Case histories
Thalassaemia

In 1858 the German pathologist Rudolf Virchow described leukaemia as a disorder of white blood cell proliferation. Virchow and others observed that people with chronic leukaemia typically had enlarged spleens, and for the next 50 years or so patients with this sign might be diagnosed with "splenic anaemia". In the early 20th century, though, this broad frame broke into several new diagnoses. One of them—thalassaemia—has been shaped by some of the most potent forces of the modern era: migration and shifting attitudes to race, molecular medicine and the pharmaceutical industry, the power of scientific medicine, and the limitations of treatment.

In his history of thalassaemia, the physician David Weatherall—a pioneer of molecular medicine—noted that the first account of the condition is usually attributed to the American paediatrician Thomas B Cooley. In a research note published in 1925, Cooley described five children with anaemia, enlarged spleens, and discoloured skin. Striking radiological changes to the skull and long bones might, he thought, reflect lesions in the bone marrow, causing a form of "myelophthisic anaemia". Cooley framed this condition in terms of its distinctive pathology, but several Italian researchers published similar accounts suggesting a strong familial component. In the early decades of the 20th century, European and American clinicians were beginning to engage with the new synthesis of mendelian genetics and population statistics, and the English physician Alfred Garrod showed that Mendel's notion of dominant and recessive genes offered a powerful explanatory frame for some inherited diseases.

Cooley's account of "myelophthisic anaemia" and Garrod's work on genetics came together in a 1932 paper by the American pathologist George Whipple and the paediatrician W L Bradford. As its title suggests, "Racial or Familial Anemia of Children" framed the condition principally in terms of its heredity. Whipple and Bradford found the condition almost exclusively in patients of Mediterranean ancestry, and coined a new name to reflect this: thalassaemia, from the Greek words for sea and blood.

In the aftermath of World War 2, new ideas and networks were transforming scientific medicine—notably, the molecular biology funded by the Rockefeller Foundation's Science of Man project, rooted in new techniques such as electrophoresis and x-ray crystallography. Genetic diseases like sickle cell anaemia and thalassaemia seemed prime candidates for "molecularisation", and by 1959 thalassaemia had been linked to mutations in the α and β globin chains in haemoglobin.

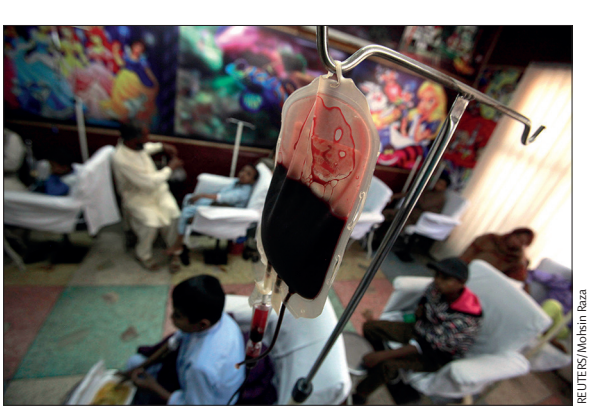
As in the case of sickle cell anaemia, this remarkable advance in clinical understanding raised a more difficult question: how would this knowledge improve the lives of patients? Treatments for other forms of anaemia were ineffective; repeated transfusions caused iron accumulation and organ damage; and most patients died before the age of 9 years. Research in the 1960s showed desferrioxamine was an effective iron chelator, but problems with administration and dosage took another two decades to solve.

If treating thalassaemia was so difficult, would prevention be more effective? A pilot counselling programme in rural Greece in the early 1970s raised consciousness of the condition but also generated anxiety and stigma around those found to be carriers. Programmes based on prenatal diagnosis proved more effective, but the attitude of the Catholic Church to abortion has proved an obstacle in some Mediterranean countries, and schemes in Islamic and Buddhist nations have faced similar difficulties.

The development of organ transplantation in the late 1960s and 1970s generated hopes that it could be used to cure thalassaemia. A team in Seattle in 1982 did the first successful bone marrow transplantation, but problems with graft-versus-host disease and increased susceptibility to infections has limited the value of the procedure.

In the last generation, research has focused on the prospect of gene therapy and new oral iron chelators. Thalassaemia patients in high-income nations generally enjoy longer lives of greater quality than in the past, but the cost of treatments and diagnostic technologies, the need for health-care infrastructure and continuity of care, and social and religious attitudes to screening programmes are all reflected in the quality of care in low-income and middle-income countries. In many developing nations "the lot of a baby with thalassaemia", in Weatherall's words, "is little better than it had been in the first half of the twentieth century".

Richard Barnett
richard@richardbarnettwriter.com



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For more on **thalassaemia** see https://www.thelancet.com/clinical/diseases/thalassaemia

Further reading

Cooley TB, Lee P. A series of cases of splenomegaly in children with anemia and peculiar bone changes. *Trans Am Pediatric Soc* 1925; **37:** 29

Wailoo K. Dying in the city of the blues: sickle cell anemia and the politics of race and health, Chapel Hill, NC: University of North Carolina Press, 2001

Weatherall D. Thalassaemia: the biography. Oxford: Oxford University Press, 2010