The shooter and the shot

Edward Abraham

Alexander Fleming: The Man and The Myth.

By Gwyn Macfarlane.

Chatto & Windus/Harvard University Press: 1984. Pp.304. £12.50, \$20.

GWYN Macfarlane prefaced his biography of Lord Florey with an aphorism attributed to Voltaire: "We owe consideration to the living; to the dead we owe only the truth". He might have saved it for this following volume. But "what is truth" said Francis Bacon's jesting Pilate. The fluent prose of *Alexander Fleming: The Man and The Myth*, a book which provides a definitive assessment of the role of Sir Alexander Fleming in the story of penicillin, should persuade readers to stay for the author's answer.

In the 1940s there was world-wide gratitude for penicillin. Fleming found that fame had been thrust upon him and that he alone had become associated in the public mind with the name he gave to an active "mould broth filtrate". But his discovery had been made in 1928. André Maurois and others have presented their views on the eclipse of penicillin during the intervening years. Gwyn Macfarlane has now written the most detailed of all the biographies and has taken pains to consult primary sources. As one who has made distinguished contributions to medical research but has no personal place in this story, his judgement deserves respect.

Fleming's Scottish background and the events which led him from an Ayrshire farm to St Mary's Hospital are the subjects of early chapters. The farm held no future for him, as a younger son, and he took the road to London, like many Scots before him. Living with a brother, he attended the Regent Street Polytechnic and then became a junior clerk in the American Line.

It was an unexpected legacy of £250 that enabled Fleming to study medicine, and he apparently chose St Mary's because he had once played water-polo against the hospital team. Later, another seeming irrelevancy — that he was a fine shot — deflected his thoughts of becoming a surgeon. To keep him in St Mary's rifle team a colleague persuaded Sir Almroth Wright to take him as a part-time research assistant. By this time we see him as a modest man who was remarkably good in examinations, and enjoyed games and company, but who was so lacking in conversation that his blue eyes were said to be sometimes immobilized in a basilisk stare.

The book contains an amusing sketch of Almroth Wright, a formidable intellectual, full of conviction that his mental powers would reveal the solutions of medical problems, on whom Bernard Shaw

modelled Sir Colenso Ridgeon in *The Doctor's Dilemma*. He had produced a vaccine that offered protection against typhoid fever and was persuaded that vaccines would cope with bacterial infections in general by stimulating phagocytosis. Fleming, who never liked to stray far from experimental facts, was as different from Wright as Florey was from Chain, but he became Wright's disciple in a newly created Inoculation Department which financed itself by the sale of vaccines.

In 1921, Fleming made an unexpected observation. While suffering from a cold, he isolated, apparently from his nasal mucus, a rare coccus which he then showed was lysed by nasal mucus and thus discovered lysozyme. Macfarlane wonders why the mucus was tested against an organism that had survived in its presence and suggests that the experiment might be placed in the random category condemned by Wright as a sin against the Holy Ghost. However that may be, Fleming regarded his work on lysozyme as his best contribution to bacteriology.

His second major discovery, in 1928, was at least as extraordinary as the first. He was not looking for an antibacterial substance but for staphylococcal variants because he had been asked to write an article on *Staphylococcus*. A seeded plate he had put aside was later found to be contaminated with a *Penicillium* and around the fungus bacterial colonies were apparently undergoing lysis. But since penicillin lyses only growing staphylococci and not fully grown colonies, how did this come about? Macfarlane accepts the convincing explanation given by Ronald Hare in *The Birth of Penicillin*: cool weather allowed the fungus to grow first and produce penicillin; it then became warmer, and the bacteria grew and underwent lysis.

Fleming deserved praise and gratitude for his acute observation and for the curiosity which prevented him from discarding an unexpected contaminant, as others might have done. He showed that his culture filtrate had selective activity against bacteria and that it was not toxic to leukocytes and a rabbit. He thought at first that it might be used for the local treatment of septic wounds, in which other antiseptics had been worse than useless because they killed leukocytes before bacteria. But when "there was no miraculous success" he was quickly discouraged and wrote in 1940 that "the trouble of making it seemed not worthwhile". In his paper on cultures of a *Penicillium* in 1929 he made "special reference to their use in the isolation of *B. influenzae*", which he had studied during the influenza pandemic of 1918, and presumably had in mind the preparation of a vaccine.

In 1936, when Colebrook was demonstrating at St Mary's the ability of prontosil to cure dangerous streptococcal diseases, Fleming carried out experiments in mice and rabbits to determine whether a

combination of vaccine and sulphonamide treatment would be beneficial, but he showed no renewed interest in penicillin. The evidence is overwhelming for the conclusion that neither he nor anyone else at that time envisaged that penicillin would be a systemic therapeutic agent. Perhaps, as Macfarlane suggests, Fleming's attitude was conditioned by a finding that penicillin

Fleming in caricature, as "Private 606". A cartoon by Ronald Gray, 1911.

disappeared rapidly from the blood and his belief that it was inactivated by serum.

Penicillin was not forgotten, however, when Howard Florey and Ernst Chain of the Sir William Dunn School of Pathology decided to make an academic study of the antimicrobial substances known to be produced by microorganisms. The decision was a consequence of Florey's earlier interest in lysozyme and the urgent need to obtain money for research. Its outcome, made possible by the efforts of a small group of people under the constraints of war, was Florey's demonstration in 1940 that even very impure penicillin could protect mice from otherwise lethal systemic

infections with streptococci and staphylococci, and the finding in 1941 that it could save patients from infections that would previously have been regarded as fatal.

