Sickle Cell Disease in Childhood

Standards and guidelines for clinical care

Detailed guidance
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Foreword

From the NHS Sickle & Thalassaemia Screening Programme

These standards are a milestone in acknowledging the care needs of children with sickle cell disorders.

Although sickle cell is the most common genetic disorder in England, expertise and services are concentrated in cities. Families living around the country have struggled to understand the condition and to access the care they need. Feedback from patients has shown patent dissatisfaction with the quality of services.

These standards provide a vital first step towards defining the care needed and the structures within which it can be effectively provided. They are important for both parents and health professionals in explaining what care is needed, who should provide it and how to access it.

Clearly there is a long journey from guidelines to practice on the ground. But what gives me hope is that these standards are based on genuine partnership. They have been developed with a wide range of clinical inputs as well as with the voluntary sector, professional bodies and parents of children with sickle cell disorders. They represent the best possible consensus of good practice.

The standards make a strong case for the development of managed care networks such as those already developed for cancer. They show the need for an holistic approach that recognises both clinical needs and the social and emotional impact. They demonstrate that when families are properly informed and supported, they can do much to help themselves.

Crucially, in the light of ever-present pressures on financial resources, they show that managed care is not only important in relieving suffering, but also effective in reducing the cost of specialist interventions. Many of the strategies help families to spot warning signs and take early action. This, in turn, reduces complications that are vastly more expensive for the NHS to address in the longer term.

Traditionally, sickle cell and thalassaemia have not had the recognition they deserved in terms of public understanding and services. In the last few years I have been delighted to see the investment in screening. The logical and crucial next step is investment in care. These standards, together with similarly developed standards for thalassaemia, provide the road map. I urge everyone involved – parents and professionals – to use them to give every affected child the best possible quality of life.

Most Rev and Rt Hon Dr John Sentamu, Archbishop of York
Chairman
Foreword

From the Sickle Cell Society

We are delighted to have been part of this important project which addresses both the medical and – importantly – the social impacts of sickle cell disorders. We are particularly pleased that the views of families living with the disorders have helped to shape the vision.

In recent months, a number of developments have backed up evidence that we hear from affected families about both the prevalence of the disorder and the uneven provision of care.

The newborn screening programme is now identifying some 300 affected babies a year and research from Dr Dick and colleagues demonstrates the strong need for improved care outside the major city areas. Evidence from both the UK and internationally demonstrates a clear correlation between support to families and improved health outcomes. We owe all families – wherever they live – the opportunity to access such care.

So, we know the size of the issue, we know the gaps in service provision. With the publication of these standards, we know what we need to do.

The standards provide the vital foundation for putting principles into practice. In particular, they highlight the importance of regular monitoring to spot problems early and avoid the suffering (and expense to the NHS) of dealing with complications. One such example, highlighted in the standards, is the provision of transcranial Doppler scanning throughout the country. This has a significant and proven impact in reducing stroke and is both an effective health measure and cost-effective for the NHS.

We welcome the standards and hope that we will see the necessary investment to ensure that they are put into practice. We look forward to doing everything we can to support the implementation process.

On a personal note, as a member of the writing group, I wish to commend Dr Dick and everyone involved in the project for their enthusiasm and commitment to the process. I hope that that same spirit of cooperation between partners will carry us forward to improve the quality of life of all children affected by sickle cell disorders.

Dr Asa’ah Nkohkwo, FRSH
Director, Sickle Cell Society

From the Department of Health

I welcome this important publication which sets out clear guidelines and standards for the delivery of care to children with sickle cell disease. Newborn screening is now universal in England and the document will be an invaluable resource for clinicians responsible for the follow-up of children diagnosed on this programme. It will provide a consistent approach and help ensure equity of care across the country regardless of levels of prevalence and expertise.

Minimum standards have been suggested against which the service can be audited and these will provide useful information for commissioners when developing sickle cell services for children, taking account of the pathway of care, delivered through a network with processes for continuing quality improvement.

Dr Sheila Shribman
National Clinical Director for Children, Young People and Maternity Services
Aim of the document

This document provides a series of recommendations for the organisation of care and management of complications in childhood sickle cell disease. Detailed guidance including the rationale for intervention and supporting evidence is found in section 4.

Sickle cell disease is now the most common genetic disorder in England, affecting over 1 in 2000 live births. However, the majority of cases occur in cities, where expertise and resources tend to be concentrated. 1 With the introduction of universal newborn screening for sickle cell disease in England by the NHS Sickle Cell & Thalassaemia screening programme, there will inevitably be affected infants identified in all parts of the country.

These guidelines have been written to support responsible clinicians in areas of low prevalence and to ensure that every infant has access to the same quality of care wherever they live. They are written primarily for paediatricians and haematologists working in local hospitals rather than sickle cell centres, and propose standards that can be monitored by hospital trusts and commissioning authorities. They refer where relevant to other related standards, eg the newborn screening programme (Appendix 1 and 2), National Service Framework for Children guidance2 and National Service Frameworks for chronic disease management in adults based on models from the USA. 4,5

The document is not intended to provide extensive clinical guidelines for the management of acute complications. There are many such guidelines, mainly from the USA. Some of these are tailored to the UK experience, such as Guidelines for the management of the acute painful crisis in sickle cell disease6.

A clinical network of local hospitals and sickle cell centres has been proposed. In this model, sickle cell centres will develop protocols with local units for treatment of acute complications and for referral where necessary.

This document outlines a model of care for children with sickle cell disease who have been identified through the newborn screening programme. It extends from newborns until transition – which is usually between 16 and 18 years. It will also have relevance for the care of children who may have missed out on neonatal screening before the programme was introduced, or who have come from abroad and been diagnosed after the newborn period. It is based on a consensus of clinicians with experience in the UK, Jamaica and the USA. The aims and rationale for care at various ages are described and the level of evidence given where available.

References
Methodology

These guidelines were formulated in accordance with the principles specified by the Appraisal of Guideline Research and Evaluation (AGREE collaboration, www.agreecollaboration.org). The writing group (see below for membership) began by constructing a list of headings and topics. These were divided and allocated to individual members on the basis of their interest and expertise. Where the group had no particular expertise eg orthopaedics or endocrinology, relevant clinicians were asked to contribute on those topics.

A search of Medline, Embase and the Cochrane Controlled Trials Register was carried out (see Appendix 3 for the search strategy) to ensure complete coverage of the evidence on which the recommendations are based. Relevant guidelines – eg the British Committee for Standards in Haematology, Royal College of Paediatrics in Child Health, National Institutes of Health USA and the National Service Framework for Children – were consulted. Members of the writing group brought their own expertise and knowledge of the literature. Recommendations from the National Service Framework for Children were taken into account.

Grading of recommendations

Grade type based on Agency for Health Care Policy & Research (AHCPR 1992) recommendations:

A

(levels 1a, 1b)
Requires at least one randomised trial as part of the body of literature of overall good quality and consistency addressing the specific recommendations

B

(levels 1a, 1b, III)
Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of the recommendations

C

(level IV)
Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Levels of evidence

Wherever possible, recommendations draw on published research. Although there is a wealth of clinical experience in paediatric sickle cell disease, there is a lack of prospective, randomised controlled trials to inform these guidelines. However, an evidence base does exist in two main areas: prevention of pneumococcal infection; and screening for cerebrovascular disease.

Against this background, the writing group has used a range of sources including published retrospective analysis of clinical data and non-randomised, non-controlled intervention, expert opinion and the views of patients and their families.
The initiative for this document came from the British Committee for Standards in Haematology with backing from the UK Forum on Haemoglobin Disorders, the NHS Sickle Cell & Thalassaemia screening programme, and the Sickle Cell Society.

Members were invited to join the writing group to represent areas of high and low prevalence of sickle cell disease; the disciplines of paediatrics, haematology, nursing, general practice and psychology; parents; and the voluntary sector. All the writers have extensive experience in managing sickle cell disease and work in areas of high prevalence. In addition, commentators with less direct experience were included to ensure relevance for the whole country. Two people were also members of the writing group for the standards for the clinical care of children and adults with thalassaemia in the UK to provide consistency where there was overlap in the management of the two conditions. There has been no external funding and there is no declared conflict of interest.

**Lead writer**

**Dr Moira Dick**
Consultant Community Paediatrician with interest in Haemoglobinopathies, Lambeth PCT & King’s College Hospital

**Authors**

**Dr Kofi Anie**
Consultant Clinical Psychologist, Brent Sickle Cell & Thalassaemia Centre, Central Middlesex Hospital

**Dr Phil Darbyshire**
Consultant Paediatric Haematologist, Birmingham Children’s Hospital

**Dr Jo Howard**
Consultant Haematologist, Central Middlesex Hospital

**Dr David Rees**
Senior Lecturer/Honorary Consultant in Paediatric Haematology, Guy’s King’s and St Thomas’ Medical School

**Ms Beverley Smalling**
Service Director, City and Hackney Sickle Cell & Thalassaemia Centre

**Dr Paul Telfer**
Senior Lecturer/Honorary Consultant in Haematology, St Bartholomew’s and the Royal London NHS Trust

**Dr Jenny Welch**
Consultant Paediatric Haematologist, Sheffield Children’s NHS Trust

**Commentators**

**Ms Lisa Farrer**
Chief Biomedical Scientist and Screening Coordinator for Electrophoresis, Leeds Teaching Hospitals

**Dr Helen Issler**
Consultant Paediatrician, Queen Elizabeth Hospital NHS Trust, Woolwich

**Dr Diana Jelley**
General Practitioner, North Shields

**Dr Simon Meyrick**
Consultant Paediatrician, Hereford Hospitals NHS Trust

**Dr Asa’ah Nkohkwo**
Sickle Cell Society

**Mr and Mrs Ogunremi**
Parents

**Dr Allison Streetly**
NHS Sickle Cell & Thalassaemia screening programme

The document has been circulated to a wide range of stakeholders including members of the UK Forum on Haemoglobin Disorders, members of the Sickle Cell Society, paediatricians and haematologists in proposed sickle cell centres, and other clinicians known to have an interest.

**Acknowledgments**

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**Reference**

1. Sickle cell disease in childhood

1.1 Conditions to be treated

Sickle cell disease (SCD) denotes all genotypes containing at least one sickle gene in which HbS makes up at least half the haemoglobin present. In addition to sickle cell anaemia (HbSS) there are four other compound heterozygous conditions which occur in the UK:

- **Haemoglobin SC**
- **Haemoglobin SD**
- **Haemoglobin S/β thalassaemia (β⁺, β⁺, δβ and Lepore)**
- **Haemoglobin SO**

Haemoglobin S/HPFH (Hereditary Persistence of Fetal Haemoglobin) is indistinguishable on neonatal screening from HbSS or Hb S/β-thalassaemia but does not cause clinical complications. Family studies and DNA testing will clarify the diagnosis. These children do not need to be followed up once the diagnosis has been established.

1.2 Incidence, prevalence and survival

SCD is now the most common genetic condition in England, affecting more than 1 in 2,000 live births. The birth prevalence in some urban areas may be as high as 1 in 300. It is found at a low frequency in all populations, the highest prevalence occurring in people of African and African-Caribbean origin. Cases also occur in families originating from the Middle East, India and the eastern Mediterranean.

Life expectancy has improved considerably over the last decades due to improved recognition and better management of acute episodes. Introduction of neonatal screening programmes in parts of the USA dramatically improved healthcare, and childhood mortality is now about 1-2% in some areas. Where programmes have been introduced in the UK, a similar benefit has been seen.

However, in the USA there is a marked geographic difference in mortality of young children with which greatly exceeds mortality of black children without the disease. This highlights the importance of having a robust follow-up programme and access to high-quality care wherever a child with SCD lives.

A US multicentre study in 1994 reported a median survival in sickle cell anaemia of 42 years in men and 48 years in women; and for haemoglobin SC disease, of 60 years and 68 years respectively. Survival estimates for sickle cell anaemia in Jamaica based on a clinic population suggested median survival for men of 53 years and 58.5 years for women. Life expectancy in the UK is not known, but is likely to be similar.

1.3 Pathophysiology

A single nucleotide substitution in the sixth codon of the β globin gene results in the substitution of valine for glutamic acid on the surface of the variant β-globin chain. This change allows HbS to polymerise when deoxygenated, the primary event in all sickle cell pathology.

Polymerisation is dependent on intracellular HbS concentration, the degree of haemoglobin deoxygenation, pH and the intracellular concentration of HbF. The polymer is a rope-like fibre that aligns with others to form a bundle, distorting the red cell into characteristic sickled forms.

These deformed sickle red cells can occlude the microvascular circulation producing vascular damage, organ infarcts, painful episodes and other symptoms associated with SCD.

There are two essential pathological processes: haemolysis and vaso-occlusion.

- Haemolysis results in anaemia and a functional deficiency of nitric oxide which results in vascular endothelial damage and may be responsible for complications such as pulmonary hypertension and stroke.
• Vaso-occlusion causes acute and chronic ischaemia and is responsible for acute pain and organ damage. A recent review gives a comprehensive account of the current understanding of pathophysiology in SCD².

1.4 Presentation

There is a wide range of clinical presentation and severity. In the unscreened population, infants may present with sudden death from pneumococcal sepsis due to splenic hypofunction, or acute splenic sequestration, before a diagnosis is made. Dactylitis is a common presenting symptom in infants between 9 and 18 months, but many children do not experience this and may only present after 2 years with vaso-occlusion affecting the long bones.

Painful episodes due to vaso-occlusion are the most common complication and account for the majority of hospital admissions, although SCD can affect any organ in the body. Strokes affect 5-10% of the paediatric population and, in addition, there may be MRI changes of silent stroke in up to 20% of the affected population before the age of 20 years. These children may experience cognitive problems or difficulties with psychological adjustment. Acute chest syndrome – which may be precipitated by infection, infarction or a combination of the two – is another serious cause of morbidity and mortality. Other complications include biliary disease, renal disease, osteomyelitis, avascular necrosis, eye complications, priapism and leg ulcers.

1.5 Variability

Some children with sickle cell anaemia are severely affected, while others remain symptom-free. This variability is not completely understood but is partly due to the presence or absence of secondary effector genes that participate in some of the pathological events related to vaso-occlusion. The fetal haemoglobin (HbF) level is constant throughout life (after stabilisation during infancy) and is a relatively good predictor of disease severity.

Concurrent α-thalassaemia trait is also thought to affect severity, but the evidence is conflicting as the beneficial effects of higher haemoglobin may be outweighed by increased viscosity. Consequently avascular necrosis and proliferative retinopathy occur more frequently in sickle cell patients with α-thalassaemia trait. However, stroke is less common and there seems to be no overall effect on life expectancy.

Haemoglobin SC disease

Although all the same complications of HbSS may occur in haemoglobin SC disease, the latter is often a much milder condition. In the absence of a screening programme it may not be detected until adulthood or a chance blood test. It accounts for half the number of acute episodes of pain compared to HbSS, and there is also less likelihood of splenic hypofunction.

References

2. Delivery of healthcare

SCD represents a unique challenge in the UK. An equitable and comprehensive care programme for children with these conditions must take into account the wide geographical variation in prevalence, combined with the known variability in the severity of sickle disorders. Any service planned for these disorders must deliver both an optimal level of care close to the patient’s home and access to specialist sickle cell centres. In addition, services should support parents and carers to manage the condition at home where at all possible.

As SCD becomes more common across the UK, every hospital should be able to provide basic inpatient and outpatient care for local patients. However, children with this chronic condition should also have the benefit of specialised knowledge. The development of a network of sickle cell centres seems an appropriate way to provide high-quality care across England.

2.1 Community care

To date, SCD has been managed almost exclusively by the acute sector. This has partly been due to SCD being seen as a specialised condition for which general practitioners may have little knowledge or training. In addition parents are often quite knowledgeable about their child’s condition and will know when home treatments are not working or when an emergency necessitates them taking their child straight to hospital.

