برنامه توانبخشی سکته حاد مغزی

(پاتولوژی و مداخلات درمانی مرحله حاد، thrombolytic therapy)

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Medical College of Kermanshah

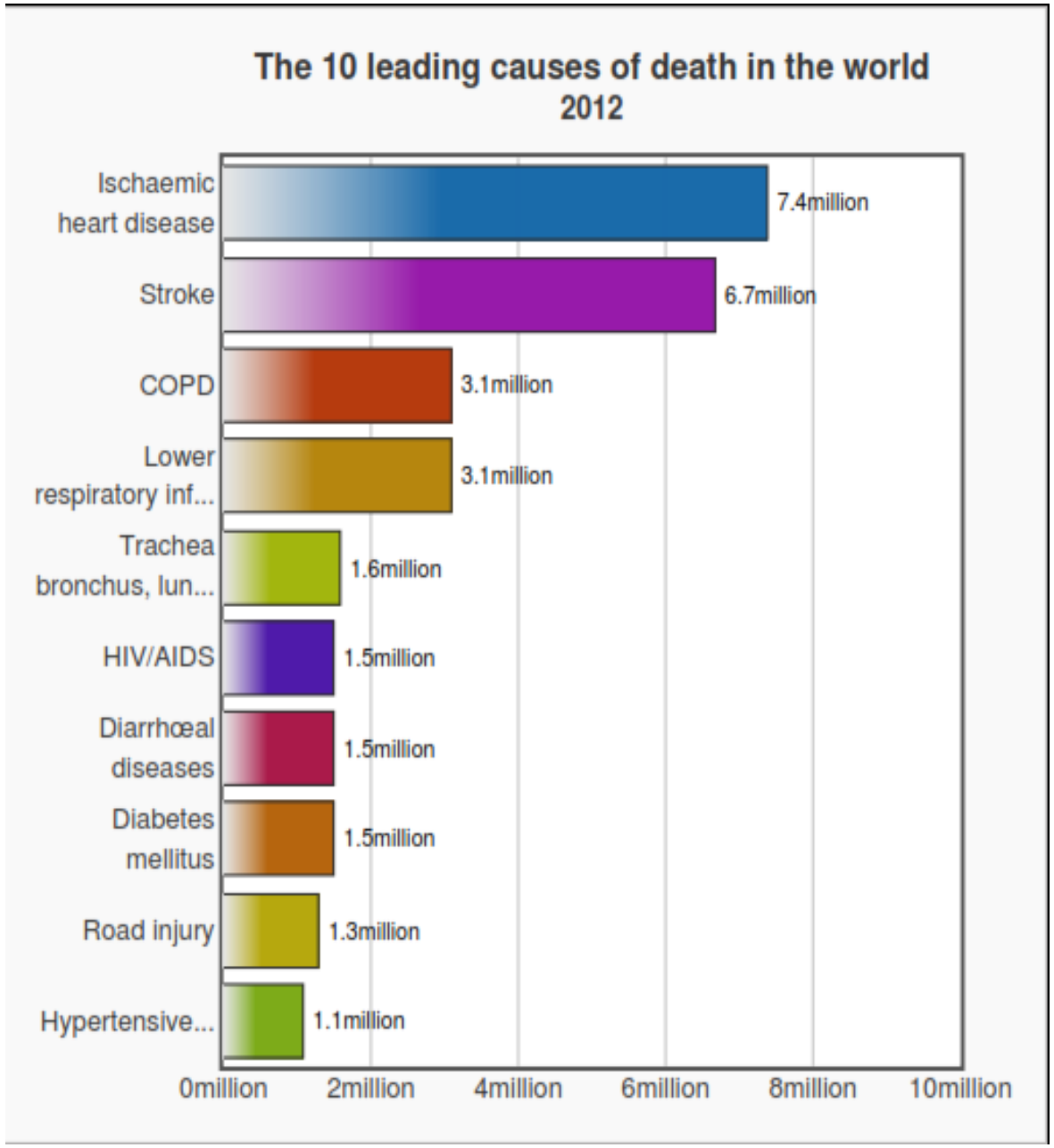
1399/07/10

بیشترین عامل مرگ ومیر ناشی از سکته های مغزی به دلیل مراجعه با تاخیر به مراکز درمانیست.

- هر سال حدود 15-17میلیون نفر در سراسر جهان دچار سکته مغزي مي شوند و ٦ ميليون نفر بر اثرآن مي ميرند
- سکته ي مغزي شايع ترين علت ناتواني بالغين در جهان مي باشد
- هر ٢ ثانيه اي که مي گذرد يک نفر دچار سکته مغزي مي شود و هر 6 ثانيه يک نفر در اثر آن مي ميرد
- از هر ۴ نفر يک نفر در طول زندگي خود دچار سکته ي مغزي مي شوند

بررسی های انجام شده در **ایران** نشان داده شده *سن سکته حاد مغزی نسبت به میانگین سن در سایر نقاط جهان پایین تر می باشد* و با مورتالیته بیشتری در مقایسه با کشورهای پیشرفته همراه است **و میانگین این عارضه در کشور ما ۵۰ سال است. ۳۰ درصد از کسانی که در ایران به سکته مغزی دچار می شوند، زیر ۵۰ سال هستند.**

در ایران سالانه ۱۵۰ هزار نفر و روزانه ۴۰۰ نفر به سکته مغزی دچار می شوند. (هر سه و نیم دقیقه یک نفر)- ۱۳۹۸


The 10 leading causes of death in the world 2012
Ischaemic heart disease
7.4million
Stroke
6.7million
COPD
3.1million
Lower respiratory inf...
3.1million
Trachea bronchus, lun...
1.6million
HIV/AIDS
1.5million
Diarrhœal diseases
1.5million
Diabetes mellitus
1.5million
Road injury
1.3million
Hypertensive...
1.1million
0million
2million
4million
6million
8million
10million

