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Obituary

Lindon Eaves: A Personal Memoir

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Nick and Lindon walking on the strand at Egmond aan Zee, October 8, 2004.

Lindon Eaves died on March 8, 2022, aged 77 years, at his home in Richmond, Virginia. His work had profound and lasting influence on the field of human quantitative genetics and all its outgrowths that include behavior and psychiatric genetics, genetic epidemiology and what we would now call complex trait genetics. Unusually, he also had a second, parallel publishing career in theology. A formal obituary enumerating his formidable list of achievements is published in parallel with this in the journal *Behavior Genetics*. Lindon was my mentor and friend for 49 years and here I wish to give a more personal account, focusing on the earlier part of his career when we worked closely together.

I grew up in Adelaide, South Australia, and had always dreamed of doing my D Phil at Oxford. After much effort and many delays, I finally made it there in October 1973 and was revelling in the dreaming spires and college life. But the intellectual milieu of my chosen department and the proposed topic for my thesis failed to inspire me. So one day, following up on an introduction from David Hay, a Birmingham genetics graduate I had met in Melbourne, I took a chance and, forcing 10p coins into the payphone in the corridor of my apartment block, clunk clunk clunk, I put through a call to Lindon who breezily invited me to visit.

Which I did on November 15, 1973; I know precisely because it was the day after Princess Anne's wedding in London which I had gone down from Oxford to watch (Lindon was incredulous that I should have made the effort). I got out of the taxi from Birmingham New Street station at 9 am, shook hands and we started to talk—and did not draw breath again till I got back in a taxi at 5 pm, elated that I had at last found my calling. It was abundantly clear that I should move my PhD enrollment from Oxford to Birmingham (I was Lindon's first PhD student). Here was someone who was interested in all the same issues that I was but had insights and expertise to bring to the problems in behavior genetics that I wanted to work on. On top of it all, Lindon had a twinkle in his eye and seemed like fun! I remarked on his trademark black clerical vest and white dog collar that it was unusual be both a geneticist and a priest (he was ordained in the Church of England). 'Oh,' said Lindon, 'there was one other bloke. I think his name was Mendel.'

So I moved to Birmingham one cold January day in 1974 and immediately was introduced to another side of Lindon. He kindly arranged for my then wife and I to stay temporarily at the Anglican Chaplaincy until we had found a flat. It was only a short walk from the University, and it provided rooms for single foreign students. Lindon was chaplain and I could see at first hand the thoughtful kindness he and his wife Sue (despite two young children to look after) invested in these often bewildered young men and women from entirely different cultures—and climates (the Chaplaincy

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was freezing!). Lindon's Christian faith was not just theoretical but hands-on, practical.

Accommodation secured, I turned up at the Department of Genetics for my first day's work to be met by Lindon who thrust a long tray of punched cards into my arms and bade me walk with him the 600 yards up to the Computer Centre; this was to be the first of thousands of such walks in the following years, to take up cards and bring back printed output, before the advent of visual display units (VDUs) and paperless computing that obviated the need for such healthy exercise (and sacrifice of forests). Lindon and I often had our best ideas on those walks. The data set he gave me was from Hans Eysenck's twin study of sexual behavior and attitudes, and it was on this that I cut my teeth using 'Birmingham methods' of analysis under Lindon's tutelage. With my own PhD students, I have always followed Lindon's example of immediately throwing them in the deep end with some data rather than have them endure months or years of preparatory courses. They flounder at first, but with every stroke successfully taken they gain confidence and are soon swimming.

Despite my elation at being there in the thick of it, after a few months I was becoming increasingly frustrated and despondent at my failure to master the logic and mechanics of the model-fitting approach to data pioneered by John Jinks, David Fulker and Lindon. One morning we were traveling up to London on the train to see Hans Eysenck, enjoying a splendid British Rail breakfast of grilled kippers, when I confessed my despondency to Lindon. He pushed the plates aside, pulled out his pen (he always called it a scriber for some reason) and wrote out on paper napkins in his neat cursive longhand, the whole logic and mathematical procedure for interative weighted least squares. Greatly relieved that I had at last finally 'got it,' when I got home I carefully hole punched these napkins and kept them in a folder. It was to be the first of many such paper napkin tutorials from Lindon; I kept them all and still have the folder in my office. I also resolved that the only way to really consolidate this knowledge was to write a program for it, which I did, LINFIT in Fortran IV, my first real engagement with Birmingham methods, though somewhat frowned upon by some in the corridor who could not see why one needed anything more complicated than a hand calculator, even for inverting matrices.

