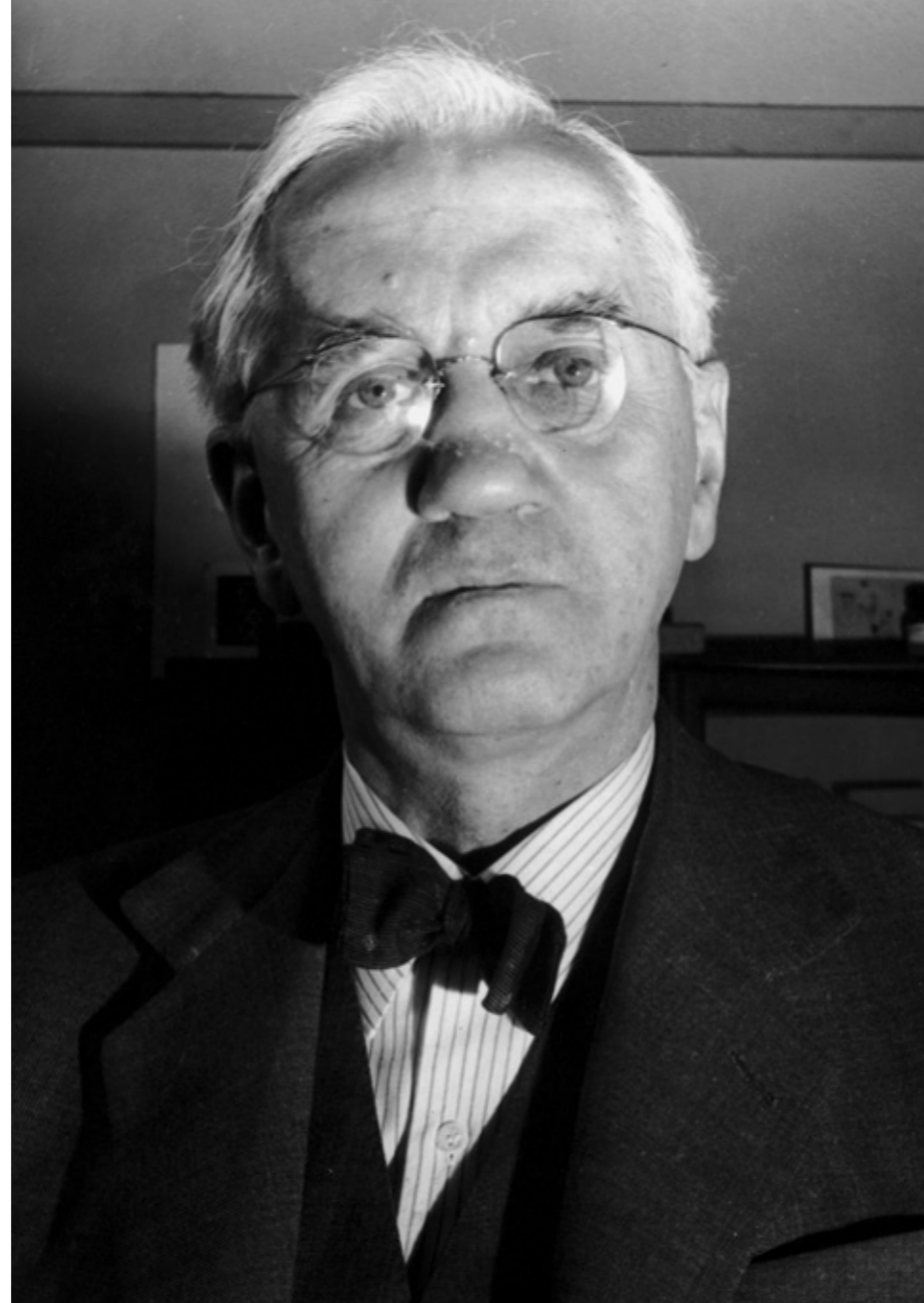


There is little prospect of further testimony from people who actually worked with Fleming. However, the existing accounts by those who knew the able but taciturn Scot well make it easier than it might otherwise be to reconcile Fleming's rather private personality with his eventually very public image as the internationally acclaimed discoverer of penicillin. Moreover, that discovery can now be seen in a historical perspective that acknowledges the contribution made by others to its realisation, and also takes account of Fleming's other, less well known, research achievements.

