



Ischemic Stroke

Objectives:

-)Not Given(

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★ Introduction to Stroke

Morbidity and Mortality:

- A leading cause of serious, long term disability #1 cause of disability
- A second to only heart disease in causing death world-wide
- According to the WHO, 15 million people worldwide suffer a stroke each year
- -30day mortality is 8-12%
- Stroke risk and mortality increase with age because of atherosclerosis which takes 20-30 years to form

The High Socioeconomic Cost of Stroke:

- For survivors aged > 65 years.
- %50 have hemiparesis paralysis on one side , 30% are unable to ambulate walk, 19% are aphasic can't talk or communicate, 35% are depressed, 26% resides in nursing home
- The increase in life expectancy will increase the incidence of stroke.
- In the US, total direct and indirect costs are \$56.8 billion annually.
- The mean lifetime cost of ischemic stroke is estimated at \$140,048.

Stroke Impact:

- The economic, social, and psychological costs of stroke are enormous.
- Many important leaders in science, medicine, and politics had their productivity end prematurely short by stroke: Louis Pasteur (at age 46), Vladimir Lenin, Woodrow Wilson, Dwight Eisenhower, Richard Nixon.

Ischemic stroke:

- Low blood flow to focal part of brain.
- Mainly caused by thromboembolism.
- Occasionally caused by hypoperfusion from low blood flow circulatory failure.
- A remarkably effective treatment for acute stroke was introduced in recent years.
- 2ry prevention depends on source of thromboembolism.
- Accounts for 85% of strokes.

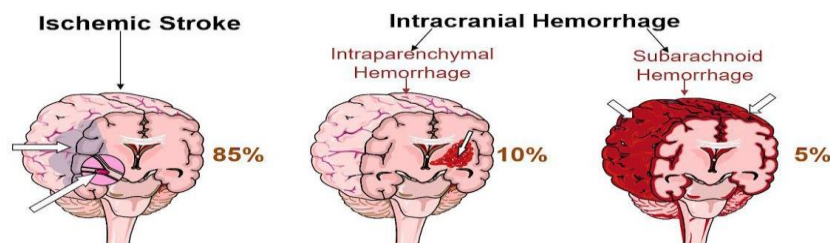
Stroke onset: Timing of FIRST neurological deficit OR last time patient was seen well.

Stroke in evolution: Is when the symptoms and signs are getting worse(usually within 24 hours of onset .(

Transient ischaemic attack (TIA :(

- Sudden transit neurological deficit. Reversible focal dysfunction.
- Symptoms lasting less than 24 hours.
- Symptoms maximal at onset.
- Normal CT/MRI of brain.
- Usually lasts minutes less than 24 hours and should have normal MRI , but most of the time it turns out that they have small strokes by MRI.
- Among TIA pts who go to ED:
 - %5)have stroke in next 2 days) (25% have recurrent event in next 3 months.(
- Stroke risk decreased with proper therapy.

Types of Stroke:



★ History Taking:

Onset: Focal neurological deficit.

- SUDDEN unilateral sensory loss/ visual loss or symptoms (monocular, homonymous hemianopia, double vision).
- SUDDEN loss of coordination.
- SUDDEN aphasia.
- SUDDEN slurred speech/language difficulty.
- SUDDEN loss of consciousness.
- SUDDEN headache characteristically with hemorrhagic stroke.
- Others it depends on which vessel will be affected the symptoms will differ (Difficulty swallowing, simultaneous bilateral weakness, imbalance, vertigo, crossed motor or sensory loss, difficult dressing or combing hair, visuospatial neglect).
- Any History of previous symptoms.
- Age.
- Gender. More in males than premenopausal females, after menopause the risk is equal.
- Prior DVT.
- Illicit drugs. Young patient and usually we do drug screen.
- Trauma. Especially in young patients.
- Heart valve disease.
- Fever. Looking for endocarditis.
- Medications (OCP Most females doesn't consider OCP a drug to ask specifically, sympathomimetic people take it to lose weight, but it causes vasospasm and stroke).
- Clues to vasculitis it is systemic condition! (arthralgia, skin rash etc.).
- Vascular risk factors: Hypertension most important risk factor, Diabetes, Dyslipidemia, Tobacco, Ischemic heart disease.

