A clinical *approach to Hemiplegia*

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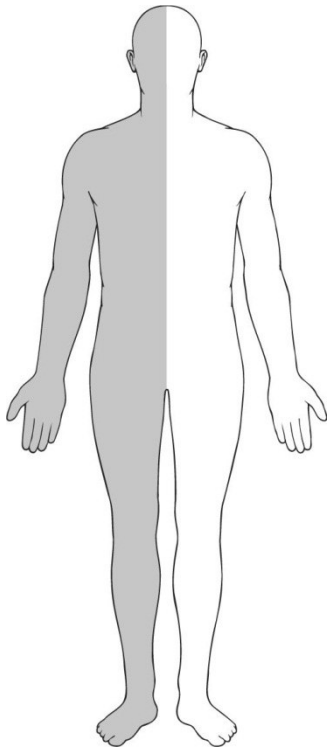
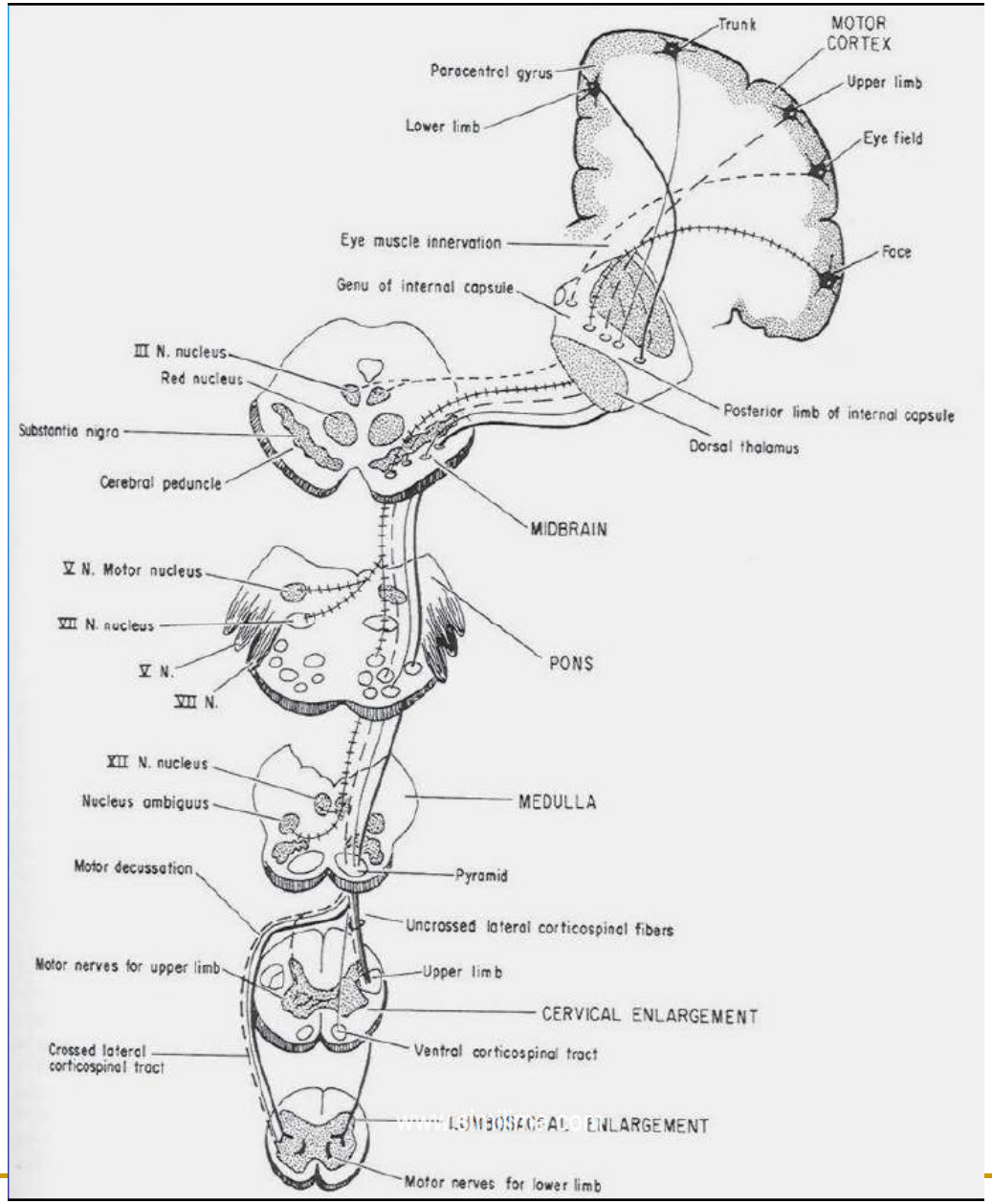
Paralysis of one side of the body