When, in the late 1940s, Fleming's fame rose to dizzy heights, it was largely as a result of his clinical colleagues' efforts to capitalize on the miracle of penicillin for the benefit of their medical school, St Mary's. This generated some resentment among scientists elsewhere whose work had brought the drug to the bedside. With Fleming being compared to Newton and Pasteur, a reaction was bound to follow; but that reaction has now perhaps swung too far, so that Fleming's justifiable reputation deserves to be revived.

### The historical perspective

Fleming's laboratory career spanned nearly 50 years. It covered much of the chemotherapeutic era, from the introduction of salvarsan almost to the first semi-synthetic penicillins. Along the way it intertwined with Almroth Wright's and Leonard Colebrook's careers and, more controversially, with those of Howard Florey and the Oxford team. The Oxford scientists purified penicillin and they were the first to apply it experimentally and clinically. In their various ways these people all helped to transform surgical practice in the first half of the 20th century. They



◀ Alexander Fleming in 1951. Hulton Archive/Getty Images

the fellowship of the Royal College of Surgeons – no mean feat.

### A fruitful partnership

By then Fleming had been recruited to Almroth Wright's 'Inoculation' Department, a branch of the St Mary's Medical School dedicated to therapeutic applications of the new science of immunology. This admirable enterprise attracted, trained and financially supported clever young graduates like Fleming. Wright's interest was in therapeutic vaccines, and whatever Fleming's reservations may have been about the efficacy of some of these preparations (his famous uncommunicativeness may have served him well in this regard), it must be said that the sale of these vaccines financed the department right up to Wright's overdue retirement in 1946 at the age of 84. The income allowed Fleming, whose habits were in any case frugal, to pursue various unrelated interests without the usual constraint of lack of funds. Furthermore, Almroth Wright's capacity for 'networking' and his reputation as a controversialist willing to offer an opinion on any matter whatever kept his department in the public eye and the reclusive Fleming 'in the swim'.

Fleming quickly became Wright's right-hand man and silent foil. The delegation to him of routine responsibilities such as management of the production of the vaccine preparations that were sold to private patients through Parke Davis may not have been welcome, and they possibly hindered Fleming's own original work; but his chief's ebullience and flair probably generated many of the research ideas, and this must have benefited Fleming. While Fleming was not necessarily an

rejected Listerian antiseptics and they promoted the aseptic approach. They investigated the sources and nature of wound infections and they drew on specific vaccine, serum and chemotherapies to overcome them. Fleming's discovery of penicillin was the single most important contribution to that transformation in surgery, as well as enabling much more in the medical treatment of infectious disease.

### Fleming's early years

Alexander Fleming grew up on a farm on the bleak uplands of Ayrshire in south-west Scotland. He was one of a close knit family of five brothers and three sisters, and was educated at small local schools and Kilmarnock Academy.

At 16 he left Scotland to join an older brother, Tom, in London. There he worked for 3 years as a shipping clerk, a job which may have given him the taste for international travel that he indulged towards the end of his life.

Office work did not extend Fleming's extraordinary capacity for disciplined and focussed observation of natural phenomena, however, and when he received a small family legacy he enrolled in 1901 as a student at the medical school of St Mary's Hospital, Paddington. There his academic career was outstanding. Contemporaries recalled him passing examinations without apparent effort, and the scholarships and gold medal he won testify to this ability. Very soon after qualification he also secured

# What manner of man was Alexander Fleming?

Almost everyone has heard of Alexander Fleming though it is now 80 years since he discovered penicillin and over 50 years since he died. **Philip Mortimer's** brief description of the character and career of the SGM's first president offers a novel perspective on Fleming's achievements.



◀ Almroth Wright, October 1929.  
Hulton Archive/Getty Images



▶ Alexander Fleming, December 1951.  
Time and Life Pictures/Getty Images

original thinker, he was a deft, and became a very experienced, bench worker. Over a period of 36 years in Wright's department he turned out a series of important contributions to laboratory medicine. The semi-protected environment of the crowded Paddington laboratory well suited this perceptive but reserved man, whose abilities were complementary to those of his extrovert chief. Fleming also owed something to his friend and contemporary, Charles Wilson, later Lord Moran. It was Moran, the consummate medical politician who, in lifting St Mary's from its Cinderella status among the London medical schools, promoted Fleming's reputation.

