The Good, the Bad, and the Ugly of being a Spoke

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Disclosures

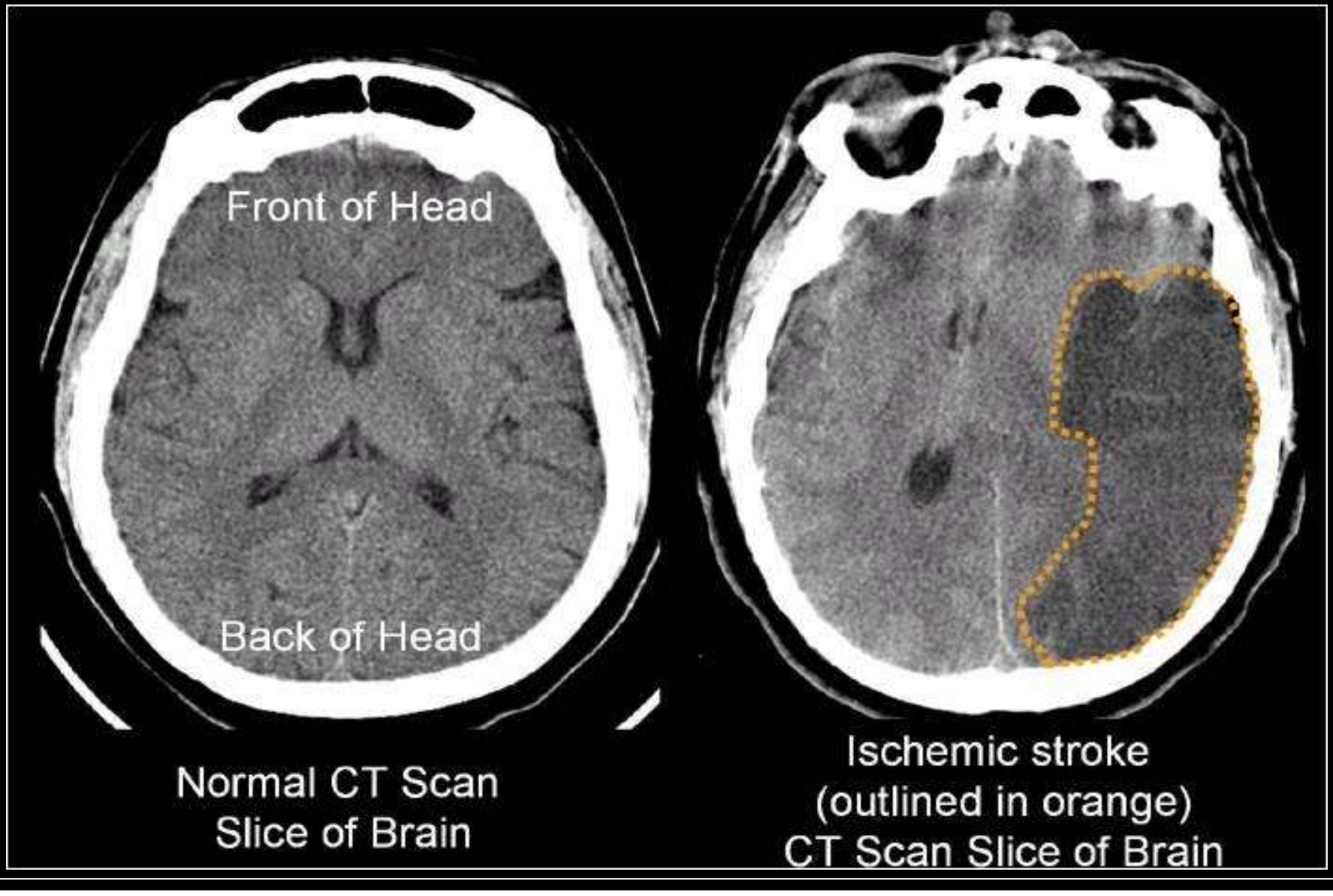
None except 2 children in college and the 3rd playing junior hockey.

Strokes

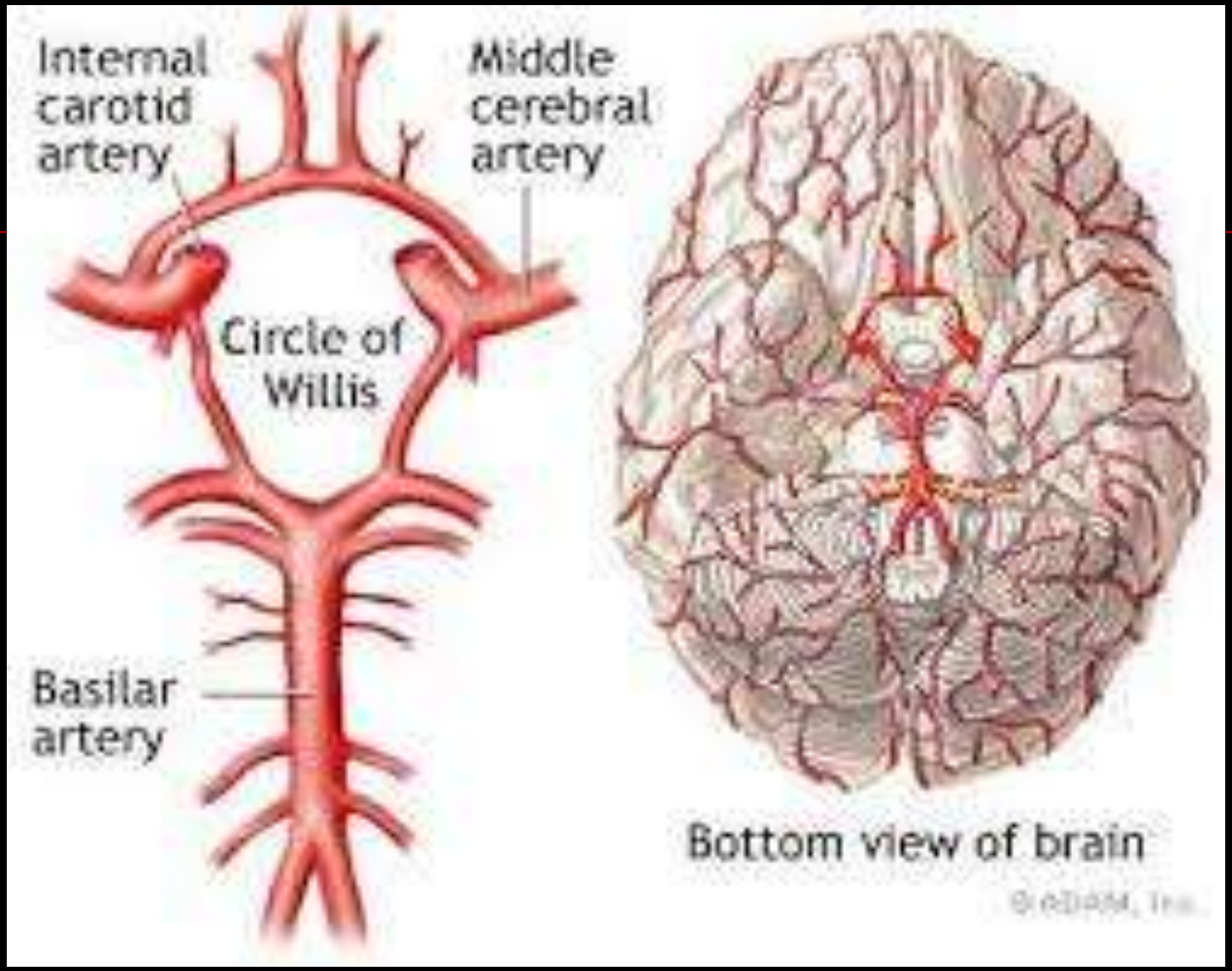
- Leading cause of disability
- 3rd leading cause of death
- More than 700,000 strokes/yr
- 100,000 recurrent strokes/yr
- 6 million stroke survivors

