Cerebrovascular Disease
TIA/Stroke

Basics and beyond basics
Medicine for Psychiatrists
Denarau 2016
Cerebrovascular disease

- Background
- Basic manifestations
- Risk factors
- Assessment and Triage
- When to refer
- Newer treatments
- Ongoing trials
Cerebrovascular Disease

- Wide disease spectrum
- Heterogeneous\(^1\)
  - pathophysiology
  - presentation
  - treatment
- Many biologic targets
- **varied response to treatment and rehab\(^2\)
  - 1 Louis R Caplan et al UpToDate:Feb26,2014
  - 2 Steven C Cramer ,”Brain repair after stroke” ESC conf,London , June 2013
CVS - Stroke

- Why the importance??? Time is Brain !!
- Every min delay - 2 million neurons lost
- Most devastating acquired adult Neurological disease!!!
- $2^{\text{nd}}/3^{\text{rd}}$ leading cause of death
- For every stroke – (at least) 5 significant others affected
- Maximize Gain & minimize Disability - Needs holistic team effort, synchronised and co-ordinated

3. Hacke et al NEJM 2008;359:1317
4. NINDS Study Group NEJM 1995; 333: 1581
5. www.stroke.org.nz/preventing-stroke
"Less deficits, better function"

Risk Factors
- TIA
- Stroke

Primary Prevention
Secondary Prevention

Residual Deficit

Acute Phase Treatment
- rt-TPA, clot retrieval
- Aspirin, dual
- Stroke Unit, Neuro surg
## CVS Spectrum

<table>
<thead>
<tr>
<th>Funny turns</th>
<th>TIA</th>
<th>Stroke</th>
<th>Stroke/Fatality/Palliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Isolated symptoms</td>
<td>• Low / High risk</td>
<td>• Minor / moderate</td>
<td>• Severe</td>
</tr>
<tr>
<td>• Dizziness</td>
<td>• ABCD² score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Light headedness</td>
<td>• &lt;3 / &gt;4⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Blurry vision</td>
<td>• 7 Day 2%-10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Gen weakness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Stroke risk &lt;2%</td>
<td></td>
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</tbody>
</table>

Transient Ischemic attack (TIA)

Classical – **Time based** “A TIA is defined as stroke symptoms and signs that resolve within **24 hours**”

Problematic!!
1. Most TIA symptoms very short lived
2. If longer symptoms, minimal resolve
3. 1/2 with TIA have evidence of recent infarction on MRI (DWI)

Hence

- AHA/ASA - **Tissue based**, focal neurological dysfunction, brain, spinal cord, retinal ischemia **without infarction**

10 Albers GW et al NEJM 2002;347:1713
11 Caplan LR et al Arch Neu 2007;64:1080
12 Redgrave JN et al Stroke 2007;38:1482
Cerebrovascular disease characteristics

TIA/Stroke
- Sudden
- Focal - vascular territory
- Maximal deficit
- Loss of function
  - Motor
  - Sensory
  - Vision
  - Speech
  - Cognition

Mimics
- Gradual
- Not in a vascular territory
- Usually no focal symptoms
- Gain in function
- Migratory secs, mins
- Tell tale signs
  - Tongue biting
  - Abnormal movements
  - Incontinence
  - Post event confusion
TIA/Stroke mimics

Frequent
• Neurological
  – Migraine
  – Epileptic seizures
  – Syncope
  – Sensory march - Amyloid
• Metabolic/Toxic encephalopathy
• Hyper/hypoglycemia
• Hyponatremia

less frequent Mimics
• Functional disorders
• Structural brain disease
• Head injury
• Encephalitis
• Peripheral nerve lesions
• Multiple Sclerosis
• CJD
# ABCD² Score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>&gt;60 yrs</td>
<td>1</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>&gt;140/90</td>
<td>1</td>
</tr>
<tr>
<td><strong>Clinical symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face, arm, leg weakness</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Speech</strong></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>&gt;60 mins</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>10-59 mins</td>
<td>1</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>7</td>
</tr>
</tbody>
</table>

7. Rothwell PM et al Neurology 2005; 64:817
ABCD2 Score

Risk Category

High Risk

Moderate Risk

Low Risk

Day 2  Stroke Risk  Day 7  Day 90

8%  12%  18%

4%  6%  10%

1%  1%  3%
TIA’s carry a poor prognosis
Cerebrovascular Disease
Risk factors

Young (<45 yrs)
- Connective tissue disease
  - SLE
  - Anti Phospholipid
  - Other vasculitis
- Dissection
- PFO
- Moyamoya disease
- Familial - CADASIL

