STROKE Definition, Epidemiology, Acute MANAGEMENT of Cerebral Ischemia

the Good, the Bad, the Ugly

- A Lecture delivered on the 26TH of OCT 2018 at the
- EAN / AFAN REGIONAL TRAINING COURSE .

- on
- Definition, epidemiology and modern emergency management of Ischemic Stroke.
- By
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- LASUCOM / LASUTH; IKEJA; LAGOS STATE NIGERIA
- Venue:. MADAGASCAR

DISCLAIMER

The following presentation may contain scientific / medical information on unapproved dosages / indications currently under clinical investigation or other scientific review.

Kindly note that the views and opinions of the speaker do not necessarily reflect those of EAN AFAN RTC

RTC recommends the use of INFORMATION only in strict accordance with the locally approved GUIDELINES

NO CONFLICT OF INTEREST.
NO COMPETING INTEREST

Current treatment of Insomnia

Lecture Overview / Outline

Holistic approach:

Need to know

what we are talking about.

Definition,
Epidemiology
modern emergency management of Ischemic Stroke
Overview of STROKE MANAGEMENT–

Challenges and the way forward

Way forward : Roadmap

- STROKE:
- Time trend defn changes
- Peculiarities of Stroke in Blacks
- Epidemiological transition
- Management: cf Gold standards Globally

- SERVICES: Equipment / Facilities
- Man Power

- Management of stroke: CI: GOOD / BAD / UGLY

- Differences / Problems identified:
- DNR/Withdrawal of Care /
- Clinical Nihilism

- Recommendations and the way forward

- ***What do our patients deserve ?***

Epidemiology:Brain Attack / Stroke

- ***Peculiarities in sSA:*** Changing global / African epidemiology

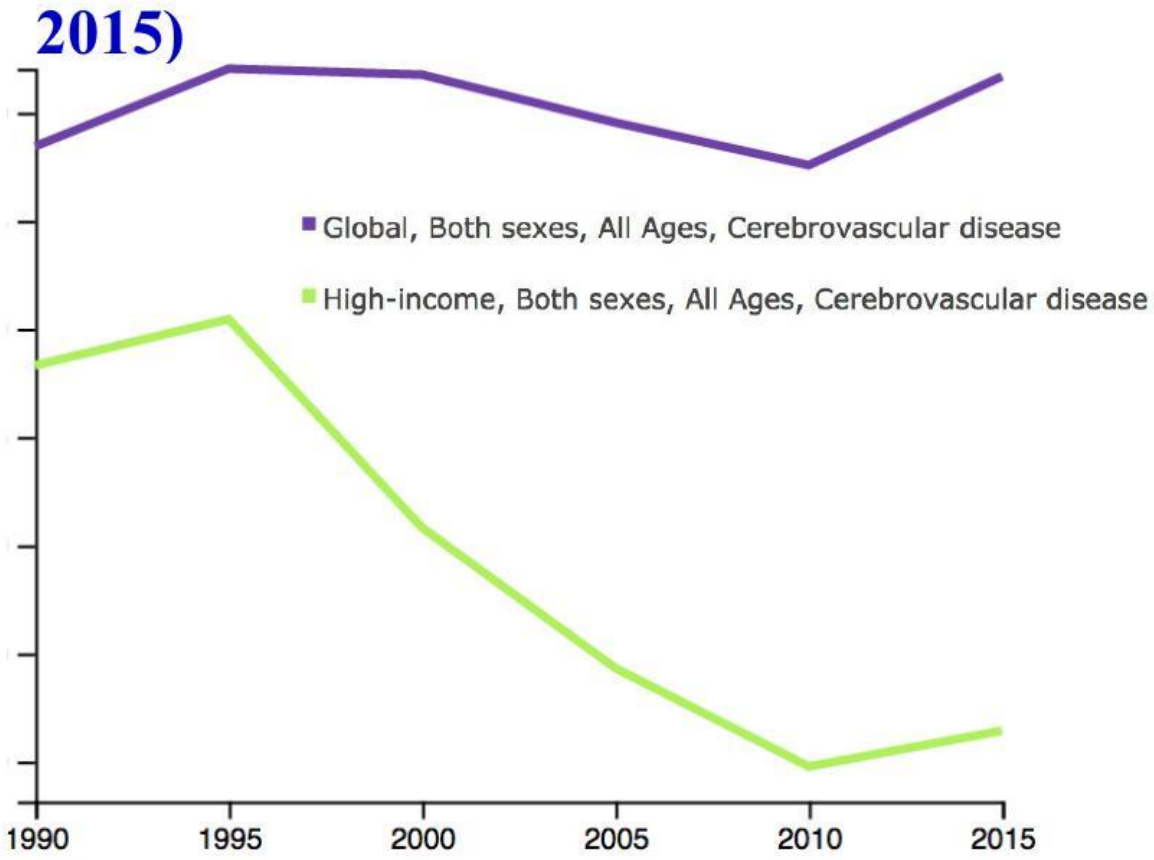
- incidence < 12% in HIC, it > by 12% in LMIC over the ***last decade***.
- exploding but neglected burden of ***NCD***s: HBP, DM, dyslipidaemia: culminate in stroke.
- ***epidemiological transition: an ageing popn, popn growth, rapid urbanisation and accompanying lifestyle changes.***

- WHO (2001): death / DALYs > 7 times higher LMIC than HIC.

- Deaths in LMIC: ***85.5% of stroke deaths worldwide (2001)***
- 87% of global stroke mortality in (2005) (a > 1.5% cf with 2001)

DALYs :disability-adjusted life years (yrs of life lost + yrs lived with disability),

Global trends in stroke incidence rates per 100,000 person-years (1990-2015



STROKE IN AFRICA

- Peculiarities of S in people of African ancestry: ***Enhanced predisposition,***
- ***different pattern of types/subtypes,***
- ***worse severity and often***
- ***poorer outcome of stroke***
- relatively ***younger age (< 15 years)***
- ***in people of African descent established.***

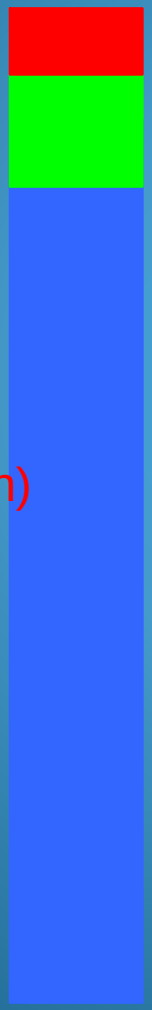
- INTERSTROKE study:
- 3types: LMIC: CI 66% ; ICH 34% ***HIC: CI*** 91%;ICH 9%
- CI subtypes: lacunar stroke; small v (27%), large (14%); cardio-embolism (25%), others (20%) undetermined (14%

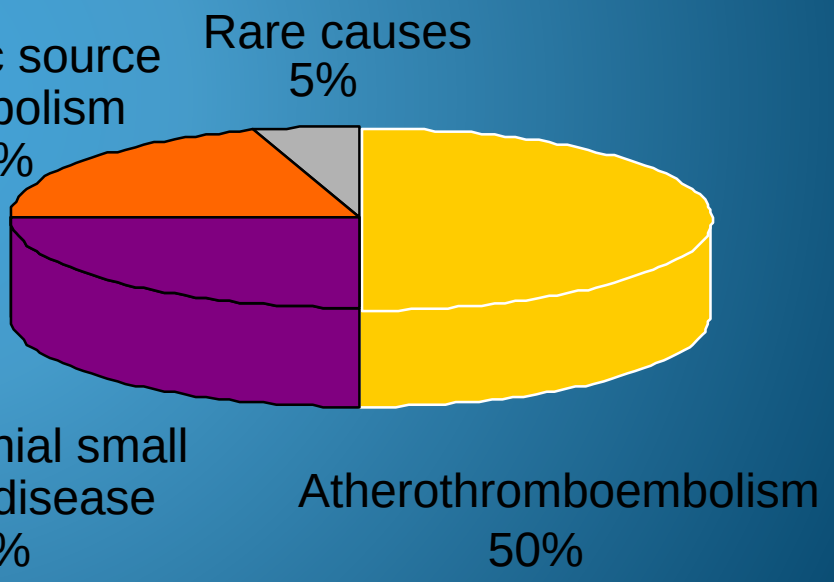
Stroke is a heterogeneous clinical syndrome –many types and subtypes

5% - subarachnoid haemorrhage

15% - primary intracerebral haemorrhage

80% - ischaemic stroke





STROKE IN AFRICA

- African Americans:
- higher predisposition,
- worse severity
- poorer outcomes cf to Caucasian Americans.
- multi-ethnic South London Stroke Registry: black stroke survivors:
- worse cognitive outcome cf to other racial groups. ?
- ?S-E differences,

- variation in rates:
- ***disparities in healthcare-seeking*** cultural ***practices***
- ***differential access to healthcare services,***
- differential exposure to environmental causes / lifestyles
- ***influence of underlying differences in genetic factors***

AHA Classes/Levels of Evidence

- Classes indicate what we should generally do
  - I: Should do it
  - II: Consider it
    - IIa - per most experts; IIb - conflicted
  - III: Don't do it
- Levels indicate how sure we are about doing it
  - A: 2 randomized trials
  - B: 1 randomized trial or nonrandomized studies
  - C: Expert opinion or case series

Comprehensive stroke unit = dedicated area (beds) in acute hospital

Assessment & monitoring

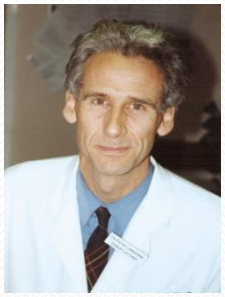
Acute management

Physiological control	Early mobilisation	Manage complications	Skilled nursing

Multidisciplinary rehabilitation

Discharge planning

Nurse



Doctor

Physiotherapy

Occupational Therapy

Speech therapy

Coordinated multidisciplinary care
= formal multi-disciplinary team meetings 1x per week)

SUTC Cochrane Library (2007)

Timeline of Care – NINDS Recommendations

- ED physician sees patient within **10 minutes**
- Stroke physician notified within **15 minutes**
- CT scan is completed within **25 minutes**
- CT interpretation is obtained within **45 minutes**
- IV rtPA should be initiated within **60 minutes**
- *Mobilize for IA therapy as rapidly as possibly*

stroke Rx : summary

5 EBM: Minimal / Essential /Advance / Service of care

1) STROKE UNIT proved by EBM– 90%

- *2) Anti-platelet agents (proved by EBM – 80%)*
- *3) Thrombolysis (proved by EBM - 30%)*
- *Anti-coagulation (limited efficacy)*
- *Neuroprotection (ABDF / NeuroAID ? proved by EBM): ? citicoline ; cerebrolysin. [Tenecteplase replaced Alteplase:*
- *Single bolus, (transporting pt easier), cheaper*
- *Knives for Stroke treatment: (surgical treatment)*
- *4) Endovascular Thromebectomy (EBM 50%)*
- *Large Vessel proximal occlusion*
- *5) Decompressive craniectomy: EBM -50%*
- *Malignant MCA occlusion (unacceptable complications)*
- *Carotid endarterectomy (limited indications)*
- *Clamp/Coil/Gluing/ Flow Diverter: aneurysm (SAH only)*
- *EC/IC bypass surgery (it works, but does not help)*

ICH: EBM.

- No FDA Approved therapy
- NONE:
- reduction on hematoma expansion
- Improvement in functional outcome

- ***Activated Factor VIIa***
- Reduce hematoma growth / expansion
- No improvement in functional outcome
- ***Intensive BP lowering:***
- No effect on hematoma expansion
- Modest functional benefit.