Involvement of corticospinal tract on the opposite side

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


Trunk
MOTOR CORTEX
Paracentral gyrus
Upper limb
Lower limb
Eye field
Eye muscle innervation
Face
Genu of internal capsule
III N. nucleus
Red nucleus
Posterior limb of internal capsule
Substantia nigra
Dorsal thalamus
Cerebral peduncle
MIDBRAIN
V N. Motor nucleus
VII N. nucleus
PONS
V N.
VII N.
XII N. nucleus
MEDULLA
Nucleus ambiguus
Motor decussation
Pyramid
Uncrossed lateral corticospinal fibers
Motor nerves for upper limb
Upper limb
CERVICAL ENLARGEMENT
Ventral corticospinal tract
Crossed lateral corticospinal tract
LUMBOSACRAL ENLARGEMENT
Motor nerves for lower limb

Cortex

- 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 = 3^{rd} N + opp. hemi
  (midbrain)
- Millard-Gubler syndr. = 6^{th} /7^{th} + opp. hemi
  (pons)
- Jackson syndrome = 10^{th}, 12^{th} + 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
  - 28weeks gest. => 1 month

- **Childhood AIS**
  - **1 month => 18years**

Epidemiology

- Childhood stroke = 2.3 – 13/100 000
- Neonatal stroke increasing

  *25 – 30/100 000 (ie.1/4000live births)

  Lynch et al, 2002 (USA); Lee et al, 2005
- Boys > girls

  Amlie-Lefond C et al, Lancet Neurol 2008
- 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

Intravascular	Vascular	Embolic
Haematologic eg. Sickle cell disease *Prothrombotic states* *Congenital:* eg. Protein S,C deficiency *Acquired:* eg. L-asparaginase Anticardiolipin	*Vasculopathies* eg. Post-varicella (TCAC) Moyamoya *Vasculitis* eg. Meningitis, SLE Takayasu	*Congenital heart disease* eg. Complex CHD *Acquired Heart Disease* eg. Rheumatic HD Infective endocard.

Examples of Childhood Arterial Ischaemic Stroke Risk Factors

Factors	Examples
1. Cardiac	- *Congenital heart disease* - *Valvular heart disease* - *Cardiomyopathies*
2. Cerebral arteriopathy	- *Focal cerebral arteriopathy* - *Moyamoya disease/syndrome* - *Dissection*
3. Infections	- *Varicella* - *Meningitides*
4. Haematological	- *Sickle cell disease* - *Thrombophilias* - *Iron deficiency anaemia*
5. Genetic	- *Neurofibromatosis Type 1* - *Homocystinuria*

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; Carlifornia)

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

Risk factors

- **Often a combination of factors in children**

*Lanthier, S, Carmant, L, David, M, et al. Stroke in children: **The coexistence of multiple risk factors** predicts poor outcome.*

Neurology 2000; 54:371.

*Strater, R, Vielhaber, H, Kassenbohmer, R, et al. **Genetic risk factors of thrombophilia in ischaemic childhood stroke of cardiac origin**. A prospective ESPED survey. Eur J Pediatr 1999; 158 Suppl 3:S122.*

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. Odds Ratios for Initial AIS Versus CSVT

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

Data were retabulated from the article by Kenet et al.[4]
MTHFR indicates *methylenetetrahydrofolate 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**

TCAC

www.thelancet.com Vol 368 July 1, 2006

Transient cerebral arteriopathy

Definitions[2]

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:[5] traumatic, inflammatory-infectious?

Spasm, toxic (eg, cocaine)?