The results obtained at Oxford transformed penicillin from a biological curiosity into a substance with great potential in medicine. A letter from Almroth Wright to *The Times*, in which he placed a laurel wreath on Fleming's brow, was followed by a flood of misleading publicity. Gwyn Macfarlane attempts to throw light on how it happened that Fleming was credited with a vision he did not have and even with work he had not done, while the discovery at Oxford, if mentioned at all, was presented as a minor development. It is clear that Florey had no wish for notoriety when so little penicillin was available and turned journalists away. As to what occurred at St Mary's the author can only surmise, but he points out that the Medical School had a history of poverty, and consequently of fund-raising, and that its Dean, Lord Moran, numbered Lord Beaverbrook (no stranger to publicity) among his influential friends.

Fleming himself made no exaggerated claims, although he acquiesced in what was happening and occasionally insinuated that the short-comings of others were responsible for his failure to exploit his discovery. Towards the end of the book we have an entertaining account of the effect of his rise to fame on his later life. Innumerable invitations, often involving long travel and coupled with scientific and social programmes that would have daunted many a younger man, were accepted without hesitation. But he received the praises of the crowds with becoming modesty and certainly never succumbed to *folie de grandeur*.

The main reason for concern about the Fleming myth was the possibility that it would permanently falsify the history of a dramatic medical advance. It had little influence on the judgement of the scientific establishment. Although the first clinical trial made it likely that penicillin's contribution to medicine would be immense, the work that had brought this about had made no comparable contribution to science. Florey wrote "The almost miraculous properties of penicillin should not blind us to the fact that the work carried out at St Mary's Hospital, London, and at Oxford introduced no new chemical or biological principles. The results, however, were new and the effects on medicine widespread". No one could have foreseen, in 1941, the chemical and biological developments which were to give the β -lactam antibiotics a scientific interest for a further forty years and continue to do so today. But this story lies outside the scope of Gwyn Macfarlane's book. □

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Arms across the waves

Laurence Martin

The Independent Nuclear State: The United States, Britain and the Military Atom.

By John Simpson.

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A KINDLY angel must have supervised the gestation of Dr Simpson's enterprising book, for he begins by explaining that he intended to write on a different subject altogether and that subsequent changes of plan have greatly delayed its completion. The result is that the book emerges at a most timely moment in both the politics and the historiography of British nuclear forces: politically because of the current and continuing debate over the British acquisition of *Trident II*, and historiographically because a great deal of hitherto highly secret information is beginning to appear in the United States. Indeed it is one of the few and unavoidable limitations of this book that already it needs updating by reference to recent disclosures. So much more closed is the British defence establishment than the American, however, that this new information affects the context rather than the substance of the British story, and Dr Simpson's heavily documented account is likely to remain standard and invaluable for some years to come.

Scientifically competent readers will doubtless take particular interest in the author's effort to put precise numbers on the scale of British military nuclear production, by means that he himself admits to be crude and disputable. For those with a more general concern for the strategic and political implications of the British nuclear force, it is instructive to note that the current generally accepted "force loading" of the British submarine strategic force of about 200 warheads, is exactly the goal set in 1948 for achievement in 1960. This may say something about the stability of British conceptions of an adequate "assured destruction" capability, especially if we assume some rough correlation between the off-station factor in the submarine force and the likely attrition of its airborne predecessor. Whereas, however, the 1948 projection was conceived to be about half the American capability, today's British force is eclipsed in scale by that of the United States. The record of the British nuclear effort is, indeed, one of being steadily overtaken, though running a very game race. In 1941 Britain was probably the leader; by the time its national programme approached the point of acquisition of weapons, a decade later, Britain was already trailing the Soviet Union and about to become the world's first "Nth nuclear power".

Dr Simpson's book, like Professor Margaret Gowing's official histories of the very early years, affords intriguing glimpses of mixed and often conflicting reasoning that has led successive British governments of both political parties to persist in a game in which the odds are uneven but in which not even the outsiders are negligible. The game is not made easier by continual changes in the rules. At the beginning the problem was to get the bomb; by the 1960s the trick was to deliver it. At the outset having the bomb was thought to be more important than knowing what it was for. In 1947 the Foreign Secretary, Ernest Bevin, was content merely to argue that Britain "could not afford to acquiesce in an American monopoly in this new development". When, in 1948, the RAF specified a force capable of attacking 59 Soviet cities — even though many members of the Labour Cabinet would not accept that the Soviet Union was an enemy, a scruple the Berlin blockade and Czech coup were to remove — policy was still concerned with tactics rather than strategy. Only in 1952, when the British Chiefs of Staff devised and later sold to Churchill when restored to power a "grand strategy" based on deterrence by nuclear retaliation, could it be said that the expensive and secret weapon programme was harnessed to a strategic theory — albeit a debatable one.

It has long been known that the incoming Eisenhower Administration drew some support from the British strategic theory in evolving its own doctrine of Massive Retaliation. The whole British story is, of course, intimately bound up with the United States. The relationship was and is a complex one, and the motives, principles and prejudices of so many different layers of the pluralistic American machine — politicians, military and scientists — made it difficult for the United States to pursue a consistent policy.

What the British needed from the United States — help in reducing costs — was rather simpler, and they were not without levers: among them their undoubted skill and know-how, even if those of the junior partner, the goodwill of past co-operation, and such legal holds on the United States as the Quebec agreement of 1942 requiring British consent for American use of nuclear weapons and agreed rights to a share in scarce uranium supplies from the Congo. Less tangible but nonetheless effective was the power Britain paradoxically enjoyed by being the weaker partner in an enterprise — the containment of the Soviet Union — of great importance to the United States. Merely by implication — often genuinely without any intention of doing so — Britain could threaten to divert its resources from supplying the conventional strength NATO needed, could show signs of paying a political price, perhaps even a price in nuclear co-operation, to win a French welcome to the European Community, or could obstruct an arms control initiative dear to America.