Older (Traditional RF)
- HT
- DM
- Smoking
- AF
- Dyslipidemia
- others
Other Risk Factors

• Age, risk of CVS increases with age
• Gender
• Family history
• Life style, ETOH, weight, diet\textsuperscript{50}
• Connective tissue disease
• Others – \textbf{APOE},\textsuperscript{51,52,53,}
• \textbf{Hyper homocysteinemia}, inc levels ass with inc risk of CAD, CVS, Isch, lacunar \textsuperscript{54}
• Rx with homocysteine reducing vitamins not beneficial for sec prevention\textsuperscript{19}

\textsuperscript{50} Furie KL et al Stroke 2011;42:227
\textsuperscript{51} McCarron MO et al Neurology 1999;53:1308
\textsuperscript{52} Schneider JA et al Stroke 2005 ;36:954
\textsuperscript{53} Sturgeon JD et al Stroke 2005;36:2484
\textsuperscript{54} Eikelboom JW et al Stroke 2000;31:1069
Assessment and triage

- Primary prevention/treatment
- Secondary prevention/treatment
- Tertiary treatments
- Restoration of function
- Limiting deficits
- Support
- Education – individual, population
Investigations

- ABCD2 score  
  <3 outpatient  
  >4 inpatient\(^\text{16}\)

- Laboratory\(^\text{17}\)  
  - FBC  
  - U&Es  
  - Glucose

- ECG

- Brain Imaging - CT, MRI, Carotid Duplex

- Other Investigations in selected cases

# Laboratory

<table>
<thead>
<tr>
<th>FBC</th>
<th>1. Hb</th>
<th>High</th>
<th>Polycythaemia hct 65, 200g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>Anaemia - clotting</td>
</tr>
<tr>
<td>2.  WCC</td>
<td>High</td>
<td>Infection, malignancy</td>
<td></td>
</tr>
<tr>
<td>3. Platelets</td>
<td>High</td>
<td>Thrombocytosis (x10^6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Penia, bleeding &lt;40,000</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>U&amp;E’s</th>
<th>1. Sodium</th>
<th>Low</th>
<th>Hyponatremia &lt;120 mmol Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Glucose</td>
<td>High</td>
<td>Ketotic coma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Hypoglycaemic coma</td>
<td></td>
</tr>
</tbody>
</table>
Other Investigations

- **ECG**
  - 1. Arrhythmia (AF)
  - 2. MI

<table>
<thead>
<tr>
<th>Imaging</th>
<th>1. Brain</th>
<th>CT/CTA, MRI/MRA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Carotids</td>
<td>Duplex USS</td>
</tr>
<tr>
<td></td>
<td>3. Heart, aortic arch</td>
<td>ECHO - TTE/TOE</td>
</tr>
</tbody>
</table>

*Young patients* 18
- Stroke screen
- Connective tissue
- Bubble study

EXPRESS Study

Early use of EXisting PREventive Strategies for Stroke

Study Setting

Oxfordshire, UK

Eligible Population

91,000 individuals registered with the 63 primary-care physicians in 9 primary-care practices in Oxfordshire, UK who are referred to the study clinic by GP on suspected TIA or stroke

Participant Population

591 Patients
EXPRESS Study

**Phase 1**
Between April 1, 2002 – Sept 30, 2004
Phase of delayed assessment and treatment

- GP
- Fax
- Report and recommendations
- Appointment

- 310

**Phase 2**
Between Oct 1, 2004 – March 31, 2007
Reduced delay of assessment and treatment

- Immediate assessment
- Assessed and treated

- 281
Hypertension

• Single biggest risk factor !!
  - (~1/5 in NZ>15yrs)⁵
  - 50% CAD, Heart failure
  - 62% Strokes²⁰

• Target range,<140/80, DM<130/80²⁰

• Evidence for treatment, BP reduction 12/5 mmHg, 30-40% RRR, both Secondary and Primary event rate 5yrs²²

• NNT: 11 patients for 5 yrs : 1 fatal or non-fatal major vascular event²³

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22 PROGRESS Collaborative Group, Lancet 2001; 358:13; 1033
23. INERACT II, SAMPARIS
Diabetes