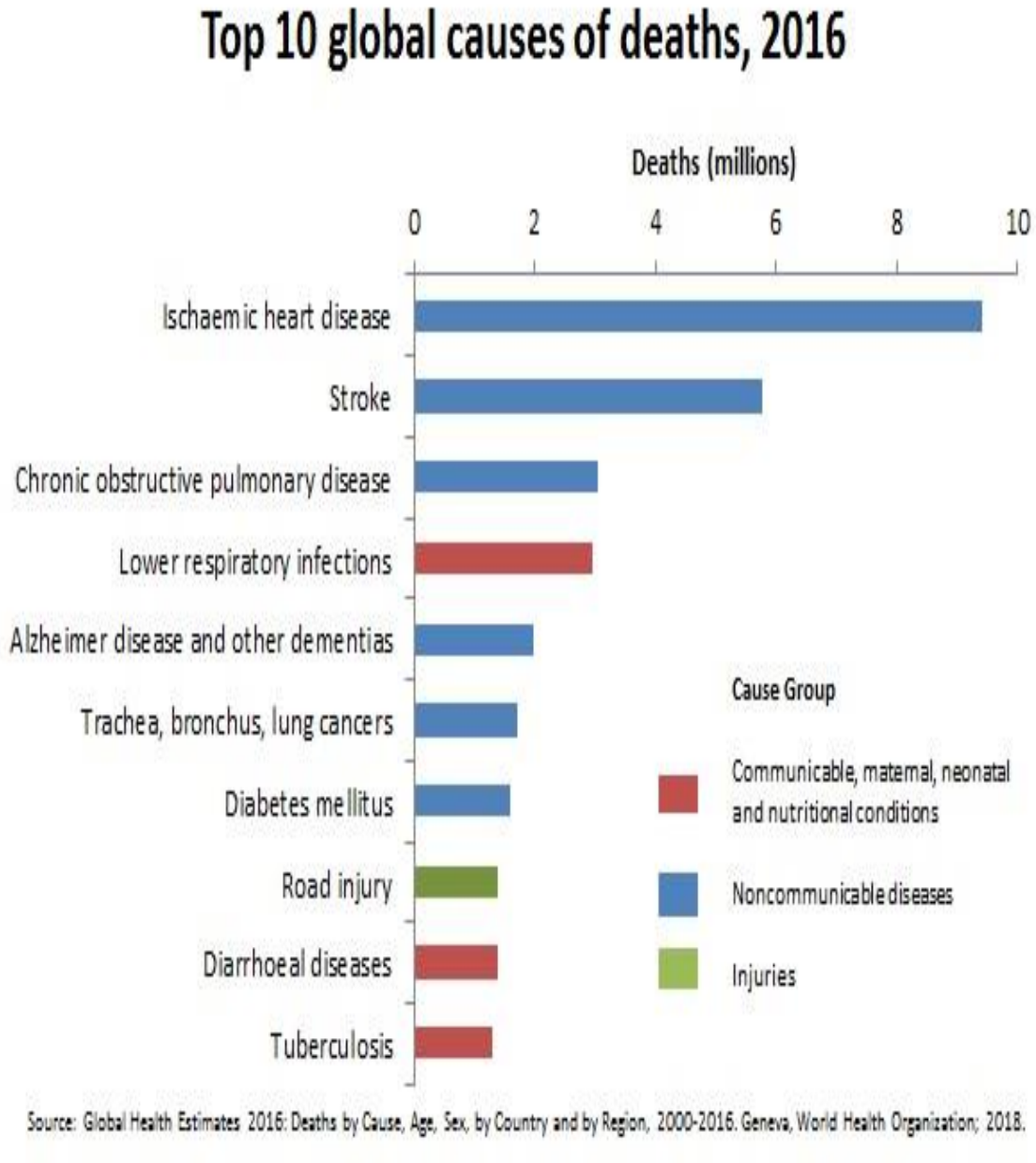
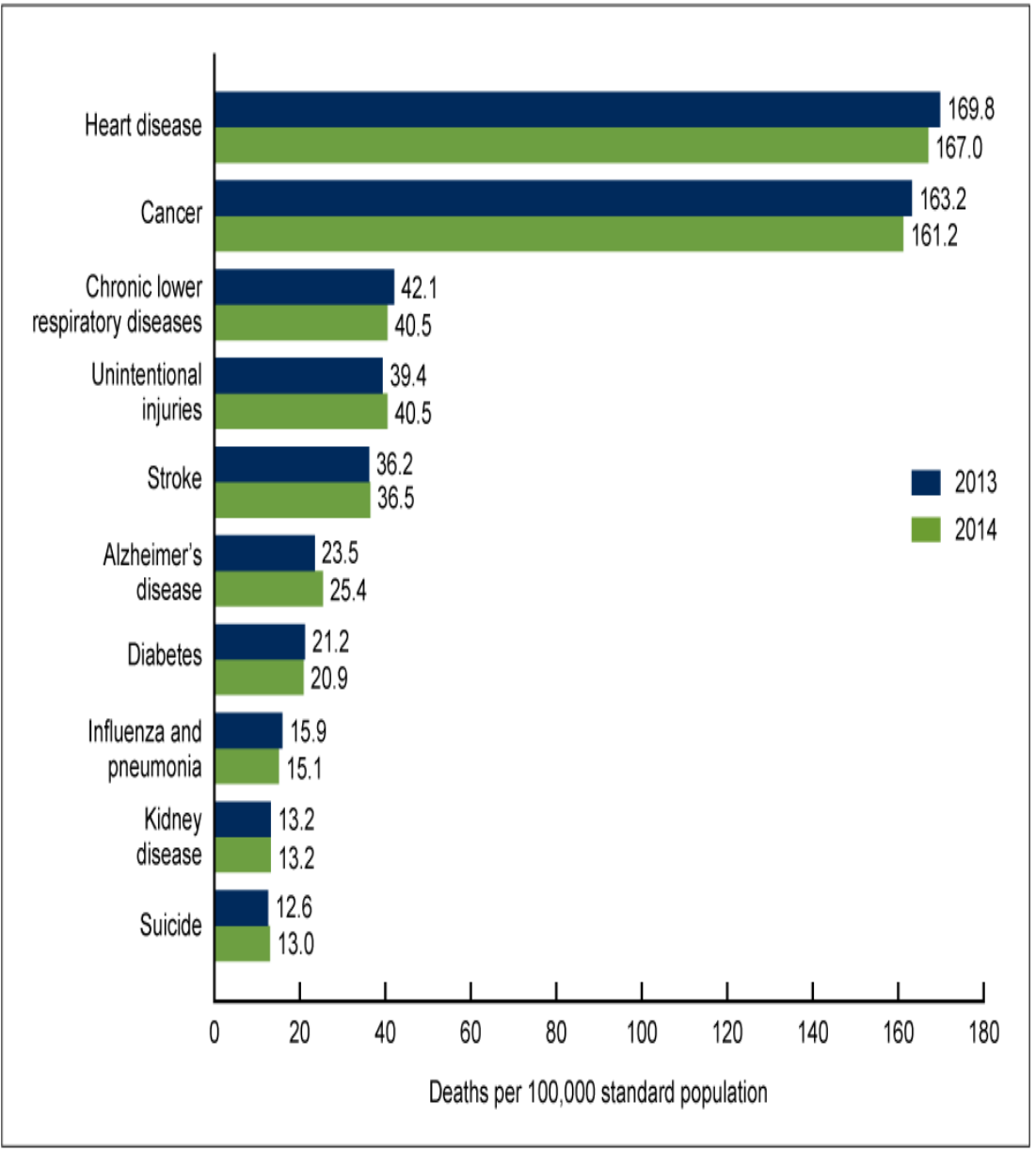

Top 10 global causes of deaths, 2016
Deaths (millions)
0
2
4
6
8
10
Ischaemic heart disease
Stroke
Chronic obstructive pulmonary disease
Lower respiratory infections
Alzheimer disease and other dementias
Trachea, bronchus, lung cancers
Diabetes mellitus
Road injury
Diarrhoeal diseases
Tuberculosis
Cause Group
Communicable, maternal, neonatal and nutritional conditions
Noncommunicable diseases
Injuries
Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.

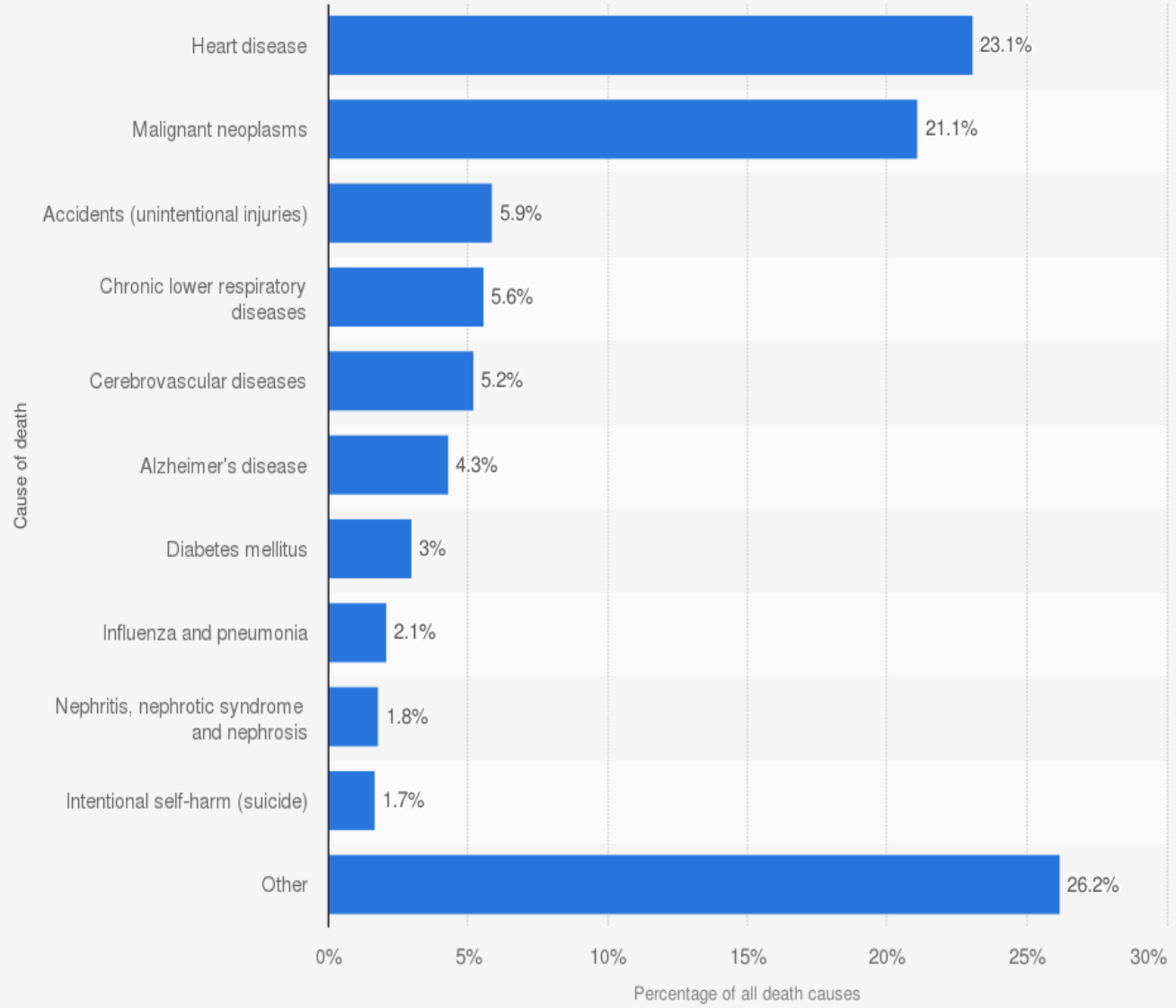
Figure 3. Age-adjusted death rates for the 10 leading causes of death: United States, 2013 and 2014



NOTES: A total of 2,626,418 resident deaths were registered in the United States in 2014. The 10 leading causes accounted for 73.8% of all deaths in the United States in 2014. Access data table for Figure 3 at: http://www.cdc.gov/nchs/data/databriefs/db229_table.pdf#1. Causes of death are ranked according to number of deaths.

