESOURCES

Video: Penicillin

http://www.history.com/topics/world-war-ii/world-war-ii-history/videos/penicillin

Video: Alexander Fleming and the Accidental Mold Juice, Open University

https://www.youtube.com/watch?v=0ZWjzcsTd5M

Infographic: The discovery of penicillin

https://visual.ly/community/infographic/health/discovery-penicillin

Text: Alexander Fleming's Nobel Prize speech

https://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-speech.html

Text: Penicillin Fact Sheet: The Challenge of Mass Production, National WWII Museum

https://www.nationalww2museum.org/sites/default/files/2017-07/penicillin-fact-sheet.pdf

Text: Discovery & Development of Penicillin, American Chemical Society

https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/flemingpenicillin.html