Ischemia

The lack of circulating blood deprives the neurons of oxygen and nutrients triggering a cascade of toxic metabolites and immune responses resulting in cell death.


Front of Head
Back of Head
Normal CT Scan
Slice of Brain
Ischemic stroke
(outlined in orange)
CT Scan Slice of Brain

Occlusion of a large vessel is rarely complete and cerebral blood flow depends on the degree of obstruction and collateral circulation


Internal carotid artery
Middle cerebral artery
Circle of Willis
Basilar artery
Bottom view of brain

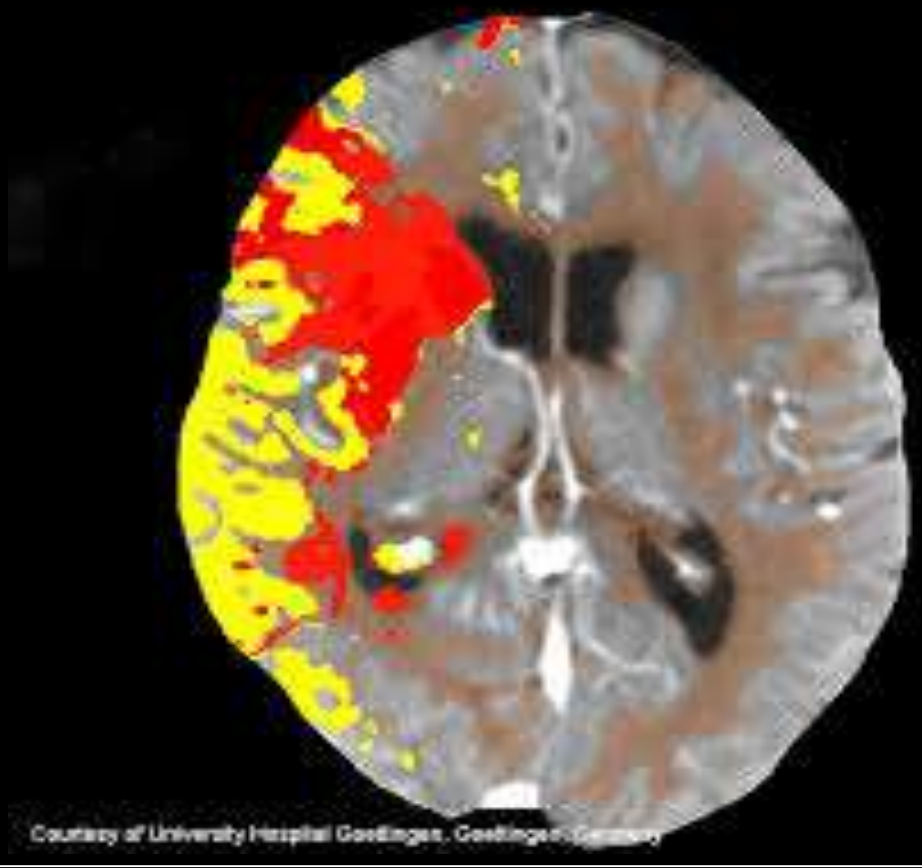
Conditions influencing progression and extent of ischemic injury

- Rate and duration
- Collateral circulation
- Systemic circulation and BP
- Coagulation abnormalities
- Temperature
- Glucose

Tissue level pathophysiology

- Ischemic thresholds
- Penumbra

Penumbra


Courtesy of University Hospital Goettingen, Goettingen, Germany

Cerebral blood flow

- Normal CBF 50-60cc/100g/min
- Loss of electrical activity 20-30cc
- Neuron death 10cc

Window of Opportunity

- Penumbra is the area that surrounds an ischemic zone with a 25-50% reduction in CBF.
- If perfusion can be returned to normal within 1 to 4.5 hrs then the viability of neuronal tissue can be preserved.