Guillaume Sébire

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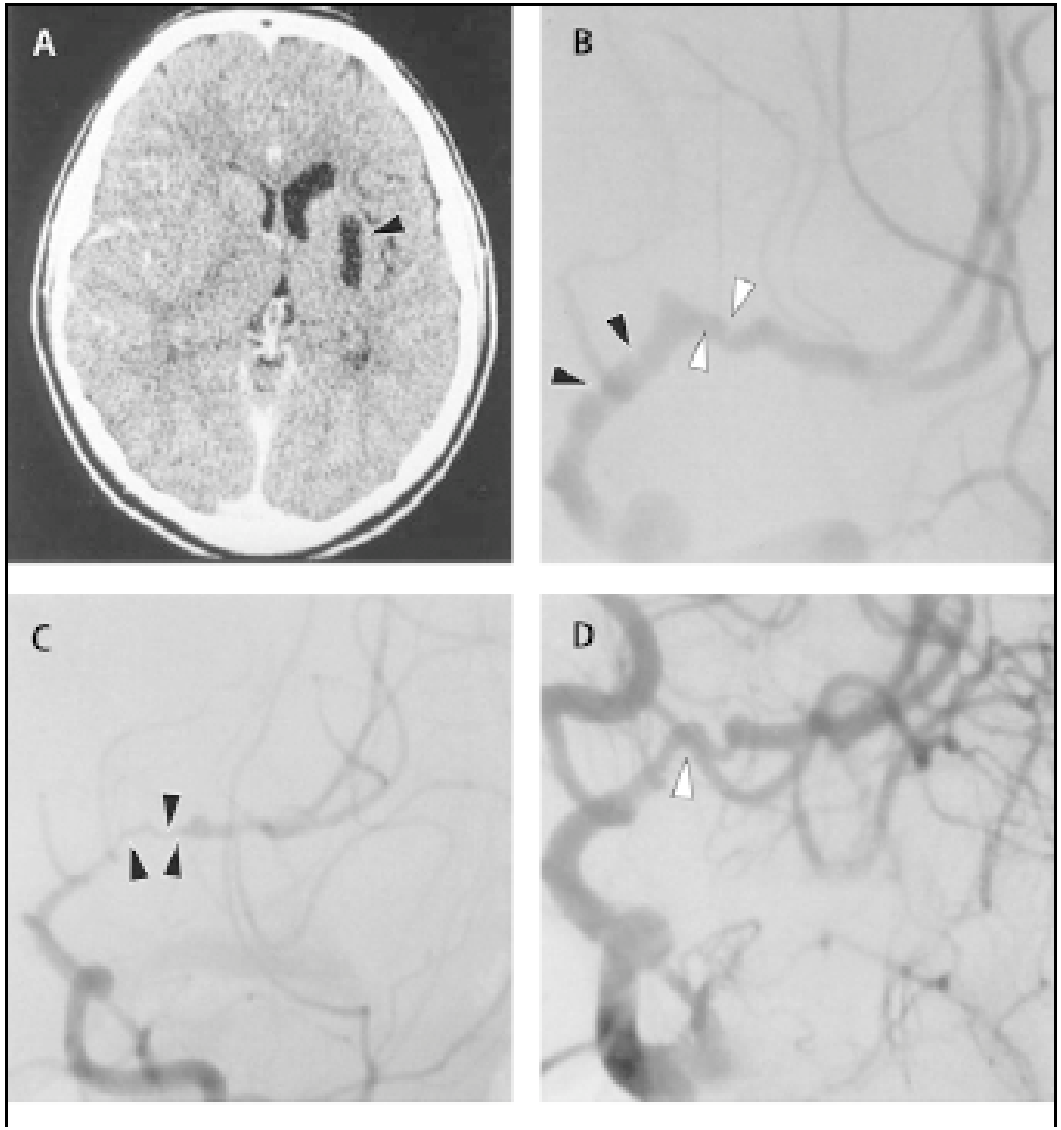


