

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/233929004>

# Jamaica, the Caribbean and Sickle Cell Disease

Article in *The West Indian medical journal* · July 2012

DOI: 10.7727/wimj.2012.200 · Source: PubMed

---

CITATION

1

---

READS

440

1 author:



[Graham Serjeant](#)

Sickle Cell Trust (Jamaica)

483 PUBLICATIONS 16,284 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Sickle cell research [View project](#)



The Manchester Project [View project](#)

# Jamaica, the Caribbean and Sickle Cell Disease

GR Serjeant

## ABSTRACT

*The development of research interests in sickle cell disease has been traced from the first recorded case, the founding of the University Hospital of the West Indies and the Jamaican Sickle Cell Unit with its influence on clinical practice in this disease worldwide.*

**Keywords:** HbS screening, Jamaica, prevention of sickle cell disease, sickle cell disease

# Jamaica, el Caribe y la Enfermedad de Células Falciformes

GR Serjeant

## RESUMEN

*El presente trabajo sigue el desarrollo del interés en la investigación de la enfermedad de células falciformes – desde el registro del primer caso, la fundación del Hospital Universitario de West Indies, y la Unidad de Anemia Falciforme en Jamaica – con su influencia en la práctica clínica de esta enfermedad a nivel mundial.*

**Palabras claves:** pesquisaje de hemoglobinas S (HbS), Jamaica, prevención de la enfermedad de células falciformes, enfermedad de células falciformes

West Indian Med J 2012; 61 (4): 331

## BACKGROUND

The Caribbean has a special place in the history of sickle cell disease since the first recorded case with homozygous sickle cell (SS) disease came from the island of Grenada in the eastern Caribbean. Studying as a dental student in the Chicago College of Dental Surgery in the United States of America (USA) between 1904 and 1907, this young Grenadian had persistent symptoms and a very unusual blood film with ‘peculiar elongated and sickle-shaped red blood cells’ (1). Having completed his studies in 1907, he returned to Grenada where he had a successful dental practice until dying from what is now known as the acute chest syndrome at the age of 32 years after enjoying a day at the races in Grenville. His identity was not known until Dr Todd Savitt visited Chicago and traced the notes made by Dr James Herrick, his physician during hospital admissions in the early 20<sup>th</sup> century, to find that his name was Walter Clement Noel (2). Dr Savitt then visited Grenada and managed to trace members of his family and an elderly lady who could still recall having received dental treatment by him in childhood.

He also found the headstone of Walter Clement Noel in the Catholic cemetery at Sauteurs in the north of the island alongside the headstone of his father, John Cornelius Noel (Fig. 1). Within three months, the second recorded case of



Fig. 1: Headstone of Walter Clement Noel (left) alongside the Gaelic cross headstone of his father John Cornelius Noel at a cemetery in Grenada. This headstone was destroyed by Hurricane Ivan in 2004.

From: Sickle Cell Trust (Jamaica), Kingston, Jamaica, West Indies.

Correspondence: Professor GR Serjeant, Sickle Cell Trust (Jamaica), 14 Milverton Crescent, Kingston 6, Jamaica. E-mail: grserjeant@cwjamaica.com

SS disease was published (3), having been observed for some years as possibly an unusual case of pernicious anaemia, but with Herrick's report, it immediately became clear that this was the same disease. The third case reported from St Louis in the USA created some confusion since both the patient and his father appeared to have sickled cells on special testing, leading to early confusion between the sickle cell trait and sickle cell disease. The fourth case was published from Johns Hopkins Hospital in 1922 by Verne Mason (4) before Mason left for Los Angeles to be a physician to the Hollywood stars and to Howard Hughes, whom he may have influenced to support medical research and became one of the early directors of the Howard Hughes Medical Institute. In reviewing these first four cases published over 12 years, Mason noted that all were black, leading to the common misconception that the disease was confined to people of African origin.

Subsequent work on early descriptions of the disease and its genetics emanated from the USA or from medical officers in colonial service in Africa with no further substantive reports from the Caribbean until the establishment of the medical school in Jamaica and of the Sickle Cell Unit.