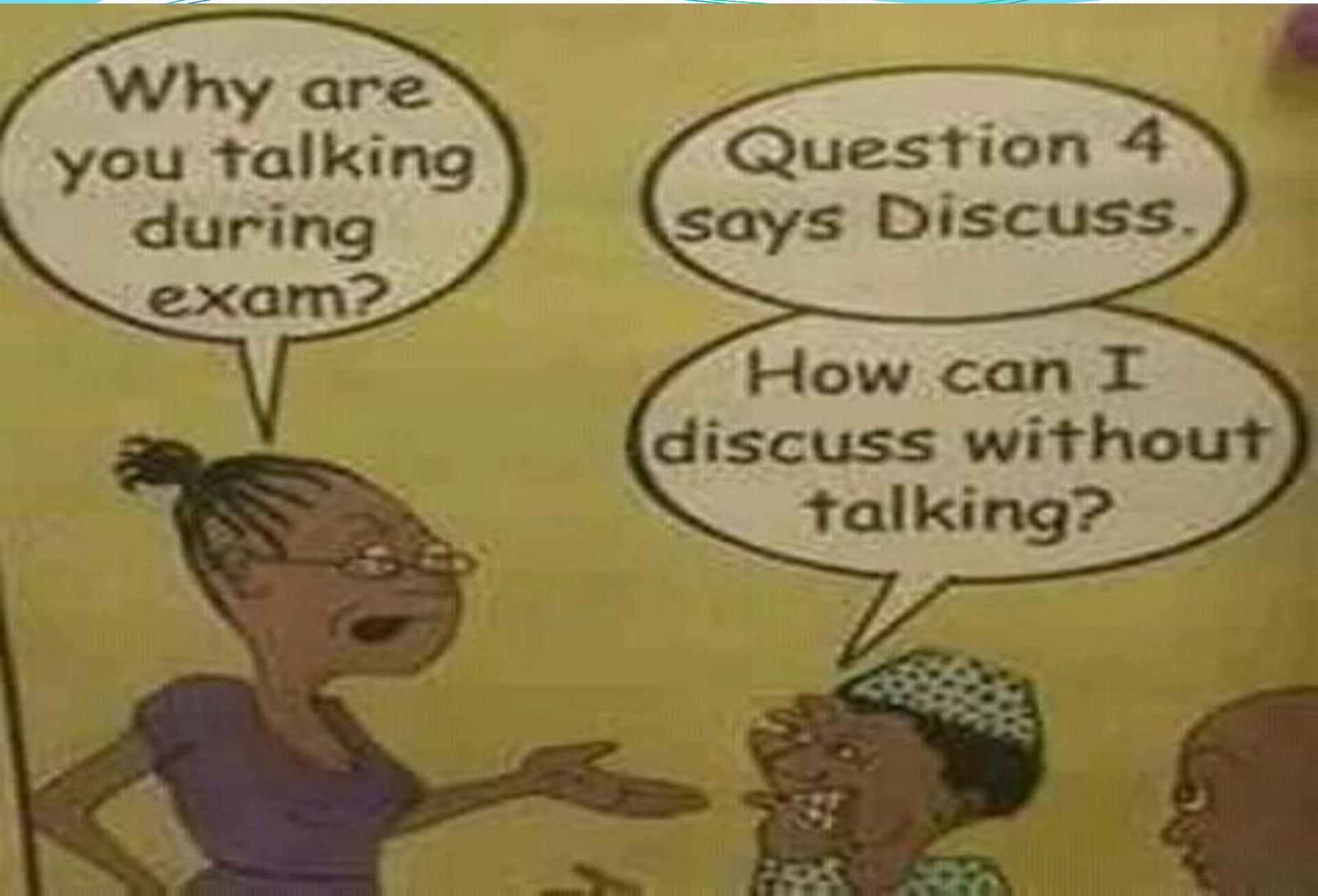
2018 Guidelines modifications

- Sonothrombolysis: adjunct to thrombolysis XX
- CRP Measurements: small vessel disease (white matter hyperintensities / microbleeds).
- Hyperhomocsteinemia: Not a significant risk factor
- ASPECTS SCORE: Dense A sign: MCA occlusion
- CT spot sign: Hematoma expansion / Active bleeding
- Factor VIIa : XX. Lack of efficacy
- Carotid End Arterectomy > 70% cin 48H – 7D
- Joint prev of stroke /dementia: commonest cvd
- Circular thinking: Silent infarct 5X > Amyloid
- >BP; > PR ; > Arterial stiffness, > Homocystein
- leads to > amyloid.

Anticipated Guidelines modifications:WSC: oct 17-20, 2018

- EXTEND STUDY: Tenecteplase 4.5 to 9 hrs
- (> Haemorrhagic Transformation, but overall benefit),
- Reactivation /Reperfusion Injury: Glymphatics
- 20 20 20: by YEAR 2020: 20% thrombolysed within 20 minutes of Door to Needle Time (DTN) ? 3- phase CT
- Donatelloc: CT features of CI disappearing between day 7 to 14, and reappear > day 14;
- Imaging of choice: CTP for CI (15minutes added) , MVA for CVT
- Collateralisation: Spheno –Palantine Ganglion Stimulation
- Focus. Rx beyond Acute Rx (CLOT dissolution / Removal)
- Recovery Rx: Brain Repair
- Post stroke Dementia: 1st stroke 10%, 2nd stroke: 30%
- Ischemic Tolerance: keeps brain tissue still active
- Cerebral Oedema: Successful trial with Glyburide/Glibenclamide
- Obstructive SLEEP APNEA: 70% of wake–up stroke (mid-point of sleep hrs)
- SAH: Delayed vasospasm factors: inflammation, thrombosis, vasospasm, Cortical Spreading Depolarisation.

If A Single Teacher Can't Teach Us All The Subjects, Then..
How Could You Expect A Single Student To Learn All Subjects??


Why are you talking during exam?
Question 4 says Discuss.
How can I discuss without talking?

QUESTION 1:

- Of PATIENTS WITH BELL'S PALSY (7th N Palsy LMNL):
- A) They have STROKE
- B) They have mild STROKE
- C) They have Partial Stroke
- D) They have STROKE in evolution
- E) None of the above

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QUESTION 2

- Of Patients with SubDural Hematoma,
- The following is correct:

- A) They have Stroke
- B) They have stroke because it is of vascular origin
- C) They have stroke because it is often post traumatic
- D) They have a stroke mimic/Stroke-like syndrome
- E) All of the above

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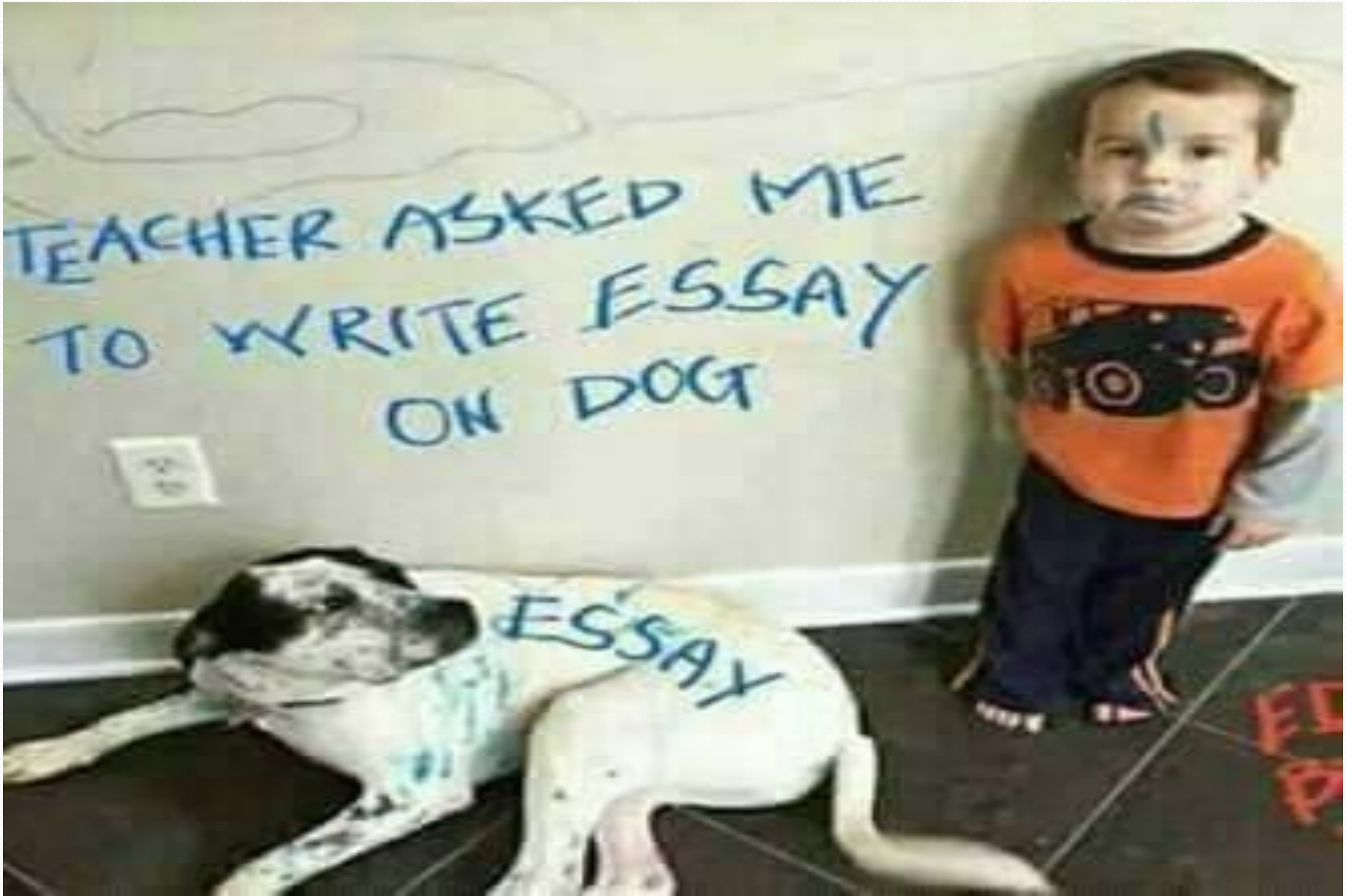

TEACHER ASKED ME
TO WRITE ESSAY
ON DOG
ESSAY

Definition

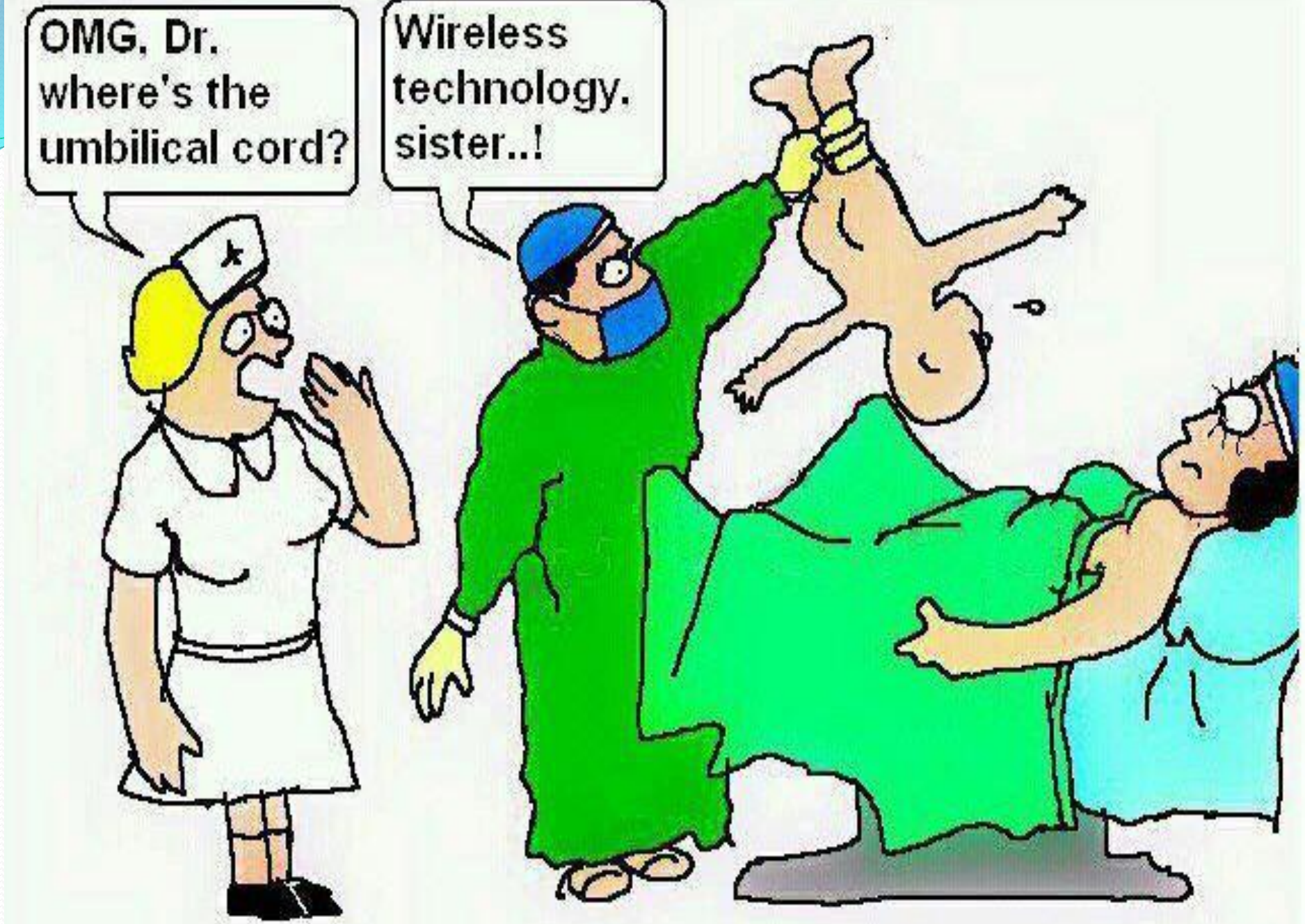
- ***WHO: 1970***

  Focal or Global Cerebral dysfn of vascular origin lasting >24 hrs or leading to death.