www.thelancet.com Vol 368 July 1, 2006

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

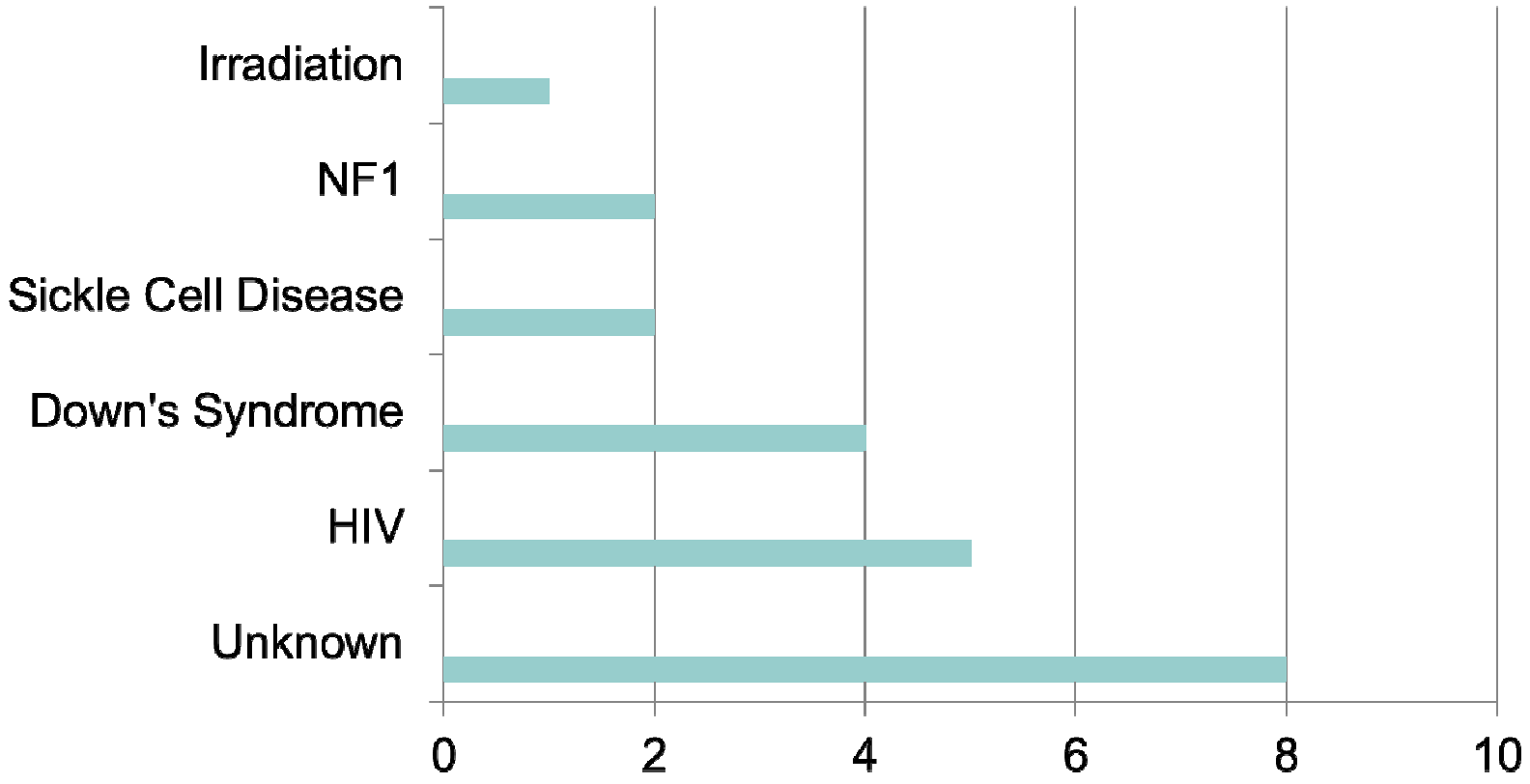
  Japan - 3-10/100 000 patient-years

Moyamoya Syndrome

Secondary to the following:

- Down's Syndrome
- Neurofibromatosis
- Sickle Cell Disease
- Homocystinuria
- Radiotherapy (brain)
- Infections (?HIV), etc.

Moyamoya associated factors:



