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NEUROZENTRUM
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Inselspital Universitätsspital Bern
Universitäre Psychiatrische Dienste Bern

Neurochirurgie
Neurologie
Neuropädiatrie
Neuroradiologie
Psychiatrie

www.strokecenter.ch **Version 09/2021**

Pediatric Stroke Guidelines

of the Bern Stroke Network

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Stroke Team Bern

Physicians on duty	Phone Numbers	Miscellaneous	Phone Numbers
Pediatric Neurology		Resuscitation (CPR)	
Emergency Department		Laboratory results	
Neurology		Bed scheduling	
Neuroradiology		Stroke Unit	
Neurosurgery			
Radiology			
Intensive Care Unit			
Cardiology			

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Apps by Stroke Center Bern


Stroke Guide


StrokeClock


Stroke Amb

Links to additional documents including pediatric stroke guidelines
www.strokecenter.ch **https://snpsr.neuropaediatrie.ch/**

Ambulance Guide

Case history	Diagnostics
• Symptom onset or last-seen-well time • Previous history/medication? • Pacemaker/artificial heart valve? • Phone number of GP/next of kin	• ABC scheme • Glucose • Temperature • GCS

Triage

See chapter on patient triage
Early information transmitted to Emergency Department and Pediatric Neurology to decide triage, fastest transportation to pediatric Stroke Center Bern.

Position

→ Supine position – if not possible max. 30°

Therapy

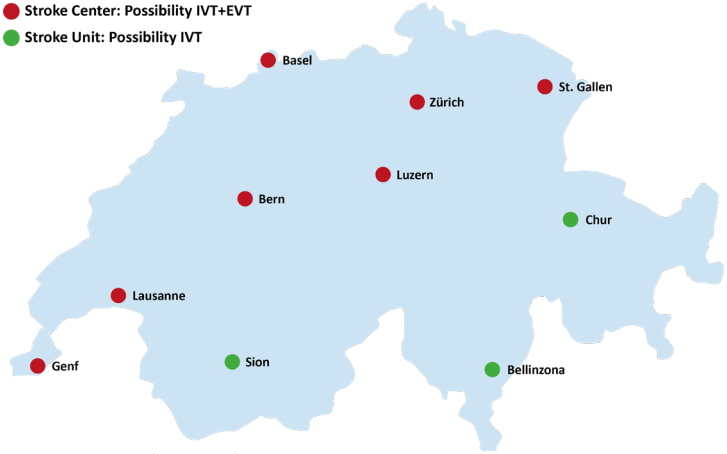
→ Venous line
→ O_2-Saturation > 92%
→ BP Aim: BP systolic and diastolic normal to max. P95
→ **WARNING** Do not administer aspirin, heparin or similar medication

Patient triage

Symptom onset < 4.5h	→ Admit to nearest Stroke Center **In University Hospital, Inselspital Bern** → Triage directly to adult's emergency department Registration is done by the ped. emergency senior physician 8110.
Symptom onset 4.5-24h	→ Admit to nearest Stroke Center **In University Hospital, Inselspital Bern** → Triage directly to adult's emergency department Registration is done by the ped. emergency senior physician 8110.
- Unclear symptom onset **- Wake-up stroke** **- Patient under (D)OAC** **- Contraindication for IVT**	→ Admit to nearest Stroke Center **In University Hospital, Inselspital Bern** → Triage directly to adult's emergency department Registration is done by the ped. emergency senior physician 8110.
Symptom onset > 24 h	→ Admit to nearest Stroke Center or Stroke Unit **In University Hospital, Inselspital Bern** → Triage directly to children's emergency department

Stroke Unit: availability of IVT
Stroke Center: availability of IVT + EVT
IVT: intravenous thrombolysis, EVT: endovascular treatment

Swiss Stroke centers and units



In Hospital Stroke

Alerting to:

Monday to Friday 07:30-17:00:	**Senior Neuropediatrics 40731**
Nighttime and Weekend:	Duty physician Pediatrics (via Intern-Phone-Number 6543) / Intensive care 6555 Duty physician Neuropediatrics 40731 / 079 652 87 42

- Senior Neuropediatrics resp. senior pediatrics goes to the patient immediately
- Monitoring of BP/pulse by monitors of the department of the corresponding ward
- Accompaniment and monitoring (also in the MRI if necessary) by the nursing staff and physicians of the corresponding ward or anesthesia (*8555), if necessary.
- Preparation of Actilyse® is done on instruction of Neuropediatrics, by nursing staff of the stroke unit: 5887

Hospital phase

be SAFE **STROKE PATH**

F A S T

Registration	**Name, Birth date, Symptoms, Symptom Onset. ABCDE. Arrival Time**
Prenotification	**Emergency OA/OAe Children's Hospital 181 8110 and UNZ 031 632 8327** **Organizes all other disciplines according to KiJu alarm scheme Shock room (Team B Neuro)** • Neuropediatrics 40731 / 079 652 87 42 • Neuroradiology *6200 • Senior Pediatric Intensive Care *6555 (24-8h) • Anesthesia *8555 • Senior Neurology *6009
Transport to	**If referral suspected stroke (paramedic, pediatrician)** • Direct transport to Stroke Center adult emergency (triage by Senior Pediatric Emergency). **If presentation on pediatric emergency/adult emergency:** • Examinations (ped-NIHSS etc. see below) directly on site, rapid transfer to MRI/CT
ED arrival	**History** • Leading symptom • Time of symptom onset • Medications (OAC/heparins?) • History, infections, varicella • Pre-existing conditions, trauma • Pacemaker/artificial valve? • Telephone number of referring physician + relatives **Management** • Supine Position, if not possible max. 30° • i.v. access (note: supply minimal volume) • Fever (fever reduction/ DD endocarditis?) • Neurological examination: pedNIHSS • Laboratory: blood count, CRP, sodium, potassium, glucose, creatinine, coagulation (Quick, aPTT, fibrinogen) • ECG, blood pressure measurement
CT or MRI 28272 / *6200	**- MRI, except in** Pacemaker, Implants not MR compatible - For children < 7years., Patient agitated or unstable: request anesthesia*8555
MRI priority?	**Priority 1** ASAP IVT/EVT indication Symptom onset <12h **Priority 2** within 20 min Presumably no IVT/EVT indication Symptom onset 12– 24h **Priority 3** within 3h TIA > 2h otherwise S2 Symptom onset > 24h

max. 10'

Arrival CT/MR	**MR questionnaire**
Monitoring MR	**HR, BP during MRI, ped-NIHSS after exiting the MRI**
Therapy decision	• Rapid therapy decision (Lead Senior Neuropediatrics) • Informing parents (Senior Neuropediatrics or delegated to Senior Pediatrics) • Usually do not wait for laboratory results • Before lysis, check BP (BP target: BP systolic <P99 for age and size). • After starting IVT or before angio: collect pedNIHSS completely

max. 15'

After Stroke-Detection	Complement coagulation (thrombin time, D dimers), ASAT, ALAT, lactate, ammonia, Consider: Lumbar puncture (WARNING contraindication until 24 h after IVT!), evaluate varicella serology (especially in focal arteriopathy!).
IVT/EVT	**IVT** Start in MR/CT **EVT** Handover patient to interventionalist + anesthesia in Neuroangiography
Aftercare	**Always performed in the pediatric intensive care unit after intervention. Otherwise also possible in a normal ward.**
Monitoring in intensive care	**Regular BP checks (see chapter Monitoring in Pediatric Intensive Care Unit).**

Indications and choice of therapy

Symptoms
Ped-NIHSS Score ≥ 4
or
Ped-NIHSS < 4 with relevant deficits (e.g. aphasia, hemianopia, distal paresis, etc.)
or
Consider in case of minor deficits and/or rapidly improving symptoms with persistent vessel occlusion

+

Vessel occlusion	Time & imaging results: < 4.5 Treatment irrespective of core-perfusion mismatch	4.5 - 9 h Usually independently of core-clinical mismatch or core-perfusion mismatch	Wake up/ Unknown onset/ 9h - at least 24h: In case of core-clinical mismatch or core-perfusion mismatch
ICA, Carotid-T, M1, M2	IVT/EVT (Bridging)	EVT[§]	EVT if mismatch[*§]
P1, A1, VA	IVT + consider EVT	EVT or IVT if mismatch[#]	EVT if mismatch[*§]
M3/4, P2, A2	IVT evt. Actilyse i.a.	IVT if mismatch[#] or Actilyse i.a. until 6h	IVT if mismatch[#]
BA	IVT/EVT (Bridging)	EVT[§]	evt. EVT[§]
No vessel occlusion	IVT	IVT if mismatch[#]	IVT if mismatch[#]
Spinal ischemia	IVT	IVT until 6h possible	

< 1 year indication for thrombectomy may be taken restrictively

* **core-perfusion-mismatch** or **core-clinical mismatch** (e.g.: ped-NIHSS ≥ 10 and MCA territory)

 # core-perfusion mismatch (core < 70mL, mismatch Ratio >1.2) or **DWI-FLAIR mismatch** (without or only minor FLAIR demarcation of the DWI lesion).