In the 1970s, we perceived two big issues holding the field back; the first was how to extend the elegant model-fitting approaches pioneered in Birmingham for the analysis of one variable at a time to the multivariate case—the causes of covariation between variables. The second was the problem of statistical power—how big do twin studies need to be to establish the presence (or otherwise) of a genetic (or other) variance component of given size. In both cases, the clue to their solution came from Lindon's extraordinarily eclectic knowledge across biostatistics, psychometrics and numerical optimization methods; and what he did not know himself he knew whom to ask to find it. Both resulting papers were published with me as first author, although Lindon made the biggest intellectual contribution—my first experience of Lindon's incredible intellectual generosity, to me and others, that has characterized his career.

In the first case, it was a tip-off from Owen White at the Institute of Psychiatry that led Lindon to the work of Swedish statistician Karl Joreskog and his analysis of covariance stuctures. Lindon immediately grasped that the multigroup case of this could be adapted to the simultaneous analysis of monozygotic (MZ) and dizygotic (DZ) twins, and thence to a maximum likelihood solution for genetic and environmental components of covariance, and indeed of variance components specific to only one variable. We published this, in deference to Joreskog, as The Genetical Analysis of Covariance Structure, but not long afterward David Fulker pointed out that it could be more elegantly formulated using Sewall Wright's path analysis and that adaptation has stuck.

The clue to solving the power problem, Lindon realized, lay in a little known paper by Richard Lewontin from 1959, in which he made use of the noncentral chisquare distribution to calculate the sample size required to detect selection of a given magnitude. Lindon figured we could use the same mathematical logic to calculate the size and composition of twin samples needed to reject false hypotheses about causes of variation. We were particularly interested in two cases: (1) where both additive genes and shared environment appeared to be important—as for social attitudes and (2) where there were both additive and nonadditive genetic effects (dominance or epistasis), as appeared to be the case for some dermatoglyphic phenotypes. How large would twin samples need to be to detect both effects with say 80% power? The answers were alarming; in the first case at least 600 twin pairs, in the second case at least 3000. These were sample sizes larger than almost anyone had used hitherto (R.C. Nichols' NMSQT study and some of the Scandinavian twin studies were exceptions) and were the spur for me to return to Australia in 1978 and start the Australian Twin Register to provide really big, powerful twin samples.

In 1977, we found out that the 2nd International Twin Congress was to be held in Washington DC in July. I tried to persuade Lindon that we should go, show our wares, but he was too much under the sway of the brilliant but dour John Jinks who dismissed international conferences as 'the idiot circuit.' Eventually, I wrote an airmail letter (long before the days of fax, let alone email) from Lindon to the conference organizer, Walter Nance, suggesting that Lindon was really a worthy invitee. About a week later somone came running down the corridor to say there was an international phone call for Lindon—it was such a big deal in those days. It was Walter Nance offering to pay our airfares and hotel to the Congress provided we agreed to visit his department in Richmond VA for a few days afterward. Lindon had never been to America before and was bemused by all he saw and heard, particularly the southern accent, which delighted him. Being at the Congress was immensely stimulating and we started friendships that have lasted ever since. We also experienced great hospitality in Richmond afterward and this too had significant longterm consequences.

But just before I left Birmingham for Canberra, overlapping with me by a week, a superbright young psychology student arrived from Oxford to do a summer project with Lindon—Andrew Heath. Little did I know how soon, and how importantly, our paths would cross again. Lindon was obviously impressed by Andrew, for not long after I left Birmingham, Lindon also left for a lectureship in Psychology in Oxford and became Andrew's PhD supervisor. But despite the stimulation of an off-the-scale student and enjoying teaching (he took the Oxford tutorial tradition to MCV), Lindon and Sue were not completely happy in Oxford, and when, in 1981, Walter Nance offered him a Distinguished Professorship on a princely salary at the Medical College of Virginia, he could not resist.