★ Differential Diagnosis:

- Migraine aura. You don't have to think of it! It has no effect on the patient.
- Seizure. Because it may come with focal weakness resolves spontaneously after minutes or hours..
- Multiple sclerosis.
- Metabolic (hypoglycemia decreased level of consciousness – dizziness – confusion but occasionally can cause focal neurological symptoms and you treat it by dextrose).
- Brain tumor. Can cause seizure or mass effect.
- Syncope conversion/somatization. Always lean towards stroke because if you give tPa to patient with somatization they won't bleed, and nothing will happen to them but if you suspected a patient with stroke to have somatization and didn't give them tPa they may die.

★ Neurological examination:

1. Cognitive assessment:

- Orientation (time, place and person).
- Attention (serial 7s) asking the patient to subtract 7 from 100 and then from 93 and so on.
- Language. Expression and comprehensive.
- Memory (recall and retrograde).
- Executive.
- Praxis (Wave, salute).
- Visuospatial (clock drawing in left lobe stroke they will draw the right half only and ignore the left one and vice versa).

2. Cranial nerve examination (olfactory, optic nerve, oculomotor, trochlear, trigeminal, abducent, facial, vestibulochlear, glossopharyngeal, vagal, accessory, and hypoglossal).
3. Motor examination.
4. Sensory examination.
5. Coordination (finger to nose and heel to chin).
6. Tone and deep tendon reflexes.
7. Gait.

Actually as neurologists we use the **NIHSS** scale to score the neurological deficit and communicate with other physicians. The larger the number the more severe deficit and the volume of the stroke. The maximum number is 42. and we also use it as follow up for the treatment and making sure that tPa is effective.

Figure 2. National Institutes of Health Stroke Scale

Category	Score	Time	Score
1a. Level of Consciousness (LOC) (Alert, drowsy, etc.)	0 = Alert 1 = Drowsy 2 = Stuporous 3 = Coma		
1b. LOC Questions (Month, age)	0 = Answers both correctly 1 = Answers one correctly 2 = Incorrect		
1c. LOC Commands (Open/close eyes, make fist & let go)	0 = Obeys both correctly 1 = Obeys one correctly 2 = Incorrect		
2. Best Gaze (Eyes open - pt follows examiner's fingers or face)	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation		
3. Visual (Introduce visual stimulus/threat to pt's visual field quadrants. Cover 1 eye and hold up fingers in all 4 quadrants.)	0 = No visual loss 1 = Partial hemianopsia 2 = Complete hemianopsia 3 = Bilateral hemianopsia		
4. Facial Palsy (Show teeth, raise eyebrows and squeeze eyes tightly shut.)	0 = Normal 1 = Mild 2 = Partial 3 = Complete		
5a. Motor Arm - Left (Elevate extremity to 90 degrees and score drift/movement. Count to 10 out loud and use fingers for visual cue.)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement NT = Amputation, joint fusion (Explain)		
5b. Motor Arm - Right (Elevate extremity to 90 degrees and score drift/movement. Count to 10 out loud and use fingers for visual cue.)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement NT = Amputation, joint fusion (Explain)		
6a. Motor Leg - Left (Elevate extremity to 30 degrees and score drift/movement. Count to 5 out loud and use fingers for visual cue.)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement NT = Amputation, joint fusion		
6b. Motor Leg - Right (Elevate extremity to 30 degrees and score drift/movement. Count to 5 out loud and use fingers for visual cue.)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement NT = Amputation, joint fusion (Explain)		
7. Limb ataxia (Finger to nose, heel down shin)	0 = Absent 1 = Present in one limb 2 = Present in two limbs		
8. Sensory (Pin prick to face, arms, trunk, and legs -compare sharpness side to side, or no feeling at all)	0 = Normal 1 = Partial loss 2 = Severe loss		
9. Best Language (Name items, describe picture, and read sentences. Don't forget glasses if they normally wear them.)	0 = No aphasia 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute		
10. Dysarthria (Evaluate speech clarity by pt reading or repeating words on list.)	0 = Normal articulation 1 = Mild to moderate dysarthria 2 = Near to unintelligible or worse NT = Intubated or other physical barrier		
11. Extinction and Inattention (Use information from prior testing or double simultaneous stimuli testing to identify neglect. Face, arms, legs and visual fields.)	0 = No neglect 1 = Partial neglect 2 = Complete neglect		
NT = Not Testable acceptable as noted above			
TOTAL SCORE:			