Microcellular neuronal injury

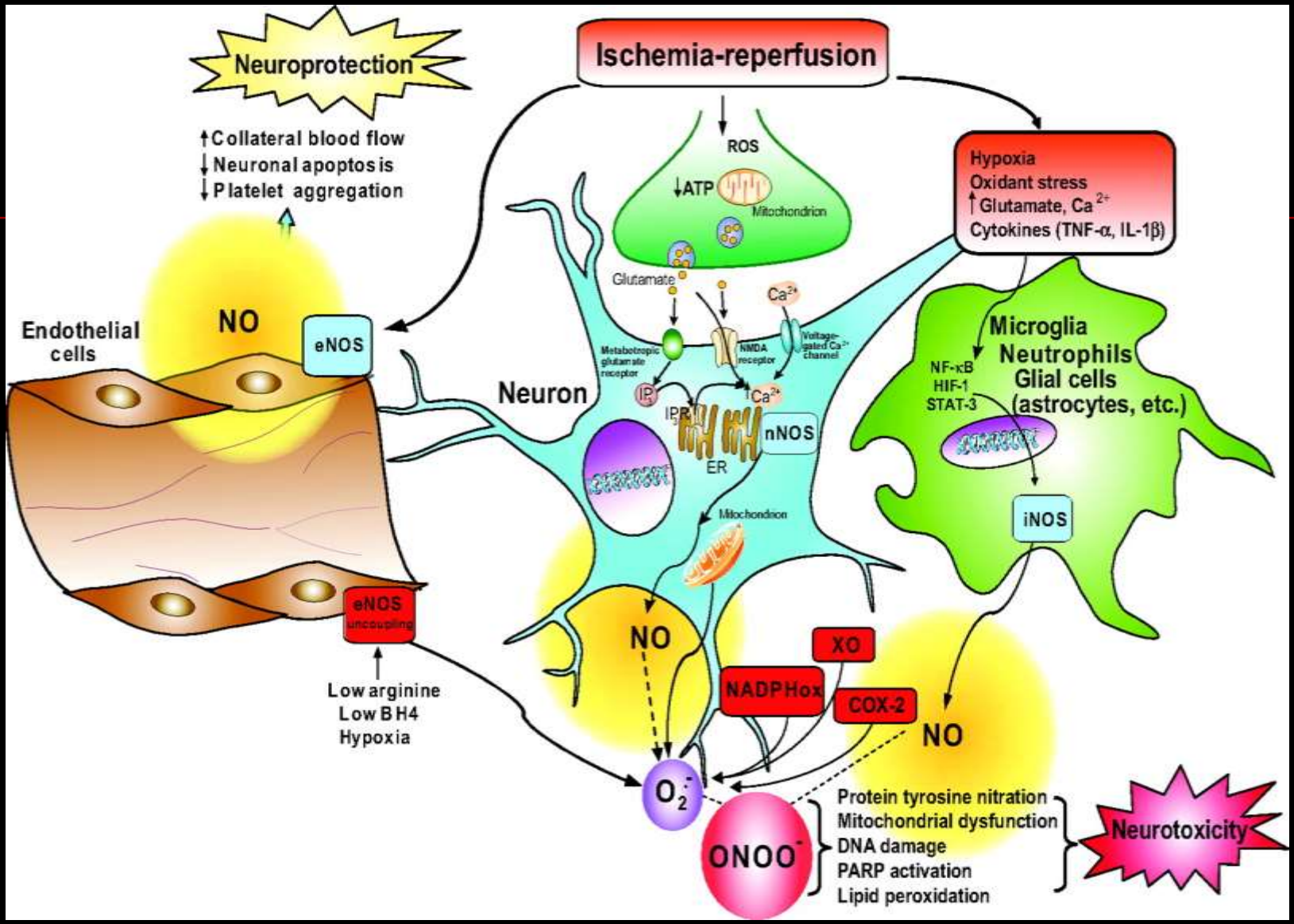
- Microthrombi
- Noxious metabolites
- Endothelial cell interaction with PMN leukocytes and platelets

These begin to trigger neuronal necrosis

Ischemia

- Depletes neuronal energy stores
- Membrane ion pumps fail
- Extracellular glutamate concentration increases
- Calcium channels open
- Influx of Ca, Na, and Cl, Outflux of K

These cause irreversible neuronal damage


Neuroprotection
↑Collateral blood flow
↓Neuronal apoptosis
↓Platelet aggregation
Ischemia-reperfusion
ROS
↓ATP
Mitochondrion
Hypoxia
Oxidant stress
↑Glutamate, Ca 2+
Cytokines (TNF-α, IL-1β)
Glutamate
Ca2+
Endothelial cells
NO
eNOS
Neuron
Metabotropic glutamate receptor
NMDA receptor
Voltage-gated Ca2+ channel
IP3
IP3R
↑Ca2+
nNOS
ER
Mitochondrion
Microglia
Neutrophils
Glial cells
(astrocytes, etc.)
NF-κB
HIF-1
STAT-3
iNOS
eNOS uncoupling
Low arginine
Low BH4
Hypoxia
NO
XO
NADPHox
COX-2
NO
O2-
ONOO-
Protein tyrosine nitration
Mitochondrial dysfunction
DNA damage
PARP activation
Lipid peroxidation
Neurotoxicity

Neuronal cell death

Evolves over 6 to 12 hrs and is attributed to the physical, chemical, and osmotic damage to the cell membrane.

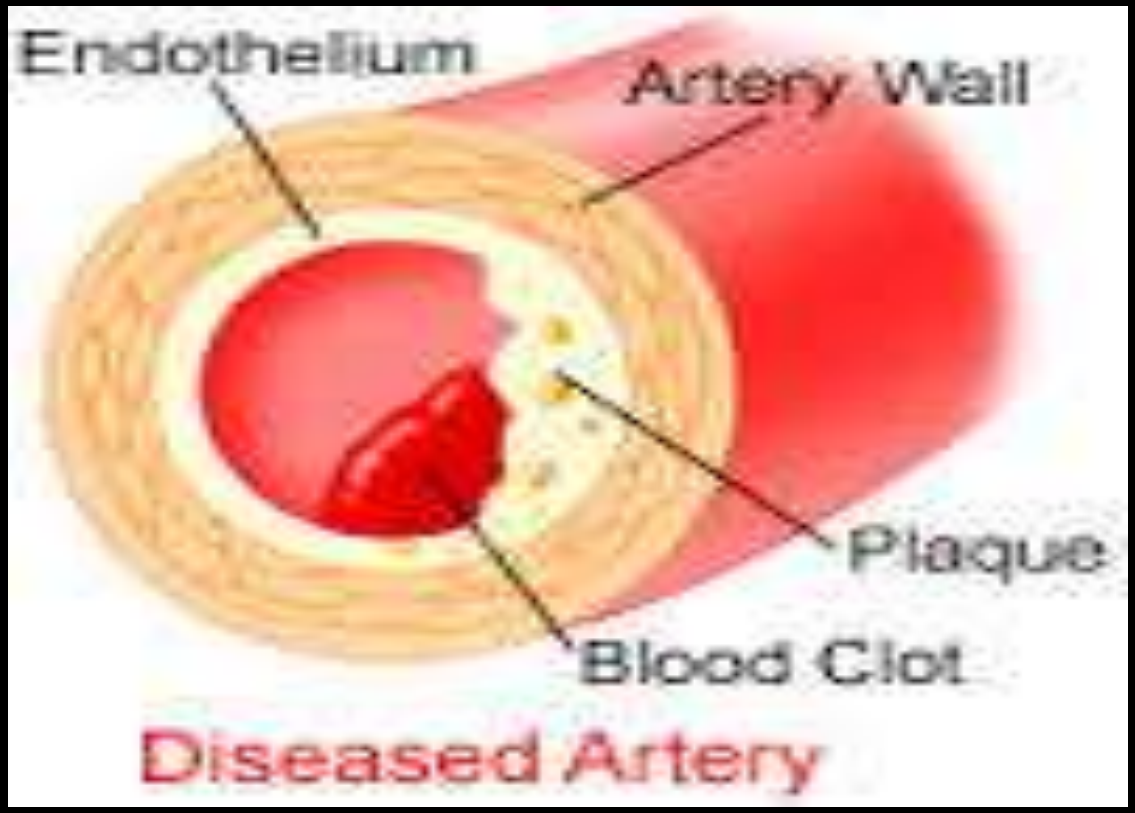
Apoptosis

- Programmed cell death
- Evolves over 2 hrs
- Caused by suicide proteins that trigger an autolytic process mediated by DNA.