§ if EVT cannot be performed due to technical/anatomical reasons: consider IVT also in case of large vessel occlusion > 4.5h after symptom onset in case of mismatch (see #)

IVT: intravenous thrombolysis, EVT: endovascular treatment, BA: basilar a., M1-4: middle cerebral a., A1-2: anterior cerebral a., VA: vertebral a., P1-2: posterior cerebral a.

Contraindications

IVT	EVT	
Absolute		Moyamoya
	Relative	Sickle cell disease,
		Septic embolization, endocarditis, encephalitis, pancreatitis
		Intracranial hemorrhage
		Surgery at non-compressible sites within the past 10 days
		INR > 1.7
		Thrombocytopenia < 100 G/l
		Severe trauma
		Intraparenchymal hemorrhage within the past 3 months
		Obstetric delivery within the past 14 days
		Gastrointestinal hemorrhage within the past 21 days
		Blood pressure not lowerable under 99.Percentile+5mmHg
Relative		Coagulopathy, incl. tumor-associated (e.g. in patients with leukemia) and prolonged aPTT
		Pregnancy (IVT may be considered as off-label treatment)
		Ischaemic stroke within the past 2 months
		Septicemia
		Hypoglycemia < 2.7 mmol/l or hyperglycemia > 22.2 mmol/l
		Sodium < 120 mmol/l or > 150 mmol/l
		Lumbar puncture < 24h
		Severe underlying disease, short life-expectancy
		Age <12 Month
		Focal Cerebral Arteriopathy, Marfan and other connective tissue disease

Monitoring during IVT + EVT

1. **Measure BP during IVT every 5 minutes** (Note no evidence available in children):
   - BP target: systolic and diastolic P50-P95 for age, sex & height*.
   - Pharmacotherapy diast./syst. Hypertension if: **one-time >P95 + 20%** or **persistent (>1h) >P95 + 15%***.
   - Important: **BP reduction slowly** (max. 25% of baseline in the first 6-8 h, normalization of BP in 48 h at the earliest**) with well titratable i.v. drug & under continuous monitoring of the child; 1st choice labetalol i.v.**
   - Pharmacotherapy diast./syst. Hypotension if: persistent <P50: generous volume administration, use vasopressors cautiously.***
   EVT: After successful reperfusion BP target <P95
2. **Respiration:** Control O2–Saturation, Ziel: > 92% SpO_2
3. **Pupils:** 3 x per hour

- In case of **clinical deterioration**, allergic reactions or **drop in blood pressure**, stop infusion immediately and inform 8888 or senior physician Neuropediatrics

*(Rivkin et al. P Neurology 2016, 56:8-17)
**(Lurbe et al. J Hypertens 2016, 34(10):1887-920)
***(Ferriero et al. Stroke 2019, 50:e51-e96)

IVT dosage

Weight	Alteplase (Actilyse®) 0.9mg/kg KG, 10% as i.v.-Bolus, 90% as i.v.-Perfusion over 1 hour with Perfusor.		
	Sum dose 0.9mg/kg KG	**Bolus** 10% over 1min	**Perfusor** over 60min
20 kg	18mg=18ml	1.8ml	16.2ml
25kg	22.5mg=22.5ml	2.3ml	20.2ml
30kg	27mg=27ml	2.7ml	24.3ml
35kg	31.5mg=31.5mg	3.2ml	28.3ml
40 kg	36mg=36ml	3.6ml	32.4ml
45 kg	40.5mg=40.5ml	4.1ml	36.4ml
50kg	45mg=45ml	4.5ml	40.5ml

Notes

IVT in patients previously treated with antiplatelet aggregation therapy:

- Monotherapy: ASA/Clopidogrel/Ticagrelor: no restrictions
- Dual therapy: ASA+Clopidogrel: no restrictions; other combinations: consider IVT carefully
  Other combinations: Consultation with Neuropediatrics
- Monotherapy or combination therapy with Prasugrel: consider IVT carefully
- Triple therapies: no IVT

Bridging (IVT + EVT):

- normally full dose Alteplase 0.9 mg/kg KG
- normally no control imaging before EVT except in the case of clinical deterioration

Possible side effects of IVT:

- Nausea, vomiting, bradycardia, fever, allergic reaction, cardiac arrhythmia and arterial hypotension, bleeding (gastrointestinal in 5%, genitourinary in 4%, cerebral in 6%).

Management elective stent placement

Extremely rarely indicated in children: Clarification before intervention according to stroke guidelines for adults

Treatment Focal Cerebral Arteriopathy (FCA-i)

Lack of evidence for steroid therapy: consider enrollment in PASTA trial

- **Day 0-2: Methylprednisolone i.v.** 30mg/kg/day (max. 1000mg), 1x/day (preferably in the morning) for 3 days. During Methylprednisolone administration: regular BP checks, glucose stix initial 1x/day, proton pump inhibitors fixed. **Attn side effects:** Arterial hypertension, increased glucose (glucosuria-ind. polyuria).
- **Day 3-13:** Prednisolone 1m/kg/day (Max. 40mg/day)
  Day 14-27: Prednisolone 0.5m/kg/day (Max. 20mg/day)
- **Additionally ASA** 3-5mg/kg/day (max. 150mg/day) first 2 weeks, afterwards 2-3mg/kg KG (max. 100mg/day)
- Severe flow-limiting stenoses: strict bed rest and positioning with max. 15° upper body elevation.
- Adjust blood pressure carefully: Aim for high-normal blood pressure (see ICU monitoring).
- For flow-related TIAs: start vasopressors.
- Follow-up MRI: After 5 days, 1 month and 6 months.

Treatment Dissection

- **Usually start with ASA** (ASA and oral anticoagulation (OAC) equivalent according to current studies)
- For higher-grade extracranial dissection-related stenosis and occlusion without major infarction or hemorrhagic infarct demarcation, consider therapeutic heparinization with LMWH or unfractionated heparin followed by LMWH or OAC
- Anticoagulation is relatively contraindicated for dissections extending to or located intradurally (increased risk of SAB)
- In case of inconclusive findings of the dissection sequences (Specially fat saturated sequences, incl. neck) on MRI, standard cause clarification and repeat dissection sequences, depending on the findings.
- Off-Label use of direct oral anticoagulation (DOAC) may be considered in individual cases if OAC is not adjustable
- Follow-up MRI at 3 months to exclude pseudoaneurysm formation.

Treatment Moyamoya

Acute phase

- **IVT and EVT contraindicated**
- Generous volume administration (aim high-normal BP)
- ASA 3-5mg/kg/day (max. 150mg/day) first 2 weeks, afterwards 2-3mg/kg KG (max. 100mg/day)
- Regular blood pressure checks (Note demand hypertension).

After stabilization of the patient

- Interdisciplinary discussion at the vascular colloqium

PFO-Closure?

- **Always individual decision**, if no clear cause of infarction closure should be discussed.
- Decision in acute phase usually not necessary - discuss decision with cardiology
- Findings that are more likely to influence the decision toward closure: 1) recurrence of stroke or TIA 2) evidence of R-L shunt by foramen in bubble echocardiography or equivalent examination, 3) hereditary risk of coagulopathy, 4) history of leg vein thrombosis or other thrombosis, 5) embolic stroke associated with Valsalva maneuver.