- **Risk x2** - vascular events
  - associated - dyslipidemia, endothelial dysfunction, platelet and coagulation abnormalities
- **IGT** May be a risk factor
- **Metabolic syndrome** - prediabetic - insulin resistance, 3 or more, high FBS, HT, low HDL, and obesity may confer increased risk
- **Target range** Strict Glycemic control reduces –
- **Microvascular complications** - retinopathy, nephropathy, neuropathy
- **Macrovascular** - RCTs no consistent evidence, MI, Strokes
- **Evidence** – UKPDS (22yrs f/u), DCCT/EDIC
- **Life style** changes – Benefits

19. AHA/ASA 2011 Guidelines
27. Holmes RR et al NEJM 2008;359:1577
Smoking

- **Risk** increased for all stroke subtypes, dose dependent\(^{30-33}\)
- **Evidence**: Observational studies
  - Nurses Health Study, smokers RR 2.58, **Disappears** 2-4yrs\(^{31}\)
  - Framingham Heart Study, OR 1.08 for moderate Carotid stenosis for every 5 pack yrs\(^{32}\)
  - Prospective Swedish cohort study (11,000 pts),~40% strokes attributable to smoking\(^{33}\)
- **Cessation** – Medicine+ therapy \(^{34,35}\)

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32. Wilson PW et al NEJM 1997;337:516
34. Stead LF et al. Cochrane Database Syst Rev 2012;10 CD008286
Dyslipidemia

- **Major risk** – CAD- Atherosclerotic disease

  Stroke relationship, complex, appears weak risk factor\(^\text{36}\)

- **Epidemiological evidence** of ischemic stroke attributable to cholesterol- in consistent and conflicting, PITFALLS**

- Weak positive ass with Ischemic Strokes with high levels > 7mmol\(^\text{37,38}\)

- Ass with hge Strokes, 4.14 mmol\(^\text{38}\)

- Dyslipidemia statin therapy and hge**\(^\text{39}\)

- Other lipid lowering therapy ?? No sig impact on Strk incidence

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37. Iso H et al NEJM 1989;320:904
38. Lindenstrom E et al BMJ 1994;309:11
Atrial Fibrillation

- **Prevalence** — increases with age

- **Evidence,** BAATAF, SPINAF, AFASAK, CAFA, SPAF\(^{40}\)
  - Primary prevention — risk stratification \(\text{CHA}_2\text{DS}_2\text{VASc}\)
  - Secondary prevention — Rx, 2011 ASA/AHA\(^{19}\)

- **Agents,** OAG, NOACS (Dabigatran, rivaroxaban, apixaban)

- **Benefits,** Reduce baseline risk by \(\frac{2}{3}\)\(^{45}\)

- **Risk** bleeding, CNS, <1% pa\(^{46}\)

- **C/E stroke** larger/severe\(^{41,42}\)

- **Silent cerebral infarcts** TIAs — Cognitive impairment\(^{43,44}\)
CHA$_2$DS$_2$VASc Score
**Referrals**

- **Outpatients** ..ABCD2 <3 – urgent, 1/52
- **Inpatients**
  - All high risk TIA’s, ABCD2 >4
  - Crescendo TIA’s
  - Atrial Fibrillation patients
  - All strokes
  - Any unstable patients
  - Discuss all with concerns
Antiplatelet therapy

- **Secondary** prevention
- Aspirin (A) RRR 18% NNT 83, IST, CAST trials
- Clopidogrel (C)
- Dipyridamole (D) RRR 17%
- Dual (A+C) RRR, MATCH, CAPRIE
- Dual (A + D) RRR 33%, ESPSII, ESPIRIT

- ACCP recommend Antiplt sec prevention, level I evidence
- Combination A+C 3 months (MATCH trial)
  - A+C 21 days dual, mono agent (CHANCE)

48.IST, CAST, Group. LANCET 1997;349:1569-1641
Recommend carotid endarterectomy

- If symptomatic carotid stenosis of 49%
  - >80% NNT 5
  - 70-80% NNT 8
  - *50-69% NNT 15 (men)
  - on same side as stroke
  - patient otherwise well
  - low surgical risk

- Early intervention!!, after 3 mths NNT 125 to prevent 1 disabling stroke/death – NASCET, Swedish Stroke Registry

49. Rothwell PM et al Lancet 2004; 363:915
TIA vs Unstable Angina
Acute stroke therapies
Time dependent

• Thrombolysis- IV, IA
• Clot retrieval
• Hemi-craniotomy
• Hematoma - ??Surgery
• Newer options
• Medications – antithrombotic- NOACS
• AF – Catheter ablation
AFFINITY

