UHL Children's Emergency Department and Children's Hospital

Stroke Guideline for Children & Child in Neonatal age group (outside neonatal unit)

[Ref: RCPCH Stroke in Childhood Guideline; American Stroke Association/ American Heart Association Neonatal Stroke Guideline]

Staff relevant to:	Clinicians working in UHL Paediatric Emergency Dept and UHL children's hospital caring for children and young people and child-in-neonatal age group (outside neonatal unit) with suspected or confirmed stroke, Paediatric intensive care unit (PICU)
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Trust Ref:	D9/2020

Contents

Child-in-Neonatal age group (outside neonatal unit) points are colour coded in blue.

1. Introduction, significance and who this guideline applies to:

Stroke is a clinical syndrome of presumed vascular origin characterized by rapidly developing signs of focal or global disturbance of cerebral functions which lasts longer than 24 hours or leads to death.

a) **Ischaemic stroke** — an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal cell death due to infarction following vascular occlusion or stenosis. This damage can have different effects, depending on where it happens in the brain
b) **Haemorrhagic stroke** — rapidly developing neurological dysfunction due to a focal collection of blood from within the brain parenchyma or ventricular system (intracerebral haemorrhage), or bleeding into the arachnoid space (subarachnoid haemorrhage) that is not caused by trauma. Rupture of cerebral arteries/ veins; also due to bleeding into site of ischemic infarct. This is also referred to as subarachnoid hemorrhage (bleeding on the surface of the brain) or intracerebral haemorrhage (bleeding within the brain)

- **Transient ischaemic attack (TIA)** is a transient (less than 24 hours) neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without evidence of acute infarction.
    - A TIA has a sudden onset and can last from a few minutes to 24 hours. Most people have complete resolution of symptoms and signs within 1 hour.

CLASSIFICATION

By age;

- **PERINATAL STROKE**: Stroke occurring from 28 weeks gestation to 28 post-natal days of life.
- **CHILDHOOD STROKE**: Stroke occurring after 28 days to 18 years of age

Perinatal stroke
• Acute perinatal stroke - newborn infants at or near birth and typically presents shortly after onset with focal seizures or encephalopathy
• Presumed perinatal stroke - chronic infarcts, diagnosed in a delayed fashion, that are presumed to have occurred in the perinatal period. Typically present with pathologic early handedness or seizures, leading to brain imaging and the diagnosis of a remote infarction.

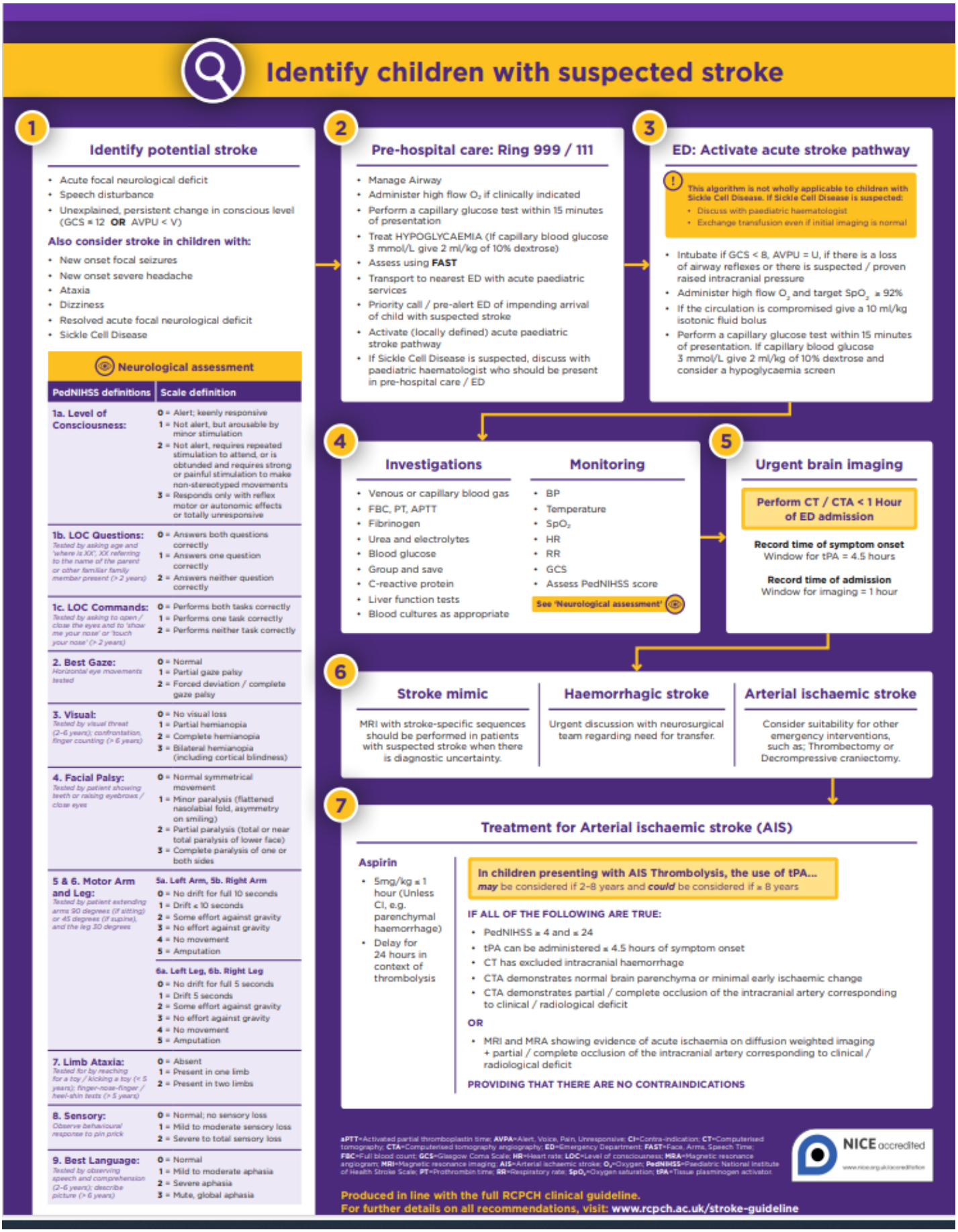
Aim of the guideline:
To help the acute recognition and diagnosis of AIS and HS; guidance on targeted investigations, help with the acute management and taking action to prevent recurrence of stroke (AIS and HS). The discussion about the cerebral sinus venous thrombosis are beyond scope of this guideline.

Key Statistics:
Over 400 children will have a stroke each year in the UK.
Incidence for overall stroke was 2.56 per 100,000 person years [The Epidemiology of Childhood Stroke in Southern England: A Prospective Study using Multiple Sources of Case Ascertainment]

This document provides guidance on the identification, diagnosis and management of Arterial Ischaemic Stroke (AIS) and Haemorrhagic Stroke (HS) in children and young people and child-in-neonatal age group (outside neonatal unit). It is beyond the scope of this guideline to discuss about the Cerebral Sinus venous thrombosis.
It includes guidance for the management of unruptured at risk vascular malformations (arteriovenous malformations, cavernous malformations, cerebral aneurysms and arteriovenous fistulae), cerebrovascular disorders, Moya moya disease, and inherited platelet and coagulation disorders.
This guideline also refers to the acute management of stroke in children with Sickle Cell Disease (SCD).

