complete absence of glucocerebrosidase was caused by homozygosity for a null mutation.[4]

This report describes an unusual association of GD type 1 and JS in a non-consanguineous family of Indonesian and white Dutch ancestry (fig 1). The proband, patient II.1, was born at term with a birth weight of 3550 g, a length of 54.5 cm, and a head circumference of 38.5 cm (>98th centile). The diagnosis of JS was made by the presence of features including episodic hyperpnoea/apnoea, agenesis of the cerebellar vermis and corpus callosum, hydrocephalus, and chorioretinal colobomata. Severely delayed psychomotor development and generalised seizures were the major clinical features until death at the age of 4 years. Unexpectedly, lysosomal enzyme investigations showed a severe deficiency of glucocerebrosidase activity in cultured skin fibroblasts. Molecular studies showed compound heterozygosity N370S/L444P, the most common genotype in patients with GD type 1 in The Netherlands. Patient II.3 was born after an uneventful pregnancy and delivery with normal weight, length, and head circumference. At the age of 2 years, she had retarded mental development and autistic behaviour. Magnetic resonance imaging of the brain was normal at 7 years. At this age, she had no clinical features of GD type 1, except for mild hepatosplenomegaly. Like her older brother, she appeared to have deficient glucocerebrosidase activity associated with compound heterozygosity for GD type 1. In the third patient (II.4) at 16 weeks of gestation hydrocephalus was detected by ultrasound. Birth weight was 3220 g and head circumference 39.3 cm (>98th centile). The patient fulfilled the diagnostic criteria for JS and he died at the age of 8 month; no material was available for analysis.

This non-consanguineous family with two boys affected by JS and a girl with autistic behaviour was identified to have the most frequent genotype of GD type 1 in the Dutch population.[6] The presence of a severe neurological disorder such as JS and autistic behaviour cannot be explained by the N370S/L444P GD genotype alone. To address the possibility that the features of GD type 1 have been masked by the early onset of severe manifestations of JS, we investigated eight additional patients with JS. In these patients, we found a normal glucocerebrosidase activity in fibroblasts. These results suggest that the JS and GD loci do not (simply) coincide.

The most likely explanation for the coexistence of the two disorders in one person is the independent association of GD and JS. In this case, our observation may be unique, since the statistical probability of this event is extremely small in a non-consanguineous and interracial relationship. The incidence of GD type 1 is estimated at 1:50 000[3] and no more than 100 cases of JS have been reported.[1] Therefore, it may be worth considering other explanations. In this respect it is of interest to note the large clinical variability among GD patients with identical mutations, even within families.[7] All patients with GD types 1, 2, and 3 have significant levels of residual glucocerebrosidase activity (3-8% of those in controls; Kleijer and Aerts, unpublished data), with the exception of a neonatal variant of GD with prenatal onset of fetal hydrops.[4] Although our patients have a residual activity of 3-8% in fibroblasts, it remains possible that a complete knock out of glucocerebrosidase activity is present in some tissues, for example, the central nervous system in patient II.1 (but not in patient II.3) by an as yet unknown factor, interacting with the transcription or translation of the gene or with the enzyme activity.

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BOOK REVIEW

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Lancelot Hogben Scientific Humanist. An Unauthorised Autobiography. Editors Adrian and Anne Hogben. (Pp xvii + 254; £14.95.) Suffolk, UK: The Merlin Press. 1998. ISBN 085036 470 1.

Unauthorised autobiographies are rare, but the title is arresting rather than accurate. After Hogben's death Professor G P Wells, who wrote an extensive obituary in the *Biological Memoirs of the Royal Society*, attempted to get a mass of papers, which was clearly an unfinished autobiography, published. Ten years ago I met Hogben's elder son, Adrian, who had retired to near Bar Harbor, and made an equally unsuccessful attempt to interest Oxford University Press. This unfinished and extensively annotated manuscript had limitations as a profitable venture unless extensively edited, when I feared it would lose more than could be gained. However, it has been edited without losing the forceful elegance of his prose and the various repetitive sections have been welded into a seamless narrative. Additions include many photographs taken by Adrian, although only a small representation of his extensive collection after, when a child, he had been given a camera by Frank Bodmer, coauthor of *The Loom of Language*. It also includes an essential, but all too brief, appendix of the cast.