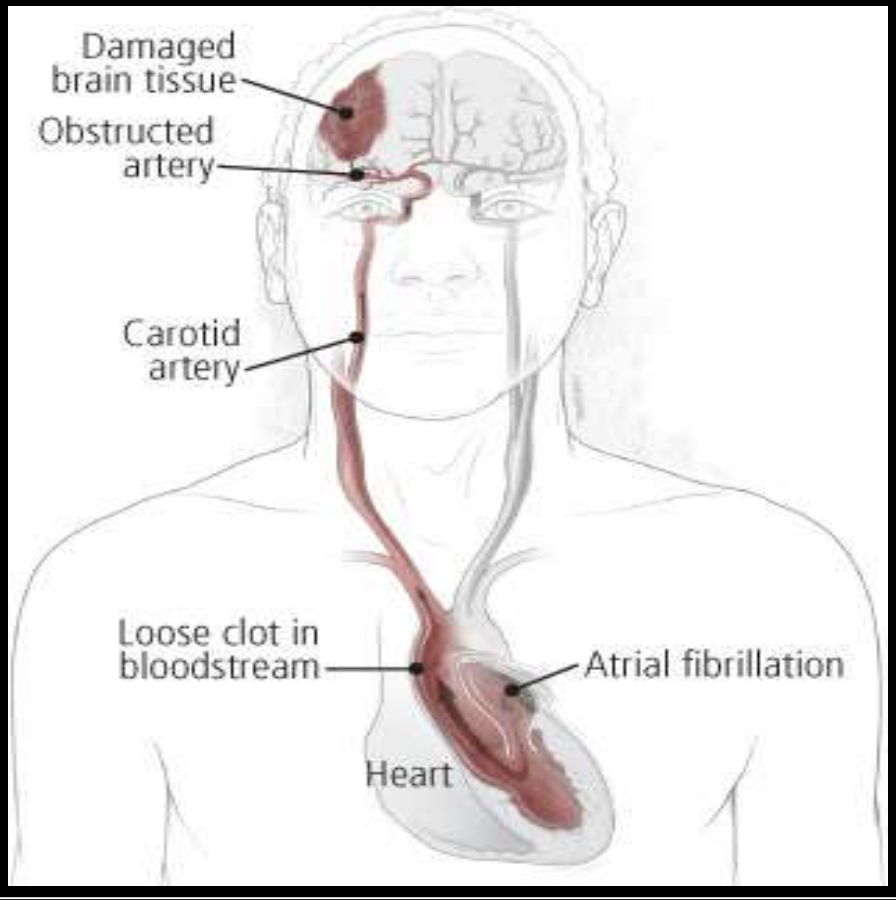
Ischemic strokes

- Thrombotic
- Embolic
- Global

Thrombotic stroke



Embolic stroke



Global Ischemia/stroke

Complications of restoration of CBF

- Damaged capillaries, arterioles
- Rupture or hemorrhage- red infarcts
- Vasogenic edema

Size of infarct, collaterals, anticoagulants, Thrombolytics.

Tissue Plasminogen Activator (TPA)

- Effective up to 4.5 hrs from onset of symptoms
- 30% better chance of no disability
- Shorter hospitalization and rehab stays
- Increased lifespan
- $2,869/QALY
- 0.6% to 6% increased risk of hemorrhage

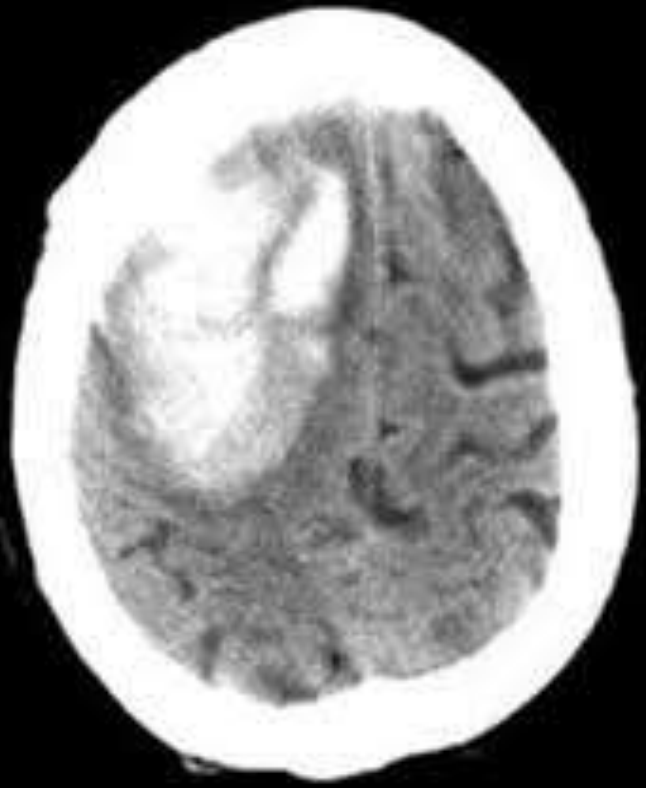
Contraindications

tPA Alteplase (Activase) is **contraindicated** if any of the following are present: (***Check if any contraindications present***)

- If CT demonstrates hemorrhage or early changes of recent major infarction such as sulcal effacement, mass effect,
  edema, thrombolytic therapy should be avoided.
- Isolated, mild neurological deficits, such as ataxia alone, sensory loss alone, dysarthria alone or minimal weakness
- *Rapidly improving neurological signs
- Evidence of intracranial hemorrhage on pre-treatment evaluation
- Suspicion of subarachnoid hemorrhage
- Intracranial neoplasm, arteriovenous malformation or aneurysm
- *Serious head trauma or another stroke in previous 3 months
- Previous intracranial hemorrhage
- Pre-thrombolytic uncontrolled systolic BP greater than 185 mmHg or diastolic BP greater than 110 mmHg
- Seizure at onset of stroke
- *Recent myocardial infarction (less than 1 month)
- *Any major surgery, history of trauma or CPR within preceding 14 days
- *Gastrointestinal or urinary bleeding within preceding 21 days
- *Any bleeding diathesis
- *Patient taking **Warfarin (Coumadin)** and INR greater than 1.7
- Heparin administration within 48 hours preceding onset of stroke and aPTT outside the normal range
- Platelet count less than 100,000/mm3
- Fibrinogen less than 120mg/dL
- Blood glucose less than 50mg/dL or greater than 400mg/dL
- *Pregnancy or delivery within 14 days
- Lumbar puncture or history of arterial puncture at a noncompressible site within preceding 7 days
- Known or suspected Bacterial Endocarditis

***May be appropriate for Intra-arterial tPA-Alteplase (Activase) Or Mechanical Clot Retrieval Device. Review these items with the stroke neurologist.**