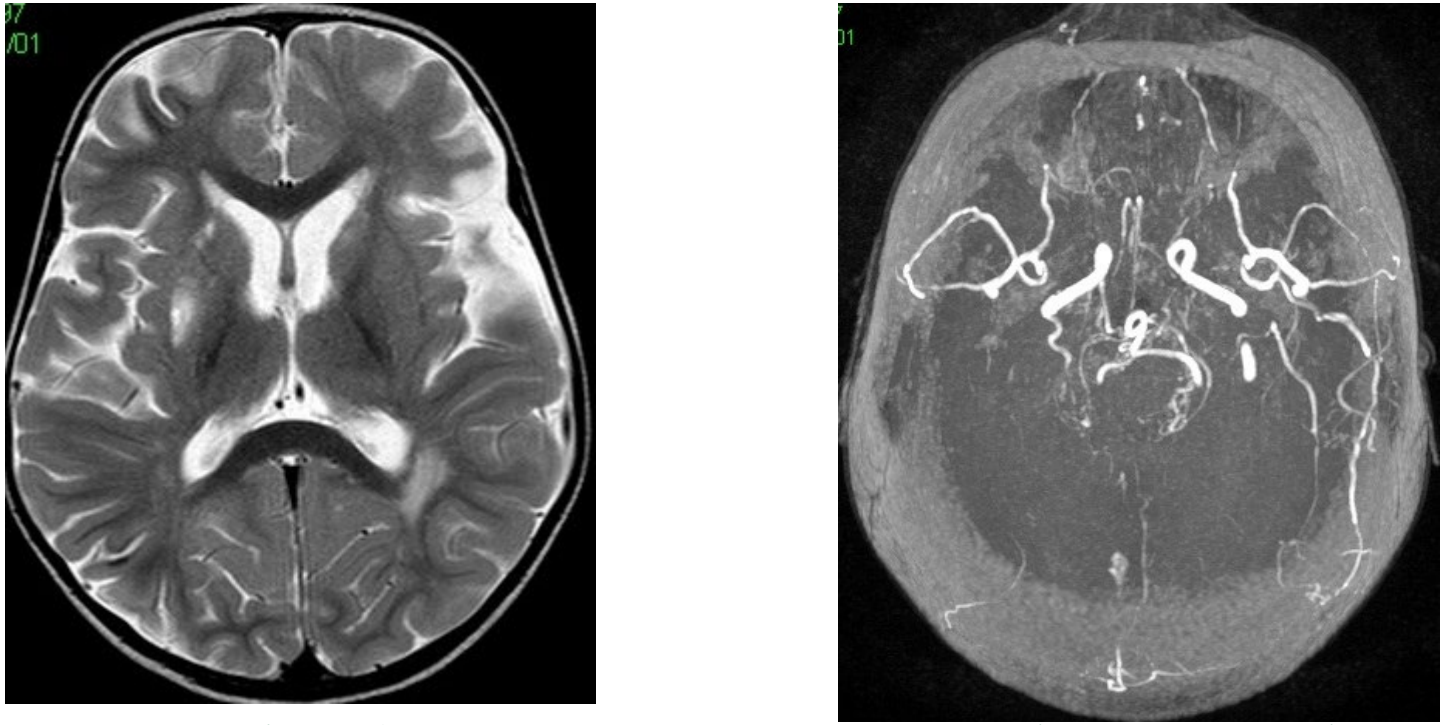


Fig 1. MRI and MRA of patient with moyamoya and Down's Syndrome

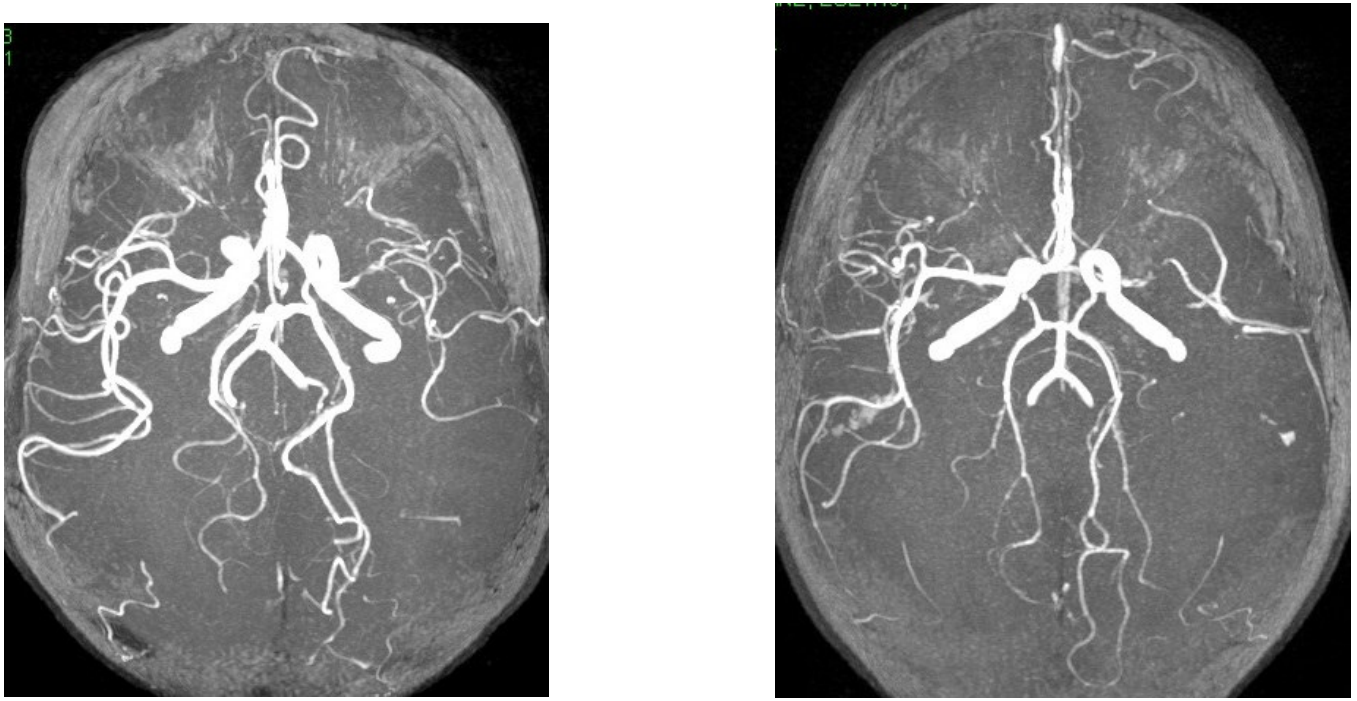
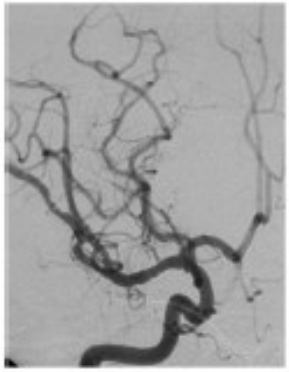
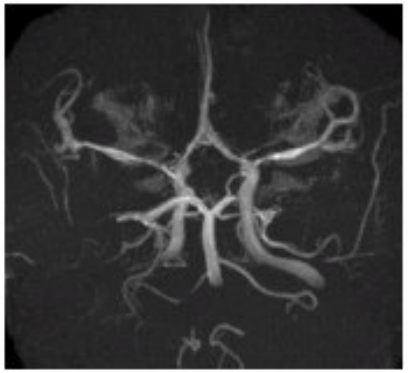
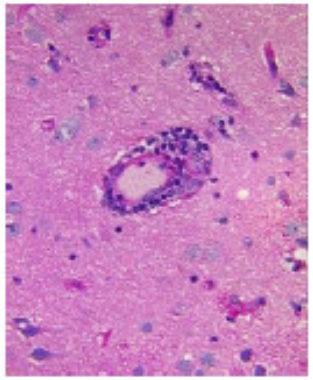
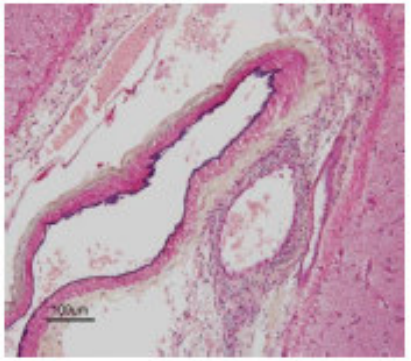


