

Ischemic Stroke

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Epidemiology

- Over 500,000 strokes/yr (USA)
- 150,000 stroke-related deaths/yr (USA)
- Leading cause of adult disability
- Second leading cause of dementia
- Third leading cause of death
- 80% of all strokes are ischemic

Risk factors

Non-modifiable

1. Age (doubles each decade after age 55)
2. Gender (M > F)
3. Race (blacks & hispanics > whites)
4. Family history of TIA/stroke

Risk factors

Modifiable – modification reduces risk

1. Hypertension
2. Smoking
3. Diabetes
4. Hyperlipidemia
5. Atrial fibrillation
6. Sickle cell disease

Ischemic stroke patterns

1. Lacunar – small-vessel infarction
2. Territorial – arterial branch occlusion
3. Distal field – watershed infarction

Lacunar infarction

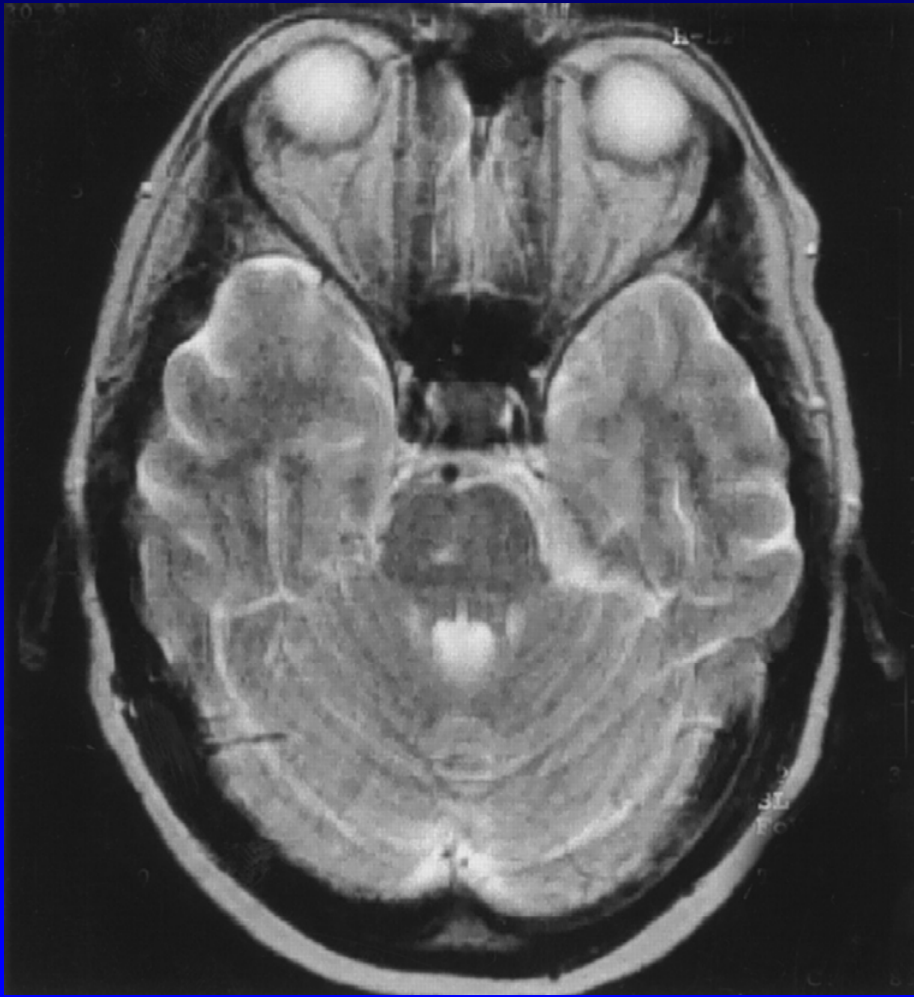
- One-third of all ischemic strokes
- Etiology: arteriosclerotic occlusion of perforators in the basal ganglia, brainstem, and centrum semiovale
- Associated with HTN and diabetes
- Lesions $< 1.5 \text{ mm}^3$
- Morbidity/mortality lowest of stroke types

Lacunar infarction

Classical clinical syndromes

1. Pure motor
2. Pure sensory
3. Sensorimotor deficits in 2 of 3 body parts
4. Ataxic hemiparesis
5. Dysarthria clumsy-hand syndrome
6. Acute hemiballismus

Lacunar infarction



T2-weighted MRI shows a right paramedian pontine lacunar infarction that lead to a left pure motor hemiparesis in a patient with diabetes and HTN.

