A clinical approach to Hemiplegia

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Paralysis of one side of the body
Involvement of corticospinal tract on the opposite side

- Cortex
- Corona radiata
- Internal capsule
- Brain-stem
  - midbrain
  - pons
  - medulla
- Spinal cord
Cortical sensory involvement

- Face + arm > leg
- Speech – if dominant hemisphere
- Seizures
- Cortical sensory involvement
Internal capsule

- Dense hemiplegia
- Hemisensory loss
- Homonymous hemianopia
Brainstem

- Crossed hemiplegia
- Ipsilateral CN palsy + opposite hemi
Brainstem

- Weber syndrome = 3rd N + opp. hemi (midbrain)

- Millard-Gubler syndr. = 6th / 7th + opp. hemi (pons)

- Jackson syndrome = 10th, 12th + opp. Hemi (medulla)
Spinal cord

- Face spared
- Cranial nerves not affected
- Hemisensory loss
- Congenital hemiplegia / Infantile hemiplegia
- Acquired hemiplegia
Congenital hemiplegia - causes

- Causes of hemiplegic CP
- Prenatal / perinatal insults
- Vascular
- Structural
pictures
Clues to congenital hemiplegia

- Asymmetric Moro
- Early handedness
- Smaller limb / hand (compare nail size)
- Delayed motor milestones
- Falls to one side
- Cortical thumb
- 20-30% seizures
- +/- 30% ID
Acquired hemiplegia

- Stroke

- Non-vascular : stroke mimics
Differential diagnosis in a child with acute hemiplegia – ‘Stroke Mimics’

- Todd’s paralysis
- ADEM (Acute Disseminated EncephaloMyelitis)
- Mass lesions, eg. Neoplasms
- Trauma (NAI)
- HSV encephalitis
- PRES (Post. Reversible Encephalopathy Syndr.)
- Complicated migraine
- Metabolic eg. MELAS (Mitochondrial)
Definitions

**Stroke:** Sudden occlusion or rupture of cerebral arteries or veins resulting in *focal cerebral damage* and *clinical neurological deficits*
Clinical stroke

A focal neurological deficit lasting more than 24 hours, with neuroimaging evidence of abnormality in an established vascular territory
The World Health Organization
‘a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 hours or leading to death, with no apparent causes other than of vascular origin’

(World Health Organization 1978).
Transient Ischaemic Attack

……. with deficits of < 24 hours

…… without neuroimaging abnormalities

(compare with Todd’s paralysis)
Others

- Bland infarct
- Haemorrhagic infarct
- Etc.
Classification

- Haemorrhagic
- Ischaemic
- Venous (CSVT)
- Arterial (AIS)
- Cardioembolic
- Thrombotic
Arterial Ischaemic Stroke

- Perinatal / Neonatal Stroke
  - 28 weeks gest. => 1 month

- Childhood AIS
  - 1 month => 18 years
Epidemiology

- Childhood stroke = 2.3 – 13/100 000
- Neonatal stroke increasing
  *25 – 30/100 000 (ie.1/4000 live births)
  
  *Lynch et al, 2002 (USA); Lee et al, 2005
- Boys > girls
  
- Black > Asian > White (including mortality)
  
  *Fullerton HJ et al, Neurology 2003
- Ischaemic > haemorrhagic
  
  *AHA (Roach et al 2008) – 55% ischaemic
Clinical presentation

- Infants may present with focal weakness

- More likely than older children present with:
  - seizures
  - altered level of consciousness

(Zimmer et al, 2007 – Age related variation in clinical signs of childhood AIS)
Clinical Presentation

Older children

- Hemiparesis
- Most commonly MCA territory
- Other focal neurological deficits
- Aphasia / dysphasia

*(Al-Sulaiman et al, 1999; Abram et al, 1996; Zimmer et al, 2007)*
Challenges in diagnosis

- Perceived to be rare – low index of suspicion
- Non-specific clinical cues
- Poor localization of signs in young children
- Misdiagnosis – ‘mimics’
- Availability of Neuroimaging
- Time delays
Underlying mechanisms/Risk Factors in Adults

- Atherosclerosis
- Hypertension
- Smoking
- Atrial fibrillation
- Diabetes mellitus
## Risk factors