- **S.A. H / C. I / I.C.H**
- **T.I.A./B.Tumors/Subdural hematoma[o]**

T. I. A. CVD - parent term = CVA (Stroke); TIA ; CITS; Cerebral arteriosclerosis; cerebral angioma ; Cerebral arterio-venous malformation ; Subdural hematoma

- Stroke Like Syndrome:
- Stroke = Vascular
- Stroke mimics = Non-vascular
- (Hemispheric tuberculoma; cryptoccocoma, toxoplasmosis, cerebral lymphpma, Kaposi sarcoma in HIV)


OMG. Dr. where's the umbilical cord?
Wireless technology. sister..!

IT age

Definition – new concept

- ***2002***
- 24 hrs time based: confusing; misleading; outdated
- Old definition does not suggest medical emergency (Brain attack).
- Not corroborate the mantra "time's neurone" (cf Time's muscle by cardiologist)
- Does not take into cognizance the use of thrombolytics within 270 mins (4 ½ hrs) in CI or Recombinant activated factor VII within 4 hours in ICH
- TIA not benign. TIA and stroke = One hour
- (90%) TIA lasts 10 mins; resolve in 30 mins. If symptoms last > I hr; chances of resolutn :15%
- ***2009***
- Tissue – based / Time – based definition
- TIA: No objective evidence of acute infarction in the affected region of brain/retina; < I hour
- Stroke : objective evidence of infarction irrespective of duration of clinical symptoms.
- (cf Angina pectoris vs Myocardial infarction)
- CT/MRI necessary to increase diagnostic accuracy
- CITS = RIND

JULY 2013 DEFN

Highlights

- Not Global, but Focal.
- No Trauma
- Neural tube structures: Brain, SC, Retina.
- Not Neural Crest structures: Cranial/ P. Nerves
- Symptomatic / Silent subtypes.
- Time definition – secondary consideration when Neuro-imaging unavailable OR Inadequate.

Epidemiology: Brain Attack / Stroke

Acute neuro-vascular syndrome

666 (Revelation 13/18)

(1 in 6 individuals dev stroke in lifetime.;

6 patients dev stroke q 1 min / Q 6s , one individual dev

q 6s 1 death recorded in its favor;

6M death worldwide

(Dementia 10% > 1st stroke; 30% > 2nd stroke: commonest CVD)

Endovascular Thrombectomy:

<6hrs; (now 16 [DEFFUSE-3]– 24 hrs [DAWN)

NIHSS >6,

CT ASPECTS Score> 6)

[ALBERTA STROKE PROGRAM EARLY CT SCORE]

The lifetime risk of stroke is 1 in 5 women and one in six men

Epidemiology: Brain Attack / Stroke

- Second leading cause of *preventable* deaths in adults worldwide.
- ***Preventable***: but preventive efforts are still far from optimal
- Primodal : NCD/CD; < salt (POLICIES ON SUGAR/SALT in food >tax);< stress, gen dx preventn: exercise, fruits/greens, no cigarrette
- Prim;
- 2º: (Aspirin/Statins).
- 3º: Reduce disability /morbidity; Improve outcome)
- ***Quatenary: Therapeutic options: CcB, Folate,***
- ***Aspirin in ICH- No; even if AF, until 1 3 6 12 (+ 2 days).***

- ***Treatable***: evidence-based Rx available, but not fully used in any region, especially low resource areas

- major PH issue international collaboration activities reqd

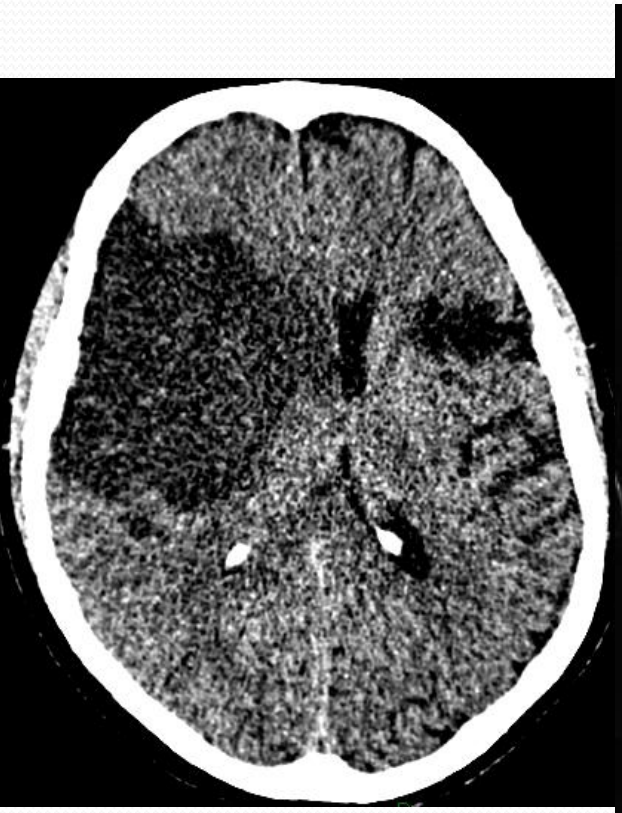
Stroke

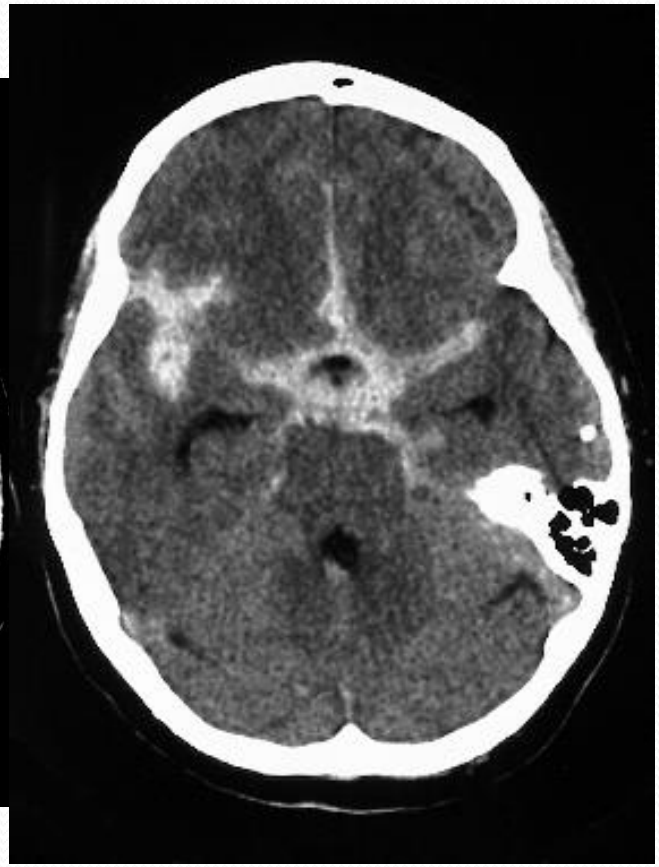
Cerebral Infarction (CI),

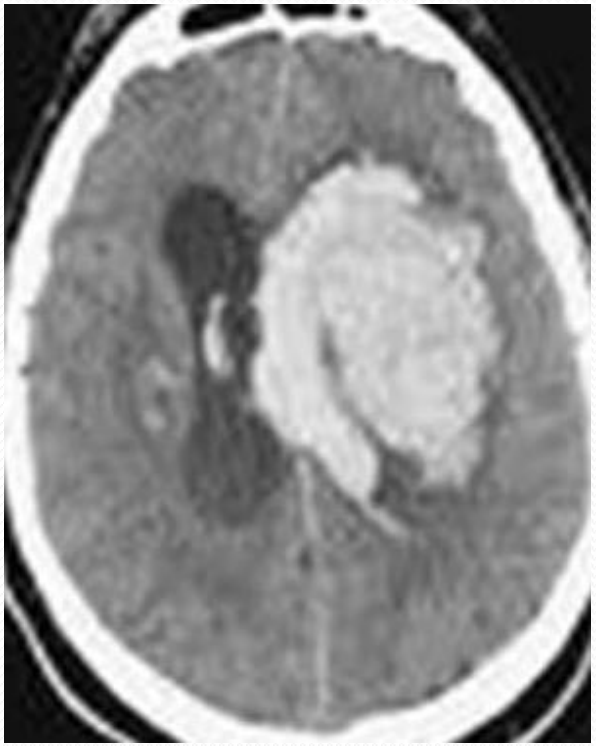
Intracerebral Haemorrhage (ICH)

Sub – Arachnoid Haemorrhage (SAH)

3 types of stroke







EXTRACRANIAL / INTRACRANIAL

EXTRACRANIAL

- endothelial plaque / plaque rupture
- Common in whites
- Common in males
- Associated with hyperlipidaemia
- Smoking
- Assoc PVD and CAD
- > CRP (? Genetics)
- > TIA

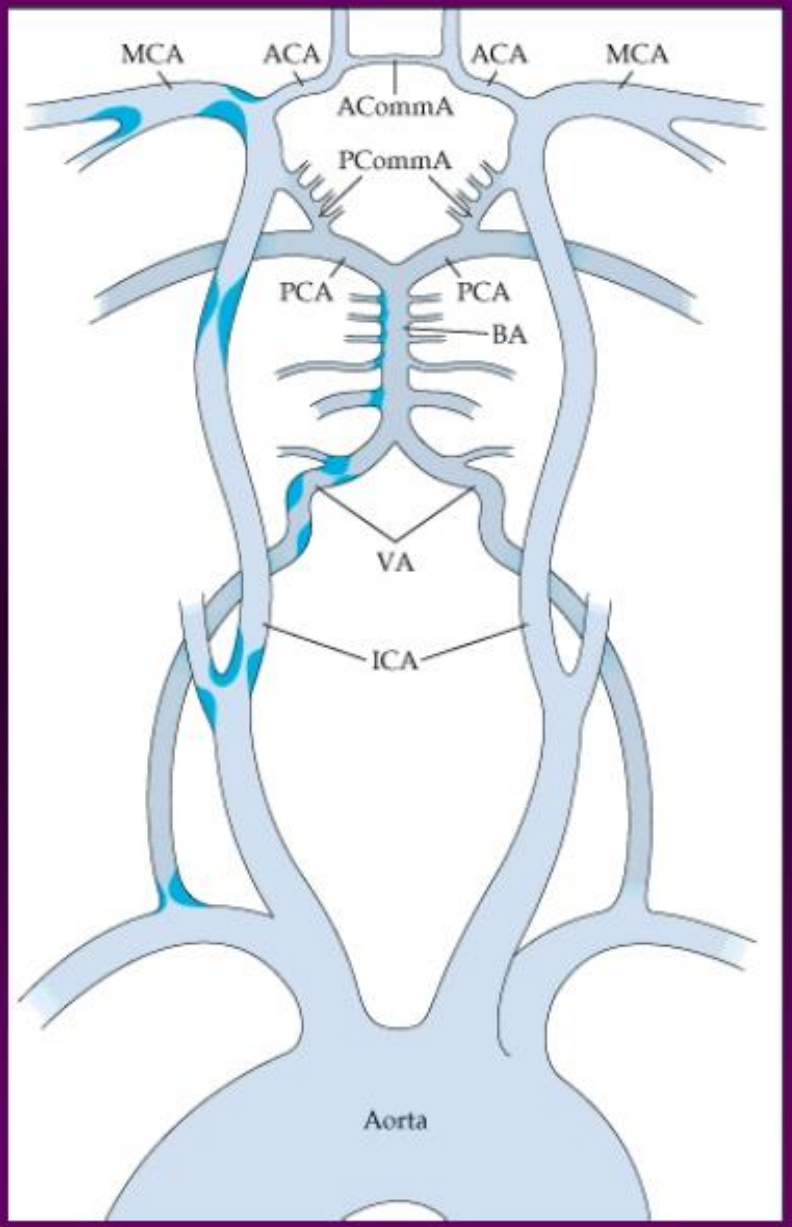
INTRACRANIAL

- Insitu thrombus
- Smaller vessels
- Common in blacks and Hispanics
- Commoner in females
- Associated with hypertension
- Associated with D.M / Metabolic Syndrome.
- > Strokes

Large vessel disease

Large Vessel Disease

- Aortic arch
- Carotid artery (extracranial)
- Vertebral artery (extracranial)
- Intracranial arteries (carotid siphon, MCA, ACA, PCA, Vertebral, Basilar)



CVD and major risk factors

Non-modifiable Risk Factors
- Age
- Sex

Behavioural Risk Factors
- Tobacco
- Diet
- Alcohol
- Physical Activity

Genes
Socio-economic, Cultural & Environmental Conditions

Intermediate Risk Factors
- Hypertension
- Blood lipids
- Obesity / Overweight
- Glucose Intolerance

Atherosclerosis

Endpoints
- Stroke
- Kidney diseas
- Ischaemic heart diseas

Retinopathy

New additions to Risk Factors

- Electronic Cigarette
- Obstructive Sleep Apnea
- High Lipoproteins

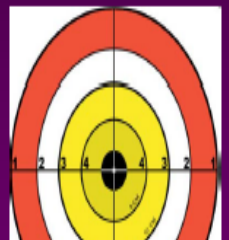
- Infectious agents (HIV; cytomegalovirus, Chlamydia pneumonia, Helicobacter pylori, herpes simplex virus, peridontal dx)

Mechanism of Stroke

Stroke Prevention: Mechanism-Specific Considerations

What is the cause of the initial cerebrovascular event?