So the Eaves moved to Richmond and enjoyed the American dream of a large modern house with all mod cons, on a large block amidst beautiful woods (which Lindon liked to look at but would not enter because he was terrified of poison ivy) and a large American car. Lindon loved it all. And the icing on the cake was to be among a population of enthusiastic church goers so Lindon could practice his Anglican/Episcopalian faith to the full. He preached to various congregations in Richmond for close on 40 years. Later, Sue was ordained too and had her own parishes.

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Lindon would have loved this example of assortative mating and debated whether it was genotypic, phenotypic or social convergence.

Walter was delighted to have Lindon there and gave him every assistance to start building a group. In 1982, I visited Richmond for three weeks in order to work with him to finish off some papers left over from my PhD. While there I met a beautiful young Anglo-Irish graduate student, Georgia Chenevix-Trench, whom Lindon had played a critical role in accepting to the department. We became friendly and after I returned to Canberra started corresponding. When the phone bill for each of us started to approach 50% of our salaries, we decided we needed to do something about this. But what ?

The problem was solved when I was awoken early one morning by a phone call from Lindon, offering me a position as assistant professor in the Genetics Department at MCV. So in April 1983 I moved to Richmond and six months later Lindon married us in St Paul's Church, the same in which his funeral has just been held, a stone's throw from Jefferson's beautiful State Capitol building.

Lindon had been busy recruiting. Arriving in Richmond at almost the same time as I had were Andrew Heath, in the final throes of his D. Phil. thesis (which eventually came in at two huge, intense volumes) and Ken Kendler, a brilliant academic psychiatrist who was determined to break into the arcane mysteries of the Birmingham methods of genetic analysis. So began a marvellous three years of intense collaboration between the four of us, in various permutations. Ken introduced us to the field of psychiatric genetics, enlightening us about the clinical aspects and considerations while we applied our multivariate genetic methods to data on symptoms of anxiety and depression from my large Australian twin sample. This resulted in our paper 'Symptoms of anxiety and symptoms of depression. Same genes, different environments?,' which has become quite a landmark as well as being a watershed in our respective careers. After that we could expand our job description from 'behavioral geneticist' to 'behavioural and psychiatric geneticist'!

In parallel, Lindon and Ken were working on the common classifier in psychiatry (and other branches of complex disease medicine) of family history positive or negative (FH+/−). Lindon had a hunch that this dichotomy was either false or had very low power and in a series of incisive simulations showed that it depended entirely on disease penetrance and family size and was weak in most realistic cases.

Also in parallel, Lindon and Andrew were continuing work on the model for the extended twin-family design (ETFD) in which the parents, sibs, spouses and offspring of MZ and DZ twins would be added to the basic classical twin design (CTD) to enable teasing apart of more subtle genetic and environmental effects. The theory was all very well but what we needed was a dataset to try it on. I was fortunate in obtaining an NIH grant to test it on alcohol phenotypes—continuous (grams per week), ordinal (symptom severity) and dichotomous (diagnosis). So began the Virginia 30,000 study (VA30k) in which we eventually collected mailed questionnaire data on nigh on that number of twins and their relatives and this gave us unprecedented power to test hypotheses about causes of variation, transmission and assortative mating. It eventually morphed and was expanded into the Mid-Atlantic Twin Registry and is a valuable resource to this day.

All of this work took place in an intensely collaborative and friendly atmosphere. We introduced the English idea of the tea-break, which the Americans initially regarded as slacking off, but we soon convinced them that the purpose was not to discuss football or the weather, but to discuss work! Similarly, we all sloped off each lunchtime to the Skull and Bones restaurant across the street from Sanger Hall where cheerful Black waitresses called us 'Honey' and served us hot pastrami sandwiches and tuna salad while we argued back and forth over latest results. These lunches would not infrequently result in Lindon pulling out his scriber and giving us another brilliant derivation on the back of a paper napkin.

But enjoyable and productive as all this was, the pull of Australia was too strong, and in mid-1986 Georgia and I left Richmond and moved to the Queensland Institute of Medical Research in Brisbane where we have been ever since. The VA30k study became the model for the Australian 23k study funded largely by a series of NIH grants PI'd generously by Andrew Heath, and much of my work since then has been based on that resource.