### **The University Hospital of the West Indies**

Opening its doors as the Hospital of the University College of the West Indies for the first medical students in 1948, the medical staff rapidly became interested in sickle cell disease. Members of the Departments of Medicine, Clinical Pathology and Chemical Pathology produced many observations between 1954 and 1960. The prevalence of positive sickling tests was examined by Jelliffe *et al* (5) and later expanded by haemoglobin electrophoresis (6). Went and MacIver carried out research throughout the early years leading to descriptions of sickle cell-*beta* thalassaemia, less common variants of sickle cell disease, megaloblastic change from folate deficiency, the aplastic crisis of sickle cell disease, and the syndrome of sickle cell-hereditary persistence of fetal haemoglobin (6).

The arrival of Dr Paul Milner in 1963 led to expansion in laboratory studies of sickle cell disease. A visit by Professor Hermann Lehmann from the Medical Research Council (MRC) Abnormal Haemoglobin Unit in Cambridge, United Kingdom (UK) in 1965 acted as a further stimulus, as having worked on sickle cell disease in Uganda, Professor Lehmann realized that the prolonged survival of many Jamaican patients was at variance with current concepts. Following his visit, Dr Milner commenced a weekly Sickle Cell Clinic for adults and Professor Robert Gray started a clinic for children. Dr Milner came from an essentially laboratory based background and collaborated with a senior registrar in the Department of Medicine for clinical assessments, a post first occupied by Dr Knox Hagley. In August 1966, Dr Knox Hagley left the University Hospital of the West Indies (UHWI) for Government service and Dr Graham Serjeant arrived from the UK to take up the vacated post in

the Department of Medicine and was requested by Dr Milner to continue working in the weekly Sickle Cell Clinic. Over the next six months, the clinic continued to grow and Dr Milner and Dr Serjeant realized that there was a great discrepancy between the descriptions of sickle cell disease in the standard medical textbooks of the time and the patients seen in the growing Jamaican clinic.

### **The Embryo Sickle Cell Unit**

It is difficult to define the beginning of the Sickle Cell Unit since this evolved gradually but the accumulating data and research potential impressed Dr Peter Williams, secretary of the Wellcome Trust, during a Caribbean tour in early 1967. He encouraged Paul Milner and Graham Serjeant to submit a research proposal on the natural history of sickle cell disease in Jamaica which was duly funded with £17 000 over two years (1967–1969). This paid the salaries of Dr Serjeant and of Mrs Beryl Serjeant, a haematology technologist, provided an early Coulter haematology analyser for Dr Milner, a Volkswagon minibus which was converted into a mobile clinical unit, and the research and clinical costs for the expanding clinic. Dr Serjeant, as a Wellcome Research Fellow in the Department of Medicine, continued to be based in Room 3, Rippel Building, where patients increasingly came on non-clinic days. The hypothesis underlying much of this early work was that textbook descriptions of sickle cell disease were biased by experience of clinic and hospital attenders and that the disease was far more diverse in its manifestations. To reduce this perceived bias, sickle cell clinics were operated every six weeks at six country hospitals (Black River, Mandeville, Montego Bay, St Ann's Bay, Annotto Bay and Morant Bay) to make it easier for patients to attend. An impression that some manifestations of the disease might ameliorate with advancing age was supported by a study of 50 patients with SS disease then aged over 30 years who had not attended the Sickle Cell Clinic for at least 10 years, and were assumed to have died. With the mobile unit, 33 patients were traced, five had emigrated, five had died, and 23 were located and well and had failed to attend clinic because their health was now better than previously. This unexpected outcome in a genetic condition illustrated the complexity of sickle cell disease. The outreach programme continued with further funding from the Wellcome Trust (1969–1972) until a moment on a cottage doorstep at Seven Rivers, St James, in the early 1970s. On visiting the family of a severely affected patient with sickle cell- $\beta^0$  thalassaemia, she was photographed alongside her symptomless sister (Fig. 2) to illustrate the effects of severe sickle cell disease on body growth and affect but a subsequent blood test on her sister revealed that she also had sickle cell- $\beta^0$  thalassaemia. It then became clear that although the bias of symptomatic selection may have been reduced, a serious bias still persisted and proper documentation of the disease would need children to be followed from birth along with normal (AA) controls in a formal cohort study.