Large vessel athero	Cardioembolism	Small vessel dz
Carotid endarterectomy Antiplatelet agent	Anticoagulation	Antiplatelet agent



PATHOPHYSIOLOGY/genesis

C.I - Occlusion in absence of adequate collateral circulation

ie: blockage of capillaries/arterioles

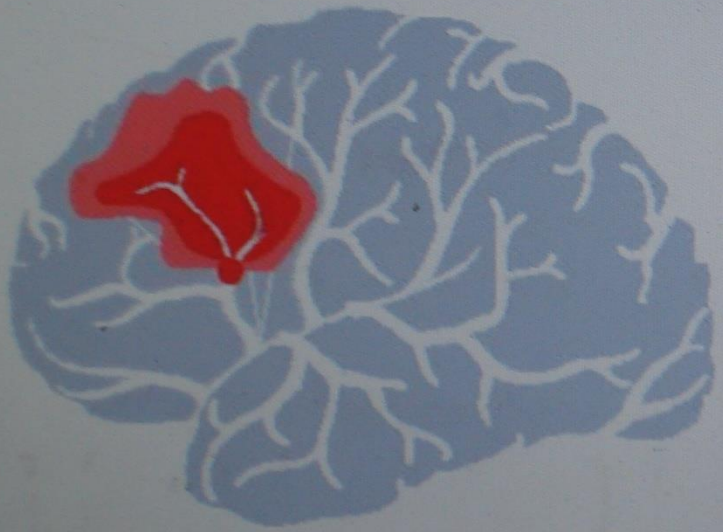
- **Collaterals (Leptomeningeal / circle of Willis);**
- **relevant with proximal occlusion.**
- **Irrelevant with lacunar infarcts b/c end arteries**

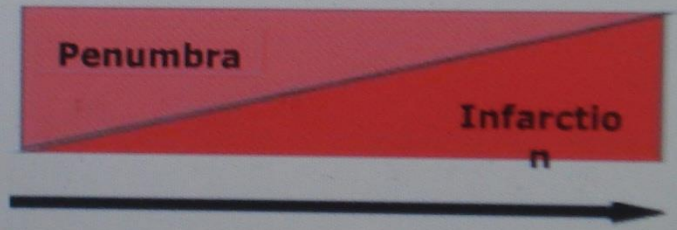
- **Thrombosis / Embolism / Vasospasm**
- **HBP: Lipohyalinosis – Charcot–Bouchard aneurysm**
- microatheroma

- **Haastrup : Penumbra (Apoptosis); Umbra (Necrosis)**
- **Penumbra = Ishaemia minus infarction**

- .

Concept of the Ischemic Penumbra





PenumbraInfarct core

1 hour 2 hours 3-4 hours 4-6 hours

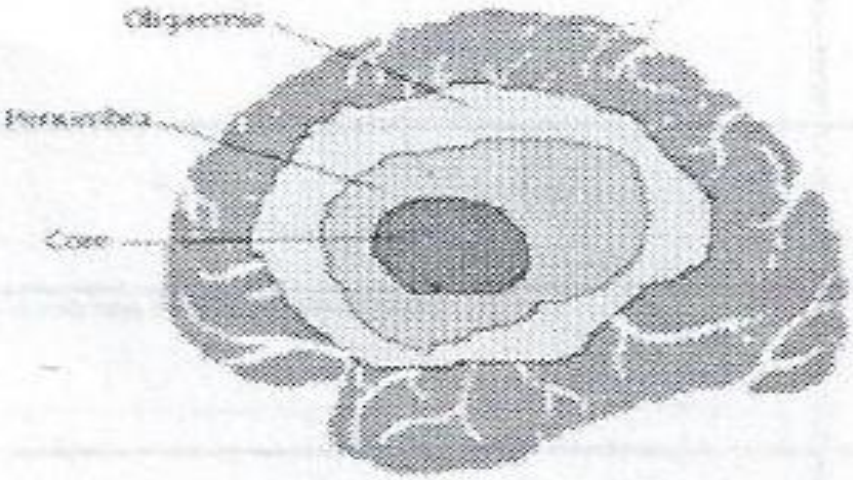
Time is Neurone / Brain

The Concept of Physiologic Time

Core: Tissue that will inevitably die and is beyond salvage

Penumbra: Total area of hypoperfusion

Benign Oligemia: Tissue that will most likely survive even without reperfusion



"Imaging of Acute Stroke." Muir et al. Lancet 2006

Pathophysiology

- **blood flow → 55ml/100g/min**
- **75ml/100g → grey; 30ml/100g → white**

<25ml – EEG diffusely slowed (met.enceph

<15ml → e- activity ceases

functional threshold: **fn ceases (penumbra)**

(apoptosis – caspace)

reversal of ischaemia: Therapeutic window

- **2-3 hrs (animal); 5-6 hrs (primates)**
- **<10ml → irreversible : *morphological threshold:* cell death ensue necrosis (Umbra): necrosis - lysosomal protease)**
- **CPP = MAP – ICP; AUTOREGULATION**
- **CPP = 70-100; MAP=100-130; ICP= 30-60**

Clinical features

- depends on location/extent

- **CLINICAL**
- **PATHOLOGICAL**
- **AETIOLOGICAL**
- **ANATOMICAL Diagnosis**

Table 1 :PHASES OF CONTEMPORARY MANAGEMENT OF STROKE

Phases	Period from onset	Activities	Prefered location
1Acute (emergency) care: Hyperacute: 4.5hrs Acute : 48hrs	1st-7th day	a)Assessment b)Early supportive care	Stroke Unit Hospital
2 Early sub-acute(supportive) care	2nd-4th week	a)prevention and treatment of complications	Hospital
3 Late sub-acute(maintanance) care	2nd-6th month	a)Rehabilitation b)Psychological support c)Prevent recurrence	Hospital/Community
4.Long-term (chronic) care	7th month onwards	a)Rehabilitation b)Psychological support c)Social support d)Prevent recurrence	Community

ACT FAST at the First Sign of STROKE

www.strokemn.org

Minnesota Stroke Association
Chapter of the National Stroke Association

If you do have a ***str***oke, act ***fast***

- Act FAST
- ***S:Smile;***
- ***T:Talk;***
- ***R: Raise arm***
- ***O***
- ***K***
- ***E***
- ***BRAIN ATTACK: Rx with the same urgency as for heart attack and acute trauma***

TIME IS BRAIN; TIME IS NEURONE

- 200 Billion Neurone in the brain
- 2 million neurone die / minute.
- **Time is brain is the key concept**
- **200 billion neurons in the brain**
- **2 million neurons lost per minute**
- **Age 3.6 years per hour of hypoxia**

Lost / hr : 830 billion synapses *(14 billion synapses /min);* Lost / hr: 714 km of myelinated fibres *(12 km fibres / min)*

- TIME IS BRAIN; TIME IS NEURONE

Timeline of Care – NINDS Recommendations

- ED physician sees patient within **10 minutes**
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- *Mobilize for IA therapy as rapidly as possibly*

Treatment

- Thrombolytic therapy
- Early antithrombotic treatment
- Treatment of elevated intracranial pressure
- Prevention and management of complications

- No 2 strokes are alike / same for 2 individuals
- Need to individualize Rx
- Response not the same for 2 individuals

Stroke Unit

- ***All stroke pts: irrespective of gender, age, stroke type, subtype and severity,***
- dedicated / geographically defined part of hosp/ specialisd staff wt coordinated. multidisciplinary expert approach to Rx/ care; Keep > = 24 hrs
- *Assessment / diagnosis* (exclude mimics)
- *early assessment of nursing / therapy* needs
- *Early mobilisation, prevention of complications,*
- *Rx of* hypoxia, >glycaemia, pyrexia and dehydration.
- 6H:Hydration, Hypoxia, Hyperglycaemia, Hypoglycaemia, Hypertension, Hyperpyrexia
- *Ongoing rehabilitation; Coordinated multidisciplinary team care; early assessments of needs > discharge*

Investigation / Assessment

- ***All pts: Brain Imaging: CT or MRI***
- Chest X-ray; ECG; Echocardiography;
- Cbc; platelet count, PT or INR, PTT; CRP/ESR

electrolytes, glucose; LFT / Renal fn; FLP

- correlation between lacunar stroke and HB, None between Hb and non-lacunar; leucocytosis is associated with poor prognosis
- **Urinalysis -** Microalbuminuria predicts haemor transformation in CI– endothelial dysfunctn
- ***In selected patients: Duplex / Doppler ultrasound TCD,*** MRA or CTA
- Diffusion and perfusion MR or perfusion CT
- Pulse oximetry and arterial blood gas analysis
- Lumbar puncture; EEG ;Toxicology screen

Stroke bio-markers

- Cf cardiac specific Troponin, CPK, LDH)
- Serum S 100 β - CI (Astroglial protein)
- Serum Glial fibrillary acidic protein (GFAP) - ICH

H –fatty acid binding protein (H-FABP)
Apo lipoprotein CI (Apo CI) - CI
Apo lipoprotein C III (Apo C III) - CI
Serum Amyloid A (SAA)
Antithrombin III (AT-III) fragment

?? N A A

- Commonly measured markers include S100 calcium binding protein B or S100B, glial fibrillary acidic protein, brain natriuretic peptide, and matrix metalloproteinase.
- None of these substances are ***routinely measured by hospital laboratories in the time frame needed to make acute care decisions*** but are a focus of clinical research.
-

- Treatment

AHA Classes/Levels of Evidence

- Classes indicate what we should generally do
  - I: Should do it
  - II: Consider it
    - IIa - per most experts; IIb - conflicted
  - III: Don't do it
- Levels indicate how sure we are about doing it
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- *Neuroprotection (ABDF / NeuroAID ? proved by EBM): citicoline ; cerebrolysin.*

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- *EC/IC bypass surgery (it works, but does not help)*
- *Clamp/Coil/Gluing/ Flow Diverter: aneurysm (limited to SAH)*

QUESTION 3

- Of patients with Sub Arachnoid Haemorrhage (SAH),
- The following is indicated irrespective of the Blood Pressure
- A) ACEI
- B) ARBs
- C) Diuretics
- E) CCBs
- F) None of the above.

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Question 4

- Of Hypertension and Stroke
- A) It is the commonest cause of stroke

- B) In ICH: The BP should be brought down within the first 6hrs to 140/90 if patient is < 60y/DM; or 150/90 if > 60y

- C) In CI: there is a place for ***permissive hypertension*** post
- stroke with an optimal BP of 185/105 (CL 111,Lev C evid)

- D) Post – stroke, there is loss of Cerebral autoregulation,
- and there is need to open collaterals (Back doors).

- E) All of the above.