This guideline has been adapted according to the proposed RCPCH guideline on Stroke in Children (2017)
Work is being done to develop a funded national registry to facilitate both data capture and critical analysis of cases considered for hyperacute treatments, monitor data from individual centres to improve the management & related services nationwide.

Flow chart for diagnosis, management and rehabilitation: Produced in line with RCPCH clinical guideline.
For further details, visit: https://www.rcpch.ac.uk/sites/default/files/2018-04/2017_stroke_in_childhood_-_pathway_poster.pdf



Stroke in Childhood and Child-in-Neonatal Age Group (Outside the neonatal unit) Flow chart for diagnosis, management and rehabilitation

1

Identify potential stroke

Most common presenting symptoms **(These do not distinguish between AIS and HS)**

- Acute focal neurological deficit/ Hemiparesis
- Aphasia/ Speech disturbance
- Unexplained, persistent change in conscious level (GCS = 12 **OR** AVPU < V)
- Child-in-neonatal age group has different presentation than the paediatric age group.

Also consider stroke in children if they present with:

- New onset focal seizures
- New onset severe headache
- Ataxia
- Dizziness
- Resolved acute focal neurological deficit (including before arrival to the hospital)

Neurological assessment

PedNIHSS definitions	Scale definition
1a. Level of Consciousness:	0 = Alert, keenly responsive 1 = Not alert but rousable by minor stimulation 2 = Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make non-stereotyped movements 3 = Responds only with reflex motor or autonomic effects or totally unresponsive
1b. LOC Questions: *Tested by asking age and 'where is XX', XX referring to the name of the parent or other familiar family member present (> 2 years)*	0 = Answers both questions correctly 1 = Answers one question correctly 2 = Answers neither question correctly
1c. LOC Commands: *Tested by asking to open /close the eyes and to 'show me your nose' or 'touch your nose' (> 2 years)*	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2. Best Gaze: *Horizontal eye movements tested*	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation/complete gaze palsy
3. Visual: ***Tested by visual threat (2–6 years); confrontation, finger counting (> 6 years)***	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (including cortical blindness)
4. Facial Palsy: ***Tested by patient showing teeth or raising eyebrows / close eyes***	0 = Normal symmetrical movement 1 = Minor paralysis (flattened naso/labial fold, asymmetry on smiling) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides
5 & 6. Motor Arm and Leg: ***Tested by patient extending arms 90 degrees (if sitting) or 45 degrees (if supine), and the leg 30 degrees***	5a. Left arm, 5b. Right arm 0 = No drift for full 10 seconds 1 = Drift ≤ 10 seconds 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement 5 = Amputation 6a. Left leg, 6b. Right leg 0 = No drift for full 5 seconds 1 = Drift 5 seconds 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement 5 = Amputation
7. Limb Ataxia: ***Tested for by reaching for a toy / kicking a toy (< 5 years); finger-nose-finger / heel-shin tests (> 5 years)***	0 = Absent 1 = Present in one limb 2 = Present in both limbs
8. Sensory: ***Observe behavioural response to pin prick***	0 = Normal; no sensory loss 1 = Mild to moderate sensory loss 2 = Severe to total sensory loss
9. Best Language: ***Tested by observing speech and comprehension (2–6 years); describe picture (> 6 years)***	0 = Normal 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute, global aphasia

2 ED: Activate acute stroke pathway

! This algorithm is not wholly applicable to children with Sickle Cell Disease. If Sickle Cell Disease is suspected:

- Discuss with paediatric haematologist, Exchange transfusion even if initial imaging is normal.

- **Intubate if GCS , 8, AVPU = U, if there is a loss of airway reflexes or if there is suspected / proven raised intracranial pressure**
- **Administer high flow O2 and target SpO2 > 92%**
- **If the circulation is compromised give a 10ml/kg isotonic fluid bolus**
- **Perform a capillary glucose test within 15 minutes of presentation. If capillary blood glucose 3mmol/L give 2ml/kg of 10% dextrose and consider a hypoglycaemia screen**

3

Investigations

- **Blood gas, Blood glucose,**
- **FBC, film, Hbpathy, clotting screen**
- **U & Es, lipid profile, TFTs, CRP, Liver function,Group and save, blood culture**
- **Blood test in Appendix 2 including thrombophilia screen, infective screen, metabolic and immunological causes including Lupus. NOT AT ADMISSION BUT AFTER STABILIZATION**
- **Tests for Child-in-neonatal age group (outside neonatal unit)- See Appendix 2**

Monitoring

- **BP**
- **Temperature**
- **SpO2**
- **HR**
- **RR**
- **GCS**
- **Assess Ped/NIHSS score**
  See 'Neurological assessment'

4 Urgent brain imaging

Record time of symptom onset
Window for tPA = 4.5 hours

Record time of admission
Window for imaging = 1 hour

Perform CT / CTA < 1 hour of ED admission

5

Stroke mimic

MRI with stroke-specific sequences should be performed in patients with suspected stroke when there is diagnostic uncertainty.

Haemorrhagic stroke

Urgent discussion with neurosurgical team regarding need for transfer

Arterial Ischaemic stroke

Consider suitability for other emergency interventions, such as: Thrombectomy or Decompressive craniectomy

Identify potential stroke

Most common presenting symptoms (These do not distinguish between AIS and HS)

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- Child-in-neonatal age group has different presentation than the paediatric age group.

Also consider stroke in children if they present with:

- New onset focal seizures
- New onset severe headache
- Ataxia
- Dizziness
- Resolved acute focal neurological deficit (including before arrival to the hospital)
- Sickle Cell Disease

6 Treatment for Arterial ischaemic stroke (AIS)

Aspirin • 5mg/kg < 1 hour (Unless CI, e.g. parenchymal haemorrhage) • Delay for 24 hours in context of thrombolysis	**IF ALL OF THE FOLLOWING ARE TRUE:** • PedNIHSS > 4 and < 24 • tPA can be administered < 4.5 hours of symptom onset • CT has excluded intracranial haemorrhage • CTA demonstrates normal brain parenchyma or minimal early ischaemic change • CTA demonstrates partial/complete occlusion of the intracranial artery corresponding to clinical/radiological deficit **OR** • MRI and MRA show evidence of acute ischaemia on diffusion weighted imaging + partial/complete occlusion of the intracranial artery corresponding to clinical/ radiological deficit **PROVIDING THAT THERE ARE NO CONTRAINDICATIONS**

In children presenting with AIS Thrombolysis, the use of tPA….
may be considered if 2-8 years and ***could*** be considered if > 8 years

1.1 Assessment of stroke using FAST criteria [Face, Arms, Speech, Time]

Face: Any facial asymmetry during smile / cry or unilateral drooping of face?
Arms: Any inability of the child to raise one arm or both arms & keep them there?
Speech: Is speech of the child is slurred / unclear / different than his/her usual one?
Time: Record time of onset of symptoms & time at presentation to hospital ED.
(Absence of FAST signs may not rule out stroke)

1.2 Assessment of Stroke for Child-in-Neonatal age group (outside neonatal unit):

Clinical assessment plus radiological help

Acute Neurological & general assessment:

This is summarized in the RCPCH poster and should be followed.