Fig. 2: The family in St James, Jamaica with the known patient (right) and her asymptomatic sister (left).

#### Medical Research Council Laboratories (Jamaica)

By late 1972, funding of the sickle cell programmes was undertaken by the British Medical Research Council and continued until the retirement of the Director, Professor GR Serjeant, in 1999. The Unit acquired the premises previously allocated to the MRC Epidemiological Research Unit opposite the Department of Social Sciences on the University of the West Indies (UWI), Mona Campus. Clinical services continued to be provided by staff in the weekly outpatients' clinic and increasingly in the Rippel Building, Room 3 and latterly, Room 4. The major undertaking of the MRC Laboratories (Jamaica) was to be a cohort study of sickle cell disease based on screening the babies at Victoria Jubilee Hospital (VJH). After consultation with senior staff and with full support of the midwives, screening of babies commenced on June 25, 1973, at a time when many authorities in the field stated that it was not possible to diagnose the disease at birth. However, Mrs Beryl Serjeant adapted procedures developed by colleagues in the USA and it soon became clear that accurate diagnosis was indeed possible and the laboratory screening was continued by Mrs Miriam Forbes along with a team of housewives whom she trained in the procedures. Screening continued for every day of the year including Christmas and bank holidays since it was believed that this conveyed the message of the importance of not missing babies. Every day, a staff member would visit VJH, check the samples collected by the midwives against the delivery

book and perform heel pricks on babies that had been missed. By these methods, the programme continued until December 28, 1981 with screening of 100 000 consecutive, non-operative deliveries. This programme detected 315 babies with SS disease, 201 with sickle cell-haemoglobin C (SC) disease, 34 with sickle cell- $\beta^+$  thalassaemia, and 13 with sickle cell- $\beta^0$  thalassaemia. The first 125 with an SS phenotype were each matched with two controls of the same age and gender with an AA phenotype (Fig. 3) providing 250 normal babies fol-



3A



3B



3C



3D

Figs. 3 A–D: Cohort 10. The mother in the centre has the baby with SS disease flanked by the AA controls of the same age and gender: (A) age 9 days, (B) age 9 years, (C) age 26 years with children, (D) meeting Her Majesty The Queen in 1994.

lowed with the same protocols. The sickle cell trait occurred in 10.1% and the HbC trait in 3.6% but other haemoglobin variants included four new haemoglobins subsequently named HbF Victoria Jubilee, HbF Kingston, Hb Caribbean and Hb Spanish Town (7).

The cohort study has taught us much about sickle cell disease and is a tribute to the suitability of Jamaica for long-term studies of the disease. With increasing age of the children, the evolution of haematological changes and the clinical complications have been documented and additional