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- ***E) All of the above.***

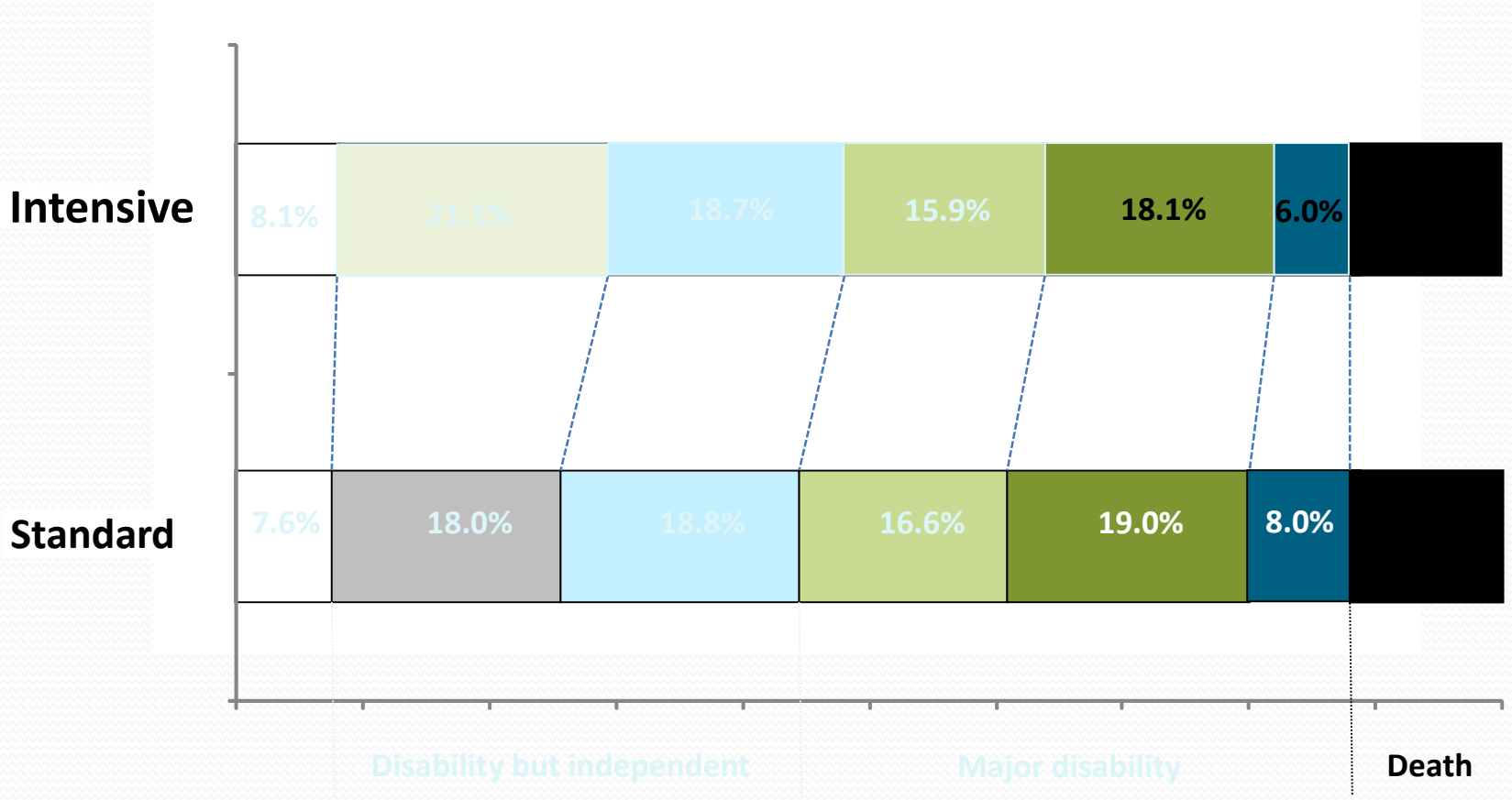
QUESTION 5

- CITICOLINE is
- A) a thrombolytic agent
- B) an anti- platelet
- C) Neuro-protective/RESTORATIVE/repair/Plasticity agent
- D) An Antihypertensive agent
- E) does not Assisst in Collateralization

QUESTION 5

- CITICOLINE is
- A) a thrombolytic agent
- B) an anti- platelet
- C) a Neuro-protective/RESTORATIVE/repair/Plasticity agent
- D) An Antihypertensive agent
- E) Does not assist in Collateralization

INTERACT-2 trial. Rapid, intensive blood pressure lowering < 6hrs in ICH to target of <140 mmHg systolic vs target < 180 mm



Odds ratio 0.87 (95%CI 0.77 to 1.00); P=0.04

Hypertension

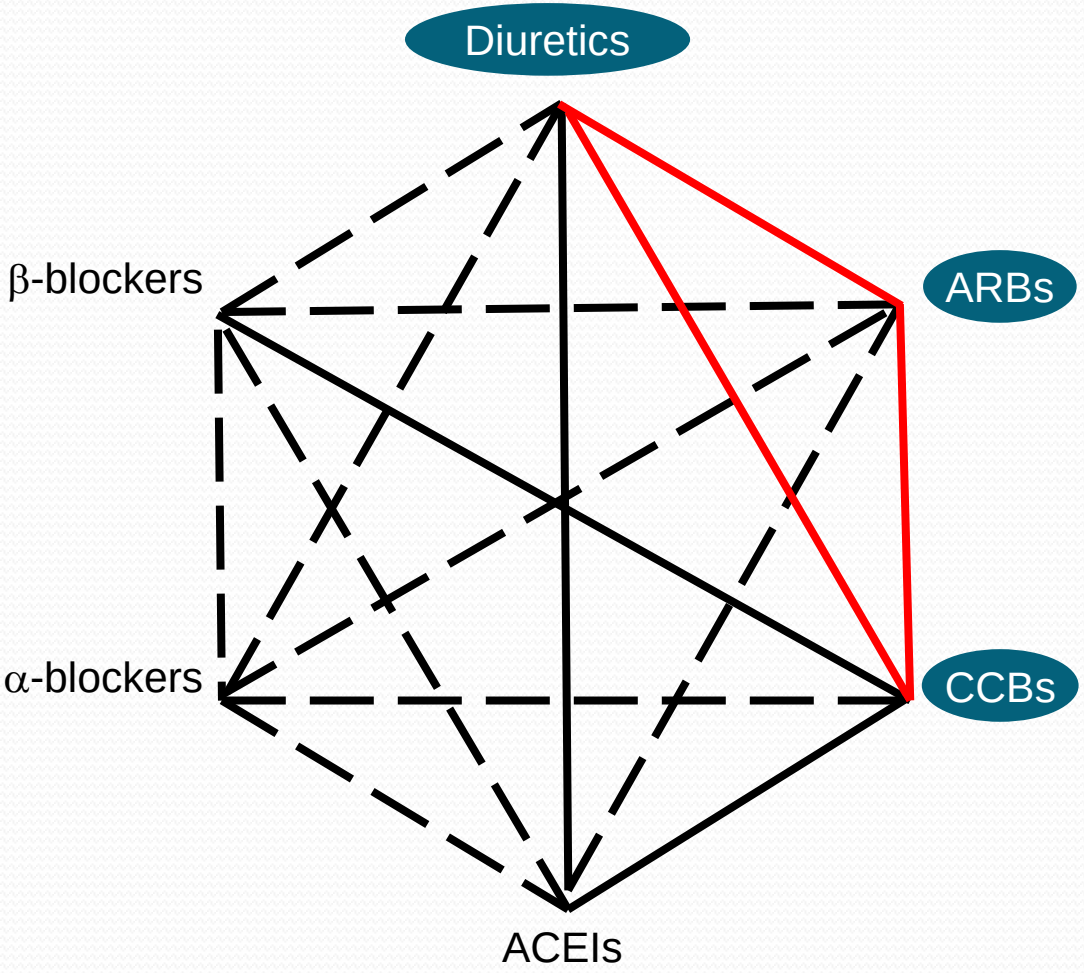
- *Variability of the BP is the key factor*.
- Systolic and diastolic troughs. (>>> systolic)

- **CcB**: reduces variability the most
  - antiplatelet effect ? Use in ICH

- **BB**: worsens variability non selective propranolol:
  - -ve inotrope, < C.output in a state of hypoperfusion.

- **ACEI**: moderate effect (effect on Renin)
- ***Nitrates: Nitroglycerines: GTN patch***
- ***MINOCYCLINE***

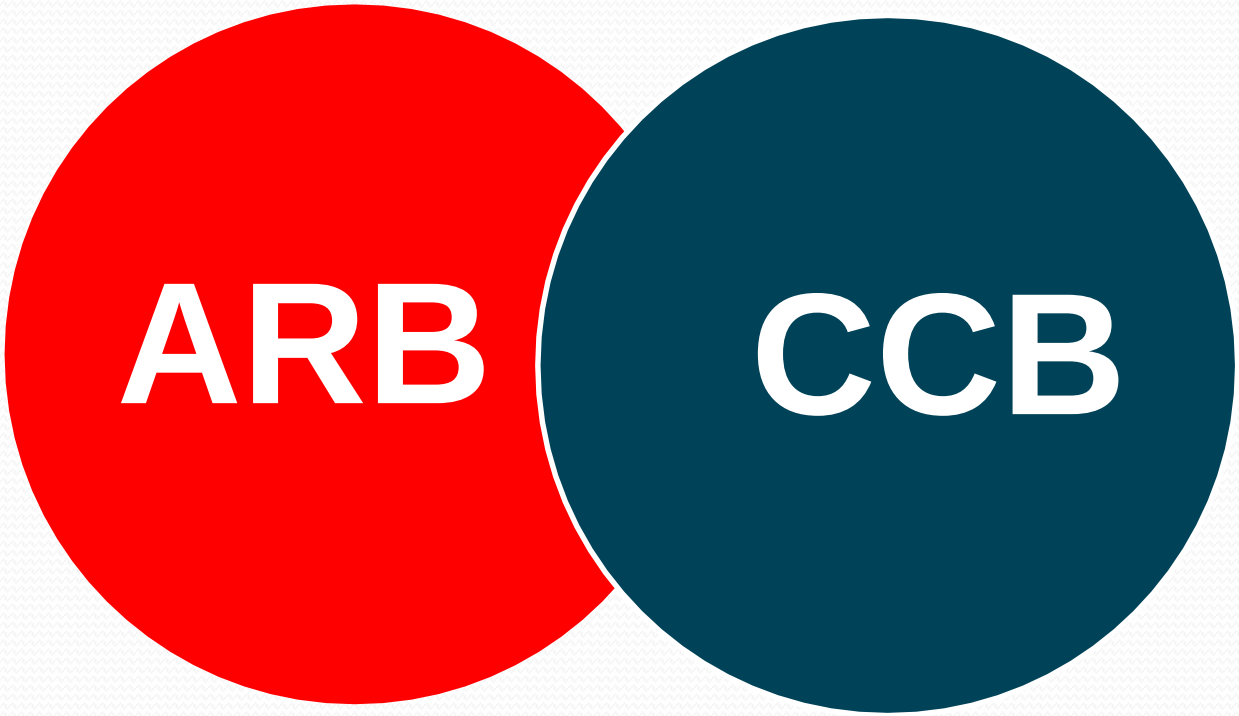
There are many possible combinations of hypertension drugs



- **ESH-ESC recommendations include**
  - **ARB + diuretic**
  - **ARB + CCB**
  - **CCB + diuretic**
- **NICE guidelines recommend triple therapy with an ACEI or ARB + CCB + thiazide diuretic at Step 3 (i.e. in patients with BP uncontrolled on 2 treatments)**

Task Force for ESH–ESC. J Hypertens 2007;25:1105–87; NICE hypertension guidelines 2006

Optimal Combination Therapy for Treating Hypertension in most people



Summary: acute stroke

Use treatments supported by evidence:

- stroke unit care,
- i.v. thrombolysis < 4.5 hrs / 9 hours
- BP lowering for acute ICH
- Prevent aspiration, DVT, urinary sepsis
- ***Intermittent pneumatic compression / VEM (Very Early Mobilisation (Passive PhysioRx) / Adequate Hydration to prevent DVT***
- Aspirin: prim P: M.I 12%; Sec P: 19%;)

- Clexane: No effect on Morbidity / Mortality
- Efficacy not established + risk of ICH.
- Benefit outweighs risk: (2B recommendation)

No evidence to support routine use of

- Aggressive BP lowering in acute ischaemic stroke
- iv heparin
- Intensive glucose control with insulin

Begin secondary prevention early:

- All stroke: Blood pressure lowering
- Ischaemic stroke + antiplatelet + statin,
- POLYPILL (STATIN + Folate + Aspirin + antihypert)

Comprehensive stroke unit = dedicated area (beds) in acute hospital

Assessment & monitoring

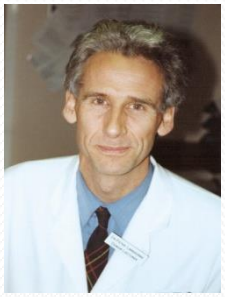
Acute management

Physiological control	Early mobilisation	Manage complications	Skilled nursing

Multidisciplinary rehabilitation

Discharge planning

Nurse



Doctor

Physiotherapy

Occupational Therapy

Speech therapy

Coordinated multidisciplinary care
= formal multi-disciplinary team meetings 1x per week)

SUTC Cochrane Library (2007)

Treatment

A) <*infarct size* (umbra) – Rxic time window

Reperfusion vis a vis recanalisation.

