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2003 WILLIAM ALLAN AWARD ADDRESS
Introductory Speech for Sir David Weatherall*

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It is a distinct pleasure for me to introduce Sir David Weatherall, the recipient of the 2003 William Allan Award of the American Society of Human Genetics. This award is the highest honor that the Society can bestow upon a scientist for contributions to human genetics. As one who has followed his career over the past 40 years, I firmly believe that this honor is well deserved and long overdue.

David Weatherall graduated from the Medical School at the University of Liverpool in 1956. After house staff training, he joined the Army for a 2-year assignment that would chart the future course of his career. Returning from military service, he took a fellowship at Johns Hopkins before returning to Liverpool, where he rose to the rank of professor. In 1974, he was appointed Nuffield Professor of Clinical Medicine at the University of Oxford, and, in 1992, he assumed the most prestigious chair, of Regis Professor of Medicine. In 1989, he founded the Institute of Molecular Medicine at Oxford, which was renamed the Weatherall Institute of Molecular Medicine in his honor, in the year 2000 (fig. 1).

David's contributions to genetic disorders and thalassemia are legend. However, it is interesting to note from his own reflection how he came to enter this field (Weatherall 2001). Two years after he qualified in medicine, he was called to serve his country, and he joined the Royal Army Medical Corps as part of his compulsory service. Having an aversion to flying, bullets, and snakes, he volunteered to serve in the United Kingdom. The army, in its infinite wisdom, shipped him to Singapore instead. And in another stroke of genius, the army put him in charge of a children's ward at the British Military Hospital (fig. 2), even though he had no pediatrics training. One of his first patients was a Gurkha child from Nepal who had a mysterious illness that required regular blood transfusions to keep her alive. With his biochemist colleague Frank Vella in Singapore, he performed hemoglobin electrophoresis on the child's parents and discovered that they had increased HbA_2. Brilliantly, they made the diagnosis of homozygous β thalassemia, no mean task in those early days. Triumphantly, they published their breakthrough findings in the *British Medical Journal,* (Weatherall and Vella 1960*)*, whereupon they were immediately called on the carpet by the Director General of Medical Services for the Far Eastern Forces. He was told that he could be court-martialed for publishing information about military personnel without permission from the War Office, and, in any case, it was bad form to reveal to the world that one of the personnel from the Gurkha regiments had bad genes. He was ordered not to do it again. Perhaps it was because of this reprimand and David's defiant nature that he decided to spend his life pursuing bad genes, and he has not stopped ever since.

After the stint in Singapore, he spent a fellowship in the Johns Hopkins Hospital under the tutelage of two

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Figure 1 The Weatherall Institute of Molecular Medicine, Oxford

giants in genetics and hematology, Victor McKusick and C. Lockhard Conley (fig. 3). His achievements since then have been so overwhelming and far reaching that I can only touch on a few highlights.

With the late Hermann Lehmann, he studied the human hemoglobin variants and described a number of novel hemoglobins, including those that cause methemoglobinemia and polycythemia. In the 1960s, David returned to the study of the genetic and molecular basis of thalassemia. With John Clegg (fig. 4), he devised a method that accurately measured the synthesis of the α- and β-globin chain in patients with various thalassemia syndromes (Weatherall et al. 1965). On a personal note, it was the sheer elegance of this measurement that attracted me to begin my own studies in thalassemia. He described or clarified many other thalassemia syndromes, such as $Hb^{ConstantSpring}$, hereditary persistence of fetal hemoglobin, and $\delta\beta$ thalassemia (Milner et al. 1971). With the advent of molecular biology, he moved with Robert Williamson's group to the studies of the genes and gene expression in these syndromes and described the deletion of the α-globin genes in α thalassemia and gene deletion in $\delta\beta$ thalassemia, among other molecular defects in thalassemia (Ottolenghi et al. 1974, 1976). He correlated the genotype-phenotype relationship of the various thalassemia syndromes. Also, he described novel cases of mental retardation associated with α thalassemia that result from the deletion of a large segment of chromosome

Figure 2 The British Military Hospital, Singapore, 1959

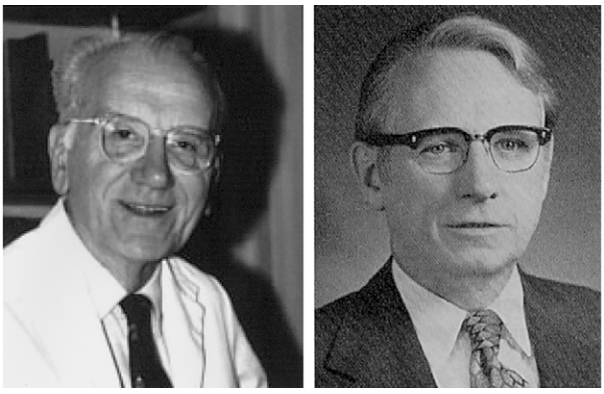

Figure 3 Victor McKusick (*left*) and C. Lockhard Conley

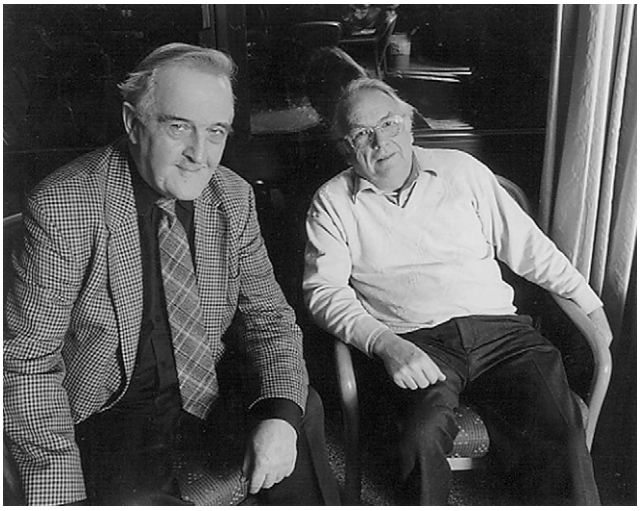

Figure 4 David Weatherall (*left*) and John Clegg

16 or from a mutation in the X chromosome that affects the expression of the α-globin gene (Wilkie et al. 1990*a*, 1990*b*). His studies in thalassemia bridged the clinical aspects of the diseases to their molecular basis and constitute the model for our studies of many genetic diseases.

In recent years, David turned his work to the HbE syndromes and their interactions with β thalassemia, an important disease entity in regions in Southeast Asia, such as Thailand and Sri Lanka (de Silva et al. 2000). He spends a great deal of time and effort in these areas, where, in Sri Lanka, he helped launch a clinic for the studies of these syndromes.

The accolades that David has received during his distinguished career are far too numerous to name here. Among his honors are many named lectures, some 24 honorary degrees, and 26 international prizes. He is a member of many international learned societies—for instance, he is a Fellow of the Royal Society and a foreign member of the National Academy of Sciences and the Institute of Medicine. For his contributions, he was knighted by the Queen in 1987.

David has trained a large number of research leaders around the world. Moreover, he educates a global audience through his tireless writings that include reviews, chapters, and original papers numbering almost 600. He has written and edited 14 books—ranging from textbooks of medicine and hematology, genetic engineering, and history of medicine—several of which have gone through multiple editions. Of course, his book, *The Thalassemia Syndromes,* now in its fourth edition, is the Bible, which everyone in the field must read.

Members of the American Society of Human Genetics, it gives me great pleasure to present to you Sir David Weatherall.

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