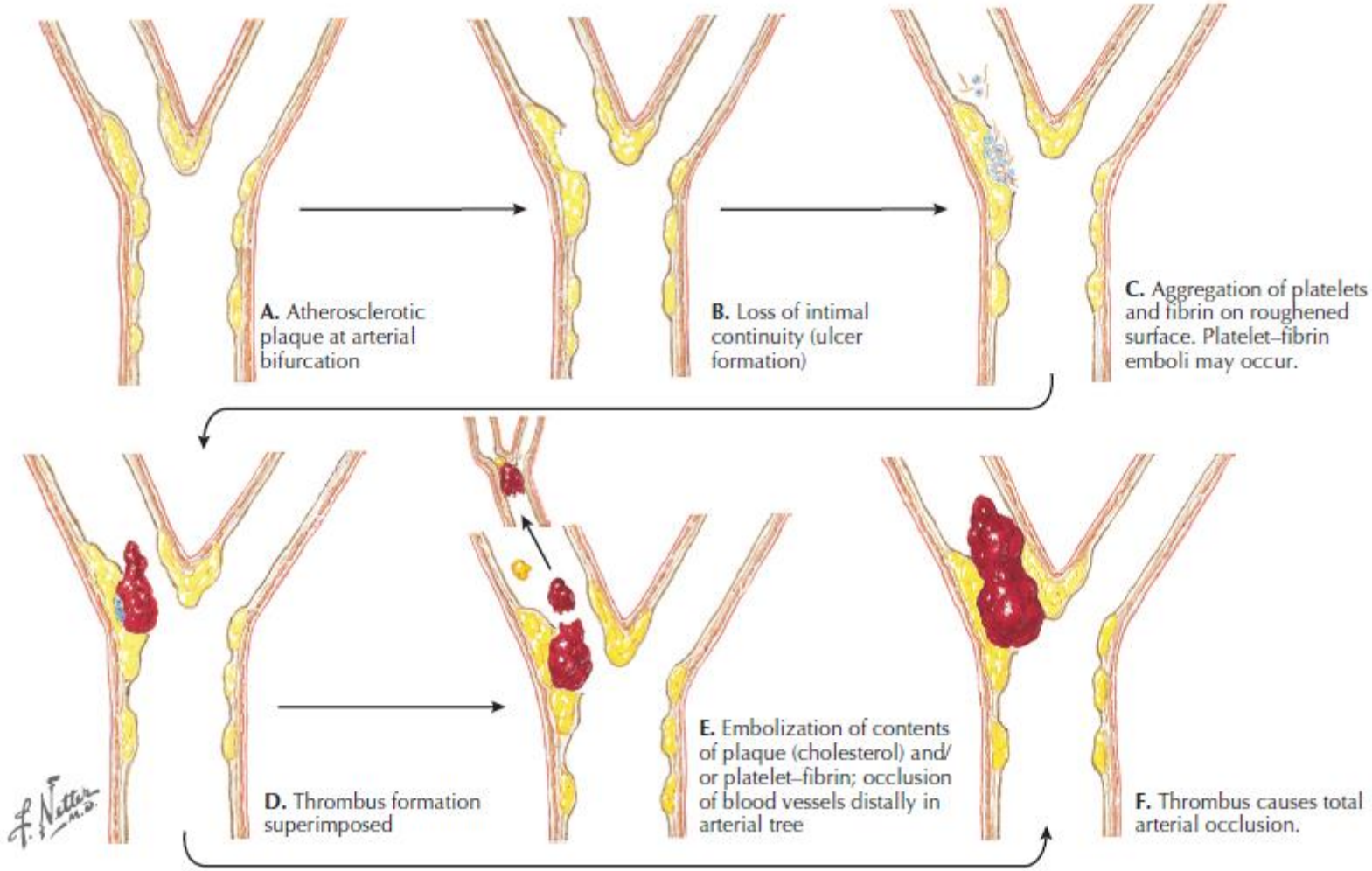
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

