

## Stroke Update for Primary Care Physicians

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SOWEGA-AHEC

CURE Activity

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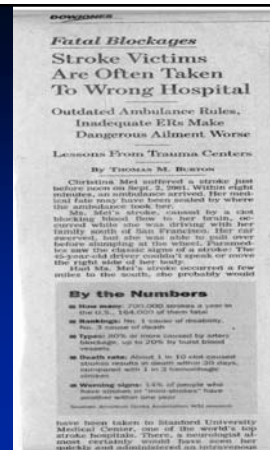
## Disclosures

- REACH CALL, Inc, Cofounder, Chairman BOD, Founder's equity
- Lundbeck, Advisory Board
- Sanofi-Aventis, Advisory Board
- Athersys, Inc, Research Contract
- Genentech, Consultant
- Boehringer Ingelheim, Consultant
- NIH, NINDS

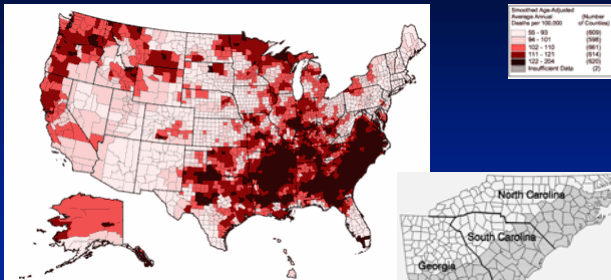
## Objectives

- List and define the types of stroke.
- Describe the diagnostic evaluation process and treatment options for acute stroke.
- Describe the stroke prevention principle.

Front Page, Wall Street Journal

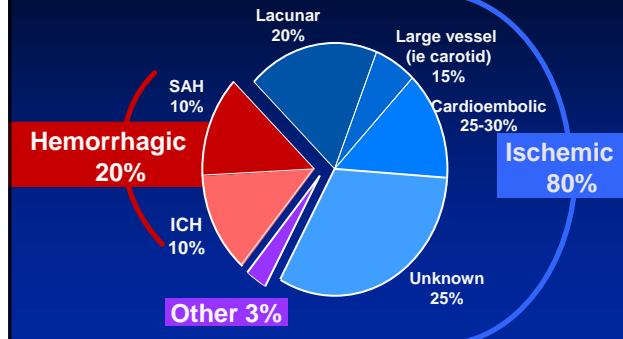


## U.S. Stroke Belt



Source: US Census Bureau Postcensal Population Estimates (DC9 430-438.9) (1981-1989)

## Stroke Subtypes



Data from NINCDS Stroke Data Bank: Foulkes et al. *Stroke*. 1988;19:547.

## Dismal Record of Acute Stroke Trials

(Kidwell, *Stroke* 2001;32:1349)

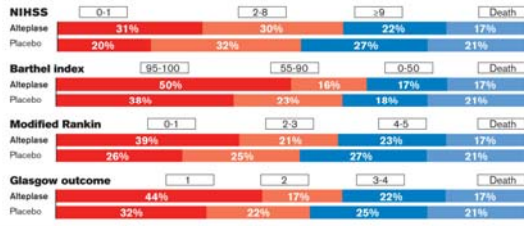
- 178 controlled acute stroke trials
- 73,000 patients
- 3 “positive trials”
- 1 FDA-approved agent

## Four “Effective” Treatments in Acute Stroke

1. tPA
2. Stroke Unit Care
3. Aspirin
4. Hemicraniectomy for “malignant edema”

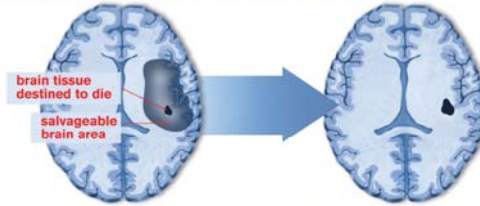
## More patients recover with minimal or no disability with Alteplase

### NINDS results at 3 months\*



■ Minimal or no disability ■ Moderate disability ■ Severe disability ■ Death  
 \*Values do not total 100% because of rounding.  
 NIHSS = National Institutes of Health Stroke Scale.  
 Scores of 51 on the NIHSS, 95 or 100 on the Barthel index, 51 on the modified Rankin scale, and 1 on the Glasgow outcome scale were considered to indicate a favorable outcome.  
 Reference: NINDS rt-PA Stroke Study Group. *N Engl J Med.* 1995;333:1581-1587.

## Potential to reverse neurologic impairment with thrombolytic reperfusion



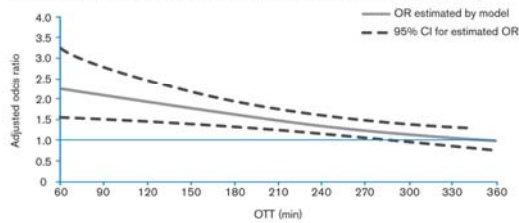
During an acute ischemic stroke, the average patient loses 32,000 brain cells every second!

