

1. Stroke Syndromes

Stroke Syndromes

Dr David E Thaler

Director

Tufts Comprehensive Stroke Center at
New England Medical Center

December 14, 2005

Tufts Comprehensive Stroke Center at
NEMC

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2. Brain Attack!

BRAIN ATTACK!

- Stroke is a brain attack
- Organ affected is the brain and NOT the heart
- Stroke is an emergency
- "Time is brain"

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3. Impact of acute ischemic stroke

Impact of acute ischemic stroke

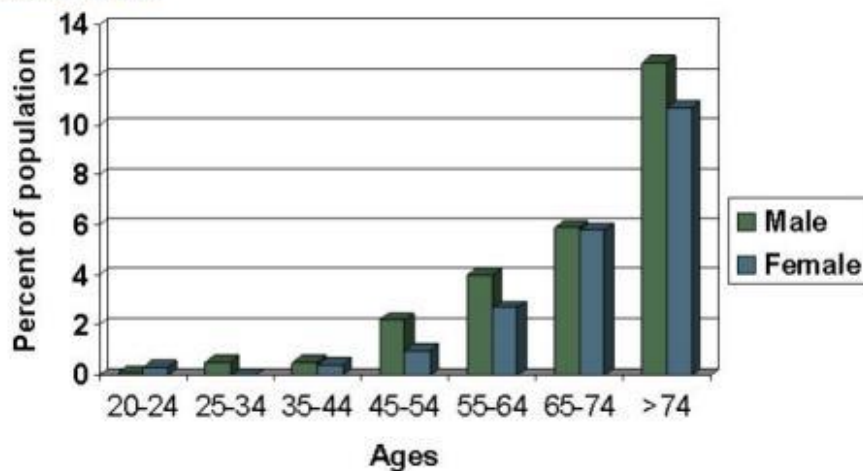
- Leading cause of serious, long-term disability
- >50% of neurological hospitalizations
- 3rd leading cause of death
- In the USA, a stroke occurs every 53 seconds
- ~600,000 strokes/year
- ~1/3 of survivors are partially dependent
- ~29% die within 1 year (higher if >65y)
- In 1995, \$3.7 billion paid by Medicare

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4. Estimated prevalence of stroke by age and sex

Estimated prevalence of stroke by age and sex



Source: AHA 1999 Heart and Stroke Statistical Update

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5. Modifiable and non-modifiable risk factors

Modifiable and non-modifiable risk factors

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6. Symptoms of stroke

Symptoms of stroke

- Sudden blurred or decreased vision in one or both eyes
- Numbness, weakness, or paralysis of the face or in an arm or leg occurring on one or both sides of the body
- Difficulty speaking or understanding
- Sudden dizziness or loss of balance
- Headache (usually severe and abrupt onset) or unexplained change in the pattern of headache

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7. Stroke Syndrome: Slide 7

Arteries at the Base of the Brain

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8. Branches of the middle cerebral artery

Branches of the middle cerebral artery

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9. Vascular territories - Coronal section

Vascular territories - Coronal section

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10. Vascular territories - Medulla