Distribution of the 10 leading causes of death in the United States in 2018

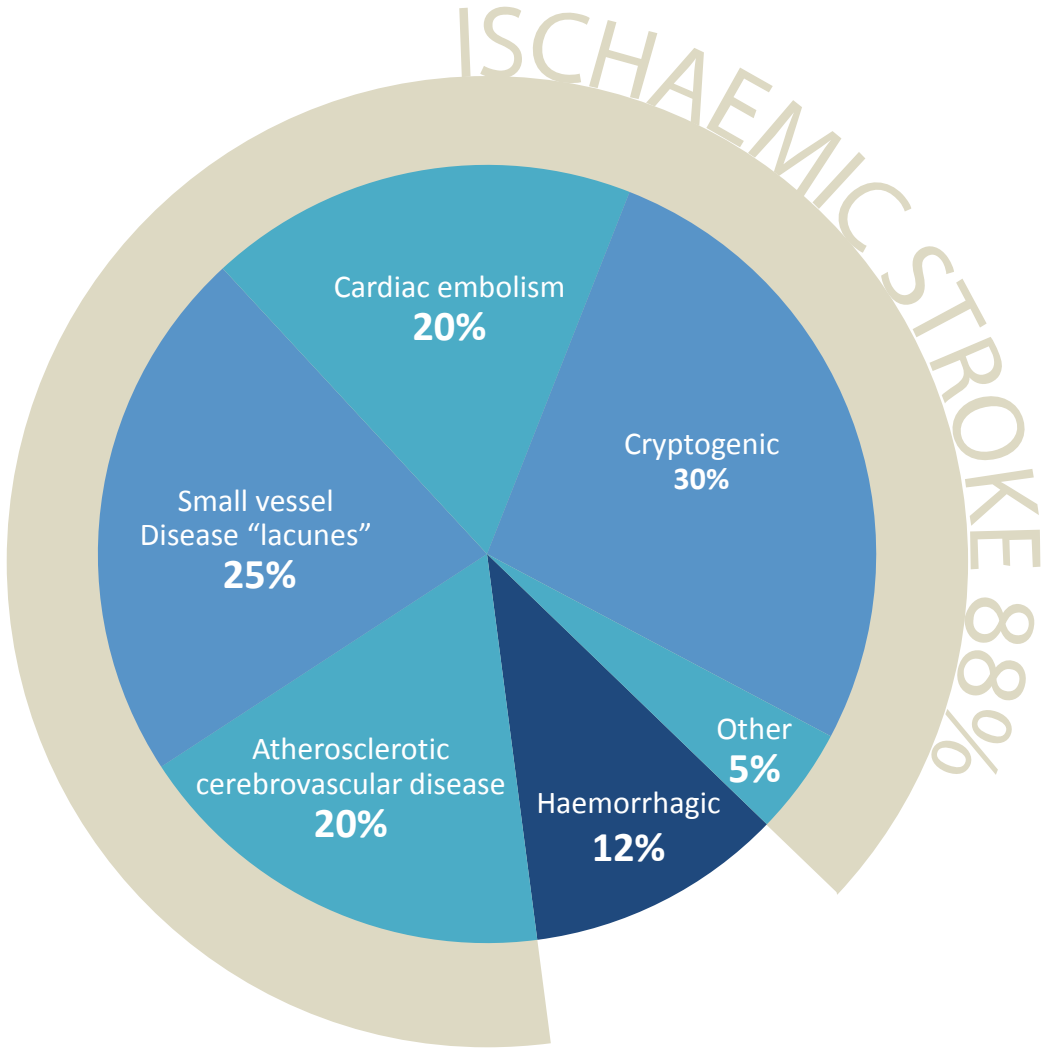


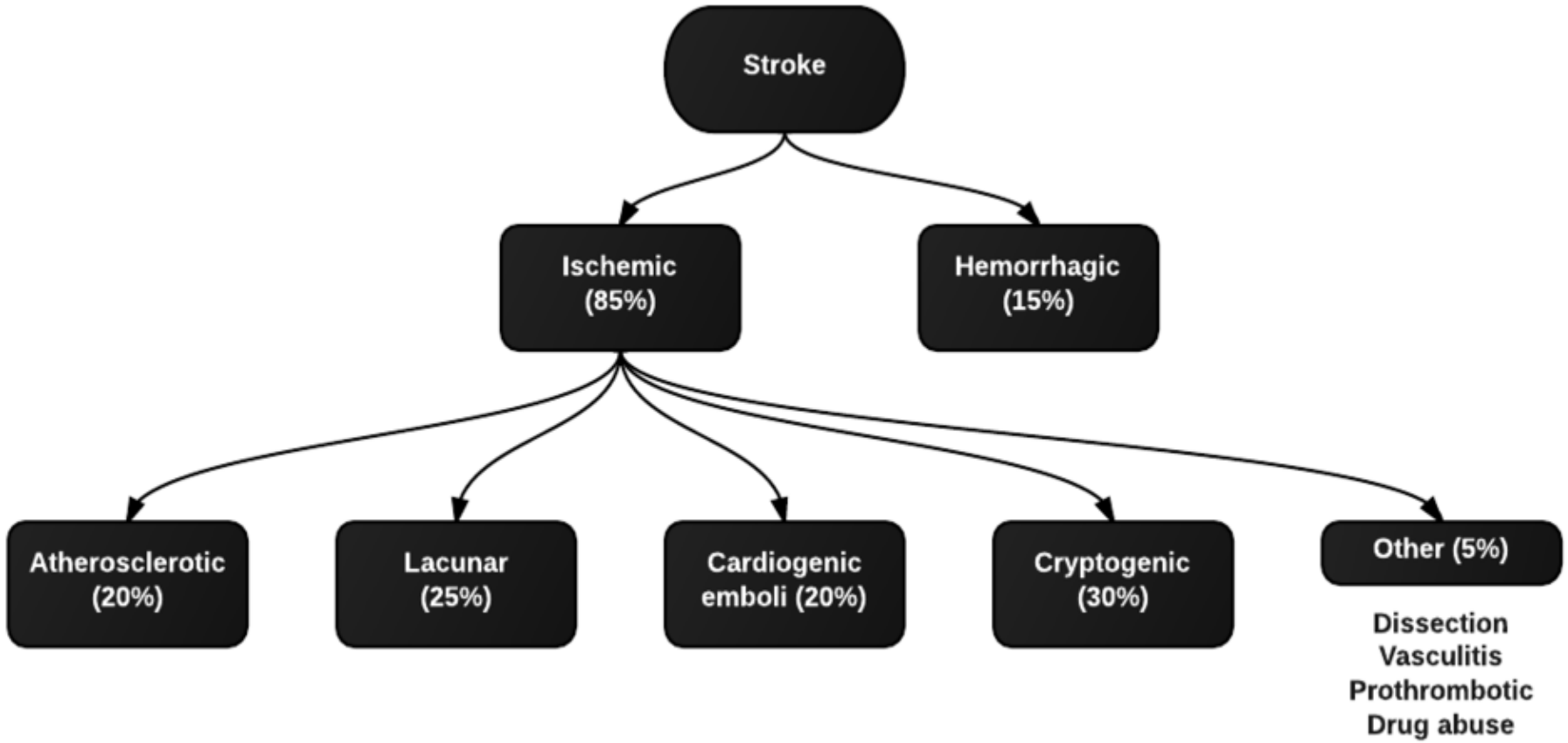
Sources
CDC; NCHS
© Statista 2020

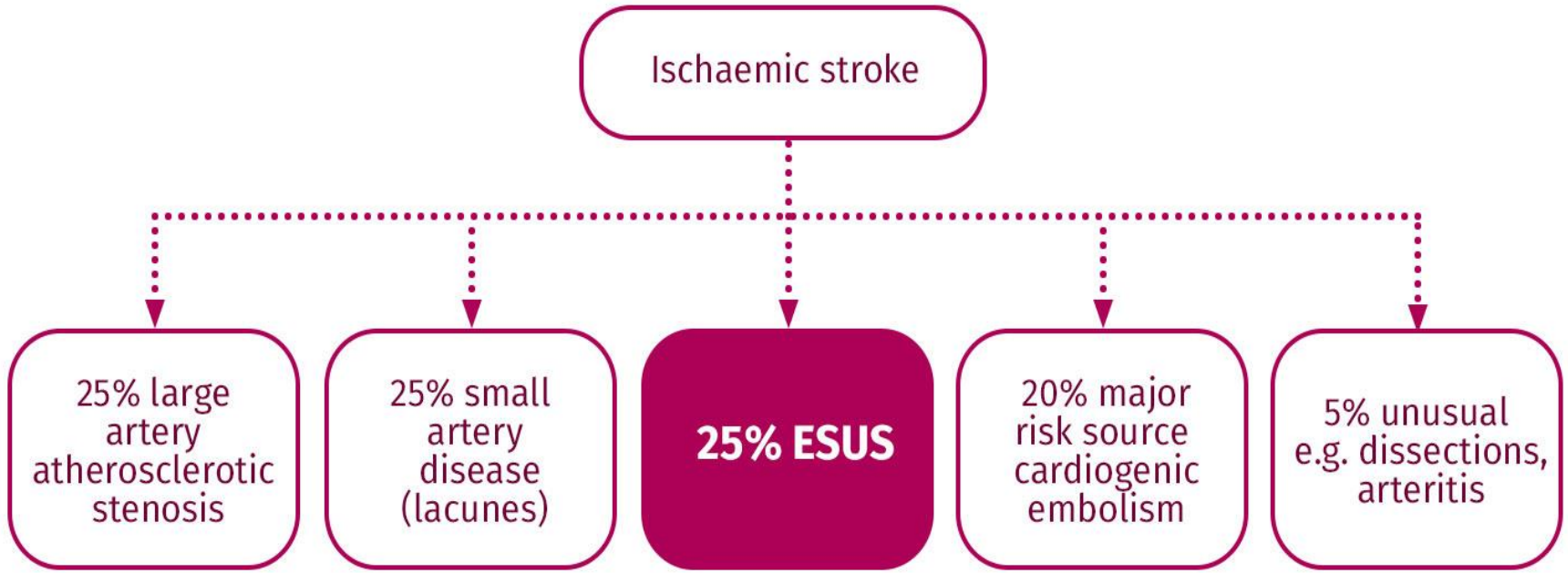
Additional Information:
United States; CDC; NCHS


A. Atherosclerotic plaque at arterial bifurcation
B. Loss of intimal continuity (ulcer formation)
C. Aggregation of platelets and fibrin on roughened surface. Platelet–fibrin emboli may occur.
D. Thrombus formation superimposed
E. Embolization of contents of plaque (cholesterol) and/or platelet–fibrin; occlusion of blood vessels distally in arterial tree
F. Thrombus causes total arterial occlusion.

Stroke types and incidence




Stroke
Ischemic (85%)
Hemorrhagic (15%)
Atherosclerotic (20%)
Lacunar (25%)
Cardiogenic emboli (20%)
Cryptogenic (30%)
Other (5%)
Dissection
Vasculitis
Prothrombotic
Drug abuse



ESUS (Embolic Stroke of Undetermined Source)

All 4 must be present:

1- Non-lacunar ischemic stroke on CT or MRI

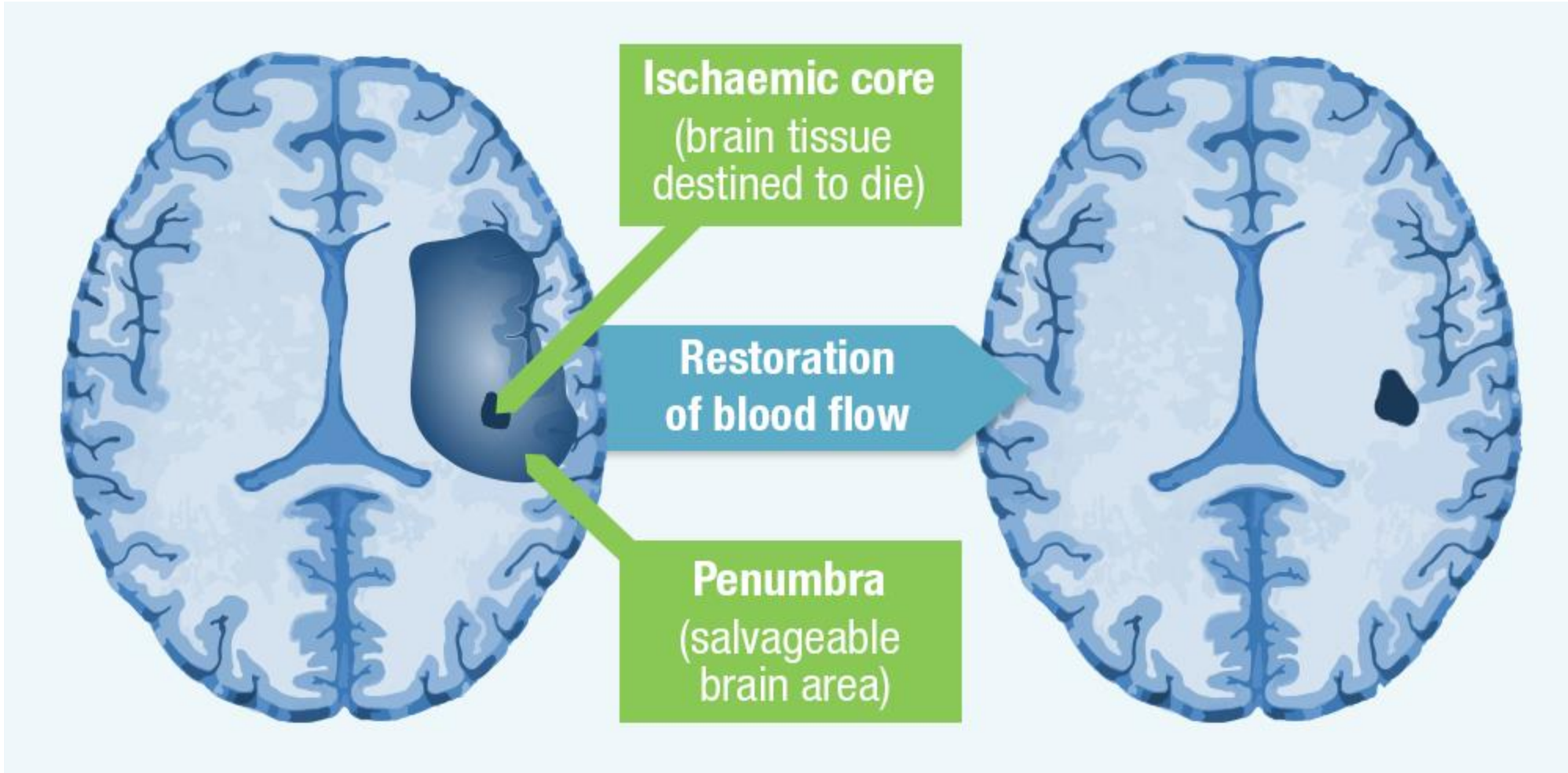
2- Absence of atherosclerosis (extra- or intracranial) causing ≥50% luminal stenosis in arteries supplying the ischemic area