Hogben, like Newton, started life as a very premature baby. His parents, who devoted their lives to missionary work in Portsmouth, and later London, espousing a hellfire brand of fundamental Methodism, provided an unusual physical and intellectual environment which changed abruptly after he went to Cambridge with a scholarship to Trinity. While there the war started, providing an extraordinary series of experiences. He became a Quaker under the influence of the distinguished trio of Doncaster, Barcroft, and Eddington—a geneticist, a physiologist, and an astrophysicist. His attempts to study medicine were interrupted by voluntary work, mainly building huts, among those dispossessed of their land in Flanders, then a quagmire of trenches and shell holes. His uncompromising integrity led him, after various duties with the Friends' Ambulance Unit in France, including giving anaesthetics, to prison in London, the fate of many objectors to war. While there he was deprived of books, pencil, or paper. Although his medical career was interrupted his further education allowed him to acquire an extensive knowledge and experience of every living thing he could observe, animal or plant, large or small. His persistence overcame numerous obstacles, initially including poverty, and later episodic thyrotoxicosis, eventually moderated by a five-hour operation to remove a retrosternal goitre.

His first major discovery was made after studying over a thousand sections of the testis of the cockroach: at last he caught chromosomes in the act of side to side synapsis, resolving the conflict between Morgan's interpretation of recombination and previous observations showing end to end synapsis. Morgan visited him. Bateson was only converted to crossing over as an explanation of disturbed cosegregation some years later in Morgan's laboratory, some 20 years after he and Punnett had first described it.

Later his career took him to Edinburgh, Montreal, Cape Town, The London School of Economics, and Aberdeen, from where he eventually got to Birmingham via trans-Siberian railway after lecturing in Oslo when the Germans invaded. As an active opponent of their eugenic activities and supporter of Jewish scientists, he was on the blackest of black lists. With his elder daughter Sylvia he escaped to Sweden, eventually returning via Russia and the USA to become Professor of Zoology in Birmingham, only to be invited to head the Medical Statistics division of the Army work in London during the blitz. He finally returned to Birmingham, where

Medawar now occupied his chair of Zoology, to have the first chair of Human Genetics to be created in Britain since Galton's endowment of the chair Pearson held, under a different name, almost 50 years earlier. The exact title was "Medical Statistics and Human Genetics", the latter half dropping out of regular use for brevity.

The book refers to his major scientific achievements so casually that only biologists are likely to grasp their importance. His microscopy defined the act of synapsis, removing the last obstacle to the mechanism of linkage. In Cape Town, his reign as Professor of Zoology started as he meant to continue: he found the students dissecting the official English species on the syllabus, dispatched from England at great expense. He threw out the entire stock and introduced local fauna, including *Xenopus,* the African four toed frog, often called a toad. He developed this as a new laboratory species, which, after he had resolved various difficult problems of its domestication, he distributed to other laboratories. Later he developed the "Hogben" test for pregnancy, replacing the similar, slower, and more expensive test on mice. The species is now widely established in laboratories. It was used by Gurdon to show the feasibility of full development of an adult frog from a tadpole nucleus. Now we have "Dolly".

The Hogben test showed the extreme conservation of some proteins in evolution. The sympathetic response of the frog's gonad to blood from pregnant women implied an unexpected near identity of both receptor and acceptor proteins after several hundred million years in diverse species. He did the first hypophysectomy in vertebrates with such success that the animals survived well, allowing observations many months later, and clarifying its pigmentary actions. He studied haemocyanin in detail, first in small quantities from snails, then on a quart from horseshoe crabs, and, after spending two weeks on a trawler off Cape Town, on a gallon of octopus blood. His approach was always direct, both professionally and socially.

His interest in language developed through fluency in Scandinavian languages. Like Darwin, a more theoretical linguist, he was fascinated by their evolution and developed an artificial archetypal language, Interglossa, which he hoped would replace Esperanto: it was partly written when fire watching in the London blitz. *The Loom of Language* provided an extensive comparative study, covering an extensive phylogeny on extensive examples. He separated from his wife Enid Charles, a Welsh speaker, who had spent the war with their children in the USA, but by then lacked the enthusiasm for Wales and its language that Hogben had developed in Birmingham. He became fascinated by the intrinsic difficulties of Welsh grammar, and later he married the woman whom he met when asked "who was murdering her language" while he tried to buy a stamp.