Stroke in sickle cell disease

See DeBaun et al, J. of Blood Advances 2020, 8:1554-1588

- Generous volume administration.
- Transfuse as soon as possible (exchange transfusion or apharesis), if exchange transfusion not possible within 2h and Hb <85 g/l perform normal transfusion.
- **Secondary prevention:** Aim for Hb level >90g/l, ASA 3-5mg/kg/day (max. 150mg/day) first 2 weeks, afterwards 2-3mg/kg KG (max. 100mg/day)
- If moyamoya is suspected, discussion at vascular colloqium.

Surveillance on pediatric intensive care unit

Immediately after patient arrival neurological examination (ped-NiHSS)

1. **Blood pressure/heart rate/rhythm:** BP limits for children (clinical experience of pediatric hypertension specialists and extrapolation of adult medicine recommendations; no data are available on BP outcomes in children with stroke)
   - BP-Target: Systolic and diastolic P50-P95 for age, sex & height*.

   - BP P50 **systolic:** 83 + (Age in years x2)
     diastolic: 1-5 years: 35 + (age in years x4); 6-16 years: 50+ age in years
   - BP P95 **systolic:** 100 + (age in years x2)
     diastolic: 1-10 years: 60 + (age in years x2); 11-17 years: 70 + age in years

   - **Pharmacotherapy diast./syst. Hypertension if: one-time >P95 + 20%** or **persistent (>1h) >P95 + 15%***.
   - **Important:** BP reduction slowly (maximum 25-30% of baseline in first 6-8 hr**) with well titratable i.v. drug and under continuous monitoring of the child; 1st choice **labetalol i.v.****
   - **Pharmacotherapy diast./syst. Hypotension if:** persistent <P50: generous volume administration (1.5x total fluid), use vasopressors cautiously.***
   - For **FCA-i/Moyamoya:** tolerate higher blood pressure values (demand hypertension).
2. **Respiration** Control of O2 saturation, target: > 92% SpO_2
   - if > 4l O2/min necessary or persistent tachypnea => physical examination, aBGA, if necessary Rx Chest
3. **Body temperature:** ≥ 38.5° C -> antipyretics (1st choice acetaminophen) + blood cultures, Screening for infectious foci, antibiotic therapy in consultation with pediatric infectious disease specialists.
4. **Neurological examinations/ped-NIHSS:** usually 2-hourly in the first 24h
5. **Laboratory:** Measure blood glucose 3x/day (Hyperglycemia associated with poor outcome, drug lowering of blood glucose controversial in literature - **target blood glucose: <7-10mmol/l)*****.

- **Prescription medication:** platelet aggregation inhibitors after IVT/i.a. urokinase DO NOT prescribe in advance (usually only after bleeding has been ruled out in course imaging).

*(Rivkin et al. P Neurology 2016, 56:8-17)
**(Lurbe et al. J Hypertens 2016, 34(10):1887-920)
***(Ferriero et al. Stroke 2019, 50:e51-e96)

Laboratory general
- Completion according to Swiss Neuropediatric Stroke Registry guidelines (https://snpsr.neuropaediatrie.ch/).

Laboratory controls approx. 24 hours after IVT/EVT
- Hb, lc, tc, CRP, glucose, sodium, potassium, creatinine, PT, INR
- In case of blood pressure problems: hs-troponin T and ECG course after 4 hours, if initially pathological.

Neuroradiological control
- 24h after IVT/EVT MRI (or CT), incl. MRA (CTA) except in renal insufficiency.
- In case of neurological deterioration, immediate CT or MR control

Secondary prevention by medication

- **ASA** 3-5mg/kg/d (max. 150mg/day) first 2 weeks, afterwards 2-3mg/kg KG (max. 100mg/day) at least 2 years; in case of persistent stenoses/vasculopathies at least 5 years, possibly lifelong
- **Clopidogrel** (Plavix®) 1mg/kg/d (Children from 2 yrs) up to max. 75 mg/d, in case of ASA intol./ineffectiveness.
- **Asasantin®** (= ASA 25mg + Dipyridamol 200mg) 2 x 1/d, alternative to Clopidogrel
- **Double platelet aggregation inhibition** with ASA 2mg/kg/d combined with Clopidogrel (risk of bleeding!) or Asasantin
- For extra- and intracranial stents, usually for at least 6 months (1 year for drug-eluting stents), followed by monotherapy with Clopidogrel or Aspirin
- **Statins** are rarely used in childhood (recommended from 8 yrs at earliest) (Drugs. 2012 Apr 16;72(6):759-72))
- **Long-term anti-hypertensive therapy in consultation with Pediatric Nephrologist.**

Mobilisation

Day 0	Day 1 (min. 24h after IVT/EVT)
Subacute stroke > 2d TIA without vessel occlusion Small infarcts, without symptoms, without vessel occlusion, conservative treatment	
Infarct, ped-NIHSS ≥ 1, without vessel occlusion, conservative treatment	
Stroke pontine/internal capsule	
Vessel occlusion/haemodynamic watershed infarcts/ symptoms, severe arterial stenosis that is flow limiting or conservative treatment	No penumbra, not pontine/internal capsule stroke Persistent penumbra, severe hypoperfusion, hemodynamic watershed infarcts/symptoms
IVT/EVT/Bridging	Reperfusion, not pontine/internal capsule stroke Persistent penumbra

Mobilization without restriction

Mobilization delayed (possibly slower in case of persistent penumbra or mobilization-dependent symptoms)

30° (*supine position if possible)

Mobilization delayed
Level 1: 30°
Level 2: sitting
Level 3: walking with assistance, if patient is steady then free mobilization is possible

Daily Checklist — visiting stroke patients

1	**Neurological evaluation - pedNIHSS and symptom-orientated functional examination**
2	**Clinical evaluation,** especially fever? Weight with high-dose steroid therapy?
3	**Monitoring** Normofrequent? BP Target? BP Actual?
4	**Mobilization?**
5	**Nutrition?** Prevention of constipation
6	**Laboratory controls?** - Acute clarifications still to be performed in regard to risk profile? Controls for high-dose steroid therapy?
7	**Medication** Antithrombotic therapy? Steroids?
8	**Neurological deterioration** ? Reinfarction ? Infarct localization: e.g. second. deterioration more frequent in internal capsula or pontine infarction ? Haemodynamic: BP associated? Associated with mobilization? ? Bleeding ? Rising ICP ? Epileptic seizure ? Infection ? Sedation ? Psychogenic and other less frequent causes

Malignant infarcts

At risk large-volume and/or infratentorial infarcts

General

- Most critical phase with risk of clinical deterioration: 24-96h
- **Usually 30° supine position**
- **BP aim:** Systolic and diastolic P50-P95 for age, sex & height.
- **BP P95:** **systolic:** 100 + (age in years x2)
  diastolic: 1-10 years: 60 + (age in years x2); 11-17 years: 70 + age in years
- **BP P50:** **systolic:** 83 + (Age in years x2)
  diastolic: 1-5 years: 35 + (age in years x4); 6-16 years: 50+ age in years
- **In case of imminent craniectomy: stop antiplatelet therapy**
- Consider as emergency medication until craniectomy:
  - Mannitol/hypertonic saline solution (dosage control of mannitol via osmotic gap, hypertonic saline solution via Na and osmolality)
  - restrictive use of hyperventilation (only briefly as an emergency measure)
- Close clinical monitoring, emergency imaging (MR or CT) if suspected.
- In infarcts with high risk of malignancy: consider protective initiation with antiepileptic therapy (Note increased blood flow intraictally => increased intracranial pressure; non-evidence-based).
- Signs of rising ICP:
  - decreasing consciousness, disturbance of pupillomotor function usually with dilatation in case of supratentorial swelling, and miosis in case of infratentorial swelling, increasing paresis, new ipsilateral paresis, pathological breathing pattern, rhythmic disorders

Decompressive craniectomy

- Indication by pediatric intensive care unit, neuropediatrics and neurosurgery
- Craniectomy if possible before relevant neurological deterioration

See: Andrade et al. Pediatric Neurology 2016, 64:44-51

Precautions before anesthesia

In flow-limiting arteriopathies (FCA-i, moyamoya, dissection, etc.), careful BP adjustment.
- Generous volume administration during fasting periods
- Start vasopressors before anesthesia to prevent BP drop.

