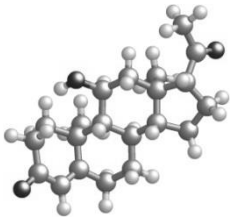

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Discovery and Development of the Antibiotic Penicillin

Introduction

In this lesson you will study various sources of information related to the discovery and development of the antibiotic *penicillin*. The articles are followed by a range of questions through which you will probe the complexities surrounding the discovery and development of this drug. Penicillin was discovered by Alexander Fleming in 1928. The antibiotic was then developed by Howard Florey and Ernst Chain, eventually coming into use between 1942 and 1945. To many people, penicillin was a wonder drug that cured illnesses which had proven fatal to previous generations. In 1945, Alexander Fleming, Ernst Chain and Howard Florey were awarded the Nobel Prize for Medicine "For the Discovery of Penicillin and its Curative Effect in Various Infectious Diseases." However, from this time until his death in 1955, it was Alexander Fleming who received most of the credit for penicillin's success.

Source A: Alexander Fleming's desire to discover a potent antibiotic

Surrounded by all these infected wounds, by men who were suffering and dying without our being able to do anything to help them, I was consumed by a desire to discover something which would kill those microbes, something like salvarsan. (**Note:** Salvarsan was an antibiotic discovered in1908 by Sahachiro Hata. It contained the toxic element arsenic.)

Alexander Fleming reflecting on his time working at a hospital for wounded soldiers in France during the First World War.

Maurois, A. (1959). *The life of Sir Alexander Fleming, discoverer of penicillin*. London: Jonathan Cape.

Source B: Alexander Fleming's discovery of penicillin

Fleming was in his little laboratory as usual, surrounded by dishes. He disliked being separated from his cultures before he was quite certain that there was no longer anything to be learned from them. He was often teased about his untidy habits. He was now to prove that untidiness may have its uses.

Fleming took up several old cultures and removed the lids. Several of the cultures had been contaminated with mould. "As soon as you uncover a culture dish," he said to Pryce, "something tiresome is sure to happen. Things fall out of the air." Suddenly he stopped talking, then, after a moment's observation said, "That's funny..." On the culture at which he was looking, there was a growth of mould, as on several others, but on this particular one, all around the mould, the staphylococci germs had been dissolved.

Fleming took a little piece of the mould with his scalpel. He obviously wanted to make quite sure that this mysterious mould would be preserved. "What struck me," Pryce says, "was that he didn't confine himself to observing, but took action at once."

Maurois, A. (1959). *The life of Sir Alexander Fleming, discoverer of penicillin*. London: Jonathan Cape.

Source C: Alexander Fleming reflects upon the importance of his discovery

Nothing is more certain than that when in September 1928 I saw bacteria fading away in the neighbourhood of a mould, I had no suspicion that I had got a clue to the most powerful substance yet used to defeat bacterial infection of the human body.

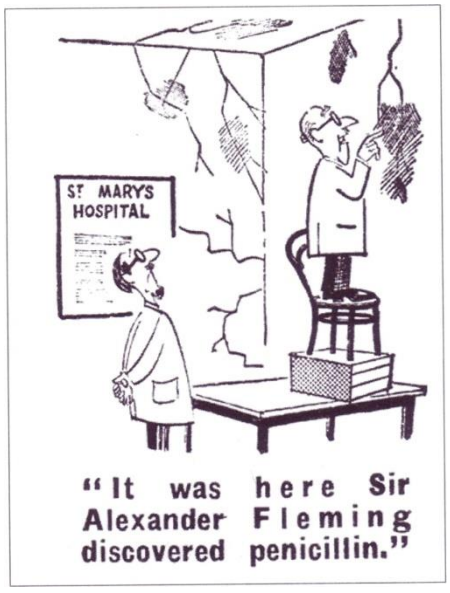
Alexander Fleming speaking to the American Pharmaceutical Manufacturers Association, 13th December 1943.

Source D: Alexander Fleming's original culture plate

Photograph of the culture plate on which Alexander Fleming observed that penicillin mould inhibits bacterial growth. The penicillin mould is located at the top of the culture plate. The small circles are colonies of bacteria.

