

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

on

STROKE Long-term sequelae, rehabilitation,

primary and secondary prevention

By

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NO CONFLICT OF INTEREST. NO COMPETING INTEREST

Current treatment of Insomnia



Lecture Overview / Outline

Holistic approach:

Need to know

what we are talking about.

Overview of

STROKE Acute/ Subacute /Short / Long-term sequelae, Rehabilitation,

Primary/Secondary prevention Challenges

Way forward : Roadmap

- STROKE:
- Peculiarities of Stroke in Blacks
- Epidemiological transition
- Management: cf Gold standards Globally GOOD / BAD / UGLY
- SERVICES: Equipment / Facilities / Man Power
- Acute / Subacute / Short /
- Long-term sequelae, Rehabilitation,
- Primary / Secondary prevention
- Recommendations and the way forward
- What do our patients deserve ?

Learning Objectives:

Define Neurorehabilitation / Repair,

2. Adaptation / Renervation / Neuroplasticity

3. Basic principles governing Neuroplasticity.

4. Documenting Neuroplasticity & effects of Neurorehabilitation

6. Neurorehabilitation Promising techniques

7. Stroke Prevention

5.

Epidemiology:Brain Attack / Stroke

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

- incidence < 12% in HIC, it > by 12% in LMIC over the <u>last decade</u>.
- exploding but neglected burden of <u>NCD</u>s: HBP, DM, dyslipidaemia: culminate in stroke.
- epidemiological transition: an ageing popn, popn growth, rapid urbanisation and accompanying lifestyle changes.
- WHO (2001): death / <u>DALYs</u> > 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),

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 (< 15Yrs)
- in people of African descent established.
- variation in rates:
- disparities in healthcare-seeking cultural practices
- differential access to healthcare services,

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

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









Nurse

Doctor

Physiotherapy



Coordinated multidisciplinary care

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

SUTC Cochrane Library (2007)

Mechanism of Stroke

Stroke Prevention: Mechanism-Specific Considerations



Table I :PHASES OF CONTEMPORARY MANAGEMENT OF STROKE

000000	Phases	Period from onset	Activities	Prefered location
	1Acute (emergency) care: Hyperacute: 4.5hrs Acute : 48hrs	1 st -7 th day	a)Assessment b)Early supportive care	Stroke Unit Hospital
	2 Early sub- acute(supportive) care	2 nd -4 th week	a)prevention and treatment of complications	Hospital
	3 Late sub- acute(maintanance) care	2 nd -6 th month	a)Rehabilitation b)Psychological support c)Prevent recurrence	Hospital/Community
	4.Long-term (chronic) care	7 th month onwards	a)Rehabilitation b)Psychological support c)Social support d)Prevent recurrence	Community

TABLE 2: ACUTE AND SUB-ACUTE COMPLICATIONS OF STROKE

		Neurological	Systemic
A	CUTE (<7 days)	 1.Cerebral oedema 2.Increased ICP 3.Hydrocephalous 4.Haemorrhagic transformation 5.Seizures 6.Transtentorial herniation 	 1.Hypoxia 2.Hypertension 3.Hyperglycemia 4.Aspiration 5.Cardiac arrythmias 6.Inappropriate ADH secretion
SI	JB-ACUTE (>7 DAYS)	 1.Seizures 2. Depression Late: 3. Vascular Cognitive Disorder / Dementia 4. Post stroke spasticity 	 1.D.V.T & Pulmonary embolism 2.Bronchopneumonia 3.Urinary tract infections 4.Septicaemia 5.Decubitus ulcers 6.Joint stiffness 7. Post stroke weight loss

After hyperacute / acute Stroke Rx, After the medications were given or the appropriate surgical procedures were done,



WHAT DO WE DO NEXT ???

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Prognosis

- Overall stroke-related case fatality = 20%35% depends on
- I) location
 - post. fossae; + / ventr. extention; deep location : poor prognosis
- 2. Size
- 3. level of consciousness on admission
- 4. later progression of neurologic signs and development of > ICP
 - 5. type of stroke ; clinical stroke syndrome.



Stroke

- Demographics:
- Leading cause of disability!
- I8M stroke cases/year worldwide
- •6M die
- •6M permanently disabled
- Overall mortality is declining
- Long-term survival post-stroke is improving



STROKE COMPLICATIONS:

EARLY / LATE

- Cerebral Infarction:
- poor clinical outcomes;
- >length of hospital stay; > readmission, > cost of care
- > delayed time to rehabilitation;
- > mortality.
- Deaths < IstWk: direct effects of CI
 - > IstWk : Medical complications.
- EARLY: in hospital settings.
- LATE: either Hospital / Rehab / Nursing Homes
- Discuss measures / Mx to < risk / rate of complications</p>

STROKE COMPLICATIONS: EARLY

Acute Reperfusion Therapy: rtpA

- rtpA anaphylaxis: Orolingual Angioedema: unilateral tongue/lips contralateral to side of CI. uncommon, 1%/8%. <2H ff infusion; Mild/transient;
- Severe cases : DC rtpA + Rx anaphylaxis
- > risk: ACEI, Frontal / insular cortices CI.
- life-threatening angioedema, laryngospasm, and hypotension
- Rx: antihistamines, IV corticosteroids, epinephrine, and endotracheal intubation for airway protection PRN : 50mg IVdiphenhydramine, 50mg IVranitidine, 10mg IVdxt
- In severe cases : 0.3 mg IM epinephrine added.

