

There's life in some old drugs yet, as **Eric Sidebottom** and his colleagues explain.



The development of penicillin as a practical treatment in medicine owes much to the work of Florey, Chain and Heatley who together developed the tools for the purification and manufacture of this antibiotic for clinical use during World War II. This ground-breaking work was undertaken at the Sir William Dunn School of Pathology in Oxford and the interesting history of this institution is currently being compiled by Dr Eric Sidebottom, a retired Lecturer in Experimental Pathology. In the course of his researches, out of the blue, Sidebottom received an email from Professor Alan Smith, based at the University of KwaZulu-Natal, South Africa, which harked backed to the 1940s.

At that time Smith worked in a pathology laboratory at Whipps Cross Hospital in London, which formed part of the war-time Emergency Medical Services (EMS). The director of the lab, Dr W. W. Walther, had been given privileged access to penicillin, which

was extremely scarce then and restricted to military use only. According to Smith, *'The penicillin was dispensed not by the pharmacy, but by the laboratory, and as the medical/nursing staff were not familiar with using dosages in units but were trained in 'grains and minims' we lab technicians did the maths for them'*.

A message in a bottle

Smith then moved on to an academic and medical career in various parts of the African continent. Many years later he rediscovered a relic of the pioneering days of antibiotics in the form of a tube of 10 penicillin tablets that were made in 1945. *'When I left Whipps Cross about 1952, the chief technician, a Mr Ernie Millwood, put all the detritus that remained of my presence in a cardboard box, and when he retired he sent it on to me and it continued to collect dust in a corner of my lab here in South Africa.'* Smith's inquisitive mind prompted him to contact Eric at the Dunn School, as he was wondering whether anybody



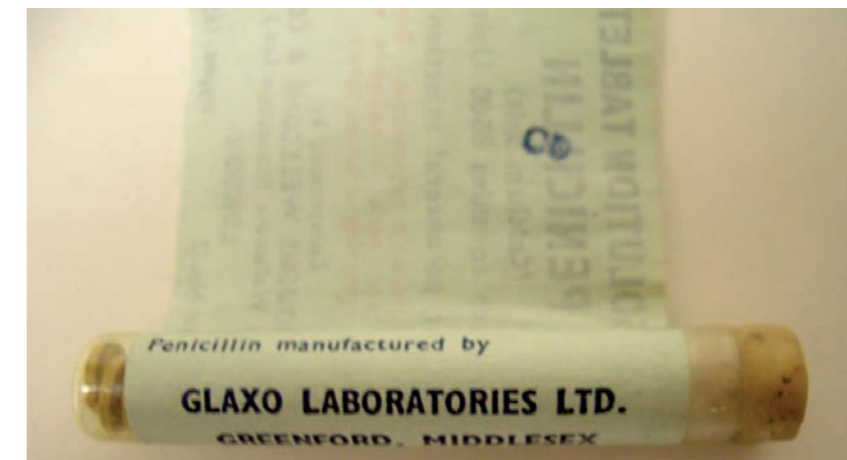
Wartime penicillin still packing a punch

there would be interested in assaying these ancient pills for antibacterial power. Sidebottom was unsure about the chances of this working and was also slightly embarrassed that the home of penicillin no longer had the capacity to perform the appropriate microbiological assays. However, undeterred, he contacted bacteriological colleague Jeff Errington who persuaded Neil Stokes at Prolysis to try some experiments.

After being shipped half way round the world, the vial was opened in Oxford and the tablets used in minimum inhibitory concentration (MIC) assays that estimate how well the drug works to kill different bacteria. Stokes determined the MICs to be 2 and 1 $\mu\text{g ml}^{-1}$ against *Bacillus subtilis* and *Staphylococcus aureus*, respectively, from triplicate assays. To relate this to modern penicillin G, he repeated the assays using a fresh batch of antibiotic from the shelf. This killed both *B. subtilis* and *S. aureus* with an MIC of 0.03 $\mu\text{g ml}^{-1}$. After correcting for the number of biochemical units of penicillin that were present in the two different tablets, he calculated that the modern penicillin is about sixfold more potent than the war-time tablet, which left him quite impressed!

Not so good old days

Unfortunately, due to the evolution of antibiotic resistance in the bacteria that penicillin was developed to kill, penicillin G itself is not as useful as it was during the 1940s. However, our ability to produce and use a wide range of antibiotics in clinical medicine has revolutionized healthcare since this time. Smith has memories of his days at Whipps Cross during the war when the supply of penicillin was not yet sufficient



▲ The tube of wartime penicillin tablets rediscovered by Professor Alan Smith. Alan Smith

◀ Left. Norman Heatley developing the penicillin assay (1940). Sir William Dunn School of Pathology Collection

◀ Right. The 'penicillin girls' harvest *Penicillium* extract from the 'bedpans' specially designed by Norman Heatley (1941). Sir William Dunn School of Pathology Collection

for the treatment of all patients alike. A child injured during the blitz had come into the hospital with serious head injuries resulting in loss of a piece of his skull caused by flying shrapnel. Smith and his colleagues visited him frequently to swab the meninges while the nurses were changing dressings and they were using an acriflavine irrigation drip to prevent sepsis, which was not helping the patient. Smith recalls the desperate situation that followed. *'Walther used penicillin on him for a few days and we tried to recover penicillin from his urine by passing it through a Seitz filter. Sadly, it was not successful as Walther was only permitted to use the small amount of penicillin for army casualties and he could not continue making false entries.'* A poignant reminder of how the development of the pharmaceutical industry and the wholesale production of antibiotics has helped put situations like this into the history books.

Eric Sidebottom and Jeff Errington

Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford OX1 3RE, UK
(e eric.sidebottom@path.ox.ac.uk)

Alan Smith

Professor and Head of Department of Virology, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, South Africa

Neil Stokes and Jeff Errington

Prolysis Limited, Oxford University Begbroke Science Park, Yarnton OX5 1PF, UK