Initial assessment of the neonate and child:

- **Assess GCS or AVPU (Alert, Verbal stimulation, Pain, Unresponsive)score:**
  - Intubate if GCS < 8, AVPU = U, if airway reflexes lost. Raised intracranial pressure to be suspected if – Headache, Vomiting, 6th Nerve Palsy, Altered Sensorium Neck stiffness
- **General Observations:**
  - BP, Temperature, HR, RR, Oxygen saturation (target>92%)
- **PedNIHSS Stroke Score assessment:**
  - See Appendix 1 for guidance as to how to do this
- **Expose and examine including the back.**
- **Check Gait, Posture & Balance:**
  - any obvious weakness
- **Tone of limbs:**
  - increased, normal or decreased;
- **Power of limbs:**
  - all joints (Grade 0-5); [see appendix]
- **Reflexes in all limbs:**
  - If unable to elicit, then should try reinforcement.
  - Biceps C5-C6, Brachioradialis C6, Triceps C7-C8
  - Knee L2-L4, Ankle S1/S2; Plantar L5-S2; [Plantars up-going till 1 year age]
- **Check Sensation:**
  - check any dermatomal distribution [see appendix]
  - Pain & Temperature - Spinothalamic tracts, light touch & proprioception - posterior column
- **Cranial nerves:**
  - most effective information from 3rd, 4th, 6th 7th cranial nerves

1.3 Immediate management: for children and child-in-neonatal age group (outside neonatal unit)

- Check Blood Pressure: altered BP is often associated with Cerebro-Vascular stroke

Hypotension: Treat with 10 ml/kg isotonic fluid bolus
Hypertension: Refer to hypertension guideline - Hypertension UHL Childrens Medical Guideline
If systolic BP>90TH centile, contact Paediatric Nephrologist via QMC switchboard for advice.
The following circumstances need to be considered:

- Hypertensive Encephalopathy
- End organ damage or dysfunction, e.g. cardiac or renal failure
- Patients eligible for IV thrombolysis but systolic BP > 95th percentile for age by > 15%

- Monitor temperature, HR, RR
- Maintain oxygen saturation (target > 92%); administer high flow O2 if needed
- Maintain fluid balance, glycaemic control, electrolyte status
- Withhold Oral Feeding until safe swallow is established
- Treat any seizure (if any) as per APLS protocol

1. 4 Urgent Radiological Investigation: for children and child-in-Neonatal age group (outside neonatal unit)

(a) Cranial CT scan:

Urgent neuroimaging should be carried out **within one hour of arrival at ED in hospital** if suspected stroke after senior clinical review which may note the following in their assessment:

- Acute focal neurological deficit / Hemiparesis

- Aphasia / Speech disturbance
- Persistent Altered Awareness (GCS < 12) or (AVPU < V)
- Alternative presentations where non contrast CT Head is suggestive of Stroke

Requests for CT should appropriately localise the symptoms, include the PedNIHSS to guide evaluation of findings, and highlight relevant risk factors in the patient's history.

(b) Cranial CT scan with review for CT-Angiogram

If no alternative pathology demonstrated on the non-contrast CT Head then proceed with CT Angiogram (Head & Neck vessels in Ischaemic Stroke)/ (Head only in Haemorrhagic stroke)

Clinical consideration is required for the appropriate way to ensure diagnostic imaging can be carried out. This may include a need for intubation.

For cases that are most likely to have a stroke, IV access is required pre-attendance for anticipated CT-Angiogram.
Review urgently CT / CT-A scan images with resident duty Radiologist in ED CT (weekends, evenings and nights) or Paediatric IP Hub Reporting (weekday day)

OUTCOME OF CT IMAGES:

- If CT images are ABNORMAL & if **SURGICAL INTERVENTION NEEDED** at any time 24 hours day / night:
  - ED team to discuss with Neurosurgery at QMC directly as the child might need to be transferred to Neurosurgical centre ASAP

- If CT images are ABNORMAL & if **SURGICAL INTERVENTION NOT REQUIRED** then;
  - Daytime (9am – 5 pm): ED team would discuss with Paediatric Neurologist at LRI OR
  - Out of hours / weekends / bank holidays: ED team would discuss with on-call Consultant Paediatrician at LRI. They would then liaise with Paediatric Neurologist from regional centre at Birmingham Children's Hospital for support if required.

(c) MR-Imaging:

This should be within 24 hours of admission if arranged as the first test, within 72 hours if supporting an abnormal CT.

- For Ischaemic stroke:
  - Stroke Sequence MRI Head + MR-Angiogram of Head & Neck vessel
- For Hemorrhagic Stroke:
  - Stroke Sequence MRI Head and MR-Angiogram of Head

MR should be provided within 24 hours if initial CT does not support a clinical diagnosis of stroke after review by a paediatric neurologist. The Paediatric neurologist from Birmingham Neurology can be contacted out of hours for support if required.

2. ARTERIAL ISCHAEMIC STROKE (AIS) in children and Child-in-Neonatal age group (outside neonatal unit)

- **Risk Factors of AIS Stroke** [Appendix – 3] includes usual neonatal AIS risk factors
- **Investigations in AIS**: [Appendix – 2] includes neonatal and maternal investigations

2.1 Confirmation of Arterial Ischaemic Stroke:
Is defined by ALL the CLINICAL CRITERIA below:

a) Acute focal neurological deficit consistent with arterial ischaemia

b) PedNIHSS score ≥ 4 and ≤ 24 [Thrombolysis could be initiated if within 4.5 hours of onset of symptoms]

Is defined by RADIOLOGICAL CRITERIA below:

a) CT and CTA demonstrates normal brain parenchyma or minimal early ischaemic change & rules out Intracranial haemorrhage
b) CTA demonstrates partial / complete occlusion of intracranial artery corresponding to clinical and/or radiological deficit
OR
c) MRI and MR-A showing evidence of acute ischaemia on diffusion weighted imaging plus partial or complete occlusion of the intracranial artery corresponding to clinical and/or radiological deficit

In case of Acute Stroke in children and young people with SICKLE CELL DISEASE (SCD) the Haematologist (Paediatric/Adult On-call) should be alerted early. Please contact through LRI Switchboard:

- Dr Kaljit Bhuller, Consultant Paediatric Haematologist,
OR
- Adult Haematology Registrar on-call

The following guidance may be helpful:

- **Sickle Cell Disease - Management UHL Childrens Medical Guideline**
- **Automated red cell exchange for paediatric sickle cell patients**

2.2 Indications for referral to Interventional Neuro-Radiology

a) Patients with AIS with disabling neuro-deficit (PedNIHSS score of ≥ 6)
b) If suitable for intra-arterial clot extraction with prior IV thrombolysis, unless contraindicated (**see list of contraindication to thrombolysis**),
c) If Symptom-Onset-to-Arterial-Puncture time of > 5 (FIVE) hours then
    - PedNIHSS score has to be > 6 (SIX)
    - Neuro-imaging showing salvageable brain tissue, in which case treatment up to 12 hours after onset may be appropriate.