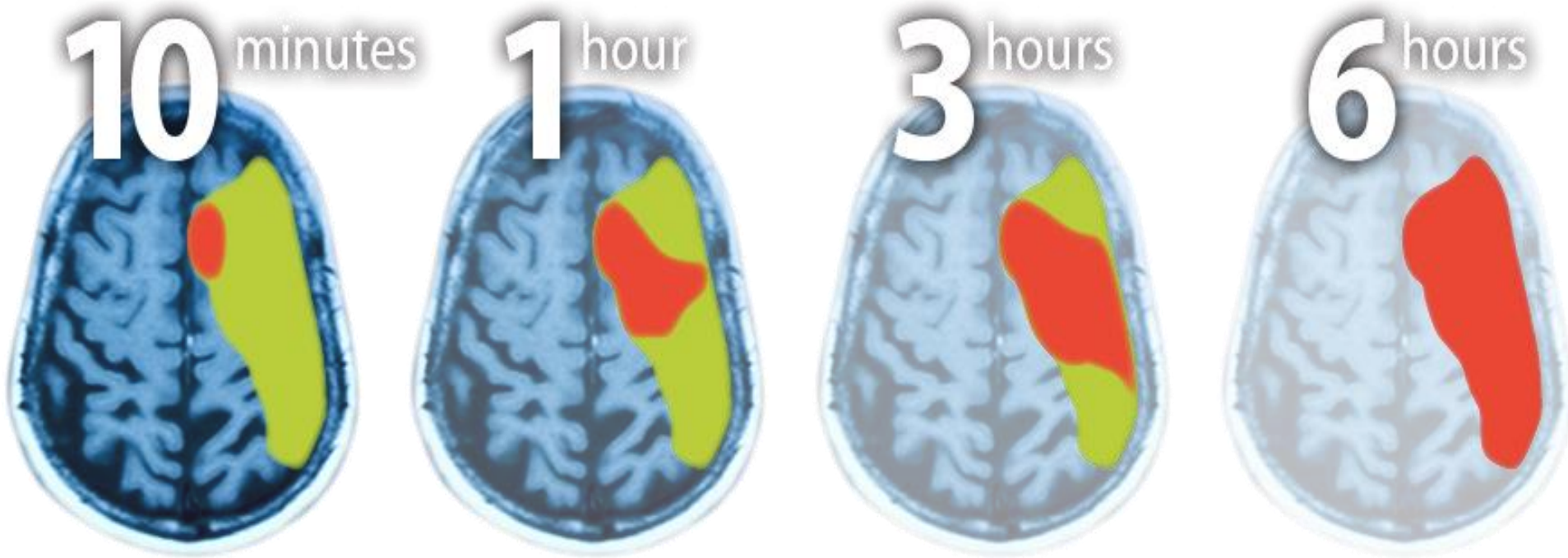
3- No major risk cardioembolic source

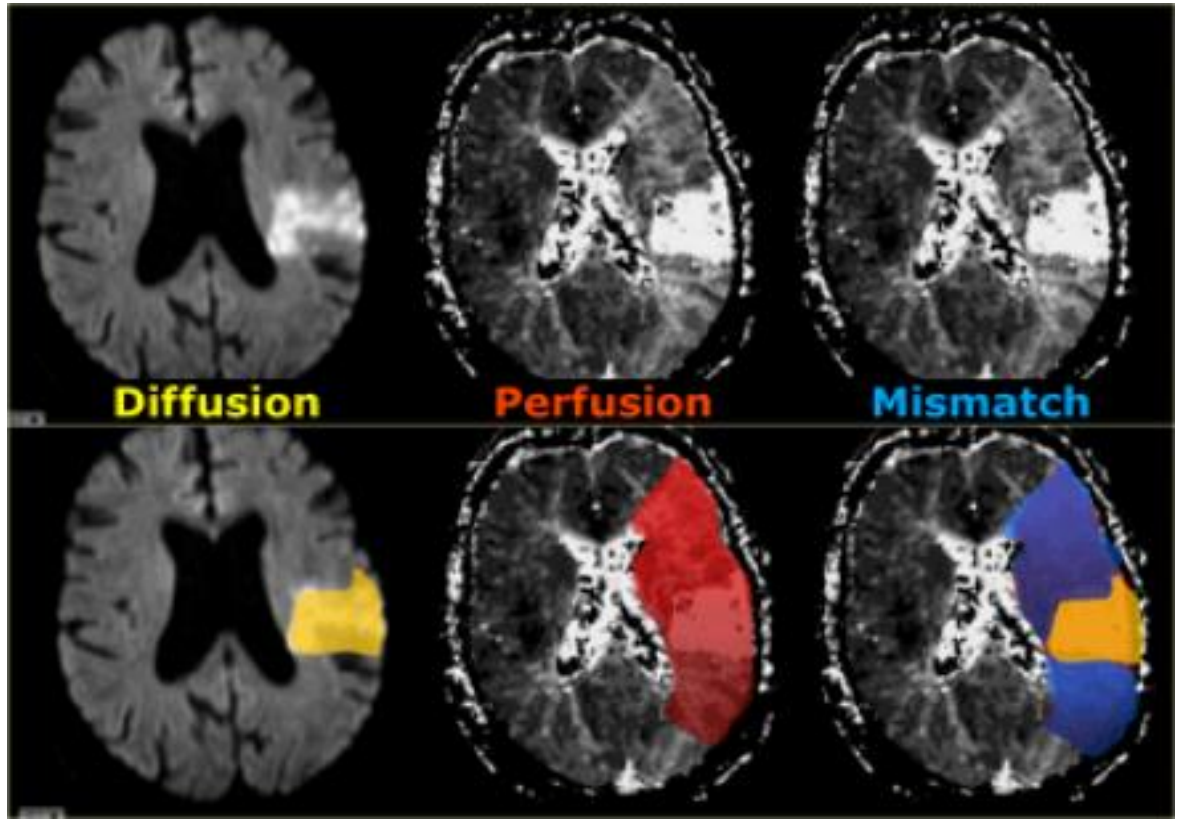
4- No other specific cause of stroke identified; e.g. arteritis, dissection, migraine/vasospasm, drug abuse

Ischemic penumbra

- Tissue surrounding the core region of infraction which is ischemic but reversibly dysfunctional.
- Maintained by collaterals.
- Can be salvaged if reperfused in time.
- Primary goal of revascularization therapies.


Ischaemic core
(brain tissue
destined to die)
Restoration
of blood flow
Penumbra
(salvageable
brain area)