Intracranial Hemorrhage



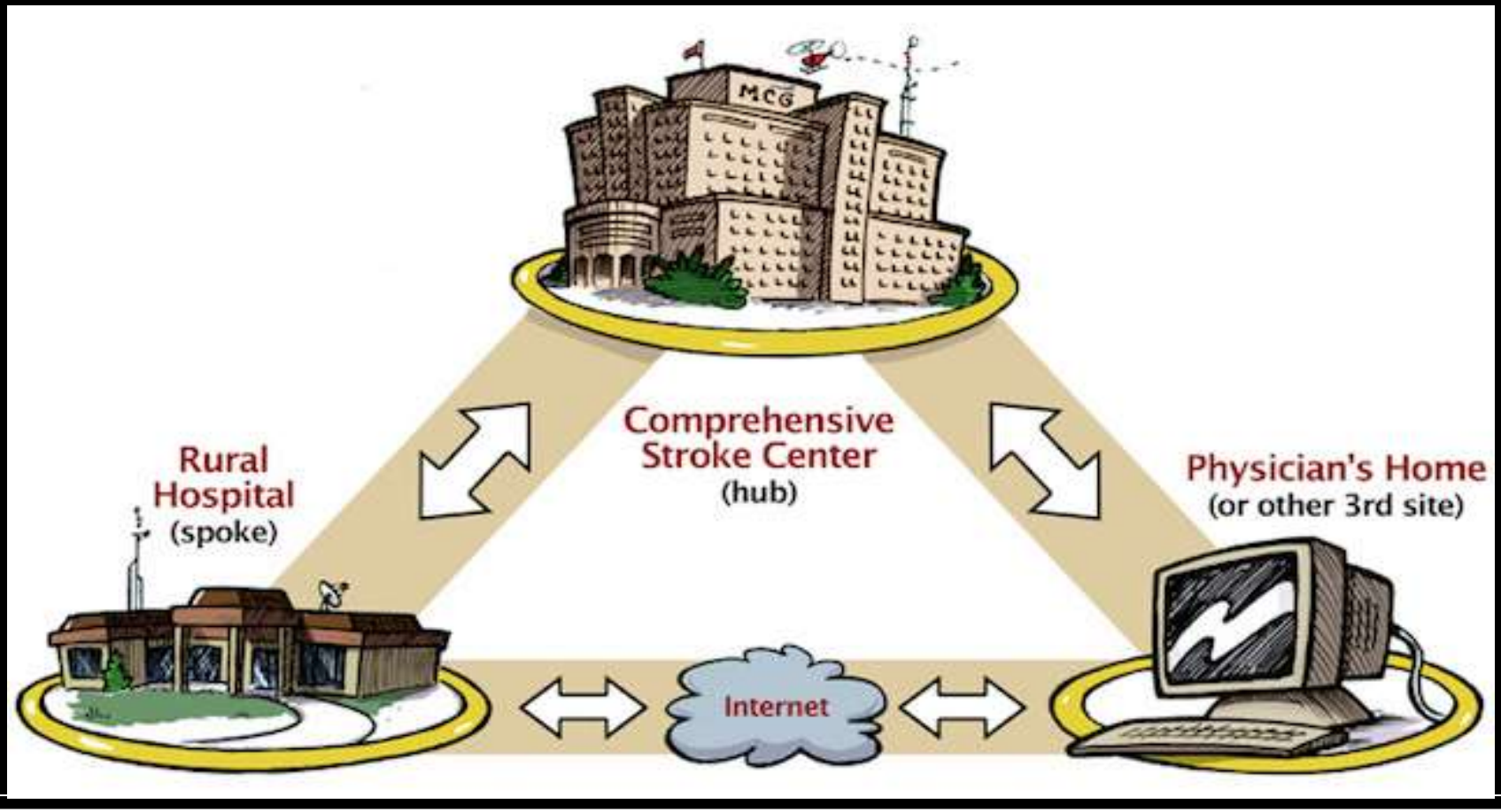
Challenges to acute stroke care delivery

- Limited stroke awareness by the patient
- Few on-call neurologists
- Rural isolation
- Narrow therapeutic time window

Sky Lakes Medical Center

Providence St. Vincent Medical Center

Hub and Spoke Model




Portland
Providence Portland Medical Center
Providence St. Vincent Medical Center
Ocean Beach Hospital – Ilwaco
Providence Seaside Hospital
Tillamook County General Hospital
Providence Newberg Medical Center
Providence Milwaukie Hospital
Providence Willamette Falls Medical Center – Oregon City
Silverton Hospital
Providence Hood River Memorial Hospital
Providence St. Mary Medical Center – Walla Walla
St. Anthony Hospital – Pendleton
Pioneer Memorial Hospital – Heppner
Wallowa Memorial Hospital – Enterprise
Curry Hospital – Gold Beach
Providence Medford Medical Center
Sky Lakes Medical Center – Klamath Falls
Lake District Hospital – Lakeview

How it works

- EMT notifies Sky Lakes ED of potential acute stroke patient
- Sky Lakes ED calls Providence St. Vincent neurologist on-call
- Patient arrives to ER, IV's placed, labs drawn, sent for HCT without contrast. Robot is set up in room

- Patient arrives back from CT, neurologist is on robot, begins interview and exam of patient (NIHSS) with the help of the ER physician or an RN.
- CT results sent directly to neurologist, labs reviewed.
- TPA being mixed in ER in anticipation
- TPA order given by neurologist