This cycle needs to be broken with clear instructions for parents on when to use primary care and the acute hospital. Practical information needs to be given to the general practitioner eg dosages of medications, steady state values, and the information that has been given to parents about the condition and ways of accessing hospital care.

In areas of high prevalence there may be sickle cell and thalassaemia community centres (see www.stacuk.org) that provide an information resource, support and advice to families, training for health and other professionals as well as genetic counselling.

Local authority services for SCD are also not well developed. Patients with SCD, unless they have a chronic disability such as stroke, do not fulfil the disability criteria for acceptance by social services departments. This is despite the fact that frequent acute exacerbations disrupt normal life and may be as disabling as other chronic conditions. Similarly, education authorities do not monitor children with SCD unless the child has been found to have a learning disability and has special educational needs. There is a need to inform these professionals that overt or silent stroke can often cause cognitive impairment that leads to learning difficulties. (This occurs in about 20% of affected children and young people under 20 years). These acquired impairments may be missed in children who started their school career without any difficulties.

SCD should be considered as a chronic illness with acute exacerbations that have far-reaching effects on education, family life, social integration and the emotional well-being of the child and family.

When organising care, it will be important to take into account local community support and health provision including Child & Adolescent Mental Health Services (CAMHS), education, social services and self management as well as hospital care. Training for general practitioners, community nursing and local authority employees will be needed along with inter-agency agreement on criteria for referral to Social Services and Education for support.

Current government thinking promotes a chronic disease model for the management of conditions such as SCD. Its main components have been constructed after a literature review and evidence from a panel of experts in the USA. This model relates mainly to adults.

In the UK, community paediatricians already have extensive experience in coordinating community services and liaising with education, social services, the voluntary sector, CAMHS and the acute sector. Community paediatricians will therefore be the key people in setting up clinical networks for this group of children as
### Roles and responsibilities for community services

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Responsibilities</th>
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<tbody>
<tr>
<td><strong>NHS</strong></td>
<td></td>
</tr>
<tr>
<td>Primary Care Trust</td>
<td>Commissioning of acute and community medical services including CAMHS&lt;br&gt;Expert Patient programme&lt;br&gt;Provision of community services</td>
</tr>
<tr>
<td>GPs</td>
<td>Register details from newborn screening programme&lt;br&gt;Prescribe penicillin by 3 months&lt;br&gt;Provide primary care for common childhood illness&lt;br&gt;Be aware of signs and symptoms that need emergency hospital assessment&lt;br&gt;Prescribe analgesics in conjunction with paediatrician</td>
</tr>
<tr>
<td>Practice nurse</td>
<td>Administer conjugate pneumococcal vaccine (Prevenar) at 2, 4, 13 months (as per routine immunisation programme) + annual ‘flu&lt;br&gt;Undertake treatments as appropriate eg dressing of leg ulcers</td>
</tr>
<tr>
<td>Health visitor</td>
<td>Routine health promotion advice and screening&lt;br&gt;Targeted visits (following local guidance for child in need)&lt;br&gt;Link in with specialist nurse counsellor where available</td>
</tr>
<tr>
<td>School nurse</td>
<td>Routine health promotion advice and screening&lt;br&gt;Liaison with school staff regarding extra needs of children and awareness of symptoms and signs&lt;br&gt;Link in with specialist nurse counsellor where available</td>
</tr>
<tr>
<td>Community paediatrician</td>
<td>Liaison with local authority (social services and education) regarding needs of child&lt;br&gt;Assessment of children with developmental delay&lt;br&gt;Coordination of community services in cases of chronic disability eg stroke&lt;br&gt;Maintenance of disability register in conjunction with local authority</td>
</tr>
<tr>
<td>Specialist nurse counsellor/nurse practitioner (may be employed by acute trust)</td>
<td>Specialist support to families&lt;br&gt;Training and support of community nurses&lt;br&gt;Liaison with primary care and hospital services&lt;br&gt;Support of care in the home</td>
</tr>
<tr>
<td>Child &amp; Adolescent Mental Health Services</td>
<td>Provision of clinical psychology assessment and management&lt;br&gt;Provision of neuropsychology services</td>
</tr>
</tbody>
</table>
recommended in the National Service Framework guidance for children and young people who are ill. Such networks include:

- Comprehensive and integrated local services recognising that children are best cared for at home whenever possible
- Managed local children’s clinical networks taking into account the particular needs of the group, geography and transport arrangements

### 2.2 Sickle cell centres

The model of local and specialised centres is well established for the treatment of such conditions as cystic fibrosis, cancer and haemophilia. The value of haemoglobinopathy centres has been well documented in the USA.

Two broad categories of sickle cell centres are proposed:

- Hospitals in urban areas with a large local population of children with SCD. These should have appropriate experience, staffing and facilities
- Hospitals in areas with few local patients. These would act as a centre of expertise for the patients in the surrounding areas. They are generally large district general or teaching hospitals which accept referrals for acute and outpatient care from other hospitals or regions

In both cases, it may be necessary to refer to a tertiary centre for intensive care. In many areas informal networks and referral patterns exist. In this case, the initial aim is to formalise these arrangements and establish a network of centres across the country (see Appendix 4 for list of proposed network of centres).

### 2.2.1 Definition of sickle cell centre

Sickle cell centres should fulfil the following criteria:

- Have a designated paediatrician/paediatric haematologist/haematologist with a specific interest in paediatric haemoglobinopathy
- Have a designated paediatric haemoglobinopathy clinic (which may be part of a larger clinic)
- Provide paediatric high dependency and intensive care, or have established protocols for the referral of patients to a hospital with paediatric HDU/ICU who have experience and protocols for the management of SCD in children
- Have CPA-accredited laboratory facilities for accurate haemoglobinopathy diagnosis
- Have established links with local neonatal screening programme and sickle cell counsellors
- Have access to transcranial Doppler (TCD) scanning
- Have links with clinical psychology for specialised treatment and neuropsychometric assessment
2.2.2 Role of sickle cell centre

- Develop shared care arrangements with local hospitals
- Support and promote management at home
- Have shared protocols and facilities for the treatment of acute complications eg acute pain, acute chest syndrome, stroke, acute anaemia, acute splenic sequestration, priapism
- Provide expert in-patient care for acute complications of SCD
- Provide and organise the management of chronic complications:
  a) Monitoring and screening for neurological complications including TCD ultrasonography
  b) Monitoring regular blood transfusion therapy, including iron stores, iron chelation and secondary effects of iron overload
  c) Initiation of hydroxyurea, long-term transfusion therapy or bone marrow transplantation
- Provide a clinical psychology service
- Carry out an annual review of all children
- Maintain a list of all children to monitor outcome and quality of follow-up
- Develop links with other specialists who need to be involved eg community paediatricians, ENT, anaesthetics, orthopaedics, paediatric surgeons, dentists, neurologists, ophthalmologists
- Take part in transition plan to the adult service
- Provide training for students, doctors and nurses
- Carry out audit and research

2.3 Role of local hospital

- Have a named paediatrician to link in with designated sickle cell centre and neonatal screening lab
- Arrange initial contact with family and provide a paediatric clinic for routine outpatient management
- Promote and support management at home by parent and GP
- Manage acute pain and acute anaemia and provide initial care for other complications before transfer to the sickle cell centre according to shared guidelines and protocols
- Liaise with sickle cell centre for annual review
- Follow-up of children who fail to attend, reporting to regional unit on annual activity
- Liaise with local authorities eg Education and Social Services
- Manage transition to the adult service

2.4 Roles and responsibilities of acute care

<table>
<thead>
<tr>
<th>Acute NHS trusts</th>
<th>Network of local hospitals and sickle cell centres</th>
</tr>
</thead>
</table>
| A&E                 | Protocols for assessment and management of children who present as an emergency  
                      Protocols for transfer |
| Outpatients         | Protocols for investigations and treatment  
                      Protocol for managing non-attenders  
                      Communication with GP and HV/SN  
                      Ongoing support of family and promotion of care in the home |
| Paediatric/surgical wards | Protocols for acute management  
                             Links with local PICU  
                             Protocols for transfer |
| PICU                | Protocols for intensive care of sickle cell complications |
### 2.5 Staffing and resources required

<table>
<thead>
<tr>
<th>Staffing/resource recommendations</th>
<th>Local unit</th>
<th>Sickle cell centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designated paediatrician</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Designated paediatrician and/or haematologist providing a lead for the service</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Named deputy for each</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Middle-grade cover (SpR/staff grade) available out of hours</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Named paediatric nurse</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Specialist nurse in SCD</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Access to clinical psychology</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Clinical psychologist with an interest in sickle cell disease and/or neuropsychologist</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Appropriate laboratory support (transfusion, haemoglobinopathy testing and other)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Access to MRI, CT and PICU</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Administration for support of clinics and maintaining local lists of children attending</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Transcranial Doppler (TCD) service</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Links with bone marrow transplant service</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Access to Paediatric Neurology</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Access to Paediatric Endocrinology</td>
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<td>✓</td>
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<tr>
<td>Access to Paediatric Ophthalmology</td>
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<td>✓</td>
</tr>
<tr>
<td>Access to Paediatric Orthopaedics</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Links with adult service for SCD</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
2.6 Shared care

Shared care arrangements will vary according to local needs and situations. It may be appropriate in some areas for the specialist to visit the local unit and in others for children and their families to travel.

2.7 Provision of PICU/HDU

Many of the proposed sickle cell centres currently do not have provision for PICU/HDU or MRI scanning. Arrangements will need to be made to develop shared protocols with regional paediatric and PICU units for the assessment and management of acute neurological complications, for exchange transfusions in an acutely unwell child, and for children needing ventilatory support.

2.8 Provision of transcranial Doppler ultrasonography

Annual imaging using TCD ultrasound scanning of children with SCD from the age of 3 years has been recommended in recent guidelines for the management of stroke in children. This is based on the findings of a randomised controlled trial on the benefits of transfusion in children with raised cerebral blood-flow velocities (see page 37). The majority of the proposed sickle cell centres do not have access to TCD scanning for children (although many will have vascular laboratories for investigation of adults with cerebrovascular disease), and most children with SCD in the UK have not yet had TCD scans. The development of accessible TCD services is vital, and sickle cell centres will need to develop this service for their network.

References


3. Standards and summary of recommendations

3.1 Audit standards

These proposed standards are based on current evidence-based practice, accepted good practice and knowledge of current resources.

3.1.1 Penicillin prophylaxis

i) 90% of infants should have been offered and prescribed Penicillin V (or alternative) by 3 months. 99% of infants should have been offered and prescribed Penicillin V (or alternative) by 6 months.

ii) Any parental refusal should be documented.

3.1.2 Pneumococcal immunisation

i) 95% of infants should have completed the primary Prevenar (conjugate pneumococcal vaccination) course by 15 months.

ii) 95% should be given Pneumovax (polysaccharide antigen) at 2 years of age (24-27 months) and 5-yearly thereafter.

3.1.3 TCD scanning

90% of sickle cell centres should have the capability of offering annual TCDs to children with SCD from the age of 3 years by 2008, and 99% should have this capability by 2010.

3.1.4 Failsafe arrangements

The sickle cell centres in conjunction with local paediatric units should have continuing responsibility for children with SCD identified on the newborn screening programme, and should maintain a list.

By 2008, 95% of sickle cell centres and local hospitals should have robust follow-up arrangements to identify and follow up any child who does not attend their hospital appointments. They should also have the capability to track children who have moved out of the area in order to make appropriate handover arrangements. 99% of sickle cell centres and local hospitals should have this capability by 2010.

3.2 Summary of recommendations

These are based on current evidence-based practice and accepted good practice. Letter in brackets refers to the grading of the recommendation (see page 7)

3.2.1 Organisation of care

- There should be a network of care consisting of primary care, the local hospital, sickle cell centre and paediatric intensive care (C)
- Parents should be put in touch with local and national voluntary organisations and sickle cell & thalassaemia centres (C)
- There should be a named paediatrician responsible for follow-up in the local hospital (C)
- There should be a named paediatrician and/or paediatric haematologist in the sickle cell centre (C)
- General practitioners and community nurses should be kept informed on a regular basis (C)
- Parents should be encouraged to acquire knowledge about their child’s condition and should be informed about initiatives such as the Expert Patient Programme (C)
• There should be a named consultant community paediatrician to coordinate the community needs of the child and to liaise with CAMHS, local authority services and the voluntary sector as needed (C)

• Local authority services (Education and Social Services) should be aware of the specific needs of children with SCD and their families (C)

• CAMHS should be aware of the specific emotional and learning needs of children with SCD and their families (C)

3.2.2 Identification of disease

i) Informing parents

• All parents/carers of an infant who has been diagnosed via the newborn screening programme should be given the result by the time the child has reached 6 weeks. This should be done in a culturally sensitive manner, respecting their dignity and individuality. An interpreter should be provided where necessary (C)

• The result should be communicated to the family GP and health visitor as soon as it is received by the specialist nurse counsellor (SNC), or named health professional (C)

• A referral to the local paediatric unit or sickle cell centre should be made by the SNC or named health professional. This will request diagnostic testing and confirmation that penicillin and conjugate pneumococcal immunisation have been prescribed (C)

• Appropriate written information about the condition should be provided for carers (C)

• Parents should be given the opportunity for genetic counselling, especially if they have not taken up this option before their child was born (C)

ii) Confirmation of diagnosis

• The diagnosis should be confirmed at the first sickle cell clinic visit in a laboratory accredited to carry out haemoglobinopathy testing (C)

• Confirmatory results should be sent to the newborn screening laboratories for quality control (C)

• DNA analysis should be requested in cases where the diagnosis is unclear (C)

• Penicillin prophylaxis should be started while waiting for clarification of diagnosis,

3.2.3 Outpatient care

i) Organisation of follow-up

• The infant diagnosed on the newborn screening programme should be seen in a sickle cell clinic by 3 months of age (C)

• At the first visit the family should meet with a doctor and/or nurse experienced in the management of SCD who can give them accurate information and advice (C)

• There should be regular communication with the primary care team and community nursing service (C)

• There should be a policy for monitoring attendance in clinic and for following up those families who fail to attend. This should include documentation of children who have moved to another area (C)

• There should be ongoing support for the family and promotion of management of straightforward illness including uncomplicated pain at home (C)

• There should be access to specialist assessment and treatment when required (C)

• Every child should be reviewed by the sickle cell centre at least once a year (C)

ii) Prevention of infection

• Twice-daily penicillin prophylaxis or alternative should be prescribed from 3 months of age and continued throughout childhood (A)

• Local negotiation should be carried out between hospitals, GPs and pharmacies to ensure a reasonable length of prescription in order to encourage compliance (C)

• Reasons that parents have for not giving their children penicillin should be explored and addressed as fully as possible (C)

• Immunisation against pneumococcal infection should include Prevenar and Pneumovax according to national schedules (C)
A course of hepatitis immunisation should be offered to the non-immune child (C)
• Annual influenza immunisation should be offered (C)
• Malaria prophylaxis should be strongly recommended and current guidance sought for the area of travel (C)

iii) Education
• Every outpatient visit should provide an opportunity for ongoing education of child and family (C)
• There should be a systematic approach to education which will vary at different ages (C)

iv) Transition to adult care
• There should be a hospital transition policy in place and preparation and planning should start at an early age, eg at age 13-14 years (C)
• A detailed review should be carried out at 15-16 years to include knowledge and understanding about SCD, management, concerns about healthcare in an adult setting, and readiness to transfer (C)
• A transition or adolescent clinic should be available to allow the adolescent to meet the adult sickle cell team and for a formal review and handover to take place (C)
• Adult and paediatric protocols for managing complications, in particular painful episodes, should correspond as much as possible (C)