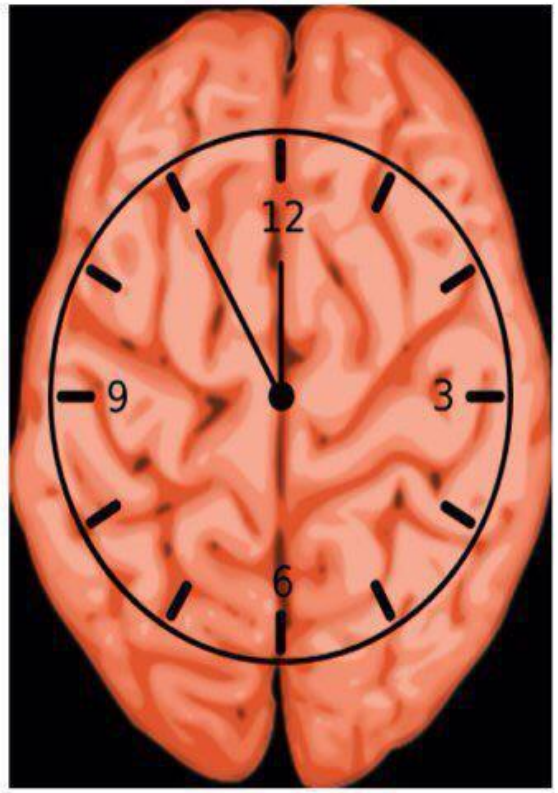

10 minutes
1 hour
3 hours
6 hours


Diffusion
Perfusion
Mismatch

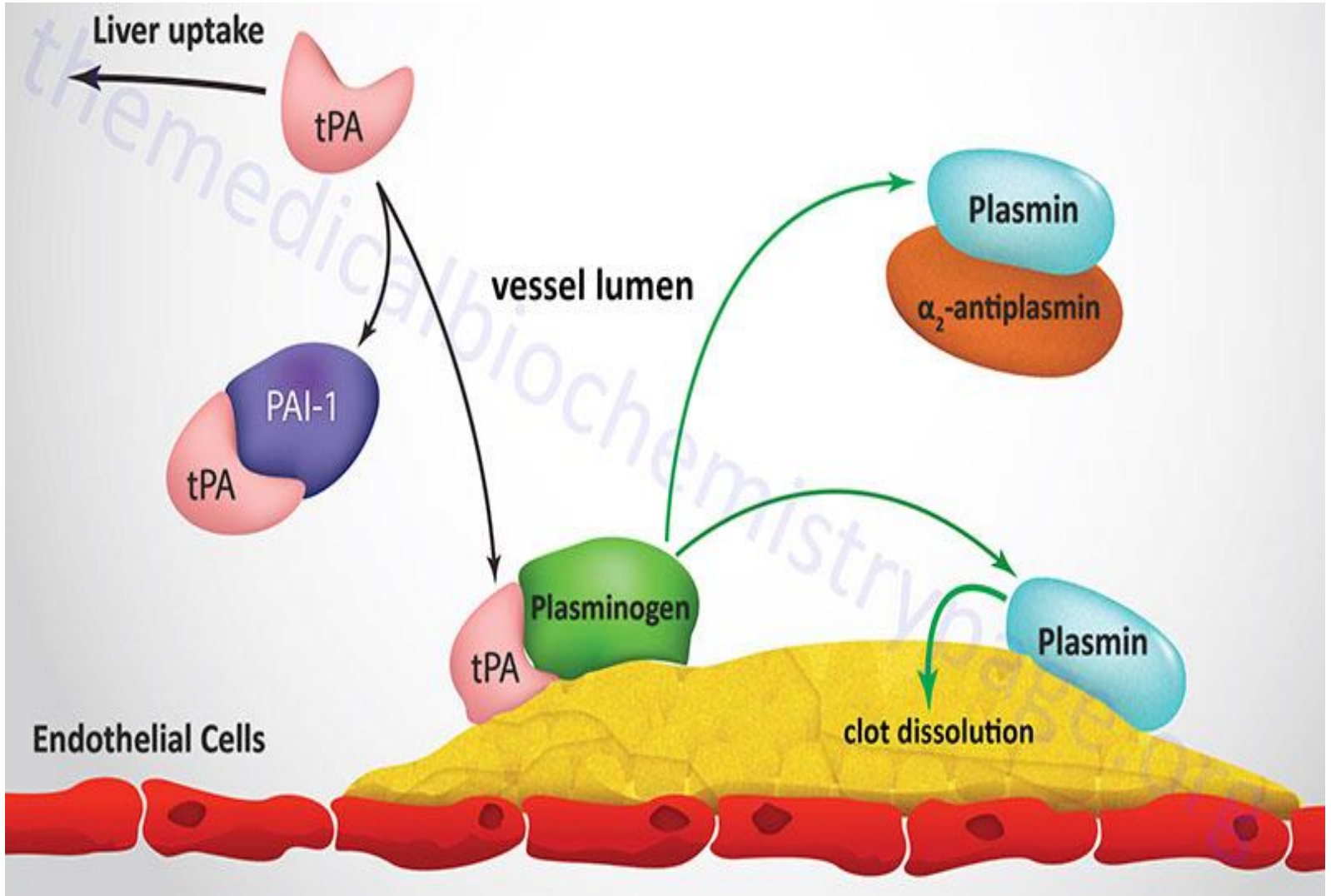
In a Typical Acute Ischemic Stroke, Every Minute Until Reperfusion the Brain Loses:

- 1.9 million neurons
- 14 billion synapses
- 7.5 miles myelinated fibers

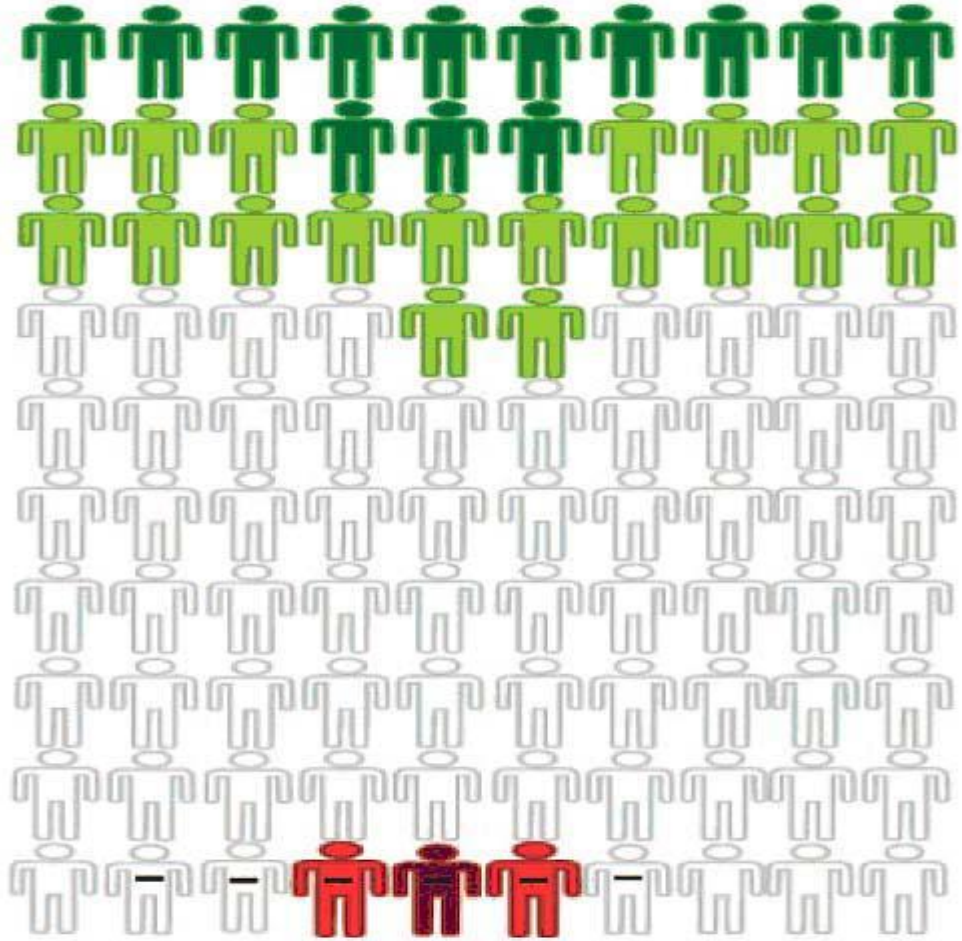
-- Saver, Stroke 2006



Alteplase


Liver uptake
tPA
vessel lumen
Plasmin
α2-antiplasmin
PAI-1
tPA
Plasminogen
tPA
Plasmin
clot dissolution
Endothelial Cells

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



Changes in final outcome as a result of treatment:

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

Early course:

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

Signs and Symptoms of Stroke:

Acute Onset of Neurologic Symptoms and Signs of Central Nervous System Nature

Face Arm Speech Test (F.A.S.T.)

TO CHECK FOR STROKE SYMPTOMS, REMEMBER F.A.S.T.

FACE DROOPING
or asymmetry on smiling

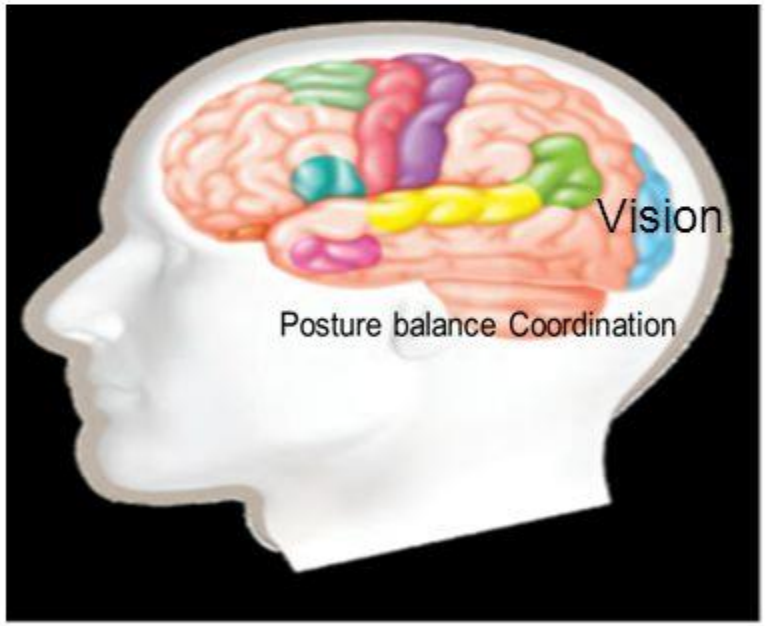
ARM WEAKNESS
or paralysis on one side

SPEECH DIFFICULTY
or slurring of speech

TIME TO CALL
the emergency services*

Beyond Fast: B.E. F.A.S.T

- **B**-Balance-Sudden trouble walking, dizziness, loss of balance or coordination
- **E**-Eyes-Sudden trouble seeing in one or both eyes



B E F A S T

Balance Eyes Face Arms Speech Time

B is for Balance: Does the person have a sudden loss of balance?

E is for Eye: Has the person lost vision in one or both eyes?

F is for Face: Does the person's face look uneven?

