

Historical Review

SIR LEONARD PARSONS AND THE SCIENTIFIC BASIS OF PAEDIATRIC HAEMATOLOGY

'Progress is marked not so much by the problems we are able to solve as by the questions we are enabled to ask'

L. G. Parsons

When considered as a subspeciality of paediatrics and a *sine qua non* of the modern academic environment, paediatric haematology is a relative latecomer. This is not surprising as diseases of the blood were for a long time considered as a minor problem when compared with the great challenges of infectious and nutritional disorders that faced the early pioneers of paediatrics. The early history of paediatric haematology is too closely interwoven with general haematology for it to be traced separately. However, the early discoveries of the pioneers of haematology (Ehrlich, Metchnikoff, Landsteiner, Minot, Castle and Whipple to mention just a few) were applied to the special problems of childhood and infancy by investigators who, with few exceptions, were paediatricians with ranging interests rather than haematologists with a specialized background. This is true even for those whose names have become immortalized through eponyms, such as Cooley, Diamond, Blackfan and Fanconi.

One name that has not been immortalized is that of Heinrich Lehndorff who devoted his life to the study of normal and abnormal haematological conditions in childhood and who published between 1906 (when 27 years old) and 1963. Lehndorff was forced to leave Austria in 1939 and found temporary shelter with the subject of this article, Leonard Parsons, before moving to the USA (Zuelzer, 1998).

Lehndorff was only one of many who was attracted to the wisdom and mentoring of Leonard Parsons, who is often regarded as the Grand Old Man of British Paediatric Haematology. Parsons was an original thinker who refused to accept the confused semantics of childhood anaemias and created his own system along pathophysiological lines.

The life of Leonard Parsons

Leonard Gregory Parsons was born in Kidderminster in 1879. He came from a family with a long tradition in farming. As a boy he attended King Edward's Grammar School, Aston, and then matriculated in zoology at Mason's College, Birmingham. What made Parsons turn to a medical career is not known, but he took his intermediate MB in 1901 and qualified MB, BS (London) in 1905 (Birmingham was not yet a University). By this time he had already

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developed other interests including the Student Christian Movement, shooting, cricket, rugby (playing for Wasps and Blackheath), winter sports, and athletics (having beaten Duffy, the American champion, over 100 yards) (Cameron, 1950).

Upon graduation, Parsons passed through several resident hospital appointments at the Queen's Hospital in Birmingham. This was followed by a few years in general practice and midwifery that probably persuaded him to specialize and, with this aim in mind, he took up the post of Casualty Officer at the Great Ormond Street Hospital for Sick Children. He obtained his MD (London) in 1907 and 2 years later became a Member of the Royal College of Physicians of London. His career progressed steadily with his appointment in 1910 as Physician to Outpatients at the Birmingham Children's Hospital.

Within 40 years, the number of beds in the Hospital increased from 60 to 300. Five years after his appointment, Parsons was appointed as Lecturer in Diseases of Children and Paediatrics. The first of approximately 50 papers (on acute tremor in polioencephalitis) was published in 1910 (Parsons, 1910), followed rapidly by papers on infantilism associated with renal disease (Parsons, 1911), spinal muscular atrophy (Parsons, 1912), polioencephalomyelitis (Parsons, 1913), variations in blood pressure associated with lumbar puncture (Parsons & Gray, 1912a), and lectures on the mechanism and treatment of shock (Parsons & Gray, 1912b).

The year 1916 found Parsons serving with the Royal Army Medical Corps in Salonika and the following year he was appointed Consultant Physician to the Serbian Army. After his return to civilian practice, he came to be regarded as the leading paediatrician for the Midlands and his reputation began to spread throughout England. In 1928 he was appointed the first Professor of Child Health at Birmingham University and the following year was selected as Sub-Dean of the Medical Faculty.

As Parsons's clinical experience increased, he realized that it was not enough just to aim at the early recognition of disease and to quest for a cure. How much more logical to prevent disease rather than wait until its appearance. With this philosophy in mind, he called together representatives of the University, the Children's Hospital and Birmingham City Council with the purpose of broadening the facilities for scientific research into paediatric disease. The outbreak of the Second World War caused an interruption in planning, but soon after peace was declared, negotiations were resumed from which came the Institute of Child Health in 1945.