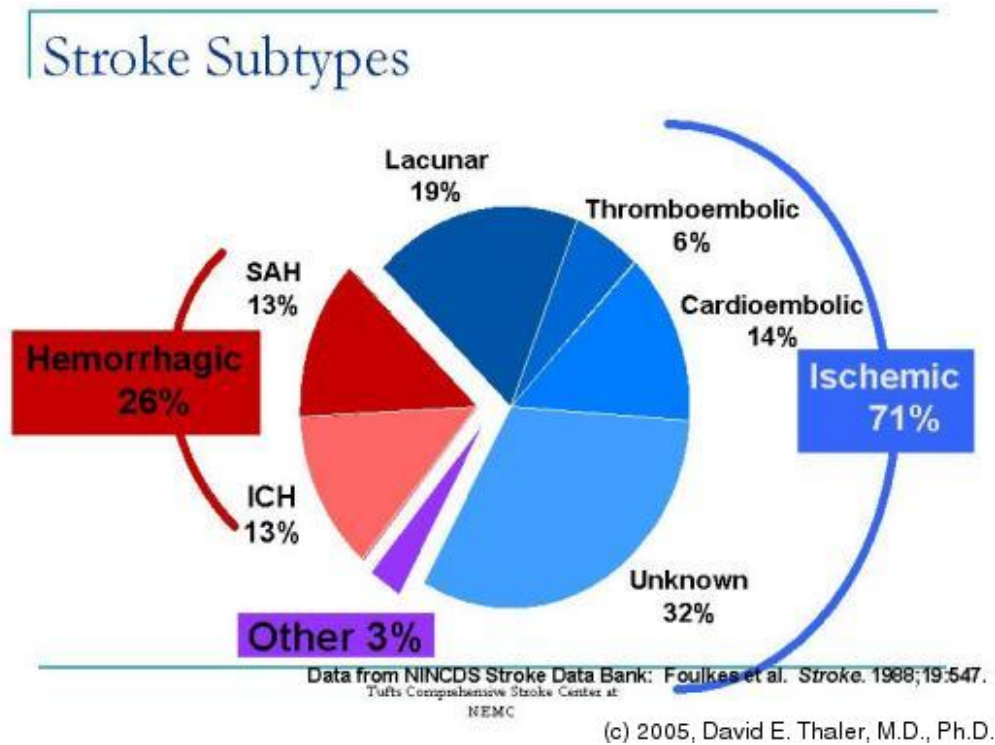
Vascular territories - Medulla

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11. Stroke Subtypes



12. Four types of intracranial hemorrhage

Four types of intracranial hemorrhage

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13. Intracerebral hemorrhage: Causes

Intracerebral hemorrhage: Causes

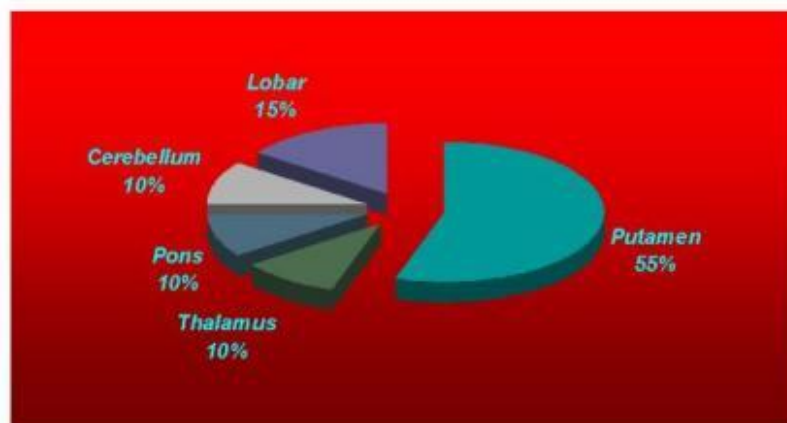
- Hypertension
- Hypertension
- Hypertension
- Congophilic (“amyloid”) angiopathy
- Hemorrhagic masses (tumor, AVM, etc)
- Hemorrhagic transformation of infarct

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14. Hypertensive ICH: Locations

Hypertensive ICH: Locations



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15. Intracerebral hemorrhage: Symptoms/Signs

Intracerebral hemorrhage: Symptoms/Signs

- *May have* sudden onset with smooth progression of deficit
- Focal deficits
- Headache
- Nausea/vomiting
- Decreased level of consciousness

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16. Lobar hemorrhage

Lobar hemorrhage

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17. Putamenal hemorrhage

Putamenal hemorrhage

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18. Intracerebral hemorrhage: Treatment

Intracerebral hemorrhage: Treatment

- No specific therapy has been shown to be useful with the exception of posterior fossa decompression for cerebellar hemorrhage
- BP management
- Supportive

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19. Aneurysms

Aneurysms

- 2mm - 2-3cm
- 90% on the circle of Willis
- Peak incidence 35-65y

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20. Cerebral aneurysms: Symptoms

Cerebral aneurysms: Symptoms

- Asymptomatic
- Mass effect
 - eg IIIrd nerve palsy
- Rupture

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21.