Point of Contact for Interventional Neuro-Radiology:

- Interventional Neuro-Radiologists (I.R) are available 7 days per week to discuss urgent neurovascular cases at following timings:
On Weekdays: 0800 AM – 1800 PM
On Weekends: 0800 AM – 1400 PM.
- Urgent cases should be referred via the Neurosurgical StR, and then discussed with the interventional radiology team:
During the week I.R could be contacted via
    - Secretaries (QMC 0115 924 9924 (Extn 81017) Paediatric I.R. team (Extn 81951) or Adult I.R. team (Extn 81949)
    - Interventional Radiology Theatres (Extn 84413).
    - At the weekend I.R can be called via QMC switchboard (Tel: 0115 924 9924)
- Non urgent cases can be referred to the weekly neurovascular MDT via 'Neuroradiology Specialist Nurse' email (Neuroradiology.SpecialistNurse@nuh.nhs.uk OR nuhnt.neurovascularMDT@nhs.net).

Consultant Interventional Radiologist:

- Dr Sujit Nair(Clinical Lead) Sujit.Nair@nuh.nhs.uk
- Dr McConachie: Norman.McConachie@nuh.nhs.uk

- Dr Robert Lenthal: Robert.Lenthall@nuh.nhs.uk
- Dr Luqman Malik: Luqman.Malik@nuh.nhs.uk

- For any paediatric case with stroke due to large vessel occlusion

Please call MECHANICAL THROMBECTOMY nurses (Sharon, Lead Nurse) on 07812 270086 (service hours 08:00 – 16:00 Mon-Friday).

- May discuss with Adult Stroke-Physicians Team in Leicester & obtain advice for an adolescent (Age ≥ 12 years) who meet above criteria & considered for referral to Interventional Neuro-Radiology.

2.3 Indications for referral to Neurosurgery in children and young people with AIS for Decompressive Hemi/Craniectomy:

a) Extensive infarction of dominant Middle Cerebral Artery (MCA) territory
b) If ≤ 48 hours after the onset of stroke
c) Level of consciousness score ≥ 1 on item 1a of the PedNIHSS scale
d) PedNIHSS score > 15
e) CT indicate infarct of ≥ 50% of the MCA territory with/without further infarct involving anterior (ACA) or posterior cerebral artery (PCA) territory on the same side
f) Neonate may need to be consider for neurosurgery for large cerebral haemorrhages.

Point Of Contact:
Referral to Neurosurgery at QMC Nottingham:

http://www.referapatient.org/ **- fill up ON-LINE REFERRAL FORM**

- Select categories on the online form to mark the referral as stroke related
- On-call trainee / fellow & consultant will send electronic reply
- Particularly in time sensitive cases, Neurosurgical team to be contacted by phone to discuss matters of great urgency**.**
- May discuss with Adult Stroke Team in Leicester & obtain advice in case of adolescent (AGE≥ 12 years), in whom Neuro-Surgical and Endovascular interventions are considered

Special Circumstances:

- **If a patient meets the BELOW criteria**, they should be ventilated and neuroprotected
- Children with the following to be discussed with paediatric neurosurgical centre with expertise in surgical revascularisation
    - Child with diagnosed Moya moya disease,
    - Child with other known progressive cerebrovascular disease.

2.4 Acute medical interventions for AIS confirmed:

a) Thrombolysis:

- strongly considered in children > eight years of age with AIS
- may consider in children ≥ two and ≤ eight years of age on a case by case basis
- Thrombolysis therapy would also be at the discretion of clinicians and parents

Criteria for Thrombolysis therapy:
Tissue plasminogen activator: (tPA) could be used for selected group of patients as given below

- Clinical & Radiological Criteria (as above) confirmed Arterial Ischaemic Stroke
- Acute focal neurological deficit consistent with arterial ischaemia
- PedNIHSS score ≥ 4 and ≤ 24
- Within 4.5 hours of onset of symptoms at beginning of Thrombolysis
- There should not be any contraindications to thrombolysis (see Appendix-9)

Patient should be nursed in high dependency area (HDU) in either Emergency department at LRI or in the HDU Paediatric unit in ward 12.

Activase® (alteplase) [tPA] (Appendix 8)

- Recommended treatment dose of Activase: 0.9 mg/kg (not to exceed 90 mg total treatment dose) to be infused over 60 minutes.
- 10% of the total treatment dose should be administered as an initial bolus over duration of 1 minute
- The remaining treatment dose should be infused intravenously over period of 60 minutes

b) Use of Anti-Thrombotic therapy: when criteria for Thrombolysis not met:

Contact Adult Haematology Registrar (mobile: 07950 867412 between 9 am – 5 pm) or through Switchboard during out-of-hours

(Team is being overseen by Haematologists S Salta (Consultant) L Sanders (Consultant) and team aware of quick correct up to date advice for Paediatric Anticoagulation Management)

In children with cardiac disease presenting with AIS, MDT discussion with Haematologist, cardiologist and paediatric neurologist is recommended.

For all other cases the following are recommended:

(i) Aspirin: Aspirin 5mg/kg (up to max 300mg) within 24 hours of diagnosis of AIS in the absence of contraindications (e.g. parenchymal haemorrhage); this is to be reduced to 1mg/kg to a max of 75mg after 14 days. Please note the following;

- Delay administering aspirin for 24 hours in patients where thrombolysis has been given.
- Aspirin should not be routinely given to children and young people with SCD presenting with AIS.

(ii) Clopidrogel: if needed dual anti-thrombotic therapy, Clopidrogel to be considered following discussion with haematologist and paediatric neurologist.

Age	<2 years	0.2 mg/kg ONCE daily
	>2 years	1 mg/kg ONCE daily

Note: Liquid form needs to be ordered for each case & then ongoing from the hospital

c) Anticoagulant therapy:

Might be needed in the circumstances below: [Appendix 4]

- Patients with recognized source of embolism (e.g. cardiac lesion)
- Patients with cerebral venous sinus thrombosis
- Patients with extracranial arterial dissection
- Patients with recurrent focal Ischaemic events even on Aspirin

(i) LMW Heparin: Usually preferred because:

i. more predictable pharmacokinetics than UFH;
ii. reduced need for frequent monitoring tests

Treatment dose: 100u / kg / dose - twice a day and monitored by Heparin Assay, therapeutic range is 0.4 - 1.0 u/ml.

(ii) Unfractionated Heparin: Recommended doses are as follows:

Loading dose = 75u/kg over 20 minutes
Maintenance dose = 25u/kg/hour for children under 1 year of age
Maintenance dose = 20u/kg/hour for children over 1 year of age

Monitored by APTT ratio: Check APTT ratio after 4 hours, aiming to achieve a ratio of 2 - 2.5 times control i.e. 50 - 80 seconds. Unfractionated heparin can be reversed more reliably than LMW heparin

3. HAEMORRHAGIC STROKE (HS) in children and Child-in-Neonatal age group (outside neonatal unit)

- **Risk Factors of Haemorrhagic Stroke** [Appendix – 5]
- **Investigations to identify underlying risk factors in HS**: [Appendix –6]

3.1 Acute medical interventions for HS:

- Check routine coagulation parameters in all children and young people presenting with HS.
    - Prothrombin time (PT),
    - Partial thromboplastin time (PTT),
    - Fibrinogen and
    - Full blood count (FBC)

- Abnormal results should be discussed with a Paediatric Haematologist (or Adult Hemostasis Consultant On call) in order that appropriate investigations can be carried out urgently to ascertain whether a coagulation abnormality is primary or secondary.
- Coagulation should be corrected prior to Neurosurgery, if surgery deemed necessary
- Liaise with Paediatric Haematologist (or Adult Hemostasis Consultant On call) about children and young people with an underlying inherited bleeding disorder (such as severe haemophilia) who have an intracerebral bleed in HS.
- Focus on maintaining normal levels of the appropriate coagulation factor for a period of intense treatment and then prophylactic treatment to prevent recurrence.
- Consider Nimodipine (see BNFc for dosing) to prevent the effects of vasospasm in children and young people with subarachnoid haemorrhage – consider liaising with Haematologist & Paediatric Nephrologist

3.2 Surgical and endovascular interventions for HS:

Needs to be discussed with Neurosurgical team on-call as mentioned above.