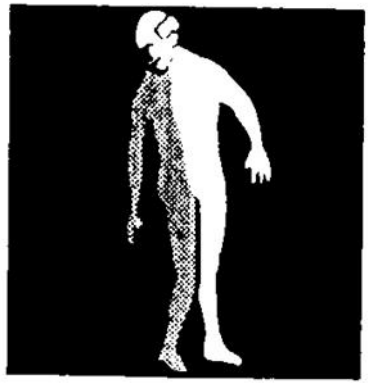
A is for Arm: Is one arm hanging down?

S is for Speech: Is the person's speech slurred? Does the person have trouble speaking or seem confused?

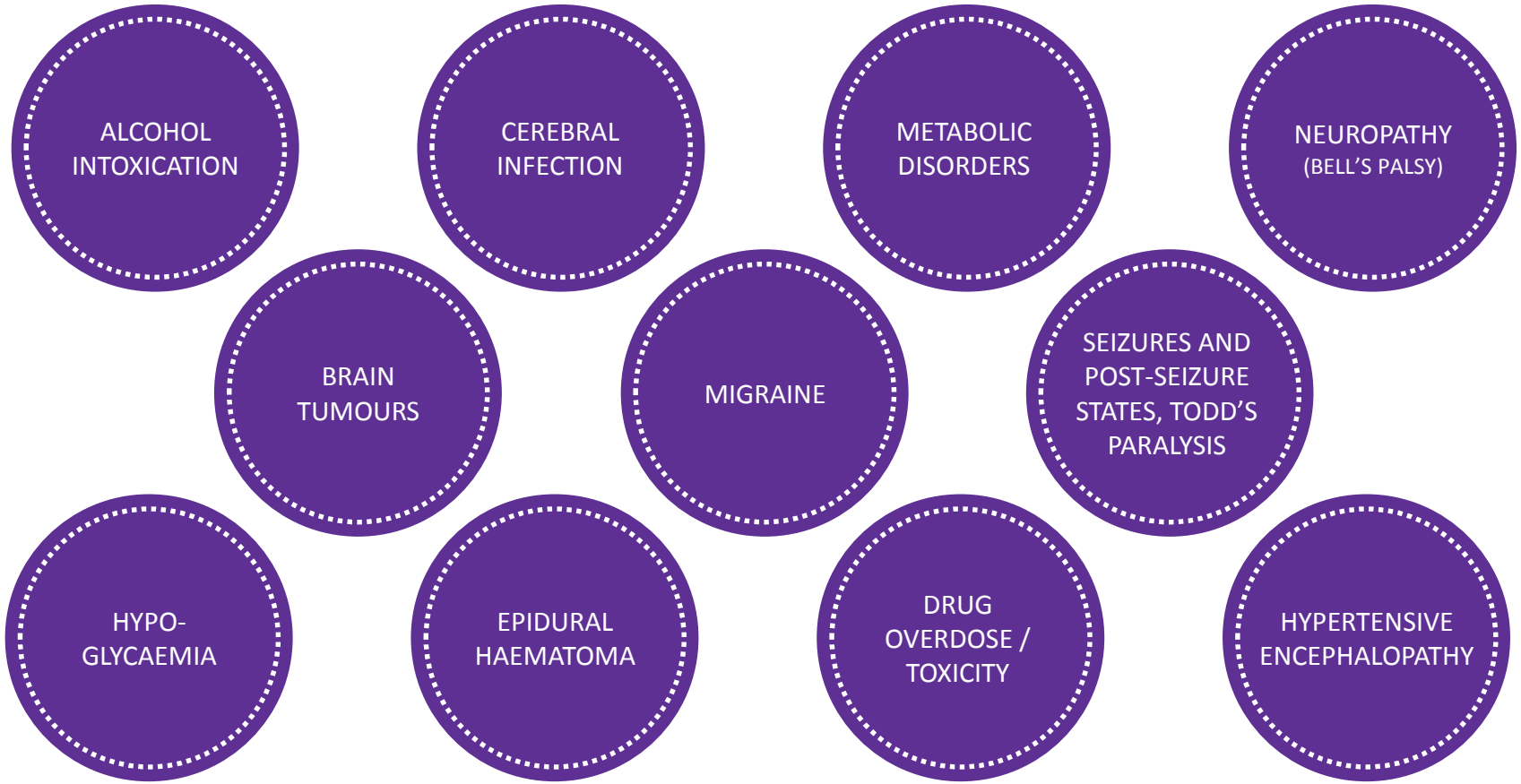
T is for Time: Call 911 now!

Acute Onset of Any of the Below symptoms:

- Hemiparesis or quadriparesis (latter in basilar occlusion)
- Facial weakness
- Aphasia
- Dysarthria
- Limb/truncal/gait ataxia +/- nausea & vomiting
- Vertigo, tinnitus, hearing deficit (posterior circ.)
- Impairment of vision in homonymous visual field defect
- Monocular impairment of vision (amaurosis fugax)
- Diplopia
- Impairment or loss of consciousness or confusion
- Hemineglect (visual or sensory)
- Headache (non-specific symptom)
- New onset seizure (3-4%) or acute new movement abnormality



Common stroke mimics



سکته مغزی قابل درمان است، اگر زمان را از دست ندهیم

اولین اقدام تماس با اورژانس

Primary Stroke Center vs Comprehensive Stroke Center

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Table 7. Treatment of AIS: IV Administration of Alteplase

Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 min, with 10% of the dose given as a bolus over 1 min.
Admit the patient to an intensive care or stroke unit for monitoring.
If the patient develops severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination, discontinue the infusion (if IV alteplase is being administered) and obtain emergency head CT scan.
Measure BP and perform neurological assessments every 15 min during and after IV alteplase infusion for 2 h, then every 30 min for 6 h, then hourly until 24 h after IV alteplase treatment.
Increase the frequency of BP measurements if SBP is >180 mm Hg or if DBP is >105 mm Hg; administer antihypertensive medications to maintain BP at or below these levels (Table 5).
Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them.
Obtain a follow-up CT or MRI scan at 24 h after IV alteplase before starting anticoagulants or antiplatelet agents.

Eligibility criteria

Inclusion criteria

- ❑ Clinical diagnosis of ischemic stroke causing measurable neurologic deficit
- ❑ Onset of symptoms <4.5 hours before beginning treatment; if the exact time of stroke onset is not known, it is defined as the last time the patient was known to be normal or at neurologic baseline
- ❑ Age ≥18 years

Eligibility criteria cont…

Exclusion criteria

Historical

- ❑ Ischemic stroke or severe head trauma in the previous three months
- ❑ Previous intracranial hemorrhage
- ❑ Intra-axial intracranial neoplasm
- ❑ ***Gastrointestinal malignancy or hemorrhage in the previous 21 days***
- ❑ intracranial or intraspinal surgery within the prior three months

Exclusion criteria cont…

Clinical

- ❑ Symptoms suggestive of subarachnoid hemorrhage
- ❑ Persistent blood pressure elevation (systolic ≥185 mmHg or diastolic ≥110 mmHg)
- ❑ Active internal bleeding
- ❑ Presentation consistent with infective endocaditis
- ❑ Stroke known or suspected to be associated with aortic arch dissection
- ❑ Acute bleeding diathesis, including but not limited to conditions defined in 'Hematologic'

Exclusion criteria cont…

Hematologic

- ❑ Platelet count <100,000/mm^3*
- ❑ Current anticoagulant use with an INR >1.7 or PT >15 seconds or aPTT>40 seconds*
- ❑ ***Theraputic*** doses of LMWH recived within 24 hours
- ❑ Current use of a direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect by laboratory tests such as aPTT, INR, ECT, TT, or appropriate factor Xa activity assays

Exclusion criteria cont…

Head CT scan

- ❑ Evidence of hemorrhage
- ❑ Evidence regions of ***obvious hypodensity*** consistent with irreversible injury

Eligibility criteria cont…

Relative exclusion criteria[¶]

- Only minor and isolated neurologic signs or Rapidly improving stroke symptoms
- ***Serum glucose <50 mg/dl***
- Major surgery or serious trauma in the previous 14 days
- History of gastrointestinal bleeding (***remote***) or genitourinary bleeding
- Seizure at the onset of stroke with postictal neurologic impairments
- Pregnancy
- ***Arterial puncture at a noncompressible site in the previous seven days***
- ***Large (>10 mm), untreated, unruptured intracranial aneurysm***
- ***Untreated intracranial vascular malformation***

Eligibility criteria cont…

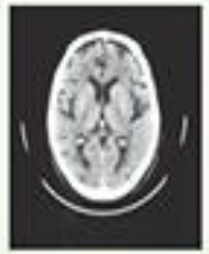
Additional relative exclusion criteria for treatment from 3 to 4.5 hours from symptom onset

- Age >80 years
- Oral anticoagulant use regardless of INR
- **Severe stroke (NIHSS score >25)**
- Combination of both previous ischemic stroke and diabetes mellitus

DTN ≤60 min: for evaluating and treating acute stroke













T=0
Suspected stroke patient arrives at stroke unit

T ≤10 min
Initial physician evaluation (including patient history, lab work initiation, & NIHSS)

IDEALLY pre-hospital

T ≤15 min
Stroke team notified (including neurologic expertise)

T ≤25 min
CT scan initiated

T ≤45 min
CT & labs interpreted

T ≤60 min
rt-PA given if patient is eligible

DTN, door to needle time, refers to in-hospital management

NINDS NIH website. Stroke symposium proceedings 1996. Updated 2011.