Territorial Infarction

- Two-thirds of all ischemic strokes
- Arterial branch or stem occlusions
- Etiology: embolic (cardiac or artery-to-artery) or local thrombosis
- Prognosis related to severity of presenting symptoms, size of lesion, and patient's age & comorbidities

Territorial infarction

Clinical syndromes

1. Supratentorial –

sudden motor/sensory deficit

Plus cortical symptoms such as aphasia, apraxia, neglect, homonymous visual deficits

2. Infratentorial –

sudden motor/sensory deficit

Plus additional brainstem or cerebellar disturbances

Territorial infarction

Clinical syndromes

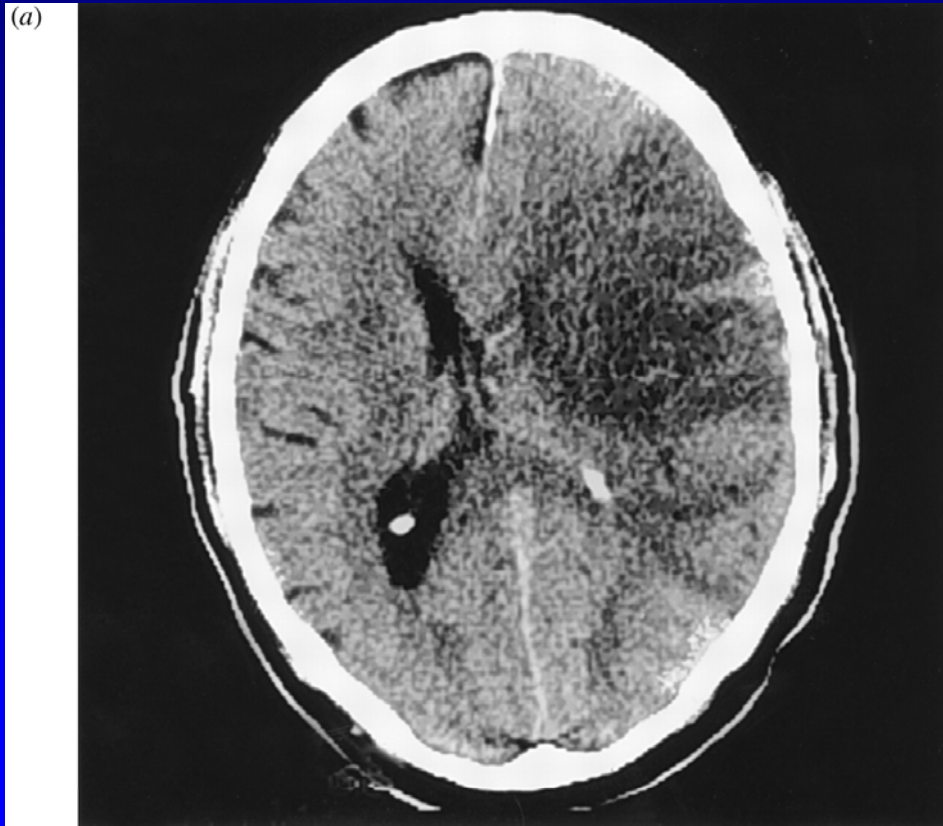
1. Embolus –

sudden onset with maximal deficit at outset

2. Thombosis –

maximal deficit occurs several hours after initial symptoms

Territorial infarction



CT shows large MCA distribution subacute infarction with significant mass effect

Distal field infarction

- Uncommon cause of ischemic stroke
- Etiology: perfusion failure due to severe stenosis/occlusion of major cranial vessel or following prolonged systemic hypotension

Distal field infarction

Clinical syndromes

1. Stereotypical TIA's
2. Unusual patterns of paresis
 - Man-in-the-barrel syndrome
3. Complex cortical syndromes
 - Balint's syndrome
 - Anton's syndrome
4. Deficits similar to territorial infarction

Distal field infarction

(a)



T2-weighted MRI shows an area of subacute infarction in the border zone between the left MCA and ACA. An angiogram revealed severe ICA stenosis.

Ischemic stroke patterns

- Although specific clinical syndromes may suggest ischemic stroke patterns, **there is considerable clinical overlap.**
- Gan et al., *Neurology*, 1997
 - As many as 25% of patients with lacunar syndromes confirmed radiologically ultimately proved to have nonlacunar infarct mechanism.