Fig.2 MRAs of 2 patients with HIV and cerebral arteriopathy

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	**Angiography-negative cPACNS**
Large vessel disease	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 2. **Acute Medical Management of Adult and Childhood Arterial Ischemic Stroke**

Acute therapy	RCP Pediatric Guidelines[24]	ACCP Pediatric Guidelines[23]	AHA Adult Guidelines[25,90]
Oxygen	Oxygen saturation should be maintained within normal limits. (D)	None	Hypoxic patients with stroke should receive supplemental oxygen. (Class I, Level of Evidence C)
Temperature	Temperature should be maintained within normal limits. (D)	None.	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)
Glucose	None.	None.	It is generally agreed that hypoglycemia should be treated in patients with acute ischemic stroke. (Class I, Level of Evidence C)
Blood pressure	None.	None.	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 >220mm Hg or the diastolic blood pressure is >120mm Hg. (Class I, Level of Evidence C)

Ann Neurol 2008;

Antithrombotic Treatments

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

Gabrielle deVeber Lancet Neurol 2005;

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

	RCP Pediatric Guidelines[24]	ACCP Pediatric Guidelines[23]	AHA Adult Guidelines[25,90]
Acute systemic thrombolysis	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."	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."	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)
Acute intraarterial thrombolysis	None.	None.	Intraarterial thrombolysis is an option for treatment of selected patients who have major stroke of <6 hours' duration because of occlusions of the MCA and who are not otherwise candidates for intravenous rtPA. (Class I, Level of Evidence B)