Neurosurgical management of HS

- Children and young people with HS, individuals with any structural vascular lesions underlying an ICH (most commonly AVM, aneurysm or cavernous malformation) should always be discussed with a neurosurgical team.
- ICH is not routinely evacuated in children and young people, except in cases where there is a rapidly deteriorating age-appropriate Glasgow Coma Scale (GCS) score.
- Treat lesions at higher risk of early re-bleeding urgently (e.g. ruptured aneurysms, arterio-venous malformations with high risk features)

Interventional Neuroradiology:

- This service does not have 24 hours cover.

- Can try contacting Interventional Radiologist at QMC Nottingham via switchboard as mentioned above & discuss patients with acute HS and vascular lesions.

4. Management of on-going care of child with stroke - Key Considerations:

- Clinical area: HDU / Paediatric ITU as clinically appropriate for the child.

- Wards & team of nurses to be informed to take stroke patient, give detailed hand over & inform their management plan

- Standards of care & observations:

    - Needs Hourly Neuro-observation for next 12 hours; close neurological monitoring for 48 hours
    - Monitor GCS / AVPU score: Intubate if GCS < 8, AVPU = U,
    - Monitor BP; Temperature, HR, RR, Oxygen saturation (target > 92%);
    - Hydration and Nutrition – Clinician & Dietician
    - Swallow safety - withhold oral feeding until assessed by Speech Therapist
    - Pain management - Clinician
    - Motor function (Physio & OT)
    - Sensation and Perception (OT)
    - Sleep & fatigue
    - Vision and Hearing
    - Maintain fluid balance / Intake-Output, glucose, electrolyte homeostasis
    - Treat any Seizure as per APLS protocol
    - Consider to treat hypertension as per Hypertension Guideline

Step down of clinical monitoring to be decided on the basis of above assessment.

5. Education and Training

- Departmental joint educational meeting to provide update, support and aid in the guideline implementation
- Ensure this guideline and accompanying materials, reach the end users & all confirmed stakeholders
- The guideline should be available to adult stroke professionals who agreed that cases may be discussed with Adult Stroke Team in Leicester in case of adolescent individual AGE>12 years confirmed case of Arterial Ischaemic Stroke or cases considered to be referred for Neuro-surgical and Endovascular interventions or considered for referral to interventional neuroradiology.
- Training in the use of the following assessment tools should be provided:
    - FAST **www.stroke.org.uk/FAST**
    - PedNIHSS **https://www.mdcalc.com/pediatric-nih-stroke-scale-nihss** & **http://stroke.ahajournals.org/content/42/3/613**
    - Clinical investigation (see appendices)
    - Specific medication and/or intervention protocols (e.g. aspirin, thrombolysis, anticoagulation, thrombectomy and decompressive surgery).

6. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
All childhood stroke cases treatment and outcomes	Departmental audit	R Samanta	Annual	M&M clinical audit meeting

7. Supporting References

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8. Key Words

Antithrombolytic, Arterial Ischaemic Stroke (AIS), Cerebral, Cerebral Arteriopathy, Cerebrovascular, Haemorrhagic Stroke (HS), Hemiplegia, Moyamoya, Neurological**,** Paediatric Stroke, Sickle Cell Disease, Thrombolysis, Transient Ischaemic Attack (TIA), Venous Sinus Thrombosis

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead (Name and Title) Rajib Samanta – Paediatric Consultant Neurologist	**Executive Lead** Chief Medical Officer
Details of Changes made during review: **29/09/2023 v2** **Update of Adult haematology Consultant contacts** **Updated Neurosurgical and Neurointerventional radiology contact details** **Discussion with Neonatal team, agreed for "Child-in-Neonatal" age group(outside neonatal unit)**	

Appendix 1: PedNIHSS Assessment Scale

Item# and Instructions	**Scale Definition and Scoring Guide**
1a. Level of Consciousness:	0 = Alert; keenly responsive. 1 = Not alert, but rousable by minor stimulation to obey, answer, or respond. 2 = Not alert, requires repeated stimulation to attend, or is obtund and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.
1b. LOC Questions: ***Modified for children, age 2 years and up. A familiar Family Member must be present for this item:***	0 = Answers both questions correctly. 1 = Answers one question correctly. 2 = Answers neither question correctly
1c. LOC Commands:	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2. Best Gaze:	0 = Normal 1 = Partial gaze palsy. This score is given when gaze is abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present. 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.
3. Visual:	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (blind including cortical blindness)
4. Facial Palsy:	0 = Normal symmetrical movement 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face)
5 & 6. Motor Arm and Leg: ***For children too immature to follow precise directions or uncooperative for any reason, power in each limb should be graded by observation of spontaneous or elicited movement according to the same grading scheme, excluding the time limits.***	**5a. Left Arm 5b. Right Arm** 0 = No drift, limb holds 90 (or 45) degrees for full 10 seconds. 1 = Drift, Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = No effort against gravity, limb falls. 4 = No movement 9 = Amputation, joint fusion explain:
	6a. Left Leg 6b. Right Leg 0 = No drift, leg holds 30 degrees position for full 5 seconds. 1 = Drift, leg falls by the end of the 5 second period but does not hit bed. 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. 3 = No effort against gravity, leg falls to bed immediately. 4 = No movement 9 = Amputation, joint fusion explain:
7. Limb Ataxia: ***In children, substitute this task***	0 = Absent 1 = Present in one limb

with reaching for a toy for the upper extremity, and kicking a toy or the examiner's hand, in children too young (< 5 years) or otherwise uncooperative for the standard exam item.	2 = Present in two limbs
8. Sensory: ***For children too young or otherwise uncooperative for reporting gradations of sensory loss, observe for any behavioral response to pin prick, and score it according to the same scoring scheme as a "normal" response, "mildly diminished" or "severely diminished" response.***	0 = Normal; no sensory loss. 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware he/she is being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.
Best Language: ***For children age 6 years and up with normal language development before onset of stroke: The patient is asked to describe what is happening in the attached picture , to name the items on the attached naming sheet, to repeat words from the attached list, and to read from the attached list of sentences (Table S1; Fig S1, S2, S3).*** ***For children age 2 yrs to 6 yrs (or older children with premorbid language skills < 6 yr level), score this item based on observations of language comprehension and speech during the examination.***	0 = No aphasia, normal 1 = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided material difficult or impossible. For example in conversation about provided materials examiner can identify picture or naming card from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory
10. Dysarthria:	0 = Normal 1 = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. 9 = Intubated or other physical barrier, explain:
11. Extinction and Inattention (formerly Neglect):	0 = No abnormality. 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.