specialists have made major contributions. Foremost among these was the team of ophthalmologists led by Professor Alan Bird of Moorefield's Eye Hospital in London who, in annual visits over 20 years, documented the eye changes with measurements of acuity and retinal drawings from the age of five years and fluorescein angiography from the age of six years. Dr Tom Walker of Reading in the UK (previously in the Department of Radiology at UWI) studied ultrasounds of the gallbladder, spleen and kidneys while the patients were waiting for eye examinations. Together these workers have produced unique datasets on the evolution of eye changes and development of gallstones over the period 1981–2000. Additional expertise was recruited for Doppler studies on skin ulcers, intelligence, psychology and many other aspects of the disease. Over the early years of the cohort study, the staff gradually grew to six doctors including an ophthalmologist, four nurses, five haematology laboratory staff, four computer staff, a social worker and other support staff. Computer programmes were developed including the Patient Management System, allowing all accumulated data for each patient to be immediately available for management and for research. After each visit, the database was updated and hard copies of visit data on self-adhesive paper were inserted in the patient's docket in the event of electronic failure. The clinic was now a formidable research tool with more sophisticated facilities than any other known sickle cell organization worldwide and with the cooperation of a patient database, which finally expanded to over 5500 patients, was set to make many original contributions in sickle cell disease. These contributions including sequential observations on growth and haematology and its relationship to clinical features, the prevalence and natural history of major complications, and through cooperation with the Department of Pathology, received excellent autopsy documentation on the cause of deaths. Examples of important advances in clinical management included the prevention of pneumococcal infection (8), the education of mothers in the early diagnosis of acute splenic sequestration which reduced the mortality from this complication by 90% (9), the identification of parvovirus B19 infection as the cause of the aplastic crisis (10), the day care management of the painful crisis (11), factors contributing to the lower intelligence quotient often described in SS disease (12), and the role of venous incompetence in the poor healing of chronic leg ulcers (13). Available through a dedicated sickle cell centre, the clinical services were now available five days weekly, providing better clinical care and increasing the completeness of data collection. Outreach continued with monthly clinics in Black River and Cornwall Regional Hospitals which had been operated since 1967 providing a diagnostic service, advice on optimal treatment and closer follow-up of cohort study patients who had moved to the west of the island.

A clinic building was completed in 1988 adjacent to the offices of the MRC Laboratories on the UWI Mona Campus about one kilometre from the original site at Room 3, Rippel

Building; a shuttle bus was donated by the local Dutch Embassy to bring patients to the Clinic, from a Sickle Cell Clinic bus stop, at the UHWI, which was donated by Alcan-Sproston.

Other facilities made possible by the dedicated centre on campus included a purpose built eye examination complex, a freezer room storing 80 000 sera and approximately 20 000 DNA samples at  $-80^{\circ}\text{C}$ , sophisticated computing facilities, a generator house and an archive room for storing the accumulated data.

### The Sickle Cell Trust (Jamaica)

This locally registered charity formed in 1986 began by raising funds for a diagnostic ultrasound instrument for studying gallstones and then launched an appeal for £100 000 to build a dedicated Sickle Cell Centre adjacent to the offices of the MRC Laboratories on the UWI campus. The completed centre was opened in August 1988 (Fig. 4) and pro-



Fig. 4: The original Sickle Cell Clinic Building which opened in 1988.

vided a reception office, four consulting rooms allowing up to four doctors to work simultaneously, an integral laboratory, a nurses/treatment room, and a four-bed day care centre, facilities that were later expanded to an eight-bed day care centre, and rooms for a social worker and for leg ulcer treatment.

With the expertise available, it became apparent that although the Unit's influence was increasingly recognized worldwide, many of the lessons were not reaching the local medical and general population. This was the background to the next appeal by the Sickle Cell Trust (Jamaica) to develop an Education Centre for sickle cell disease. The appeal attracted the attention of Mr Mayer Matalon, then chairman of the Jamaica Telephone company who generously donated J\$7 million for the building, furnishing and equipment. The Education Centre was built on the roof of the Sickle Cell Clinic and became operational in 1994 (Fig. 5) and administered by Ms Karlene Mason who had served the Unit for many years as a medical technologist and then counsellor and educator. With an external entrance, the Education Centre could function independently of the Sickle Cell Clinic and provided a seminar room capable of seating 80 people, the laboratory of the Jamaican Government Newborn Screening Programme, offices for the Sickle Cell Support



Fig. 5: The final Medical Research Council (MRC) complex after the addition of the Education Centre in 1994.

Club, rooms for interactive CD-ROM tutorials, a small studio for producing teaching video films and offices for research fellows.