Stroke Syndrome: Slide 21

3rd nerve proximity to the PComA

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22.

Subarachnoid hemorrhage: Symptoms

Subarachnoid hemorrhage: Symptoms

- *Sudden onset* headache
- Stiff neck
- Photophobia
- Nausea/vomiting
- Transient loss of consciousness

**Does NOT need to be “the
worst headache of my life”**

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23. Subarachnoid hemorrhage: Signs

Subarachnoid hemorrhage: Signs

- Meningismus
 - Stiff neck
 - Pain with eye movement
 - Photophobia
- Subhyloid hemorrhages in fundus
- Focal signs are rare

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24. Subarachnoid hemorrhage: Diagnosis

Subarachnoid hemorrhage: Diagnosis

- History
 - ~50% have "sentinal bleed"
- CT scan (~90% sensitive)
- Lumbar puncture shows red blood cells and xanthochromia
- Angiography (MRA, CTA, conventional)

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25. Subarachnoid hemorrhage

Subarachnoid hemorrhage

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26. Subarachnoid hemorrhage

Subarachnoid hemorrhage

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27. Hunt and Hess Classification of subarachnoid hemorrhage

Hunt and Hess Classification of subarachnoid hemorrhage

Grade 1: Asymptomatic, mild headache, slight nuchal rigidity

Grade 2: Moderate to severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy

Grade 3: Drowsiness / confusion, mild focal neurologic deficit

Grade 4: Stupor, moderate-severe hemiparesis

Grade 5: Coma, decerebrate posturing

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28. Subarachnoid hemorrhage: Major concerns

Subarachnoid hemorrhage: Major concerns

- Rebleeding (~20% in 2 wks)
- Vasospasm (peaks day 3-14)
- Seizure (rare but preventable)
- Increased intracranial pressure

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29. Subarachnoid hemorrhage: Management

Subarachnoid hemorrhage: Management

- Bedrest with sedation
- BP tightrope
- Surgical clipping as soon as possible
- Prophylactic anticonvulsant
- Nimodipine
- “Triple H” - hypertension (pressors), hypervolemia (colloids), and hemodilution (Hct ~33)

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30. Arteriovenous malformation (AVM)

Arteriovenous malformation (AVM)

A tangle of abnormal vessels which form
an aberrant communication between
arterial and venous systems

Abnormally thinned walled vessels

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31. Arteriovenous malformation (AVM): Symptoms

Arteriovenous malformation (AVM): Symptoms

- Subarachnoid hemorrhage
- Intraparenchymal hemorrhage
- Seizures
- Headaches

Signs

- Any focal deficit
 - Cranial bruits
-

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32. Arteriovenous malformation (AVM)

Arteriovenous malformation (AVM)

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33. Arteriovenous malformation (AVM): Treatment

Arteriovenous malformation (AVM): Treatment

Obliteration of malformation by:

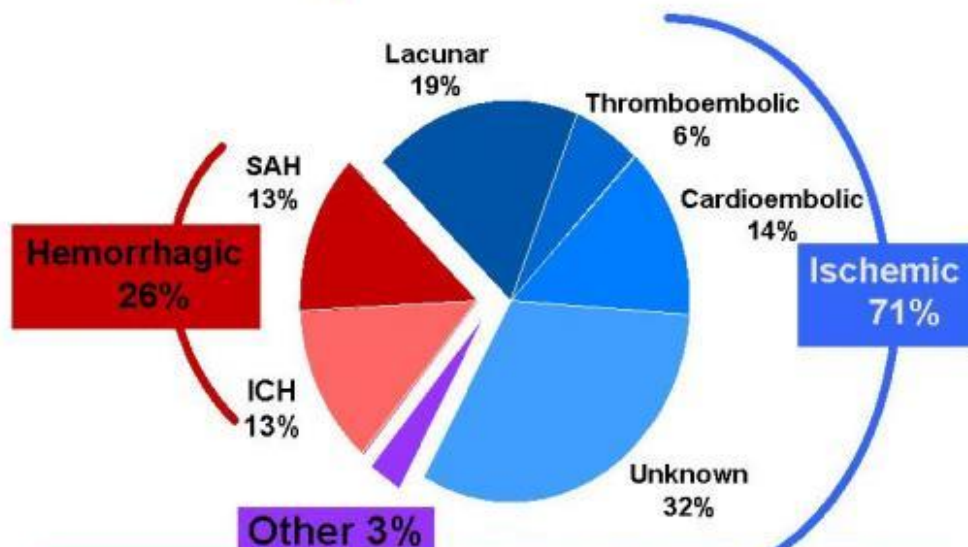
- Surgical excision
- Endovascular thrombosis
- Radiation - including Gamma knife

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34. Stroke Subtypes

Stroke Subtypes



Data from NINCDS Stroke Data Bank: Foulkes et al. *Stroke*. 1988;19:547.
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35.

Stroke: Definition

Stroke: Definition

“Sudden onset neurological deficit in a vascular territory”

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36.

Stroke defined by pace

Stroke defined by pace

- TIA - <24 hours
- RIND
- Completed stroke
- Stroke in progression

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37. What is the underlying mechanism?

What is the underlying
mechanism?

***“Stroke is an
observation not a
diagnosis”***

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38. Common mechanisms of cerebral ischemia

Common mechanisms of cerebral
ischemia

- “Small vessel disease” - lipohyalinosis
- Embolism
 - Artery-to-artery (carotid, aorta, other)
 - Cardiac source
 - Paradoxical
- Decreased perfusion through a fixed stenosis

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39. Etiology of ischemic stroke

Etiology of ischemic stroke

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40. Small vessel disease

“Small vessel disease”

- Associated with hypertension, diabetes, cholesterol
- “Lacune” ≠ small volume or small deficit

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41.

Stroke Syndrome: Slide 42

Intimal thickening

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42.

Major lacunar syndromes (C.Miller Fisher)

Major lacunar syndromes

(C.Miller Fisher)

- Pure motor stroke
- Pure sensory stroke
- Sensorimotor stroke
- Ataxic hemiparesis
- Clumsy hand - dysarthria

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43. Lacunar stroke (0.2-15mm³)

Lacunar stroke (0.2-15mm³)

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44. Other causes of cerebral ischemia

Other causes of cerebral ischemia

- Vasculitis
- Collagen vascular diseases: isolated angiitis of the CNS, temporal (giant cell) arteritis, polyarteritis nodosa, Wegener's granulomatosis, Takayasu's arteritis, syphilis
- Meningitis: tuberculosis, fungi, syphilis, bacteria, herpes zoster
- Arterial dissection: carotid, vertebral, basal intracranial arteries
- Hematologic disorders: polycythemia, thrombocytosis, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, dysproteinemias, hemoglobinopathies (sickle cell disease)
- Miscellaneous: cocaine, amphetamines, moyamoya disease, fibromuscular dysplasia, CADASIL
- Hypercoagulable states: secondary to systemic disease, carcinoma (especially pancreatic), eclampsia, oral contraceptives, lupus, factor C or S deficiency, factor V mutation, etc.
- Vasospasm: following subarachnoid hemorrhage
- Reversible cerebral vasoconstriction: idiopathic, migraine, eclampsia, trauma
- Venous: Dehydration, pericranial infection, postpartum and postoperative states, systemic cancer

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45.

Ms I.C.

Ms I.C.

- 46 y/o LH F with recent tooth abscess, on antibiotics, presented with L-face and arm weakness, dysarthria
- Still had tooth pain in R-upper teeth
- No vascular risk factors or family history of stroke

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46.