Table 2. Abbreviated NIH Stroke Scale

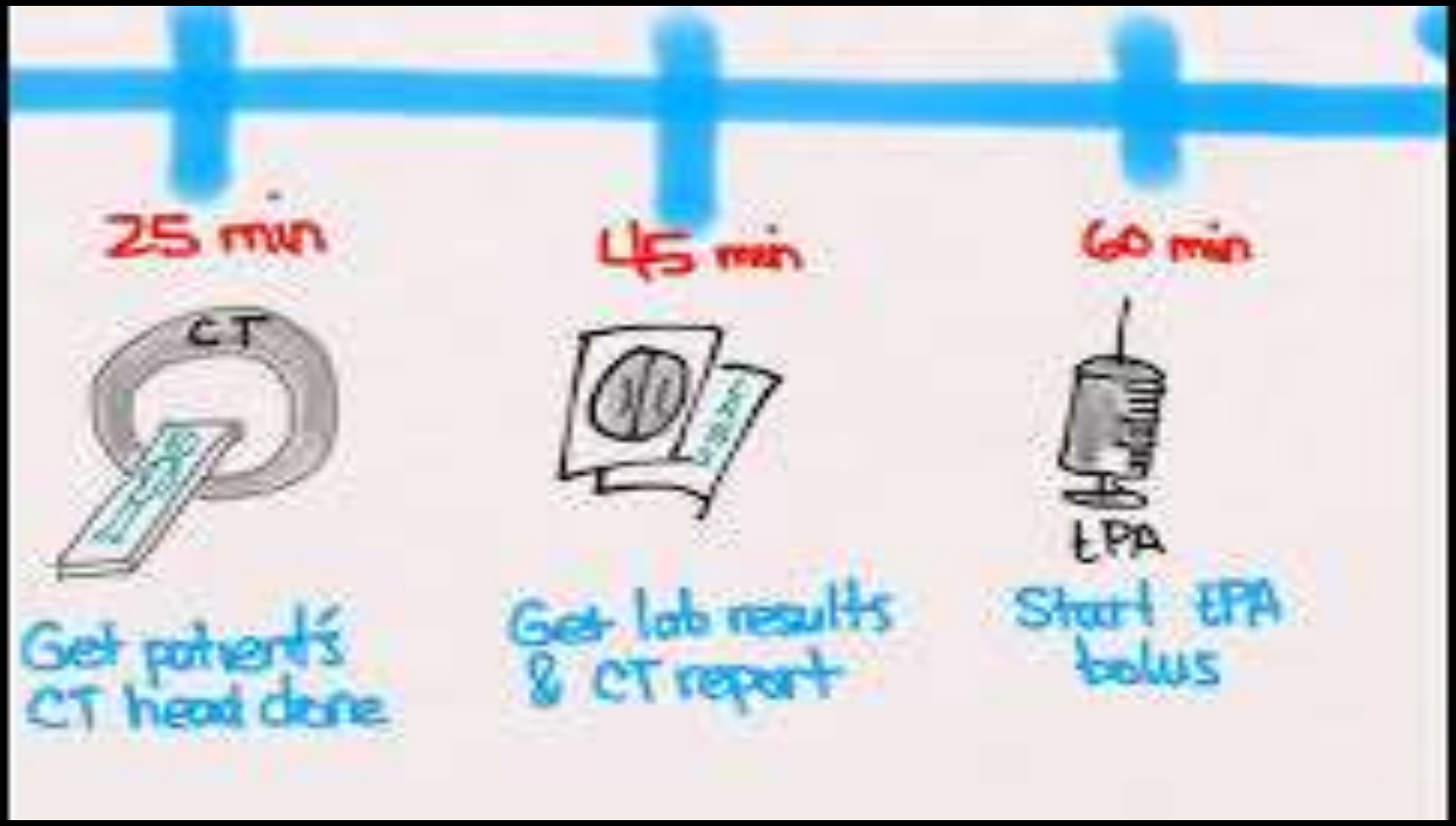
Points	Description
	1. Level of consciousness
0 - 3	a. Alertness
0 - 2	b. Orientation
0 - 2	c. Follows command
0 - 2	2. Best gaze
0 - 2	3. Visual fields
0 - 2	4. Facial palsy
	5. Motor function (arm)
0 - 4	a. Right
0 - 4	b. Left
	6. Motor function (leg)
0 - 4	a. Right
0 - 4	b. Left
0 - 2	7. Limb ataxia
0 - 2	8. Sensory
0 - 3	9. Language (aphasia)
0 - 2	10. Dysarthria (articulation)
0 - 2	11. Neglect

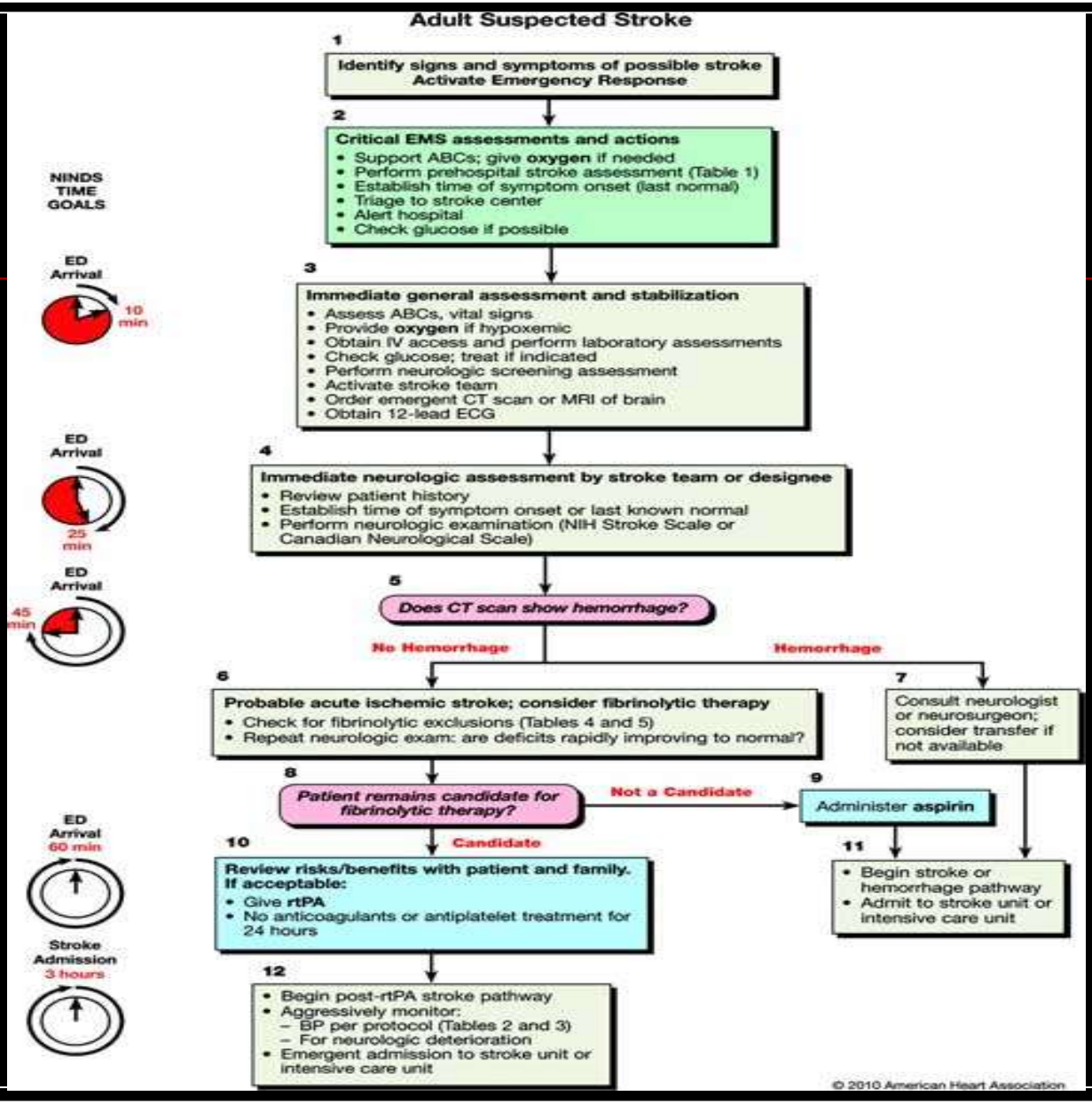
NIH: National Institutes of Health
Level of stroke severity: 0 = no stroke; 1-4 = minor stroke; 5-15 = moderate stroke; 15-20 = moderate/severe stroke; 21-42 = severe stroke.
Source: References 3, 9.