In addition to providing physical facilities, the Sickle Cell Trust (Jamaica) also developed, printed and distributed a variety of educational materials including posters, pamphlets, booklets, slide sets, videos and DVDs. Interactive CD-ROM tutorials were developed in association with the Wellcome Trust and, most recently, an internet-based training course in sickle cell disease was developed in association with the Virtual University of Monaco ([umvm.net](http://umvm.net)). The Education Centre also allowed broader programmes of public education hosting the general public, offering illustrated lectures on the disease to school groups, and a focus for genetic counselling courses advertised throughout the Caribbean.

The most recent initiative of the Trust has been the conception and conduct of the Manchester Project for prevention of sickle cell disease, described in a later section (The Future).

### **Caribbean Organisation of Sickle Cell Associations (COSCA)**

With the increasing awareness of sickle cell disease in the Caribbean, several island territories established local Sickle Cell Associations. These tended to develop their own educational materials and to avoid unnecessary duplication as well as to provide an 'umbrella' organization which might make these associations more effective in dealing with their local Governments, the Caribbean Organisation of Sickle Cell Associations (COSCA) was launched in St Lucia on October 3, 1997, and was registered as a regional charity in 2001. Operating under the current President, Mrs Paula Calderon, of St Lucia, COSCA has organized regional genetic counselling courses, acts as a repository for educational materials and functions as a source of expert advice throughout the region.

### **Influence of the Sickle Cell Unit throughout the Caribbean and the World**

The results of the clinical research programmes have all been published in the international medical press and so are widely available. With funding from the Department for Interna-

tional Development (DFID), private and other Government sources, Unit staff has been asked to advise on the development of sickle cell services in Uganda, Congo Brazzaville, Cameroon, Brazil, Bahrain, Saudi Arabia and throughout central India where sickle cell disease is a major public health problem. Core funding continued from the British Medical Research Council, but was supplemented by support from the National Institutes of Health (NIH) for the role of argon laser in the treatment of proliferative sickle retinopathy over 10 years, and drug company support for specific therapeutic trials. Recognizing the educational potential of the facility prompted generous support from Guinness who funded outreach programmes around the Caribbean, genetic counselling courses and Guinness Sickle Cell Fellowships for suitable candidates from the UK, Nigeria and Ghana.

In addition to its role in education, the Sickle Cell Unit also developed cost-effective models of care appropriate to other societies with limited resources and it is believed that this has been achieved without compromising the quality of clinical care. The large numbers of patients and the relatively limited resources have led to alternative models of care which have been utilized in areas of sub-Saharan Africa and especially central India. Jamaica is fortunate in having good primary healthcare, relatively low rates of infectious disease and no malaria, all of which contribute to a relative amelioration of the clinical course. Furthermore, interventions developed during the cohort study, especially pneumococcal prophylaxis and parental detection of acute splenic sequestration significantly improved survival (14) and estimates of overall survival are similar, if not better, than those in the USA (15). Data from the cohort study also confirmed the benefits and importance of newborn screening for sickle cell disease, culminating in an NIH sponsored Consensus Conference advocating newborn screening for sickle cell disease (16).

Another vital ingredient was the enthusiasm and competence of the clinical and ancillary staff which grew to 28 highly dedicated and professional personnel. Residents were regularly seconded from the Department of Child Health and other research fellows were welcomed from local or international sources. A further stimulus to research was provided by 30–50 elective medical students annually from the Caribbean or internationally who assisted with research projects within the Unit's programmes.

### **The Future**

#### *Newborn Screening*

Implementation of newborn screening for sickle cell disease throughout the Caribbean is so clearly cost-effective and beneficial that it is regrettable that diagnostic services remain so poorly developed. Partly on the basis of the benefits of newborn screening demonstrated in Jamaica, this has become routine in the USA and in the UK, yet in Jamaica, which was the first country in the world to have extensive newborn screening for sickle cell disease, programmes have not been

