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# The birth of antibiotics: cutting a long story short. Part 1

**Peer review status:**

No

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**Article ID:** WMC005591

**Article Type:** Original Articles

**Submitted on:** 31-Aug-2019, 07:23:13 PM GMT **Published on:** 04-Sep-2019, 07:42:14 AM GMT

**Article URL:** [http://www.webmedcentral.com/article\\_view/5591](http://www.webmedcentral.com/article_view/5591)

**Subject Categories:** INFECTIOUS DISEASES

**Keywords:** Penicillin, bacteria, arsenic, mercury, Salvarsan, magic bullets

**How to cite the article:** Una Cidon E. The birth of antibiotics: cutting a long story short. Part 1. WebmedCentral INFECTIOUS DISEASES 2019;10(9):WMC005591

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**Source(s) of Funding:**

N/A

**Competing Interests:**

N/A

# The birth of antibiotics: cutting a long story short.

## Part 1

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### A difficult beginning

Nowadays we are so used to the antibiotics that we take them for granted. However, there was a time where common bacterial infections were at ease and minor scratches or simple cuts were fatal.

All started when syphilis, although known for centuries, became the 19th century version of today's AIDS epidemic. This sexually transmitted disease infected and killed millions worldwide. Mercury had been used to treat it but unsuccessfully and with a high risk of poisoning.

In 1880, Robert Koch found a way of staining bacteria to identify them. Paul Ehrlich, a member of his team, took this idea further. He thought that a dye could be used not just to stain the bacteria, but hopefully to kill them (and not the patient) as well. He began experimenting with several arsenic compounds in treating syphilis in rabbits. In 1909 and after trying 606 chemicals, he and his assistant Sahachiro Hata, a Japanese bacteriologist, experienced success with the compound 606, later called *Salvarsan*, or the "magic bullet". This was highly toxic and in 1912 Ehrlich created Neo-salvarsan, safer than its ancestor and this became the standard treatment for syphilis until replaced by penicillin.

It was in 1928 when a Scottish scientist, Alexander Fleming returned from a holiday trip to discover that a mold had accidentally contaminated Petri dishes containing cultures of the bacteria *Staphylococcus*. He realised that no bacteria grew up near the mold. Further tests showed that other bacteria died as well after being exposed to the mold known as *Penicillium notatum*. This seemed to contain an agent that inhibited the growth of bacteria initially called "mold juice", later penicillin. Fleming wrote: "When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I guess that was exactly what I did." But sad news, he could not successfully isolate pure penicillin from the mold juice and the experiments stopped in 1931.

Other researchers were working to find the "second magic bullet". This was a red dye called

Prontosil which killed bacteria causing blood poisoning. Gerhard Domagk in 1932 injected mice with a lethal dose of a streptococcal infection and then with Prontosil, which cured them. He also cured his daughter when she became seriously ill with the same infection.

Further investigations showed that the active ingredient of Prontosil was a sulphonamide and this led to the cure of gonorrhoea, pneumonia, scarlet fever and reduced mothers post-birth mortality from 20% to 4.7%.

### Penicillin was not forgotten

Luckily for us, Howard Florey and Ernst Chain solved the chemical issues of extraction and purification of penicillin with the help of Norman Heatley (a young biochemist).

In 1940, they designed an experiment with 50 mice infected with the deadly *Streptococcus* bacteria. Half of them received penicillin and lived while all of the others died.

In September 1940, Albert Alexander a 48-year-old Oxford police constable had suffered a minor scratch on his face from a rose bush and it became infected. Alexander was overwhelmed by sepsis and did not respond to sulphonamides. Florey and Chain asked his doctors to try penicillin. After five days he started to recover, but penicillin supplies ran out before the infection was completely eradicated, and Alexander died.

In 1942, Anne Sheafe Miller was dying with a streptococcal septicaemia after a miscarriage but saved her life with unrefined penicillin.

Mass production of penicillin continued to be the major issue. Over 2,000 litres of mold culture were needed to get enough penicillin to treat one person. World War II brought a huge need for antibiotics. Florey went to the USA with Heatley and asked large pharmaceutical companies for assistance. In 1943 a laboratory assistant May Hunt, arrived with a cantaloupe melon from the market covered with a golden mold, *Penicillium Chrysogenum*. It yielded 200 times the amount of penicillin and when exposed to X-rays, the mutant generated produced 1000 times more penicillin than *Penicillium notatum*. The mass production of

penicillin was finally possible!

By the end of 1943, hundreds of million units of pure penicillin were produced every month. The impact on the war was enormous. First time in history that the major killer in a war was not infection. Also the survival rate of bacterial pneumonia increased from 20% in 1937 to 85% in 1964.

## The continuation

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This led to several pharmaceutical industries to start checking other natural products for antibacterial activity and many other antibiotics were discovered.

Now probably you think that we have won the war against infection. Well, unfortunately not. The happy boom of antibiotics led to misuse and now multidrug-resistant bacteria or superbugs have appeared with the risk that old diseases could come back.

Research needs to continue and should open the door to another chapter.

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## References

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