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REVIEW

What if Fleming had not discovered penicillin?

Sulaiman Ali Alharbi [a,*], Milton Wainwright [a,c], Tahani Awad Alahmadi [b], Hashim Bin Salleeh [b], Asmaa A. Faden [d], Arunachalam Chinnathambi [a]

[a] Department of Botany and Microbiology, College of Science, King Saud University, P.O. Box 2455, Riyadh 11451, Saudi Arabia
[b] Emergency Medicine Department, Pediatric Emergency Unit, College of Medicine, King Saud University, P.O. Box (56) 2925, Riyadh 11461, Saudi Arabia
[c] Department of Molecular Biology and Biotechnology, University of Sheffield, Sheffield S10 2TN, UK
[d] College of Dentistry, King Saud University, P.O. Box 60169, Riyadh 11545, Saudi Arabia

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Abstract What would have happened had Alexander Fleming not discovered penicillin in 1928? Perhaps the obvious answer is that, someone else would have discovered penicillin during 1930s and the Oxford group, would still have purified it sometime in the early 1940s. Here, however, in this counterfactual account of the penicillin story, it is argued that without Fleming, penicillin might still be undiscovered and the antibiotic age would never have dawned. As a result, many of the recent developments in medicine, such as organ transplantation, might have been delayed or, at best, made more hazardous. Penicillin might have come onto the scene a few years later but, had Fleming overlooked the discovery, it seems certain that penicillin would not have saved countless Allied lives, during and after D-Day. Instead of having enjoyed fifty and more years of the antibiotic age, it is argued here, that we would have had to rely upon highly developed sulphonamides, so-called ''supasulfas'', and other chemically-derived antibacterial drugs. Indeed, it might be the case that, even well into this new millennium, the antibiotic age has yet to dawn, and medicine is still waiting for someone to chance upon penicillin. Here we discuss what might have happened had Fleming not discovered penicillin and come to the conclusion that the medical armoury available today would have been far different and might have relied solely upon highly developed varieties of sulphonamides or similar, synthetic, non-antibiotic antibacterial agents.

* Corresponding author. Address: Department of Botany and Microbiology, College of Science, Building Number 05, King Saud University, P.O. Box 2455, Riyadh 11451, Saudi Arabia. Mobile: +966 555232656.
E-mail address: sharbi@ksu.edu.sa (S.A. Alharbi).
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1. Introduction

It is September, 1928; a forty-seven year old man walks, somewhat wearily, up the steps to his place of work. He would rather not be there. Summer is not yet over and he has had to return to London because of an emergency, otherwise he would still be enjoying life at his rural cottage in Suffolk. On entering his room, one of his assistants exchanges pleasantries and he doubtless responds with a few mild curses. The man sits at the bench; he is a scientist and this is his laboratory. Casually, he picks up a few old petri dishes on which he has been growing bacteria. He glances through them until he comes to one that looks unusual. A colony of mould has somehow found its way into the dish and is dissolving the bacteria around it. He shows the unusual plate to his assistant who shows only mild interest and then hands it back without comment. The scientist has one last casual look, decides the phenomenon is of no importance, and drops the dish into a bucket of disinfectant. Our scientist then picks up his bag and hurries off to catch the train back to Suffolk, unaware that he has just thrown away the opportunity to save millions of lives, win a Nobel Prize and become one of the most famous and feted men in history.

The above is of course a counter-factual account of how Alexander Fleming failed to discover penicillin, the standard story having been given many times elsewhere (Diggins, 1999; Garrod, 1947; Hare, 1982; Lignam, 2000; Wainwright and Swan, 1986; Wainwright, 1987, 1990, 2008).

Andrew Roberts, in the introduction to *What Might Have Been*, a book devoted to counterfactual studies, suggests that while battles, and many other events in history, can be successfully studied from a counterfactual perspective, the exposure of scientific discoveries to such a process tends to be less successful (Roberts, 2004). This is simply because, it is generally assumed, that if a scientist misses a discovery then sooner or later someone else will get there; gravity for example, would have still be open to discovery had Sir Isaac Newton never seen an apple tree!. However, here I wish to suggest that had Fleming not discovered penicillin then it is likely that, the first and most important of the antibiotics would remain undiscovered. There would also have been various time-related consequences; notably, insufficient penicillin would have been available for use by the Allies from D-Day onwards and other antibiotics (notably, the anti-TB drug, streptomycin) might never have been developed in time to back a number of major developments in modern surgery such as open heart and transplant surgery.

But, if Fleming had missed his chance, surely someone else would have discovered penicillin? Possibly, but it should be remembered that penicillin, although discovered by Fleming in 1928, was not purified and developed for medicine until the early 1940s, and there is no reason to believe that anyone was close to discovering penicillin in the interim. At best, without Fleming's discovery penicillin would have languished for perhaps another five or ten years.

Let us begin our counterfactual journey by going back to that fateful moment in September, 1928 when Fleming missed the opportunity to discover penicillin. . .what happened next?

Has as we have seen, although Fleming discovered penicillin in 1928 and wrote his first penicillin paper in 1929, the drug was not made available for medical use (and then largely restricted to the military) until the early nineteen forties, following the intervention of Florey, Chain and co-workers at the Oxford University. Of course penicillin could have been discovered the day after Fleming missed the opportunity, but in reality there was no parallel discovery took place. As a result, anyone taking an interest in penicillin during the 1930s did so in the knowledge of Fleming's work. In particular, there seems no reason to believe that Florey and Chain would have discovered penicillin, since their work depended on Fleming's famous paper and their access to one of his penicillin-producing cultures.

Since penicillin was, in reality, not available during the 1930s few events and lives would have been materially altered if Fleming had missed the discovery. Fleming's first penicillin paper refers to its use as an additives to bacteriological media to selectively isolate the bacterium *Bacillus influenzae*, then thought to cause influenza. A couple of workers reported using penicillin in this way, but their work was far from earth shattering, and the world of medicine would have happily continued without it. Similarly, without Fleming's discovery an American student, called Roger Reid, would have needed to find another research topic for his MS thesis; no doubt his supervisor would have come up with another topic and the young man's career would not have suffered unduly.

The absence of penicillin in the 1930s would however, have had more serious consequences for the lives of three people living in the steel city of Sheffield in England, who benefited from treatment with penicillin-rich filtrates. In 1930 such filtrates were used by Cecil George Paine to cure infections which might have left the children blind. Paine had worked in Fleming's laboratory (and had seen the famous plate). On graduating, he left London to work in Sheffield. This, his first job, was described as being conjoint, that is his efforts were to be divided acting as a Pathologist at the Royal Infirmary and lecturing at the nearby Sheffield University. The young man, was required to do some research and remembering the penicillin plate, he obtained a culture of the penicillin-producing mould from Fleming. This, he cultured and used penicillin-rich filtrates to treat infections. His first attempts, against the skin infection sychosis barbae were unsuccessful, so he turned his attention to eye infections, arguing that the penicillin filtrates would be more likely to reach pathogens in the eye, than in puss-rich skin infections. Paine treated three eye patients, a local coal miner, whose eye had become infected after an accident, and two new born babies. All the infections were cured by the simple act of irrigating the infected eye with mould filtrates. The two babies were suffering from ophthalmia neonatorum caused by *Gonococcus* and diphtheroids. Such infections in the new-born were common before the advent of purified