3.2.4 Ongoing issues and chronic complications

i) Management of pain at home
• Parents/carers and older children should be given clear guidance on how to assess and manage pain at home. This should include the type and dose of analgesia to be used for different levels of pain intensity, and also guidance on when to seek medical advice (C)
• Parents/carers should be informed about non-pharmacological therapies for pain such as massage. Children should be encouraged to use psychological coping strategies, including distraction techniques such as games, computers, and television (C)
• Children should be encouraged to identify and avoid factors that trigger painful crises such as exposure to cold weather, excessive physical activity, and dehydration (C)

ii) Nutrition and growth
• Heights and weights should be measured at each visit and plotted on appropriate growth centile charts (C)
• A referral to a dietitian should be made to consider extra caloric input if the child is hospitalised for frequent or long periods (C)
• Zinc supplementation should be considered if growth is retarded (C)
• Children with delayed growth should be reassured if there is evidence of delayed skeletal maturation. However they should be referred to a paediatric endocrinologist if there are no physical signs of puberty at 14 years in a girl and 14.5 years in a boy (C)

iii) Nocturnal enuresis
• If nocturnal enuresis is present over the age of 6 years, this should be documented and parents should be given information and advice on treatment (C)
• If the history is suggestive of obstructive apnoea and snoring, this should be documented, overnight oxygen saturations should be measured, and referral made for an ENT opinion (C)
• Desmopressin therapy should be considered in children who do not respond to routine advice and management (C)
• The child should be referred for specialist management (eg an enuresis clinic) if there is no response to basic measures after the age of 7 years (C)

iv) Liver disease
• Annual steady-state liver function tests should be carried out (C)
• Abdominal pain should be investigated with an ultrasound of liver and biliary tree (C)
• Elective cholecystectomy should be carried out in symptomatic biliary disease (C)
v) Avascular necrosis
- Where there is persistent hip or shoulder pain, an MRI scan should be carried out (C)
- The radiological stage of avascular necrosis should be documented (C)
- A referral to an orthopaedic surgeon with an interest in SCD should be undertaken if pain persists or if avascular necrosis is stage III or more (C)

vi) Leg ulcers
- Debridement of the ulcer and antibiotic therapy should be started if infection is present (C)
- Adequate pain relief should be prescribed (C)
- Compression bandaging and physiotherapy should be arranged to improve ankle mobility (C)
- Oral zinc sulphate should be considered in children with persistent leg ulcers (C)

vii) Cerebrovascular disease
- Annual TCD scans should be performed on all children with SCD from 3 years. The scans should be performed and categorised as ‘high risk’, ‘conditional’, ‘standard risk’ or ‘inadequate’, according to the criteria of Adams et al. (A)

- High-risk and conditional TCD scans should be repeated within 2 months. For those remaining at high risk, the risks and benefits of starting regular blood transfusions should be fully discussed with the parents (C)
- Appropriate imaging studies to assess the extent of cerebrovascular disease should also be arranged if there is evidence of cerebral vessel narrowing on TCD, learning difficulties, atypical symptoms such as unusual behaviour during acute pain, frequent headaches, fits, or other unexplained neurological, psychiatric or psychological symptoms (C)
- Blood pressure should be measured and recorded annually (C)
- Overnight oxygen saturation monitoring should be recorded if there is a history of snoring, nocturnal enuresis after the age of 6 and low steady-state oxygen saturations on air (<95%) (C)

- Children should have access to a neuropsychologist to assess cognitive function, learning and behavioural difficulties (C)
- Transfusion therapy should be continued throughout childhood for the secondary prevention of stroke (B)

viii) Kidney disease
- Any child with a urinary tract infection should be treated and then investigated according to RCPCH guidelines (C)
- Macroscopic haematuria should be fully investigated according to local protocols (C)
- Blood pressure, urea, creatinine and electrolytes should be measured on a yearly basis and renal investigations initiated if hypertension is present or there are raised creatinine and urea levels (C)

ix) Lung disease
- Children with either two or more episodes of acute chest syndrome in the last 2 years, or one episode requiring ventilatory support, should be offered hydroxyurea (A)

- Oxygen saturations in air should be recorded on an annual basis using pulse oximetry when the patient is well and seen in outpatients. If saturations are <95%, overnight oxygen saturation monitoring should be performed (C)

- If the mean overnight oxygen saturation is <95%, the child should be investigated for cerebrovascular disease and obstructive sleep apnoea. Formal pulmonary function tests and echocardiography should also be arranged (C)

- If pulmonary function tests suggest chronic sickle lung, the child should be monitored with regular pulmonary function tests. Overnight pulse oximetry and high-resolution CT scan of the lungs should be considered. Treatment with home oxygen, hydroxyurea or regular blood transfusions should be considered in cases of deterioration (C)

- Echocardiography to assess pulmonary hypertension should be arranged if there is evidence of chronic sickle lung, chronic unexplained hypoxia (oxygen saturations <95%) or other symptoms/signs suggestive of pulmonary hypertension (C)
• A child with significant pulmonary hypertension should be referred to a respiratory physician with an interest in SCD (C)

x) Priapism
• Adolescent boys and their parents should receive information about priapism and know to seek treatment early (C)
• An enquiry about priapism should be included as part of the outpatient consultation for pubertal boys (C)
• For minor events, complete bladder emptying before sleep, pain relief, and warm baths should be recommended (C)
• Oral etilefrine should be considered in cases of stuttering priapism (C)

xi) Eye complications
• Children and their carers should be made aware of this potential complication (C)
• Any visual symptoms should be reported immediately and the child referred urgently for an ophthalmologic opinion (C)

Reference

3.2.5 Peri-operative care
• A clear management plan agreed by all involved health professionals should be written in the patient’s notes before surgery (C)
• Sickle cell centres should have guidelines to share with local hospitals on pre-operative transfusion in patients with SCD. The transfusion laboratory should have an extended red cell phenotype and recent antibody screen performed in case blood transfusion becomes necessary before or after the operation (C)
• Sickle cell centres should have guidelines on the procedure for surgery to share with local hospitals, including the use of fluids, oxygen therapy and antibiotics and post-operative care (C)

3.2.6 Specific treatments
i) Hydroxyurea
• Hydroxyurea should be considered in patients who have recurrent episodes of acute pain (more than three admissions in the previous 12 months, or are very symptomatic in the community) or who have had two or more episodes of acute sickle chest syndrome (A)
• The decision to start hydroxyurea should be made with the specialist centre, although the local hospital will have a role in monitoring blood counts and side effects. The specialist centre should have a written protocol which is shared with the local hospital. This should include information about dose regimen, frequency of blood test monitoring, management of myelosuppression and contraindications for use of hydroxyurea (C)
• The patient and/or their parents should be given a patient’s information sheet and the use of hydroxyurea should be discussed with them on at least two separate occasions. Current knowledge about side effects, including cytopenias and the possible risk of leukaemia or other malignancies, should be discussed. This discussion should be documented in the patient’s notes (C)

ii) Use of blood transfusion
• At diagnosis or first clinic attendance, all patients should have an extended red cell phenotype performed (C)
• All blood transfused should be fully Rh and Kell compatible. If alloantibodies are identified, further transfusions should be negative for corresponding antigen. CMV-negative blood should be used in all CMV-negative children (C)
• Red cells for transfusion to patients with SCD should be sickle-test negative and less than 7 days old if possible (C)
• Exchange transfusion should be used in the management of acute chest syndrome and acute cerebrovascular events (C)
• Long-term transfusion regimens should be used after a cerebrovascular event to prevent recurrence and considered if cerebral vessel velocities are >200cm/sec on TCD ultrasonography according to the STOP criteria (A)

• Iron chelation should be started in all children on regular blood transfusions according to standard protocols (C)

• Immunisation against hepatitis A and B should be offered to all those on long-term transfusion programmes (C)

• Children receiving regular monthly blood transfusion should have a specific annual review (C)

iii) Bone marrow transplantation

• All patients or families with a child with SCD should be offered the opportunity to discuss bone marrow transplantation as a treatment option. This should not depend upon the family having an available donor at the time (C)

• Bone marrow transplant should be performed in centres experienced in transplants for haemoglobinopathies. Transplants from any donor other than HLA identical family members should only be undertaken after careful consideration and extensive counselling. This should be done by a team experienced in such work. Each sickle cell centre should have clear referral links to such a transplant centre (C)

3.2.7 Psychological management

• All children and their families should have access to a clinical psychology service (C)

• Cognitive behavioural therapy should be considered in addition to standard management in children experiencing frequent pain episodes (C)

• A detailed neuropsychological assessment should be carried out in all children who have had a stroke, and repeated annually (C)

• Regular developmental assessments, neuropsychological screening or monitoring of school attainments in standard assessment tests (SATs) should be carried out on a regular basis to assess for possible silent stroke (C)

3.2.8 Management of acute complications

i) General considerations

• Parents and carers should be made aware of the symptoms and signs associated with severe and life-threatening complications and know where to take their child if these occur (C)

• A care pathway should be in place in the local unit for assessment of the child in casualty, and for transfer to a designated ward if admission is necessary (C)

• Protocols should be available to cover the management of all acute sickle cell complications. These should include worsening anaemia, febrile episodes, acute pain, acute neurological complications, acute chest syndrome, and priapism (C)

• A designated consultant paediatrician and/or paediatric haematologist should be responsible for the management of all children in the local hospital and sickle cell centre, with a named deputy. Junior doctors involved in assessment and treatment of acute sickle admissions should be made aware of acute complications and the local treatment protocols through regular education/training sessions (C)

• Communication between the local centre and expert opinion in the sickle cell centre should be possible 24 hrs/day for discussion of difficult cases and possible transfer of the patient. The means of communication should be made explicit (C)

• Communication and transfer to a specified paediatric ITU will be readily available according to an agreed procedure (C)

ii) Acute pain in hospital

• Pain assessment should include the use of a validated pain assessment tool that is developmentally age-appropriate (C)

• There should be a policy in the accident and emergency department regarding triage, pain assessment and length of acceptable time from arrival to administration of analgesia (C)

• Children should be managed according to a standard local analgesia protocol. This should be developed by collaboration between the local hospital and sickle cell centre and should include input from a
pain control team, paediatric pharmacist and a paediatric anaesthetist designated for this purpose. The protocol should provide clear guidance on drugs, route of administration, dosage, and monitoring for analgesic effect and side effects (C)

- Medical and nursing staff involved in treating children for acute pain should have regular training in pain management and in the application of the local analgesic protocol (C)

- Children should be monitored regularly for effectiveness of analgesia and for signs of adverse effects (eg opiate-induced narcosis and hypoventilation, acute sickle chest syndrome etc) (C)

- The psychological needs of the child and family regarding coping with pain and avoiding sickle crises should be addressed during the admission (C)

iii) The febrile child in hospital

- A protocol for antibiotic treatment of suspected or proven acute infection should be prepared by the sickle cell centre in collaboration with the local clinic and with a designated paediatric microbiologist (C)

- Cultures of blood, urine and other possible sites of infection should be done routinely on any child presenting with acute pain and fever (C)

- Malaria films should be sent if there is any suspicion of malaria or if a patient has returned from a malarious region in the previous year (C)

iv) Acute anaemia

- There should be a protocol for recognition and investigation of children presenting with pallor with or without pain in hospital (C)

- Parents should be aware of the need to bring the child to hospital if they detect pallor and/or an enlarging spleen, and should be aware of the local procedure for emergency assessment (C)

- Medical staff assessing children with acute sickle cell complications should be made aware of these complications through regular training/education sessions (C)

- A local protocol for management, including indications for transfusion, should be available (C)

- Children with two or more episodes of acute splenic sequestration should be considered for splenectomy (C)

v) Acute chest symptoms

- Parents, patients and carers should be made aware of this complication. They should know how to recognise the symptoms, and should be familiar with the local procedure for emergency assessment (C)

- Children with chest pain, cough, respiratory distress, new chest signs or worsening hypoxia, either presenting in casualty or during the course of a hospital admission, should be carefully assessed and monitored and have an urgent chest X-ray (C)

- Incentive spirometry should be used in children with acute chest and back pain (A)

- Oxygen saturation monitoring should be used routinely, particularly in those children with respiratory signs and symptoms, acute pain affecting the trunk and girdle regions, and those treated with opiates (C)

- A local protocol should be prepared for management of the acute chest syndrome. This should include clear guidance on analgesia, observations, oxygen delivery, antibiotics, iv fluids, bronchodilators, physiotherapy, incentive spirometry, and nursing observations. The indications for top-up transfusion, exchange transfusion and ventilatory support should be specified. There should also be a local protocol covering the practical issues of carrying out an exchange transfusion (C)

- Medical and nursing staff should be made aware of this complication. Regular training and education sessions should advise on how to recognise it and provide updates on the local policy for management (C)

- An agreement should be reached with the local paediatric intensive care unit about indications for transfer, means of communication, and the protocol for treatment in the intensive care unit (C)
vi) Acute neurological complications

- Each sickle cell centre should have access to a designated paediatric neurologist who can assess and advise on acute neurological complications (C)

- Each sickle cell centre should have a clear plan for access to a neurosurgical unit for managing children and adolescents with cerebral haemorrhage and subarachnoid bleeds (C)

- RCP guidelines on the management of acute stroke should be followed and specific guidelines for acute stroke in SCD should be prepared by the sickle cell centre for the local unit (C)

- Each sickle cell centre should have access to neuroimaging facilities including paediatric CT, MRI/MRA, and EEG (C)

vii) Fulminant priapism

- A policy for the management of severe fulminant priapism should be drawn up with the sickle cell centre and the urology team (C)

- Adolescent males and their carers should be aware of the policy and know how to access emergency treatment (C)

- Aspiration and irrigation with etilefrine or ephedrine should be the initial treatment of choice (C)

Reference


Suggested audit topics based on these guidelines can be found in Appendix 5.
4. Detailed guidance

4.1 Identification of affected infants

All children born in England are to be offered screening as part of the newborn bloodspot screening programme from April 2005. The diagnosis will be made by designated screening laboratories. Standards have been set for laboratories, as well as for the initial contact with the parent and registration in paediatric follow-up (Appendices 1 and 2).

The aim of the programme is to reduce early mortality and morbidity in SCD.

Objectives include:

- To ensure effective and acceptable follow-up, care and support for affected infants and their carers
- To offer and start parental education and child treatment in a timely manner
- To minimise any possible adverse effects of screening – including failure to follow-up screen-positive infants; inaccurate or inadequate information; unnecessary investigation and follow-up; and inappropriate disclosure of information

4.1.1 Initial communication by newborn screening programme

Bloodspots from newborn screening are sent to designated laboratories and the results of all infants with SCD are sent as a matter of urgency (eg by fax or email) to the nominated coordinating centre and named individual. The centre confirms receipt.

The parents of every affected child are informed by personal contact and by the GP, in writing, by 6 weeks after birth. Every area has a named health professional who may be a paediatrician or a nurse. In some high prevalence areas the nurse will be a specialist in SCD.

4.1.2 Informing parents

Although women and their partners should have been offered antenatal screening and counselling, and should have been fully informed of their risk, this may not always be the case and it may still come as a shock to learn the diagnosis. Early communication by the local named paediatrician or nurse in a culturally sensitive way is important to provide accurate information and to ensure that the infant has timely access to prophylactic treatment.

The primary care team need to know the diagnosis as soon as possible to provide ongoing medical and emotional support and to begin penicillin treatment and immunisation with conjugate pneumococcal vaccination (see 4.2: Outpatient care, page 27). Arrangements for outpatient follow-up should be made so that the infant is seen by 3 months.