Symptomatic Intracranial Hemorrhage:

- < 36H of Rx; neurologic decline: 6.4%;</p>
- NIHSS >= 4 more than baseline. 2.4% of Rx 3 to 4.5H.
- Hemorrhagic transformation 4 subtypes :

Hemorrhagic transformation: 4 subtypes

Hemorrhagic infarction :

scattered heterogeneous petechiae along the margins CI

Hemorrhagic infarction 2:

>confluent; heterogeneous petechiae within CI

Parenchymal hematomal:

homogeneous hematoma< 30% CI vol; mild SOL effect

Parenchymal hematoma2:

dense hematoma>30%Cl volume, significant SOL effect

- HII, HI2, PHI < 36 hours of stroke onset: Benign
- Parenchymal hematoma2: early deterioration; > 3-month mortality
- RISK > higher stroke severity/older age ; heart failure, IHD, AF, hyperglycemia, DM, renal impairment, HBP < 24H, preceding antithrombotic use, thrombocytopenia, leukoaraiosis (cerebral white matter dx), persistent arterial occlusion after IV rtPA</p>

Hemorrhagic transformation assessment

Table 1. Anatomic Description of Intracranial Hemorrhages

Class	Туре	Description		
1.	Hemorrhagic transformation of infarcted brain tissue			
1a HI1		Scattered small petechiae, no mass effect		
1b	HI2	Confluent petechiae, no mass effect		
1c	PH1	Hematoma within infarcted tissue, occupying <30%, no substantive mass effect		
2	Intracerebral hemorrhage within and beyond infarcted brain tissue			
	PH2	Hematoma occupying 30% or more of the infarcted tissue, with obvious mass effect		
3	Intracerebral hemorrhage outside the infarcted brain tissue or intracranial-extracerebral hemorrhage			
3a	Parenchymal hematoma remote from infarcted brain tissue			
3b	Intraventricular hemorrhage			
3c	Subarachnoid hemorrhage			
3d		Subdural hemorrhage		

HI indicates hemorrhagic infarction; and PH, parenchymatous hematoma.



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Haemorrhagic transformation: Rx:

- Cryoprecipitate: initial dose 10 units. If contraindicated / unavailable
- Antifibrinolytic agents:
- IV tranexamic acid 10 mg/kg-15 mg/kg over 20 minutes
- ΙV ε-aminocaproic acid 5
- Prothrombin complex concentrate: EFFECTIVE
- Fibrinogen levels can be checked after administering reversal agents;
- if <150 mg/dL, additional cryoprecipitate can be given.</p>
- Fibrinogen
- Platelets, or fresh frozen plasma: Ineffective
- Surgical INTERVENTION if rtpA reversed.
- Endovascular thrombectomy: no significant difference in rates of ICH bt ET and standard care.

Risk of ICH: anticoagulant induced

- Fresh Frozen Plasma : No
- Rx: Prothrombin Complex Concentrate Yes
- < hematoma growth > FFF, ? Effect on fnctnal outcome
- Idarucizumab for NOAC Dabigatran
- No improvement in functional outcome
- 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 dep^{11/6/2018} severity; 7th Mth if sICH ²¹

Malignant Cerebral Edema

- 5%/10%.Neurologic deterioration within 72 to 96H earliest clinical sign:
- < level of arousal: > worsened motor fn.
- somnolence precede pupillary changes/anisocoria Tissue swelling; shift of thalamus /

brainstem Herniation;

- rather than due to a significant >ICP
- Large vessel occlusion of the terminal internal carotid artery / proximal middle cerebral artery with a large infarct volume; usually bilateral
- Features: Vomiting, female sex, CHF, leukocytosis

Malignant Cerebral OEdema

- Medical Mx:
- Normothermia (Hypothermia may < CO)
- Avoid Hypercarbia,
- Euvolemia ; Correct Hyponatremia.
- Avoid Hypoosmolar / hypotonic solutions:
- 5% D in H2O inefficient aggravates HYPOOSMOTIC CO
- Glucose between 140 mg/dL / 180 mg/dL.
- Mannitol: 0.5g I g/kg IV every 4/6H X 24h / pre-op.
- 0.25 0.5g/kg over 20 mins; rpt 4/6 hrly max = 2g/kg
- Goal serum osmolarity bt 310/320 mOsm/L; osmolar gap of < 10.
- Mannitol toxicity: renal tubular cells/renal impairment:

relative CI: hypotension / hypovolemia.