- **1) restore blood flow + nutrients (glu + o_2)**

- **Thrombolysis →within 1st 4.5 hrs (3-15% pts)**
- **rtPA, alteplase; streptokinase; urokinase, desmoteplase, (Reteplase, Tenecteplase)**
- **Door to needle < 1 hr.**

20% success rate: recanalisation / unblocking.

Needs more agents:

- **hemodilution / induced HBP/ hyperbaric o_2**
- **encephabol° (Piritinol) – cerebral steal effect.**

Tenecteplase: cheaper, single bolus, better, ease of transporting patients

Risk of ICH: anticoagulant induced

- Rx: **Prothrombin Complex Concentrate** - Yes
- < hematoma growth > FFF, ? Effect on functnal outcome
- No improvement in functional outcome
- **Fresh Frozen Plasma** : No
- **Idarucizumab** for NOAC - Dabigatran
- **Andexanet / Aripazine** for Factor X inhibitors.
- Rx: iv **Vit K** 10mg bc half life of all above 2-3 h.
- ***Platelet infusion***: harmful.

- ***ICH develops AF /DVT. ? Risk of Cardio-embolic***
- Recommence Antiplatelets / Anticoagulants:
- ***1 3 6 12 (+/- 2)*** Days Principles depn on severity

Neuroprotective agents (Neuroprotectants)

- Neurorestorative / Neuroregenerative / Neurogenesis
- Neuroprotective / Neuroproliferative /Neurotrophicity
- /REWIRING / NEUROPLASTICITY
- BDNF pathways are ***involved in cell survival, neuron – protection, brain plasticity and neurogenesis.***
- NeuroAiD: stimulates production of BDNF
- Promotes neurogenesis
- >neurites growth and synaptogenesis (neuronal connections)
- Provides a ***better post stroke recovery of Neurological function*** in pts with severe stroke.
- CITICOLINE:

CITICOLINE

- CYTIDINE 5 DIPHOSPHOCHOLINE / CDP–choline: Nprotective/Nrepair/Nplasticity:>dendritic plasticity/ complexity/spine density:
- < volume of ischemic lesion: Inhibits apoptosis
- Hyrolyzed to choline and cytidine triphosphate Stimulates Ach synthesis:
- > choline availability - essential intermediate - activates the biosynthesis of structural PL in neuronal membranes integrity . Inhibits activation of PLipases
- Prevents accumulation of fatty acids/Formation of free radicals, avoiding destruction of membranous systems Preserving antioxidant defence systems (glutation) >cerebral oedema reabsorption/BBBrestoration integrity

CITICOLINE

- Preserves neuronal energetic reserve,
- Accelerates recovery of consciousness/motor deficit
- Facilitates rehabilitation/Sensorimotor function recovery/ integration .
- >cerebral metabolism and noradrenaline/dopamine levels in CNS/ Potentiates the effect of L-Dopa.
- positive effect on memory, behaviour and clinical global impression.
- **post-stroke vascular cognitive impairment (VCI):** Stroke surv
- new case of dementia every 7S/ 2nd most common type of D
- > temporal orientation/attention/executive fns /> ADL with more efficient/accurate responses to cognitive demands/ better Qol and improves cognitive status
- PERIHEMATOMA ISCHEMIA: due to a vascular compression/local inflammatory reaction, > vasoactive substance
- Meta-analysis: beneficial Rx effect, without safety concerns

Treatment of ICH

- Reduce Hematoma expansion
- Reduce peri-hematoma cerebral oedema
- Brain Necrosis/ Atrophy
- Treatment of elevated ICP
- Prevention and management of complications

- No 2 strokes are alike / same for 2 individuals
- Need to individualize Rx
- Response not the same for 2 individuals

ICH: EBM.

- No FDA Approved therapy
- NONE:
- reduction on hematoma expansion
- Improvement in functional outcome

- ***Activated Factor VIIa***
- Reduce hematoma growth / expansion
- No improvement in functional outcome
- ***Intensive BP lowering:***
- No effect on hematoma expansion
- Modest functional benefit.

Neurosurgical treatment - ICH

- **CH: evacuate hematoma > 12 hrs.**
  60% mortality at 30 days
  (mortality not different from conservative)

- **CT guided stereotactic surg. + hemolysis**

- **conservative Mx if volume < 100 mls**

- **CRANIOTOMY. Vs. CRANIECTOMY**
- **ENDOSCOPY**
- **MIS:** < Trauma; < Clot removed, Steep learning curve
- Expensive equipments
-

ICH Rx

- ICU ; ventilatory support,
- Haemodynamic ; Glucose; Fluid ; temp mgt
- ?? Bld pressure reduction High BP – worsens cerebral oedema ; > haemorrhage recurrence Labetalol < 15% reduction)
- ***140/90: DM; <60YRS; 150/90 > 60YRS***
- Rx Recombinant actvatd factor VII (rFVIIa)< 4h
- reduce hematoma expansion
- mortality and disability
- Angioplasty and stenting (Endovascular Rx)
- Intracranial pressure monitoring
- Ventricular drainage (pts with intra ventricular haemorrhage and acute hydrocephalus)

- Rx requiring further testing in randomised clinical trials:
- Haemostatic agents (TXA, rFVIIa)
- Minimally invasive surgery
- Hypothermia

Surgical Rx:neurovascular intervn

- Occlusive large Vessel dx:Artero-venous malformation
- Intra-Luminal thrombosis; Fibro muscular dysplasia
- Collateral channels of blood flow; Intra cranial Stenosis.; Artherosclerosis
- **Embolectomy:** Mechanical Embolus Removal in Cerebral Ischaemia (MERCI)
- Endovascular Cockscrew embolectomy
- **Vascular reconstruction:**BalloonAngioplasty/stenting Cf : Aorto-Femoral stenting of coronary
- **Thromboendarterectomy**
- Extracranial – Intracranial By Pass Surgery- ineffective
- **Hemicraniectomy (Malignant MCA occlussin)**
- **Devices**

Devices

- Microwires / micro catheters
- Ballon snare
- Ballon stent
- Sunction thrombectomy
- Clot retriever (aligator clot retrieval device)
- Any above + low dose urokinase
- Stents – use only aspirin b/c no endothelial attachment

Carotid end-arterectomy

- >70% CS : 18% risk of stroke
- **(12-17% (1st yr); 7% thereafter)**
- **(>C.O)–if >70% CS** ? Age
- < risk of stroke by 48%; lower benefit in females
- (more ICA affectation)
- < 70% CS : 7-8% risk

- **Balloon angioplasty + stenting—randomised trial in progress.**

Hemicraniectomy

- Malignant MCA occlusion / CI – usually bilateral
- 100 % mortality: Options:
- 50% mortality :20% mild disability
- 30% moderate disability.
- Family choice.
- Age below 60 years
- Dominant hemisphere (Aphasia + depression vs hemi-neglect)
- Surgery within 48 hrs; > 12 cm diameter
- Replace flap 6-8 /52. (Do not misplace)

Rx of Complications

- **DVT: 75% of hemiplegic leg**
- **Pul. Embolism: 9-13% of all stroke deaths;**
- **25% of late death (>1wk).**
- ***< Risk: good hydratn/v.early mobilizatn / IPC***
- Frequent changes of the patient's position in bed q2-4hrs;pulmonary physical Rx(airway care
- **??5000 units sc. Heparin 8/12 hrs (>48hrs)** Low-dose LMWH; Dabigatran / Rivaroxiban
- ***Aspiration pneumonitis: 51% dysphagia: w***ithhold oral feeding until intact swallowing, (**swallow test: 50mls of water):** NGT > 48hrs / > 2 days
- Percutaneous Endoscopic Gastrostomy(PEG)>2wks

Steroids

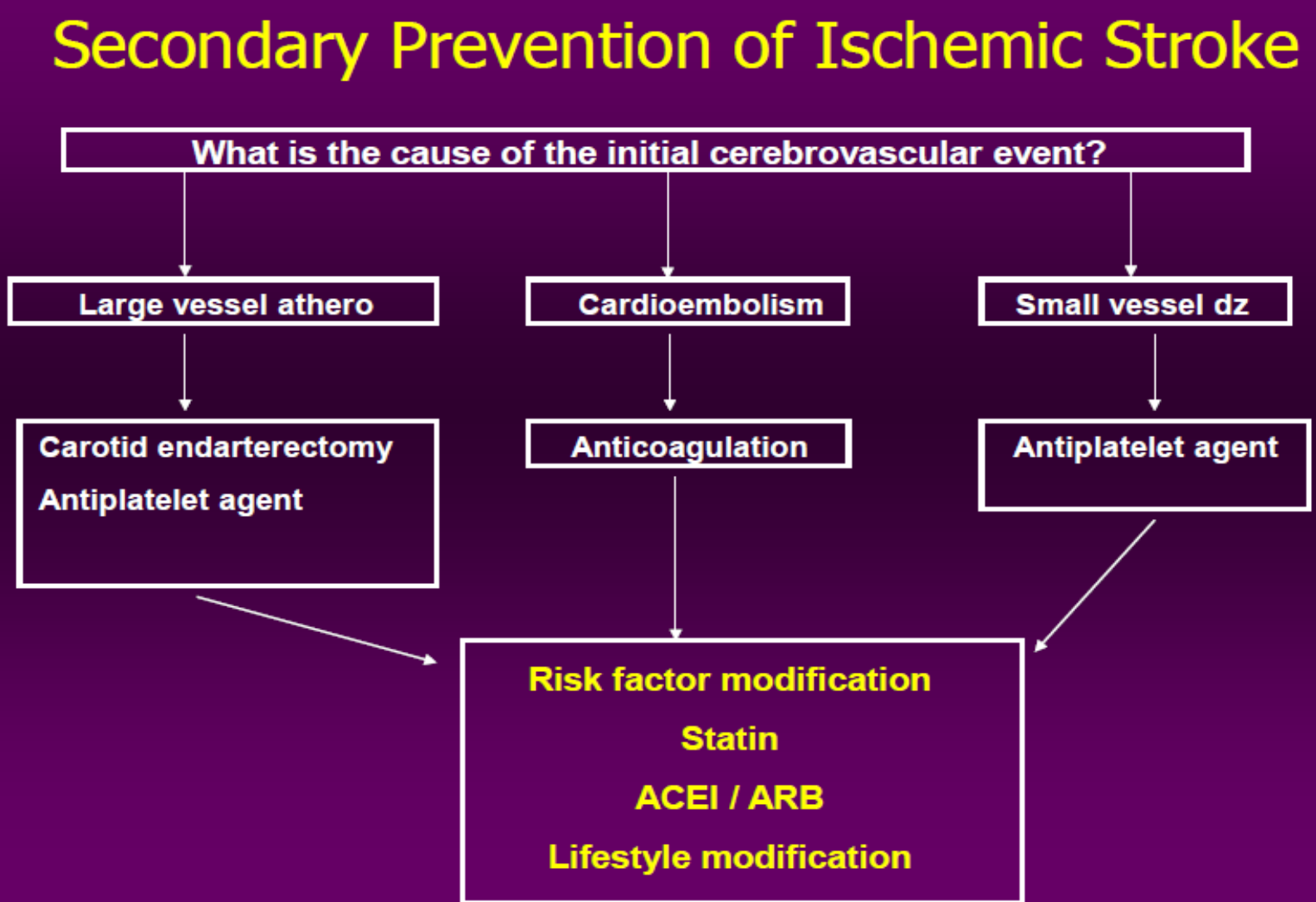
- **Counteract stress factor;**
- **<Cerebral Oedema;**
- **< 1CP;**
- **Strengthens the BBB;**
- **< cytokines: IL-1; TNF; prostaglandin**

dexamethasone⁰ cytotoxic oedema⁰ (vasogenic oedema+)
early death – 6 days vs 15 days

Steroids have been shown to rapidly enhance intraischemic CBF& reduce cerebral infarct size-upregulate eNOsynthase.