### Treating syphilis

So what was the substance of Fleming's career? In 1910 Wright's friendship with the famous German chemist Ehrlich secured the gift of samples of the new anti-spirochaetal drug, salvarsan ('606'), for clinical use. These were handed on to Fleming who put them to good effect.

Fleming's first scientific work had involved the application of von Wasserman's ground-breaking laboratory test for syphilis. That test has never been a laboratory exercise for the faint-hearted, and back in the 1900s the technical tinkering needed to get it to work must have been an appealing challenge for Fleming. That achieved, Fleming's next success was in devising satisfactory means of administering the salvarsan he had acquired. This synthetic compound was unstable and poorly soluble; and when given intramuscularly it was painful and necrotizing for tissue. Fleming overcame this by infusing the drug intravenously. Consequently, he developed a private practice discreetly treating cases of syphilis with '606' and its successor, '914'. These were universally used to cure syphilis for the following 30 years, and had seen it off as an endemic disease long before penicillin, the present drug of choice, made its clinical debut.

### World War I

The next phase of Fleming's work had a terrible and lasting relevance. It concerned the management of war wounds, and raised an issue that has yet to be resolved even in modern peacetime surgical practice. In France, between 1915 and 1918, Fleming showed that most battlefield injuries became infected, first with anaerobic and then with aerobic organisms. The problem, a forerunner of today's hospital-acquired clostridial and MRSA infections, was superimposed on grossly contaminated war wounds, and Wright, sustained by Fleming's supportive research findings, railed against the incontinent application of disinfectants to these wounds.

### From lysozyme to the conquest of sepsis

Returning to St Mary's in 1919, Fleming made his first major scientific discovery, that human tears and nasal secretions contain 'lysozyme' (the word was coined by the classically

educated Wright). Lysozyme rapidly dissolves a wide range of bacterial cells in the laboratory, and it was found to be widespread in nature. It was assumed to be a common animal defence against bacterial infections. For Fleming it opened up a path of discovery semi-independent of Wright's scientific interests, and it would alone have assured Fleming a place in the history of microbiology. However, the achievement was (or more accurately was later judged to be) overshadowed by the discovery of penicillin in 1928. That story has often enough been told not to be repeated here (but see Kevin Brown's specially commissioned article on p. 12).

In retrospect, Fleming should obviously have persevered with penicillin longer than he did; but he was, according to his younger colleague Hare, 'no chemist'. However, Fleming's interest in antibacterial substances did not flag, and he pursued the general goal of finding effective, non-toxic antibacterial substances that might be of clinical use. In the later 1930s he studied the sulfonamides as they appeared and, like Colebrook, used them successfully to treat streptococcal infections, whether pneumonic, puerperal or other. Wright, Fleming and Colebrook shared the view that antisepsis had been a crude weapon dependent on the use of tissue-toxic chemicals. Conversely asepsis needed, in order to maintain it, non-toxic antibacterials that were specific for particular infections.

### Fleming's biographers

Fleming has been lucky in his many biographers. The most distinguished, the French writer Andre Maurois, produced a literary triumph in 1959. He obtained written testimony from a host of Fleming's acquaintances, none of them willing to criticize a recently dead national treasure. And Maurois himself, already the biographer of several French notables, was anxious to expiate some incautious remarks he had made in 1940 on the subject of British perfidy. However, the British hero he chose to write about was far removed from his own culture and, not really understanding Fleming's world, Maurois was too generous to his subject. His was an uncritical, even hagiographic, account.

Posterity is more indebted to Ronald Hare who both wrote the best book on the penicillin phenomenon and drew attention to Fleming's other scientific achievements. Hare wrote affectionately about 'Flem', admiring his technical ability and modest demeanour, but acknowledging his pawky humour, extreme economy with words, and child-like pleasure in games and tricks such as painting with chromogenic bacteria. These latter characteristics may have diminished Fleming in the eyes of the English scientific establishment; they almost certainly led its members to undervalue his intellect.