Acute stroke management

Dedicated stroke units = reduced stroke-related morbidity and mortality

- Langhorne et al., *Lancet*, 1993.
- Jorgensen et al., *Stroke*, 1995.

Initial work-up

- H&P
 - Neurologic exam
 - Medical exam (BP, O₂ sats, cardiac fxn, etc.)
- EKG and admitting labs
- Immediate head CT (or MRI)
 - Differentiates ischemic stroke from other etiologies of focal neuro deficits (hemorrhage, brain tumor)

Medical management

Anti-platelet agents

- Aspirin (160-300 mg QD) < 48 hrs stroke
 - International Stroke Trial, *Lancet*, 1997
 - CAST, *Lancet*, 1997
 - Reduction of 10 deaths or recurrent strokes per 1000 ischemic strokes
 - Note: aspirin should not be given in first 24 hrs after intravenous rt-PA

Medical management

Anti-platelet agents

- Aspirin + dipyridamole (50 / 200 mg BID)
 - Diner et al., J. Neurol. Sci., 1997
 - Superior to aspirin alone for secondary stroke prevention
 - Unclear whether combination is superior in acute stroke setting?

Medical management

Anti-platelet agents

- Clopidogrel (75 mg QD)
 - CAPRIE, *Lancet*, 1996
 - Shown to reduce relative risk of ischemic stroke
 - Can be used as alternative for patients with contraindications to aspirin

Medical management

Anticoagulation

- 5000 SQ heparin BID recommended
 - Prevention of DVT / PE
 - Higher doses associated with increased bleeding and no increased protection

Medical management

Anticoagulation

- Dose-adjusted intravenous heparin
 - Early treatment with iv heparin in ischemic stroke remains unresolved (conflicting studies)
 - RAPID trial to address this issue is ongoing

Medical management

Current recommendations for IV heparin

1. Atrial fibrillation
2. High-risk cardiac embolic sources
 - Acute MI, artificial valve
3. Coagulopathies
4. Arterial dissection
5. *Symptomatic high-grade carotid stenosis awaiting surgical therapy*

Medical management

Systemic thrombolysis

- Intravenous rt-PA (NINDS, *NEJM*, 1995)
 - Selected patients within 3 hours of ischemic stroke should receive rt-PA (0.9 mg/kg, 10% as bolus & 90% over 60 min)
 - FDA approved, strongly supported by AAN and AHA
 - Mechanism of action: presumably fibrinolysis
 - Yet response to rt-PA is rarely acute and rt-PA has been found unexpectedly effective across all ischemic stroke types

Systemic thrombolysis eligibility

- Age ≥ 18
- Reliable onset of symptoms < 3 hrs
- Early infarct signs $< 1/3$ of MCA territory
- No rapidly improving deficits
- No seizure
- No stroke/head injury/cranial surgery in past 3 mo.
- No GI/GU bleeding in past 3 weeks
- No recent MI
- Pretreatment BP $\leq 185/110$
- Normal coagulation profile

Medical management

Systemic thrombolysis

- Ancrod (Sherman et al., *JAMA*, 2000)
 - Purified fraction of Malaysian pit viper venom, which stimulates release of plasminogen activator from endothelium
 - Found effective in patients treated within 3 hours of ischemic stroke onset

Medical management in review

1. rt-PA if < 3 hrs from symptom onset
2. ASA, ASA + dipyridamole, or clopidogrel
 - within 48 hrs of symptom onset
 - wait 24 hrs if rt-PA administered
3. Heparin 5000 U SQ BID
4. Intravenous heparin in select patients only

Intra-arterial thrombolysis

- PROACT, *Stroke*, 1998; no benefit
- PROACT II, *JAMA*, 1999
 - 180 patients with acute ischemic stroke
 - Angiographically proven MCA occlusion
 - Intra-arterial pro-urokinase plus heparin
 - Better outcome at 90 days
 - (Rankin score ≤ 2 in 40% vs. 25%)
 - Increased early symptomatic ICH (10% vs. 2%)

Intra-arterial thrombolysis

Current recommendations

- May be appropriate for patients > 3 hrs out whose clinical syndrome and transcranial Doppler suggest MCA occlusion.

Disease specific treatment

Diseases to be considered...