<table>
<thead>
<tr>
<th>Intravascular</th>
<th>Vascular</th>
<th>Embolic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematologic</strong>&lt;br&gt;eg. Sickle cell disease</td>
<td><strong>Vasculopathies</strong>&lt;br&gt;eg. Post-varicella (TCAC)&lt;br&gt;Moyamoya</td>
<td><strong>Congenital heart disease</strong>&lt;br&gt;eg. Complex CHD</td>
</tr>
<tr>
<td><strong>Prothrombotic states</strong>&lt;br&gt;<strong>Congenital:</strong>&lt;br&gt;eg. Protein S,C deficiency&lt;br&gt;<strong>Acquired:</strong>&lt;br&gt;eg. L-asparaginase Anticardiolipin</td>
<td><strong>Vasculitis</strong>&lt;br&gt;eg. Meningitis, SLE Takayasu</td>
<td><strong>Acquired Heart Disease</strong>&lt;br&gt;eg. Rheumatic HD Infective endocard.</td>
</tr>
</tbody>
</table>
Examples of Childhood Arterial Ischaemic Stroke Risk Factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cardiac</td>
<td>- Congenital heart disease</td>
</tr>
<tr>
<td></td>
<td>- Valvular heart disease</td>
</tr>
<tr>
<td></td>
<td>- Cardiomyopathies</td>
</tr>
<tr>
<td>2. Cerebral arteriopathy</td>
<td>- Focal cerebral arteriopathy</td>
</tr>
<tr>
<td></td>
<td>- Moyamoya disease/syndrome</td>
</tr>
<tr>
<td></td>
<td>- Dissection</td>
</tr>
<tr>
<td>3. Infections</td>
<td>- Varicella</td>
</tr>
<tr>
<td></td>
<td>- Meningitides</td>
</tr>
<tr>
<td>4. Haematological</td>
<td>- Sickle cell disease</td>
</tr>
<tr>
<td></td>
<td>- Thrombophlias</td>
</tr>
<tr>
<td></td>
<td>- Iron deficiency anaemia</td>
</tr>
<tr>
<td>5. Genetic</td>
<td>- Neurofibromatosis Type 1</td>
</tr>
<tr>
<td></td>
<td>- Homocystinuria</td>
</tr>
</tbody>
</table>
Risk factors

- Hospital-based vs population-based
- Cardiac constitute about 30% (*hospital*)

- Cerebral Arteriopathy – 24%
- Infection (meningitis, sepsis) – 23%
- Cardiac – 12%
- No identifiable cause – 27%

*Fullerton et al, 2007 (n=97; California)*

- Thrombophilia (?) ; Sickle cell disease (3%)
Risk factors

- Often a combination of factors in children


Embolic

- Cardiac eg. Congenital HD

- Large vessels eg. Dissection
Intravascular factors / Haematological

- Thrombophilias
- Sickle Cell disease (+ vascular)
- Iron Deficiency Anaemia
Thrombophilias

- Isolated thrombophilias
- Primary or secondary?
- Combinations more important
- Venous vs arterial
- Type of thrombophilia
## Thrombophilias

<table>
<thead>
<tr>
<th>Thrombophilia</th>
<th>Odds Ratio (95% Confidence Interval) for AIS</th>
<th>Odds Ratio (95% Confidence Interval) for CSVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 Genetic traits</td>
<td>18.75 (6.49–54.14)</td>
<td>6.12 (0.87–43.07)</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>11.0 (5.13–23.59)</td>
<td>6.30 (1.56–25.40)</td>
</tr>
<tr>
<td>Antiphospholipid antibodies</td>
<td>6.95 (3.67–13.14)</td>
<td>*</td>
</tr>
<tr>
<td>Lipoprotein(a) elevation</td>
<td>6.53 (4.46–9.55)</td>
<td>*</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>3.70 (2.82–4.85)</td>
<td>2.74 (1.73–4.34)</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>3.29 (0.70–15.48)</td>
<td>18.41 (3.25–104.29)</td>
</tr>
<tr>
<td>Factor II G20210A</td>
<td>2.60 (1.66–4.08)</td>
<td>1.95 (0.93–4.07)</td>
</tr>
<tr>
<td>MTHFR thermolabile</td>
<td>1.58 (1.20–2.08)</td>
<td>*</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>1.49 (0.32–6.92)</td>
<td>5.27 (1.53–18.21)</td>
</tr>
</tbody>
</table>

Data were retabulated from the article by Kenet et al.4

*MTHFR* indicates *methylene tetrahydrofolate reductase.  
*Insufficient data.*
Vasculopathies

- **FCA** – Focal Cerebral Arteriopathy of Childhood
- **Post-varicella** Arteriopathy
- **(TCAC – Transient Cerebral Arteriopathy of Childhood)**
- **Moyamoya** – Disease/Syndrome
- **Vasculitis – cPACNS;** post-infectious
- **Arterial Dissection**
Transient cerebral arteriopathy

Definitions²
On initial vascular imaging, unilateral focal or segmental stenosis or occlusion involving distal part of internal carotid and initial segments and branches of anterior and/or middle cerebral artery. In some cases, none or only minimum stenosis, with maximum stenosis or occlusion observed within 3 months of initial imaging (figure A, B). On follow-up imaging 6 months after initial stroke, non-progression (or regression) of arterial lesions compared with baseline 3-month angiogram (figure B, C, and D).