implemented islandwide. In 2009, the Sickle Cell Unit at UWI screened approximately 15 700 deliveries at the VJH and hospitals at the University and Spanish Town or 39% of the estimated 40 000 all-island births. The Sickle Cell Trust's Manchester Project screens approximately 8500 deliveries throughout Clarendon, Manchester and St Elizabeth or 21%; these two programmes cover 60% of births, leaving 40% unscreened representing deliveries in the west, north and east of the island. With the undoubted cost-effectiveness of such screening and the effectiveness of simple clinical intervention preventing many serious, life threatening complications during follow-up of detected cases, it is difficult to understand why such cheap benefits are not implemented by local Ministries of Health. Similar criticisms apply to other areas of the English-speaking Caribbean with the notable exception of St Lucia where the Sickle Cell Association, under the able presidency of Mrs Paula Calderon, has funded the Government's newborn screening. It is understood that comprehensive screening programmes occur in Francophone Guadeloupe and Martinique.

### *Prevention*

There can be little doubt that the long-term management of sickle cell disease will depend upon prevention of as many cases as possible. With conservative estimates of populations and birth rates, it can be calculated that at least 250 000 babies with SS disease will be born each year in sub-Saharan Africa. The scale of this public health problem is such that countries will not have resources adequate to provide effective clinical care with the result that median survival is likely to be less than five years. Only by reducing the scale of this problem will the limited available resources in many developing societies begin to provide adequate programmes of clinical care. To a large extent, such prevention must rest upon population education and facilities to accurately detect the carrier states of abnormal haemoglobin genes such as HbS and HbC. Affected populations deserve the ability to determine their genotype and to understand its significance. Only then can they be empowered to make informed decisions. Models of disease control based on premarital screening have been developed in Bahrain and Saudi Arabia. In Bahrain, a trial of voluntary premarital screening halved the apparent frequency of births with SS disease (17), an effect so striking that Royal Decrees were passed in both Bahrain and Saudi Arabia in 2004 making premarital screening mandatory. All prospective partners are tested for the sickle cell gene and counselled, and families receive reports that these proposed marriages are compatible or 'not compatible'; in the latter case, the families may still proceed but they have been warned that the relationship might produce offspring with SS disease. This model may be appropriate in these Islamic societies with traditions of arranged marriages but would have limited application in most of sub-Saharan Africa. In these societies, it becomes important to know whether identification of haemoglobin genotypes associated

with counselling on genetic risk might influence decisions on the choice of partner and this is the question addressed by the Manchester Project in Jamaica.

Manchester is a parish in central Jamaica where, since 2008, genotype identification and counselling has been offered to senior school students aged 16–19 years attending 14 secondary schools in the parish. Compliance with testing has risen annually from 56% to 88% and of the 2700 students tested annually, 14% are found to be carriers of genes which could give rise to babies with sickle cell disease. To determine the outcome of this intervention, newborn screening has been established throughout the three parishes of southern central Jamaica where the tested students are most likely to deliver their children: Manchester, St Elizabeth and Clarendon. Dried blood samples from newborn babies in these parishes arrive at a central laboratory in Mandeville, the capital of Manchester, where 8500 or 98% of all deliveries are tested for haemoglobin genotype and babies with clinically significant genotypes are confirmed and incorporated into Sickle Cell Clinics currently held in Mandeville and May Pen. The effect of the genotype detection and education programme among the students must await a significant number becoming parents, and although 662 of the female school students have now become mothers, it is too early to see the results of this intervention.

### **CONCLUSIONS**

The University Hospital of the West Indies and the Sickle Cell Unit, in particular, have been fortunate to make many contributions to the better understanding of sickle cell disease. Most of these advances would not have been possible without the active cooperation and compliance of the patients who contributed greatly to our increased understanding of the disease and of course, to the suitability of the island of Jamaica for long-term clinical studies. The generally good primary healthcare, good communications and extended family structures have assisted in the long-term tracing and follow-up of patients; the relatively sophisticated diagnostic and investigative facilities have also contributed. Although the Jamaican population is primarily of West African origin, admixture from other racial groups has contributed to the variety of genetic conditions, often providing instructive interactions. These have included the variety of beta thalassaemia genes and also the beta globin haplotypes of the disease. It was in the village of Lacovia, St Elizabeth, that an extensive family pedigree with part Indian ancestry and 10 members with SS disease, characterized by unusually high levels of fetal haemoglobin, were found to have an unusual DNA structure (18). It was only when Unit staff was working in sickle cell disease with colleagues in Orissa State, India in 1985 and 1986 that the same DNA structure was found to characterize the disease in India and subsequently became known as the Asian haplotype (19). This story is yet another example of the fertile field for clinical research offered by the island laboratory of Jamaica.

