A short history of antibiotic discovery and development

In 1909, the antibiotic era began: discovery of the first drug against syphilis, Salvarsan. 606 chemicals screened before success

Discovery of salvarsan was made possible by the work of three scientists, Paul Ehrich, Alfred Bertheim and Sachachiro Hata.

In 1912, neosalvarsan was introduced. Similar to salvarsan the drug had fewer side effects; it was used until the discovery of penicillin.

In the 1920s a huge screening of chemical compounds against bacteria led to the discovery of KL730, which later became known as prontosol.

The discovery of prontosol was by Bayer chemists: Josef Klarer, Fritz Mietzsch and Gerhard Domagk. prontosol gave rise to the sulphonamides.

In 1943, Lord Moran and Brigadier Bradford saved Winston Churchill from pneumonia with the use of a new sulphonamide called sulphapyridine.

Domagk was awarded 1939 Nobel Prize for discovery of antibacterial effects of prontosol; Nazi Germany government forced him to decline.

Hitler banned acceptance of Nobel Prizes after Carl von Ossietzky, an outspoken activist against fascism, was awarded a Nobel Peace Prize.

In 1947, a formal award ceremony was held to present Domagk with his Nobel Prize diploma and medal.

In 1939, René Dubos isolated tyrothricin; first antibiotic in history to show strong antimicrobial activity experimentally in a mouse.

It was also the first antibiotic found by large-scale screening of soil bacteria; this method led to discovery of many more antibiotics.

On 3rd Sept 1928, after a holiday, A. Fleming discovered Penicillin when finding a mould contaminated petri dish had killed bacteria closely.
Fleming found penicillin was unstable and hard to produce, thus, he spent time trying to get chemists interested in it.

Howard Florey, Ernest Chain and Norman Heatley took penicillin from the petri dish to large-scale production.

In 1941, policeman Albert Alexander was dying from a scratch from a rose bush. Given penicillin, he recovered until stocks ran out. He died.

In March 1942, Anne Sheafe Miller had septicaemia after miscarriage, luckily John Fulton, Howard Florey’s friend was in the next room.

Using 5.5g of crude penicillin Anne’s life was saved. This was the first successful use of penicillin.

Penicillin V made in 1945 was the first successful penicillin to take by mouth.

In 1945, Dorothy Hodgkin worked out the structure of penicillin by using X-rays. She was later awarded the Nobel Prize in Chemistry.

In 1942, G.F. Gause & his wife M. Brazhnikova found Gramicidin S; within a year Russian hospitals used it. It was on the front line by 1943.

In 1943, streptomycin, the first aminoglycoside & effective drug against TB, was isolated and developed by Albert Schatz and Selman Waksman.

Global soil samples were analysed by Benjamin Duggar & in 1948 he revealed the discovery of chlortetracycline, the first tetracycline.

Chlortetracycline had a broad range of targets and proved itself in 1948 saving 5-year-old Tobey Hockett’s life, when all other antibiotics failed.

In 1947, Ehrlich and colleagues discovered the first amphenicol (called chloramphenicol).
Interestingly, in the same year Gottlieb and colleagues also came across chloramphenicol.

In 1949, erythromycin producing bacteria were isolated by A. Aguilar from Iloilo City, Philippine Islands and sent to the Eli Lilly Company.

Erythromycin was the first macrolide and was an essential alternative for people allergic to penicillin as it inhibited similar bacteria.

In 1952, a sample of soil was sent from a missionary in Borneo to his friend E. C. Kornfield. Vancomycin was discovered from this sample.

Vancomycin was the first glycopeptide and with the rise of methicillin-resistant bacteria, proved an essential treatment.

In June 2002, the first case of vancomycin resistant Staphylococcus aureus was isolated from a Michigan patient aged 40.

In 1950, Y. Koyama in Japan isolated the 1st polymyxin, colistin. Replaced in the 70s by less toxic drugs, AMR has forced its revival.

As of 1959, metronidazole treated non-bacterial infections, when accidently in 1962 it proved able to cure a bacterial infection, gingivitis.

Metronidazole was the first nitroimidazole and is still a commonly prescribed drug for a number of infections.

In 1957, J.C. Sheeman was the first to chemically make penicillin; leading to hundreds of new penicillin variations including ampicillin.

Penicillin was unstable and hard to make; Sheeman said building it in the lab was like "placing an anvil on top of a house of cards".

In 1945, Giuseppe Brotzu found a fungus from seawater near a sewage outlet in Sardinia; the first cephalosporin was isolated from this.
Giuseppe Brotzu went on to become president of the Sardinian Regional Council and later Major of Cagliari.

Edward Abraham & Guy Newton were responsible for isolating Cephalosporin C, Abraham patented it and set up trust funds with proceeds.

In 1976, Merck found a new class of β-lactam antibiotics, carbapenems, these proved able to kill bacteria resistant to other β-lactams.

Carbapenems are drugs of 'last resort'; although resistant bacteria have emerged. If carbapenems fail, there are few alternative treatments.

In 1957, a crude material was isolated from *N. mediterranei*, this material was nicknamed rififi after a popular French crime film.

This nickname formed the basis of the group of antibiotics that were subsequently isolated, the rifamycins.

By chemical modification of the rifamycins, rifampicin was created. This drug has proved essential in the treatment of TB.

Linezolid was introduced to the marketplace in 2001. It was the first of a new class of antibiotics known as the oxazolidinones.

In 1957, the Umezawa group in Japan, isolated kanamycin. It was a break-through drug for killing penicillin and streptomycin resistant bacteria.

In 1985, Barry Marshall swallowed a petri dish of *Helicobacter pylori* to prove they caused stomach diseases such as peptic ulcers.

He cured himself of the infection with antibiotics and was later awarded the Nobel Prize with his collaborator J. Robin Warren.