Carotid dissection

Carotid dissection

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47. Mimics of cerebral ischemia

Mimics of cerebral ischemia

- Migraine
- Seizure
- Subdural hematoma
- Tumor
- Syncope
- Cardiac arrhythmia
- Panic attack
- Hypoglycemia
- Demyelinating disease
- Amyloid angiopathy
- Brain abscess
- Encephalitis

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48. Risk for stroke after transient ischemic attack (TIA)

Risk for stroke after transient ischemic attack (TIA)

- 4% to 8% in first month
- 12% to 13% in first year
- 24% to 29% in five years

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49. Unstable angina of the brain

“Unstable angina of the brain”

**TIA = “Treat Ischemia
Aggressively”**

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50. Transcranial ultrasound

Transcranial ultrasound

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51. Baseline: Conventional T2 vs. Diffusion

Baseline: Conventional T2 vs.
Diffusion

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52. 24 Hours: Conventional T2 vs. Diffusion

24 Hours: Conventional T2 vs.
Diffusion

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53. Diffusion/Perfusion mismatch

Diffusion/Perfusion mismatch

73-year-old 3 with L-HP.

- A. 6 hours after the onset of symptoms.
- B. 6 hours: *larger area* of hypoperfusion on the rCBF map Image removed due to copyright.
- C. Infarct growth at 27 hours
- D. 1 week

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54. Diffusion/Perfusion match

Diffusion/Perfusion match

71-year-old 9 with L-HP

- A. 15 hours after the onset of symptoms.
 - B. 15 hours a *matching* area of hypoperfusion.
 - C. No significant growth is seen in the infarct at 39 hours
 - D. 1 week. Note the hemorrhagic transformation at 1 week (dark regions representing the breakdown products of hemoglobin).
- Image removed due to copyright.

[Kärmen et al Stroke. 1999;30:1583-1590](#)

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55. Conventional angiography

Conventional angiography

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56. Carotid angiogram Internal carotid artery stenosis

Carotid angiogram

Internal carotid artery stenosis

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57. Carotid artery disease

Carotid artery disease

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58. Carotid artery stenosis: Treatment

Carotid artery stenosis: Treatment

Asymptomatic		Medical management
Asymptomatic and progressing		Consider surgery
Asymptomatic and severe		Consider surgery
Symptomatic and	> 70%	Surgery
	> 50%	Consider surgery
	< 50%	Medical management

Medical management = risk factor control, antiplatelet agent, and
HMG-CoA reductase inhibitor (?)

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59. Proximal aortic atherosclerosis

Proximal aortic atherosclerosis

■ Amerenco (1992) - Autopsy series

Ulcerated aortic plaque seen in:

- Non-stroke neurological disease 5%
- Stroke of known cause 20%
- Cryptogenic stroke 58%

■ French study (1996) - Transesophageal echo

Stroke recurrence at 48 months

- Plaque thickness ≥ 4 mm 40%
- Plaque thickness 1-3.9mm 9%
- Plaque thickness < 1 mm 8%

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60. Cardiac conditions associated with cerebral embolism

Cardiac conditions associated with cerebral embolism

- High risk ($> 1\%$ /year)
 - Atrial myxoma
 - Infective endocarditis
 - Dilated cardiomyopathy
 - Atrial fibrillation
 - Anterior MI with thrombus
 - Ventricular aneurysm
 - Prosthetic cardiac valves
 - Nonbacterial thrombotic endocarditis

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61. Cardiac conditions associated with cerebral embolism

Cardiac conditions associated with cerebral embolism

- Low risk (<1%/year)
 - Mitral valve prolapse
 - Lone AF
 - Inferior MI
 - Bioprosthetic aortic valve
- Unclear risk
 - Patent foramen ovale
 - Atrial septal aneurysm
 - Left atrial spontaneous echo contrast ("smoke")

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62. Investigations for hypercoagulable states