Recommendations

1 All parents/carers of an infant diagnosed via the newborn screening programme should be given the result by the time their child has reached 6 weeks. This should be done in a culturally sensitive manner, respecting their dignity and individuality. An interpreter should be provided where necessary (C)

2 The result should be communicated to the family GP and health visitor as soon as it is received by the named health professional (C)

3 A referral to the local paediatric unit should be made for diagnostic testing and confirmation that penicillin and conjugate pneumococcal immunisation have been started (C)

4 Appropriate written information about the condition should be provided for the carers (C)

5 Parents should be given the opportunity for genetic counselling, especially if this offer has not been taken up before their child was born (C)

References


Literature available for parents and carers:


4.2 Outpatient care

4.2.1 Organisation of follow-up

The majority of a child’s care will take place at home, in outpatients, or in a GP surgery. Many children require hospital admission at some time but only a minority will require frequent admissions. As SCD is a lifelong condition it is important to engage the family early, not only to establish the diagnosis and start treatment but also to provide advice, education and support.

The US Department of Health and Human Services clinical practice guideline outlines the importance of early entry into care for pneumococcal prophylaxis and the parents’ ability to recognise and manage signs and symptoms of illness. In a Jamaican cohort study, parents were able to accurately define spleen size in cases of acute splenic sequestration, a potentially fatal complication if presentation is late.

It is generally accepted that penicillin prophylaxis should start by 3 months of age as the level of fetal haemoglobin starts to decline and the risk of splenic hypofunction increases. The Cooperative Study of Sickle Cell Disease, initiated in the USA in 1978 showed a significant number of acute events including bacterial meningitis and sepsis before the age of 6 months. Although there is no evidence for splenic hypofunction in HbS and HbS/B+ Thalassaemia, the Cooperative Study showed a significant incidence of pneumococcal infections in HbSC in the first 2 years of life, indicating that these children should receive the same treatment and education as children with HbSS. In order to achieve this, children should be registered for follow-up in the sickle cell clinic by 3 months.

The value of specific follow-up programmes for SCD, particularly after identification by neonatal screening, has been confirmed over the past 20 years. A US review of 10 years of newborn screening for SCD described changing trends in survival, resulting not only from the introduction of penicillin but also from the integration of children into routine follow-up and care. Improved survival has also been shown in a cohort study in Jamaica. Enlistment in follow-up programmes following neonatal screening has been found to reduce morbidity and mortality to about 1%. More recently, the benefit of regular TCD scans to

4.1.3 Confirmation of diagnosis

Newly diagnosed infants should be registered in the sickle cell centre by 3 months so that the diagnosis can be confirmed and other family members offered screening tests if required.

Samples for diagnostic testing should be sent to a laboratory that is CPA-accredited and that takes part in quality control schemes for haemoglobin testing. There should be organised links with the neonatal screening laboratory to confirm cases identified on the newborn screening programme.

In the absence of the father’s haemoglobin phenotype it may be difficult to get a definitive diagnosis, as HbSS, HbS/β-Thalassaemia and HbS/HPFH all have an FS phenotype on screening. If there is any doubt, DNA analysis should be requested from a specialist unit. Treatment should be instituted for all children until the diagnosis is clarified. There is no evidence that infants with HbS/HPFH need ongoing care and prophylactic treatment, but this diagnosis should not be confused with a child with HbSS and a persisting high level of Hbf, which is a relatively common finding.

Recommendations

1. The diagnosis should be confirmed at the first sickle cell clinic visit in a laboratory accredited to carry out haemoglobinopathy testing (C)
2. Confirmatory results should be sent to the newborn screening laboratories for quality control (C)
3. DNA analysis should be requested in cases where the diagnosis is unclear (C)
4. Penicillin prophylaxis should be started while waiting for clarification of diagnosis, if this is delayed (C)
identify those children at risk of cerebrovascular disease (see 4.3.7, page 37) and prevent stroke has been shown in a randomised controlled trial.

The aims of regular attendance in a local paediatric clinic and annual review by a sickle cell centre should be: to encourage adherence to treatment – particularly prophylaxis and immunisation programmes; to continue education; to offer screening tests; and to monitor general health, nutrition and growth. Treatment options can be offered depending on the nature of complications, and transition to the adult clinic can be organised in a timely fashion. A policy for frequency of attendance at the sickle cell clinic can be helpful eg a minimum of 3-monthly during the first 2 years; 6-monthly until the age of 5 years; and annually thereafter.

Every child with SCD, regardless of where they live, should be offered annual access to a full range of specialist professionals and services to ensure that their care is optimised. Some children may also need to be seen at the sickle cell centre before their annual review is due, in order to discuss particular management issues.

It is important that all families feel supported and have access to specialist advice and treatment. A qualitative study of pain management showed that where families were supported and able to cope with their child’s condition, the young adult was more likely to be able to manage their condition.

There should be regular communication with primary care and, where appropriate, the wider multidisciplinary team; and the parent-held book (provided to all newborns) should be completed on every visit. Arrangements for follow-up and shared care should be made explicit. A policy for tracking children who do not attend should be in place.

Recommendations
1. The infant diagnosed on the newborn screening programme should be seen in a sickle cell clinic by 3 months of age (C)

2. At the first visit the family should meet with a doctor and/or nurse experienced in the management of SCD who can give them accurate information and advice (C)

3. There should be regular communication with the primary care team and community nursing service (C)

4. There should be a policy for monitoring attendance in clinic and for following up those families who fail to attend, including documentation of children who have moved to another area (C)

5. There should be ongoing support for the family and promotion of management of straightforward illness, including uncomplicated pain at home (C)

6. There should be access to specialist assessment and treatment when required (C)

7. Every child should be offered a review by the sickle cell centre at least once a year (C)

References


4.2.2 The consultation

The following gives a guide to what should be included in each consultation. The list is not exclusive.

The history should include:

- Current symptoms and a review of painful episodes, illnesses, A & E attendances and hospital admissions since the last consultation
- A systematic enquiry about symptoms eg abdominal pain, pica, priapism, headaches, snoring, other neurological symptoms suggestive of ischaemia
- Adherence to penicillin prophylaxis
- How pain and fever is managed at home
- Regularity of school attendance and reasons for absence
- Outcome of developmental screening tests, school progress and achievement in national tests (eg SATs, GCSEs)
- Travel plans

The examination should include:

- Height and weight measurements that are plotted on a centile chart
- Assessment of puberty (Tanner staging)
- A general physical examination that should take particular note of any pallor, jaundice, spleen size, presence of heart murmur
- Blood pressure

At the first consultation, investigations should include:

- Full blood count
- Haemoglobin electrophoresis
- Reticulocyte count
- Blood group and extended red cell phenotype

As G6PD deficiency is common in the same ethnic groups and also induces haemolysis, it is advisable to test for G6PD at the first newborn visit when the degree of reticulocytosis is unlikely to produce falsely elevated results.

At subsequent consultations

The reason for blood and urine tests and other screening tests in well children is to provide a baseline should the child become unwell, and to screen for conditions that may benefit from treatment. Blood tests should generally be performed annually unless there is clinical concern. Steady-state oxygen saturations should be recorded.

TCD scans should be carried out annually from age 3 years.

4.2.3 Prevention of infection

A major aim of neonatal screening and follow up care is to reduce the morbidity and mortality from preventable disease by antibiotic prophylaxis and immunisations. Splenic hypofunction resulting from splenic infarction, usually from the first 6 months of life, means that children are at a greatly increased risk of infection by organisms expressing polysaccharide antigen such as pneumococcus and Haemophilus influenzae.

Children with SCD are more likely than the general population to be transfused for complications such as acute splenic sequestration or aplastic crisis; some 5-10% may be enrolled on a chronic transfusion programme at some time in their life. Protection against hepatitis B should be arranged before exposure is likely to occur. Many families travel to parts of the world where malaria and meningococcus are endemic, and they should receive appropriate advice and prophylaxis. Malaria is likely to be serious due to splenic hypofunction and families should be aware that having SCD does not make a person immune to malaria.

Adherence may be a problem: published reports show about 70% compliance with treatment. Failure to administer penicillin may be due to parental health beliefs and practicalities of renewing prescriptions. A synthesis of qualitative studies shows a widespread resistance in general to taking medication for any condition over prolonged periods.

Penicillin prophylaxis

In a randomised controlled trial it was shown that penicillin was effective in reducing the mortality from pneumococcal sepsis. Published guidelines recommend that penicillin prophylaxis is lifelong. As compliance is likely to decline and the incidence of pneumococcal infection in the community reduces significantly after the age
of 5 years, the emphasis should be on excellent adherence in early childhood. Penicillin V should be offered to all children according to the following dosage schedule: 62.5mg po bd <1yr, 125mg po bd 1-5yr, 250mg po bd >5yr. Erythromycin is a suitable alternative if penicillin allergy is documented.

**Pneumococcal immunisation**

Guidelines on the immunisation of the immunocompromised child recommend immunisation with conjugate pneumococcal vaccine (Prevenar), 5-yearly polysaccharide vaccine (Pneumovax) from age 2 years, and annual influenza vaccinations in children with SCD. It is planned that Prevenar becomes part of the routine primary immunisation course for all children in 2006/7.

The current schedule (2005) is as follows:

Prevenar (heptavalent conjugate pneumococcal vaccine licensed for use in infants) should be given according to the following schedule:

**Infants aged 2-6 months:** three doses, each of 0.5ml, the first dose usually given at 2 months of age and with an interval of at least 1 month between doses. A fourth dose is recommended in the second year of life.

**Previously unvaccinated older infants and children:** Infants aged 7-11 months: two doses, each of 0.5ml, with an interval of at least 1 month between doses. A third dose is recommended in the second year of life.

**Children aged 12-23 months:** two doses, each of 0.5ml, with an interval of at least 2 months between doses.

**Children aged 24 months to 5 years:** one single dose.

The need for a booster dose after these immunisation schedules has not been established.

This will change for the primary course as follows:

Prevenar: 3 doses to be given at 2, 4 and 13 months

If Prevenar is not given during the first year, two doses should be given 2 months apart in the second year

Pneumovax (23 valent polysaccharide pneumococcal vaccine) should be given in addition at 2 years (and 5-yearly thereafter) at least 2 months after Prevenar.

**Proposed vaccine schedule (universal and sickle-specific)**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP/Hib/IPV + Prevenar</td>
<td>2 months</td>
</tr>
<tr>
<td>DTaP/Hib/IPV polio + MenC</td>
<td>3 months</td>
</tr>
<tr>
<td>DTaP/Hib/IPV + MenC + Prevenar</td>
<td>4 months</td>
</tr>
<tr>
<td>Hep B + Hib/Men C</td>
<td>12 months</td>
</tr>
<tr>
<td>MMR + Prevenar + Hep B</td>
<td>13 months</td>
</tr>
<tr>
<td>Hep B</td>
<td>18 months</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>2 years</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>7 years</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>12 years</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>17 years</td>
</tr>
<tr>
<td>Influenza</td>
<td>Annually from 6 months of age</td>
</tr>
</tbody>
</table>

DTaP/Hib/IPV is a single vaccine that protects against diphtheria, tetanus, pertussis, *Haemophilus influenzae* and polio.

Hib/MenC is a combined vaccine that protects against *Haemophilus influenzae* and meningitis C.

**Travel requirements**

When travelling abroad to areas that are endemic for meningococcus, children should be offered MengiVac A+C in addition to other recommended travel vaccinations and malaria prophylaxis.

**Recommendations**

1. **Twice-daily penicillin prophylaxis or alternative should be prescribed from 3 months of age and continued throughout childhood (A)**

2. **Local negotiation should be carried out between hospital, GPs and pharmacies to ensure a reasonable length of prescription to encourage compliance (C)**

3. **Reasons that parents have for not giving their children penicillin should be explored and addressed as fully as possible (C)**
4 Immunisation against pneumococcal infection should include Prevenar and Pneumovax, according to national schedules (C)

5 A course of hepatitis immunisation should be offered in the non-immune child (C)

6 Annual influenza immunisation should be offered (C)

7 Malaria prophylaxis should be strongly recommended and current guidance sought for the area of travel (C)

References


4.2.4 Education

The following topics should be emphasised at every clinic visit or contact with the team. The aim is to educate parents (and then the children themselves) to manage uncomplicated problems at home. In addition they should be taught to recognise the onset of serious complications so that the child is brought promptly for hospital treatment. Where possible, this information should be backed up by written material in the first language of the parents and interpreters should be available. The following list is not exclusive:

- A simple understanding of the condition
- Importance of penicillin
- Importance of staying up-to-date with all vaccinations

- Management of pain at home
- Need to seek early advice for fevers, respiratory symptoms or other signs of infection, and how to access advice and admission if necessary

- Recognition of unusual pallor and need to seek early treatment
- Need to seek early medical advice if weakness (without pain), tingling, or loss of speech are observed

- Detection of an enlarged spleen by palpation
- Recognition of dactylitis and other painful crises
- When to consult the GP
- When to come to hospital in an emergency
- Need for reporting any visual symptoms
- Need to report any developmental concerns or falling-off in school achievement

- General advice regarding keeping warm and avoiding sudden changes in temperature, care when swimming, maintaining a good fluid intake

- Information that should be shared with child’s school
- The need for any planned surgery to be managed jointly with the surgeon, anaesthetist and the SCD team
- Travel advice
• Genetic counselling, contraception
• Avoidance of smoking and alcohol

Recommendations

1. Every outpatient visit should provide an opportunity for ongoing education of child and family (C)
2. There should be a systematic approach to education which will vary at different ages (C)

4.2.5 The annual review

This should include assessment of progress in general and a review of the patient’s and family’s knowledge of the condition by an experienced doctor, usually the consultant and a clinical nurse specialist or nurse counsellor. If possible, a clinical psychologist should be available at the same visit.

• Review of information provided by local unit – to include any investigations taken, treatment given
• Clinical review
  – Number of hospital admissions
  – Number and severity of crises (include days off school)
  – Other complications eg splenic sequestration, aplastic crisis, priapism, gallstones, chest syndrome, stroke
  – Nocturnal enuresis >6 years
  – Assessment of child development
• Review of infection prevention
  – Penicillin V dosage and compliance
  – Immunisation record
• Clinical measurements – undertaken at visit or results of investigations since last visit reviewed
  – Clinical examination – heart, lungs, liver, spleen
  – Weight and height (plotted on centile charts)
  – Assessment of puberty
  – Blood pressure
  – Oxygen saturation
  – Urinalysis

• Consideration and discussion of other treatments eg hydroxyurea, bone marrow transplantation (see pages 22, 23)

4.2.6 Transition to adult service

Transition is ‘the purposeful planned movement of adolescents and young adults with chronic physical and medical conditions from child-centred to adult-oriented health care systems’.

The importance of transitional care has been highlighted in the Children’s National Service Framework Hospital Standards, Improving the transition of young children with long term conditions to adult health services and the intercollegiate report, Bridging the gaps: health care for adolescents. This includes a requirement for children and adult services to take the needs of this group of patients into consideration when planning and developing services.

The 2004 National Service Framework for Children emphasises the importance of transition and states that within 10 years, ideally ‘Transition to adult services for young people is planned and coordinated around the needs of each young person to maximise health outcomes, their life chance opportunities and their ability to live independently.’

There is a need to involve the GP and community services early in the process, as they may be expected to take on a wider role as children leave the holistic care of paediatric outpatients.

In paediatric care, services place very few medical management expectations on the adolescent (these being placed instead on their parents), and clinicians are generally knowledgeable about the patient’s condition. In contrast, adult healthcare services may know less about patients and/or how their condition affects them, but generally have higher expectations for medical self-management. In addition, adolescents, by definition, are having to cope with numerous changes as they develop their individual identity and deal with personal priorities of school, work, friends, family, social relationships, and independent living.

Perhaps the biggest fear for adolescents is how their painful episodes are going to be
managed in hospital on an adult ward. There may be significantly lower supervision and direct nursing care on the adult ward and a reasonable expectation that the adolescent will take a more active role in managing painful episodes. There may be fewer visits from doctors and less structured activity including school-work supervision. In addition the medical staff will initially be unfamiliar with the individual, and the ‘adult’ analgesic regimen may differ from the paediatric one.

