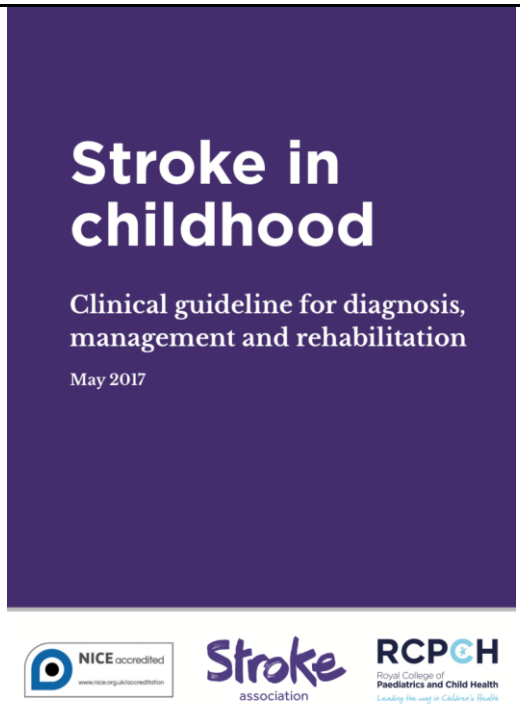
Stroke in Childhood: Clinic guideline for diagnosis, management and rehabilitation (2017)

Background

- Nationally developed evidence-based clinical guideline
- Funded by the Stroke Association
  - Guideline Development Group chaired by Dr Vijeya Ganesan
  - 32 members
  - 27 stakeholder organisations
  - Three parents of affected children
  - Clinical guideline accompanied by parent guideline
- First clinical guideline on stroke in children developed by RCP in 2004



Clinical Guideline

- Guideline
  - Full guideline 169 pages
  - 357 pages of Appendices
  - Major sections
    - Acute diagnosis of stroke in childhood
    - Referral pathways and further investigations
    - Acute management
    - Arterial ischaemic stroke
    - Haemorrhagic stroke
    - Discharge from hospital
    - Rehabilitation
    - Long-term care: transfer and transition
    - Implications for practice
    - Research recommendations

Key Recommendations Relevant to SCD

Acute diagnosis of stroke in childhood (Chapter 3)
Clinical presentation (Chapter 3.1)

- Use the FAST ('Face, Arms, Speech Time') criteria to determine stroke in children and young people, but do not rule out stroke in the absence of FAST signs.
- Undertake urgent brain imaging of children/young people presenting with symptoms (e.g. acute focal neurological deficit, aphasia, or a reduced level of consciousness).

To access full recommendations, see Chapter 3.1.

Diagnosis (Chapter 3.2)

- Ensure that a cranial computerised tomography (CT) scan is performed within one hour of arrival at hospital in every child with a suspected stroke; including computerised tomography angiography (CTA), if the CT scan does not show haemorrhage, ***OR*** CTA limited to intracranial vascular imaging, if haemorrhagic stroke (HS) is demonstrated.
- Initial scan images should be reviewed on acquisition and if necessary transferred immediately to the regional paediatric neuroscience centre for review.

Acute medical interventions for AIS (Chapter 6.2.1)

Use of thrombolysis or anti-thrombotic therapy

- Prescribe and deliver 5mg/kg of aspirin up to a maximum of 300mg within 24 hours of diagnosis of AIS in the absence of contraindications (e.g. parenchymal haemorrhage). After 14 days reduce dose of aspirin to 1mg/kg to a max of 75mg.

- The off label use of tissue plasminogen activator (tPA) ***could*** be considered in children presenting with AIS who are more than eight years of age and ***may*** be considered for children aged between two and eight years of age on a case by case basis when the criteria detailed in 6.2.1 have been met.

- Aspirin should not be routinely given to children and young people with SCD presenting with AIS.

