

Professor Geoffrey J F Dutton (1924–2010)



Brian Burchell (University of Dundee)

Geoff Dutton was a distinguished scholar and a man of culture, intelligence and humour, who made an outstanding contribution to biochemistry, environmental biology and literature. He played a major role in the development of the Biochemistry Department in Dundee (now a leading Life Sciences Institute), especially during its earlier years, when his research excellence held off the threats of transfer of the subject from Queen's College, Dundee.

His many interests and achievements exhibit the common theme of exploration of the response of the organism to its environment in the widest sense.

The son of Anglo-Scottish parents, living in Cheshire, the teenage Geoffrey Dutton spent his Saturday afternoons in the chemically intriguing surroundings of a pre-World War II pharmacy. Following war service, this experience influenced his decision to study biochemistry in Edinburgh, a return to his beloved Scotland. After graduating in 1948, Dutton fell under the influence of G.F. Marrian, a steroid biochemist who had established the structures of pregnanediol and oestriol and shown that they were excreted

as glucuronides. Marrian held the Chair of 'Chemistry in Relation to Medicine' in Edinburgh and his friendship with John Gaddum, then Professor of Pharmacology, provided one of the early stimuli to establish biochemical pharmacology in Britain. Marrian employed Dutton as an Assistant in Biochemistry, which allowed him to work part-time for a PhD under the supervision of Ian Storey on the enzymic formation of glucuronides.

Dutton's postgraduate work was 'steeped in' chemistry-related-to-medicine in a department of steroid metabolism where steroid glucuronides in vats of urine were considered to be important; he studied glucuronide biosynthesis by night, and was a teaching assistant during daylight hours.

Glucuronides were discovered in 1879 and the conjugates were established as an important metabolic modification of endogenous and exogenous compounds. The substrates include bilirubin, steroids and other hormones as well as a plethora of drugs and toxic chemicals.

At that time, the ability of B-glucuronidase to cleave glucuronides was well established, but although some claimed this enzyme could also catalyse the synthesis of the conjugates, this proposal was very controversial.

Dutton discovered a new sugar nucleotide, UDP-glucuronic acid in 1950 and subsequently a sugar-transferring enzyme family, UDP-glucuronosyltransferases, which catalysed the biotransformation of toxic chemicals by conjugation with glucuronic acid. The glucuronide biosynthetic pathway was 'drilled into shape' using a variety of modern techniques in the early 1950s such as tissue homogenates, cell fractions and chromatographic separation. Geoff was a key participant in the worldwide investigation of chemical defence in the dawn of biochemical pharmacology. He described the first molecular mechanism of detoxication of organic chemicals by conjugation with a

common sugar made from glucose. These findings were first presented to the Biochemical Society in 1951. This work, performed for his PhD under the supervision of Ian Storey, was the first unequivocal demonstration of the biochemical mechanism for any reaction of drug metabolism reaction¹.

Biomedical Science is now increasingly aware of environmental toxicity caused by natural toxins, pollutants, pesticides, carcinogens and even drugs. Geoff Dutton was a pioneer in our understanding of chemical defence; how these toxic chemicals could be rendered harmless.

This most important mechanism is easily recognized in bilirubin metabolism, where neonatal jaundice reveals the temporary absence of this detoxication mechanism. Likewise, the newborn are not able to eliminate apparently safe drugs, such as chloramphenicol, because detoxication through glucuronidation has not developed. "A baby is not a small adult when considering detoxication mechanisms".

These significant discoveries starting in 1953 brought worldwide scientific recognition and invitations to present keynote lectures at a spectrum of international meetings, often referred to by Geoff as the biochemical, medical, toxicological, oncological and pharmacological "circuses".

He moved to Queen's College, Dundee, in 1954 from the Wilkie Research Institute and the "blacksuited tyrants" in Edinburgh to the embryonic Biochemistry Department with R.P. Cook. Dundee then became a world centre of detoxication studies and continues to be so to date. Continuous MRC support, publications, a succession of PhD students such as Ian Stevenson and Brian Burchell and many overseas collaborators laid the foundation for some of the current developments in life sciences in Dundee.

The Dutton group was assiduous in its studies of the microsomal UDP-glucuronosyltransferase, examining successively its substrate specificity, ontogenesis and control

by various hormonal influences as well as differences in activity across species. The group's careful classification of both endogenous and exogenous substrates and the study of the remarkable deficiency of the formation of certain glucuronides in the domestic cat presaged the identification of UGT isoenzymes, evidence strengthened by studies on the differential effects of enzyme inducers, as this phenomenon was investigated from the 1970s onwards. This was followed much later by work on the differential regulation of the synthesis of various isoenzymes, which support the majority of their early conclusions.