Research indicates that adolescents with SCD have concerns, opinions and expectations about their future health care and medical management. They need guidance, support and information about available services to help meet daily challenges. Adolescents with SCD may have problems of adjustment during a transition phase; and it is important to identify factors that would guide appropriate interventions.

Arrangements need to be flexible, as children reach maturity at different ages and puberty in general is delayed. Hospital policy may demand that all children are admitted to adult wards at the age of 16 years, even when they are emotionally and sexually immature. The following recommendations are based on experience from existing transition clinics in sickle cell centres.

Recommendations

1. There should be a hospital transition policy in place and preparation and planning should start at an early age, eg at age 13-14 years (C)

2. A detailed review should be carried out at 15-16 years to include knowledge and understanding about SCD, management, concerns about healthcare in an adult setting, and readiness to transfer (C)

3. A transition or adolescent clinic should be available to allow the adolescent to meet the adult sickle cell team and for a formal review and handover to take place (C)

4. Adult and paediatric protocols for managing complications, in particular painful episodes, should correspond as much as possible (C)

References


3. Improving the transition of young children with long-term conditions to adult health services, 2006 DH gateway ref 5914 product code 271588 www.dh.gov.uk/publications


4.3 Management of ongoing issues and chronic complications

4.3.1 Management of pain at home

Quite commonly, children experience pain at home. This is usually mild to moderate and it will not be necessary to bring the child to hospital. Frequent pain may lead to other problems, including negative mood, and considerable loss of schooling.

It is important for older children, parents/carers and family members to know how to manage pain at home with appropriate analgesia for the level of intensity. In addition, coping strategies have to be examined since these have been shown to predict both pain experience and the utilisation of health services.

Paracetamol and ibuprofen are the analgesics of choice in mild-to-moderate pain. Codeine phosphate can be added for more severe pain but it should be recognised that at least 20% will not respond due to the lack of the enzyme to convert it to morphine. If there is no response to these, the child should be assessed in hospital. An individual care plan should be available for all children in the A&E department (or children’s ward if there is a direct admission policy). It is usual to advise an increase in fluid intake if the child is unwell, as dehydration will tend to prolong the painful episode.

Recommendations

1. Parents/carers and older children should be given clear guidance on how to assess and manage pain at home, including the type and dose of analgesia to be used for the level of intensity and when to seek medical advice (C)

2. Parents/carers should be informed about non-pharmacological therapies for pain such as massage and children should be encouraged to use psychological coping strategies such as distraction techniques e.g. games, computers, and television (C)

3. Children should be encouraged to identify and avoid factors that trigger painful crises such as exposure to cold weather, excessive physical activity, and dehydration (C)

References


4.3.2 Nutrition and growth

Impaired growth, poor nutritional status and delayed skeletal and sexual maturation are common in children with SCD.

In HbSS, growth retardation may become apparent after 6 months of age – possibly due to decreased absorption of nutrients and/or an increase in metabolic rate. Poor appetite is frequently reported, and anorexia associated with febrile or painful episodes is common.

Studies of body composition show a significantly lower fat mass in prepubertal children and lower fat-free mass in all children, with muscle wasting and low protein stores. There is some evidence that growth can be accelerated by providing extra calories via naso-gastric feeding.

There is little evidence of specific nutrient deficits, although a randomised control trial showed some improvement in height and weight after supplementation with zinc sulphate. Another controlled trial showed a reduction in infections and hospital admissions in those taking zinc supplements.

As a hypochromic microcytic blood picture may be caused by an associated α-thalassaemia trait, iron supplementation should be given only if iron deficiency is documented. There is no evidence that folic acid supplementation is beneficial, although this remains controversial.

Vitamin D deficiency is very prevalent in non-white children of all ages in the UK and there has been a resurgence of rickets. Advice should be given regarding vitamin supplementation, an adequate calcium intake and exposure to sunlight. The Consensus Development for the Supplementation of Vitamin D in Childhood and Adolescence recommends 400 IU vitamin D daily in the first year of life, regardless of manner of feeding, and 200 IU to the age of 50 years.
Some clinicians recommend the use of ethnically appropriate growth charts, but not specific sickle cell charts. Puberty may be delayed by about 6 months in haemoglobin SCD and by 2-3 years in HbSS. Delayed skeletal maturation during adolescence allows for a longer growth period in the long bones. This results in normal adult height, and hence children and their parents can usually be reassured. Hormonal treatment may be indicated in children with physiological delay if they are very concerned by their short stature. An endocrinology opinion should be sought if there are no physical signs of puberty in a girl at 14 years and a boy at 14.5 years. It should also be recognised that children on long-term transfusion programmes with significant iron overload may develop pituitary +/- primary gonadal deficiencies.

Recommendations

1. Heights and weights should be measured at each visit and plotted on appropriate growth centile charts (C)
2. A referral to a dietitian should be made to consider extra calorific input if the child is hospitalised for frequent or long periods (C)
3. Zinc supplementation should be considered if growth is retarded (B)
4. Children with delayed growth should be reassured if there is evidence of delayed skeletal maturation. However they should be referred to a paediatric endocrinologist if there are no physical signs of puberty at 14 years in a girl and 14.5 years in a boy (C)

References


4.3.3 Nocturnal enuresis

Nocturnal enuresis is common in all children, and approximately 15% of children aged 5 years and 3% of 15 year olds still wet the bed. There is an increased rate of nocturnal enuresis in SCD, particularly boys with HbSS; but, as in the normal population, most will resolve spontaneously. The reason for this is not entirely clear. Children pass large quantities of dilute urine and have nocturia, but this should not necessarily lead to incontinence. Overnight urinary volumes greater than maximum functional bladder capacity have been posed as a possible cause. Parents report that their children are heavy sleepers. It has been shown that children with adenoidal hypertrophy and obstructive apnoea are more likely to have nocturnal enuresis and it is possible that hypoxaemia plays a role in the aetiology of nocturnal enuresis.
On the whole, sickle cell children do not respond to behavioural management techniques such as star charts or mattress alarms but can be ‘trained’ by intermittent alarms and parental waking to achieve continence. Many children respond to oral or nasal desmopressin, and this is a useful adjunct, particularly for school trips.

**Recommendations**

1. Nocturnal enuresis if present over the age of 6 years should be documented and parents given information and advice on treatment (C)

2. Snoring and obstructive apnoea should be documented and overnight oxygen saturations measured if the history is suggestive of obstructive apnoea, and a referral made for ENT opinion (C)

3. Desmopressin therapy should be considered in those children not responding to routine advice and management (C)

4. The child should be referred for specialist management eg an enuresis clinic if there is no response to basic measures after the age of 7 years (C)

**References**


**4.3.4 Liver disease**

Gallstones occur in over 50% of children over the age of 10 years in the UK. They are usually asymptomatic and may not be the cause of intermittent abdominal pain, which is relatively common. There is no evidence to recommend cholecystectomy in asymptomatic cases, but cholecystectomy is advised in symptomatic biliary disease.

**Recommendations**

1. Annual steady-state liver function tests should be carried out (C)

2. Abdominal pain should be investigated with an ultrasound of liver and biliary tree (C)

3. Elective cholecystectomy should be carried out in symptomatic biliary disease (C)

**Reference**


**4.3.5 Avascular necrosis of the femoral and humeral head**

This may occur in all genotypes, and children with high HbF levels are not protected. The shoulder joint is more likely to be affected in older age groups. Although weight-bearing makes femoral head necrosis more likely to cause severe joint destruction, healing with minimal destruction may be the outcome if it occurs before closure of the femoral epiphysis.

X-ray changes will not be apparent until the repair process has changed the density of the bone. Hence MRI scanning is the investigation of choice in an persistent painful hip or shoulder. It is usual to use some form of radiological staging to evaluate the development and progression of the disease. Initial treatment should be conservative, with analgesia, partial weight-bearing on crutches, and physiotherapy support.

**Recommendations**

1. An MRI scan should be carried out where there is persistent acute pain in the hip or shoulder (C)

2. The radiological stage of avascular necrosis should be documented (C)

3. A referral to an orthopaedic surgeon with an interest in SCD should be undertaken if pain persists at stage III or more (C)

**Reference**

4.3.6 Leg ulcers

These are relatively uncommon in children in the UK. Nearly all ulcers develop in the ankle region near the malleolus, and often exist bilaterally. They may be painless or extremely painful. The pathogenesis of this condition is uncertain but is likely to result from poor microvascular bloodflow of abnormal red cells combined with reduced oxygen delivery.

Low serum zinc levels have been reported in non-sickle patients with venous leg ulcers. However, low serum zinc levels are found in all patients with SCD and do not correlate specifically with leg ulcers. A controlled study of a small number of patients taking oral zinc sulphate did however accelerate healing of leg ulcers1.

There has been a randomised double blind controlled trial using granulocyte-macrophage colony stimulating factor (GM-CSF) in non-sickle patients with chronic venous leg ulcers with acceleration of healing2. Another study showed good response using topical GM-CSF in a small number of sickle patients.3 Best practice is not clear in this group, and neither regular transfusion therapy nor hydroxyurea therapy seem to influence outcome.

In the first instance ulcers should be treated with frequent dressing, support bandages and antibiotics if infected. Physiotherapy to increase ankle mobility and venous return is also likely to be helpful.

Recommendations

1 Debridement of the ulcer and antibiotic therapy should be started if infection is present (C)
2 Adequate pain relief should be prescribed (C)
3 Compression bandaging and physiotherapy should be arranged to improve ankle mobility (C)
4 Oral zinc sulphate should be considered in children with persistent leg ulcers (B)

References


4.3.7 Cerebrovascular disease

In the multicentre sickle cell cooperative study in the USA, the overall incidence of stroke in sickle cell anaemia (HbSS) was 0.6/100 patient years. The highest incidence was between 2 and 5 years (1.02/100 patient years) and by the age of 20, about 11% of people with sickle cell anaemia have had a clinically evident stroke1. In the absence of primary screening and prophylaxis, there is no reason to expect rates to differ in the UK.

In children, the cerebral ischaemic damage is often in the territory of supply of the internal carotid/middle cerebral artery. However, damage in a watershed distribution between the anterior and middle cerebral artery, or middle and posterior cerebral artery, are also commonly observed. Stroke is associated with cerebrovascular stenotic lesions commonly in the distal internal carotid, and proximal portions of the middle cerebral and anterior cerebral arteries. The high bloodflow velocities through these stenotic segments can be detected using TCD ultrasound scanning.

A large prospective follow-up study showed that a high-risk group for stroke can be identified by time-averaged mean velocities in the ICA/MCA/ACA segments >200cm/sec. The risk is also increased to a lesser extent in those with conditional velocities (170-200cm/sec) and in those with absent or low signal. This randomised, controlled trial showed that a first stroke could be prevented by regular blood transfusions in children with sickle cell anaemia and abnormal TCD scans.

The recent UK guidelines for diagnosis and management of stroke in childhood has incorporated the conclusions from this and other studies, and recommends annual screening for stroke in children with SCD from the age of 3 years.
Another important indicator of risk for stroke is a history of transient ischaemic attacks. Other reported risk factors – such as low baseline haemoglobin, high baseline leukocyte count, low overnight oxygen saturation, acute chest syndrome in the previous 2 weeks, frequent episodes of acute chest syndrome, and high systolic blood pressure – are too insensitive to be of any value in evaluating a child, although high blood pressure obviously requires appropriate investigation and management. Stroke is more prevalent in HbSS and HbS/β thalassaemia compared to HbSC and HbS/β+thalassaemia, although there is limited information regarding HbS/βthalassaemia.

Haemorrhagic stroke is relatively rare in childhood, becoming more common in the third decade. Identified risk factors include low haemoglobin and high white cell count. Intracerebral aneurysms are more common in SCD, and can be multiple. The pathogenesis is unclear. There are no established or proven ways of screening for increased risk of haemorrhagic stroke.

About 17% of children with sickle cell anaemia have silent infarcts on MRI scan that are not associated with overt neurological episodes or symptoms. These are relatively small white-matter lesions, often in the anterior watershed distribution. They are associated with mild cognitive impairment, which may be picked up by neurocognitive screening tests. TCD screening in these patients shows normal results in 75% of cases; and there is, as yet, no evidence that strokes can be prevented by blood transfusion or other intervention. The relative hazard for overt stroke in a patient with a silent infarct is approximately 14 times those with a normal MRI. (This compares to 18 times normal in a patient with a high-risk TCD). Chronic transfusion has been established as effective secondary stroke prevention, reducing the risk of recurrent stroke from 50-75% to about 13%. The aim of the transfusion regimen is to maintain haemoglobin 5 below 30%. Some patients may be able to reduce the intensity of transfusions after 3 years to maintain haemoglobin 5 at 50%.

The second stroke prevention trial in sickle cell anaemia in the USA recommends that transfusion therapy should be continued throughout childhood. This is because a significant number of children reverted to the high-risk range of TCD velocities, or developed overt stroke after discontinuation. As iron overload is a serious consideration in long-term transfusion therapy, clinical decisions will need to be reached on a case-by-case basis.

See page 52 for the management of acute stroke and other neurological complications.

Recommendations

1. Annual TCD scans should be performed on all children with SCD from the age of 3 years. The scans should be performed and categorised as ‘high risk’, ‘conditional’, ‘standard risk’ and ‘inadequate’ assessed according to the criteria of Adams et al (A)

2. ‘High risk’ and ‘conditional’ TCD scans should be repeated within 2 months. For those remaining at high risk, the risks and benefits of starting regular blood transfusions should be fully discussed with the parents (C)

3. Appropriate imaging studies to assess the extent of cerebrovascular disease should also be arranged if there is evidence of cerebral vessel narrowing on TCD, learning difficulties, atypical symptoms such as unusual behaviour during acute pain, frequent headaches, fits, or other unexplained neurological, psychiatric or psychological symptoms (C)

4. Blood pressure should be measured and recorded annually (C)

5. Overnight oxygen saturation monitoring should be recorded if there is a history of snoring, nocturnal enuresis after the age of 6 and low steady-state oxygen saturations on air (<95%) (C)

6. Children should have access to a neuropsychologist to assess cognitive function, learning and behavioural difficulties (C)

7. Transfusion therapy should be continued throughout childhood for the secondary prevention of stroke (B)
References


4.3.8 Kidney disease

Renal complications are relatively common in SCD, particularly with increasing age. Renal failure primarily due to SCD is rare in childhood, but other paediatric complications include urinary tract infections, haematuria, microscopic albuminuria and renal papillary necrosis. There is little good information on the frequency of these problems in childhood or whether screening for renal disease in childhood, such as by microscopic albuminuria, leads to intervention that can prevent problems in later life.

Recommendations

1 Any child with a urinary tract infection should be treated and then investigated according to RCPCH guidelines (C)

2 Macroscopic haematuria should be fully investigated according to local protocols (C)

3 Blood pressure, urea, creatinine and electrolytes should be measured on a yearly basis and renal investigations initiated if hypertension is present or if there are raised creatinine and urea levels (C)

Reference


4.3.9 Lung disease

Acute chest syndrome is a well-characterised complication of SCD in childhood. It is a potentially fatal complication, and there is good evidence that recurrent episodes can be prevented by hydroxyurea.

Chronic lung complications are increasingly recognised, particularly in adults. Two main chronic problems are recognised: chronic sickle lung, with a restrictive lung picture; and pulmonary hypertension. Both are predominantly a problem in adulthood, but with increasing recognition in older children and adolescents.