- Carry out the following investigations in children and young people with a diagnosis of AIS:
  - haematological investigations, including full blood count, iron status (e.g. iron, ferritin, total iron binding capacity) and haemoglobinopathy screen
  - biochemistry tests, including total plasma homocysteine, alpha galactosidase, fasting blood sugar, fasting cholesterol, and Lipoprotein(a)
  - lupus anticoagulant and ACLA, and discuss beta 2GP1 testing with haematology if necessary
  - cardiac evaluation: electrocardiogram (ECG), echocardiogram (to identify structural lesions and R to L shunts)
  - cerebrovascular imaging from the aortic arch to vertex, with computed tomography angiography (CTA) or magnetic resonance angiogram (MRA) at the time of CT or MRI respectively
  - transcranial Doppler in patients with SCD
- Clinically evaluate all patients for history of prior infection (especially VZV), immunisation, dysmorphic features, neurocutaneous stigmata, autoimmune disease and evidence of vascular disease in other organ systems.

Risk Factors for Stroke in Sickle Cell Disease

Sickle Cell Disease	Additional factors in children and young people with SCD: • genotype (sickle haemoglobin (HbS) & HbSβ thalassaemia more than other genotypes) • abnormal transcranial Doppler studies • arteriopathy (intracranial & extracranial) • absence of alpha thalassaemia trait • acute anaemia • silent infarction
	• prior transient ischaemic attack (TIA) • high systolic blood pressure, acute chest syndrome • anaemia, high reticulocyte count

Acute AIS treatment in children and young people with SCD

- Treat children and young people with SCD and acute neurological signs or symptoms urgently with a blood transfusion, to reduce the HbS to less than 30%, and increase the haemoglobin concentration to more than 100–110g/l. This will usually require exchange transfusion.
- Provide a small top up transfusion to bring Hb to 100g/l to improve cerebral oxygenation if the start of the exchange is likely to be delayed by more than six hours.
- Provide other standard supportive stroke care.

- Prioritise exchange transfusion over thrombolysis.

AIS recurrence prevention in SCD

- Start regular blood transfusions as secondary stroke prevention in children and young people with SCD, aiming to keep the pre-transfusion HbS less than 30% and keeping the pre-transfusion haemoglobin above 90g/l. This can be done with either exchange or simple top-up blood transfusion.
- Ensure that all children and young people with SCD and their siblings are HLA typed. Children and young people with HLA-identical siblings and recurrent stroke or worsening vasculopathy despite optimum haematological treatment should be referred for discussion of HSCT.
- Monitor children with regular neurocognitive testing, MRI and TCD; frequency should be determined on a case-by-case basis.
- Intensify treatment if there is evidence of progressive cerebrovascular disease, if identified through either TCD or magnetic resonance angiography. Options may include:
  - intensified transfusion with lower HbS target
  - the addition of hydroxycarbamide or antiplatelet agents during red cell transfusions
  - consideration of surgical revascularisation (in the presence of arteriopathy)
  - referral for alternative-donor HSCT
- Children and young people's cases should be discussed in an appropriate multidisciplinary team (MDT) with experience of managing children and young people with SCD prior to referral for either surgery or alternative-donor HSCT.
- Hydroxycarbamide should be considered as part of a secondary stroke prevention programme when suitable blood (e.g. multiple alloantibodies or hyperhaemolysis) is not available, or when continued transfusions pose unacceptable risks (uncontrolled iron accumulation).
- Hydroxycarbamide may be used as an alternative to blood transfusion if transfusion is genuinely unacceptable to the parents/carers and child. It is imperative that the decision to stop transfusions and switch to hydroxycarbamide is taken by a MDT.

- Consider using anticoagulation or antiplatelet agents only when there are other risk factors for cerebrovascular disease that justify their use.

SCI progression prevention in SCD

- Discuss the possible benefits of transfusion with children, young people and families if SCI are identified on MRI. Factors favouring the implementation of a treatment program involving regular blood transfusions include:
  - impaired cognitive performance
  - progressive deterioration in cognitive function
  - evidence of increase in size or number of SCIs on serial MRIs
  - evidence of intracranial or extracranial vasculopathy on MRA
  - other co-existent morbidities of SCD which may benefit from regular blood transfusions, including frequent episodes of acute pain, progressive pulmonary damage, and progressive renal impairment.
- Consider haematopoietic stem cell transplantation in children and young people starting transfusions.
- Consider starting hydroxycarbamide as an alternative therapy if repeated transfusions are declined or contra-indicated.