Reperfusion offers the potential to reduce the extent of ischemic injury<sup>2,3</sup>

References: 1. AHA Stroke Journal Report, May 8, 2006. 2. Thomas et al. *N Engl J Med.* 2006;354:2263-2271. 3. NINDS. *N Engl J Med.* 1995;333:1581-1587.

## Pooled analysis confirms favorable outcomes with Alteplase\*

### Estimation of odds ratio for favorable stroke outcome at 3 months compared to placebo by onset to treatment (OTT)



\*Treatment only indicated within 0-3 hours after symptom onset.

Reference: Adapted from ATLANTIS, ECASS, and NINDS rt-PA Study Group Investigators. *Lancet* 2004;363:368-374.

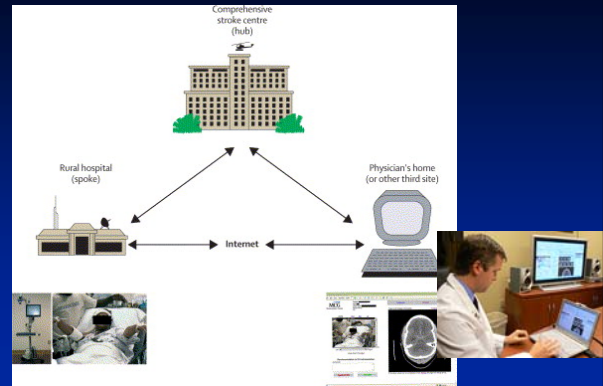
## ECASS III Clinical Trial

- tPA window extended safely to **4.5 hours**
- But TIME still CRITICAL!!!!
- “Having more time does not mean we should take more time”

## The Geographic Penalty

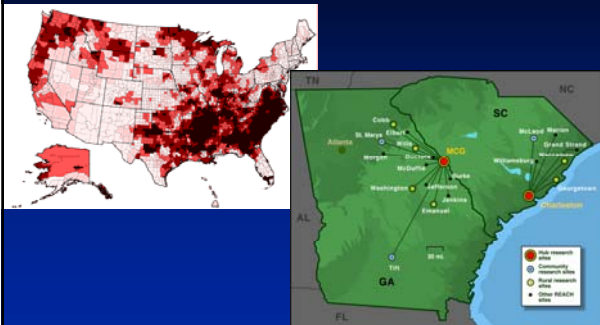
- The quality of stroke care is dependent upon the hospital you go to
- If you live in a rural area or “underserved acute stroke care” area you will NEVER receive tPA
- There is a GEOGRAPHIC penalty for stroke care

