ACUTE STROKE MANAGEMENT

.... Before the Specialist Arrives

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ACTIONS taken during the 1st few hours of stroke will determine the quality of patient’s existence for the rest of his LIFE.
N= 259 patients

- 97% of acute stroke patients are seen initially by non-neurologist
Infarction
• CBF < 10 ml/100 gm/min
• Cytotoxic edema
• Irreversible ischemia

Ischemic Penumbra
• CBF – 18 -35ml / 100 gm/min
• Neuronal Paralysis
• Reversible ischemia
How to salvage the Penumbra?

1. RECANALIZATION STRATEGIES: THROMBOLYTIC

In carefully selected patients.....

- 30% more likely to have minimal to no disability at 3 months if given within 3 hrs

- rTPA treatment produced an absolute increase of 11-13% in favorable outcome

How to salvage the Penumbra?

2. NEUROVASCULAR PROTECTION – strategies singly or in combination that antagonize the injurious biochemical & molecular events leading to cell death

A. Physiologic – BP, Oxygen, Glucose, Temperature, Fluid

B. Pharmacologic – Citicoline, Cerebrolysin
5 H OF Neurovascular Protection

- **Temperature**: Brain damage increases as temperature increases.
- **Blood Glucose**: Brain damage decreases as blood glucose decreases.
- **pO₂**: Brain damage decreases as pO₂ decreases.
- **Blood Pressure**: Brain damage decreases as blood pressure decreases.
The Problem with Ischemic Stroke: 
Fate of the Penumbra

Ineffective 
Reperfusion & Neuroprotection over Time
The Problem with Hypertensive ICH

- Hematoma expansion can occur within the first 24 hours
- Frequently associated with early neurological deterioration or death
What to do in acute stroke?.....
IMPORTANT LINKS in STROKE CHAIN of SURVIVAL & RECOVERY

• Rapid recognition and reaction to stroke warning signs

• Rapid EMS dispatch

• Rapid EMS transport to facilitates capable of acute stroke care

• Rapid diagnosis & treatment in the hospital
US Brain Attack Alert Program, 1996

STROKE CHAIN of SURVIVAL & RECOVERY

7 “D” Program

1. Detection
2. Dispatch
3. Delivery
4. Door
5. Data
6. Decision
7. Drugs
Recognition of Stroke: Identify the signs of Stroke

Stroke Warning Signs:
- Sudden numbness or weakness of the face, arm, or leg, especially on one side of the body.
- Sudden trouble walking, dizziness, loss of balance or coordination.
- Sudden severe headache with no known cause.
- Sudden trouble seeing in one or both eyes.
- Sudden confusion, trouble speaking or understanding.

Recognize: the signs of Stroke
Detection by Patient or witness

React !
Call for help or Go immediately to ER
TIME OF ONSET

ASSESS FOR:

- Facial asymmetry
- Arm weakness
- Speech difficulty

“Cincinnati Prehospital Stroke Scale”

ASK FOR:
Alert: receiving hospital

- If possible, check glucose and administer oxygen
To the Internists & Generalists: Remember

Management Priorities (A, B, C)

Emergent Diagnostics

Early Specific Treatment
ER Stroke Therapy Timelines:

**Before the specialists...**

**0 min** – ED arrival. Immediate TRIAGE

**≤ 10 mins**
- Complete MD evaluation
- Assess ABCs
- Establish time of onset
- Obtain IV access and blood samples
- Provide oxygen if hypoxemic
- Check glucose. Correct hypo or hyperglycemia
- Obtain 12 L ECG, Neuroimaging
- Alert Brain Attack Team
General assessment

- Immediate stabilization of the ABCs
- Secondary assessment of neurological deficits & other co-morbidities
  - Rule out stroke mimickers
  - Identify other conditions requiring immediate attention
  - Determine potential causes of stroke for early secondary prevention
Sudden, focal, negative signs / deficits
Establish time of onset (single most important info!)
Perform focused neurological exam (GCS, NIHSS)
Inquire from History & rule out Mimickers