★ **Four Major Stroke Syndromes for Rapid Recognition in the ED:** All occur suddenly

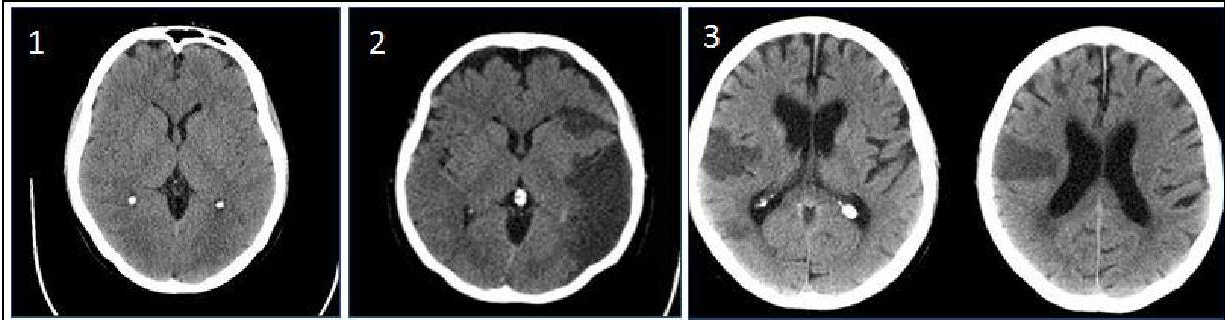
Left (dominant ¹) cerebral hemisphere Most people are right-handed so here is their language center	<ul style="list-style-type: none"> ● Aphasia (Broca's and wernicke's areas). ● L gaze preference². ● R visual field deficit. ● R hemiparesis. ● R hemisensory loss.
Right (nondominant) cerebral hemisphere	<ul style="list-style-type: none"> ● Neglect = (L hemi-inattention) they neglect their left side of Everything. ● R gaze preference. ● L visual field deficit. ● L hemiparesis. ● L hemisensory loss.
Brainstem because it contains the cardio respiratory symptoms they may present with tachycardia	<ul style="list-style-type: none"> ● Hemi or quadriparesis (if both sides of brain stem affected). ● Sensory loss in hemibody or all 4 limbs. ● <u>Crossed signs</u>³ (face 1 side, body other side(facial weakness and numbness. ● Diplopia, dysconjugate gaze, gaze palsy⁴. ● Vertigo, tinnitus. ● Nausea, vomiting. ● Hiccups, abnormal respirations. ● Decreased consciousness.
Cerebellum	<ul style="list-style-type: none"> ● Truncal = gait ataxia⁴. ● Limb ataxia.

¹The dominant cerebral hemisphere is the side that controls language function.