HS recurrence prevention in SCD

- Perform neuroimaging as recommended for other children and young people with acute HS.
- Consider administering a transfusion to decrease HbS less than 30% prior to direct intra-arterial injection of contrast for catheter angiography.
- Provide anti-sickling treatment to children and young people with SCD and HS, and either a regular blood transfusion or a haematopoietic cell transplantation from a human leukocyte antigen (HLA)-matched sibling (or alternative donors in rare circumstances).
- Provide regular blood transfusions if there is clear evidence of arteriopathy (e.g. occlusive lesions or aneurysms) to keep HbS less than 30%.
- Ensure that all children and young people with SCD and their siblings are HLA typed. Children and young people with HLA identical siblings and recurrent stroke or worsening vasculopathy despite optimum haematological treatment should be referred for discussion of haematopoietic stem cell transplantation (HSCT).
- Consider children and young people with HS and isolated small aneurysms and no other cerebral vasculopathy for treatment with hydroxycarbamide or regular blood transfusions in addition to evaluation for endovascular or surgical treatment.
- Follow-up children and young people with HS in SCD, long-term with repeat neurocognitive testing, MRI and TCD to assess evidence of progressive cerebrovascular disease.

Transition

• Children with sickle cell disease (SCD) on long-term transfusion for prevention of stroke should be referred to an adult unit where transfusion therapy can continue to be provided and support is given to continue transfusion during and after the transitional period.

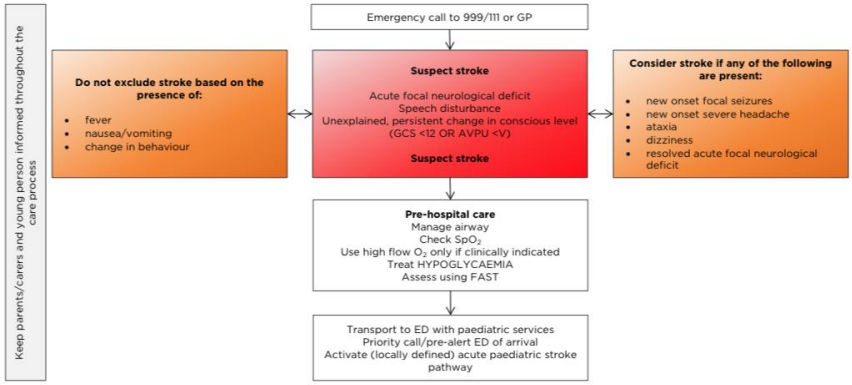


Diagram 4.1. Pre-hospital pathway for the management of suspected childhood stroke.

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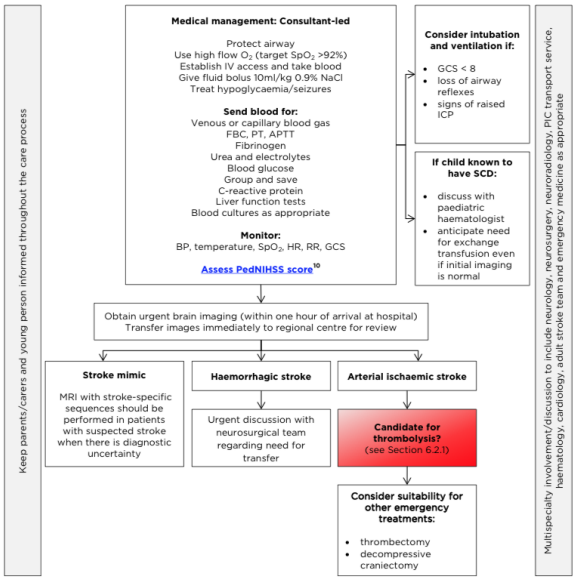

Diagram 4.2. Acute paediatric stroke pathway (according to locally agreed arrangements for delivery).

Summary

- RCPCH guidelines on stroke management exist and are useful
- Largely coincide with current stroke management in SCD
- Questions raised by guidelines
  - Antiplatelet agents in SCD and stroke
  - Thrombolysis in SCD and stroke