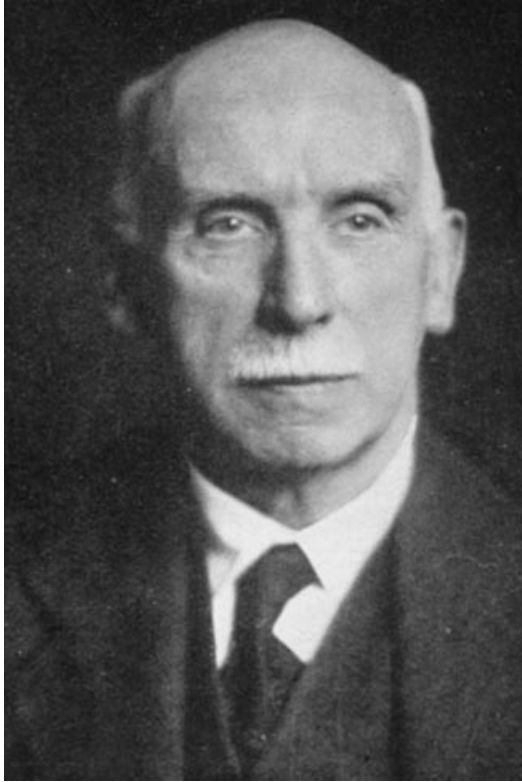


Fig 1. Sir Leonard Parsons, FRS, MD, FRCP, FRCOG.

Parsons served his University and Medical School well. He was a great supporter of building the new Medical School on the Edgbaston site, he became Dean of the Medical School in 1948 and was elected Fellow of the Royal Society in 1948. He was knighted in 1946 in recognition of his work for children during the war years. He died suddenly on 17 December 1950, aged 71 years (Fig. 1).

The scientific work of Leonard Parsons

Much of Leonard Parsons's achievements were owing to his personality and ability to nurture human relationships. He was able to gather around him a group of devoted workers to whom his obligations were great, but never forgotten. The following account is limited to topics that were peculiarly his own.

The haemolytic anaemias of childhood. It was in the field of anaemias of childhood that Parsons achieved his greatest research success and hence this subject provides the backbone of this review.

In the 1920s, the condition known as 'icterus neonatorum' was well recognized. This 'yellow jaundice' may be present in the first few days of life and usually rectifies itself without serious long-term effects (Cameron, 1950). However, some babies were recognized as having a much more severe jaundice that appears soon after birth and progresses to drowsiness, convulsions and even death. This may be associated with severe anaemia, organomegaly and generalized oedema, contributing to an overall picture of hydrops fetalis and post-mortem evidence of kernicterus and

persistence of extramedullary erythropoiesis (erythroblastosis). It was appreciated that the common factor was excessive red cell destruction, but the cause of this haemolysis remained unknown.

Parsons began his investigations in 1930 (Parsons, 1931). In 1933, he wrote 'Sometimes in the newborn child haemolysis is severe and unchecked and a profound anaemia of the haemolytic type develops within a few days of birth. This form of haemolysis occurs in familial icterus gravis. As a result the bone marrow is stimulated and the extramedullary centres of the erythron recalled into activity, and a form of erythroblastosis of the newborn is produced' (Parsons *et al.*, 1933). Parsons put his emphasis on the haemolytic red cell destruction as the main causative factor and differed from American workers who attributed icterus gravis to the persistence of foetal erythroblastosis into post-uterine life.