Table S1. Language testing items for PedNIHSS

Table S1. Language testing items for PedNIHSS: Repetition	Each of 4 word-repetition tasks is presented: a. Stop b. Stop and go c. If it rains we play inside d. The President lives in Washington
Reading	Each of 3 items is presented for the child to read in Fig 1. Adjust expectations according to child's age/school level
Naming	Pictures are presented and of a clock, pencil, skateboard, shirt, baseball, bicycle (Fig 2).
Fluency and word finding	The picture (Fig 3) is presented and the child is asked to describe what he/she sees.

Fig.1 Reading items for PedNIHSS

Stop

See the dog run

Little children like to play outdoors

Fig. 2 Pictures to test naming for Item 9 Best Language of PedNIHSS

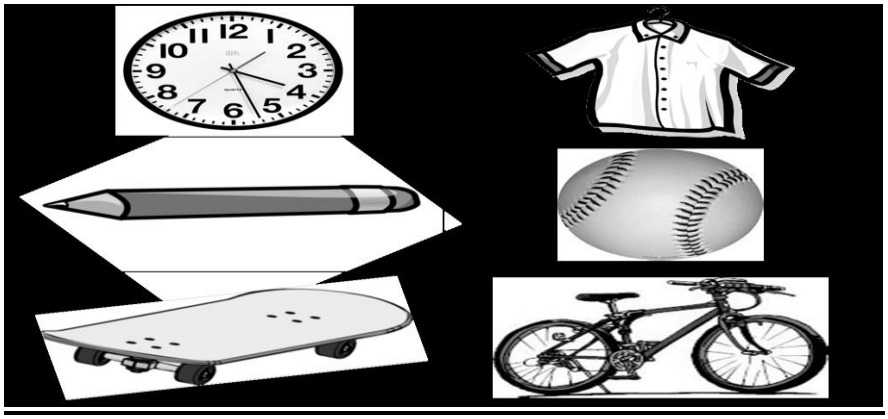
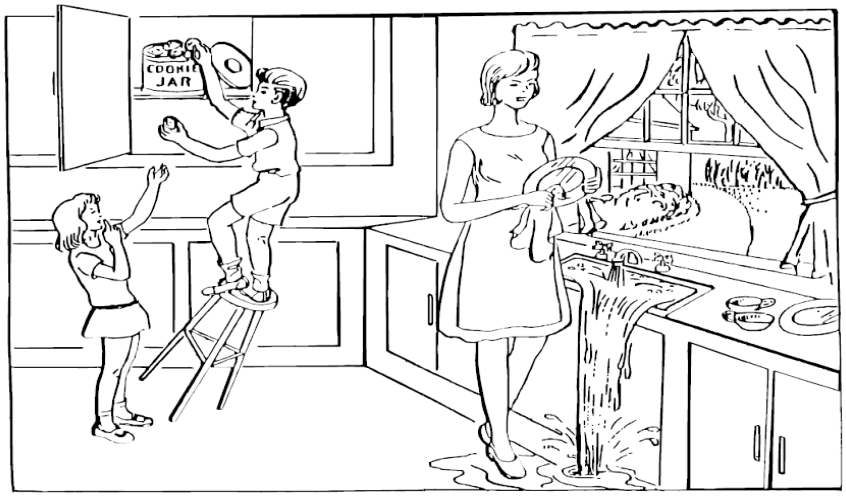


Fig. 3 Picture to test story-telling for Item 9 Best Language of PedNIHSS



Appendix 2: Investigations – Arterial Ischaemic Stroke

On admission Next day

Investigations:	Type of Sample
Haematology: On admission- Full blood count, Haemoglobinopathy screen, Blood Film Next day- Plasma Viscosity	EDTA
Haematology: Coagulation profile On admission- INR, PT, APTT, Fibrinogen	Green top
Biochemistry On admission- U&Es, LFT, Bone profile, Mg, TFT, Lab Glucose, Lipid Profile Next day- Lactate , Ammonia, CK, Lipoprotein(a), Iron, Ferritin, total iron binding capacity.	Yellow top (on ice) Orange top (on ice) Yellow top White/brown top
Biochemistry: Next day-Vit-D, Vit-B12, Folate	White
Special Biochemistry: Next day- Transferrin Glycoform, Homocysteine, Carnitine profile, Alpha Galactosidase Next day- Urine Organic Acid, Bedside dip stix, Protein, Sugar	White top Orange top EDTA
Special Haematology: Next day- Lupus anticoagulant - repeat after 12 weeks if found +ve Next day– special haematology Thrombophilia screen- Protein C & S, Antithrombin-3, Factor V Leiden mutation, Prothrombin gene mutation	Green top Green/EDTA
Immunology: Next day- Anti-Cardiolipin Ab, beta 2 GlycoProtein Antibodies, ANCA, Phospholipid Ab, Anti TPO, ANA repeat after 12 weeks if found +ve Next day- Antibody titres- Herpes Simplex, Varicella, Mycoplasma, Chlamydia pneumoniae, Helicobacter pylori, Borrelia Burgdorferi,	White top
Cardiac evaluation: ECG – 12 leads - Within 48 hrs Echocardiogram (to identify structural lesions and R to L shunts) Transcranial Doppler in patients with SCD	

Stroke Investigations to be done in Child-in-Neonatal age group (outside neonatal unit)

- Maternal blood investigations
- Full coagulation profile, Fibrinogen
- Thrombophillic tests: Protein C, protein S, Antithrombin III
- Lipoprotein (a), Homocysteine
- Anti-phospholipid and Anticardiolipin antibodies, Lupus anticoagulant
- Factor V Leiden (FVL), Beta 2 glycoprotein and Prothrombin gene mutation

Appendix 3: Aetiology of Arterial Ischaemic Stroke (AIS): Risk factors for first AIS:

Risk Category	Included factors/diagnoses
Arteriopathy	Focal cerebral arteriopathy of childhood Moyamoya Arterial dissection Central nervous system Vasculitis Henoch-Schonlein Purpura, PolyArteritis Nodosa, Kawasaki disease
Cardiac disease	Congenital cardiac disease, Children and young people with acquired cardiac disease: Right to Left shunt, Increased Lipoprotein(a), Anticardiolipin antibody (ACLA), Combined prothrombotic disorders
Cardiac surgery/interventions	History
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, High Reticulocyte Count, Silent infarction Prior Transient Ischaemic Attack, High Systolic Blood Pressure, Acute Chest Syndrome
Infection	Varicella infection, Upper resp tract infection, Multiple infections
Gender / ethnicity	Black ethnicity, Asian ethnicity, Male gender
Thrombophilia	Genetic: Factor V Leiden (FVL), PT20210, MTHFR c677T, Protein C deficiency, increased Lipoprotein(a) (Lp(a)), more than 2 genetic Thrombophilia traits, High Homocystinuria (HCY), Acquired: Antiphospholipid syndrome
Miscellaneous	Iron Deficiency Anaemia, Radiotherapy, High Alpha-1 Antitrypsin (AT), Trauma, Under-vaccination, Multiple factors
Metabolic	Fabry disease in children and young people
Conditions may be clinically important in relevant cohorts	Trisomy 21, Neurofibromatosis, Malignancy, long-term effects of treatment for malignancy (especially cranial radiotherapy) Auto-immune diseases, e.g. systemic lupus erythematosus Substances of abuse / recreational drugs (e.g. cocaine)