CO: EXTRACELLULAR/VASOGENIC : > vascular permeability
Intracellular – cytotoxic – Na –K Atpase – no energy source
Hyposmotic: SIADH / No hypotonic infusion
Hydrostatic: High BP,
INTERSTITIAL: High csf leakage - hydrocephalus etc

Stroke prevention



Primary prevention

- **Removal of risk factors**
- **HTN-control reduces risk by 40%**
- **Discourage smoking /**
- **Discourage alcohol (> Triglyceride / HDL)**
- **D.M control**
- **maintenance of normal weight**
- **regular exercise**
- **Life style changes/modification: dietary, cholesterol /hyperhomocystenaemia control**

How can we improve stroke Outcome?

- The real challenge of stroke therapy at the outset of this millennium is ***how to translate basic pathophysiologic evidence of ischemic neuronal injury into novel neuroprotective therapies*** either independently or combined with **thrombolysis**

- The management of stroke is changing rapidly as new ideas appear for acute treatment, rehabilitation and secondary prevention

We Need Better Arrows

4 main targets areas;

- 1) Population strategy in stroke care,
- 2) The role of the physician in preventive care
- 3) Managing the acute stroke patient
- 4) The place of rehabilitation and prevention of recurrence.

1 Population strategy in stroke care

- ***Public awareness programs are important***
- Studies have shown that delays in presentation are caused mostly by lack of awareness of stroke*
- The definition of stroke using 24hr leads to patient apathy and physician inactivity for such a long time.
- **All patients within the age range and with a high stroke risk should know the symptoms of strokeThe** need to present early for evaluation, treatment and prevention of further attacks must be discussed at various levels

- Information about stroke should be made widely available to the public

- ***Stroke issues should be introduced in schools, churches, mosques, plays on television, in the theater and brought to national attention.***

The population should be educated on lifestyle modification to prevent/manage cardiovascular disease

•SLYTER H. Guidelines for the management of patients with acute ischemic stroke. Stroke 1995;26(137-138).

2-The role of the physician in preventive care – strategy for risk factor control

- Stroke study groups and development of local guidelines .
- Physicians must identify patients at risk
- ***This risk assessment include taking a good history of risk factors, a thorough clinical examination and simple tests such as measurement of BP, pulse (ECG if concerned), and cholesterol level, level of C-reactive protein* and calculate the body mass index***.

- Stroke Unit: < mortality by 30%;Improves functional outcomes; < disability / need for institutionalised care

- Calculation of individual patient's risk of stroke

*BLAKE GJ, RIDKER PM. KUNTZ KM. Projected life-expectancy gains with statin therapy

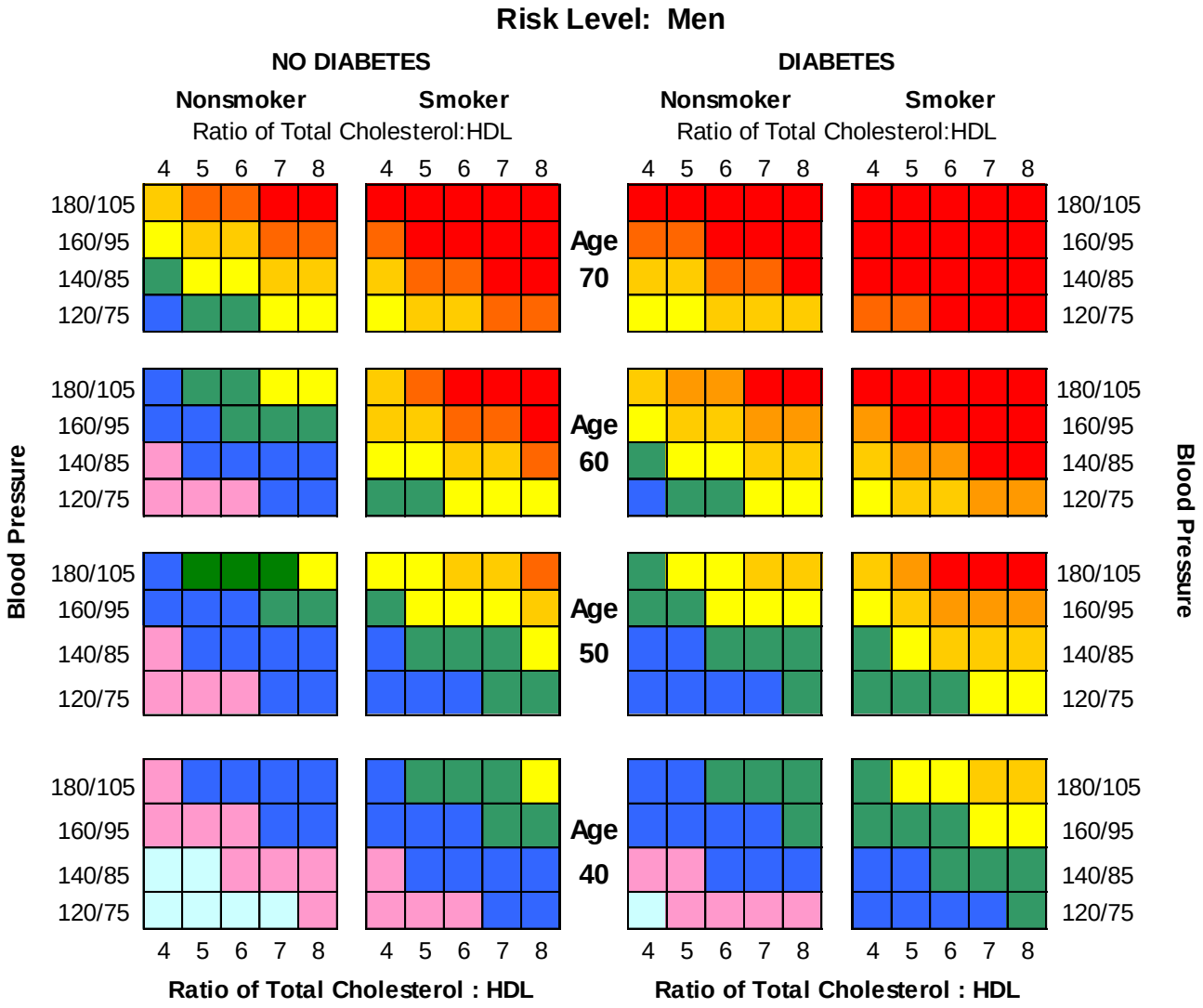
Stroke Risk Scorecard

Each box that applies to you equals 1 point. Total your score at the bottom of each column and compare with the stroke risk levels on the back.

National Stroke Association

Risk Factor	High Risk	Caution	Low Risk
Blood Pressure	> 140/90 or I don't know	120-139/80-89	<120/80
Cholesterol	>240 or I don't know	200-239	<200
Diabetes	Yes	Borderline	No
Smoking	I still smoke	I'm trying to quit	I am a non-smoker
Atrial Fibrillation	I have an irregular heartbeat	I don't know	My heartbeat is not irregular
Diet	I am overweight	I am slightly overweight	My weight is healthy
Exercise	I am a couch potato	I exercise sometimes	I exercise regularly
I have stroke in my family	Yes	Not sure	No
Score (each box=1)			

Assessing absolute CVD risk: the New Zealand guidelines



Present challenges

- Overall, the management of stroke patients in Nigeria / Africa is sub-optimal.
- Stroke units are not yet developed.
- Neuro-imaging centers are very few and assess limited by cost and distance.
- ***Most patients settle for intravenous infusion of hypertonic / isotonic infusion, medical decompression with steroid or mannitol, use of free radical scavengers, folate supplement, statins, anti-platelets and antihypertensives when indicated***.
- A significant proportion is seen by non-Neurologist and general practitioners who inadvertently bring down the blood pressure and compromise cerebral perfusion with its attendant poorer prognosis.
- Furthermore, multidisciplinary rehabilitation team management is difficult because of dearth of paramedical staff, physiotherapists, occupational therapists and stroke nurses.
-

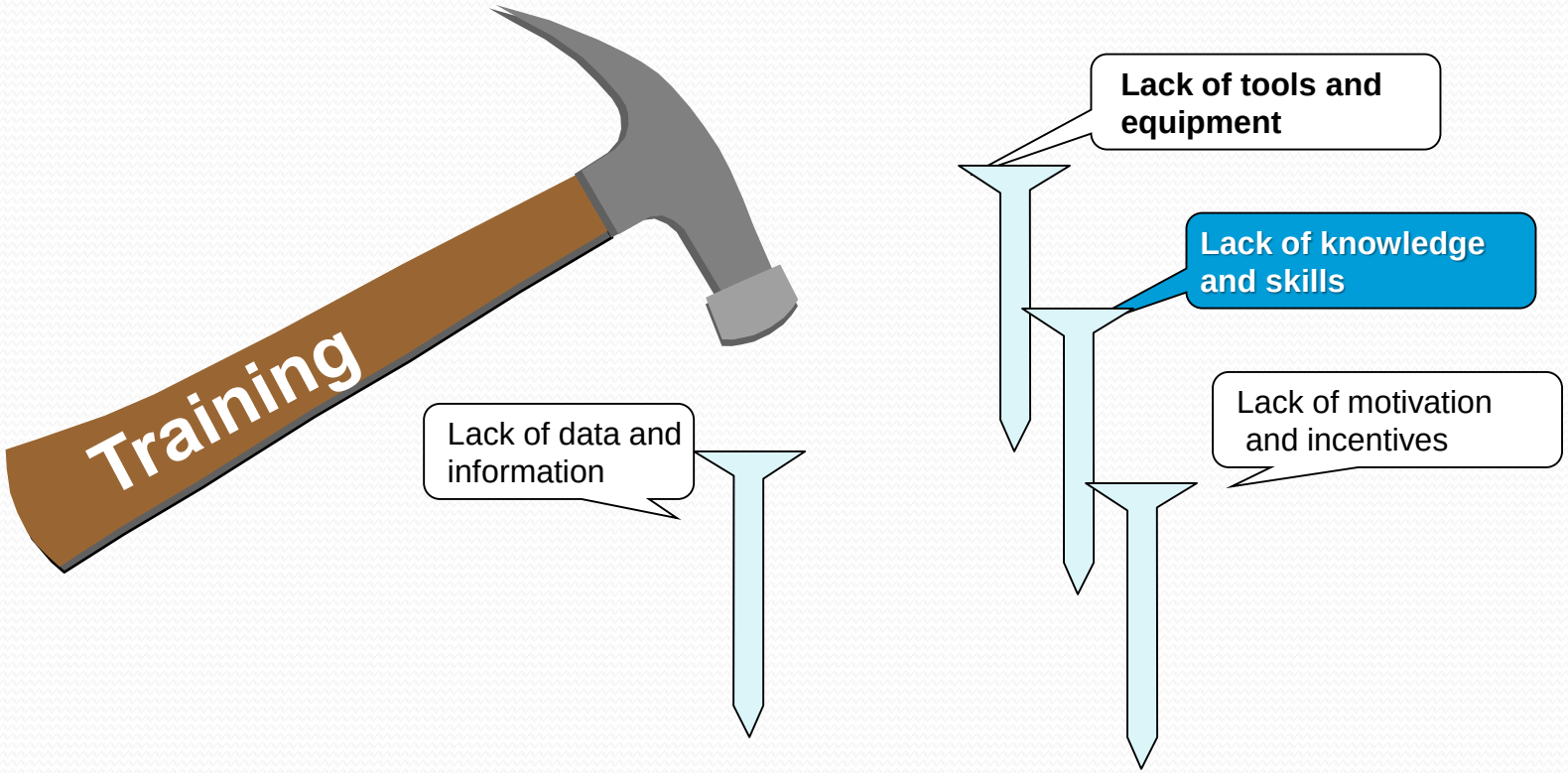
What do our patients deserve?