Mann, J. (1992). *Murder, magic and medicine*. Oxford: Oxford University Press.

Source E: The Media's perception of how penicillin was discovered



A cartoon about Alexander Fleming's discovery of penicillin.

Source F: Alexander Fleming notes penicillin's potential as an antibiotic

It is suggested that penicillin may be an efficient antiseptic for application to, or injected into, areas infected with penicillin sensitive microbes.

From Fleming's article of 1929 in the *British Journal of Experimental Pathology*.

Source G: Alexander Fleming recognises the importance of penicillin

He was well aware of the therapeutic potentialities of penicillin, and was extremely keen that it should be purified, because, he said, it was, "The only product capable of killing microbes such as the staphylococci, without injuring the white corpuscles."

Dr. L. Holt, a biochemist who worked with Alexander Fleming in 1934.

Maurois, A. (1959). *The life of Sir Alexander Fleming, discoverer of penicillin*. London: Jonathan Cape.

Source H: The media's opinion of Alexander Fleming – Part 1

The man who made possible this incalculable alleviation of human suffering is Dr. Alexander Fleming, discoverer of the anti-bacterial effect of the mould from which penicillin is made. He is a short, retiring Scot with somewhat dreamy blue eyes, fierce white hair and a mind which, when it moves, moves like a cobra. It will be hard to say who the great men of the 20th century are, but Dr. Alexander Fleming is certainly one of them. He belongs in the tradition of the scientific seers which includes Galileo and Isaac Newton.

Penicillin is already big business, yet Dr. Fleming (who discovered it) and Dr. Florey (who made it tick) have got nothing out of it but praise.

Time magazine, 15th May 1944.

Source I: The Media's opinion of Alexander Fleming – Part 2

When a man of genius is modest and simple, the world is liable to undervalue what he has done. Alexander Fleming was a genius of this rare kind. During his life in his own land, recognition of his genius was grudging. I became indignant on his behalf. I was anxious that justice should be done to this great pioneer. It seems to me that it was a duty laid on me as the proprietor of newspapers in Britain, the country which gained a measure of reflected glory on account of Fleming's immense achievement.

Lord Beaverbrook writing in *The Evening Standard*, 5th January 1956.

Source J: The limitations of Alexander Fleming's work

Fleming used penicillin as a local antiseptic on a scientist's eye that had conjunctivitis. The infection cleared-up, but when he used it in deep wounds, it did not work. It also took a long time to produce enough penicillin to treat just one person.

In 1929, Fleming wrote all his findings in a paper. Nobody at the time took any notice. This was probably Fleming's fault. He had not tried injecting penicillin; he had only used it as a local antiseptic. This meant that he had not provided the evidence that it was an important breakthrough. He did write at the time, "It is quite likely that penicillin will be used in the treatment of septic wounds."

A description of Fleming's early work with penicillin.

Source K: Howard Florey begins research on penicillin

I enclose some proposals that have a very practical bearing at the moment. The properties of penicillin hold out promise of its finding practical application in the treatment of infections. In view of the great practical importance of the above mentioned bactericidal (germ-killing) agents it is proposed to prepare these substances in a purified form suitable for injection and to study their antiseptic action in living creatures.

Application from Howard Florey to the Medical Research Council for money to finance penicillin research,

6th September 1939, three days after the outbreak of World War Two.

Source L: Penicillin's first clinical trial

The policeman had a sore on his mouth about a month previously, and the infection had spread to his scalp. He'd had an abscess there. It had spread to both his eyes and one of them had to be removed. He had abscesses open on his arm. He had abscesses on his lung – he was well on his way towards death from the terrible infection. We'd nothing to lose and everything to gain. So we thought we'd have a try.

The shortage of penicillin was such that after the first day I collected all his urine and I took it over to where Florey was working so that the penicillin could be extracted from the urine and used again.

On the fourth day he was really dramatically improved. He was sitting up in bed and his temperature had gone down. On the fifth day the penicillin began to run out and we couldn't go on. Of course, when they'd extracted the penicillin from the urine they couldn't get it all back and it gradually ran out. He wasn't cured. He gradually relapsed and eventually died.