Anecdotal evidence suggests that in chronic sickle lung, deterioration can be prevented by hydroxyurea or regular blood transfusions. It is therefore potentially important to detect early development of these problems in children. Low blood-oxygen saturations, as assessed by overnight oxygen by pulse oximetry, have been linked to both cerebrovascular disease and frequent episodes of acute pain. Referral to a respiratory physician with an interest in SCD should be made if there is significant pulmonary hypertension with a TR (tricuspid regurgitation) jet velocity >2.9m/s as measured by echocardiography.
Recommendations

1. Children with either two or more episodes of acute chest syndrome in the last 2 years, or one episode requiring ventilatory support, should be offered hydroxyurea (A).

2. Oxygen saturations in air should be recorded on an annual basis using pulse oximetry when the patient is well and seen in outpatients. If saturations are <95%, overnight oxygen saturation monitoring should be performed (C).

3. If the mean overnight oxygen saturation is <95%, the child should be investigated for cerebrovascular disease and obstructive sleep apnoea (see management of acute neurological complications section page 52). Formal pulmonary function tests and echocardiography should also be arranged (C).

4. If pulmonary function tests suggest chronic sickle lung, the child should be monitored with regular pulmonary function tests and overnight pulse oximetry and high-resolution CT scan of the lungs should be considered. Treatment with home oxygen, hydroxyurea or regular blood transfusions should be considered in cases of deterioration (C).

5. Echocardiography to assess pulmonary hypertension should be arranged if there is evidence of chronic sickle lung, chronic unexplained hypoxia (oxygen saturations <95%) or other symptoms/signs suggestive of pulmonary hypertension (C).

6. A child with significant pulmonary hypertension should be referred to a respiratory physician with an interest in SCD. (C)

References


4.3.10 Priapism (see also management of fulminant priapism, page 53).

Priapism mainly affects adolescents and adults, and may go unreported. Bicorporal priapism occurs in 3-5% of pre-pubertal boys and has a better prognosis for normal erectile function than tricorporal priapism in post-pubertal boys. Events may be classified as stuttering (occurring for less than 3 hours’ duration but several times a week), minor (isolated or infrequent episodes of less than 3 hours’ duration), or major (events usually lasting more than 3 hours – see section on acute management). Major episodes are often preceded by bouts of stuttering priapism.

In minor episodes bladder emptying, exercise such as jogging, warm baths and analgesia may help abort an attack. Oral etilefrine may reduce the frequency of stuttering priapism and, in a prolonged episode, aspiration and irrigation of the corpora cavernosa with epinephrine or etilefrine is now the treatment of choice. Children and their carers should be advised to seek treatment early and should attend hospital as an emergency if priapism persists for more than 2 hours.

Recommendations

1. Adolescent boys and their parents should receive information about priapism and know to seek treatment early (C).

2. An enquiry about priapism should be included as part of the outpatient consultation for pubertal boys (C).

3. For minor events, complete bladder emptying before sleep, pain relief, and warm baths should be recommended (C).

4. Oral etilefrine should be considered in cases of stuttering priapism (C).

References


4.3.11 Eye complications

Sickle cell vaso-occlusive events can affect every vascular bed in the eye and may have serious and permanent visual consequences. Detectable retinal disease is very rare in childhood, being found most commonly between the ages of 15 and 30 years. Patients with HbSC and HbS/βthal are more likely than those with HbSS to have serious ocular problems.

The clinical manifestations are grouped according to whether there is neovascularisation or not. In non-neovascular or ‘non-proliferative’ cases, there are rarely any visual consequences. In contrast, revascularisation and proliferation may proceed to vitreous haemorrhage and retinal detachment. However, there is a high rate of spontaneous regression or non-progression, and indications for treatment are not clear. Given the uncertainty about the natural history of this complication, there is no evidence to support routine ophthalmologic screening of children. Children and their carers should report any change in vision and be referred for an ophthalmologic opinion as a matter of urgency.

Recommendations

1. Children and their carers should be made aware of this potential complication (C)

2. Any visual symptoms should be reported immediately and the child referred urgently for an ophthalmologic opinion (C)

References


4.4 Routine surgery and peri-operative care

As well as needing operative procedures for sickle cell complications such as acute splenic sequestration or gallstones, children may need routine operations for adenoidal hypertrophy, serous otitis media, orchidopexy, dental extractions and other complications that occur in childhood. There is no consensus amongst anaesthetists and haematologists as to which children need pre-operative transfusion, and some units are very much more conservative in their approach than others.

Peri-operative management plan

All patients with SCD, even if not previously severe, are at increased risk of sickle complications at time of surgery. Certain patients are at greater risk of peri-operative complications:

- Severe sickle-related problems such as acute chest syndrome, cerebrovascular disease and frequent painful episodes
- Severe obstructive sleep apnoea

The peri-operative management of patients with SCD requires good communication between surgeons, anaesthetists, haematologists, paediatricians and nursing staff. A clear management plan should be written in the notes prior to surgery.

Pre-operative transfusion

The optimal pre-operative transfusion policy in SCD is not clear. There is only one randomised controlled trial, which showed that a conservative transfusion regimen which raised haemoglobin to 10g/dl was as effective in preventing peri-operative complications as an aggressive exchange regimen which reduced HbS to <30%.

Transfusion may not be necessary at all for many procedures, including cholecystectomy and adenotonsillectomy. A randomised trial is currently being initiated by the National Blood Service in conjunction with the MRC Clinical Studies Unit. This is comparing those who receive no transfusion with those who receive additive or exchange transfusion.

Recommendations

1. A clear management plan agreed by all involved health professionals should be written in the patient’s notes before surgery (C)
2. Sickle cell centres should have guidelines on pre-operative transfusion in patients with SCD to share with local hospitals. The transfusion lab should have a red cell phenotype and recent antibody screen performed in case blood transfusion becomes necessary before or after the operation (C)
3. Sickle cell centres should have guidelines on the procedure for surgery to share with local hospitals, including the use of fluids, oxygen therapy and antibiotics and post-operative care (C)

References

4.5 Specific treatments

4.5.1 Hydroxyurea

Hydroxyurea promotes fetal haemoglobin synthesis, improves red cell hydration, decreases neutrophil count, modifies red cell-endothelial cell interactions and acts as a nitric oxide donor.

There have been two randomised controlled trials looking at efficacy of hydroxyurea in SCD. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) showed a reduction in frequency of painful episodes, incidence of chest syndrome and transfusion requirement without serious short-term side effects. A paediatric study in Belgium showed similar beneficial results. Long-term data from the MSH study, has shown a reduction in mortality in the hydroxyurea group.

There are a number of side effects, of which myelosuppression is the most common in the short term. In conditions already predisposed to leukaemia (eg polycythaemia rubra vera), there is an increase in the incidence of leukaemia in patients who received hydroxyurea treatment. There is no evidence to date from its use in SCD to suggest that children on hydroxyurea are more at risk. Teratogenic risk is also not known, but sexually active girls taking hydroxyurea should be advised to use contraception.

Hydroxyurea is of benefit to both children and adults with moderate to severe SCD. There are still some areas which need clarification: the optimal dose; impact on long-term organ function; and risk of malignancy. For these reasons, its use should be monitored with collection of data about long-term outcomes.

Recommendations

1. Hydroxyurea should be considered in patients who have recurrent episodes of acute pain (more than three admissions in the previous 12 months, or are very symptomatic in the community) or who have had two or more episodes of acute sickle chest syndrome (A)

2. The decision to start hydroxyurea should be made by the specialist centre, although the local hospital will have a role in monitoring blood counts and side effects. The specialist centre should have a written protocol which is shared with the local hospital. This should include information about dose regimen, frequency of blood test monitoring, management of myelosuppression and contraindications for use of hydroxyurea (C)

3. The patient and/or their parents should be given a patients’ information sheet and the use of hydroxyurea should be discussed with them on at least two separate occasions. Current knowledge about side effects, including cytopenias and the possible risk of leukaemia or other malignancies, should be discussed. This discussion should be documented in the patient’s notes (C)

References


4.5.2 Use of transfusion therapy

(see also sections on lung, cerebrovascular disease and peri-operative management)

Transfusion is an essential and life-saving therapy for some acute complications of SCD and has been shown to reduce the risk of chronic progressive organ damage in the case of ischaemic stroke.1,2

There may be a beneficial effect in preventing other forms of organ damage, but studies are currently lacking. Transfusion should not be undertaken without careful consideration of the benefits and risks. Informed consent from the parents, or child where appropriate, should always be obtained prior to transfusion.

There is an incidence of about 18% of alloimmunisation following blood transfusion in the sickle population, and two thirds of antibodies described are in the Rh or Kell
systems. This is in part because the blood-donor population and sickle-patient population are from different ethnic origins. The risk of alloimmunisation can be reduced by transfusing only if absolutely necessary and using blood that is fully Rh and Kell typed.

There is an incidence of delayed haemolytic transfusion reactions in SCD of between 4% and 22%, which is significantly higher than in other patients. These can mimic sickle cell crises, and the clinician should have a high index of suspicion for investigating for the development of antibodies when crises develop in the post-transfusion period. Once an alloantibody has been identified, antigen-negative blood should be given. Hyperhaemolysis has also been described post-transfusion without the development of antibodies. This may be due to bystander haemolysis, and one study has shown a benefit of high-dose steroids and intravenous immunoglobulin.

Viscosity of blood-containing sickled cells increases with increasing haemoglobin, so it is important to balance target haemoglobin levels with haemoglobin S concentrations. With this in mind, the target of a top-up transfusion for the treatment of acute anaemia is to the steady-state haemoglobin level. In monthly top-up transfusions (eg for the management of stroke where the haemoglobin S is being maintained <30%), the target haemoglobin is between 12 and 13g/dl. In partial-exchange transfusions, the aim is to reduce the haemoglobin S to less than 30%, whilst keeping the haemoglobin between 10-12g/dl.

As children may be candidates for bone marrow transplantation, CMV-negative blood should be used in all CMV-negative children.

Simple top-up or additive transfusion may be indicated if there has been an acute fall in haemoglobin, usually to below 5g/dl. The haemoglobin should be raised to the patient’s normal steady-state haemoglobin.

Indications:
- Acute splenic sequestration
- Aplastic crisis
- Prior to surgery
- Acute chest syndrome (may need to be converted into exchange)

Partial-exchange transfusion is indicated when it is necessary to reduce the percentage of haemoglobin S quickly in acute life-threatening complications.

Indications:
- Severe cases of acute chest syndrome
- Acute stroke
- Multi-organ failure
- Urgent preparation for major surgery

Regular simple top-up blood transfusions, usually on a monthly basis, maintain haemoglobin S <30% and haemoglobin 12-13g/dl to prevent ongoing organ damage. However, there is only anecdotal evidence of benefit in the treatment of avascular necrosis and leg ulcers. Hydroxyurea would be the preferred option for treatment of recurrent painful episodes.

Indication:
- Secondary stroke prevention
- Primary prevention of stroke in children with high-risk TCD velocities

Recommendations
1. At diagnosis or first clinic attendance, all patients should have an extended red cell phenotype performed (C)
2. All blood transfused should be fully Rh and Kell compatible. If alloantibodies are identified, further transfusions should be negative for corresponding antigen. CMV-negative blood should be used in all CMV-negative children (C)
3. Red cells for transfusion to patients with SCD should be sickle test negative and less than 7 days old if possible (C)
4. Exchange transfusion should be used in the management of acute chest syndrome and acute cerebrovascular events (C)
5. Long-term transfusion regimens should be used after a cerebrovascular event to prevent recurrence and considered if cerebral vessel velocities are >200cm/sec on TCD ultrasonography, according to the STOP criteria (A)
Iron chelation should be started in all children on regular blood transfusions according to standard protocols (C)

Immunisation against hepatitis A and B should be offered to all those on long-term transfusion programmes (C)

Children receiving regular monthly blood transfusion should have a specific annual review (C)

References

4.5.3 Bone marrow transplantation
Stem-cell transplantation is the only treatment for SCD which is potentially curative. Published experience describes a 92-94% survival rate and a 75-84% disease-free survival rate. 1-3 There is no recurrence of clinical vaso-occlusive events in patients with stable engraftment, but 10% of patients experience rejection or recurrent SCD. The majority of patients have an excellent quality of life after bone marrow transplantation (BMT).

There are, however, significant risks associated with BMT. The most common early complications are acute graft-versus-host disease (GVHD) and neurological events, including intracerebral haemorrhage and seizures. Chronic GVHD is the most common cause of late mortality and morbidity, with an incidence of 5% in the UK. Other late complications include gonadal dysfunction and an increased risk of malignancy.

Unlike β-thalassaemia major, where the clinical course is fairly predictable, there is a large variation of severity in SCD and in view of this and the high risk of mortality and morbidity from the procedure, BMT is not appropriate in every patient.

The British Paediatric Haematology Forum suggested criteria for selection. 4,5

Acceptance
• <17 years with HLA-identical sibling and informed consent
• One or more of these SCD-related complications:
  – CNS disease
  – Recurrent acute chest syndrome
  – Stage I/II chronic sickle lung disease
  – Recurrent, severe, debilitating pain (>3 hospital admissions/year in 3-4 years)
• Problems relating to future care

Exclusions
• Donor with a major haemoglobinopathy
• One or more of the following:
  – Karnofsky performance <70%
  – Portal fibrosis (moderate or severe)
  – Renal failure (GFR <30%)
  – Major intellectual impairment
  – Stage III or IV chronic sickle lung disease
  – Cardiomyopathy
  – HIV infection
Since the publication of trials using hydroxyurea, some of the recommendations have been modified, as recurrent pain and chest disease are probably now best treated initially with hydroxyurea, with BMT reserved for those patients who do not respond to hydroxyurea. The exclusions, however, are still relevant.

Recommendations

1. All patients or families with a child with SCD should be offered the opportunity to discuss BMT as a treatment option. This should not depend upon the family having an available donor at the time (C)

2. BMT should be performed in centres experienced in transplants for haemoglobinopathies. Transplants from any donor other than HLA-identical family members should be undertaken only after careful consideration and extensive counselling by a team experienced in such work. Each sickle cell centre should have clear referral links to such a transplant centre (C)

References


4.6 Psychological management

Psychological issues for people with SCD and their families result mainly from the impact of pain and symptoms on their daily lives, and society’s attitudes to the condition and those affected.

There is considerable variability in how people with SCD cope with their condition. People with SCD experience different levels of health, and such variations can lead to differences in psychosocial functioning. Some people cope relatively well, attend school or work, and are active physically and socially. Their efforts should be recognised and encouraged where necessary.

Others lead more limited and secluded lives. Nonetheless, this may not necessarily be a consequence of severe disease, and the reasons should be sought and addressed. Quality of life in people with SCD may therefore be lower than that of the general population, and with severe disease may deteriorate as people grow into adulthood. Children are also at greater risk of stroke, with consequent impairment of their psychosocial functioning and cognition.

Studies on providing psychological therapy as a standard adjunct to routine medical management have shown encouraging results. The overall goal is to help patients cope better, fulfil roles, and achieve better quality of life. In addition there are specific indications for psychological intervention in the management of pain and stroke. A review of psychosocial interventions for pain and adherence outcomes demonstrates that cognitive behavioural techniques are probably efficacious in treating sickle cell pain.

4.6.1 Psycho-education

Psycho-educational interventions primarily focus on improving knowledge and understanding of patients about their illness, while at the same time providing psychological support. Group interventions have been shown to identify issues and concerns in children and adolescents with SCD and family interventions improve knowledge. The rationale behind this approach is that information can lead to improved knowledge and better coping with the condition and children who feel isolated may benefit from the support and motivation of others through shared experience.

4.6.2 Cognitive Behavioural Therapy

Cognitive Behavioural Therapy (CBT) comprises two psychological approaches: cognitive and behavioural techniques. The premise underlying CBT is that difficulties in living, relationships and general health have their origin in (and are maintained by) thoughts, emotions, and behaviours.

