Revolution and Evolution in Stroke Care and Treatment

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Vice President
University of Kansas Health System
Marilyn M. Rymer, MD

• NO DISCLOSURES
Kansas City
Irene Bettinger, MD
First IV tPA  1994

Graham Lee, MD
First IA Urokinase  1993

Debbie Summers, APN
Founder – AHA Nursing Symposium; Lead author of AHA stroke guidelines

Naveed Akhtar, MD
First mechanical embolectomy  2002

Colleen Lechtenberg, MD
Director – One of first five Comprehensive US Stroke Centers  - 2007

Kansas City leads innovation in Stroke Care
1 in 6 people worldwide will have a stroke in their lifetime.
Epidemiology of Stroke Worldwide

• *Stroke is the second leading cause of death worldwide; 1st in China*

• *Every 6 seconds*, stroke kills one person.

• *Every other second*, stroke attacks one person, regardless of age or gender.

• *15 million people* experience stroke each year; 6 million of them do not survive.

• *About 30 million people* have had a stroke; most have residual disabilities.
## Time is Brain -- Quantified

(Saver J. Stroke 2006; 37: 263-66)

<table>
<thead>
<tr>
<th></th>
<th>Neurons lost</th>
<th>Synapses lost</th>
<th>Myelinated fibers lost</th>
<th>Accelerated aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per stroke</td>
<td>1.2 billion</td>
<td>8.3 trillion</td>
<td>4470 miles</td>
<td>36y</td>
</tr>
<tr>
<td>Per hour</td>
<td>120 million</td>
<td>830 billion</td>
<td>447 miles</td>
<td>3.6y</td>
</tr>
<tr>
<td>Per minute</td>
<td>1.9 million</td>
<td>14 billion</td>
<td>7.5 miles</td>
<td>3.1 wk</td>
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<tr>
<td>Per second</td>
<td>32,000</td>
<td>230</td>
<td>218</td>
<td>8.7 hr</td>
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The Early Days

• 1954  Warfarin approved by the FDA

• 1965  Dr. Clark Millikan at Mayo Clinic described transient cerebral ischemia and its mechanisms.
Brain Imaging

- CT scans of the brain became available in the mid 1970s

- MRI scans: early to mid 1980s
  In 1982 there were no MRI scanners in Kansas City. The closest one was in Columbia, MO
ED stroke case – no hurry!
Thrombolytics for Stroke

• Late 1980s and early 1990s several trials of streptokinase were abandoned due to excessive bleeding.

• The tPA study group began dose escalation trials and determined that there was excessive bleeding above 0.9mg/kg (lower than the cardiac dose). The lowest necessary dose for efficacy was not determined.
Who Remembers This Guy??
IV tPA

- 1994 – First case treated in Kansas City
- 1995 – NEJM landmark paper
- 1996 – FDA approval

MAJOR BARRIERS TO ADOPTION
Radiology and Pharmacy

RX
Treatment with IV tPA is Complex

**Acute Stroke Process**

1) ABC ASSESSMENT
2) NEURO ASSESSMENT (NIHSS)
3) GOWN ON PT
4) IV STARTS X 1
5) BRIEF HR (HIGHLY TIME VARIABLE) TO ESTABLISH ONSET TIME
6) LAB DRAW
7) BLOOD GLUCOSE
8) VS
9) O2
10) EMS VERBAL REPORT
11) 12-LEAD EKG

**STROKE PANEL LABS (BMP, CBC, Coags, Trop, Mg) & NON-CONTRAST HEAD CT ORDERED BY ED MD**

**iSTAT** (lab person @ bedside)

**QUICK ADMIT**

**COMPUTERIZED DOCUMENTATION & CODE STROKE FORM**

**TRANSPORT TO CT (ED RN + Code Neuro RN)**

**NON-CONTRAST HEAD CT**

**TRANSPORT BACK TO ED**

**CT INTERP** (APN + Radiologist)

**IF tPA CANDIDATE**

- **INR ORDER PLACED**
  - **COMPUTERIZED DOCUMENTATION, CNN COMPLETES CODE STROKE FORM, PT PLACED ON PORTABLE MONITOR, O2, ED RN CALLS REPORT TO ICU, NEUROLOGY/APN, COMPUTING ORDERS, CHART COPIED**
  - **CNN TRANSPORTS PT TO INR, APN PROVIDES FAMILY EDUCATION & INSTRUCTION**
  - **CNN & 2nd RN or TECH TRANSPORTS PT TO ICU, APN PROVIDES FAMILY EDUCATION & INSTRUCTION**