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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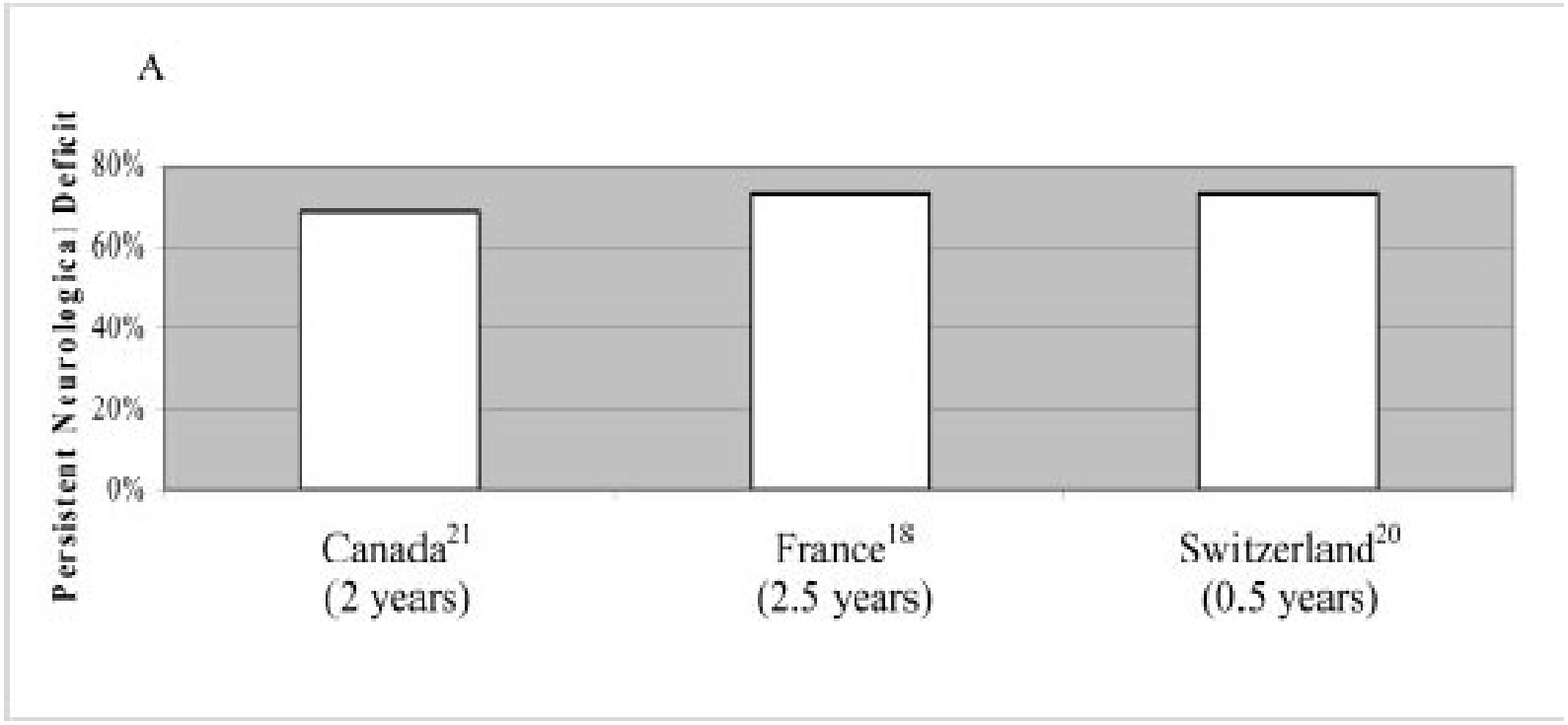