Specific causes

Cause	Key symptom	Diagnostics
Arteriopathies		
Focal Cerebral Arteriopathy of the inflammatory type (FCA-i)	TIA or acute stroke Borrelia, varicella or other viral infections	MR-Angiography, Dark blood or enhanced. Infection-, vasculitis-parameters, serologies. CSF puncture (opening pressure, serologies).
Moyamoya	Recurrent cerebrovascular Events. (Assoc. with trisomy 21, neurofibromatosis type 1, sickle cell anemia).	MRI including angiography (MRA), neurovascular ultrasound (nvUS)
Arterial dissection	Trauma (including minor trauma), Infection	MR Angiography, fat-suppr.-sequences of neck vessels, conv. angiography.
Fibromuscular dysplasia	Arterial hypertension	BP, Imaging: renal vessels
Rotational compression of vertebral artery	Recurrent posterior circulation strokes, especially in boys	Rotational angiography; cervical spine
Hereditary Arteriopathies	Family history and clinics (vascular) Imaging	e.g. NF1; SMAD3, ACTA2, ADA2, COL4A1, COL4A2, PHACES (sporadic)
Cardial		
Congenital malformations, Cardiomyopathy	Personal history, physical examination	Echocardiography, ECG
Endocarditis	Reduced general condition, fever, microemboli	Blood cultures, echocardiography
Hematological diseases		
Hereditary coagulopathies	Family and personal history, risk situations	Basic clarification: venous Thrombophilia-Block (Anti β2-GP IgG/IgM, Antithrombin, APC Resistence, aPTT, Cardiolipin IgG/IgM, D-Dimers, FII, FV, FVII, FVIII, FX, Fibrinogen Clauss, INR, Lupus Anticoagulant, Protein C, Protein S, PT, Quick, TAT-Complex, Thrombintime) Plus: Homocystein, Lipoprotein a, Further clarification.: FIX& FXI
Lupus-/Antiphospholipid-Antibodies-Syndrome	Clinical Evaluation	Cardiolipin-IgG/-IgM, Lupus-Anticoagulant, Anti-beta2-Glykoprotein-IgG /-IgM
Sickle Cell Disease	Anemia, splenomegaly	Hb-Elektrophoresis/Chromatography(External shipping, Laboratory Aarau), nvUS
Anemia, Iron deficiency	Pallor	Blood count, reticulocytes, ferritin, CRP, plus transferrin/transferrin saturation if necessary.

Specific causes

Cause	Key symptom	Diagnostics
Vasculitides		
Lupus, systemic disease, CNS-Vasculitis, u.a.	Clinical evaluation	BSR, pathological coagulation (aPTT), ANCA, Lupus-, other antibodies, MRI, MRA, SPECT
Primary Angiitis of medium to large sized vessels	Progr. symptoms before stroke (headache, cognitive)	Lumbar puncture (incl. opening pressure), MR-Angiography, consider FCA-i as a differential diagnosis
Connective tissue and metabolic diseases		
Ehlers-Danlos-Syndrome	Cutis laxa and joint hypermobility	Genetic, skin biopsy
Marfan-Syndrome	Habitus, family history	Genetics, echocardiography
"Congenital Disorder of Glycosylation" (CDG)-Syndrome	Retinitis pigmentosa, Deformities (multi-organ disease)	Transferrinelectrophoresis, MRI
Molybdenum cofactor deficiency	Epileptic seizures	Uric acid, AA in plasma Urine: sulfite test, AA and organic acids
Mitochondriopathies (Rather stroke like episode, not a classical Vasculopathy)	Family history, failure to thrive, occipital infarcts.	Lactat (Blood, CSF), Genetics, Enzyme diagnostics in muscle and skin biopsies
Urea Cycle Disorders (Rather stroke like episode, not a classical Vasculopathy)	Acute, fluctuating neurological symptoms.	Ammonia, urea, amino acids (AA) Urine: AA and organic acids

Cause clarification

- **Echocardiography** / ECG if not already performed
- **Laboratory during hospitalization:** Venous Thrombophilia-Block (Anti β2-GP IgG/IgM, Antithrombin, APC Resistance, aPTT, Cardiolipin IgG/IgM, D-Dimers, FII, FV, FVII, FVIII, FX, Fibrinogen Clauss, INR, Lupus Anticoagulant, Protein C, Protein S, PT, Quick, TAT-Complex, Thrombintime)
  BSR, Ferritin, Homocystein, Lipoprotein A, Prothrombin Mutation, MTHF-Mutation, ANA, Lactate, Ammonia, Amino Acids in plasma, organic acids in urine, Lipid profile
  Lumbar puncture (especially if focal cerebral arteriopathy is suspected - Attn. contraindicated until 24h after IVT and during heparinization): Opening pressure, cells, glucose, protein, lactate, Lyme disease index, varicella /herpetic serologies, plus spec. additional serologies.
- **Laboratory only 6-12 weeks after stroke:**
  Protein S-, Protein C-Activity, D-Dimers
- **Laboratory only 4 weeks after discontinuation of anticoagulation:**
  Thrombophilia-Block venous (see above) without molecular genetics, D-Dimers
- **Level-2 Testing (for special indication)**
  See https://snpsr.neuropaediatrie.ch/Formulare

Cerebral venous and sinus thrombosis therapy

- Low molecular weight heparin: Enoxaparin (Clexane®) therapeutic (dosage 1mg/kg 2x/d) (in its efficacy as well as complications (bleedings) might be superior to unfractionated heparin (UFH) (non-rand. study in adults)
- Alternative UFH (UFH-Anti-Xa controlled) especially in case of possible surgical intervention
- Discuss changeover to OAC during course-in children, mostly therapy over months with LMWH and inflo-jetspreferred (fewer therapy controls)
- Consider alternative Rivaroxaban (Connor et al. Blood Adv. 2020, 4(24):6250-6258)

- IVT of mechanical recanalization in exceptional cases or i.R. study (TO-ACT)
- If hemorrhagic from venous stasis occurs, continue heparin therapeutically
- In cases of large hemorrhagic infarcts and impending lateral herniation, decompressive craniectomy should be performed rapidly, but without simultaneous hematoma or infarct evacuation

- Duration of OAC 4-6 months (except in case of progression of thrombosis on follow-up MRI or thrombophilia/ pos. family history)
- Coagulation clarification after stopping OAC (see below)

Cerebral venous & sinus thrombosis diagn. work-up

- Laboratory: blood count, electrolytes (dehydration), lactate, BSR, CRP, ferritin, anticardiolipin antibodies, ammonia, amino acids in plasma, organic acids in urine. Lyme serology
- Coagulation: **acute:** Quick/INR, aPTT, fibrinogen,
  in the course: Prothrombin mutation, homocysteine, lipoprotein A, MTHFR mutation, thrombophilia block venous (anti- β2-GP IgG/IgM, antithrombin, APC resistance, aPTT, cardiolipin IgG/IgM, D-dimers, FII, FV, FVII, FVIII, FX, fibrinogen Clauss, INR, lupus anticoagulant, protein C, protein S, PT venous, Quick, TAT complex, thrombin time).
  after 6-12 weeks/4 weeks after discontinuation of anticoagulation: protein C and protein S.
- **Lumbar puncture (only with special indication):** opening pressure, cells, glucose, protein, lactate, glucose ratio
- **Further clarifications according to https://snpsr.neuropaediatrie.ch/**

Therap. heparinization with Unfract. Heparin

Blood count and coagulation status (Tc, Quick/INR, aPTT, fibrinogen) before starting.