Investigations for hypercoagulable states

- Protein S
- Protein C
- Antithrombin III
- Factor V Leiden (= activated protein C resistance)
- Antiphospholipid antibodies
 - Lupus anticoagulant
 - Anticardiolipin antibody
 - Antiphosphatidylserine antibody
- Prothrombin gene mutation (A ⇒ G)
- Antiphosphatidylserine antibodies

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63. Progression of ischemic stroke

Progression of ischemic stroke The “ischemic penumbra”

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64. Strategies for acute stroke treatment

Strategies for acute stroke treatment

- Revascularization
 - “Plumbing approach”
- Preventing damage from ischemic cascade
 - “Neuroprotection”

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65. The Plumbing Approach

The Plumbing Approach

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66. National Institute of Neurological Diseases and Stroke (NINDS) t-PA

National Institute of Neurological Diseases and Stroke (NINDS) t-PA trial

- *New England Journal of Medicine*, December 14, 1995
- First major trial to demonstrate the efficacy of ANY treatment for acute stroke
- Patients with stroke treated within 3 hours of symptom onset had a ~30% better chance of recovery without symptoms.

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67.

NINDS t-PA Trial

NINDS t-PA Trial:

1 year follow-up *NEJM* 1999 (340): 1781

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68.

Symptomatic hemorrhages

Symptomatic hemorrhages

- Cases 1 and 2 are placebo
- 4 ICHs outside of distribution of stroke: 4, 9, 16, 17
- = 1.3% of all t-PA patients

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69.

NINDS t-PA Trial

NINDS t-PA Trial:

1 year follow-up *NEJM* 1999 (340): 1781

- Benefit of t-PA therapy was across all ischemic stroke subtypes
- For every 100 patients treated 11 will have a better outcome

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70.