Mortality

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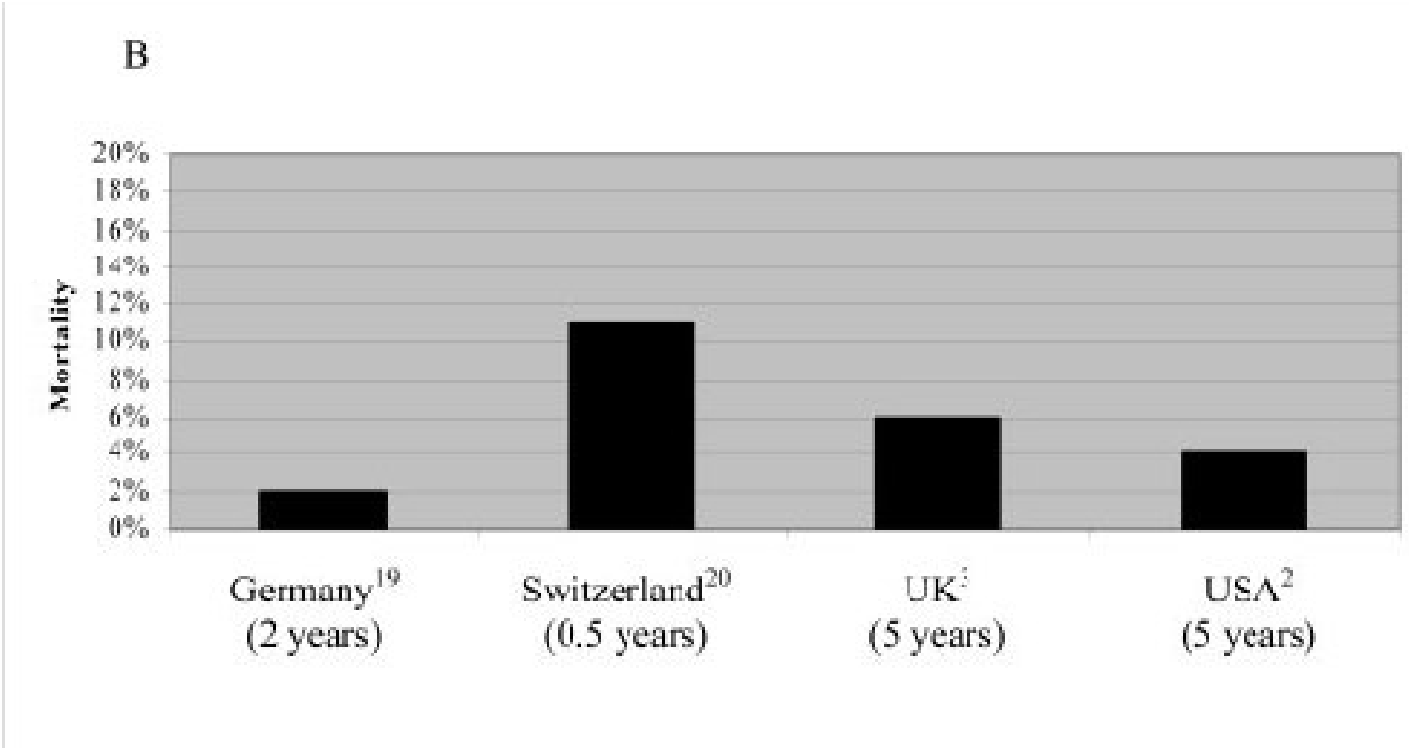

Recurrence

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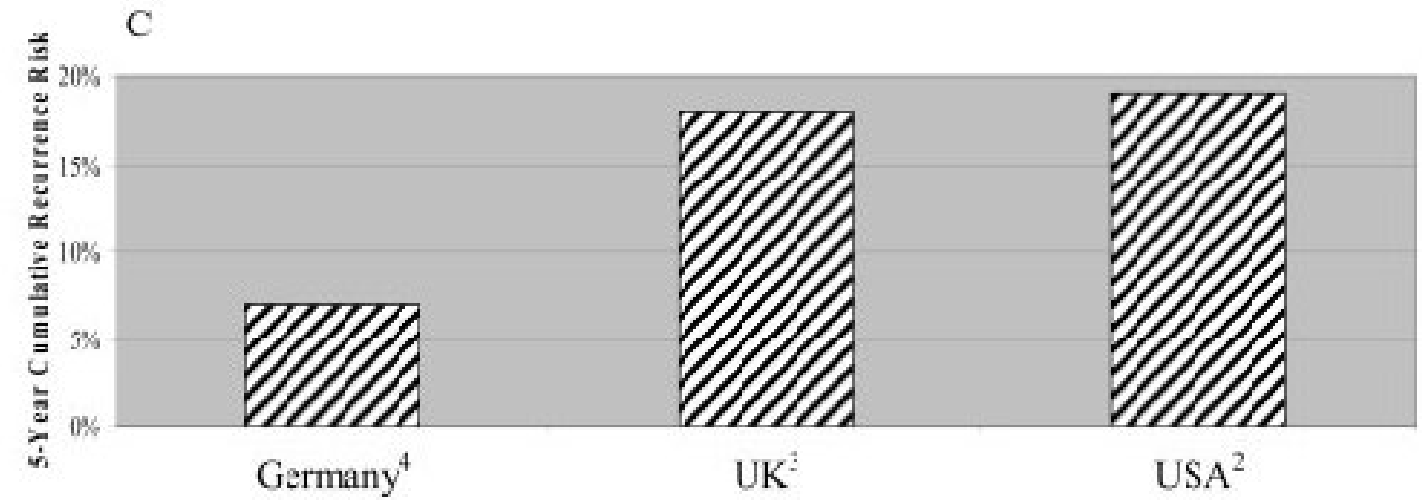

THANK YOU !!!