## REACH Hub & Spoke Telestroke Model

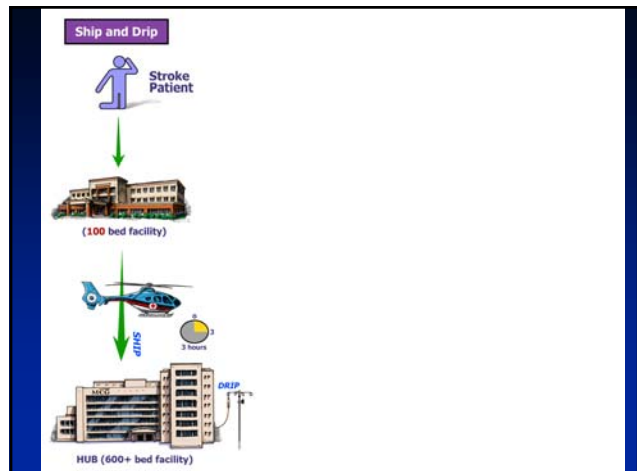


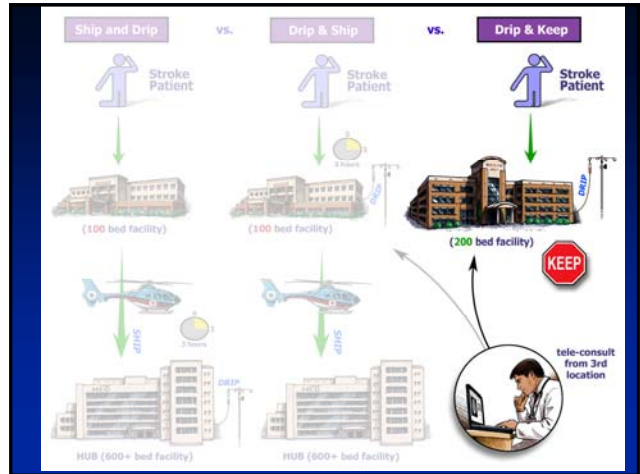
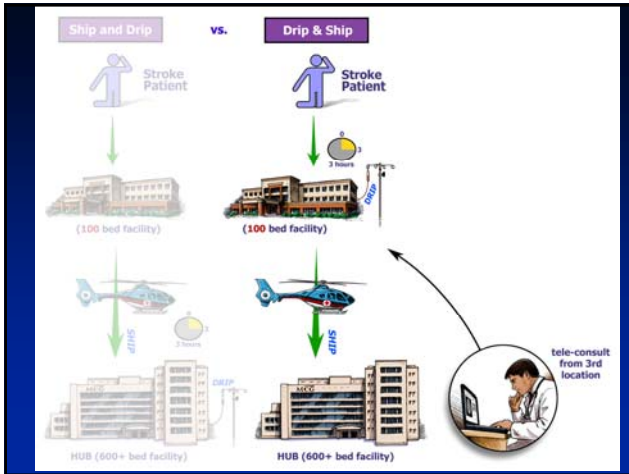
Hess DC et al. Lancet Neurol. 2006; 5: 275-6

## U.S. Stroke Belt and MCG-MUSC Telestroke Network



Source: US Census Bureau Postcensal Population Estimates (IC9 430-438.9) (1991-1995)





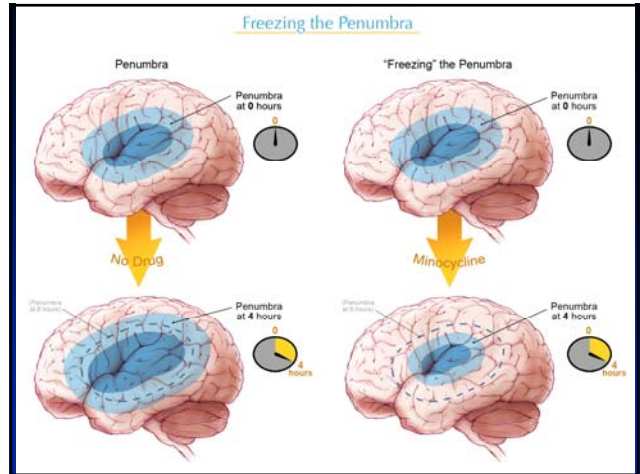
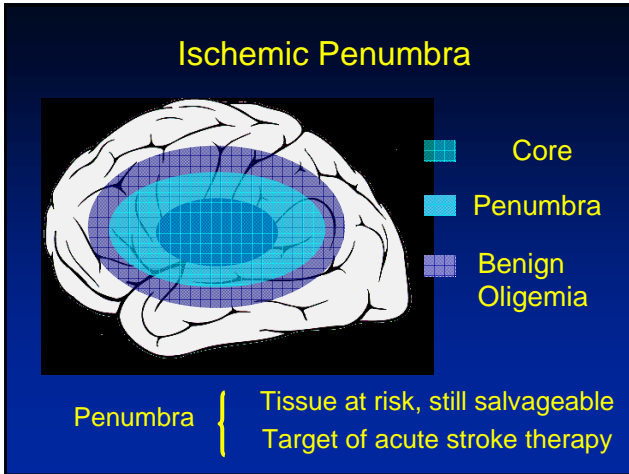
## What about heparin?



- NO SOLID DATA
- The strong trend in stroke centers is NOT to use it in acute stroke

## New Treatments Under Development

- Pipeline is running at a "drip"
- Many past failures
- Big Pharma views acute stroke as a "financial drain" and a "loser"
- Hypothermia, magnesium, albumin, minocycline in clinical trial



- ### Combination Treatment with tPA
- Reduce risk of ICH associated with tPA
  - Extend window of tPA beyond 3 hours
  - Added protective effect

### Minocycline: "Repurposing" An Old Drug with New Tricks

$C_{22}H_{24}N_2O_8 \cdot HCl$  MW = 480.90

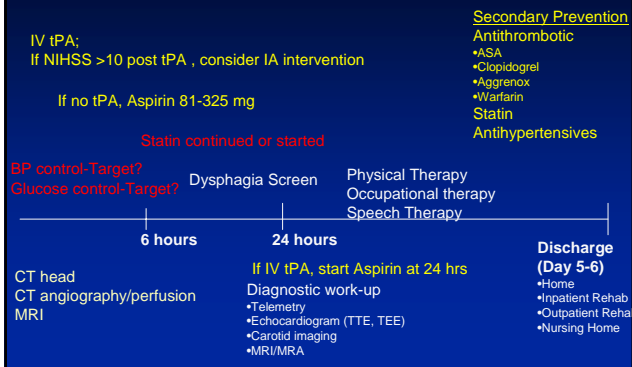
Tetracycline

$C_{23}H_{26}N_2O_7 \cdot HCl$  M.W. 483.95

Minocycline

- Developed as antibiotics
- Dental use (MMP inhibitors)
- Acne
- Effective in rheumatoid arthritis (MIRA Trial, Tilley BC, Ann Intern Med 1995; 122:81)