- Hypertonic saline: different concentrations, with goal serum sodium of 150/155 mEq/L.: volume overload ? heart failure.
- 2.34%; 23.4% Saline given as bolus over 30 mins creates osmotic gradient (B = osmometer)

Elevated ICP / Cereb Oedema: Basic Mx

- Head elevation(Day 1:0°; day 2:45°; day 3:90°;
- sit out of bed > 4 hrs from day 4)
- Pain relief and sedation; THAM-buffer
- Hypertonic / hyperosmolar agents: glucose; sucrose; urea; mannitol; sorbitol; glycerol; dextran
- Glycerol improves mortality, functional recovery^o subclinical hemolysis; rebound > ICP^o
- Diuretics acetazolamide; frusemide
- Ventilatory support: Controlled respiration using a ventilator Hyperventilation⁰- ineffective
- Sedation: Barbiturates ? high dose; coma; Paralysis

• ; Phosphodiesterase inhibitors: pentoxyfilline

Steroids

- Counteract stress factor;
- <Cerebral Oedema;</p>
- < ICP;
- Strengthens the BBB;
- < cytokines: IL-I;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 / hypotonic infusion Hydrostatic: High BP, INTERSTITIAL: High csf leakage - hydrocephalus etc

Hypothermia

- Immediate cooling to 35^oc+0.5 rewarming q12h
 Traditional surface cooling: cooling Blanket
- IV temp mgt: extracorporeal circulation
- Multi-lumen spray catheter: intranasal cooling with perfluorochloride spray
- Neck collar + helmet
- Drug induced cooling / shivering prophylaxis
- Cooling whilst on life support-33C; achieve34-3°c
 Neurosurgical implantation or intraventricular injection

Decompressive hemicraniectomy: < death/disability, but no complete freedom from disability; < 60YRS

- I00 % mortality: Options:
- 50% mortality :20% mild disability
- 30% moderate disability.
- Family choice.
- Dominant hemisphere (Aphasia + depression vs hemi-neglect)
- Surgery within 48 hrs; > 12 cm diameter
- Replace flap 6-8 /52. (Do not misplace)

Venous Thromboembolism

- DVT: 1st Wk ; 11% -15% within first M; **75% of hemiplegic leg**
- PE: W 2 / 4; 1% -3%; 13% to 25% of early/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)
- **PREDI**SPOSING F: Prolonged Immobilization, dehydration, elderly, Hx of malignancy, previous DVT; clotting disord
- Rx: Unfractionated / LMW Heparin
- Contraindication : ICH, recent thrombolytic Rx, and active extracranial haemorrhage.
- Chemical DVT prophylaxis: initiated at presentation if not on thrombolytics.
- if had IV rtPA: initiation of heparin 5000 units 8/12 hrs, sc. prophylaxis delayed until > 24H/48h, to continue during th hospitalization / until regains mobility.
- Low-dose LMW heparin: best benefit/risk ratio for VTE prophylaxis. <risk of DVT / PE with no significant > in risk of major hemorrhagic events?? Clexane: No effect on Morbidity / Mortality; Efficacy not established + risk of ICH.

Benefit not outweigh risk: 2B recommendation) Consider Dabigatran / Rivaroxiban

- Alternatives : IPC, Aspirin ; inferior vena cava filter placement; Catheter or surgical embolectomy
- IPC: contraindications: PVD causing leg ischemia/ulcerations/ edema. dermatitis

Therapeutic anticoagulation:

• Risks :Hemorrhagic Transformation, hematoma expansion/recurrent bleeding Icranial / Extracranial hemorrhage.

Dysphagia and Nutritional Considerations

- **51% dysphagia:** (<u>+</u>impaired mental status).
- Fluids/Nutrition orally: adequate hydration wt isotonic fluids
 - >risk : Male; > 70 years of age; Severe stroke;
- Impaired pharyngeal response, Incomplete oral clearance,
- Palatal weakness or asymmetry.
- A wet voice/spontaneous cough after swallowing are predictors of high aspiration risk: water swallow test 50mls of water
- high risk: Video-fluoroscopic evaluation of swallow or Fiber-optic endoscopic
- Rx: evaluation of swallow / early dysphagia screening;
- Adequate hydratn; NG/NDuodenal Tube > 48hrs / 2 Days,
- Percutaneous Endoscopic Gastrostomy (PEG)>2wks

Infection

- Fever : pneumonia; UTI.
- **Prop**hylactic antibiotic use: Not recommended.
- Fever Rx (T>37.5):vasodilation : worsens C.O.
- Aspiration pneumonitis: withhold oral feeding until intact swallowing.
 Most common cause of fever < 48H: -
- Aspiration in 60% of cases, immobility and atelectasis.
- Post stroke Reduced Immunity / Lazy Leukocyte syndrome; Intubation,
- Preventive measures: ventilation in a semi-recumbent position, appropriate airway positioning, suctioning of secretions, and daily assessments for potential extubation.
- Nausea should be addressed and Rxed to prevent vomiting.
- UTI: 11/15% < first 5 days/3 months
- Independent predictor of worse outcomes/prolonged hospitalizations.
- Indwelling catheters avoided : catheter-associated UTI.
- ?acute urinary retention / obstruction or when strict monitoring of urinary output is NEEDED. ? intermittent catheterization; Paul's tubing; condom