- Therapy: Bolus i.v. 75E/kg, then continuous infusion 25E/kg/h
- Afterwards withheld or reduce boluses if there is significant bleeding risk
- Usually Anti-Xa-Target: 0.35-0.7 U/ml (see Monagle et al. Chest 2012)
- Check anti-Xa level after 3, 6, 12, 24h, then depending on the setting see below.
- Weekly blood count checks (exclusion of HIT-II)

Dosage adjustment (see Monagle et al. Chest 2012, 141(2 Suppl):e737S-e801S, Trucco et al. J. of Thromb. 13(5):788-794)

Anti-FXa[U/ml]	Bolus	Hold [min]	Rate change	Repeat Anti-Xa
<0.1	50 U/kg	-	Increase 10%	After 4h
0.11-0.34	-	-	Increase 10%	After 4h
0.35-0.7	-	-	No adjustment	Confirm after 6h, then 1x/d
0.71-0.99	-	-	Decrease 10%	After 4h
1.0-1.19	-	30-60	Decrease 10-20%	After 4h
>1.2	-	60-120 until Anti-Xa <1.0	Decrease 15-30%	After 4h

Therap. heparinization with LMWH (Clexane®)

- Before start: Tc, Quick/INR, aPTT, thrombin time, fibrinogen, anti FXa activity
- Dosage: Children <2 Month **initial**: 1.5mg/kg/dose s.c. every 12h, **Titration based on Anti-Xa-Spiegel**
  Children >2 Month **initial**: 1.0mg/kg/dose s.c. every 12h, **Titration based on Anti-Xa-Spiegel**
- target level for therapeutic anticoagulation is an anti-Xa level of 0.5 - 1 IU/ml measured 4 - 6 hours after subcutaneous injection (or 0.5 - 0.8 IU/ml measured 2 - 6 hours after injection).
- **If high doses are needed** (children <2 months: >3.0mg/kg/dose; children >2 months: >2.0mg/kg/dose), **consult DA/DAe Hematology.**
- Note: No ASA or antiplatelet agents during therapy.
- Regular blood count checks (platelets?). If platelets drop (for example by 50% in 1-2 days), think of heparin-induced thrombocytopenia (HIT) and involve hematology!
- Before invasive procedures (e.g. lumbar puncture): Stop heparin (suspend 2 doses before procedure)

Dosage adjustment

Anti-FXa [U/ml]	stop	adjustment	Anti-FXa-control
<0.35	no	+25%	4 h after next morning dose
0.35-0.49	no	+10%	4 h after next morning dose
0.50-1.0	no	0	1x/week 4h after morning dose, if stable also possible every 14 days or 1x/month
1.01-1.50	no	-20%	4 hrs after next morning dose
1.60-2.0	no	-30%	Before and 4 h after next dose
>2.0	yes, until <0.5E/ml	-40%	Before (possibly every 12 h if not <0.5E/ml) and 4 h after dose reduced by 40%.

Rivaroxaban (Xarelto®)

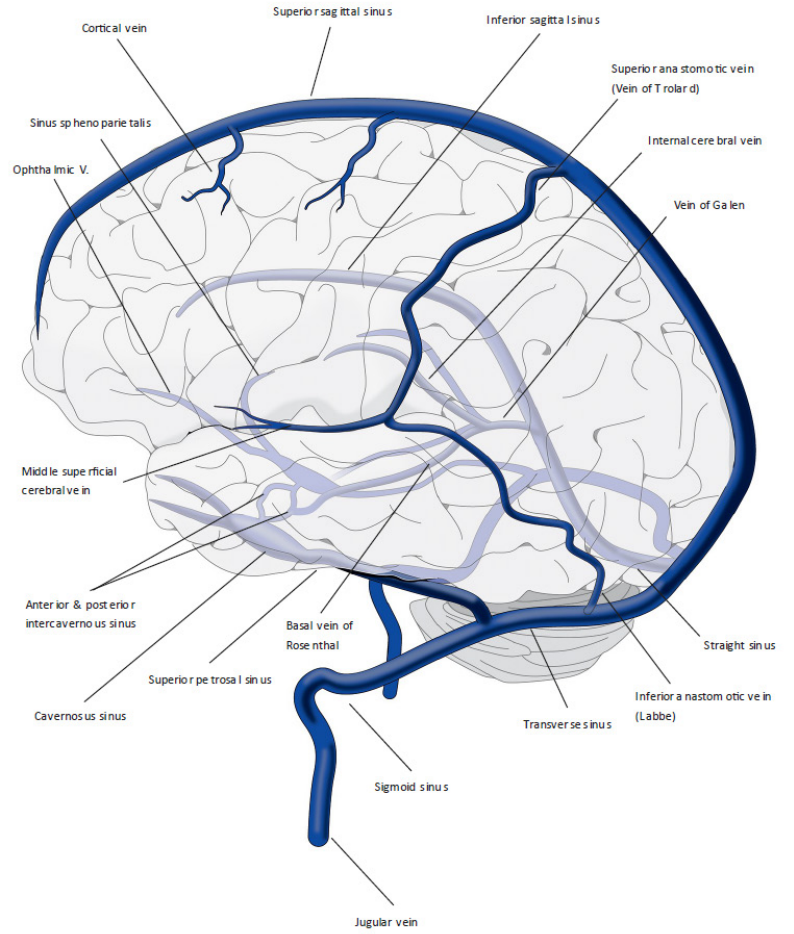
Conditions (see Connor et al. Blood Adv. 2020, 4(24):6250-6258):

1) GFR >30ml/min/1.73m² (For children <1 year: serum creatinine <97.Pc). For patients with GFR 30-50ml/min no dose adjustment necessary.
2) Age >0.5 years (or >37 weeks gestation, body weight >2600g, and oral feeding >10 days).
3) No act. bleeding or not at high risk for bleeding (hepatic dis., Tc <50,000, etc.), no uncontrolled hypertension.
4) Blood pressure values systolic and diastolic <95. Pc.

→ Start after administration of unfractionated heparin: 4h after end of heparin therapy.
→ Onset after 1x daily administration of low molecular weight heparin: 24h after last administration.
→ Onset after 2x-daily administration of low-molecular-weight heparin: 12h after last administration.

- Therapy duration: 6-12 months
- **Attn: Interactions with drugs affecting CYP3A4 and P-glycoprotein activity.**

Body weight	Dosage	Body weight	Dosage
2.6-2.9kg	0.8mg, 3x/day (=2.4mg/day)	**9.0-9.9kg**	2.8mg, 3x/day (=8.4mg/day)
3.0-3.9kg	0.9mg, 3x/day (=2.7mg/day)	**10.0-11.9kg**	3.0mg, 3x/day (=9.0mg/day)
4.0-4.9kg	1.4mg, 3x/day (=4.2mg/day)	**12.0-29.9kg**	5mg, 2x/day (=10mg/day)
5.0-6.9kg	1.6mg, 3x/day (=4.8mg/day)	**30.0-49.9kg**	15mg, 1x/day (=15mg/day)
7.0-7.9kg	1.8mg, 3x/day (=5.4mg/day)	**≥ 50kg**	20mg, 1x/day (=20mg/day)
8.0-8.9kg	2.4mg, 3x/day (=7.2mg/day)		


Superior sagittal sinus
Cortical vein
Inferior sagittal sinus
Superior anastomotic vein
(Vein of Trolard)
Sinus sphenoparietalis
Internal cerebral vein
Ophthalmic V.
Vein of Galen
Middle superficial
cerebral vein
Anterior & posterior
intercavernous sinus
Basal vein of
Rosenthal
Straight sinus
Superior petrosal sinus
Inferior anastomotic vein
(Labbe)
Cavernous sinus
Transverse sinus
Sigmoid sinus
Jugular vein