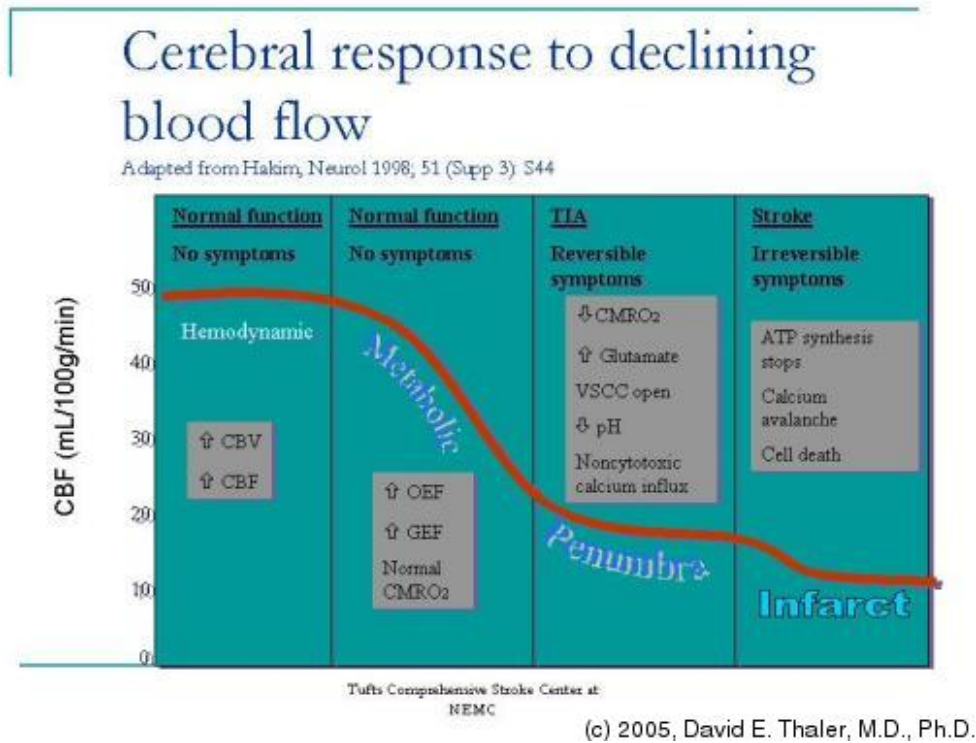
Neuroprotection

Neuroprotection

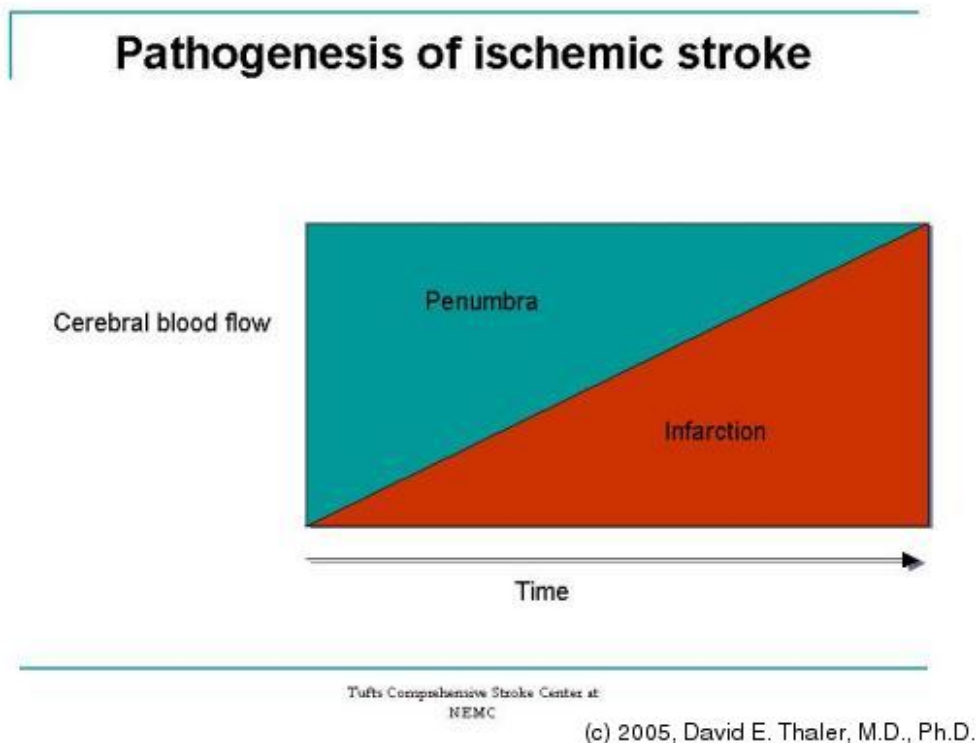
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71. Cerebral response to declining blood flow



72. Stroke Syndrome: Slide 73



73. Neuroprotectant mechanisms and some tested compounds

Neuroprotectant mechanisms and some tested compounds

NMDA antagonists	<ul style="list-style-type: none">▪ Dextrophan▪ Selfotel (CGS 19755)▪ Cerestat (aptiganel)▪ Magnesium▪ CP 101, 606	GABA agonists	<ul style="list-style-type: none">▪ Clomethiazole
Glycine site antagonist	<ul style="list-style-type: none">▪ ACEA 1021▪ GV 150526	Membrane stabilizers	<ul style="list-style-type: none">▪ Citicoline
Ca²⁺-channel blocker	<ul style="list-style-type: none">▪ Nimodipine	Ischemic injury cascade inhibitors	<ul style="list-style-type: none">▪ Lubeluzole
Opiate antagonists	<ul style="list-style-type: none">▪ Naloxone▪ Cervene	Inhibitors of leukocyte adhesion	<ul style="list-style-type: none">▪ Enlimomab▪ Hu23F2G

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74. Timing, timing, timing

Timing, timing, timing

How often do patients with stroke arrive at the hospital early enough for treatment and what factors contribute to early arrival?