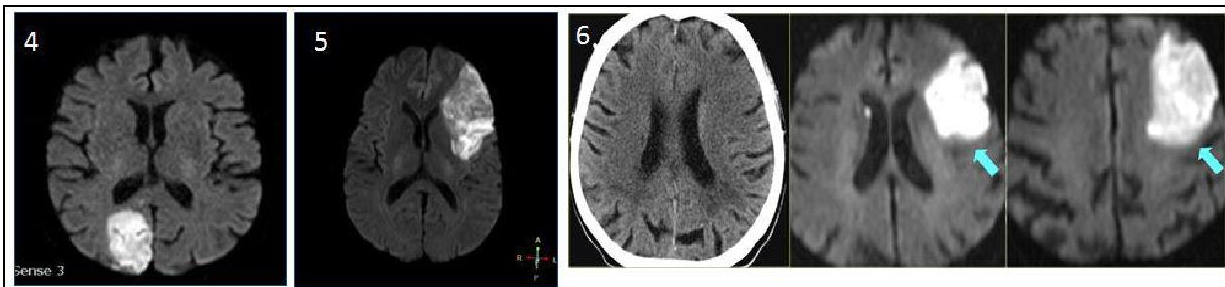
²Acute inability to produce gaze contralateral to the side of the lesion.

³The presence of ipsilateral motor and sensory cranial nerve signs and symptoms, and contralateral long tract dysfunction like hemiplegia.

⁴failure of coordinated movements of the eyes.



:1 Normal CT scan of the brain. Ischemic stroke looks hypodense (darker grey) on the CT scan. With time if the area turned to necrosis and filled with fluid it will be dark black.
 :2 CT shows old stroke stroke .Very dark and filled with fluid.
 :3 Wedge-shaped hypodense area indicating stroke “dead tissue” and it is most likely embolic stroke.

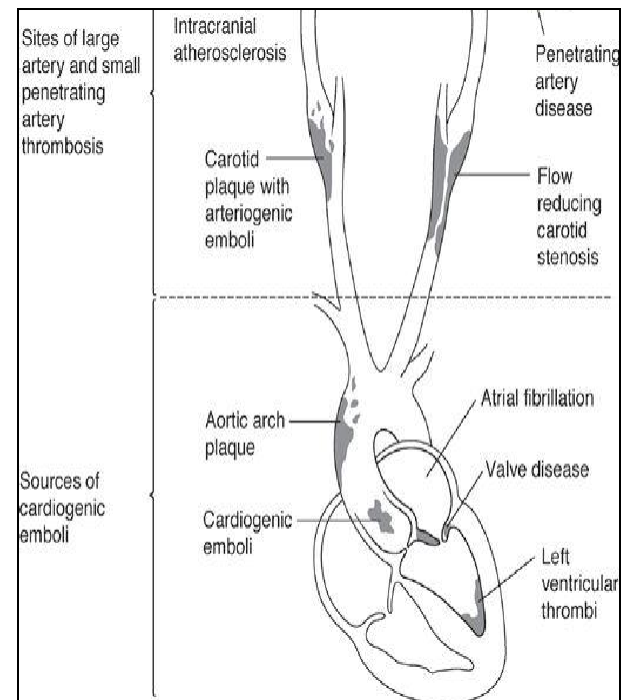


:5 MRI showing embolic stroke.
 6: MRI shows the stroke earlier (after 30 mins) while CT scan takes several hours to show a stroke.

★ Ischemic Stroke Major sites and sources of ischemic stroke: Important!

Knowing the Etiology of the stroke will dictate the prevention. If the blood supply to the brain is cut, it will die immediately; why? because neurons won't have energy storages like ATP.

- In elderly you would also think of embolism caused by Afib. The atrium is not bumping it is fibrillating. We have to do 24 holter monitor.
- If we have problem in the bumping of the heart or low ejection fraction the blood will not reach the brain. So you have to do echo to measure ejection fraction.
- If you have valvular heart disease it will cause thromboembolic stroke.
- Thrombus formation in the ventricle may cause stroke.
- Then I have to look at the vessels of the neck to rule out stenosis (by doppler) if stenosis is more than 70% you send the patient to surgery. If it is 50-70% you measure the risks and benefits weather to do surgery or not. Less than 50% stenosis won't have any difference between surgery and aspirin plus risk factor modification.
- MRA or CT angiography of the brain is done to see the vessels on the brain.