In the 1930s, haemolytic anaemias were considered as an 'unsatisfactory disease group for which there is no clear nor accepted definition and a useful dumping ground for obscure blood diseases' (Lancet, 1938). Parsons was unhappy with this definition. He recognized the importance of underlying abnormalities of the 'erythron' and, hence, susceptibility to haemolysis. Such conditions included acholuric jaundice (spherocytosis), sickle cell anaemia, Cooley's anaemia (thalassaemia) and paroxysmal nocturnal haemoglobinuria. Parsons believed that the commonest cause of haemolytic anaemia in the newborn was either infection or a 'lysin'. 'The picture produced by an acute infection may be indistinguishable from the acute haemolytic anaemia of Lederer or icterus gravis' (Parsons, 1938). Parsons's 'lysin' achieved greater relevance with the elaboration of blood grouping and the description of the 'rhesus factor' by Landsteiner and Wiener in 1940. These discoveries opened a new understanding into haemolytic disease of the newborn. The part played by Parsons team was of great importance, for it was based on a firm foundation of painstaking, meticulous, clinical and pathological study that led to the elucidation of many confusing varieties of anaemia. With characteristic simplicity, Parsons was able to correlate these complex varieties when he recognized that they 'owe their clinical characters to permutations and combinations of the erythronic response to injury' (Parsons, 1947). He maintained that 'The various forms of anaemia described should not be regarded as hard and fast types or separate diseases but as manifestations of varying behaviour of blood'.

Antenatal paediatrics. Parsons had a life-long interest in fetal development and, in particular, the influence of maternal nutrition (Parsons, 1946). He recognized that maternal disease or inadequate diet affected fetal development, particularly during the last trimester, and that intrauterine infection or prematurity could have similar consequences.

He also appreciated that, during the last 3 months of pregnancy, the fetus is particularly vulnerable to nutritional disorders that can develop rapidly during extrauterine life if storage during pregnancy has been defective as a result of prematurity, inadequate nutrition or maternal disease. Such

conditions include haemorrhagic disease of the newborn, nutritional anaemia, tetany, rickets and scurvy.

Wasting diseases in infants. Coeliac disease was first described in 1888 by Samuel Gee, a physician to University College and St. Bartholomew's Hospital. He described the loss of appetite, diarrhoea and marked failure to thrive. Parson's contribution to this condition was the appreciation that many of the symptoms of coeliac disease, especially scurvy, tetany, rickets and malabsorption, are evidence of a deficiency disorder (Parsons, 1936). He and his co-workers recognized the defect in fat absorption from the intestine and, hence, reduced absorption of vitamin D.

Rickets and associated diseases. Parsons maintained an interest in this deforming disease throughout his life. The importance of sunlight in preventing rickets was established around the time of the First World War when the therapeutic benefit of ultraviolet therapy was shown. In the 1930s, it was realized that the potential to cure rickets could be conferred on certain food stuffs by exposing them to ultraviolet irradiation. Parsons was the first to substantiate this in humans by administering irradiated cholesterol to Birmingham children suffering from rickets and showing that such treatment gave complete and rapid cure (Parsons, 1926). Subsequently, it was shown that the curative action of sunlight and artificial ultraviolet irradiation in rickets was owing to the synthesis of vitamin D. 'Thus we have the appearance and development of rickets associated with the progress of civilization and in particular, with the rise of industrialization and the decline of breast feeding' (Cameron, 1950).

Parsons and paediatric research. Parsons held clear views on research in paediatrics and expressed them so well on many occasions that he came to exert an influence on this branch of medicine far beyond his immediate field of activity. 'Paediatrics is concerned with the study of disease in infancy and childhood as well as the study of the infancy and childhood of disease. Clearly, the study of disease in infancy and childhood enables us to recognize the genesis and evolution of many chronic diseases in the adult'. Parsons felt strongly that the burden of research must fall to the lot of the clinician in the first instance. So long as the observer of disease is careful, honest and untiring in his pursuit of facts, he will succeed. 'The search for specimens of disease and the observations of their habits must be made in the wide, sometimes unexplored, continents of practice. This is the province of the clinician, but having secured his specimens he must take them to the laboratory for closer investigation and dissection, and in this laboratory must not only be clinicians but, far more important, chemists and physicists, who not only have to find the solution of problems that arise in the investigation, but who, in their turn, may produce not only ideas for clinical inquiry but detailed methods for its pursuit' (Cameron, 1950).

Parsons was once asked why he had decided to devote so much time to the study of disease in children. He gave two reasons. First, that he liked children and, second, that he believed that the problems of paediatrics were probably to prove the most profitable for study while biochemistry and clinical pathology were in their infancy, because they were relatively simple in comparison with those of adults and, he added with a laugh, he got on better with simple things.

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