Almost in my last week in Richmond there were two new arrivals. The first was John Hewitt, who had done a PhD in London with David Fulker in parallel with mine in Birmingham with Lindon. He bought our enormous American car and took our tuxedo cat, but before long John was snaffled up by the Institute for Behavior Genetics in Boulder and is now its director. The other new arrival was Mike Neale, another brilliant young PhD student of David's who has become a central figure in the subject (think Mx) and has stayed in Richmond, working with Lindon till the end.

Despite now being on the other side of the world, I didn't have to wait long before I saw Lindon again—at the International Congress of Twin Studies in Amsterdam in September 1986. The congress showed that there was great interest in the work coming out of our group and that many researchers would like to acquire our analytic methods. In the lobby at tea-break, I proposed to Lindon that what we needed was to hold a workshop where, in one week, we could teach the 'Birmingham methods' for twin analysis and we should teach it in the Birmingham way with a heavy emphasis on hands-on practicals and running of programs to solve problems. Dorret Boomsma was a local host and also enthusiastic about the idea and together we put it, then and there in the lobby, to our Belgian friends Bob Vlietinck and Robert Derom. Robert was, in common parlance, a mover and shaker, and in no time came up with some funding from his university to hold the first twin analysis workshop in Leuven. Being Belgian he also insisted we should all eat dinner together and made a very pleasant arrangement with a local restaurant to this end; this combination of high scholarship with good living is a tradition that has continued to this day. Only 23 'students' (many of them senior academics, and even one NIH director) attended the first workshop. Lindon was the star of course; with his humorous but scholarly and incisive teaching style he held the audience in the palm of his hand. And continued to do so for the next 30 years or so as the workshop grew and grew (we now cap enrolment at 100) first alternating between Europe and US but now settled on Boulder for the persuasive reason of over 20 years' continuous NIH funding (thanks to David Fulker and John Hewitt). Lindon's opening lecture always set the workshop off on a good course, and his lively, questioning style won many recruits to the subject. For me, the prospect of seeing and catching up with Lindon was a huge drawcard in going to Boulder each year—always something new, always a quirky, funny perspective, all too often a devastating insight that undercut my last year's work.

There have been many other meetings at conferences and elsewhere in the intervening years but two come particularly to mind. The first was occasioned by Lindon's award of an honorary degree

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from the Free University in Amsterdam in the Spring of 2000. Dorret had arranged a wonderful symposium (starring Lindon of course) held the in the august rooms of the KNAW (Dutch equivalent of the Royal Society) and splendid social program to make the most of the warm spring evenings, including an excellent performance of Stravinsky's *The Rake's Progress*, with a moralistic ending she thought would appeal to a man of the cloth; it did. The second was a visit to Brisbane in about 2007 by Lindon and Sue and younger son Thomas. Having espoused Frequentism all his life, Lindon had become an enthusiastic Bayesian, and with the zeal of a new convert came out to teach us how to use BUGS to solve various problems in psychometric genetics still intractable by traditional maximum likelihood methods. Lindon managed to convince us all and had the whole class using enormous amounts of computer grunt to do burn-ins. And in the evenings we had splendid dinners and parties and convinced them, I think, that life is endurable in the Antipodes.

Most of all on this visit it was wonderful to see Lindon engaging in a new intellectual challenge with the same energy, intellect and boyish enthusiasm as had charmed me to be his student 30+ years before—always challenging the accepted wisdom, asking how one could test the truth of some hypothesis, seeing the nuances and qualifications where others saw only black and white. Above all, he always stressed the paramount importance of 'getting it right' (John Jinks); his other favourite quotes were 'The truth will out' (Kenneth Mather), 'Reality cannot be fooled' (Richard Feynman) and 'Look at the bloody data!' (LJE). He lived by those rules himself and impressed them on those around him. His wife Sue comments, 'It would be good to mention the humility with which he approached the encounter with truth whether it be science or religion. He was one of the most humble people I have known—humble in the sense that he was fierce and rigorous about the search and its possible truths, but essentially modest about his place in that journey.' He is irreplaceable.

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