The aim of cognitive interventions is to challenge and ultimately change inappropriate, self-defeating thoughts and allow the patient to lead a more productive and satisfying life. On the other hand, behavioural methods follow from the premise that inappropriate behaviours are learnt, and therefore can be unlearnt. CBT has been shown to reduce health service utilisation in both children and adolescents with SCD. It has also been shown to reduce pain and improve mood and coping in adults.

4.6.3 Neuropsychology

Neurological complications in SCD result in both obvious and subtle neuropsychological deterioration. There is intellectual impairment with an increase in frontal-lobe problems of attention and executive functioning following overt stroke. However, children who have silent infarct also experience learning and behavioural problems and are twice as likely to have school difficulties as other children.

The Intercollegiate Working Party for Paediatric Stroke recommends a detailed assessment of the child’s cognitive and social functioning following a stroke. Although MRI can detect silent infarcts, it is impracticable to scan every child on a regular basis. However, there is evidence that neuropsychological screening provides a useful means of identifying those who may have suffered silent stroke.
Recommendations

1. All children and their families should have access to a clinical psychology service (C).

2. Cognitive behavioural therapy should be considered in addition to standard management in children experiencing frequent pain episodes (C).

3. A detailed neuropsychological assessment should be carried out in all children who have had a stroke, and repeated annually (C).

4. Regular developmental assessments, neuropsychological screening or monitoring of school attainments in SATs should be carried out on a regular basis to assess for possible silent stroke (C).

References


4.7 Management of acute complications

4.7.1 General considerations

SCD is characterised by both acute and chronic complications. Acute complications will inevitably present initially to the local hospital and may be associated with significant mortality in childhood. Mortality rates have been reduced through effective antimicrobial prophylaxis, parental education and appropriate acute intervention coordinated in dedicated sickle centres employing experienced and well-trained staff.1,2

Recommendations

1. Parents and carers should be made aware of the symptoms and signs associated with severe and life-threatening complications and know where to take their child if these occur (C)

2. A care pathway should be in place in the local unit for assessment of the child in casualty, and for transfer to a designated ward if admission is necessary (C)

3. Protocols should be available to cover the management of all acute sickle cell complications. These should include worsening anaemia, febrile episodes, acute pain, acute neurological complications, acute chest syndrome, and priapism (C)

4. A designated consultant paediatrician and/or paediatric haematologist should be responsible for the management of all children in the local hospital and sickle cell centre, with a named deputy. Junior doctors involved in assessment and treatment of acute sickle cell admissions should be made aware of acute complications and the local treatment protocols through regular education/training sessions (C)

5. Communication between the local centre and expert opinion in the sickle cell centre should be possible 24hrs/day for discussion of difficult cases and possible transfer of the patient. The means of communication should be made explicit (C)

6. Communication and transfer to a specified paediatric ITU will be readily available according to an agreed procedure (C)

References


4.7.2 Management of acute pain in hospital

Pain is the most common cause of acute morbidity in SCD, and frequent hospital admission with acute pain has been associated with increased mortality.1,2 Recurrent painful episodes have a negative psychological impact, and the experience of poorly managed episodes in hospital, together with perceived negative attitudes of some staff, are often reported.

These attitudes make it more difficult to develop effective long-term pain-coping strategies, and may lead to problematic behaviour on the ward.3 There are UK guidelines for pain management in SCD4 and RCPCH guidelines on the recognition of acute pain in children in hospital.5 Validated pain assessment tools should be used to measure the child’s self-report and behaviour.6 These should include parental and health professional assessment. Developmentally age-appropriate self-report tools should be used whenever children are able to participate.

Recommendations

1. Pain assessment should include the use of a validated pain assessment tool that is developmentally age-appropriate (C)

2. There should be a policy in the A&E department regarding triage, pain assessment and length of acceptable time from arrival to administration of analgesia (C)

3. Children should be managed according to a standard local analgesia protocol. This should be developed by collaboration between the local hospital and sickle cell centre and include input from a pain control team, paediatric pharmacist and a paediatric anaesthetist designated for this purpose. The protocol should provide clear guidance on drugs, route of administration,
dosage, and monitoring for analgesic effect and side effects (C)

4 Medical and nursing staff involved in treating children for acute pain should have regular training in pain management and in the application of the local analgesic protocol (C)

5 Children should be monitored regularly for effectiveness of analgesia and for signs of adverse effects (eg opiate-induced narcosis and hypoventilation, acute sickle chest syndrome etc) (C)

6 The psychological needs of the child and family regarding coping with pain and avoiding sickle crises should be addressed during the admission (C)

References


4.7.3 Management of the febrile child

All children with sickle cell disorders are at increased risk of infection due partly to hyposplenism. In addition, defects in opsonisation and in cell-mediated immunity have been demonstrated. The risk is highest for the HbSS genotype, and in infants up to the age of 5. This is the time of particularly high risk for infection with encapsulated bacteria.

In the days before immunisation programmes and prophylactic antibiotics against Haemophilus influenzae and pneumococcus, infections with these bacteria were common and caused septicaemia, pneumonia and meningitis. Salmonella osteomyelitis, pneumonia due to typical and atypical organisms, and malaria, particularly in children returning from holidays in Africa, may also occur. Other infections, such as urinary tract infection and acute cholecystitis, are common. Parvovirus B19 causes temporary red cell aplasia. The reason for the increased susceptibility to salmonella osteomyelitis is not known.12

Diagnostic problems can occur. It is common for a child with a simple acute painful episode to present with a fever and no obvious evidence of infection. Some young children present with painful, swollen joints or areas of swelling in a long bone. In these cases, it may be difficult to differentiate between acute bone infarction due to sickling and an osteomyelitis or septic arthritis. Blood cultures should always be taken, and if there is a high level of suspicion (eg high swinging fever, septic child, localized very tender swelling) imaging on ultrasound looking for subperiosteal fluid collection and surgical drainage should be considered before starting antibiotics. Prophylactic penicillin should always be continued in hospital if a different antibiotic is not prescribed to treat an acute infection.

Empirical antibiotics should be given appropriate for the range of likely infectious agents. An agent active against pneumococcus should always be included. Cover for suspected chest infection should include agents against atypical organisms.

Recommendations

1 A policy for antibiotic treatment of suspected or proven acute infection should be prepared by the sickle cell centre in collaboration with the local clinic and with a designated paediatric microbiologist (C)

2 Cultures of blood, urine and other possible sites of infection should be routinely done on any child presenting with acute pain and fever (C)

3 Malaria films should be sent if there is any suspicion of malaria or if a patient has returned from a malarious region in the previous year (C)
4.7.4 Management of acute anaemia

The most common causes of an acute fall in haemoglobin of more than 2g/dl below steady-state haemoglobin level are acute splenic sequestration and temporary red cell aplasia (TRCA). This is usually due to parvovirus B19 infection.1

Acute splenic sequestration has been defined as an acute fall of haemoglobin and markedly elevated reticulocyte count, together with an acute increase in spleen size. It is a serious complication of SCD, and if unrecognised, carries significant mortality.2 Mortality rates can be reduced substantially by parental education, regular palpation of the abdomen at home to detect early signs of splenic enlargement, and prompt intervention with transfusion.3,4 Recurrent splenic sequestration is an indication for splenectomy.

TRCA is characterised by a drop in haemoglobin over a period of about a week, often to levels as low as 3g/dl. It may be associated with fever, headache and abdominal pain. In a young child, it may be difficult to differentiate between TRCA and acute splenic sequestration, as the spleen may still be palpable. In contrast to acute splenic sequestration, the reticulocyte count will be very low or absent, and IgM for parvovirus B19 will be present. Recovery may be spontaneous, but a top-up transfusion is usually indicated.

Recommendations

1. There should be a protocol for recognition and investigation of children presenting with pallor with or without pain in hospital (C)

2. Parents should be taught how to palpate for splenic enlargement and should be aware of the need to bring the child to hospital if they detect pallor and/or an enlarging spleen. They should be aware of the local procedure for emergency assessment (C)

3. Medical staff assessing children with acute sickle cell complications should be made aware of these complications through regular training/education sessions (C)

4. A local protocol for management, including indications for transfusion should be available (C)

5. Children with two or more episodes of acute splenic sequestration, should be considered for splenectomy (C)

References


4.7.5 Management of acute chest symptoms

The acute sickle chest syndrome is characterised by pleuritic chest pain, fever, abnormal chest examination and new pulmonary infiltrates on the chest X-ray. It is an important cause of morbidity and mortality in SCD.1,3

It is particularly common in early childhood4 although, at that time, the clinical features are generally more typical of pneumonia. In later childhood and adulthood, the syndrome can develop during a painful crisis, or after anaesthesia.5 Early intervention with an effective treatment protocol including analgesia, oxygen, physiotherapy, antibiotics and transfusion can significantly reduce morbidity and mortality. A randomised controlled trial has shown that incentive spirometry performed regularly every 2 hours reduces the risk of acute chest syndrome in patients with chest and back pain.6
Recommendations

1. Parents, patients and carers should be made aware of this complication and how to recognise the symptoms, and should be familiar with the local procedure for emergency assessment (C).

2. Children with chest pain, cough, respiratory distress, new chest signs or worsening hypoxia, presenting either in casualty or during the course of a hospital admission, should be carefully assessed and monitored and a chest X-ray organised urgently (C).

3. Oxygen saturation monitoring should be used routinely, particularly in those children with respiratory signs and symptoms, acute pain affecting the trunk and girdle regions and if treated with opiates (C).

4. Incentive spirometry should be used in children with acute chest and back pain (A).

5. A local protocol should be prepared for management of the acute chest syndrome, to include clear guidance on analgesia, observations, oxygen delivery, antibiotics, IV fluids, bronchodilators, physiotherapy, incentive spirometry, and nursing observations. The indications for top-up transfusion, exchange transfusion and ventilatory support should be specified. There should also be a local protocol covering the practical issues of carrying out an exchange transfusion (C).

6. Medical and nursing staff should be made aware of this complication, how to recognise it, and the local policy for management through regular training/education sessions (C).

7. An agreement should be reached with the local paediatric intensive care unit about indications for transfer, means of communication, and the protocol for treatment in the intensive care unit (C).

References


4.7.6 Management of acute neurological complications (see also management of cerebrovascular disease, page 37)

Acute neurological complications are relatively common in children with HbSS, and are potentially devastating. Cerebrovascular disease, particularly proximal vessel stenosis, predisposes children to acute cerebral infarction. Occasionally older children present with subarachnoid or intracerebral bleeds, which may be related to single or multiple cerebral artery aneurysms. Acute neurological ischaemia is more likely to occur in children with pre-existing cerebrovascular lesions during acute anaemic events, or acute sickle cell crises.

Other acute neurological complications include behavioural changes, seizures, and loss of consciousness. The causes of these complications are not always clear, even after extensive imaging).

Symptoms suggestive of meningitis require urgent investigation, including lumbar puncture, blood culture and prompt antibiotic treatment. Acute ischaemic events require urgent investigation with CT and/or MRI scan to define the event and exclude a haemorrhagic component. This should be followed by exchange transfusion as soon as possible to reduce the risk of progression of the lesion.

Intracerebral or subarachnoid bleeds defined by such imaging may need to be followed by lumbar puncture (if safe), and, in some situations, surgical intervention. Although stroke in a child with SCD is likely to be secondary to cerebrovascular pathology, it is important to remember that stroke in childhood can result from alternative pathology,
particularly a source of cardiovascular emboli. These should be actively excluded. The RCP, with the paediatric stroke working party, has published guidelines on the management of all causes of acute stroke in childhood.2

Recommendations
1 Each sickle cell centre should have access to a designated paediatric neurologist who can assess and advise on acute neurological complications (C)
2 Each sickle cell centre should have a clear plan for access to a neurosurgical unit for managing children and adolescents with cerebral haemorrhage and subarachnoid bleeds (C)
3 RCP guidelines on the management of acute stroke should be followed and specific guidelines for acute stroke in SCD should be prepared by the sickle cell centre for the local unit (C)
4 Each sickle cell centre, should have access to neuro-imaging facilities including paediatric CT, MRI/MRA, and EEG (C)

References

4.7.7 Management of fulminant priapism (see also p40)

Priapism is a sustained, painful and unwanted erection. A prolonged attack, lasting more than 3 hours should be treated as a surgical emergency as, if untreated, cavernosal fibrosis and impotence may ensue. The condition becomes more common in adolescence and minor attacks may go unreported due to reluctance to tell parents or health professionals.1 Minor attacks may be aborted by emptying of the bladder, taking a warm bath and use of oral analgesia. Frequent minor attacks or ‘stuttering priapism’ may be treated with oral etilefrine.2 A prospective study of 15 young patients showed that aspiration and irrigation with dilute epinephrine produced immediate detumescence in 37 out of 39 occasions.3 Etilefrine may also be used.4 In the event that this is not successful, a glans-corporal shunt may need to be performed and if no relief occurs the urologists may need to go on to perform a bilateral non-parallel spongiosum corporal shunt or a corporal-venous shunt.5 Blood transfusion may be indicated as part of the overall management if a shunt needs to be performed.

Recommendations
1 A policy for the management of severe fulminant priapism should be drawn up with the sickle cell centre and the urology team (C)
2 Adolescent males and their carers should be aware of the policy and know how to access emergency treatment (C)
3 Aspiration and irrigation with etilefrine or ephedrine should be the initial treatment of choice (C)

References
Appendix 1

Newborn screening programme (NHS Sickle & Thalassaemia screening programme: www.screening.nhs.uk/sickleandthal)

Programme aims

To achieve the lowest possible childhood death rate and to minimise childhood morbidity from sickle cell disorders.

Overall outcome to be achieved at national level

Mortality rate in children under 5 of less than 4 per 1000 person-years of life (2 deaths per 100 affected infants) by 2010.

Programme objectives

1. To offer screening for sickle cell disorders to all infants.
2. To process tests in a timely manner.
3. To identify and arrange timely follow-up of infants identified as needing further investigation.
4. To accurately diagnose infants born with specific conditions where early intervention is likely to be beneficial.
5. To ensure effective and acceptable follow-up, care and support for affected infants and their carers.
6. To offer and start parental education and treatment in a timely manner.
7. To minimise the adverse effects of screening – including failure to follow up screen-positive infants, inaccurate or inadequate information, unnecessary investigation and follow-up, and inappropriate disclosure of information.
8. To ensure that responsibility, accountability and performance management for all aspects of the programme are clear and that these link together from local to national level and between the newborn and antenatal programme.

Outcome measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Criteria</th>
<th>Minimum standard (core)</th>
<th>Achievable standard (developmental)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best possible survival for infants detected by the programme</td>
<td>Mortality rates expressed in person-years</td>
<td>Mortality rate in children under 5 of less than four per 1000 person-years of life (two deaths per 100 affected infants)</td>
<td>Mortality rate in children under 5 of less than two per 1000 person-years of life (one death per 100 affected children)</td>
</tr>
<tr>
<td>Accurate detection of all infants born with major clinical significant abnormality</td>
<td>Sensitivity of the screening programme</td>
<td>99% for HbSS 98% for HbSC 95% for other variants</td>
<td>99.5% for HbSS 99% for HbSC 97% for other variants</td>
</tr>
<tr>
<td></td>
<td>High quality newborn laboratory services</td>
<td>All newborn laboratories meet minimum requirement by end 2006 (including EQA scheme and sharing data)</td>
<td>All newborn laboratories meet achievable standards by end 2007</td>
</tr>
</tbody>
</table>
Appendix 2

Issuing laboratory reports

The parents and GP should be informed of all the outcomes of screening. The approach adopted should follow general guidance from the UK Newborn Bloodspot Programme Centre. www.newbornscreening-bloodspot.org.uk

Laboratories are responsible for sending all screening results to child health departments or their equivalent in a timely manner. This information will be used to assess coverage of the screening programme and to provide a mechanism for reporting ‘normal’ results to parents and other healthcare professionals. Presumptive positive results should be reported immediately by the laboratory to the designated healthcare professional.