- **BP MNGMT INDICATED**
  - **INITIATE BP DRIPS**
    - Obtain order, prep med, admin med, monitor pt
  - **FAMILY DISCUSSION & CONSENT FOR INR**
    - INR MD, ED MD, Neurologist, CNN, ED RN - APN & ED RN
  - **RETURN TO ED FOR HOLD LIFE, TV PLUN ESTABLISHED**
    - Reconstruction of CTP/CTA & Interp of Scans
  - **BACK TO ED FOR HOLD LIFE, TV PLUN ESTABLISHED**

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**CNS TRANSPORTS PT TO INR**

**APN PROVIDES FAMILY EDUCATION & INSTRUCTION**

**BACK TO ED FOR HOLD LIFE, TV PLUN ESTABLISHED**

**RECONSTRUCTION OF CTP/CTA & INTERP OF SCANS**

**COMPUTERIZED DOCUMENTATION, CNN COMPLETES CODE STROKE FORM, PT PLACED ON PORTABLE MONITOR, O2, ED RN CALLS REPORT TO ICU, NEUROLOGY/APN, COMPUTING ORDERS, CHART COPIED**

**CNN TRANSPORTS PT TO INR**

**APN PROVIDES FAMILY EDUCATION & INSTRUCTION**

**RETURN TO CT SCAN FOR CTA/CTP**

**Code Neuro, Neurologist, APN & ED RN**

**OBTAIN DOCUMENT VS & NEURO CHECKS q 15min x 2hrs (estimate 3hrs)**

**CTA/CTP (ordered by Neurologist & ED MD & NOTIFY IR TEAM & CT OF POSSIBLE TABLE HOLD)**

**NEUROLOGIST & APN COMPLETE HISTORY & NEURO ASSESSMENT**

**REVIEW OF LABS**

- **tPA PREP**
  - 2nd IV Start, Foley (w/ UA C&S + Pregnancy if Applicable) & HANG IV FLUIDS
  - **No**
  - **Yes**
- **OBTAIN DOCUMENT VS & NEURO CHECKS q 15min x 2hrs (estimate 3hrs)**
- **RETURN TO CT SCAN FOR CTA/CTP**
  - Code Neuro, Neurologist, APN & ED RN
- **BACK TO ED FOR HOLD LIFE, TV PLUN ESTABLISHED**
  - Reconstruction of CTP/CTA & Interp of Scans
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The **Golden Hour**
ED Stroke Response

*** EMS CALL TO ED ***

** EMS REPORT:** Last Time Known Well, Vital Signs, Glucose, Symptoms
** TRIAGE REPORT:** Last Time Known Well, Vital Signs, Symptoms, Ensure Patient Armband is Scanned by Admitting
** PAGE CODE NEURO:** 440-1139; Code Neuro to Activate Code Ischemic Stroke; Overhead Page Admitting at 25599 Upon Patient Arrival

*** Patient Arrives ***

** Immediate General Assessment & Stabilization **
§ Address ABCs, Oxygen
§ Establish Last Time Known Well
§ Ask ED Physician to See Patient Immediately
§ Discuss Patient w/ Neurology
§ NIHSS
§ Obtain IV Access x2 & Stat Stroke Panel
§ Electronic Order Entry
§ Check Glucose at Bedside; Treat if Indicated
§ Obtain 12-Lead EKG

** Immediate Neurological Assessment by Stroke Team Member or Designee **
§ Review Patient Chief Complaint & Past Medical History
§ Obtain CT Head (Non-Contrast)
§ Complete Physical Assessment
The Golden Hour
ED Stroke Response (Continued)

ED DOOR TO CT INTERP 45 MINS

Does CT Show Hemorrhage?