Professor C. M. Fletcher, a member of Howard Florey's team, speaking on *Horizon*, BBC television, 27th January 1986.

Source M: The use of penicillin during World War 2

We had enormous numbers of infected wounded, terrible burn cases among the crews of the armoured cars. Sulphonamides had absolutely no effect on these cases. The last thing I tried was penicillin. I had very little penicillin, something like 10 000 units, maybe less.

The first man I tried it on was a young New Zealand officer called Newton. He had been in bed for six months with compound fractures of both legs. His sheets were soaked with pus and the heat in Cairo made the smell intolerable. Normally he would have died in a short time. I gave three injections a day of penicillin and studied the effects under a microscope... The thing seemed like a miracle. In ten days time the left leg was cured and in a month's time the young fellow was back on his feet. I had enough penicillin left for ten cases. Nine of them were complete cures.

Lt. Col. Pulvertaft, an army doctor in North Africa, 1943.

Maurois, A. (1959). *The life of Sir Alexander Fleming, discoverer of penicillin*. London: Jonathan Cape.

Source N: Howard Florey describes what motivated his work on penicillin

There are a lot of misconceptions about medical research. People sometimes think that I and the others worked on penicillin because we were interested in suffering humanity – I don't think it ever crossed our minds about suffering humanity; this was an interesting scientific exercise. Because it was some use in medicine was very gratifying, but this was not the reason we started working on it. It might have been in the background of our minds – it's always in the background in people working on medical subjects – but that's not the mainspring.

Lord Howard Florey in an interview in Australia, 1967.

Source O: The influence of the media – Part 1

28th August 1942

Sir, in the leading article on penicillin yesterday, you refrained from putting the laurel wreath for discovery around anybody's brow. It should be given to Professor Alexander Fleming of this research laboratory. For he is the discoverer of penicillin and was the author also of the original suggestion that the substance might prove to have important applications in medicine.

I am, Sir, yours faithfully,
Almroth Wright,
Inoculation Department
St. Mary's Hospital

A letter written to the Editor of *The Times* newspaper by Alexander Fleming's superior at St. Mary's Hospital, Paddington.

Source P: The Influence of the media – Part 2

I have now quite good evidence, from the Director General of the BBC in fact, and also indication from some people at St. Mary's, that Fleming is doing his best to see the whole subject is being presented as being foreseen and worked out by Fleming, and that we in this department just did a few final flourishes.

Letter from Howard Florey to Sir Henry Dale, President of the Royal Society, 11th December 1942.

Source Q: The Influence of the media – Part 3

My policy here has been never to interview the press or allow them to get any information from us by telephone. This has been rigidly adhered to in spite of protests from some of my colleagues (especially Chain).

In contrast, Fleming has been interviewed apparently without cease, photographed etc. (we have ample evidence of this here) with the upshot he is put across as the discoverer of penicillin (which is true), with the implication that he did all the work leading to the discovery of its properties (which is not true).

Many of my colleagues feel things are going much too far, and are getting naturally restive at seeing so much of their own work going to glorify or even financially enrich someone else.

Letter from Howard Florey to the Secretary of the Medical Research Council, January 1944.

Source R: Frederick Lister's work on penicillin predates that of Alexander Fleming

There was a centuries old *folk-medicine* tradition that various mouldy substances cured infections. In 1940, a patient of Lister's described to Dr. Fraser-Moore the treatment she had received at King's College Hospital in 1881, when she was a young nurse. Injured in a street accident, she sustained a wound that became infected. Various antiseptics failed to clear the infection and then something was used that worked so dramatically that she asked Lister's Registrar to write the name of it in her scrap book. The writing in her book, which she showed to Fraser-Moore, was *Penicillin*.

MacFarlane, G. (1984). *Alexander Fleming: the man and the myth*. London: Chatto and Windus.