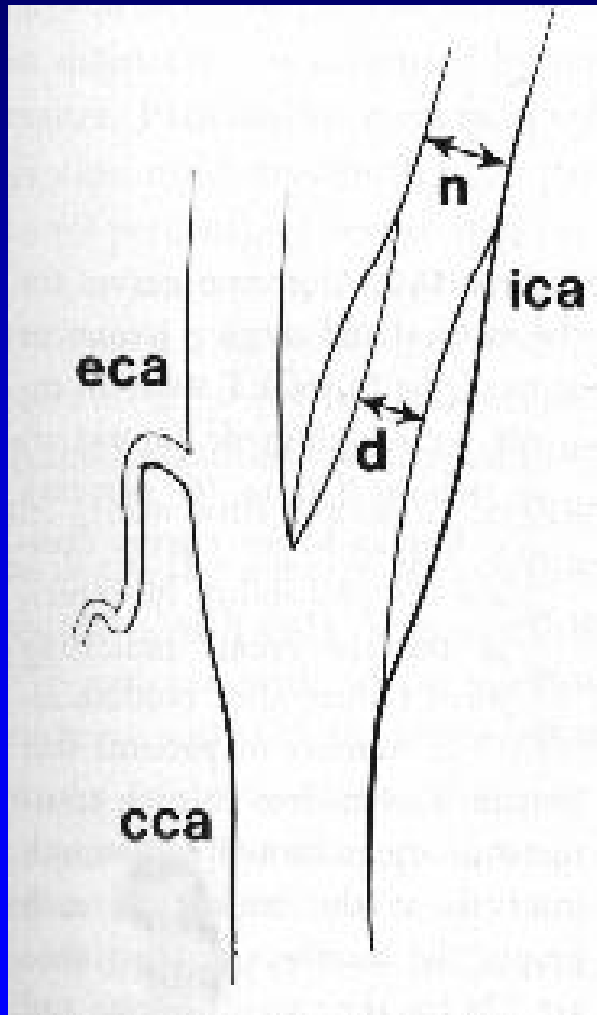
1. Extracranial carotid artery stenosis (CAS)
2. Intracranial arterial stenosis
3. Tandem carotid stenosis
4. Distal perfusion failure
5. Infarct-related cerebral herniation

Extracranial CAS

CEA for symptomatic CAS

- NASCET, *NEJM*, 1991
- ECST, *Lancet*, 1991
- VACS, *JAMA*, 1991
- CEA reduces recurrent stroke and death in patients with symptomatic high-grade stenosis

NASCET criteria



$$\% \text{ stenosis} = d / n * 100$$

Extracranial CAS

CEA for asymptomatic CAS

- ACAS, *JAMA*, 1995
- CEA reduces stroke and death in asymptomatic patients with high-grade stenosis
- Patient's medical condition important, as efficacy of CEA does not become statistically significant until 5 years following surgery

Extracranial CAS

Current indications for CEA

1. Symptomatic high-grade stenosis
 - 70% to 99% by NASCET criteria
2. Symptomatic moderate-grade stenosis
 - 50% to 70% by NASCET criteria
3. Asymptomatic high-grade stenosis
 - 60% to 99% by NASCET criteria

Extracranial CAS

Early vs. late CEA after stroke: unsettled...

- Secondary analysis of NASCET data
 - In patients with minor stroke, no difference was noted between those operated on within 30 days and those operated on later.
 - However, 5% of patients medically managed after initial stroke had recurrent stroke within 30 days
- Recommendation: early CEA can be considered in patients with high-grade stenosis presenting with TIA or minor stroke

Balloon angioplasty and stenting

CAVATAS trial

- 504 patients with carotid stenosis randomized to carotid stenting or endarterectomy
- equally effective at preventing stroke recurrence for up to 3 years
- concerns about re-stenosis in endovascular group
- Endovascular technique changed significantly during patient accrual for this study

Balloon angioplasty and stenting

Further prospective, randomized trials ongoing

Current recommendations:

- Patients with contraindications to CEA
 - radiation-induced stenosis, FMD, etc.
 - medically infirm
 - other lesion to be addressed by endovascular means (e.g. intracranial aneurysm)

Intracranial arterial stenosis

Medical therapy

- BP control and antiplatelet agents
- Anticoagulation added if symptoms continue

Interventional therapy

- If symptoms persist despite maximal medical therapy, endovascular balloon angioplasty and stenting should be considered.

Tandem carotid stenosis

Definition

- simultaneous occurrence of stenosis at both the carotid sinus and carotid siphon secondary to atherosclerotic disease

Tandem stenosis: pathology

Atherosclerosis:

- continuum from fatty streaks to fibrous plaques to complicated lesions (calcification, hemorrhage, intimal ulceration, or mural thrombus)

Carotid sinus vs. carotid siphon:

- severe stenosis and complicated plaques are more common at the carotid sinus

Tandem stenosis: treatment

Treatment directed toward cervical CAS first.

