



10 DOWNING STREET

*From the Private Secretary*

14 September 1984

I enclose a copy of a letter which the Prime Minister has received from Sir James Gowans, Secretary of the Medical Research Council.

BT1  
I should be grateful if you would let me have a draft reply for the Prime Minister to send to Sir James Gowans, to reach this office by Friday 28 September.

I am sending copies of this letter and its enclosure to Steve Godber (Department of Health and Social Security), Robin Nicholson (Cabinet Office) and John Gieve (Chief Secretary's Office, HM Treasury).

David Barclay

Miss Elizabeth Hodkinson,  
Department of Education and Science.

NR

# MRC

Ack'd on 14/9  
Medical Research Council  
20 Park Crescent, London W1N 4AL

telephone 01-636 5422  
telex 24897 (Medresco London)

from the Secretary

13 September 1984

Sir James Gowans, CBE FRS

Dear Prime Minister,

Lord Jellicoe has already written to thank you for your kindness in allowing us to explain to you personally the consequences of the financial problems facing the Medical Research Council. As we told you, we are concerned that the future of medical research in the UK is being severely damaged by the progressive erosion of the Council's budget.

In addition to the erosion of the Council's grant-in-aid, there are other factors outside our control to which Lord Jellicoe drew your attention which, if corrected, would help the Council to plan effectively for the future. May I outline again the most important of these:

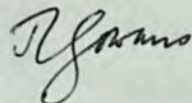
1. Pensions The Council has to supplement its pension fund from its grant-in-aid. This year, following a review by the Government Actuary, an extra £600,000 was required.
2. International Subscriptions The revaluation of subscriptions and currency fluctuations require increased payments for which we are not compensated. This year an extra £200,000 had to be found.
3. Restructuring in other Research Councils The Advisory Board for the Research Councils plans to deduct £0.9 m and £1.8 m in 1985/86 and 1986/87 respectively from our grant-in-aid to assist the re-organisation of AFRC and NERC. The imposition of these cuts does not conform to the precedent set for the universities which were provided with an extra fund to aid restructuring.

The most important problem besetting the Research Councils generally and starkly exposed this year for the MRC is the inability to fund about half the outstanding (∞) applications from the universities. I am sure you will understand that the prospects for the future of scientific research in the UK are bleak if the resources of the Research Councils fall to a level at which a substantial fraction of the very best workers in the universities cannot secure funds.

May I add my personal thanks for allowing us to discuss so frankly and informally the difficulties which the MRC is facing.

Yours sincerely,

The Prime Minister  
The Rt. Hon. Margaret Thatcher, MP  
10 Downing Street  
London SW1

  
James Gowans

MRC

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20 Park Crescent, London W1N 4AL

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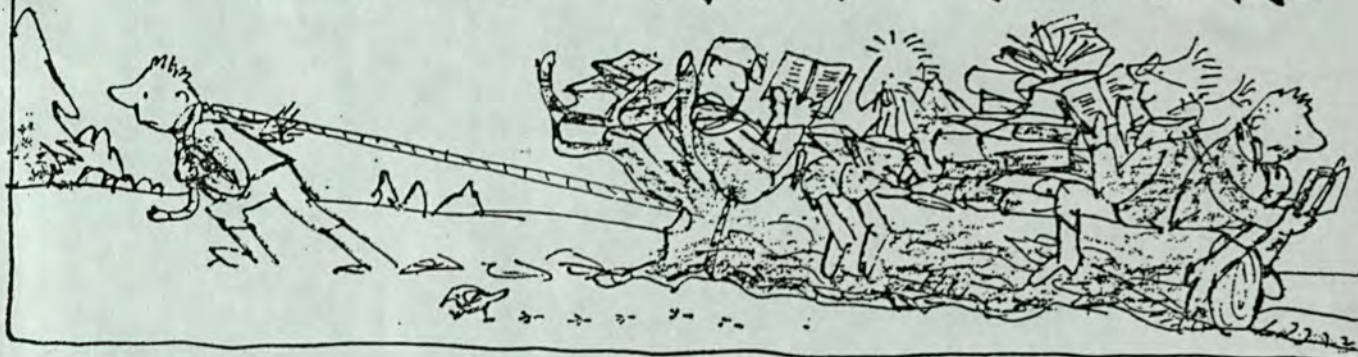
13/9/84

reference

You mentioned Lord Florey during our talk.  
I enclose a review of a book about him  
which touches briefly on one of the issues  
you raised. I wonder if you might be  
interested to see it.