❖ Risk factors for neonatal AIS

- Maternal and neonatal factors- e.g. recurrent miscarriages in maternal anti-phospholipid antibodies or similar e.g. maternal SLE and lupus anti-coagulant.
- Activation of coagulation factors in mother and triggering the same in infant just before and after the time of delivery may contribute to increased risk of stroke.
- Inherited thrombophilia in Neonates
- Other risk factors include cardiac lesions, coagulation disorders, infection, trauma, and asphyxia

- Porencephaly and intrauterine stroke linked to Col4A1 mutation subunit of type IV collagen. Mutations in Col4A1 should be considered in neonates with cerebral hemorrhage, porencephaly, glaucoma, and/or cataracts

❖ **Risk factors for Recurrent Arterial Ischaemic Stroke:**

- Arteriopathy (metabolic or post-infective aetiology if progressive on interval imaging)
- Moya moya disease
- Arteriopathy in Sickle Cell Disease
- Congenital heart disease (especially if either infection was present at sentinel stroke or if there is a thrombotic state)
- Thrombophilia (e.g. homozygosity for MTHFR mutation, protein C and/or protein S deficiency)
- Low birthweight/ Prematurity

APPENDIX 4: Anticoagulant therapy and Monitoring:

The groups of patients in whom anticoagulation may be considered are: [23]

- Patients with a recognised source of embolism (e.g. cardiac lesion)
- Patients with cerebral venous thrombosis
- Patients with extracranial arterial dissection
- Patients with recurrent focal ischaemic events on aspirin

Low Molecular Weight (LMW) heparin:

LMW heparin has almost 100% bioavailability compared to unfractionated heparin, which binds to plasma proteins. For this reason, LMW heparin has both a more predictable antithrombotic effect with fewer bleeding complications (Counsell 2000). LMW heparin also has a longer half-life compared to unfractionated heparin. Consider insertion of an indwelling subcutaneous device (Insufflon) to minimise trauma to the child.

Treatment dose:	LMW heparin 100u / kg of Dalteparin Sodium twice a day.
Monitoring of treatment:	By performing Heparin Assay Blood should be taken 4 hours after the morning dose to measure the level of LMW heparin. (On request form, please request HEPARIN ASSAY and state the type of heparin i.e. Dalteparin and the time that the last dose was given & please ring Extn 7531 to alert Special Haematology)
Therapeutic range:	0.4 – 1.0 u/ml. This is rarely achieved in the initial days of therapy but the drug is cumulative. If levels are very low, the dose can be increased by 25%. It is unusual for further increments in dose to be necessary.
Platelet count:	should also be monitored in order to detect heparin induced thrombocytopenia, although this is extremely rare in children.

Monitoring for Heparin Induced Thrombocytopaenia
- If exposed to heparin within the previous 100 days

Check FBC within 24 hours of starting the heparin, then on alternate days until day 14.
- If not exposed within the last 100 days

Check FBC on alternate days from days 4 -14 of starting heparin

For most patients there is no need to monitor therapy. The exceptions to this are:

- patients with body weight < 40kg
- patients with renal impairment (CrCl < 30ml/min)

LMW Heparin is recommended where possible for the reasons outlined above. However, for patients at high risk of haemorrhage (e.g. venous thrombosis in a patient with AVM) it is preferable to use unfractionated heparin for rapid reversal in the event of a haemorrhage.

Unfractionated heparin:
It has to be given intravenously and therapy needs to be monitored using the APTT ratio. Unfractionated heparin can be reversed more reliably than LMW heparin.

Recommended doses of unfractionated heparin are as follows:
- loading dose = 75u/kg over 20 minutes
- maintenance dose = 20u/kg/hour for children over 1 year of age
- maintenance dose = 25u/kg/hour for children under 1 year of age

Monitoring treatment:
Check the APTT ratio after 4 hours, aiming to achieve a ratio of 2 - 2.5 times control i.e. 60 - 80 seconds.

Adjustment of Heparin Dose:

APTT (s)	Bolus (u/kg)	Hold (min)	Rate change (u/kg/h)	Repeat APTT
<50	50	0	Incr by 20%	4 hours
50-59	0	0	Incr by 10%	4 hours
60-85 (target range)	0	0	0	24 hours
86-95	0	0	Decr by 10%	4 hours
96-120	0	30	Decr by 10%	4 hours
>120	0	60	Decr by 15%	4 hours

Warfarin

Where the decision is made to initiate medium to long-term anticoagulation, warfarin is recommended. Timing of initiation of warfarin needs to be decided on an individual basis. There is some logic to delaying this for a few days as; theoretically, warfarin will reduce levels of protein C and S.
Warfarin is relatively contraindicated in infants under 1 year of age; therapeutic anticoagulation is difficult to achieve with warfarin in milk fed infants. If anticoagulation is to be used in this age group LMW heparin may be recommended. All cases should be discussed with a haematologist.

The recommended loading dose of warfarin is 0.2mg/kg. On days 2 - 4, the recommended dose relative to the INR is given below:

INR	Dose of warfarin
1.1 – 1.3	0.2mg/kg
1.4 – 3.0	0.1mg/kg
3.1 – 3.5	0.05mg/kg
>3.5	Withhold for 1 day and then restart at 50% previous dos

The target INR is usually in the range 2 - 3; however, in particular "high risk" patients, it may be desirable to maintain the INR in the range 3 - 4. This will need to be decided on an individual basis.
It is best to arrange monitoring of the INR through the local anticoagulation service if possible as

this is much more practical for the child and family. This can be done by referring the patient to the Consultant Haematologist responsible for the local service.

Appendix – 5 : Risk factors for First HS:

Risk factors	Included factors / diagnoses
Vascular disorders	AVM, with arterial phase aneurysms, varicosities or venous stenoses on the draining veins cavernous malformations, especially Zabramski type 1 & 2 cerebral arterial aneurysms moyamoya
Clotting disorders	severe platelet disorders/low platelet count all severe inherited bleeding disorders anticoagulation severe vitamin K deficiency
Sickle Cell Disease	
Illicit Drug Use	Amphetamine Cocaine
Gender / Ethnicity / Age	Age 15-19 years Black Ethnicity Male Gender
Information on risk factors should be delivered in face-to-face conversation with parents/carers and young people (where appropriate) and supported where possible with web-based or written materials for later reference. The information provided should be age-appropriate and multi-format.	

