Appreciation

Dr Norman Heatley
10th January 1911–5th January 2004

Norman Heatley died on 5th January 2004. His passing, a few days before his 93rd birthday, marks the end of a living link between the present day and members of Florey’s team that developed penicillin in Oxford in the early 1940s. Obituaries in newspapers from many parts of the world have paid tribute to his contributions to this project. It was in fact extremely lucky that he was working in Oxford at that time, as he had been offered a Rockefeller Fellowship in Copenhagen, but had decided to stay in England due to the imminent threat of war. He was directly responsible for devising ways of measuring the activity of penicillin in fermentation liquors in concentrations far too low for chemical methods. He also worked out how to extract the highly unstable penicillin from very dilute and heavily contaminated solutions, and at a later phase of development tirelessly grappled with the many problems involved in growing large volumes of culture with the high surface:volume ratios necessary for optimal antibiotic production. These problems were exacerbated by the difficulties imposed at that time in the UK by wartime restrictions on manufacturing, which meant that Heatley had little or no access to purpose-made apparatus, forcing him at first to improvise with great ingenuity in order to make do with everyday objects. It was his idea that ceramic could take the place of the prohibitively expensive glass culture flasks required to make enough penicillin for the first human trials. In 1941, Heatley accompanied Florey to the USA, on a transatlantic flight that was potentially perilous, there being a very real possibility of being shot down by the enemy. In anticipation of such an event, Heatley had, as had become his practice, rubbed spores of the *Penicillium* species into the seams of his overcoat, so that there would be a chance of the penicillin-producing mould being recovered if and when his corpse was found. On arriving at their destination, appropriate facilities were made available, and Heatley stayed on until 1942 to collaborate in the deep culture techniques that made possible the production of sufficient amounts of penicillin to treat casualties of the war. After the end of the Second World War, considerable bad feeling emerged between the UK and USA when US patents were issued regarding the commercial production process on which Heatley had collaborated. Heatley’s name had been omitted from a publication crucial to the patents. It is typical of Heatley’s attitude that he was amused rather than upset by this.

Unlike Fleming, Florey and Chain, the main players involved in the discovery and exploitation of penicillin, Heatley received scant recognition. However, his scientific and technical achievements have earned him a particular place of honour amongst his peers. Obituaries in The Daily Telegraph and The Times refer to his humanity, modesty and charming personality, and I would like to add to these with a few reminiscences from my personal knowledge of Heatley, whom I met when I was a postdoctoral Fellow at The Dunn School between 1967 and 1970. Seeing his picture in the obituary column took me back instantly to my very first practical class in Bacteriology at Cambridge in October 1959. The class was set to spend 2 hours entirely with glass tubing, making and calibrating 50-droppers and mercury piston pipettes. The latter were capable of repetitive and highly accurate dispensing of microlitre volumes of fluid, and were the forerunner of modern Gilson and Eppendorf pipettes. They were just the sort of Heath Robinson devices brilliantly conceived and made by Heatley, entirely from ordinary laboratory supplies, in this case, glass tubing, cotton wool, sealing wax, rubber tubing and mercury, and he may well have invented them. He never wasted anything, probably due to his experiences of shortages of materials during the war years; I recall him on one occasion attending a Journal Club taking notes in tiny precise writing with a mapping pen on the inside of a used envelope that he had carefully torn open.

His generosity of spirit to younger and considerably more junior colleagues can be illustrated by two examples: Heatley happened to hear a third party grumbling that I had damaged yet another expensive commercial 5 µL pipette in the course of my experiments. He then proceeded, unasked, to make for me from glass and rubber tubing a micropipette that he diffidently assured me would accurately dispense exactly 1.32 µL. Just before starting at The Dunn School, I had submitted a paper to the *Journal of General Microbiology*; shortly after my arrival, Heatley, who was at that time an Editor of that journal (a fact of which I was ignorant), spontaneously sought me out with a few reminiscences from my personal knowledge of Heatley, whom I met when I was a postdoctoral Fellow at The Dunn School between 1967 and 1970. Seeing his picture in the obituary column took me back instantly to my very first practical class in Bacteriology at Cambridge in October 1959. The class was set to spend 2 hours entirely with glass tubing, making and calibrating 50-droppers and mercury piston pipettes. The latter were capable of repetitive and highly accurate dispensing of microlitre volumes of fluid, and were the forerunner of modern Gilson and Eppendorf pipettes. They were just the sort of Heath Robinson devices brilliantly conceived and made by Heatley, entirely from ordinary laboratory supplies, in this case, glass tubing, cotton wool, sealing wax, rubber tubing and mercury, and he may well have invented them. He never wasted anything, probably due to his experiences of shortages of materials during the war years; I recall him on one occasion attending a Journal Club taking notes in tiny precise writing with a mapping pen on the inside of a used envelope that he had carefully torn open.

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this class on only two previous occasions and that in those days name badges were not used.

Heatley’s very pleasant personality makes one wonder at the reasons behind the depth of ill-feeling he had for Chain, whom he hated so much that every time Chain left a room heatley immediately left the room. This often presented considerable problems, as it was essential that they collaborate during the penicillin project, and Abraham had often occasions to act as go-between spokesman. Even 30 years after these events, Heatley and Abraham remained tight-lipped about what was behind this enmity.

Turning from Heatley the man to Heatley the scientist, his contribution to the penicillin project was crucial. His realization that penicillin could be extracted from acidified broth into ether and back extracted into water held at pH 7 was the key step to the purification process, and his tireless energy in pursuit of the necessary equipment to enable scaling up of penicillin production at The Dunn School maintained the momentum generated by the rest of the team. However, his permanent gift to microbiology was to lay the foundations for the whole art and practice of microbiological antibiotic assay, which led in turn directly to diffusion methods of susceptibility testing. While others before him (for example, Fleming) had demonstrated inhibition of bacterial growth in agar by broth cultures of an antibiotic-producing organism, this had only been done in a qualitative way; quantitative assay was previously done in liquid cultures. Heatley hit on the concept of making a reservoir of broth culture in the agar, contained in such a way as to prevent the producer organisms in the broth contaminating the agar, while allowing the antibiotic-rich broth to diffuse out into the agar. This was done at first using fish spines, then porcelain cups and finally stainless steel cylinders, the latter still being in daily use in Abraham’s laboratory 30 years later. Heatley went on to work on protein constituents of pancreatic secretions, and staphylococcal α-lysin, and maintained his fascination for all things micro. The latter is illustrated by a paper describing how to dialyse volumes of fluid between 100 and 5 µL, and also by his hobby in retirement of making dolls’ furniture out of bird feather quills.

Memories soon turn into history; let us therefore remember the magnitude of the debt we owe to Heatley, a great scientist and a quiet gentleman. He is one of the few the application of whose science has outlived the person.

Acknowledgements

I am deeply grateful to Professor David Greenwood for several historical facts. Also, both myself and the Journal are extremely grateful to Maggie Bristol ARPS for her permission to reproduce the photograph of Dr Heatley.

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