- Our patients deserve timely access to quality services appropriate to their needs.
- ***The most important strategy for stroke treatment is modification of risk factors and life style modification (excercise , diet, no smoking, modest alcohol (+/-)***
- The existing evidence strongly implies that good care of patients with stroke starts with ***organization of the entire stroke chain; from the prehospital scene, through the emergency room, to the stroke unit.***
- Without structured stroke services no pharmacological or intervening therapy is likely to improve the outcome Thrombolysis apart, our patients deserve better care from the moment they have their first TIA.
- Patients with mild stroke should be managed in a specialist stroke/TIA clinic.
- managed on an acute stroke unit for stabilization, CT scanning and other investigation, and diagnosis, and then referred, if possible, to a specialist stroke rehabilitation unit.
- *Attention should be paid to risk factors to prevent recurrence. This is the ideal that requires modification for the situation in N**g***

We must not set our standards too low if we are to compete in the global village!

What's the big deal about Jacuzzis?

"If all you have is a HAMMER... everything around looks like a NAIL."



(Died and Buried – ***The BAD)***

(Where we are presently)

THE UGLY

THE ROAD TO SUCCESS (THE GOOD)

CHALLENGES

- If you can't fly, run
- If you can't run, walk
- If you can't walk. Crawl
- Whatever you do, please keep moving.

(Where we are going)

THE GOOD

National Institute of Neurological Sciences, Nigeria

Prayer

"The young chick in the claws of the preying hawk says that she cries ***so that the world may learn of her plight;***

It knows the hawk will not let go!"

(Igbo proverb)

Merciful God, may those who can change things listen to our plight.

(15419)

Where there is a will, there is a way

Strength through Unity

Knowing is not enough

We must apply

- Willing is not enough

We must do

(15419)

Yes, we can !
Yes, we can !
Yes, we can !
Yes.....

YES YES YES

- Yes We will !
- Yes We will !!
- Yes We will !!!
- Yes Yes Yes

The Lecture is over - please wake-up and wake your neighbours

- ***Worshiping God is the***
- ***beginning of Intellectual wisdom***

Thank You

Blood pressure

Hypertension and Stroke

The most important and treatable risk factor for all types of stroke : 60-92% of ICH (60 -90)

33-62% of CI (30-60)

19-30% of SAH (20-30)

undiagnosed or untreated in 60%

10%: asymptomatic; life-long Rx; adequately controlled

- > diastolic BP 10 mm Hg: > risk of first stroke > by > 50%
- < diastolic BP 6 mm Hg: < stroke risk by > 33%
- Antihypertensive therapy: < stroke risk by about 38%

Antihypertensives

Weight of available evidence – Rx⁰ x 10 D
Rx if MAP > 145 (SBP > 220; DBP>120)
"absence of evidence" is not "evidence of absence")

- **Aim: MAP = 130; DBP = 105; (185/105)**
- **Why high BP is required ???:**
- **loss of C. autoregulation; (> O2 extraction fraction)**
- **CPP = MAP – ICP**
- **keep collateral channels open**

Blood Pressure

Optimal BP Management for Nonreperfusion Candidates?

- Potential Strategies
  - Keep it the same?
    - Maintain home BP meds (COSSACS)
  - Lower it?
    - Start BP med (ACCESS, SCAST)
  - Raise it?
- Current AHA Guideline
  - Permissive hypertension (up to 220/120) (Class I, Level of Evidence C)

Indications for Rx of HBP

Extra-cerebral complications:

- **dissecting aortic aneurysm**
- **Ischemic heart dx / Myocardial Ischemia.**
- **Acute pulm. Oedema.**
- **Rapid decline in renal function.**

***Antihypertensives of choice*:**

- **CcB: nifedipine; isradipine; nimodipine oral nimodipine : cerebrospp + cytoprotective:**
- ACEI
- BB worsens variability, next ACEI. Best is CaCB

Hyperglycaemia

Hyperglycemia

- Hyperglycemia (>140 mg/dL) during the first 24 hours after stroke is associated with poor outcomes
- Higher serum glucose concentrations (possibly 140 to 185 mg/dL) probably should trigger administration of insulin (Class IIa, Level of Evidence C)

Hyperglycaemia & Ischemia

- > Glycolysis (lactate production); rather than oxidative phosphorylation.
- Metabolic acidosis – > > H+ / K+ - denatures enzymatic / structural proteins:- interferes with function (non-enzymatic glycation /glycosylatn) AGEP (Advanced Glycation end product)– Toxic to endothelia + production of free radicals
- Haemorrhagic transformation incidence higher glucose – toxic to vasculature
- **hyperglycaemia – Rx as appropriate: insulin**
- BS>180mg%/10mmol; ensure HbA1c < 7%

Services

- At all times, you want the best for your patients but occassionally, you cannot achieve this.
- ***This is partly sequel to bad planning of health delivery system to meet "the demands" of the people rather than their "needs".***
- lack of neuro-imaging support: Non-availability of essential investigative tools (Thanks to the Public – Private initiative).

- ***No stroke unit***. Thrombolytics (recombinant Tissue Plasminogen activator / Activated factor VII – unavailable.
- Lack of ***neurosurgical*** support:
- ***Late presentations***: 80% of our patients with stroke do not present until after 24 hrs.

SERVICES / PRACTICE
The Good; the bad ; the ugly

- ***The Good:***
- A stroke patient brought in unconscious, speechless and densely hemiplegic and the patient talked and walked home.
- Thus, Neurologists seen as "The Jesus christ of our time"-and the Lame walked ***(Mark 2 v 11-12)***

- ***The Bad*** : and the patient died !!!. Nothing could be worse than this !!! – in spite of all your efforts. The enemies have done their worst even at the age of over 3 scores and ten !! as stipulated biblically(***Psalm 90; v 10)*** . The witchcraft or wicked mother-in-law Theory

- ***The ugly-:*** Misdiagnosis and mismanagement.
- Misdiagnosis of stroke reported in 13.5% of cases. Surgically correctable cases such as Giant brain tumors (Pitutary Adenoma, Giant Meningioma), cerebral abscess, subdural hematoma, Epidural Haematoma: were misdiagnosed and mismanaged as stroke

The Ugly

- *No CT scan support in most centers until lately.* Head CT scan is an essential first step in the Mx of stroke any where in the world, but even at that o*nly 9% of our stroke population could afford the cost in 2005, 21% in 2015.*
- No NS opinion sought in several cases as we may not have NS
- Some other basic investigations were unaffordable/available.
- No Thrombolytics. (especially if early presentation < 4.5hrs) Pts presenting after visit to spiritual /prayer houses, declining admission and prefer Mx in Churches, Traditional healers, or at best as an out-patient ! See helpless patients dying !!
- ***Inadequate knowledge of stroke on the part of patients and health workers. Majority were seen by non-neurologists***.
- No National ***guidelines and policies*** on stroke.

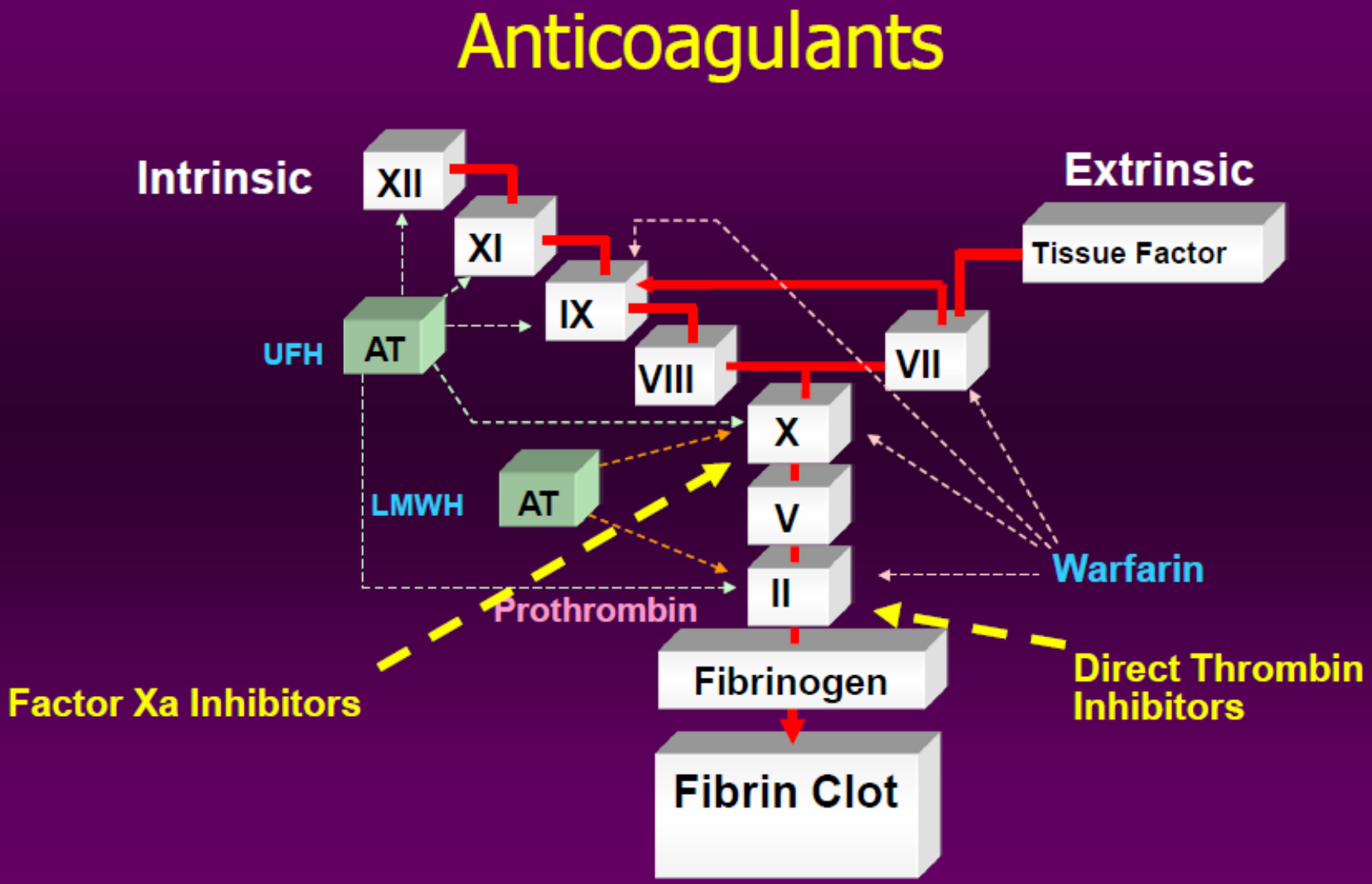
WAY FORWARD: *Stroke*

- ***Endovascular intervention*** knowledge would be rewarding.
- Knowledge on ***Tele – Medicine*** to Mx pts in rural /remote centers.
- There is dearth of ***Neuro imaging facilities***, expertise and skill.
- approach to Health education of the populace
- **stroke club**, its administration and relevance in stroke Rehabilitation
- organization of ***Rapid ambulance services*** to convey S pts, Training on Pre-hospital arrival Mx of S by ambulance drivers / relevant medical/ nursing personnel.
- Air ambulance services in stroke Mx.
- Prompt ***response of the S Team***, response time, 24/7 availability .
- Organization of CT suite/commencement of Thrombolysis at suite
- progressive ***improvement in the DOOR to NEEDLE*** time.
- ***Rehabilitation*** activities and post hospital care of pts with stroke

Other treatment options

- Newer Anti-thrombotics
- Statins
- Neuroprotectants (Mg So4) – vasodilator)
- Stem cell Transplantation
- +IV cooling with iced saline via IVC
- USS clot lysis
- Endovascular Rx.
- Mechanical recanalisation

Anti coagulants



Stem cell transplantation

- Rationale:a)Replace necrotic cell / take over fn
- B)Secrete trophic factors to maintain marginally surviving cells or enhance local environment
- C)Sprouting new axons and synapse formation .
- Sources: A)Fetal stem cells
- B)Neuroprogenitor cells (fd in periventricular region of developing/adults B. –migrates to area of injury and differentiate. autologous neural progenitor: paracrine / indirect effect
- eg: adipose tissue derived is minimally invasive
- Concept of Neurovascular unit hypothesis must be upheld

- C) Bone marrow stromal cells: diffrentiate to multiple cell types including N
- D) Multipotential cells: from umbilical cord blood
- E) Immortalised cell line : Human embryonic carcinoma derived

Stem cell transplantation

- PD: dopaminergic cell replacement.
- Stroke:
- multiple cell types and neurotransmitters lost.
- Several Potential pitfalls;
- Success in animals yet to translate to humans
- Cautious optimism and healthy skeptical reserve;
- Ethical concerns
- Depends:
- Subtypes of Stem cell/time after ictus