Source S: Alexander Fleming reflects on the work of Frederick Lister

Alexander Fleming had just been told of Frederick Lister's experiments of 1871 using a penicillium mould to kill bacteria. Fleming: "What a pity that his experiment of November 1871 didn't come off. He had the idea of penicillin, but he had the wrong mould or the wrong bacteria or both. If fate had been kind to him, medical history might have been changed and Lister might have live to see what he had always been looking for, a non-poisonous antiseptic. From the time of Pasteur and Lister, workers had been trying to kill one bacteria with another. The idea was there, but the performance had to wait until Fortune decreed that a mould spore should contaminate one of my cultures, and then for a few years more until the chemists busied themselves with the products of this same mould to give us pure penicillin. Lister would indeed have rejoiced to have had such a thing.

Alexander Fleming talking to Lord Webb-Johnson in the 1950s.

Maurois, A. (1959). *The life of Sir Alexander Fleming, discoverer of penicillin*. London: Jonathan Cape.

Source T: The discovery of penicillin was inevitable

We would have started a research programme (into anti-bacterial substances provided by micro-organisms) even if Fleming's paper had never been published, and if we had not done so, someone else somewhere in the world would have taken this initiative. As a result, some interesting anti-bacterial substances would have been discovered and a general screening programme would have started. This would undoubtedly have revealed the existence of the penicillin-producing penicillia. The development of the antibiotic field might have been delayed by a few years, but it would inevitably have taken place with the same final results that we have now.

Ernst Chain, *Proceedings of the Royal Society*, 1971.

Source U: The Nobel Prize for Physiology or Medicine – 1945

Sir Alexander Fleming, Doctor Chain, and Sir Howard Florey. The story of penicillin is well-known throughout the world. It affords a splendid example of different scientific methods cooperating for a great common purpose. Once again it has shown us the fundamental importance of basic research. The starting-point was a purely academic investigation, which led to a so-called accidental observation. This gave the nucleus, around which one of the most efficient remedies ever known could be crystallized. This difficult process was made possible with the aid of modern biochemistry, bacteriology, and clinical research. To overcome the numerous obstacles, all this work demanded not only assistance from many different quarters, but also an unusual amount of scientific enthusiasm, and a firm belief in an idea. In a time when annihilation and destruction through the inventions of man have been greater than ever before in history, the introduction of penicillin is a brilliant demonstration that human genius is just as well able to save life and combat disease.

Exert from the speech made by Professor G. Liljestrand during the presentation of the Noble Prize for Physiology or Medicine, 10th December 1945.

Source V: Alexander Fleming's reflections on the Nobel Prize

Fleming told me often that he didn't deserve the Nobel Prize, and I had to bite my teeth not to agree with him. He wasn't putting on an act – at least around 1945/6. At the same time he would tell me that he couldn't help enjoying all his undeserved fame, and I liked him for that. With me and others of his scientific colleagues he had the sense to know that none of us were more impressed by him than he was himself.

Letter from Dr. W. E. Van Heuningen to Dr. G. McFarlane, 3rd August 1980.

MacFarlane, G. (1984). *Alexander Fleming: the man and the myth*. London: Chatto and Windus.

Questions

Read through *all* of the questions in the table provided on page 8. Choose and answer the *one question* from *each row* that is most appropriate for your level of ability, interest and learning style.

References

Shephard, C., & Rees, R. (2004). *Medicine investigations*. John Murray Publishers: London.

Scott, J., & Culpin, C. (2004). *Medicine through time*. Collins Educational: London.