A later biographer, Gwyn Macfarlane, was an Oxford physician who had previously written about Florey and

understood the politics of the controversy that arose between Florey's Oxford group and Fleming's St Mary's based associates concerning where the credit for penicillin lay. The Londoners, abetted by the Beaverbrook press, had special reasons for claiming the triumph of penicillin as their own, and they antagonized some of the Oxford scientists. Nevertheless, Macfarlane gives a balanced assessment of Fleming's part in what was a huge shared achievement that also had important American involvement. Fleming's own way of dealing with the contention between Oxford and St Mary's was to stay aloof, though he enjoyed – and why not? – the belated public and academic acclaim accorded to him.

During his semi-retirement, Fleming travelled widely by plane and ocean liner, latterly with his second wife, Amalia. There is here an amusing parallel with the outstanding laboratory worker of the previous generation of microbiologists, Robert Koch. Both men, once freed of their laboratory responsibilities, circled the world accepting academic plaudits, accompanied by their young wives. Macfarlane quotes an anecdote describing the sort of reception Fleming was often given abroad

*'In Spain, when he was walking in procession from the graduation ceremony to a bullfight, members of the crowd fell to their knees to kiss the hem of his latest colourful robe. He later resented a cynical suggestion that he had been mistaken for a new cardinal.'*

### Significance as a scientist

Though Fleming was a gifted laboratory-based doctor, he was, again like Koch, neither articulate nor gregarious enough to occupy a leading place in his country's medico-scientific establishment. British scientists do not rank their peers according to the esteem in which they are held by the lay public – this is more likely to attract envy than respect. The more ungenerous of Fleming's

scientific contemporaries viewed his observation of a mould on a discarded plate in 1928 as a kind of fluke; but they perhaps ought to have taken the opportunity to read his other scientific articles, virtually all published before he became a household name. These are skilfully written and varied in content, and several have been influential.

Fleming's descriptions of the Wasserman test and of an apparatus for infusing salvarsan have already been referred to. His studies on the bacterial flora of war wounds focused on the haemolytic streptococci, and Fleming was one of the first to use beta haemolysis of blood agar as the touchstone of streptococcal pathogenicity. In 1919 he published a paper on the collection of blood into citrate solution for subsequent transfusion which anticipated and partially solved several of the difficulties that the first generation of professional blood bankers encountered some two decades later. Thereafter, as well as his well-known papers on lysozyme and penicillin, Fleming wrote papers on the use of the sulfonamide M&B 693.

Harking back to his experience of treating neurosyphilis, Fleming, in 1942, successfully treated a case of pneumococcal meningitis intrathecally with precious penicillin given him by Florey. Long after it was necessary to minimize its consumption, clinicians still chose to give penicillin in a small intrathecal dose to begin the treatment of meningitis, and Fleming's influence may also have been a factor in choosing the same route to administer streptomycin to children with tuberculous meningitis. The latter was frequently a life-saving intervention.

### Conclusion

Fleming made not one but several important contributions to the development of chemotherapy. Taking the long perspective, he ranks not on a solitary pedestal but equal among several pioneers of antibiotics, and this, to be fair, is where he would probably have

placed himself. He would also have pointed to the ironies that the first organism he showed to be sensitive to penicillin, *Staphylococcus aureus*, was the first to develop resistance to it (over 50% of hospital isolates by 1950), and that those who later met that problem with newer antibiotics did not, and have not since, been accorded the recognition he got.

Lord Moran, who knew Fleming as well as anyone, later wrote: *'Alexander Fleming had lived in obscurity and in some disfavour ... He seemed to his profession to be disgruntled by criticism and by neglect, a sour, rather silent Scot. And then, on the verge of old age, he discovered penicillin. He, too, had found a place in the sun ... Fleming seemed to spend the rest of his days travelling over the world, making modest little speeches ... everywhere he went he won their hearts by his happy simplicity.'*

In fact, Fleming was very good at whatever he chose to do, and perhaps being aware of his weakness as an exponent of his work he accepted the long-delayed praise showered on him with dignity but few words. What more could one ask of a rather unlikely hero than that he should have known his limitations and not bored his audiences by reading out long speeches?

#### Philip Mortimer

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### Further reading

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