Causes
Inflammatory/infectious: varicella zoster virus, other agents (eg, enterovirus, borrelia, bartonella)?
Intracranial dissection: traumatic, inflammatory-infectious?
Spasm, toxic (eg, cocaine)?
Moyamoya

- “Moyamoya” is a rare cerebrovascular disorder
- Involves stenosis or occlusion of terminal internal carotids
- There are collateral vessels at base of the brain
  - best visualised on cerebral angiography
  - appearance of “puff of smoke” hence the Japanese term “Moyamoya”
Moyamoya Disease

- Primary or Idiopathic form
- Seen mostly in Japan and East Asia
- Estimated incidence:
  - USA - 0.09/100 000 patient-years
  - Japan - 3-10/100 000 patient-years
Moyamoya Syndrome
Secondary to the following:
- Down’s Syndrome
- Neurofibromatosis
- Sickle Cell Disease
- Homocystinuria
- Radiotherapy (brain)
- Infections (?HIV), etc.
Moyamoya associated factors:

- Irradiation
- NF1
- Sickle Cell Disease
- Down's Syndrome
- HIV
- Unknown
Fig 1. MRI and MRA of patient with moyamoya and Down’s Syndrome
Fig. 2 MRAs of 2 patients with HIV and cerebral arteriopathy
Vasculitis

- Primary or Secondary to systemic disease
- CNS vasculitis in adults – 1959
- Primary CNS vasculitis of childhood recently described
Primary CNS Vasculitis of Childhood

Angiography-positive cPACNS
Large vessel disease

Angiography-negative cPACNS
Small vessel disease

Benseler 2005, 2005
Elbers, 2011
Panel of Investigations

- Neuroimaging – CT vs MRI/MRA (head & neck)
- Infection screening – including CSF
- Echocardiography
- Connective tissue screening
- Thrombophilia screening
- HIV testing (where clinically indicated)
- Metabolic (eg. Homocystinuria)
Treatment

- Neuroprotective
- Antithrombotic
- Thrombolysis (experimental)
- Rehabilitation
- Revascularisation
Acute management includes

- Oxygenation
- Perfusion / cerebral perfusion
- Glycaemic control
- Temperature
- ? Anaemia correction
## Supportive care measures

<table>
<thead>
<tr>
<th>Acute therapy</th>
<th>RCP Pediatric Guidelines</th>
<th>ACCP Pediatric Guidelines</th>
<th>AHA Adult Guidelines[25,90]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>Oxygen saturation should be maintained within normal limits. (D)</td>
<td>None.</td>
<td>Hypoxic patients with stroke should receive supplemental oxygen. (Class I, Level of Evidence C)</td>
</tr>
<tr>
<td>Temperature</td>
<td>Temperature should be maintained within normal limits. (U)</td>
<td>None.</td>
<td>It is generally agreed that sources of fever should be treated and antipyretic medications should be administered to reduce temperature in febrile patients with stroke. (Class I, Level of Evidence C)</td>
</tr>
<tr>
<td>Glucose</td>
<td>None.</td>
<td>None.</td>
<td>It is generally agreed that hypoglycemia should be treated in patients with acute ischemic stroke. (Class I, Level of Evidence C)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>None.</td>
<td>None.</td>
<td>It is generally agreed that patients with markedly increased blood pressure may have their blood pressure lowered. A reasonable goal would be to reduce blood pressure by 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is unknown, but consensus exists that medications should be withheld unless the systolic blood pressure is &gt;220 mm Hg or the diastolic blood pressure is &gt;120 mm Hg. (Class I, Level of Evidence C)</td>
</tr>
</tbody>
</table>
# Antithrombotic Treatments