Diagn. algorithm non traumatic intracerebral hemorrage

1. On ED: CT or MRI depending on availability. If possible, with angiography - evidence of macrovascular source of bleeding (AVM, aneurysm, stasis bleeding in SVT, etc.)?
2. If no trauma & no clear evidence of cavernous malformation: conv angiography.
3. Generous indication for invasive angio. (IADSA): interdisciplinary decision Neuropediatrics/NRAD/NCH.
4. Treatment plan: Rapid evaluation with neurosurgery regarding emergency intervention (decompression) if necessary, discuss further measures interdisciplinary with Neuropediatrics/NRAD/NCH.
5. Possible causes:
   - AVM, cavernous malformation, rarely aneurysm
   - Small Vessel Disease (SVD) in sickle cell disease and moyamoya.
   - Brain tumor
   - Bleeding diathesis: especially hemophilia or vitamin K deficiency (especially infants)
   - Cerebral venous sinus thrombosis
   - Trauma X (non-accidental head injury; especially in combination with (1) ecchymosis of the neck/head, (2) rib fracture, (3) fracture of the long tubular bones, (4) retinal hemorrhage, (5) epileptic seizure, (6) apnea. See „Prediction Tool for Abusive Head Trauma," Cowley LE et al. Pediatrics 2015)
6. Follow-up imaging (preferably MRI) after 24h to evaluate hematoma expansion (prognostic marker and quality control).
7. EEG and anti-epileptic therapy generously for seizures/alteration of consciousness***.
8. In case of **missing cause repeat imaging** after hemorrhage resorption with question for vascular malformation + Additional examinations after consultation **with paed. Hematology**

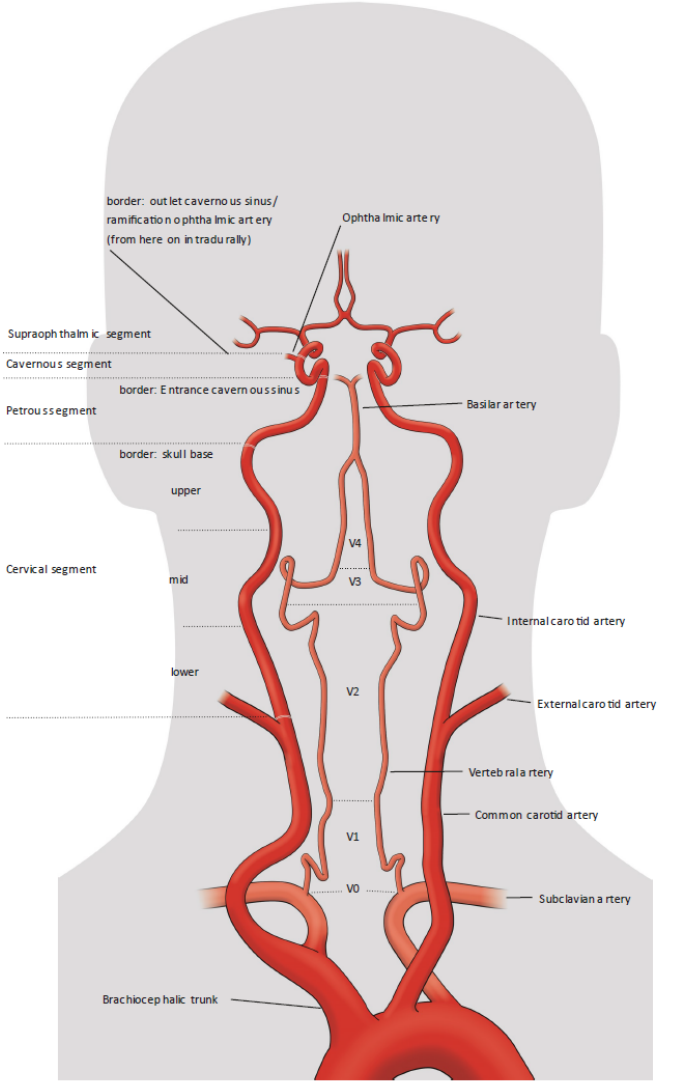
- **Blood pressure limits for children** (clinical experience of pediatric hypertension specialists and extrapolation of recommendations from adult medicine; no data are available on blood pressure outcomes in children with stroke):
  BP target range normal to P95 for age, sex and size **(but depending on cause of bleeding)**
  BP P95: systolic: 100 + (age in years x2)
  diastolic 1-10 years: 60 + (age in years x2); 11-17 years: 70 + age in years
- **Important:** BP reduction slowly (maximum 25-30% of baseline in the first 6-8 h, normalization of BP in 48 h at the earliest**) with well titratable i.v. drug and under continuous monitoring of the child; 1st choice i.v. labetalol.

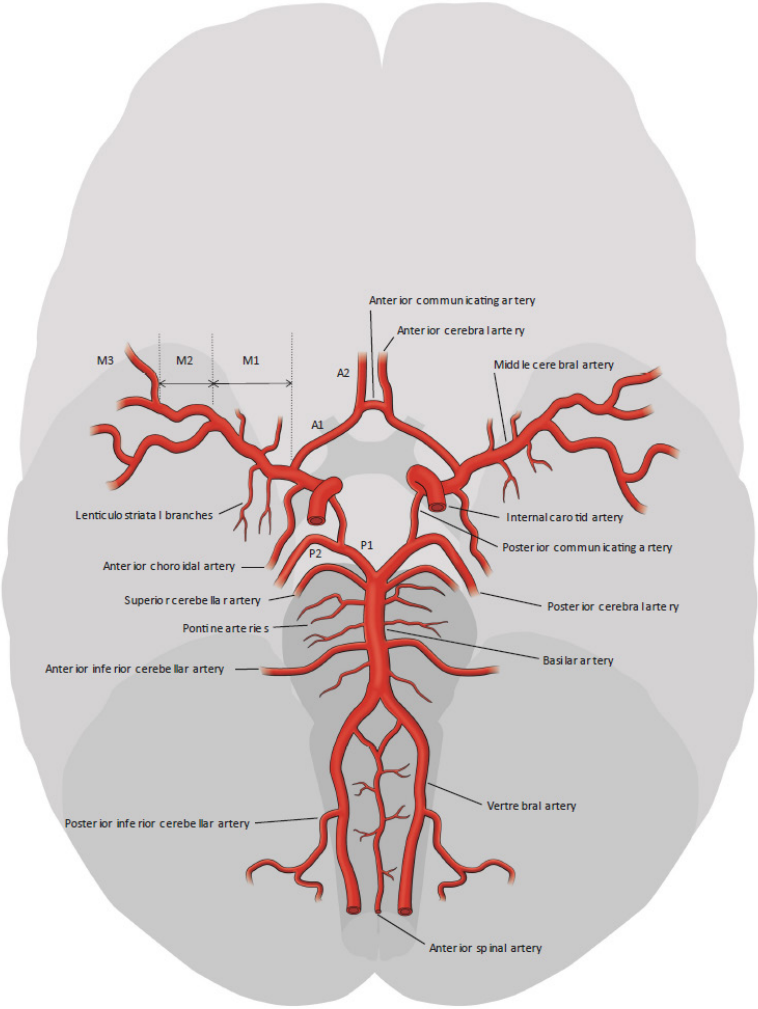
**(Lurbe et al. J Hypertens 2016, 34(10):1887-920)
***(Ferriero et al. Stroke 2019, 50:e51-e96)

