

complete absence of glucocerebrosidase was caused by homozygosity for a null mutation.³

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 months; 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 000³ 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.

A VAN ROYEN-KERKHOF
B T POLL-THE

University Children's Hospital "Het Wilhelmina Kinderziekenhuis", Nieuwegein 137, 3512 LK Utrecht, The Netherlands

W J KLEIJER
O P VAN DIGGELEN

Department of Clinical Genetics, University Hospital, Erasmus University, Rotterdam, The Netherlands

J M F G AERTS
Department of Biochemistry, Academic Medical Centre, University of Amsterdam, The Netherlands

J J HOPWOOD
Department of Chemical Pathology, Women's and Children's Hospital, North Adelaide, Australia

F A BEEMER
Clinical Genetics Center Utrecht and Department of Clinical Genetics, University Children's Hospital "Het Wilhelmina Kinderziekenhuis", Utrecht, The Netherlands

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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*, at-

tempted 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

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 Gratzner'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@mail.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