- Risk factors for atherosclerosis
- Previous stroke (Infarct / ICH)
- Seizures
- Migraine
- Infection
- Head Trauma
- Psychiatric or conversion disorder
- Previous or recent surgery
- History of Bleeding
- Recent MI
- Medications
### Stroke vs stroke mimicker

Check if patient fulfills criteria for dx of stroke: acute onset, neurological syndrome referable to a vascular territory, lasting for few minutes (TIA) or hours

<table>
<thead>
<tr>
<th>Stroke / TIA likely</th>
<th>Stroke/TIA less likely</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) stroke risk factor</td>
<td>No vascular risk factor</td>
</tr>
<tr>
<td>Definite focal signs/symptoms</td>
<td>Isolated facial nerve involvement</td>
</tr>
<tr>
<td>Clear, exact time of onset</td>
<td>Isolated dizziness, vertigo</td>
</tr>
<tr>
<td>Irregular cardiac rhythm</td>
<td>Seizures at onset; fever at onset</td>
</tr>
<tr>
<td>Abnormal visual fields</td>
<td>Weakness with atrophy</td>
</tr>
<tr>
<td>Abnormal eye movements</td>
<td>Signs &amp; symptoms not consistent with neuroanatomic or vascular distribution</td>
</tr>
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</table>
## ROSIER SCORE
Recognition of Stroke in the Emergency Room

<table>
<thead>
<tr>
<th>NEW SYMPTOMS</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral facial weakness</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral arm weakness</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral leg weakness</td>
<td>1</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>1</td>
</tr>
<tr>
<td>Visual field defect</td>
<td>1</td>
</tr>
<tr>
<td>Loss of consciousness or syncope</td>
<td>-1</td>
</tr>
<tr>
<td>Any seizures</td>
<td>-1</td>
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</tbody>
</table>

**Score > 0 strongly suggests acute stroke**

**Score -2 to 0 are less likely to be stroke**
IN THE ER, prioritize:

1. CBC with platelet count
2. PT-INR, PTT
3. CBG
4. Non-contrast Cranial CT scan or Cranial MRI-DWI
5. 12 L ECG
Rationale of Early Neuroimaging Assessment

- Identify the lesion (is it a stroke?)
- Determine the type of stroke (ischemic or hemorrhage?)
- Localize the stroke (where is it?)
- Quantify the lesion (how large is it?)
- Determine the age of the lesion (old or new?)
- If hemorrhagic, what is the possible etiology?
Conventional Non-Contrast CT scan

- Fast, widely available, relatively inexpensive
- Easily obtained on patients with monitors
- Excludes hemorrhage, mimickers such as tumors
- Used to determine eligibility for rTPA treatment

**BUT** may be normal in 60% in the first 0-6 hrs of ischemic stroke (limited sensitivity)
Cranial MRI in Acute Stroke

- Markedly increased sensitivity for acute ischemic stroke
- DWI positive within 90 minutes of stroke
- Must include GRE sequence to rule out hemorrhage

CT scan at 1.5 hrs
MRI-DWI scan at 2.5 hrs
ER Stroke Therapy Timelines:

With the Neurology specialists…. 

0 min – ED arrival. Immediate TRIAGE

≤ 10 mins
ED staff

≤ 15 mins

- Neurologist Assessment
- Review history
- Review Neuro exam
4 Door

5 Data

6 Decision for IV rTPA

≤15 min Notify stroke team (including neurologic expertise)

≤25 min Initiate CT scan

≤45 min Interpret CT scan and labs
Review patient eligibility for Activase

≤60 min Give Activase bolus and initiate infusion in eligible* patients
THERAPY of ACUTE STROKE means more than just THROMBOLYSIS .....
CONCEPT OF NEUROVASCULAR PROTECTION

**PHYSIOLOGIC**

- Hypertension
- Hyperglycemia
- Hypoxia
- Hyperthermia
- Hypovolemia

**PHARMACOLOGIC**

- Citicoline
- Cerebrolysin
BP Management in Ischemic Stroke

Allow permissive hypertension please …!