R. Gwynne.

# MORE CHRISTMAS BOOKS



*James Gowans*

## The penicillin men

*Howard Florey: The Making of a Great Scientist.* By Gwyn Macfarlane. Oxford £7.95

This book is about a remarkable man and a remarkable achievement. In outline the story is simple. Howard Florey, in wartime Oxford, transformed penicillin from an academic curiosity into the most powerful agent for the treatment of human infections hitherto available in medical practice. In due course he received accolades that marked him out nationally and internationally as a great scientist: a life peerage, OM, Nobel laureate, President of the Royal Society and Chancellor of the Australian National University.

In 1968, after Florey died, his achievements were compared with those of Jenner, Pasteur and Lister. Yet strangely, in the public mind, it is Fleming alone who remains the hero. Indeed, when Gwyn Macfarlane proposed to one publisher that he wished to write about Florey he was advised to write a biography of Fleming instead. The creation of the 'Fleming myth' by the media and public ignorance of Florey's achievements is something which, Macfarlane says, saddened those who knew him and is, in itself, interesting and alarming. One of the reasons for writing this book was the wish to put the record straight; the other was to trace the life and career of a great scientist.

Florey came to Oxford in 1922 as the Rhodes Scholar for South Australia, and before he returned to Oxford as Professor of Pathology in 1935 he had established for himself a considerable reputation as an

experimental scientist. He had also acquired the reputation of being an abrasive character, although this did not prevent Sir Edward Mellanby, the Secretary of the Medical Research Council (who could match Florey's forcefulness), from swinging the electors to the Oxford chair in Florey's favour after arriving two hours late for the meeting. Even without penicillin, Florey would have exerted a considerable influence as the founder in Oxford of a distinguished school which brought the ideas and techniques of physiology and biochemistry to the study of a wide range of topics in human pathology. But it is the work on penicillin which forms the centrepiece of the book.

Penicillin illustrates dramatically the element of chance in scientific discovery. Alexander Fleming had a genius for noticing the unusual, but for reasons of temperament and training he did not press the analysis of his observations very far. Scientifically, his best work was the discovery of an antibacterial substance, lysozyme, which he found as a normal constituent of certain body secretions. This was a new natural defence against infection. Subsequently he discovered penicillin, again because he was an astute observer, but partly, it is interesting to note, because he worked in a messy laboratory which modern standards of hygiene would probably have condemned.

Fleming was studying the properties of an organism which sometimes causes human infections—the staphylococcus—and he observed on some discarded dishes that the growth of the bacteria had been inhibited in a zone around a contaminating mould (no, it almost certainly did not blow in through

## STMAS BOOKS



an open window!). Macfarlane describes the part played by chance in this discovery: the strain of penicillin-producing mould which settled on Fleming's plate was a rare contaminant; if the laboratory had been equipped with the usual vessels of disinfectant for the disposal of bacterial plates, they would have been immediately submerged and destroyed; more speculatively, if alternate periods of warm and cool weather had not provided the correct laboratory temperatures, the relative rates of growth of the mould and the bacteria would not have been optimal for bacteria inhibition to have occurred; if a visitor to the laboratory had not turned Fleming's thoughts to the discarded plates, he might never have made the observations at all.

But none of this should detract from the quickness of eye and mind which enabled Fleming to make his chance observation and to exploit it. The paper which described penicillin in 1929 made little impact; indeed, Fleming's main interest in penicillin was as a kind of selective bacterial weed-killer, a substance which prevented the growth of unwanted bacteria in a mixed culture. He did suggest that it might be useful as a local application to infected areas, but his failure to carry out protection experiments on infected animals showed that he did not foresee its potential for treating severe general infections. Fleming virtually lost interest in penicillin after the publication of his paper and, in the interval before the Oxford work, he did nothing obvious to promote its use in therapy. But as Macfarlane says, Fleming made a brilliant observation, and we should not criticise him for the things he did not do; it is just that Macfarlane would like us to get the facts straight.

