



Dr H. B. F. (Hal) Dixon (1928-2008)

The Wilson's Disease Support Group-UK (WDSG-UK) will have special memories of Hal Dixon, who died in Cambridge on 30th July 2008. Hal was a Fellow of King's College, Cambridge, and through this connection he was able to arrange for several of our annual meetings to be held in King's College. These meetings concluded with Hal taking us for a 'private' view of the world-famous chapel of King's College followed by a visit to the Fellows' Garden. Hal's Fellowship at King's College spanned fifty-five years and the commentary and insights that Hal was able to provide us with for these privileged tours around King's reflected his commitment and service to the college.

'Insight' is an apt word to describe Hal Dixon, and it was displayed most notably for the benefit of Wilson's disease patients when John Walshe told him in the mid-1960s about the problem of a patient who had become intolerant of D-penicillamine. Hal's doctorate and later scientific work were in biochemistry, in protein chemistry, but he had a very deep understanding of organic chemistry. Hal suggested that the well-known chelating agent triethylenetetramine (trien) (a bottle of which happened to be sitting on his laboratory bench) was a likely candidate for treating Wilson's disease. It had been known from the early 1950s that trien, a quadridentate ligand, forms very stable complexes with cupric ions and with other metals. But Hal also realised that the similarity of the chemical structure of trien to some naturally occurring polyamines meant that it would probably not be toxic to humans if used as a drug.

A few other chelating agents (not related to trien) were also tested in animals around this time, but trien was the most promising agent of those selected for testing. The bottle of triethylenetetramine on Hal's shelf was a 'technical grade' product and was also a liquid. In order to be suitable for patients, trien had to be very pure and in a solid form. Trien is a strong base and can combine with acids to form salts. Salts are invariably crystalline in nature, and can be purified by recrystallisation from suitable solvents. Hal's next insight, based on his knowledge of protein chemistry, was to suggest that the dihydrochloride of trien was the most suitable salt to purify and to use as a drug. John Walshe, Hal Dixon, and Kay Gibbs in Cambridge University put these ideas to practical use, and by the 1970s triethylenetetramine dihydrochloride (now referred to more often by its 'official' INN name, trientine, rather than trien) was recognised as a drug of second choice for treating Wilson's disease.

I came to know Hal firstly through his *Lancet* papers on trientine, and later personally in Cambridge and at the WDSG-UK meetings. At one of these meetings (in Nottingham) I mentioned the problem of the bioavailability of trientine and in particular how to chelate intracellular copper. Hal offered a solution to this problem immediately, based on a paper tucked away in his mind. This solution was both ingenious and synthetically relevant. I think he made some progress experimentally, and I often suggested to him that he should publish at least the idea, if not the practical results.

Hal was always ready to share his scientific knowledge with others, and this willingness to communicate enabled him to carry on with useful scientific work all his life. He was a very courteous man with beautiful manners and a deep interest in his fellow man. It was a privilege to have known him.

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Honorary Member of the Wilson's Disease Support Group UK. February 2010