Action required for particular categories of results

Infants with sickle cell disease
Results should be sent by the laboratory as a matter of urgency (fax/electronically, etc) to the designated healthcare professional where the child was born, and confirmation of receipt documented. Parents should be informed by personal contact. Copies of all reports should be sent to the GP and health visitor.

Infants found to have a condition other than sickle cell disease which requires follow-up
Results should be sent by the laboratory to designated healthcare professional and confirmation of receipt documented. Parents should be informed by personal contact. Copies of all reports should be sent to the GP and health visitor.

Infants heterozygous for a haemoglobin variant
Results should be sent by the laboratory to the designated healthcare professional and confirmation of receipt documented. Parents and GPs should be informed by a locally agreed mechanism.

Infants with no abnormality detected
Results should be provided in written form by the Child Health Department or equivalent for the parent(s) of the child and the child’s GP.

Child Health computer systems or their equivalent should have links to laboratories to allow the notification of receipt of samples and the reporting of results.

Follow-up procedures

Infants with sickle cell disorders
Diagnostic testing should be undertaken before 3 months of age. Parental samples (where required) should also be tested at the same time. Samples for diagnostic testing for sickle cell disease should be sent to a specialist laboratory, which has expertise in haemoglobinopathy analysis.

Other clinically significant conditions
Diagnostic testing (when required) should be undertaken before 3 months of age, and it is recommended that parental samples should also be tested at the same time. Samples should be sent to a specialised laboratory which has expertise in haemoglobinopathy analysis.

Carriers of common haemoglobin variants (Hb S, C, Dpxjab, E)
Using screening techniques, second-line testing can confirm the presumed identity of the haemoglobin variant, and it should not be necessary to take a further blood sample. Carriers are usually asymptomatic but can be at risk under particular high-stress situations. It is helpful if their families are made aware of their carrier status and screening of parents offered.

Rarer haemoglobin variants
Most of these will be infants who are heterozygous for the rarer variants and will have no clinical or haematological manifestations. However, some rare variants, particularly unstable haemoglobins or those with altered oxygen affinity, can produce clinical manifestations even in the heterozygous form, although not all of these will be detected by screening. Local policies should be in place for the follow-up of these babies whilst guidance to support clinicians and ensure effective use of resources
is developed by the programme. If it is decided to establish the identity of the variant, further samples on the neonate and/or parents should be referred to a laboratory with expertise in haemoglobin analysis and its clinical significance. It may be easier to test parental samples at this stage rather than re-bleed the neonate. Once the nature of the condition is established, medical follow-up can be provided if necessary. An example of a letter that could be used as a template to send to parents is given in Appendix 1.

Transfused infants
Any infant who is known to have had a blood transfusion prior to the dried bloodspot sample being taken must have a repeat test taken at least 4 months after the last transfusion. Any quantity of red cell transfusion, at any time (in utero or postnatally) should be regarded as significant and the test repeated.

Premature infants
Hb A is normally detectable by 30 weeks gestation and is sometimes detected by 24 weeks. Results from premature infants should be interpreted with caution. Premature infants who show no Hb A need repeat testing to check for the presence of a sickle cell disorder or homozygous ß-thalassaemia.

Quality assurance
Timeliness
Bloodspot card samples should be taken 5-8 days after birth (ideally day 5), sent to the laboratory within 24 hrs of being taken and received in the screening laboratory within 4 working days of being taken (see UK Newborn Bloodspot Screening Programme Centre guidance – Standards 1 and 2). The report should be issued in line with National Standards to enable arrangements to be made so that affected children can be immunised with pneumococcal vaccine by 8 weeks and attend a specialist clinic by 3 months of age.

NHS numbers
The bloodspot card should have both the baby’s NHS number, to ensure correct identification and to confirm coverage of the programme, and ideally the mother’s NHS number to allow linkage with antenatal records.

Reports
The recommendations made in the ‘Reporting results for the newborn screening programme’ section should be followed.

Storage of bloodspot cards
Laboratories will be expected to comply with the ‘Code of Practice for the Retention and Storage of Residual Spots’ published in the Policies and Standards of the UK Newborn Screening Programme Centre.

Lines of responsibility

The midwife is responsible for:
• Informing the parent(s) or guardian of the reasons for testing
• Providing relevant information to parents
• Offering the test, collection of the dried bloodspot sample 5-8 days after birth, labelling and sending off the sample as soon as it has been taken
• Obtaining informed consent or written notification if the parents wish to opt out of testing

The screening laboratory is responsible for:
• Documentation of the infant's demographics, specimen analysis and issuing of results within a timely manner after receipt of the sample
• Reporting non-normal results to the designated healthcare professional responsible for the follow-up of affected infants
• Reporting all results to the relevant child health department

The designated healthcare professional with relevant skills and training is responsible for:
• Informing parents of the results and arranging clinical follow-up of infants with sickle cell disease
• Informing parents of the results and arranging clinical follow-up of infants with other potentially clinically significant conditions
• Providing information and counselling for the parents of infants who are carriers or have other benign conditions detected
• Arranging repeat testing as indicated by the laboratory
• Ensuring that infants are not lost to clinical follow-up before enrolment in a clinic

The Child Health Department is responsible for:
• Checking that all newborn babies are offered screening
• Recording the results of screening in the child health record
• Disseminating the normal results

Laboratory Standards for Newborn Sickle Cell Screening Programme

1 The laboratory must be accredited by an appropriate body, eg Clinical Pathology Accreditation UK (Ltd).

2 When the programme is fully implemented, the workload of the screening laboratory should exceed 25,000 specimens per year (ideally 50,000), to give appropriate economies of scale and confidence in the interpretation of abnormal results. This needs to be linked to the requirements of the UK Newborn Screening Programme Centre.

3 There must be a senior member of the laboratory staff at consultant level responsible for the haemoglobinopathy screening service, with defined lines of accountability and authority for all laboratory aspects of the service.

4 The initial screening test must be performed using HPLC or IEF, with a confirmatory test for the positive results being performed on the original blood spot, using a different technique from the initial screening test.

5 Screening laboratories must demonstrate a plan for developing a comprehensive laboratory computer system capable of being interfaced with the appropriate child health computer systems and antenatal screening records, for reporting of results, monitoring and audit purposes.

6 There must be a documented risk management policy for the laboratory aspects of the haemoglobinopathy screening service.

7 The laboratory must participate in an accredited External Quality Assessment Scheme (EQAS), appropriate for newborn screening, eg UKNEQAS, and be able to demonstrate satisfactory performance.

8 Appropriate internal quality control procedures must be undertaken and documented, eg recording of reagent lot numbers, recording of turnaround time for reports, results of internal quality control specimens, etc.

9 The laboratory must participate in audit at local and regional level, with the effectiveness of the screening programme being published in a local annual report.

10 The laboratory must be willing to release information on screening performance to any appropriate monitoring group of the National Screening Committee and the NHS Sickle Cell and Thalassaemia Screening Programme Centre, and be open to inspection by the commissioners or their representatives at any time by mutual agreement.

Support services

Clinical network arrangements:
It is recommended that a clinical network be formally established, with a recognised specialist/regional centre and a named specialist, for annual review of all affected infants. A process to formalise existing informal networks is being developed with support from the Department of Health and relevant professional groups, including the British Society of Haematology, the UK Haemoglobinopathy Forum, the Royal College of Paediatrics and other interested parties.

Support services for timely follow-up and treatment need to be in place and coordinated across the area covered by a programme, to ensure that the potential benefits of the programme are realised. Experience from the USA shows that the main reason for the failure of a screening programme is failing to ensure that identified infants are enrolled in a programme of treatment and care or, having been enrolled, are subsequently lost to follow-up.
Specific arrangements for counselling women and their partners with an affected infant need to be in place for all areas covered by a newborn screening programme.

**Fail-safe arrangements:**
Each local area needs to have fail-safe arrangements in place, with designated individuals responsible from the relevant professional disciplines. These are distinct from the care pathway for individual users of the service and also from the responsibilities of individual professionals in following up particular actions for individual patients.

For the newborn programme this includes having a system to ensure that there is a review of screen-positive infants, together with the success of enrolling them in appropriate follow-up care and starting them on a defined programme of treatment with a relevant local service provider (and a recognised specialist unit, as appropriate).

For both the newborn and the antenatal programmes, this includes a requirement for a formal independent process, such as a regular audit meeting, for the review of all screen-positive results and action taken to follow-up screen-positive cases. This should be undertaken on a regular basis, with specified individuals involved and clear accountability, to ensure that processes of care operate smoothly and in a timely manner.
Appendix 3

Literature search strategy
Sources searched: Medline, Embase, Cochrane Controlled Trials Register
Dates of search: Jan 1980 to Aug week 2 2006
Search Strategy

OVID Medline
1. exp Hemoglobinopathies/
2. exp Hemoglobin, Sickle/
3. (hemoglobinopath$ or haemoglobinopath$).tw.
4. sickle cell.tw.
5. sickle-cell.tw.
6. meniscocytic.tw.
7. drepanocytosis.tw.
8. (hemoglobin s or haemoglobin s).tw.
9. (hemoglobin sc disease or haemoglobin sc disease).tw.
10. (sickling and (blood or plasma)).tw.
11. 1 or 2 or 3 or 4 or 5 or 7 or 9 or 10

Combined with RCT strategy below:
1. RANDOMIZED CONTROLLED TRIAL.pt.
2. CONTROLLED CLINICAL TRIAL.pt.
3. Randomised Controlled Trials/
4. Random Allocation/
5. Double-Blind Method/
7. 1 or 2 or 3 or 4 or 5 or 6
8. Animals/
9. Humans/
10. 8 not 9
11. 7 not 10
12. CLINICAL TRIAL.pt.
13. exp Clinical Trials/
15. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
16. Placebos/
17. placebo$.ti,ab.
18. random$.ti,ab.
19. Research Design/
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 20 not 10
22. 20 not 11
23. 11 or 22

Results
All search results were imported into a Reference Manager database and duplicates removed.
The search retrieved a large number of citations about diabetes, and also picked up a number of review articles, comments and letters, so these were removed leaving 1998 citations remaining.

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<th>Database</th>
<th>No. of citations retrieved</th>
<th>Exclusive</th>
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<tr>
<td>Cochrane Controlled Trials Register (CCTR)</td>
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<td>1960</td>
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<td>Embase</td>
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# Appendix 4

## Proposed networks of clinical care

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<tr>
<th>Region</th>
<th>Newborn screening lab</th>
<th>Proposed network of sickle cell centres</th>
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<tr>
<td><strong>East of England &amp; Bedfordshire</strong></td>
<td>Cambridge Great Ormond Street</td>
<td>Addenbrooke’s Cambridge Luton &amp; Dunstable</td>
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<tr>
<td><strong>East Midlands</strong></td>
<td>Sheffield</td>
<td>Nottingham, Leicester</td>
</tr>
<tr>
<td><strong>London</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southeast Essex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast &amp; Essex</td>
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<td></td>
</tr>
<tr>
<td>North Central</td>
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</tr>
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<td><strong>Northwest &amp; Hertfordshire</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>South East &amp; Kent/Sussex</strong></td>
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<tr>
<td>Southwest &amp; Surrey</td>
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<td><strong>Southeast, Thames Valley</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>West Midlands</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>North, North East</strong></td>
<td></td>
<td></td>
</tr>
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<td>Northeast Yorkshire</td>
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<td>Royal Victoria, Newcastle St Jame’s Hospital, Leeds, Sheffield</td>
</tr>
<tr>
<td><strong>Yorkshire &amp; Humberside</strong></td>
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<tr>
<td><strong>West Midlands</strong></td>
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<td><strong>North West</strong></td>
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<td>Manchester Children’s Hospital Alder Hey Children’s Hospital</td>
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<td>Bristol Royal Infirmary Derriford Hospital, Plymouth</td>
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<tr>
<td><strong>South West</strong></td>
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<td>Royal Berkshire Hospital, Reading The John Radcliffe Hospital, Oxford (Milton Keynes) Southampton</td>
</tr>
<tr>
<td><strong>South East</strong></td>
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<tr>
<td><strong>South</strong></td>
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Appendix 5

Suggested audit topics

1. Breaking the news and confirmation of diagnosis
   a) The screening practitioner will communicate with the primary care team and local paediatrician within 1 week of receiving result
   b) The result will be communicated to parents by the paediatrician or specialist nurse within 1 week of the screening practitioner receiving result
   c) The paediatrician or specialist nurse will refer for paediatric follow-up within 1 week of informing the parents
   d) Evidence that literature (translated where necessary) on the care of the infant and early signs and symptoms of the condition has been given to the carer

2. Initial outpatient visit
   a) Outpatient appointment with consultant paediatrician and/or paediatric haematologist within 2 weeks of diagnosis or by 3 months of age if parents have received a home visit from specialist nurse
   b) Documentation in notes that care plan and written information have been given
   c) Written communication to GP, HV, screening practitioner
   d) Confirmation of diagnosis in notes and to local unit by 3 months of age
   e) Documentation that penicillin prophylaxis has been started by 3 months of age
   f) Documentation that immunisation with conjugate pneumococcal vaccine (Prevenar) has been prescribed

3. Annual review
   a) A minimum of four monthly outpatient appointments in first 2 years, 6-monthly until age 5 years and yearly thereafter.
   b) A written policy and procedures for tracking families who do not attend
   c) Documentation of height and weight on centile chart in the child’s notes
   d) Documentation of spleen size in notes
   e) Record of education/discussion with family
   f) Evidence that an annual review has been offered and information provided to sickle cell centre
   g) Individual treatment and care plan in notes
   h) Evidence of communication with parent, local unit, GP, health visitor or school nurse
   i) Evidence of transition planning from age 14

4. Transition
   a) Transition policy in place
   b) Adult sickle cell service identified

5. Prevention of infection
   a) Evidence of prescription of penicillin V or alternative documented in notes
   b) Completion of Prevenar course by 15 months documented in notes
   c) Documentation of Pneumovax at 2 years, 7 years, 12 years
   d) Documentation of hepatitis immunisation completed by 2 years
   e) Offer of influenza vaccine documented

Suggested audit topics

Appendix 65
Screening for cerebrovascular disease
a) All children with sickle cell disease offered annual transcranial Doppler imaging from the age of 3 onwards.
b) Blood pressure measured and recorded annually in notes

Monitoring of nutrition and growth
a) Evidence of completed height and weight chart in notes
b) Radiological assessment of bone age in growth delay

Common paediatric problems
Local procedures and guidelines in place for the investigations and management of growth delay, nocturnal enuresis, renal problems, stroke, lung disease, priapism, leg ulcers, biliary disease, avascular necrosis, eye complications

Peri-operative management
a) Pre-operative sickle screening is in place
b) Policy and protocols are in place for peri-operative management

Use of hydroxyurea
a) Evidence of patient information literature regarding the use of hydroxyurea and side effects
b) Evidence of discussion regarding this treatment at annual review
c) Evidence of informed consent
d) Policy and protocols for the commencement and monitoring of treatment

Use of blood transfusion
Policy and procedures in place for the use of transfusion in sickle cell disease

Indications for bone marrow transplantation
a) Patient literature available regarding use of bone marrow transplantation in SCD
b) Evidence of discussion regarding this treatment at annual review

Psychological interventions
a) Named clinical psychologist with an interest in SCD
b) Annual neuropsychological assessments for children who have had stroke documented in notes

Management of acute complications
a) Written guidance for families on how to access hospital treatment
b) Written policy and procedures on the management of acute complications
c) Written policy and procedures on transfer to sickle centre or intensive care