ATE COMPLICATIONS

- Falls, Seizures, Sleep-disordered breathing, Depression; VCD / Dementia
- > apparent ff acute hospitalization.
 - FALL : 70% First 6M ; 5%: acute hospitalizatn.
- Poststroke Fractures : paretic side; accidental falls;
- < mobility: < bone mineral density; asses Ca²⁺vitamin D supplementn
- Hospitalizatn: Formal fall prevention program + Balance training
- Fall prevention program: Identify patients at high risk.
- Counselling/Encouraging patient / family to seek assistance; preventing delirium.
- Minimizing use of mechanical restraints,
- using bed/chair alarms, ceiling lifts to facilitate transfers,
- Risk: cognitive impairment, depression; sensory impairment; non-dominant
- neglect, anosognosia, polypharmacy; > stroke severity/disability.
- Worse: TIA, HBP, CAD, <Vit D, 2[°]hyperPT, high bone resorptn, >serum vit B12, anxiety
- To improve bone strength and < fracture rates:
- Exercise, calcium supplements; bisphosphonates. Rx Atrial Fibrillation PRN

Seizures

- Focal onset wt 2[°]generalizatn (Focal to Bilateral Tonic Clonic
 - **Early**: Late: >rate of epilep
- most common cause of seizures > 35 years of age.
- Focal at onset with < 10% CI develop Sx.</p>
- Incidence/risk: Stroke severity, hemorrhagic transformatn. cortical location:
- Early-onset: ion shifts/ > excitotoxic neurotransmitters in C cascade. Prophylactic antiepileptic Rx: not recommended
- Late-onset: > 2W: common 6M 24M
- Permanent lesion causing an alteration in neuronal excitability/epileptogenicity.
- Seizures: Rx PRN ; Agitation: Causal Rx must precede sedation or antipsychotic Rx
- **Rx PR**N ;Agitation: Causal Rx must precede sedation or antipsychotic Rx

Sleep-disordered Breathing

- Obstructive / Central sleep apnea (OSA / CSA) / Hypopnea : 70%;
- Stroke Risk: strong independent assoctn wt sleep apnea in gen. popn. Neurologic deterioration.
- An apnea-hypopnea index of >= 5 events/H
- Preexisting undiagnosed OSA / central sleep apnea (CSA),
- Stroke localisatn: Medullary respiratory centers OSA / CSA or both
- Bihemispheric strokes: Cheyne-Stokes respiration.
- Reversed Robin Hood synd: proximal large vessel occlusions/sleep apnea. Compensatory vasodilatation during hypercapnia > blood flow velocity /BFV in unaffected vessels. < BFV in vessels supplying CI territory (CEREBRAL STEAL phenomena) ?? Encephabol / piritinol

• Nocturnal desaturations:

- Rx supplemental oxygen, CPAP, or bilevel positive airway pressure.
- Polysomnography evaluation: necessary part of Mx of 2° stroke preventn.

Depression

- I/3 stroke survivors; cumulative incidence: 55%.
- 20/40%; underdiagnosed/Rxed, Highest frequency: IST year;
 - > mortality/morbidity; poor fnal outcomes. recovery not optimized.
- limit the benefits of rehab; counteract them.
- Symptoms: Fatigue, < motivation, loss of confidence / attention concentration difficulties) + Anedonia
- cause: poorly understood; psychological + biological factors.
- Risk: stroke severity dominant hemispheric wt aphasia, >disability, cognitive impairment, prestroke depression, previous stroke, FSHx psychiatric disorder, Female sex.
- Inot demonstrated relationship bt depression vs stroke size / locatn
- Rx depression leads to improved fnal recovery
- Dopaminergic deficit : Restores balance of central neurotransmitters,
- > motivation to work with rehab Rxsts; > medication compliance
- SSRIs : citalopram (20 mg/d), sertraline (50/100 mg/d), Fluoxetine(20 mg/d), Tricyclic antidepressants 1/2 Wks for effect
- Fluoxetine for Motor Recovery After Acute Ischaemic Stroke (FLAME) trial: significant improvement in motor fn + <
 depression

Post stroke Fatigue/wt loss/Decubitus ulcer/ Hydrocephalus/Dementia

- **Post-stroke fatigue:** Occurs in absence of depression, difficult to Rx. Fatigue assoc wt depression: potentially alleviated when depression is Rxed. Rx: Nonpharmacologic / Pharmacologic
- Post stroke weight loss: > proteasome activity in muscle > after stroke; correlate with infarct size;
- > catabolic signal /< anabolic signal
- Rx : Physiotherapy
- Decubitus Pressure ulcer: support surfaces: Pp mattress frequent repositioning, optimizing nutritional status, and moisturizing sacral skin
- Hydrocephalus: csf drainage (ventriculostomy) / surgical decompression (? Cerebellar infarct wth BS compression)
- Post Stroke Dementia:

Rehabilitation / Recovery

- Recent advances in acute stroke/Neurocritical care.
- = > survivals / disability.
- Familiar with acute stroke Rxs/preventn strategies;
 < wt rehabilitation.
- Educate stroke survivors/families:
- Prognosis / 2° complicators
- identify barriers to recovery / develop individualized plans.
Common terms used in Rehabilitation