Treat only if with any of the ff:

- \( SBP \geq 220 \) or \( DBP \geq 120 \) or
- \( MAP > 130 \text{mm Hg} \)

\[ MAP = \text{SYSTOLIC} + 2 \times \text{DIASTOLIC} / 3 \]
Why Rapid Lowering of BP in Acute Stroke is NOT Recommended

1. In acute ischemic stroke, autoregulation is paralyzed in the affected tissues with CBF passively following MAP. Rapid BP lowering can lead to further ↓ perfusion in the penumbra.

2. HPN is typically present in acute stroke, with spontaneous decline within the first 5 - 7 days.

3. ↑ ICP during the acute phase of large infarcts reduces the net CPP.
4. Several reports document neurological deterioration from significant pharmacologic lowering of BP

Oliveiria - Filho J. et al. Neurology 2003
Castillo, J et al. Stroke 2004
Candesartan for the Treatment of Acute Stroke (SCAST)

2029 pts within 30 hrs of stroke

SBP > 140

Candesartan 4 mg day 1 to 16 mg day 3 - 7

Placebo

N = 1017
N = 1012

Outcome: MI, Stroke & vascular Death during the 1st 6 months

: Functional outcome (mRS) at 6 months

Candesartan for the Treatment of Acute Stroke (SCAST)

Candesartan – 170 / 90  
Placebo – 171 / 90

Candesartan – 147 / 82  
Placebo – 152 / 84
## Candesartan for the Treatment of Acute Stroke (SCAST)

<table>
<thead>
<tr>
<th>Event</th>
<th>Candesartan</th>
<th>Placebo</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke, MI /Vascular Death</td>
<td>120 (12%)</td>
<td>111 (11%)</td>
<td>1.09</td>
<td>0.52</td>
</tr>
<tr>
<td>Progressive Stroke</td>
<td>65 (6 %)</td>
<td>44 (4%)</td>
<td>1.47</td>
<td>0.04</td>
</tr>
<tr>
<td>Poor Functional Outcome</td>
<td></td>
<td></td>
<td>1.17</td>
<td>0.048</td>
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</table>

How to lower BP in Acute Ischemic Stroke

- BP GOAL: MAP 110
- Not > 10 – 15% lowering from baseline MAP
- AGENT: Use easily titratable IV or short acting oral antiHPN meds
Remember ....

No sublingual agents please ...!
Cerebral Blood Flow (ml/100g/minute)

Mean Arterial BP (mmHg)

Cerebral Autoregulatory Curve & Target MAP

Normotensive

Hypertensive

Mean Arterial BP (mmHg)
Sample Computation

BP = 210/110
MAP = 143 mmHg
15% of 143 = 21

Compute for the desired MAP:
143 – 21 = 122

The desired BP should not be lower than 180/90.
BP Management in Acute ICH

In Hypertensive ICH: Goal is to minimize hematoma expansion & limit tissue injury

Treat only if with any of the ff:
- SBP > 180
- MAP > 130mm Hg

Target MAP ≈ 110 or SBP ≈ 160

*Acute BP lowering to SBP = 140 is safe and can help limit hematoma expansion (INTERACT). BUT Clinical benefit remains to be determined.
Hypo-hyperglycemia in Stroke

• Prompt determination & monitoring of blood sugar
• Treat with insulin titration if CBG > 180 mg %
• Avoid glucose containing IV fluids
• Target normoglycemia (110 - 180 mg / dl as early as the 1st 24 hrs up to first 3-5 days)
Hyperglycemia decreases Penumbral salvage.
Fluid Management in Stroke

1. Use normal saline (0.9% NaCl) to maintain a balanced fluid status
2. Correct dehydration promptly, if present
3. Start IVF rate of 75 – 100 ml/hr
4. Avoid glucose containing or hypotonic solutions
5. Monitor intake & output regularly. Include Mannitol, IV fluids & NGT flushes in the computation of total fluid intake
• Hypotonic solutions may worsen cerebral edema