## Ischemic Stroke: Admission to Discharge in U.S. Hospital (Joint Commission Primary Stroke Center)



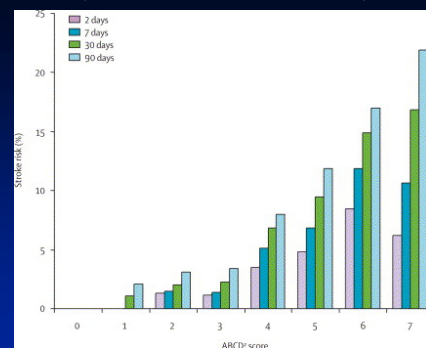
## Diagnostic Work up for Stroke Patient

- Carotid ultrasound
- Echo (TTE or TEE)
- Telemetry (a fib)
- CBC, platelet, ESR, lipid profile, PT, aPTT
- MRI/DWI and MRA

## Risk scoring for TIA: ABCD<sup>2</sup>

- Age > 60 1 point
- Hypertension >140/90 1 point
- Diabetes 1 point
- Duration
  - ◆ 10-59 minutes 1 point
  - ◆ >60 minutes 2 points
- Clinical features
  - ◆ Unilateral weakness 2 points
  - ◆ Speech disturbance, no weakness 1 point

(Johnston SC et al Lancet 2007;369:283)



**ABCD<sup>2</sup> scores**      **2 day stroke risk**

High risk (6-7 pts)	8.1%
Medium risk (4-5)	4.1%
Low risk (0-3)	1.0%

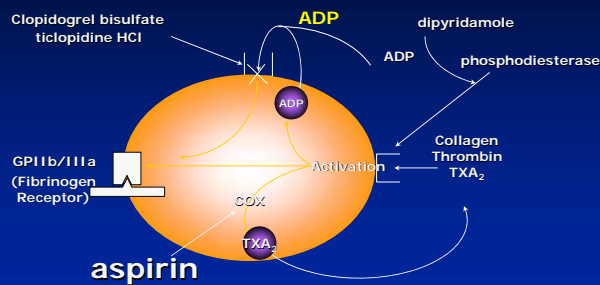
The end result of inadequate management of TIAs



## Stroke Prevention Cocktail

- Antiplatelet agent {aspirin (RRR 15%), Aggrenox (RRR 37%), clopidogrel}
- Thiazide diuretic and ACE inhibitor (RRR 43%)
- Statin (RRR 30%)

## Oral Antiplatelet Agents: Mechanisms of Action



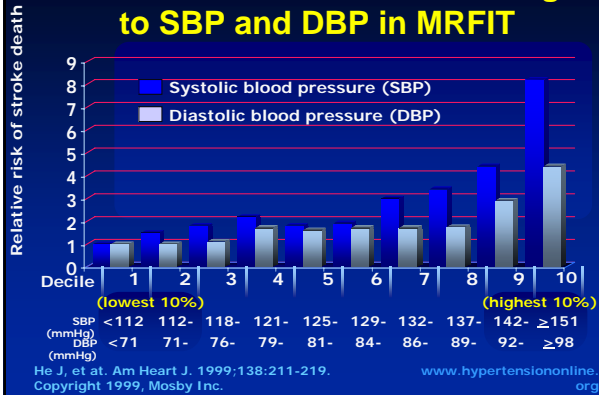
ADP = adenosine diphosphate, TXA<sub>2</sub> = thromboxane A<sub>2</sub>, COX = cyclooxygenase.

Plavix® (clopidogrel bisulfate) Prescribing Information.  
Schafer AI. *Am J Med.* 1996;101:199-209.

## Hypertension

- Treating hypertension is the biggest bang for your buck in stroke prevention!

## Risk of Stroke Death According to SBP and DBP in MRFIT



## The "Polypill"

Wald and Law, BMJ 2003; 326:1419

- Pill consisting of a statin, 3 anti-hypertensives, folic acid, aspirin
- Reduce ischemic heart disease by 88% (CI 84-91%)
- Reduce stroke by 80% (CI, 71-87%)
- Target over age 55 and pre-existing CV disease
- If started at age 55, 1/3 would benefit with 11 years of life stroke and IHD-free

## QUESTIONS



## Evaluation

- Attended Live Activity on July 13, 2010  
<http://www.surveymonkey.com/s/CURE6>
- Attended Archived Activity July 14, 2010 or later  
<http://www.surveymonkey.com/s/CURE6Archived>