1. High-grade stenosis and presence of complicated plaques are much more common at the carotid sinus
2. Indications and clinical benefit for intervention are well defined
3. Early concerns that patients with tandem stenosis were at higher risk during CEA are unsubstantiated by more recent retrospective studies
 - Schuler et al., Roederer et al., Mackey et al., & Mattos et al.
 - 1171 cases reviewed; no statistically significant difference in peri-operative stroke, peri-operative mortality, or late ischemic events

Tandem stenosis: treatment

If symptoms persist/recur following CEA

1. Re-study cervical carotid
2. If no cervical carotid disease, treat with maximum medical therapy (ASA, then anticoagulation).
3. If symptoms persist despite maximal medical therapy, endovascular treatment indicated.

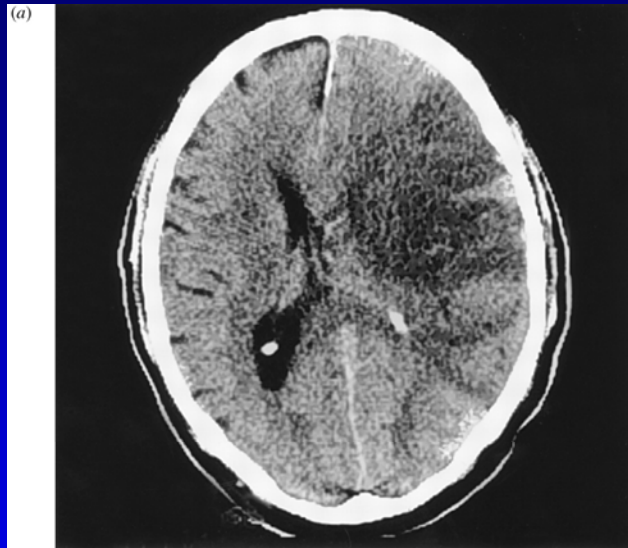
Distal perfusion failure

- Seen in patients with large-artery occlusion
- Treat symptomatic patients with antiplatelet agents and/or anticoagulation
- If symptoms persist, obtain SPECT or PET scan and consider EC-IC bypass in those with demonstrable hypoperfusion
- Grubb et al., *JAMA*, 1998
 - Increased oxygen extraction measured by PET scanning identified subgroup of patients who were at high risk for recurrent stroke despite maximal medical therapy

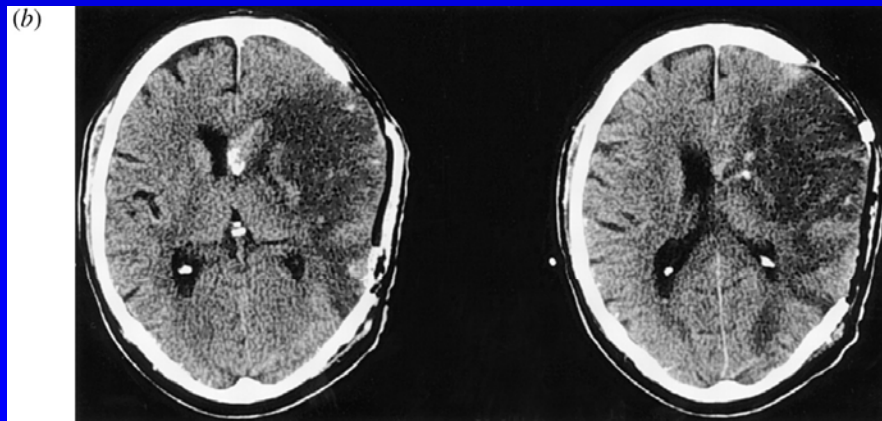
Infarct-related cerebral edema

- Mortality from large-hemispheric stroke syndromes due to space-occupying territorial infarct is up to 80%
- Prospective, randomized trials underway
- Current recommendation: consider decompressive surgery for patients < 70 yo, $GCS \geq 7$, and CT showing evidence for severe intracranial pressure and midline shift. Also consider hemispheric dominance.

Infarct-related cerebral edema



CT showing a large subacute infarct of the left MCA with space-occupying edema leading to midline shift and beginning subfalcial herniation.



CT after decompression surgery showing normal midline structures and extension of the edematous infarct tissue extending over the former bone limits