- Patient is then transferred to the ICU under the care of the hospitalists with continuing consultation from the neurologist.
- If further decline, hemorrhage, then possible transfer to Providence St. Vincent’s via air.

Goals

- 1 min patient is activating EMS
- 10 min Door to ED doc
- 15 min Door to neurology consult
- 25 min in CT scanner
- 45 min CT and lab results available
- 60 min TPA given


25 min
CT
Get patient's CT head done
45 min
Get lab results & CT report
60 min
tPA
Start tPA bolus


Adult Suspected Stroke
1
Identify signs and symptoms of possible stroke
Activate Emergency Response
2
Critical EMS assessments and actions
• Support ABCs; give oxygen if needed
• Perform prehospital stroke assessment (Table 1)
• Establish time of symptom onset (last normal)
• Triage to stroke center
• Alert hospital
• Check glucose if possible
NINDS TIME GOALS
ED Arrival
10 min
3
Immediate general assessment and stabilization
• Assess ABCs, vital signs
• Provide oxygen if hypoxemic
• Obtain IV access and perform laboratory assessments
• Check glucose; treat if indicated
• Perform neurologic screening assessment
• Activate stroke team
• Order emergent CT scan or MRI of brain
• Obtain 12-lead ECG
ED Arrival
25 min
4
Immediate neurologic assessment by stroke team or designee
• Review patient history
• Establish time of symptom onset or last known normal
• Perform neurologic examination (NIH Stroke Scale or Canadian Neurological Scale)
ED Arrival
45 min
5
Does CT scan show hemorrhage?
No Hemorrhage
Hemorrhage
6
Probable acute ischemic stroke; consider fibrinolytic therapy
• Check for fibrinolytic exclusions (Tables 4 and 5)
• Repeat neurologic exam: are deficits rapidly improving to normal?
7
Consult neurologist or neurosurgeon; consider transfer if not available
8
Patient remains candidate for fibrinolytic therapy?
Not a Candidate
9
Administer aspirin
ED Arrival
60 min
Candidate
10
Review risks/benefits with patient and family. If acceptable:
• Give rtPA
• No anticoagulants or antiplatelet treatment for 24 hours
11
• Begin stroke or hemorrhage pathway
• Admit to stroke unit or intensive care unit
Stroke Admission
3 hours
12
• Begin post-rtPA stroke pathway
• Aggressively monitor:
– BP per protocol (Tables 2 and 3)
– For neurologic deterioration
• Emergent admission to stroke unit or intensive care unit
© 2010 American Heart Association

Obstacles

- Patient is unaware of stroke symptoms
- In a rural setting transfer to a hospital can be prolonged
- Lab results can be prolonged late at night
- CT tech is on-call and not in hospital
- TPA is not stored in the ER

Post TPA care

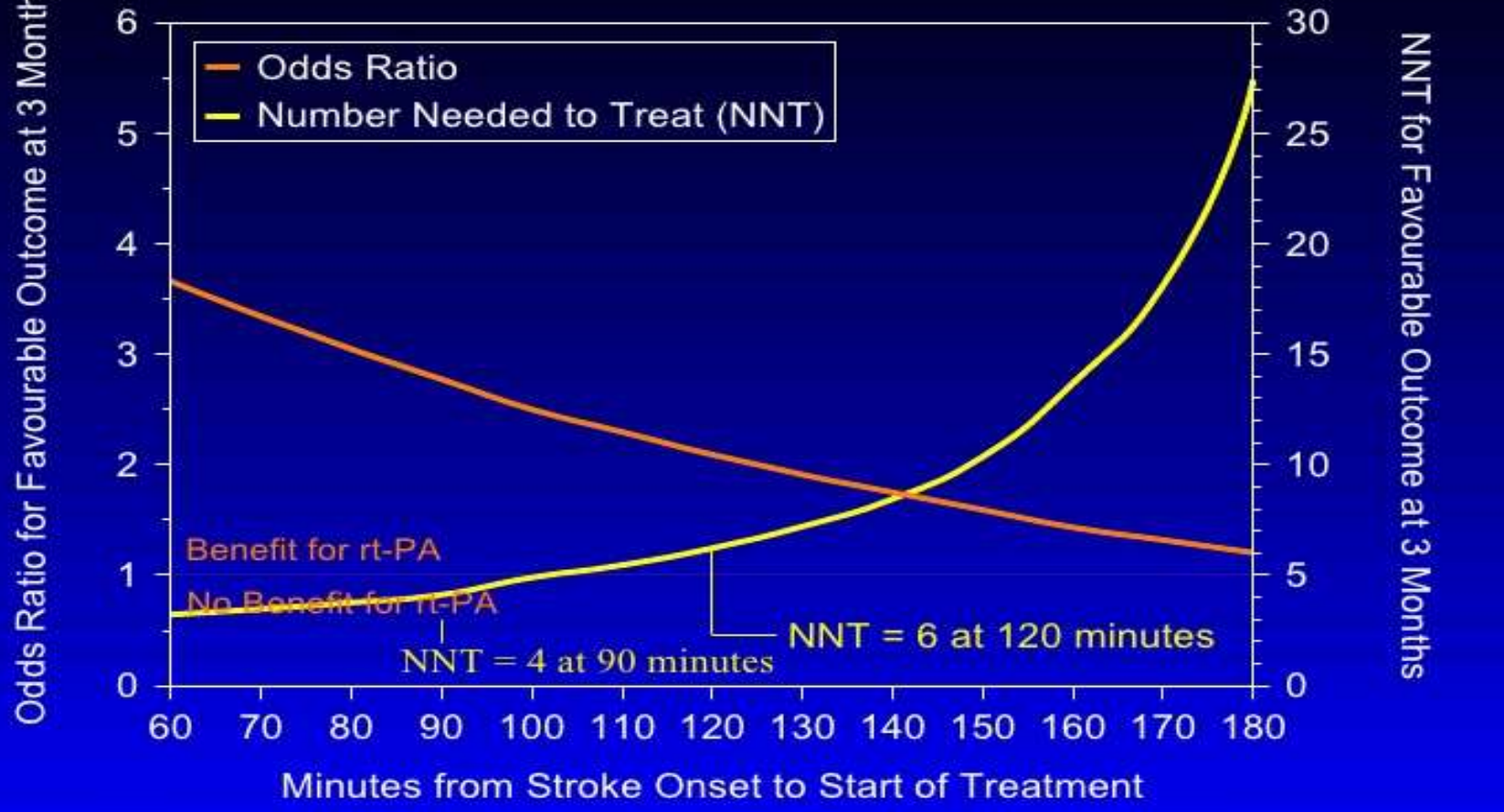
Guidelines for IV thrombolysis

~ Care during the first 24 hours after administration of tPA

71

- Admission to a skilled care facility (ICU or acute stroke unit)
- Careful monitor and management of BP
  - Keep SBP<185 mmHg, DBP<110 mmHg
- No use of anticoagulants and antiplatelet
- Central venous access and arterial punctures are restricted
- Placement of an indwelling bladder catheter should be avoided during drug infusion and for at least 30 minutes after infusion ends
- Insertion of a nasogastric tube should be avoided
- Careful neurological evaluation (NIHSS at 1st, 2nd, 24th hours)