Complications Associated with rtPA

- Symptomatic intracerebral haemorrhage is one of the most serious and feared complications of IV rtPA therapy reported in **1.7 to 8.0%** of treated patients,

- The risk of SICH is roughly **6%** in patients with stroke treated with IV r-tPA

Table 8. Management of Symptomatic Intracranial Bleeding Occurring Within 24 Hours After Administration of IV Alteplase for Treatment of AIS

Class IIb, LOE C-EO
Stop alteplase infusion
CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match
Emergent nonenhanced head CT
Cryoprecipitate (includes factor VIII): 10 U infused over 10–30 min (onset in 1 h, peaks in 12 h); administer additional dose for fibrinogen level of <200 mg/dL
Tranexamic acid 1000 mg IV infused over 10 min OR ε-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled (peak onset in 3 h)
Hematology and neurosurgery consultations
Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

surgery is controversial with 2 exceptions:

(1)patients with cerebellar hemorrhage who are deteriorating neurologically and/or who have brain stem compression and

(2) patients with a lobar hemorrhage within 1 cm of the surface and measuring >30 mL

For how long after r-tPA administration is it reasonable to attempt to reverse the lytic effects if SICH occurs?

Although r-tPA is short acting with rapid clearance, its effects on the coagulation profile (prolonged PT/PTT and reduced fibrinogen levels) may last 24 hours or more postinfusion. we propose a window of 24 hours for lytic reversal in SICH(early ICH).

However, as NINDS, SITS-MOST, and DEFUSE all define hemorrhages attributable to thrombolysis as occurring within 36 hours, one could argue that a 36-hour window for lytic reversal is also appropriate, especially when considering the likelihood of poor prognosis and high mortality.

[1] Department of Neurology, Division of Cerebrovascular Diseases, Mayo Clinic, Phoenix, AZ, USA

Angioedema

- Orolingual angioedema occurring in 1 to 5%
- In most cases the symptoms of angioedema are mild and transient, associated more with lesions in the frontal and insular cortex and contralateral to the ischaemic hemisphere .
- Severe acute orolingual angioedema is a rare but potentially life threatening situation as it may cause partial airway obstruction that may require urgent airway management. CT of the tongue can distinguish haematoma from angioedema in this setting .
- The risk of developing angioedema is increased with the use of angiotensin converting enzyme (ACE) inhibitor medications.

Clinical Management

Management of angioedema include discontinuing rtPA infusion, administering antihistamines and corticosteroids, as well as intubating patients who develop stridor.

Table 9. Management of Orolingual Angioedema Associated With IV Alteplase Administration for AIS

Class IIb, LOE C-EO
Maintain airway
Endotracheal intubation may not be necessary if edema is limited to anterior tongue and lips.
Edema involving larynx, palate, floor of mouth, or oropharynx with rapid progression (within 30 min) poses higher risk of requiring intubation.
Awake fiberoptic intubation is optimal. Nasal-tracheal intubation may be required but poses risk of epistaxis post-IV alteplase. Cricothyroidotomy is rarely needed and also problematic after IV alteplase.
Discontinue IV alteplase infusion and hold ACEIs
Administer IV methylprednisolone 125 mg
Administer IV diphenhydramine 50 mg
Administer ranitidine 50 mg IV or famotidine 20 mg IV
If there is further increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL
Icatibant, a selective bradykinin B_2 receptor antagonist, 3 mL (30 mg) subcutaneously in abdominal area; additional injection of 30 mg may be administered at intervals of 6 h not to exceed total of 3 injections in 24 h; and plasma-derived C1 esterase inhibitor (20 IU/kg) has been successfully used in hereditary angioedema and ACEI-related angioedema
Supportive care

Aim: Organized Stroke Care System To..

Tenecteplase

- Tenecteplase is a three-point-mutated variant of alteplase bioengineered to achieve longer half-life, higher fibrin specificity, and increased resistance towards plasminogen activator inhibitor-1.

Tenecteplase

Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial

Nicola Logallo, Vojtech Novotny, Jörg Assmus, Christopher E Kvistad, Lars Alteheld, Ole Morten Rønning, Bente Thommessen, Karl-Friedrich Amthor, Hege Ihle-Hansen, Martin Kurz, Håkon Tobro, Kamaljit Kaur, Magdalena Stankiewicz, Maria Carlsson, Åse Morsund, Titto Idicula, Anne Hege Aamodt, Christian Lund, Halvor Næss, Ulrike Waje-Andreassen, Lars Thomassen

Tenecteplase was not superior to alteplase and showed a similar safety profile

Phase IIB/III Trial of Tenecteplase in Acute Ischemic Stroke

Results of a Prematurely Terminated Randomized Clinical Trial

E. Clarke Haley, Jr, MD; John L.P. Thompson, PhD; James C. Grotta, MD; Patrick D. Lyden, MD; Thomas G. Hemmen, MD; Devin L. Brown, MD, MS; Christopher Fanale, MD; Richard Libman, MD; Thomas G. Kwiatkowski, MD; Rafael H. Llinas, MD; Steven R. Levine, MD; Karen C. Johnston, MD, MSc; Richard Buchsbaum; Gilberto Levy, MD, MS; Bruce Levin, PhD; for the Tenecteplase in Stroke Investigators

The trial began as a multicenter, randomized, double-blind, controlled clinical trial comparing 0.1, 0.25, and 0.4 mg/kg tenecteplase with standard 0.9 mg/kg rtPA in patients with acute stroke within 3 hours of onset.

choose a best dose of tenecteplase to carry forward;

Symptomatic intracranial hemorrhage rates were highest in the 0.4-mg/kg tenecteplase group.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 26, 2018 VOL. 378 NO. 17

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collecutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis, for the EXTEND-IA TNK Investigators*

EXTEND 1A-TNK

- Patients with ischemic stroke who had occlusion of the internal carotid, basilar, or middle cerebral artery and who were eligible to undergo thrombectomy to receive tenecteplase (at a dose of 0.25 mg per kilogram of body weight; maximum dose, 25 mg) or alteplase (at a dose of 0.9 mg per kilogram; maximum dose, 90 mg) within 4.5 hours after symptom onset.

- The primary outcome was reperfusion of greater than 50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment.

- Secondary outcomes included the mRS at 90 days.

- Safety outcomes were death and symptomatic intracerebral hemorrhage.

CONCLUSIONS (NEJM):

Tenecteplase before thrombectomy was associated with a higher incidence of reperfusion and better functional outcome than alteplase among patients with ischemic stroke treated within 4.5 hours after symptom onset.

Stroke Thrombolysis With Tenecteplase to Reduce Emergency Department Spread of Coronavirus Disease 2019 and Shortages of Alteplase

Box. Workflow Advantages of Tenecteplase Relative to Alteplase That Reduce Staff Exposure to Contagion

- Shorter time to prepare
- Shorter time to administer (5 s versus 1 h)
- Does not require that a second, dedicated intravenous catheter be inserted and maintained
- Does not require an intravenous infusion pump
- Shorter time to initiate interfacility transfer after intravenous lytic administration

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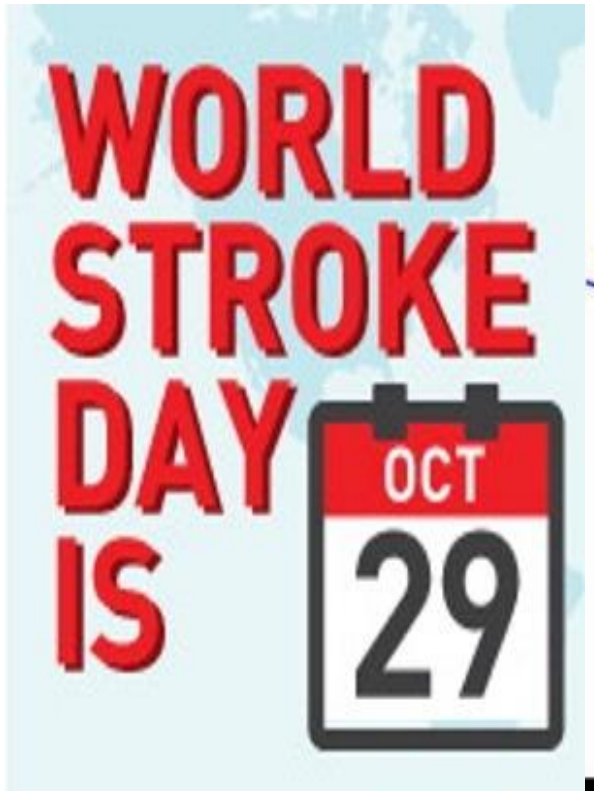

Iranian Stroke Organization

انجمن سکته مغزی ایران

روز جهانی سکته مغزی

هفتم آبان

ازهرچهارنفر، یک نفر دچار سکته مغزی می شود
تلاش کنیم آن یکنفر ما نباشیم.


Thank You All
for your patience
hearing !!