- •Impairment-refer to the loss of bodily structures or function
- **Disability**-refer to limitations or restrictions resulting from the impairments
- •Handicap-refer to the inability to perform social/vocational functions resulting from impairment
- Key aspects in neurorehabilitation:
- Repetitive multi-disciplinary assessment
- Problem definition & measurement
- Goal-setting & treatment planning: INDIVIDUALIZED
- Rx delivery:
- Evaluation of effectiveness & re-assessement
- Skill retraining by Physiotherapy ; Occupational; Cognitive & speech & language therapy
- -May include : facilitation of adaptation to loss, by the patient/family
- -prescription of appliances/environmental modifications

REHABILITATION / RECOVERY

- differentiate b/t stroke recovery / rehabilitation. interchangeably **Rehabilitation** : process of stroke care: < disability / improves participation in ADL
- Regain former abilities / achieve Optimum Physical, Mental, Social , Vocational capacity
- Recovery: improvements of outcomes: Biologic / Behavioural
- Biological / Neurologic: improvement on performance
- Behavioural: Activity-based Behavioral measures.
- Outcome measures: Thresholds for defining successful recovery: GOALS
- Not necessarily reflect fnal improvement: Tailor defn of recovery to individual
- Develop rehabilitation plan to reach defined recovery goals.
- Brain recovers: Adaptation, Regeneration, Neuroplasticity.

Rehabilitation / Recovery

Rehabilitation techniques: incorporate > 1 of these processes. Eg:Adaptation: reliance on : Alternative physical movements / Devices compensate for deficits: Nondominant hand to feed Assistive devices: Walker for gait / balance dysfunction.

Prisms in glasses to compensate for visual field deficits.

- Adaptation helpful, BUT
- harmful to the recovery process: learned disuse phenomenon
- Limiting use of the limb can also limit its recovery.

Rehabilitation Objectives:

- prevent deterioration / improve fn.
- Achieve highest possible level of independence
- (physically, psychologically, socially, financially)
- within limits of persistent stroke impairments
- **Rx / t**raining are provided to return to normal life.
- Regaining and Relearning skills of ADL
- Major rehabilitation approaches.
- Goals of each approach:

STROKE RECOVERY

- **Regeneration**: growth of neurons/associated cells / circuity to replace those damaged.
- < useful in Rehabilitatn:
- ? CNS capacity for regrowth after injury limited.
- Focus of attention: stem cell/growth factor intervention
- ? type / Subtypes of stem cell to use, time after ictus
- how to deliver it (IV, via surgical resection, or endovascularly),
- dosing, and long-term safety effects / Ethical concerns
- PD: dopaminergic cell replacement.
- Stroke: multiple cell types / neurotransmitters lost
- Several Potential pitfalls;
- Success in animals yet to translate to humans
- Cautious optimism and healthy skeptical reserve
- Holds hope for the future.

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 cell lines. 41

Stroke recovery

- **Neuroplasticity**:/Remodelling
- principles of task specificity, repetition, challenge (TSRC). Capability of brain/CNS) to reorganize by forming new neural connections /Rewiring throughout life.
- Neurons in brain compensate for injury/disease
- Adjust their activities in response to new situations / environ changes.
- Different functions recover differently.
- Swallowing, facial movement, gait > recovery language/dominant hand fn
- ULmotor recovery predictn:
- voluntary finger extension/shoulder abdctn
- Generally accepted practice:
- Acute/hyperacute settings: PASSIVE; < intense Rx</p>
- Outpatient settings: ACTIVE; > intensity, tolerable.

Neuroplasticity

Changes / Rewiring neural network : main recovery process.

Acute: <activation in cortical areas/ change in localization of tasks: movement.

Acute/subacute: disrupted neural networks, reconnect in adjacent areas; and coincide with clinical recovery.

- Functional neuroimaging techniques:
- As hand fn improves, cortical representation that once subserved the hand moves toward the cortical face. This, in turn, causes activation in the peri-ischemic/ischemic area with return of laterality to fns: alteratn of representative cortical maps.
- Amount of recovery: correlate wt degree of activatn

 For plasticity to fully occur: rehabilitation interventns must be task specific/goal directed rather than general/nonspecific movements.

Goal-directed tasks: Challenging/interesting to maintain individual's attention / allow for repetition through multiple attempts

Mechanism of Neuroplasticity

- angiogenesis
- Axonal sprouting (neurogenesis)
- Unmasking of latent synapses
 (synaptogenesis)
- Regeneration from neural stem cells in the subventricular regions migrating to the periinfarct area.