Dutton edited two important volumes, *Glucuronic Acid Free and Combined* (1966) and *Glucuronidation of Drugs and Other Compounds* (1980) which remain landmarks in this field and are widely consulted to the present day. Over 50 years, the field which Dutton founded has moved from being a revolutionary novelty to one of the cornerstones of drug metabolism, as important as cytochrome P450 system, which began in Britain and where British contributions are sustained today.

The research laboratory and medical teaching moved from the 'old stables' to the plush Medical Sciences Institute in 1970 and he continued his internationally recognized research in drug metabolism and perinatal pharmacology until 1983. He was the Head of the Department of Biochemistry from 1979 to 1983. He was awarded Dundee's first DSc in 1968, became Professor of Pharmacological Biochemistry in 1977, elected FRSE in 1973 and was given Honorary Degrees by University of Kuopio, Finland, in 1978 and University of Nancy, France, in 1980, indicating his international esteem.

Dutton spent almost 30 years of his academic career in the Biochemistry Department in Dundee where he fostered a series of influential colleagues, including Ian Stevenson and Brian Burchell. As the subject developed, Brian Burchell led a move into the Medical School in Dundee in 1988, where

he was joined by Michael Coughtrie. Drug metabolism continues to flourish in Dundee, the impact of this group being added to by the recruitment in 1992 of Roland Wolf, who now leads the Biomedical Research Centre in the University of Dundee. Together, these contributions to drug metabolism play an important role in the overall excellence of Dundee in the biomedical sciences.

One of the main interests of Professor Dutton was 'enzyme ecology'. This outlook was encouraged by his studies in wider ecology. Whereas weekdays were spent in Dundee, weekends were for ecological experiments in biology, horticulture and forestry in a few mountain acres. This study developed into the renowned 'Marginal Garden', a subject of TV, radio and magazine articles, reviews in *The Times* and two books where Geoff was designated the Gilbert White of the 21st Century by reviewers.

Weekends were also for exploration of mountains and wild waters. He edited the *Scottish Mountaineering Club Journal* for 13 years and was awarded honorary membership of that exclusive club. These experiences led to his celebrated contribution of "classic wit and humour" to mountain literature, 'The Doctor's Stories'. His book on wildwater swimming received an award in North America.

This writing exploration has also extended to four published books of verse, three of which were awarded prizes by the Scottish Arts Council (the prizes were taxed – much to Geoff's disgust!), the fourth a Poetry Book Society recommendation.

Geoff was in great demand as an after-dinner speaker at scientific meetings, where presentations were given in the style of McGonagall or Pope. One creation was the imaginative use of biochemistry to describe personal events, such as retirement: "The deadly peptide reminisin activates a cascade of events releasing high levels of pontific acid and other peptides such as haverin and bletherin and the lachrymatory maudlin."

There is a link between all these excellent achievements. Exploration of rock, ice, rivers or lakes, horticulture or molecular biology requires the same self-imposed discipline and obsessive behaviour, all of them being intellectually demanding and equally rewarding.

We celebrate his scientific achievements, both for their value to science, medicine and the environment, and for their support, through the difficult times, of a Department, a College, and subsequently a University. Ultimately, in contribution to the conception of the Wellcome Building. He is one example of a phenomenon that small departments containing excellence cannot be written off, but may be better poised to expand into new exciting work, by introducing diversity, which was the hallmark of developments in Dundee.

Geoff Dutton was an outstanding ambassador for Dundee University as an internationally renowned scholar of many letters. His lifelong commitment to environmental exploration was the embodiment of this scholarship.

He was awarded an Honorary Degree by the University in 1998.

Geoff was a family man and his children fondly remember their highland home, *Druimchardain*, where he and his wife Elizabeth entertained friends and colleagues from all over the world. He was a great inspiration to all his PhD students and many undergraduates throughout his academic career.

He is survived by Elizabeth and their three children and several grandchildren.

Dutton was a member of the Editorial Board of the *Biochemical Journal* from 1976 to 1981; his festschrift appeared in *Transactions of the Biochemical Society* in 1984 (12, 1–105) and an autobiographical memoir was published in *Drug Metabolism Reviews*². ■

References:

1. Dutton, G.J. and Storey, I.D.E. (1954) *Biochem. J.* **57**, 275–283
2. Dutton, G.J. (1997) *Drug Metab. Rev.* **29**, 997–1024