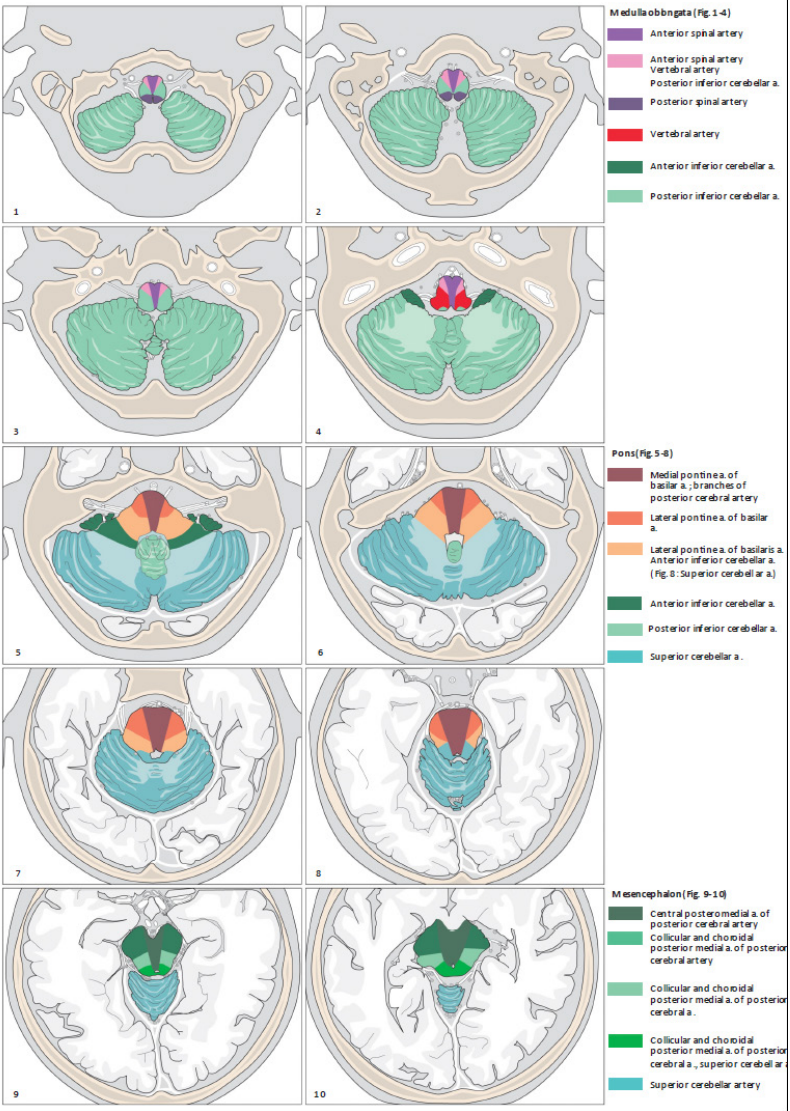
Pediatric ICH Score

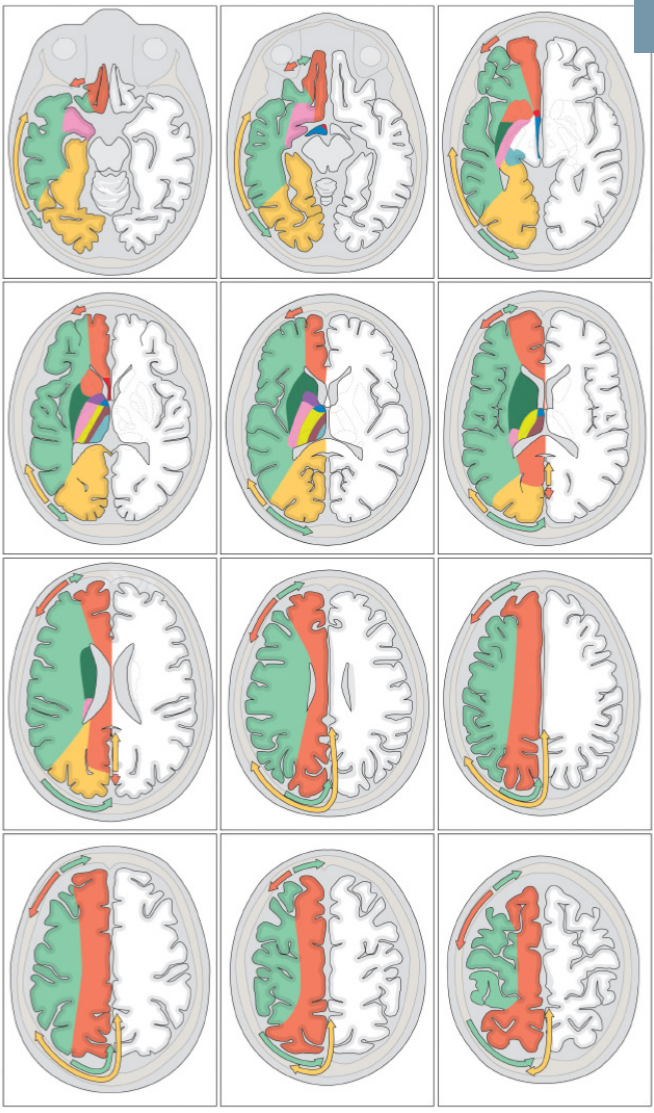
		Points
Volume of hemorrhage in % of brain volume	≤ 2 2-3.99 ≥ 4	0 1 2
Hydrocephalus	No Yes	0 1
Herniation	No Yes	0 1
Infratentorial	No Yes	0 1

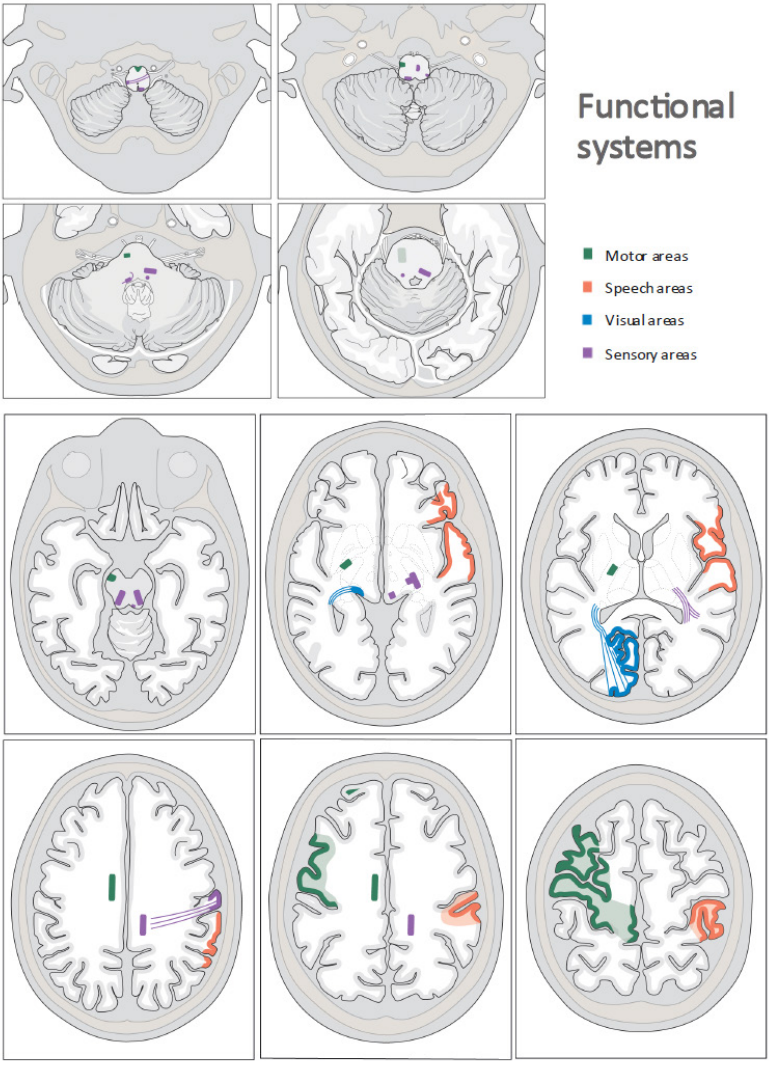
Score ≥ 1: Prediction for moderate disability or worse (sensitivity 75%, specificity 70%).
Score ≥ 2: Prediction for severe disability or death (sensitivity 90%, specificity 68%)


border: outlet cavernous sinus/
ramification ophthalmic artery
(from here on intradurally)
Ophthalmic artery
Supraophthalmic segment
Cavernous segment
border: Entrance cavernous sinus
Petrous segment
Basilar artery
border: skull base
upper
V4
Cervical segment
mid
V3
Internal carotid artery
lower
V2
External carotid artery
Vertebral artery
Common carotid artery
V1
V0
Subclavian artery
Brachiocephalic trunk


Anterior communicating artery
Anterior cerebral artery
M3
M2
M1
A2
Middle cerebral artery
A1
Lenticulostriatal branches
Internal carotid artery
Posterior communicating artery
P2
P1
Anterior choroidal artery
Superior cerebellar artery
Posterior cerebral artery
Pontine arteries
Basilar artery
Anterior inferior cerebellar artery
Vertebral artery
Posterior inferior cerebellar artery
Anterior spinal artery