Question 1: Refer to **Source T**. What are the implications and consequences for the discovery of penicillin if neither Alexander Fleming nor Howard Florey had ever lived?	**Question 2:** Refer to **Source R** and **Source S**. To what extent do these sources prove that Alexander Fleming did *not* discover penicillin?	**Question 3:** Refer to **Sources B**, **E**, **R**, **S**, **T**, **U** and **V**. What assumptions are made, what information is taken into account and what points of view are considered / ignored when it is claimed that "Alexander Fleming discovered penicillin?"
Question 4: To what extent is **Source E** a fair and accurate interpretation of the information contained within **Source B** and **Source D**? What point of view does the artist who drew **Source E** have?	**Question 5:** Refer to **Sources B**, **D** and **E**. Draw a cartoon or short comic strip that portrays the discovery of penicillin from a different perspective or point of view compared to the one that is shown in **Source E**.	**Question 6:** It is widely accepted within the scientific community that *chance* played a significant part in Alexander Fleming's discovery of penicillin. Alexander Fleming seems to accept this himself in **Source V**. Research to investigate which other drugs have been discovered by chance. What are the more rational and scientific methods by which drugs are discovered?
Question 7: Refer to **Sources A**, **B**, **C**, **D**, **E**, **F** and **G**. Write a front page newspaper article reporting on Alexander Fleming's discovery of penicillin at St. Mary's Hospital in Paddington, London, in September 1928.	**Question 8:** Review **all** of the sources. Write an article to be published in a scientific journal or magazine which argues convincingly that penicillin was the most important drug to be discovered during the 20th Century.	**Question 9:** Which major diseases, for which there are no absolute known cures, pose a threat to humanity? From the diseases that you have identified, which *single* disease most urgently requires a "wonder drug" like penicillin? Use convincing arguments to justify your answer.
Question 10: Review the literature to identify which other scientists have been awarded either the Nobel Prize for Chemistry or the Nobel Prize for Physiology or Medicine due to their work on antibacterial compounds. Briefly summarise the contribution that each scientist made to this area of study.	**Question 11:** Refer to **Sources B**, **E**, **G**, **H**, **J** and **V**. Evaluate the information contained within these sources, and any other sources of your choice. Did Alexander Fleming deserve to be awarded the Nobel Prize for Physiology or Medicine in 1945? Justify your answer.	**Question 12:** Dorothy Hodgkin was awarded the Nobel Prize in Chemistry in 1964, "For her determinations by X-ray techniques of the structures of important biochemical substances." One of these biochemical substances was penicillin. Which other women have been awarded the Nobel Prize in Chemistry? How many men have been awarded the Nobel Prize in Chemistry? What are the possible reasons and implications of your findings?
Question 13: What are the ideal properties that a drug should possess? You may have already generated a list of ideal properties while developing *drug* as a concept in a previous lesson. Refer to **Sources D**, **G**, **L** and **M**. To what extent does penicillin fulfil the ideal properties of a drug?	**Question 14:** To what extent do Howard Florey's comments in **Source N** surprise you? Identify some of the misconceptions that he talks about and state clearly what you think the "mainspring" or motivation for his research into penicillin was.	**Question 15:** Refer to **Sources B, J, K and L**. Compare and contrast the scientific methodologies shown by Alexander Fleming and Howard Florey. What possible reasons are there for any differences that you identify? From your own knowledge of the scientific method, propose how their methodologies could be improved.
Question 16: Refer to **Sources J**, **K** and **L**. How far would the development of penicillin have got without the intervention of Howard Florey and Ernst Chain?	**Question 17:** Refer to **Sources E**, **H**, **I**, **O**, **P** and **Q**. Evaluate the role of the media in influencing peoples' decisions with respect to who played the greater part in penicillin's success.	**Question 18: Either** Review **all** of the sources. Actively participate in a discussion / debate in which you must defend **either** Alexander Fleming **or** Howard Florey as the most important scientist in penicillin' success. **Or** Review **all** of the sources. To what extent is it important for the scientific community to answer the question, "Who deserves the credit for the discovery of penicillin?" Write your own answer to this question.
Question 19: Review **some** of the sources. Use the **two** item Venn Diagram template provided to summarise the similarities, differences and interactions between any **two** of the following: • Alexander Fleming. • Howard Florey. • Penicillin. • Bacterial infections. • The scientific method. • Another item of your choice.	**Question 20:** Review **most** of the sources. Use the **three** item Venn Diagram template provided to summarise the similarities, differences and interactions between any **three** of the following: • Alexander Fleming. • Howard Florey. • Penicillin. • Bacterial infections. • The scientific method. • Another item of your choice.	**Question 21:** Review **all** of the sources. Use the **four** item Venn Diagram template provided to summarise the similarities, differences and interactions between any **four** of the following: • Alexander Fleming. • Howard Florey. • Penicillin. • Bacterial infections. • The scientific method. • Another item of your choice.