<table>
<thead>
<tr>
<th></th>
<th>UK guideline</th>
<th>Chest guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonatal AIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>Not addressed</td>
<td>No anticoagulants or ASA</td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>Not addressed</td>
<td>UFH or LMWH for 3 months</td>
</tr>
<tr>
<td><strong>Acute childhood AIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>ASA 5 mg/kg</td>
<td>UFH or LMWH for 5 to 7 days and until cardioembolic and dissection excluded</td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>Exchange transfusion to HbS &lt; 30%</td>
<td>Intravenous hydration and exchange transfusion to HbS &lt; 30%</td>
</tr>
<tr>
<td>Allopase</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Maintenance therapy in childhood AIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>ASA 1-5 mg/kg/day</td>
<td>For all children with AIS treat with ASA 2-5 mg/kg/day after anticoagulation therapy has been stopped</td>
</tr>
<tr>
<td>Dissection</td>
<td>Consider anticoagulation until evidence of vessel healing or up to 6 months</td>
<td>After 5-7 days UFH or LMWH, treat with LMWH or warfarin for 3-6 months</td>
</tr>
<tr>
<td>Carciogenic embolism</td>
<td>Consider anticoagulation after discussion with the cardiologist managing patient</td>
<td>After 5-7 days UFH or LMWH, treat with LMWH or warfarin for 3-6 months</td>
</tr>
<tr>
<td>Vasculopathy</td>
<td>ASA 1-3 mg/kg/day</td>
<td>ASA 2-5 mg/kg/day after anticoagulation therapy has been stopped</td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>Blood transfusion every 3-6 weeks to HbS &lt; 30%</td>
<td>Long-term transfusion programme</td>
</tr>
<tr>
<td></td>
<td>After 3 years aim for HbS &lt; 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If no transfusion, hydroxyurea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider bone-marrow transplant</td>
<td></td>
</tr>
<tr>
<td>Recurrent stroke on ASA</td>
<td>Consider anticoagulation</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>
Recommendations – Childhood AIS

- For secondary prevention in underlying **cardiac disorders** and **vascular dissection**:
  - *low molecular weight heparin*
  - these patients MUST be referred and managed in conjunction with relevant specialists – cardiologist, haematologist, neurologist.

Growing evidence for heparin in **CSVT**
Recommendations for Treatment of Cerebral Venous Sinus Thrombosis

Class I Recommendations

1. Supportive measures for children with CVST should include appropriate hydration, control of epileptic seizures, and treatment of elevated intracranial pressure (Class I, Level of Evidence C).

2. Children with CVST should have a complete blood count (Class I, Level of Evidence C).

3. Children with a CVST and a suspected bacterial infection should receive appropriate antibiotics (Class I, Level of Evidence C).
Childhood AIS

- Low dose aspirin for children with AIS
- All patients with vasculopathy
- Patients with unknown aetiology
- ?Duration of aspirin
Sickle cell disease - STOP

- Transfusions
- Target HbS <30%
- Transcranial Doppler
- Hydroxurea
## Thrombolysis (Hyperacute)

**Bernard et al: Childhood AIS Treatment, Ann Neurol 2008**

<table>
<thead>
<tr>
<th></th>
<th>RCP Pediatric Guidelines&lt;sup&gt;24&lt;/sup&gt;</th>
<th>ACCP Pediatric Guidelines&lt;sup&gt;23&lt;/sup&gt;</th>
<th>AHA Adult Guidelines&lt;sup&gt;25,90&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute systemic thrombolysis</strong></td>
<td>No specific guideline, but the following comment: “There is currently no evidence to support use of thrombolytic agents such as tissue plasminogen activator (tPA) in the acute treatment of arterial ischaemic stroke in children.”</td>
<td>No specific guideline, but the following comment: “The use of thrombolytic agents in children with AIS, however, has been rare, and the risk/benefit ratio is unknown at this time.”</td>
<td>Intravenous rtPA (0.9mg/kg; maximum dose, 90mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke. (Class I, Level of Evidence A)</td>
</tr>
<tr>
<td><strong>Acute intraarterial thrombolysis</strong></td>
<td>None.</td>
<td>None.</td>
<td>Intraarterial thrombolysis is an option for treatment of selected patients who have major stroke of &lt;6 hours’ duration because of occlusions of the MCA and who are not otherwise candidates for intravenous rtPA. (Class I, Level of Evidence B)</td>
</tr>
</tbody>
</table>
Rehabilitation

- Physio
- OT
- Speech Therapy

- CIMT - *Constraint-Induced Movement Therapy*
- TMS - *Transcranial Magnetic Stimulation*
Outcomes

- Normal
- Neurological deficits
- Epilepsy
- Death
- Migraine

NB: Pre-Wallerian degeneration on Diffusion studies = poor prognosis
Neurological deficit

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A

Persistent Neurological Deficit

Canada\textsuperscript{21} (2 years)
France\textsuperscript{18} (2.5 years)
Switzerland\textsuperscript{20} (0.5 years)
Mortality

Annals of Neurology Vol 63 No 6 June 2008
Recurrence

Annals of Neurology Vol 63 No 6 June 2008
THANK YOU !!!