## REFERENCES

- Herrick JB. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. *Arch Intern Med* 1910; **6**: 517–21.
- Savitt TL, Goldberg MF. Herrick's 1910 case report of sickle cell anemia. The rest of the story. *JAMA* 1989; **261**: 266–71.
- Washburn RE. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. *Virginia Med Semi-Monthly* 1911; **15**: 490–3.
- Mason VR. Sickle cell anemia. *JAMA* 1922; **79**: 1318–20.
- Jelliffe DB, Stuart KL, Wills VG. The sickle cell trait in Jamaica. *Blood* 1954; **9**: 144–52.
- MacIver JE, Went LN. Further observations on abnormal haemoglobins in Jamaica. *West Indian Med J* 1958; **7**: 109–22.
- Serjeant GR, Serjeant BE, Forbes M, Hayes RJ, Higgs DR, Lehmann H. Haemoglobin gene frequencies in the Jamaican population: a study of 100,000 newborns. *Br J Haematol* 1986; **64**: 253–62.
- John AB, Ramlal A, Jackson H, Maude GH, Waight-Sharma A, Serjeant GR. Prevention of pneumococcal infection in children with homozygous sickle cell disease. *Br Med J* 1984; **288**: 1567–70.
- Emond AM, Collis R, Darvill D, Higgs DR, Maude GH, Serjeant GR. Acute splenic sequestration in homozygous sickle cell disease: natural history and management. *J Pediatr* 1985; **107**: 201–6.
- Serjeant GR, Serjeant BE, Thomas P, Anderson MJ, Patou G, Pattison JR. Human parvovirus infection in homozygous sickle cell disease. *Lancet* 1993; **341**: 1237–40.
- Ware ME, Hambleton I, Ochaya I, Serjeant GR. Sickle cell painful crises in Jamaica: a day care approach to management. *Br J Haematol* 1999; **104**: 93–6.
- Knight S, Singhal A, Thomas P, Serjeant G. Factors associated with lowered intelligence in homozygous sickle cell disease. *Arch Dis Child* 1995; **73**: 316–20.
- Clare A, FitzHenley M, Harris J, Hambleton I, Serjeant GR. Chronic leg ulceration in homozygous sickle cell disease: the role of venous incompetence. *Br J Haematol* 2002; **119**: 567–71.
- Lee A, Thomas P, Cupidore L, Serjeant B, Serjeant G. Improved survival in homozygous sickle cell disease: lessons from a cohort study. *Br Med J* 1995; **311**: 160–2.
- Wierenga KJ, Hambleton IR, Lewis NA. Survival estimates for patients with homozygous sickle-cell disease in Jamaica: a clinic-based population study. *Lancet* 2001; **357**: 680–3.
- Consensus conference: Newborn screening for sickle cell disease and other hemoglobinopathies. *JAMA* 1987; **258**: 1205–9.
- Al Arrayed S. Campaign to control genetic blood diseases in Bahrain. *Community Genetics* 2005; **8**: 52–5.
- Wainscoat JS, Bell JI, Thein SL, Higgs DR, Serjeant GR, Peto TEA et al. Multiple origins of the sickle mutation: evidence for  $\beta^S$  globin gene cluster polymorphisms. *Mol Biol Med* 1983; **1**: 191–7.
- Kulozik AE, Wainscoat JS, Serjeant GR, Kar BC, Al-Awamy B, Essan GJ et al. Geographical survey of  $\beta^S$ -globin gene haplotypes: Evidence for an independent Asian origin of the sickle-cell mutation. *Am J Hum Genet* 1986; **39**: 239–44.