Last October, Birmingham celebrated the half century of the founding of the first chair including the title Human Genetics at a meeting organised by the late Professor Sarah Bundey. His son Adrian and his wife, coeditors of the book, and his daughter, his first child, Sylvia and her husband, and their children and grandchildren were present. The University library displayed to them its extensive archives, including the papers from which the edited version was assembled.

His combination of inborn, if not always conventional, good manners, even when compromised by his directness of speech and action, exposed him to scenes of hospitality he could not reciprocate. His wide range of hosts included H G Wells, the father of G P Wells, The Webbs, Lady Ottoline Morrell, and Beveridge. His close but usually intermittent friendships included F A E Crew and Julian Huxley, up to Lysencko's activities, which Huxley denigrated as "the New Genetics". After this Professor C A B Smith told me he would avoid the University college area in case he met Haldane.

His appointments were never without problems. In Montreal he became a member of the Society for Cultural Relations with the Soviet Union, which was considered evidence for espousing free love, making him a hazard to women assistants. In Cape Town he was among the first to combine opposition to both Apartheid and the application of eugenic and educational arguments to political biology, and probably surprised some colleagues by his preference for Jewish company. The closed group of church and senate in Aberdeen, which he describes in some detail, may not have appreciated his agnosticism, socialism, or casual hospitality. Nor could the rhetorical question in one of his books "would you prefer to be cast up on a desert island with a Jamaican or an East Coast Scot", have helped, even if sometimes misunderstood. His opposition to racism and his credentials in pacifism, socialism, and feminism (he named his firstborn after Sylvia Pankhurst) allowed him to be uninhibited by political correctness in his many books and lectures. He did not approve of what he termed "package faiths".

He was not much more tactful in Birmingham where he declined to be in the same room as Zuckerman. His much quoted comment that it was "no longer possible to get into the Royal Society on the backside of a baboon" hardly smoothed matters. His common remark "where there's death there's hope", although less cutting by then, was doubtless heard loud and clear in his earlier attempts to influence university gerontocracies in the days before universities had introduced retirement. He maintained a steady, entertaining, and usually well mannered opposition to the biometric genetics of Mather and Jinks, whose Latin square plots he overlooked from the Staff Club. His chairing a prestigious lecture by Mather at the Genetical Society was concluded, not by a conventional vote of thanks, but by "Unless anyone can suggest any other way to make simple matters more complicated I think we should go and have tea". He particularly objected to Galton, a "local boy", both as a renegade Quaker and as sponsor of the biometric approach of Pearson, and his endowing the chair he was to occupy. His opinion of Fisher was not charitable, but reciprocated. He held court in the Staff Club bar, and was generous in buying drinks on the grounds that, when he was poor, H G Wells was always generous. He told me he considered his major achievement was to have got 12 of his technicians into University chairs, competing in this with Sharpey-Shafer, with whom he had worked briefly in the Animal Breeding Research Department in Edinburgh, teaching cytology and working on pigmentation.

He could not understand how anyone professing a knowledge of biology or medicine could, or should, contemplate a null hypothesis except in limited fields, including therapeutic trials, on whose numerical inadequacy he had strong views: many local enthusiasts "sent their washing to London". He tried to dispel various illusions in a remarkable book on Statistical Theory combining logical rigour, algebraic and historical accuracy, and ironic prose. He was a consistent enemy of the "cook book" approach to statistics allowing apparent rigour divorced from understanding, but did not live to see its worst manifestations with the computerised "cook books" now well established in genetics and epidemiology. In this major and little recognised book on Statistical Theory he distinguished, perhaps for the first time with such clarity, the forward look before collecting data and the backward look afterwards. In genetics he exploited the finite difference calculus, which is difficult for humans but simple for the computers he did not live to use, although he was among the first users of punched cards, the integer's friend, in establishing the Birmingham Cancer Registry. He developed a code involving numbers for names based on their frequency distribution, accompanied by birth date, initiating both the Birmingham Cancer Registry and, under McKeown, the Malformation Registry. His scientific integrity compelled him to avoid what he could not both understand and visualise. He was always unhappy with the differential and integral calculus; his book, *Mathematical Genetics*, in which I have failed to interest either Norton's, its original publishers, or the Dover Press, in reprinting, managed to avoid what he regarded as the "fudge" of treating integers as close neighbours of real numbers rather than their original landlords. Like Eddington he liked to restrict his inference to models he could visualise, and they had to be finite; in his several popular books they were largely based on card packs and chess boards, avoiding the smooth curves which others used to clothe and, in his opinion, to conceal. One, *Choice and Chance through Cardpack and Chess Board* achieved even greater feats of alliteration than his three great "primers for the age of plenty": *Mathematics for the Million*, *Science for the Citizen*, and *The Loom of Language*. His integrity sometimes verged on cruelty, from which even death was no escape. The second sentence on the first page states he came from "poor but intellectually dishonest" parents: neither statement is supported by the facts. Some of the well established dead, including Hugh Gaitskell, fared no better. But at least he justified his remarks: he was a primary witness and, where appropriate, his criticism includes fine ironic prose. For more examples, see a superb review by Gratzer (*Nature* 1998;**391**:452-3).