Mechanism of Neuroplasticity

Neurotrophins

•Regular exercise is ass. w/ the upregulation

of a number of genes that promote plasticity

- I. NGF-nerve growth factor (1920s)
- 2. BDNF-brain-derived neurotrophic factor (1970s)
- 3. Synaptotagmin 5 (neurotrophins)
- 4. Neuronal activity-regulated pentraxin (a neurotrophin)
- Animal studies suggest that BDNF is a key mediator in synaptic efficacy, neuronal connectivity and use-dependent plasticity

NATURAL hx of STROKE:

- Stroke deficits: highest rate of recovery 6w 6m.
- > 6M, reaches a plateau phase without additional significant improvement. Exceptions exist: improvement continue for several years.
- Swallowing, facial movement, and gait: better recovery than other deficits.
- Bihemispheric CORTICAL representate as part of normal feal anatomy.
- Cortical fns: language/spatial attention; dominant hand movement:
- Iateralized in fnal anatomy and recover > slowly.
- FACTORS: Spontaneous recovery / Recovery plateau ; limitations
- Factors hindering recovery:
- Poststroke depression: < recovery of measures; cognitive deficits/mortality.</p>
- Medication SE: excessive benzodiazepine use, antiepileptic/antihistaminergic
- Physical comorbidities: cervical spine disorders.

SPECIFIC ISSUES IN STROKE REHABILITATION

- Impeding overall recovery and quality of life.
- Shoulder pain; Spasticity // Shoulder Syndrome:
 - Loss of arm fn; shoulder pain; 70% of UL dysfunction.
- delays recovery/painful joints; limits rehab; participation; mask improvement motor fi
- Causes: subluxation, impingement, complex regional pain syndrome, thalamic pain syndrome, spasticity, radiculopathies.
- Flaccid UL paresis: shoulder subluxation / traction in the glenohumeral capsule
- Spasticity: velocity-dependent>tonic stretch reflexes lead>tone
- adversely affects fnal outcomes in chronic phase
- Mx of spasticity: Intrathecal Baclofen, Nerve blocks, serial casting: limited bc of SE;
- Botulinum toxin Commence >6W.
- cf oral route, muscle-relaxing properties at significantly < doses, limiting systemic SE.
- Rx: Proper positioning: supporting distal forearm from elbow down to reduce strain at shoulder; < tension on shoulder; slings provide additional support.
- Strapping / taping UL to shoulder /clavicle.
- intraarticular steroids glenohumeral joint

NATURAL HISTORY OF STROKE: RECOVERY

- **Predict recovery:** Recovery begins in proximal UL/LL; and progresses.
- voluntary finger extension/shoulder abduction
- **PRE**SENT: < 48H probability of a good outcome: 98%.
- NOT PRESENT: < 48H, probability of good outcome:25%.//9D: likelihood of complete UL recovery 14%.
- TIMING / INTENSITY OF REHABILITATION:
- ?optimal timing / intensity. Recovery: time sensitive Inverse relationship bt start date / fnal outcome;
- No learned disuse: experience dependent
- ?mobilized:worse outcome: mRS < 3, cf to standard care shorter ; > frequent sessions of VEM improved chances of regaining independence.
- early rehabilitation< 48H, benefit in 6M survival/fnal outcomes ICH
- enlargement in areas of ischemia correlating with poor fn when constraint Rx is applied >intense than conventional Rx, > ischemic demand exists, which cause neurologic injury. (loss of ischemic tolerance)

THERAPY APPROACHES TO REHABILITATION

- GOAL:
- Facilitate relearning of skills possible b4 stroke,
- SOME ? focus of rehabilitation:
 - adaptation / compensation for deficits.
- Begins during hospitalization :
- Motor skill retraining, preventing complications, and teaching adaptive techniques using a comprehensive approach.
- 3 post hospital dispositions / placement.
- Home with outpatient Rx,
- Home with home health Rx,
- Inpatient rehabilitation facility / skilled nursing facility
- based on: nature / severity of deficits, comorbidities, insurance / reimbursement.

Inpatient rehabilitation facilities

- Factors: medical issues requiring physician supervision,
- a reasonable expectation of resuming community living.
- Length of stay: dependent on severity of neurologic deficits, medical comorbidities, rehabilitation progress;
- Rehabilitation TEAM: a team-based approach
- Physical / Occupational / Speech and Language Rx for 3Hrs/D
- Setting goals, re-evaluating goals on a regular basis, and making adjustments to rehabilitation plan PRN; caregiver training
- Physical Rxsts: evaluations: movement / balance.
- Exercises to strengthen muscles for walking, standing, and other activities.
- Occupational Rxsts: learn strategies to Mx ADL: Eating, Bathing, Writing, Cooking, Dressing.
- Focus of physical Rx: LL impairments
- Focus of Occupational Rx: UL

Rehabilitation Techniques

- Speech and language pathologists/SLT (speech Rx)
- learn strategies to overcome swallowing / language deficits.
- Acute: dysphagia / swallowing evaluations
- Recommend alternatives: NGT / PEG percutaneous endoscopic gastrostomy.
- Subacute / outpatient settings: aphasia focus of SLT.
- develop a program/provide exercises using principles of
- Neuroplasticity: task specificity, repetition, challenging
- Important goal: Teaching of compensatory/adaptive techniques
- Train patient/family activities: safe transfers, assisted ambulation, proper feeding, provision of appropriate adaptive techniques.