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75. Immediate management of patients with suspected stroke

Immediate management of patients with suspected stroke

- Neuroimaging
- Keep head of bed flat
- *Do not* treat hypertension
- Hydrate with isotonic fluids
- Cardiac monitor

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76. Immediate management of patient with suspected stroke

Immediate management of patient with suspected stroke

- | | |
|------------------|-------------------------|
| ■ ABCs | |
| ■ CBC | CONSIDER |
| ■ ESR | R/O MI |
| ■ BUN/creatinine | Lumbar puncture |
| ■ electrolytes | Hypercoagulable studies |
| ■ INR | RPR |
| ■ Lipid profile | Sickling tests |
| ■ ECG | ANA |
| ■ CXR | ANCA |

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77. Short-term complications

Short-term complications

Non-neurological

- MI
- Arrhythmia
- Pneumonia
- DVT/PE

Neurological

- Edema/herniation
- Recurrence
- Hemorrhagic transformation
- Seizure

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78. Prevention of DVT

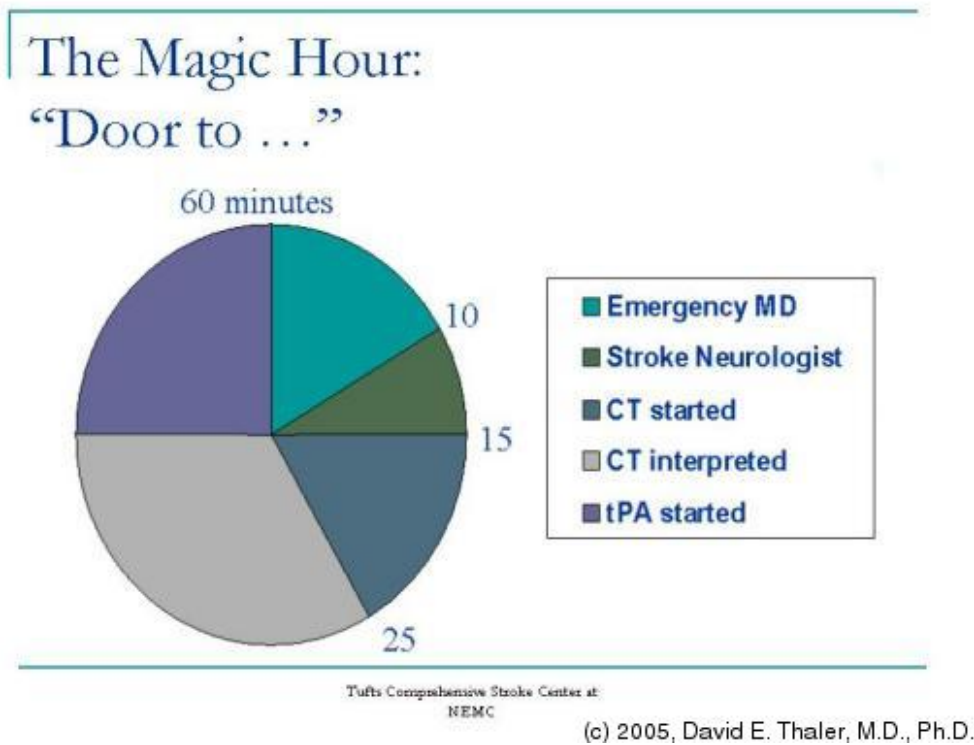
Prevention of DVT

- Heparin 5000u s/c bid
- TED stockings
- Intermittent compression boots
("pneumoboots")
- Mobilization

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79. The Magic Hour



80. Time: Traditional vs. Emerging Views

Time:
Traditional vs. Emerging Views

	<i>Traditional View</i>	<i>Y2K View</i>
Patient	Wait and see if symptoms disappear	Stroke is a “Brain Attack” – Call 911
Pre-hospital	Low-priority transport	High priority transport
Acute	Wait and watch	Stroke Codes, protocols, and clinical pathways

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81.

Brain Attack!

BRAIN ATTACK!

- Stroke is a brain attack
- Organ affected is the brain and NOT the heart
- Stroke is an emergency
- "Time is brain"

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