- D5 W
- D5NM
- D5 0.3% NaCl
- D5LR

• D5 containing IVFs may promote lactic acidosis, increase free radical production, worsens cerebral edema and weakens blood vessels
Monitor by pulse oximeter, ABG determination
Use O₂ supplementation if hypoxic - target O₂ saturation > 95%
Secure airway in patients with impaired sensorium or with brainstem dysfunction
Proper head positioning (neutral, 30 degree)
Hyperpyrexia and Stroke Outcome

Fever burden – maximum temperature measured during hospitalization minus 100°F (37.8°C) X no of days with temp. > 100°F

Cohort study – 1,361 stroke patients

Temperature Management in Stroke

- Search and treat source of fever
- Use paracetamol, surface cooling measures & cold saline IVF if temp $\geq 37.5$
- Endovascular cooling
- Maintain normothermia
Oral Citicoline in Acute Ischemic Stroke
An Individual Patient Data Pooling Analysis of Clinical Trials

Antoni Dávalos, MD, PhD; José Castillo, MD, PhD; José Álvarez-Sabín, MD, PhD; Julio J. Secades, MD, PhD; Joan Mercadal, BS; Sonia López, BS; Erik Cobo, MD, PhD; Steven Warach, MD, PhD; David Sherman, MD; Wayne M. Clark, MD; Rafael Lozano, MD

Citicoline treatment among pts with moderate to severe stroke within 24 hours results in 33% odds of complete recovery at 3 mos

OR 1.33 [1.10 - 1.62]; p = 0.0034

Citicoline (CDP choline)

- Essential intermediate in synthesis of phospholipids (phosphatidylcholine)
  which are important constituents of neuronal membranes
Organized care in Acute Stroke Unit

Stroke Unit Trialists Collaboration
25 trials, N = 4195 pts

REDUCTION IN:

- Death
- Dependency
- Need for chronic institutional care
SUMMARY

1. Early recognition & intervention is needed in all acute stroke patients with the goal of salvaging the penumbra in Cerebral infarct while addressing hematoma expansion and edema in ICH

2. Because of time constraint, diagnostic investigations should be prioritized in the ER
3. While rTPA therapy is best decided on by the specialist, neuroprotective strategies remain as important in acute stroke.

4. For patients who are rTPA ineligible, administration of neuroprotectant drugs and careful management of physiologic parameters (5H) can be easily done even by internists and generalists.
It would be wonderful if all physicians & personnel were to “work closely together”

Louie Caplan, 2003
Thank you!
**Cerebrolysin**

- Neurotrophic peptide-based drug that mimics the activity of endogenous Neurotrophic Factors.

**Neurotrophic factors**
 *(Endogenous Brain’s Defense Mechanism)*
- regulate processes of development and modeling of CNS
- Regulatory role and guide recovery processes in the brain tissue as important part of natural response to injury
N = 1070 pts with ischemic stroke
Can be randomized within 12 hrs NIHSS 6 - 22

Cerebolysin 30 mg IV x 10 days; n = 509

Placebo (0.9% NaCl) N = 541

- Primary Efficacy Criteria
  Modified Rankin Scale, Barthel Index, NIH Stroke Scale
  Evaluation as scales (as global scale) at day 90
CASTA Results

Mann Whitney test statistic
Global test of Efficacy Variable
(1-sided test for superiority, 97.5% CI)

- 0.50 = equality
- 0.56 = slight superiority
- 0.64 = relevant superiority
- 0.71 = large superiority

Global test resulted in \( MW = 0.5002 \)
(no significant difference found between the study groups)
It is a well known fact that patients with mild strokes might recover with receiving standard of care only. & no further improvement can be shown with the use of Cerebrolysin.
Applying NIHSS outcome criteria among those with baseline NIHSS > 12 indicate trend for **beneficial effects** of Cerebrolysin

OR = 1.2724; 95 % CI LB 0.97 p= 0.04 )