Medullaobbngata (Fig. 1-4)
Anterior spinal artery
Anterior spinal artery
Vertebral artery
Posterior inferior cerebellar a.
Posterior spinal artery
Vertebral artery
Anterior inferior cerebellar a.
Posterior inferior cerebellar a.
1
2
3
4
Pons(Fig. 5-8)
Medial pontine a. of basilar a. ; branches of posterior cerebral artery
Lateral pontine a. of basilar a.
Lateral pontine a. of basilaris a. Anterior inferior cerebellar a. (Fig. 8 : Superior cerebellar a.)
Anterior inferior cerebellar a.
Posterior inferior cerebellar a.
Superior cerebellar a.
5
6
7
8
Mesencephalon (Fig. 9-10)
Central posteromedial a. of posterior cerebral artery
Collicular and choroidal posterior medial a. of posterior cerebral artery
Collicular and choroidal posterior medial a. of posterior cerebral a.
Collicular and choroidal posterior medial a. of posterior cerebral a., superior cerebellar a.
Superior cerebellar artery
9
10


Anterior cerebral a.
Middle cerebral a.
Middle cerebral a., lenticuolostriate branches
Posterior cerebral a.
Anterior choroidal a.
Posterior choroidal a. (from P2)
Anterior communicating artery
Posterior communicating artery
Thalamoperforating A. (from P1 or BA; if jointly main trunk: Percheron artery)
Thalamogeniculata a. (from P2)
Internal carotid a.


Functional systems
Motor areas
Speech areas
Visual areas
Sensory areas

Impressions Score SOI-Score (PSOM SNE)

Explanation of the test: See explanatory video on the SNPSR-Homepage (https://snpsr.neuropaediatrie.ch/)

A. Sensorimotor deficit (any motor or sensory abnormality including cranial nerve deficits, visual, hearing)	Right	Left
None	0	0
Mild but no impact on function	0.5	0.5
Moderate with some functional limitations	1	1
Severe or Profound with missing function	2	2
Not tested	n/t	n/t
Observed sensorimotor deficit: □ Global development delay □ Global hypotonia or hypertonia □ Hemiparesis □ Hemifacial weakness □ Hemiataxia □ Dysarthria □ Other motor deficit □ Hemisensory deficit □Other sensory deficit □ Difficulty with vision □ Difficulty with drinking, chewing, swallowing □ Other		
B. Language deficits - Production (exclude dysarthria)		
None	0	
Mild but no impact on function	0.5	
Moderate with some functional limitations	1	
Severe or Profound with missing function	2	
Not tested	n/t	
C. Language deficits—Comprehension		
None	0	
Mild but no impact on function	0.5	
Moderate with some functional limitations	1	
Severe or Profound with missing function	2	
Not tested	n/t	
D. Cognitive or behavioural deficits □ Cognitive □ Behavioural		
None	0	
Mild but no impact on function	0.5	
Moderate with some functional limitations	1	
Severe or Profound with missing function	2	
Not tested	n/t	
Total Score	**___/10P.**	

Ped NIHSS

Explanation of the test: See explanatory video on the SNPSR-Homepage (https://snpsr.neuropaediatrie.ch/)

Score	Test	Instructions (red: Modification for children)
☐	**1a Level of consciousness**	**For children < 2 yrs, multiply score 1a by three and omit items 1b and 1c** **0** Alert; keenly responsive **1** Not alert, but arousable by minor stimulation to obey, answer, or respond. **2** Not alert, requires repeated stimulation to attend, or is obtunded 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** Anarthria, Intubation=1, Coma=2	**<2 years.: omit, see above** Ask about age and **counting finger/where is Mama/Papa** **0** Answers both questions correctly **1** Answers one question correctly. **2** Answers neither question correctly
☐	**1c LOC Commands**	**<2 years.: omit, see above** Request to open and close the eyes and non-paretic hand or touch nose **0** Performs both tasks correctly. **1** Performs one task correctly. **2** Performs neither task correctly
☐	**2 Best Gaze** Insufficient Cooperation=1, Coma=2	**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 Fields** not consecutive=0, Neglect=1, Coma=3, in aphasia evaluate visual threat	**Visual threat in children 4 Month to 6 years** **0** No visual loss **1** Partial hemianopia **2** Complete hemianopia **3** Bilateral hemianopia (blind including cortical blindness)
☐	**4 Facial Paresis** grimace in response to noxious stimuli coma=3	**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).
left ☐ **right** ☐	**5 Motor Arm** amputation, joint fusion= 0, coma=4	**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

Ped NIHSS

Score	Test	Instructions (red: Modification for children)
left ☐ right ☐	**6 Motor Leg** amputation, joint fusion= 0, coma=4	**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.
☐	**7 Limb Ataxia** coma, aphasia, complete paresis=0	Ask to reach for a hand or for a toy **0** Absent. **1** Present in one limb **2** Present in two limbs
☐	**8 Sensory** bilateral=2, coma=2 if no reaction to noxious stimuli, in case of aphasia mor likely 1	**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
☐	**9 Best Language** Intubated patient should be asked to write, Coma=3	Children ≥ 2 years: **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. **2** Severe aphasia; communication through fragmentary expression. Range of information that can be exchanged is limited. Examiner cannot identify materials provided from patient response. **3** Mute, global aphasia; no usable speech or auditory comprehension Children 4 month to 2 years **0** Alerts to sound; spatial orientation to sound visually or by behavior **1** Alerts to sound, does not have spatial orientation to sound **2** Does not alert or orient to sound
☐	**10 Dysarthria** coma=2	**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
☐	**11 Extinction and Inattention** Not testable=0, coma=2	Children ≥ 2 years **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 Children 4 month to 2 years: **0** No abnormality. **1** Either a sensory or motor deficit **2** Sensory and motor deficits on neurological examination


12
1
2
3
4
5
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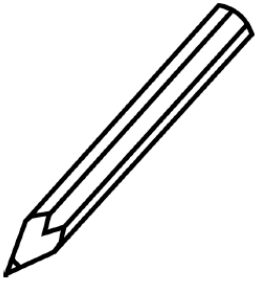
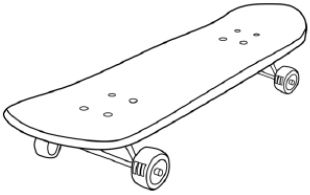
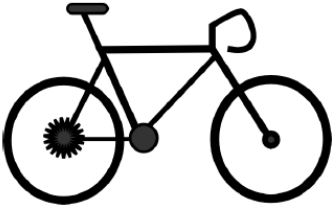
7
8
9
10
11







Close your eyes

He‘s a chip off the old block.

Harm set, harm get.

HUCKLEBERRY

BASEBALL PLAYER

Blood Pressure Percentiles

	Boys				Girls			
Age	P50	P95	>15% above P95	>20% above P95	P50	P95	>15% above P95	>20% above P95
5	105/65	116/74	133/85	139/89	103/66	115/74	132/85	138/89
6	106/66	118/75	136/86	142/90	104/66	116/74	133/85	139/89
7	106/66	119/75	137/86	143/90	105/66	118/74	136/85	142/89
8	107/66	120/75	138/86	144/90	107/66	119/74	137/85	143/89
9	108/67	121/75	139/86	145/90	108/66	120/74	138/85	144/89
10	109/67	123/75	141/86	148/90	109/66	121/75	139/86	145/90
11	110/67	125/76	144/87	150/91	110/66	122/75	140/86	146/90
12	113/67	127/76	146/87	152/91	111/67	123/76	141/87	148/91
13	115/67	130/76	150/87	156/91	112/67	124/76	143/87	149/91
14	118/68	133/77	153/89	160/92	113/67	125/76	144/87	150/91
15	121/68	136/77	156/89	163/92	114/68	125/77	144/89	150/92
16	123/69	138/78	159/90	166/94	115/68	126/77	145/89	151/92

Lurbe et al. J Hypertens 2016, 34(10):1887-920