In Birmingham, I first met him at my last successful formal interview, in so far as any activity involving him could be formal, and some 20 years later held the chair in Human Genetics he had initiated. I did not anticipate so distinguihed a scientist having rooms underneath the hospital laundry, where he found the high temperature suited his intolerance to cold. I was greeted by an elegantly if unconventionally dressed man with radiation scars over his thyroid and a myxoedematous voice, possibly worsened by radiation damage to his larynx. The police once mistook this intonation, and his attempt to prove his sobriety by deriving the distribution of chi-squared did not achieve the effect he had hoped: he was meant to draw a straight line and walk along it. He was then living in the

Staff Club during the week, ascending each night with a jam jar full of sharpened pencils, which had to be the right hardness, a pad of yellow paper, and a bottle of brandy, descending in the morning with neat copy ready for the printer, blunt pencils, and an empty bottle. His last act, while admitted to Wrexham Hospital, was to request hard pencils and yellow paper to modify his will: he died while they were being purchased.

When I last saw him in hospital he asked me if I knew that a small bottle of Johnny Walker whisky fitted up the sleeve. The next day, on leaving him, the ward Sister informed me that, by some coincidence, the professor of Surgery, in whose ward he was, the professor of Medicine, and myself had all visited him that morning and all had stiff arms.

Readers of reviews need to know if the book is worth reading, buying, or advising a librarian to buy. The answer must be yes, yes, and sometimes. It is essential for libraries of Departments of English, Modern History, and the History of Science. It is a fine work of English prose, and a fine document to the political, social, and academic environment of the period. But it has limited claims on a library of a Department of Genetics or a hospital. The publishers are to be congratulated on both their standard of production and their price.

It should create a need for a second edition with more photographs, a more extended appendix, maps of the "grand tour" from Oslo to Aberdeen, some facsimile pages of the original, and more details of the several centres of excellence he visited in the USA en route from Aberdeen to Birmingham. To know more read Gratzer's review in *Nature*.

JOHN H EDWARDS

NOTICES

6th International Congress on Amino Acids

The 6th International Congress on Amino Acids will be held at the University of Bonn, Germany on 3-7 August 1999. For further information contact Dr Olga Labudova/Prof Dr Hermann Rink, Exp Radiol/ Strahlenbiologie, Univ Bonn, Sigmund Freud Str 25, D-53105 Bonn, Germany. Fax: 0228/287-4457. Email: hrink@mailer.meb.uni-bonn.de

4th European Forum on Quality Improvement in Health Care, and 4th Swedish QUL Conference

This three day conference will be held in Stockholm, Sweden on 25-27 May 1999. The aims of the forum are: to provide education on how to improve health care; to exchange sound, practical ideas in improving health care; to provide a setting for deep discussion and shared learning among those charged with leading improvements in health care; to build the scientific base of methods to improve health care; to accelerate the improvements in health care; to make change happen. For further information contact: Marchella Mitchell, British Medical Association, Conference Unit, BMA House, Tavistock Square, London WC1H 9JR, UK. Tel: +44 (0)171 383 6478. Fax: +44 (0)171 383 6869. Email: MMitchell@bma.org.uk