Rehabilitation Techniques

- Device-based / adjunctive therapies: robotic arms / bodyweight support treadmills
- Nontraditional strategies: improved efficacy cf traditional Rx
- Constraint-induced movement Rx: alternative UL motor rehabilitation Rx technq: unaffected UL is constrained with a mitt, forcing use of affected hand
- Melodic intonation Rx: > recovery aphasia: musical elements melody / rhythm
- language is localized in dominant hemisphere, but singing/melody localize to the nondominant hemisphere. Engage language-capable regions in the nondominant hemisphere. most beneficial : expressive (Broca) aphasia, with some retained expressive abilities / absent bihemispheric damage

• Functional electrostimulation / Electrical stimulation (FES)

> motor recovery : applying electrical stimulation devices to muscles

Techniques in Neurorehab

- Constraint-Induced Movement Therapy (CIMT) Functional
- Mirror Therapy (Mirror Visual Feedback)
- **EMG** biofeedback
- Repetitive Transcranial Magnetic Stimulation (rTMS)
- Computer Games and Rehabilitation:
- Virtual Reality: approach to user-computer interface involving real time stimulation of an environment, scenario/activity that allows for user interaction via multiple sensory channels.
 Engaging, Entertaining & fun(+) Visual and Auditory Feedback from TV monitor: biomarkers must be developed.
- Brain Imagery/ Mental Practice / Brain stimulation
- Systems of care level: Telemedicine /Telerehabilitation play role in acute Mx/ expand to recovery phase.
- Networks: assess / evaluate the rehab needs; focus on wellness/self-training; novel pharmacologic agents,
- Stem Cells Therapy.

Techniques in Neurorehabilitation PRINCIPLE No. 1: BODY PARTS COMPETE FOR BRAIN REPRESENTATION!

•Ex: CIMT-constraint induced movement therapy .. One of the very
Useful techniques in
Neuro-rehab.



Constraint-Induced Movement Therapy (CIMT)



- Principle of FORCED USE to avoid the Learned Nonuse of the paretic side for Stroke patients
- Mainly for training of upper extremity



Mirror Therapy

- Mirror Therapy (Mirror Visual Feedback)
 - form of motor imagery in which a mirror is used to convey visual stimuli to the brain through observation of one's unaffected body part as it carries out a set of movements.



PHARMACOLOGIC APPROACHES TO STROKE REHAB

- Rehabilitation setting: appropriate / optimized / individualize.
- Medications promoting stroke recovery: Fluoxetine
- Rx depression; selective serotonin reuptake inhibitors (SSRIs) + impact motor recovery: neuroplastic mechanisms.
- Antidepressant / neuro-modulating agents + benefits:
- Cholinesterase inhibitors / glutamatergic agents: improve aphasia
- Dopaminergic medications: depression / attention; impair recovery: in acute period. Based on mechanistic effect on neurotransmitters:
- AEDs: phenobarbital, diazepam, phenytoin: impede synaptic formation / synaptogenesis
- Newer-generation AEDs should be first-line Rx
- Antihistamines: sedation in elderly /compromise attn for motor /cognitive tasks: impede plasticity through inhibition of long-term potentiation.
- Proton pump inhibitors are preferable to H2 blockers: (famotidine/ranitidine)

Return to Work / Driving : medical / professional clearance

- Return to work: >important factors: severity of physical/cognitive impairments, younger age,level of skill/education, and prestroke professional status. NOT severity of physical / cognitive impairments
- Financial independence; full integratn into society, enjoy subtle benefits from employment: > self-esteem / confidence; serves as key to independence.
- < driving ability: hemiparesis; visual field, cognitive, coordination deficits; Sx
- viewed as metric for return to normalcy/independence, inability to return to driving affect ability to return to work;
- Formal driving assessment for ability to drive
- Medical / Fnal assessment clearance needed
- Medical evaluation: performed by a health care professional: visual field, cognitive, motor deficits not severe enough to impact driving ability
- Sx control is compliant with local laws.
- Assess other medical comorbidities: cardiac condns
- complex aspects of driving: planning, motor coordination, reaction times, difficult to ascertain in the office.
- A formal driving assessment helpful to evaluate these skills: conducted on a driving simulator or by in-car evaluation by a specialist assessor.

Important Points

- "Improved fn may occur with vigorous/intensive task-oriented Rx, strong motivation/good cognition; provided some selective hand movement is present"!*
- **Recov**ery in Stroke Depends on:
- Location/extent of damage
- Activation of secondary areas / Contralateral areas
- •"Neuroplasticity occurs better in motivated & moving patients".
- Multidisciplinary approach due to complex problems of the nervous system
- Stroke rehabilitation is a complex process:
- multiple health care specialties / multiple approaches
- Timing/Dosing of Rx and novel approaches have not been validated/established



Summary

 If a stroke patient is to recover, he must do/try all of these activities by himself!!!