If some would regard Fleming as a brilliant amateur, Florey was a brilliant professional who commanded a team to tackle problems systematically and in detail. In

1935, an enthusiastic Ernst Chain joined the Oxford team, and it was Chain who subsequently came across Fleming's paper when the decision was taken to study the antibacterial properties of a number of natural products. Again chance played its part, for it is not clear why penicillin was among the substances chosen for study; it was certainly not the only candidate in the literature. Whatever the reasons for the choice, Florey became convinced by 1939 that penicillin was worth serious study. What followed was a saga of ingenuity, organisation and prodigious industry by a group of whom Florey was the undisputed leader. The penicillin-producing mould was grown on progressively larger volumes of nutrient fluid, and the key problem of extracting and concentrating the unstable active material was solved.

By 1940 they were ready to bring about what Macfarlane calls 'one of the turning points in medical history'. He describes how, on Saturday, 25 May 1940, while the German Panzer columns were outflanking the Maginot Line, four out of eight mice which had been infected with a lethal dose of streptococci were successfully treated with penicillin while the four untreated controls were soon dead. As Macfarlane says, against the gigantic backcloth of the battles in France, 'the fate of eight white mice may seem of ridiculously small consequence.' Yet in terms of human lives and suffering the consequences were profound.

Further extensive animal tests convinced Florey's team of the remarkable properties of this powerful but non-toxic antibacterial drug, and eventually they improvised a pilot plant which produced enough material for a successful clinical trial in man. The problem now was to persuade industry to undertake the large-scale production of penicillin for human use. The companies which Florey approached in the UK were either unable or unwilling in wartime to undertake the pro-

duction of penicillin, and he exerted his considerable powers to initiate its production in the United States. American patents were taken out on new processes which enabled large-scale production to proceed more efficiently.

This has led to recriminations about the failure to take out patents in the UK, but Florey was advised against this by both the Secretary of the Medical Research Council and by the President of the Royal Society. This advice is unfortunately not on record, but the argument appears to have been that the patenting of penicillin would be unethical, and that it should be a gift to mankind. At this distance such idealism seems unworldly and certainly, even at the time, Chain was furious. But at least the same mistake was not made twice, and cephalosporin, another antibiotic developed by Abraham and Newton in Florey's laboratory, became the largest earner of royalties by the government agency set up to handle such matters, the National Research Development Corporation.

Gwyn Macfarlane has not written an anti-Fleming book. Indeed, Fleming's contributions to penicillin are fully and generously described. But he does seek to explain why Florey is not also a public

hero. Part of the explanation was undoubtedly Florey's refusal to receive the press when the results of the clinical success of penicillin were first published. His motives were partly a dislike of publicity, but also a desire to avoid a sensationalism which would create a demand for penicillin which could not be met. Fleming, on the other hand, was more welcoming. Does it matter? After all the three essential players, Chain, Fleming and Florey, shared the Nobel Prize. Gwyn Macfarlane thinks it does matter, and he explains why.

There remains the problem of bringing to life the character of Howard Florey for those who never met him. Even for those who knew him it is not easy to explain what it was about his personality that captured us. I started my own career in research under Florey in 1947, and remained in his laboratory up to and beyond his retirement in 1962. When Mellanby suggested that I should try my luck in Oxford, he said to me of Florey: 'He is the only person in the country who is any good at experimental pathology but you won't like him.' Well, I did like him, although it took some time to see beyond his obvious scientific virtues. At the outset he would tell his students that they would probably be no good at research and that there was no money in it; we would have a job as long as we continued to live successfully by our wits. He had a nice line in deflationary wit which made it unlikely that anyone who passed through his laboratory would ever in later life fall for obsequious flattery, or flattery of any kind. 'You were lucky, Gowans, it was a poor field,' was his comment when I was successful in obtaining a minor appointment.

But what infected us was his zest for experimental science, his own skill and industry and above all his total honesty and lack of pretension. The basic currency in the laboratory was not what he derisively called 'hot air' (i.e., facile speculation) but the simple, telling experiment. If you could pass that test, you were accepted and encouraged. Of his own contribution to penicillin he wrote: 'Nor should anyone suppose that we think we have performed any great intellectual feats here. All we did was to do some decent experiments and have the luck to hit on a substance with astonishing properties.' Anyone who wants to know more about this tough, reserved, modest man and the qualities which made him 'the most effective medical scientist since Lister' should read Gwyn Macfarlane's excellent biography.

## STREETS

Janos Nyiri

'An exciting first novel'  
*Donal Foley, Irish Times.*

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book about the Hungarian  
Revolution' *George Mikes*

'Impressive . . . a vivid  
panorama of an intensely  
dramatic period' *Noel  
Clark, BBC.*

'Succeeds wonderfully.'  
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