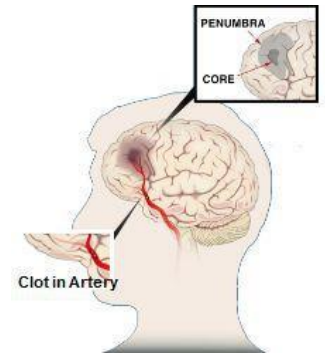


★ **Investigations:**

- Blood pressure/ejection fraction.
- Thrombophilia panel.
- Vasculitis panel.
- Echocardiogram.
- 24/72-hour holter.
- Carotid doppler.
- CT angiogram/MRA brain and neck.
- TEE (Occasionally instead of echo).
- Conventional angiogram. Rarely nowadays.

★ **Thromboembolytic treatment of acute ischemic stroke:**

- Prior to two decades ago, no treatment was offered for acute stroke victims because of the misconception that arterial occlusion in the brain leads to irreversible necrosis and dead tissue within minutes.
- Stroke was wrongly named Cerebrovascular accidents (CVA).
- Stroke care was focused on supportive care, stroke prevention and rehabilitation.



Stroke Penumbra: “Time is Brain”

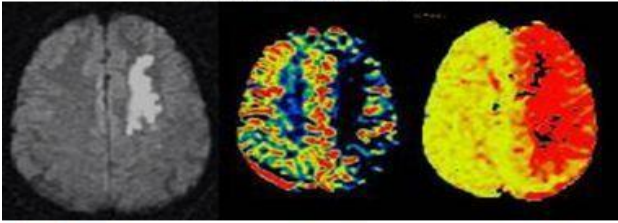
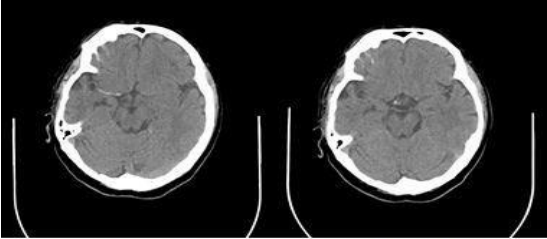
- **Penumbra** is zone of **reversible** ischemia around core of irreversible infarction.
- In every ischemic stroke there is ischemic core which dies within few minute and penumbra.
- Penumbra salvageable in the first few hours after ischemic stroke onset due to the **collateral arteries** that supply the penumbral zone. but eventually the penumbra will die if you don't save it, why? because if any time the pt goes to sleep and the BP goes down, blood will not go through the collaterals and necrosis will happen.
- Penumbra is the region of tissue at risk of being recruited into the ischemic core.
- Ischemic Penumbra presents a **Window of Opportunity**.

<p>Perfusion CT Scans Obtained 1 Hour 45 Minutes after the Onset of Ischemia in the Territory of the Right Middle Cerebral Artery. In (Panel C) the map suggest a <u>large penumbra</u> and a <u>small infarct core</u> , with the <u>penumbra</u> shown in <u>green</u> and the suggested infarct <u>core</u> in <u>red</u>.</p>	<p>“Penumbra is The Target of Acute Ischemic Stroke Treatment → TIME IS BRAIN: SAVE THE PENUMBRA”</p>

Perfusion means **Ischemia** and diffusion means **Necrosis** .

So if you see on perfusion CTA (large perfusion area and a small diffusion area) , that means you still can save the penumbra, INTERVENE!

If there is good collaterals you will have better prognosis and vice versa.