• ?neuroprotection
• Flame 2011, Lancet Neurology
• 26.6% vs 9.9% placebo
• UK- FOCUS
• Sweden - EFFECTS
ECST -2 Trial

• Surgery vs OMT (optimal medical therapy)
• CAR score- (carotid artery score)
• PROBE - Trial design
• Currently – tPA, Stent Thrombectomy
TPA Trial

• Tenectaplastase – easier to use – a bolus
• ?more clot specific
• Phase III trials – ATTEST, Aust TNK study
• WUS – wake up stroke, extending thrombolysis time window
Respect ESUS

- Cryptogenic Stroke
- Dabigatrin vs Aspirin
- ATTUNE
- OAG in Ischemic stroke within 7 days
STROKE

Ischaemic
70-90%
- Thrombus
- Embolus
- Hypoperfusion

Haemorrhage
10-30%
- HTN
- Amyloid
ICH Haematoma expansion & Mortality

Volume (60ml / 60% mortality)
GCS <8
Site

0-5 hours
6-24 hours
2 weeks
1 year

RISK OF HAEMATOMA EXPANSION

Time from Onset

56 Cerebrovasc Dis 1999 Mar-Apr;9(2):102-8
Ischaemic Stroke

- Ischaemic Penumbra
- Infarcted Tissue
- MABP
- Collateral Blood Flow
Ischaemic Strokes Classification

- Oxfordshire (OSCP, Bamford) Classification
  - **TACI** – total anterior circulation infarct
  - **PACI** – partial anterior circulation infarct
  - **POCI** – posterior cerebral infarct
  - **LACI** – lacunar infarct

- 1 yr mortality
  - 60%
  - 19%
  - 16%
  - 11%

Oxford Stroke Classification

- **TACS:**
  - Total anterior circulation stroke
  - Large cortical stroke in middle / anterior cerebral artery areas.

- **PACS:**
  - Partial Anterior Circulation Syndrome (PACS)
  - Cortical stroke in middle / anterior cerebral artery areas.

- **POCS:**
  - Posterior Circulation Syndrome

- **LACS:**
  - Lacunar Syndrome (LACS)
  - Subcortical stroke due to small vessel disease.
  - No evidence higher cerebral dysfunction and

**Diagnosis:**
All three of the following:
1. Unilateral weakness (and/or sensory deficit) of face, arm and leg
2. Homonymous hemianopia
3. Higher cerebral dysfunction (dysphasia, visuospatial disorder)

**Diagnosis:**
Two of:
1. Unilateral weakness (and/or sensory deficit) of face, arm and leg
2. Homonymous hemianopia
3. Higher cerebral dysfunction (dysphasia, visuospatial disorder)

**Diagnosis:**
One of
1. Cerebellar or brainstem syndromes
2. Loss of consciousness
3. Isolated homonymous hemianopia

**Diagnosis:**
one of:
- Unilateral weakness (and/or sensory deficit) of face and arm, arm and leg or all three.
- Pure sensory stroke.
- Ataxic hemiparesis.

Bamford classification

MQ
Lacunar Infarct (LACI) Classification

- LACI – 5 Major syndromes
  - Pure motor
  - Pure Sensory
  - Mixed
  - Dysarthria clumsy hand
  - Ataxic hemiparesis

- Small discrete infarcted area - penetrating artery occlusion.
- Lipohyalanosis – HT, DM, embolism
- Due to location normally don’t affect higher cortical cognitive function.

89 Jamary OF et al Lacunar infarcts UpToDate Aug20,2013
Many Sources of Variance affecting Stoke outcome - Heterogeniety

- Pre-Stoke Disability
- Genetics
- Age
- Handedness
- Medical co-morbidities
- Initial and final deficits
- Injury mechanism, side topography, volume

- Effects on brain function
- Acute stroke interventions
- Time post-stroke
- Post-stroke depression
- Medication (+ and -)
- Caregiver, social factors
- Quantity, quality, and timing
- Of post–stroke therapy
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- Of post –stroke therapy
Remember!!!

• Time is Brain, Action is salvation
• Move - talk field – work field !
• Treat immediately, aggressively
• Holistic team effort - maximize Gain
  - minimize disability
  - insync, coordinated
• Thank you