Number Needed to Treat Increases Exponentially with Time



Adapted from Marler JR et al., *Neurology* 2000;55:1649-1655

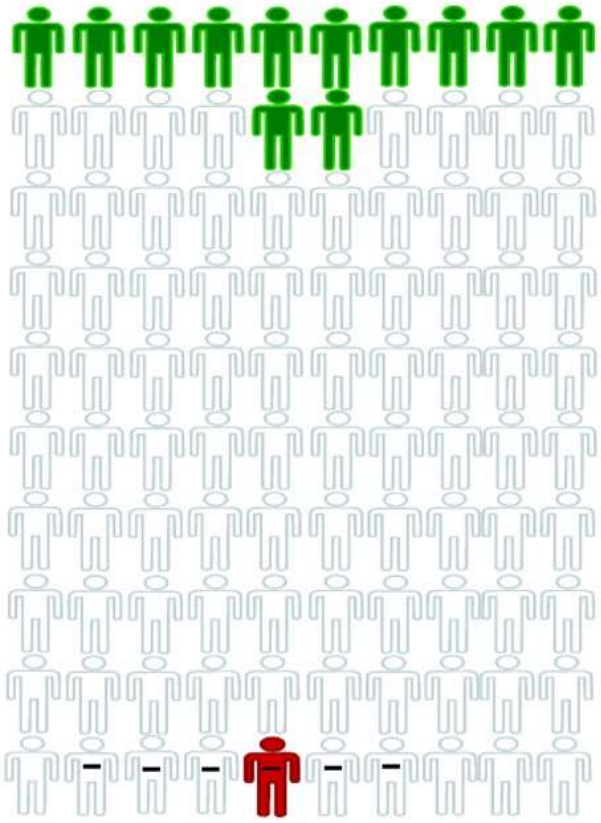
Created by Tex

Numbers Needed to Treat

- NNT of 3 if TPA given within 3 hrs to improve disability
- NNT of 6 if TPA given 3 to 4.5 hrs to improve disability

TPA for Cerebral Ischemia within 3 Hours of Onset-Select Changes in Outcome Due to Treatment

A1



Changes in final outcome as a result of treatment:

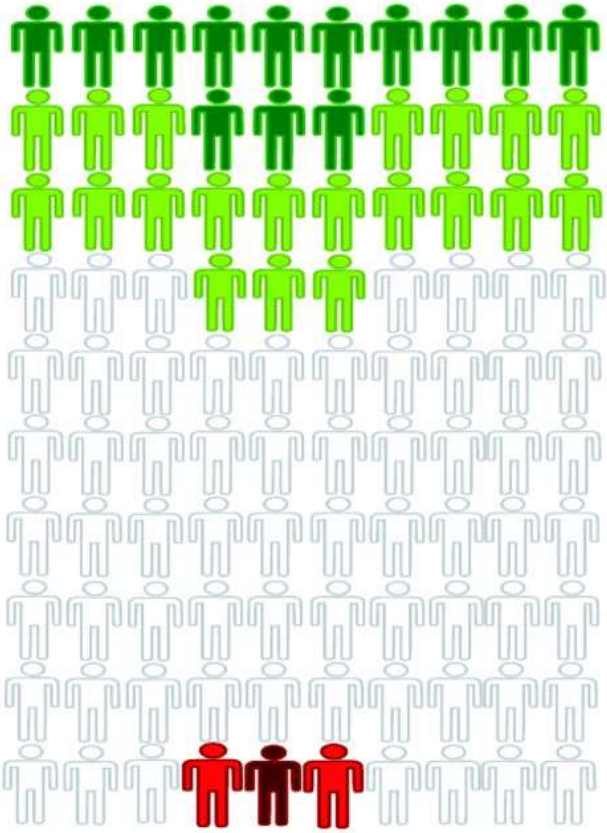
- Normal or nearly normal
- No major change
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

TPA for Cerebral Ischemia within 3 Hours of Onset- Changes in Final Outcome Due to Treatment

A2



Changes in final outcome as a result of treatment:

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Sky Lakes Medical Center

- Prior to 2013 TPA was almost never given to the appropriate patient. Primary reason was the ED docs felt they were not trained to make this decision or willing take the responsibility.

2016 Treatment with Telestroke and TPA

Arrive by 2 hr, treat by 3 hrs is 100%

Arrive by 3.5 hrs, treat by 4.5 hrs is 100%

Those not treated were excluded by the neurologist.

Time to TPA less than 60 mins was 100%.

Post stroke care 2016

Anticoag for Afib/flutter- 100%

Smoking cessation education-100%

VTE prophylaxis-100%

Dysphagia screen- 95.6%

Assessed for rehab-100%

Stroke education- 100%

Post stroke care

NIHSS- 72.7%

Intensive statin therapy- 47.4%

Transient Ischemic Attacks (TIA)

A brief episode of neurologic dysfunction resulting from focal temporary cerebral edema.

Classically defined as symptoms lasting less than 24 hrs.

Realistically symptoms lasting less than 1 hr.

Transient Ischemic Attacks (TIA's)

- Aggressive, timely imaging
- ABCD2- 2 or less can be worked up as outpatient but should be within just a couple of days.

  4 or more should be hospitalized for this work-up

Primary prevention

- BP control
- Treatment of dyslipidemia
- Physical activity
- Obesity
- Diet
- Diabetes
- Smoking cessation
- Alcohol consumption

Aspirin

- Men ages 45-79
- Women ages 55-79

USPTFS recommendation Grade A

When the benefits outweigh the risk of gastrointestinal bleed.

Summary

Time = Brain

- Telemedicine allows timely, expert consultations and treatment in rural areas
- Quick, aggressive work-ups of TIA's
- Ideally should be preventing TIA's/Strokes through primary care

“ I tried to think but nothing happened”

Curly Howard

Questions?