PREVENTION

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



Endpoints



Kidney diseas
Ischaemic

heart disease

Glucose
 Intolerance

Overweight

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)

Epidemiology: Brain Attack / Stroke

Second leading cause of preventable deaths in adults worldwide.
 Preventable: but preventive efforts are still far from optimal
 Primedal: NCD/CD: < calt. (POLICIES ON SUCAP/SALT in feed)

- Primodal : NCD/CD; < salt (POLICIES ON SUGAR/SALT in food
 >tax);< stress, gen dx preventn: exercise, fruits/greens, no cigarrette
- Prim;
- 2⁰: (Aspirin/Statins).
- 3⁰: Reduce disability /morbidity; Improve outcome)
- Quatenary: Therapeutic options: CcB, Folate,
- Aspirin in ICH- No; even if AF, until 1 3 6 12 (<u>+ 2 days).</u>
- Treatable: evidence-based Rx available, but not fully used in any region, especially low resource areas
- major PH issue international collaboration activities reqd

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

Stroke prevention

Secondary Prevention of Ischemic Stroke



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 stroke The 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 G.L 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

High Risk	Caution	Low Risk
Or	120-139/80-89	<120/80
>240 or	200-239	<200
8280	Borderline	No
I still smoke		I am a non-smoker
I have an irregular heartbeat	I don't know	My heartbeat is not irregular
I am overweight	I am slightly overweight	My weight is healthy
I am a couch potato	I exercise sometimes	I exercise regularly
Yes	Not sure	No
	 > 140/90 or I don't know > 240 or I don't know > 240 or I don't know Yes I still smoke I still smoke I have an irregular heartbeat I am overweight I am a couch potato 	> 140/90or120-139/80-89I don't know200-239or200-239or1I don't knowBorderlineYesBorderlineI still smokeI'm trying to quitI have an irregular heartbeatI don't knowI am overweightI am slightly overweightI am a couch potatoI exercise sometimes

Assessing absolute CVD risk: the New Zealand guidelines



Risk Level: Men

ACT FAST at the First Sign of STROKE



www.strokemn.org



If you do have a stroke, act fast

- Act FAST
- S:Smile;
- T:Talk;
- R: Raise arm
- 0
- 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

AHA/ASA 2011 Recommendations for Lifestyle and Risk Factor Management in TIA or Ischemic Stroke

Factor	Recommendation	LOE
HTN	Initiate Rx beyond 24 hours; individualize Rx, consider ACEI/diuretics; BP reduction of 10/5 mm Hg	Class I, LOE A Class IIa, LOE B
Diabetes	Use existent guidelines for glycemic & BP targets; aim for hemoglobin A1c = 7%</td <td>Class I, LOE B</td>	Class I, LOE B
Smoking	Discontinue smoking Counseling, NRT, and oral smoking-cessation medications	Class I, LOE A
Alcohol use	Eliminate heavy drinking or reduce Men = 2 drinks/day and non-pregnant women<br 1 drink/day	Class I, LOE C Class IIb, LOE B
Obesity	Goal BMI 18.5 to 24.9 kg/m ² and waist circumference women (<35 inches) and men (<40 inches)	No study shows weight reduction reduces stroke recurrence risk
Physical activity	If capable, at least 30 minutes of moderate-intensity to break a sweat or raise heart rate, 1-3x/wk	Class IIb, LOE C
ACEI = angiotensin converting enzyme inhibitor; BMI = body mass index; HTN=hypertension NRT = nicotine replacement therapy; RX = treatment source: Furie KL et al. Stroke 2011; 42: 227-276		

Lifestyle Modifications for BP Reduction

Modification	Recommendation	*SBP Reduction (Range)		
1. Weight Reduction	Target: 18.5-24.9 kg/m2	5-20 mm Hg/10 kg		
2. DASH Diet*	Diet rich in fruits, veggies, low-fat dairy & reduced saturated & total fat	8-14 mm Hg		
3. Lower Sodium Intake	Target: 2400 mg Na+/day; 1500 or 1000 mg Na+/day provides further lowering of BP	2-8 mm Hg		
4. Physical Activity	Aerobic (e.g., brisk walking) 30 min./day most days	4-9 mm Hg		
5. Alcohol	2 drinks (24 oz. beer, 10 oz. wine, 3 oz. 80-proof whiskey) for men & 1 drink for women or those lighter weight	2-4 mm Hg		
*Dietary Approaches to Stop Hypertension Source: Go AS, Bauman MA, Coleman King SM, et al. Hypertension DOI: 10.1161/HYP.00000000000003				



Mum told me not to touch it



FAST FOOD and ISCHAEMIC stroke

neurology Today April 16, 2009 Lewis B. Morgenstern, MD, professor of neurology and director of the Stroke Program at the University of Michigan Health System in Ann Arbor.

- SAN DIEGO-People who live in neighborhoods with lots of fast food restaurants are at increased risk of CI, a population-based study suggests.
- cf with individuals living in areas with the lowest concentration of fast-food outlets, people living in neighborhoods with the highest density are at 13 percent higher risk of stroke, study does not prove cause-and-effect.
- ? whether fast food actually > risk of stroke or whether a high density of fast-food restaurants (FFR) is a marker of unhealthy neighborhoods.
- where we live has a profound effect on our health.
- public health standpoint: neighborhoods with FFR targeted for stroke prv
- Many studies have implicated fatty and fried fast foods in the dev. of CAD Rethink our fast-food diets, based on associatn stroke risk with proximity
- Research into factors account for > strokes rates in areas where FFR abound
- My intention is not to implicate FFR, but to take a better look at these neighborhoods with higher stroke rates. In addition to fast food itself,?

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















Stroke Unit management