<p style="text-align: center;">Perfusion/Diffusion MRI</p>  <p style="text-align: center;">Diffusion rCBV MTT</p>	 <p style="text-align: center;">CT Prior to IV t-PA CT Post IV t-PA</p>
<p>Diffusion MRI shows a large area of necrosis that can't be treated, because it's dead tissue already.</p>	<p>Occluded MCA hyperdense. after the tPA it disappeared, and the patient is normal now.</p>

★ National Institute of Neurological Disorders and Stroke (NINDS) Trial:

- 624 acute stroke patients were randomized to either Placebo or 0.9mg/kg. of IV rt-PA it dissolves the blood clot within 3 hours from the stroke onset.
- Primary outcome: complete or nearly complete neurological recovery at 3 months after stroke. So the outcome was in favor of IV tPa despite the higher possibility of intracranial hemorrhage.
- Those treated with IV rt-Pa were 30% more likely to have no or only minor disability at 3 months post stroke.
- Absolute risk reduction of poor outcome in the t-PA patients is 13%.
- Odd ratio for favorable outcome (MRS 0-1) in the t-PA patients 1.9.
- No difference in mortality between the two groups.
- 6.4 symptomatic hemorrhage in the t-PA group compared to 0.6% in the placebo group.
- Based on the NINDS trial results, the FDA in 1996 approved IV t-PA for the treatment of acute ischemic stroke within 3 hours from stroke onset.

★ European cooperative acute stroke study (ECASS 2)

- Acute stroke patients were treated with either 0.9 mg/kg rt-Pa or placebo within 6 hours after stroke onset and results showed increase intracerebral hemorrhage in this t-Pa group. They missed the window of opportunity.

★ European cooperative acute stroke study (ECASS 3)

- A total of 821 acute stroke patients were treated with either 0.9 mg/kg rt-PA or placebo within 4.5 hours of the stroke symptoms onset.
- Additional exclusion criteria to the NINDS trial include age >80, oral anticoagulants, NIHSS>25, CT showing > 1/3 MCA infarct, and history of both stroke and diabetes.
- The results were encouraging with great outcomes. So it is effective.
- Absolute risk reduction pf poor outcome is 7%.
- A second pooled analysis including ECASS and EPITHET showed consistent results.
- The AHA, ASA, and ESA endorsed use of alteplase within 4.5 hours of symptoms onset.
- Because of the narrow window of treatment opportunity (4.5 hours), the majority of stroke patients are deprived of the treatment.

★ Advanced neuro-imaging techniques for acute stroke:

- In acute stroke patients, Diffusion/perfusion sequence and CTA/CTP head and neck should be performed to assess for LVO and eligibility for endovascular therapy.
- Recently a much more effective and efficient endovascular devices has been introduced.
- Stent-retriever technology (2nd generation devices for mechanical thrombolysis): 1. Solitaire device. 2. Trevo Stent-retriever. Open the vessels immediately.

★ **Stent-retriever:**

- They work by temporally deploying a stent that captures the thrombus and at the same time instantly restores blood flow to the affected brain territory by displacing the clot peripherally against the artery wall.
- And theoretically, such flow restoration can enhance the efficacy of systemic thrombolytic drugs if already in the circulation.

★ **Mechanical thrombolysis in AIS:** Within 6 hours from the symptom onset

- Mechanical thrombectomy is a landmark change in stroke management, and guidelines should recommend mechanical thrombectomy as a level 1 evidence-based treatment worldwide. In terms of technical aspects of mechanical thrombectomy, stent retrievers (Solitaire FR or Trevo device) as the primary method.
- After 6-24 hours, there must be a mismatch between the severity of the clinical deficit and the infarct volume (mismatch between NIHSS and infarct volume). Infarct volume was assessed with the use of DW MRI/CT perfusion and was measured with automated software (RAPID software). Outcomes for disability and functional independence at 90 days were better with thrombectomy plus standard care than with standard care alone.

★ **Acute Ischemic Stroke Treatment in 2020 (Conclusion):**

- IV t-PA, within 4.5 hours from the symptoms onset of acute ischemic stroke, is effective and the standard of care.
- Endovascular treatment using stent retriever +/- t-PA within 6 hours from the onset of stroke symptoms, is effective and the standard of care.
- In selected patients within 6-16 hours of last known normal who have a large vessel occlusion in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.
- In selected patients within 6-24 hours of last known normal who have large vessel occlusion in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy with a stent retriever is reasonable.