- **Risk factors for Neonatal Haemorrhage (ASA/AHA guidelines for Neonatal and Childhood Stroke)**

- Coagulopathy, thrombocytopenia, trauma and, rarely, structural vascular lesions
- Post-maturity, emergency caesarean delivery, fetal distress, and male gender
- Mutations in Col4A1 should be considered in neonates with cerebral hemorrhage, porencephaly, glaucoma, and/or cataracts
- Some hemorrhagic lesions, such as periventricular hemorrhagic venous infarction, may represent hemorrhagic conversion of an arterial or venous infarction
- Acquired or congenital/hereditary coagulopathy including Haemophilia A and others.
- Hemorrhagic disease remains problematic in areas of the world where supplemental vitamin k not routinely administered to newborns
- Breastfeeding infants may also develop vitamin k deficiency
- Babies whose mothers ingested warfarin, phenytoin, or barbiturates during pregnancy sometimes develop a vitamin k-related coagulopathy

- **Risk factors for recurrent HS:**

Be aware of increased risk of recurrence in children/young people with HS and the following risk factors	Arteriovenous malformation (AVM), Cerebral arterial aneurysms, Cavernous malformations, Moyamoya, SCD, All severe bleeding disorders, Ongoing anticoagulation, Illicit drug use e.g. amphetamines and cocaine
Be aware that in arteriovenous malformations, which have already bled	The greatest risk of a re-bleed is from the part of the malformation which was responsible for the initial haemorrhage. Intranidal /perinidal aneurysm, venous varicosiy/stenosis are sinister features

APPENDIX 6: Investigations to identify underlying risk factors in HS:

Category	Investigations
Haematological investigations:	• coagulation screen including activated partial thromboplastin time (aPTT), prothrombin time (PT), fibrinogen (taken by a free-flowing venous sample), full blood count (FBC), haemoglobinopathy screen. • discuss any abnormality of these haematological tests with a paediatric haematologist so that they can advise on further testing including specific clotting factor assays. • establish whether the parents are consanguineous to suspect rare severe recessive bleeding disorders that cannot be ruled out with a normal blood count and coagulation screen.
Imaging Investigations:	• discuss the child's case in a neurovascular multidisciplinary team (MDT) to plan further investigations to identify/exclude underlying vascular malformation; • plan any interventional treatment; • such investigations may include non-invasive angiography such as computed tomography angiography (CTA) or MRA, as well as formal catheter angiography (CA)
If the child is known to have SCD, additional tests should include TCD and an extended blood group phenotype (e.g. ABO, Rh C, D and E, and Kell).	

Appendix 7: Treatment of Acute AIS & Interventions to prevent recurrent AIS

Treatment of Acute AIS in child with sickle cell disease (SCD)

- Team should work closely with Consultant Haematologist Dr Kaljit Bhuller & Blood bank to ensure that appropriate blood is available as soon as possible.
- No RCT / large studies assessing acute management of stroke in SCD were identified by the systematic review; therefore, following recommendations are based on the consensus of the GDG.
- Acute management is focused on reducing percentage of HbS in the blood and correcting anaemia.
- Exchange transfusion is usually necessary to achieve this, unless the patient is severely anaemic, when a simple transfusion can be adequate.
- Treat children/young people with sickle cell disease (SCD) and acute neurological signs or symptoms urgently with a blood transfusion, to reduce the sickle haemoglobin (HbS) to less than 30%, and increase the haemoglobin concentration to more than 100–110g/l. This will usually require exchange transfusion.

Medical interventions to prevent recurrence of AIS

- Continue antithrombotic treatment initiated acutely in children and young people with AIS. Reduce dose of aspirin from 5mg/kg to 1mg/kg after 14 days.
- Treat all children, young people with AIS with aspirin, unless they have SCD or are receiving anticoagulation e.g. for a cardiac source of embolism.
- Maintain adequate levels of hydration in patients with occlusive arteriopathies including moyamoya, especially when fasting or during intercurrent illness.
- Clopidogrel - It can be considered in older children in discussion with the neurologist/haematologist. Documented dose in the literature is 1 mg/kg per day up to the maximum of 75 mg
- Anticoagulant therapy: [Appendix – 4] Using Low Molecular Heparin should be considered in the following groups of patients for secondary prevention are: [23]
    - Patients with a recognised source of embolism (e.g. cardiac lesion)

- Patients with cerebral venous thrombosis
- Patients with extracranial arterial dissection
- Patients with recurrent focal ischaemic events on aspirin

The recommended duration of anticoagulation in extra-cranial dissection is 3-6 months [24]. In children with a risk of cardiac embolism, it is reasonable to continue either LMWH or warfarin from 6 month up to 1 year or until the lesion responsible for the risk has been corrected [24]. If the risk of recurrent embolism is judged to be high, it is reasonable to continue anticoagulation indefinitely as long as it is well tolerated.

Prevention of recurrence of AIS 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.
- Monitor children with regular neurocognitive testing, MRI and transcranial doppler ultrasonography (TCD); frequency should be determined on a case-by-case basis.
- 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).

Appendix 8: Alteplase information

Altepase – detailed guidance (pdf)
https://www.gene.com/download/pdf/activase_prescribing.pdf

Altepase – Dose & administering guidance:
https://www.activase.com/ais/dosing-and-administration/dosing.html

Refer to Childrens Medusa Monograph and BNFC for detailed information on prescribing, administration and side effects

Appendix 9: Contraindication of Thrombolysis:

Absolute Contraindication:

- Large infarct volume, on CT / MRI involving ≥ one-third of affected cerebral hemisphere. [In contrast to the subtle radiographic signs of early ischemia, frank hypodensity on CT reflects more severe and irreversible brain injury and increases the risk of hemorrhagic transformation] = pre-tPA PedNIHSS score > 24
- History of prior intracranial haemorrhage
- Clinical suspicion of subarachnoid haemorrhage, though neuro-image is negative
- Diagnosed cerebral arterial venous malformation, aneurysm or neoplasm
- Intracranial haemorrhage on pre-treatment head CT and MRI
- Intracranial dissection
- Stroke due to Subacute Bacterial Endocarditis (SBE), Moyamoya, Sickle Cell Disease (SCD), Meningitis, bone marrow, air, or fat embolism
- Uncontrolled hypertension - see Hypertension UHL Childrens Guideline
- History of stroke, major head trauma, or intracranial surgery < three months
- History of Central Nervous System (CNS) vasculitis.
- Thrombocytopenia; platelets < 100

- Coagulopathy; PT >15 sec, INR > 1.7, or APTT > upper limits of the normal
- Known allergy to recombinant tissue plasminogen activator
- Patient received heparin <four hours – needs APTT to be in in normal range
- Low molecular weight heparin (LMWH) < 24 hrs (APTT & INR will not reflect LMWH effect)
- Patient with malignancy or within one month of completion of treatment for cancer
- Patients with underlying significant bleeding disorder. (Patients with a mild platelet dysfunction, mild von Willebrand disease, or other mild bleeding disorders are not excluded)
- Patients anticoagulated with oral factor Xa inhibitors apixaban or rivaroxaban
- Clinically consistent with acute MI/post-MI pericarditis, needs cardiac assessment before treatment

Relative Contraindication:

- Seizure at onset of stroke symptoms with residual postictal state
- Unknown time of symptoms onset
- Pregnancy
- Patient who would decline blood transfusion if indicated
- Glucose less than 2.78 mmol/L or more than 22.22 mmol/L
- Major surgery or parenchymal biopsy within 10 days
- Gastrointestinal or urinary bleeding within 21 days

Arterial puncture at non-compressible site or LP within seven days. [Patients who had cardiac catheterization via a compressible artery are not excluded]