NO HEMORRHAGE

tPA Candidate

Probable Acute Ischemic Stroke; Consider t-PA Therapy
§ Check for Fibrinolytic Inclusions & Exclusions
§ Repeat Neurological Exam Prior to Tx Option
§ BP Must be <185/110 to Administer IV tPA

Neurologist or ED MD Will Review Risks/Benefits w/ Patient & Family
§ Tx Options: Depend on Time & Images
  ➢ 0-4.5 hrs: IV tPA
  ➢ 3-6hrs: IA tPA - Specials
  ➢ 3-8hrs: Clot Retrieval, Specials
§ Clinical Trial Candidate: Assess by Code Neuro RN & Research RN
§ Collaborate w/ Code Neuro RN for Further Imaging Orders or Arteriogram

ED DOOR TO DRUG 60 MINS

HEMORRHAGE

Not a tPA Candidate

§ Consult Neurosurgeon if Surgical Candidate or Hospitalist if Non-Surgical Candidate
§ Treat BP if Indicated by ED MD

Initiate Admission Process
§ Report to Receiving Unit
§ History & Physical
§ Stroke Onset History
§ NIH Stroke Scale Review
§ Treatment
  ➢ Dose of IV tPA
§ If Patient to IR, Code Neuro RN to Provide Further Patient Report
Stroke Center Certification

• 2000 BAC published criteria for primary stroke centers
• 2004 ASA/JC certification began and by 2005 15 reviews per month. Currently 1100 PSC (JC) and more via DNV.
• 2005 BAC paper regarding CSC with certification beginning in 2007. Currently 118 JC CSCs
• JC ASRH certified hospitals = 22
• Many states have state certification
Get With the Guidelines - Stroke

• Development of quality measures has improved performance though there is still a long way to go.

• At least 25% of cases of AIS reach the hospital within the time limit for IV tPA, yet about half of those are treated. This led to rewriting the package insert, making inclusion easier.

• Treatment window expanded to 4.5 hours
Drip and Ship – Expanding treatment to smaller hospitals
The Quest for Neuroprotection – extending the window for treatment – mid to late 1990s

- Cervene 1995, 1996 (III)
- Lubeluzole 1996
- SAINT II (NXY-059)
- CHANT (ICH)
- DAIICHI (Piclozotan)
- ALIAS
- ASPII (Ancrod)
- Neurothera
- BrainsGATE
- CoAxia

NEST 3
NN104 Rhapsody
Hypothermia trials
Endovascular Therapy

• First IA urokinase case in Kansas City – 1993 (never approved by FDA despite impressive PROACT Trial results.)

• First MERCI device case in Kansas City – 2002. Device approved for clot retrieval 2004
MERCI Retriever “The Corkscrew”
Clot/Thrombus Samples
Basilar artery blocked
Basilar artery opened up
RANDOMIZED TO DEVICE GROUP

RANDOMIZED TO CONTROL GROUP
The Evolution of Endovascular Treatment

IA drip
IA drip & wire
Merci
Penumbra
Stents
Stentriever
IA STUDY POPULATION

- **All ICA or M1 MCA Occlusions**
- **ESCAPE**
- **EXTEND**
- **SWIFT PRIME**

- **Unlikely**
- **Likely**
- **tPA Tx**
- **Time from Onset**

- 12h
- 6h
- 2h

- low ASPECTS
  - poor collaterals
  - large core

- good ASPECTS
  - good collaterals
  - small core

ALL SHOWED BENEFIT OF ENDOVASCULAR TREATMENT

Slide credit: M. Goyal ESCAPE Trial Presentation
Summary of New Randomized Clinical Trials of Endovascular Therapy

<table>
<thead>
<tr>
<th>Trial</th>
<th>Good Outcome (%)</th>
<th>Rankin 0-2 @ 90 days</th>
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<tbody>
<tr>
<td>MR CLEAN (0% RAPID)</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>ESCAPE (0% RAPID)</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>SWIFT PRIME (69% RAPID TMM)</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>EXTEND-IA (100% RAPID TMM)</td>
<td>71%</td>
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Endovascular: 33% 53% 60% 71%
Control: 19% 29% 36% 40%
Small Core + Proximal occlusion
Small core with complete reperfusion

Baseline CTP

CBF (0.3 threshold) 1 ml
Hypoperfusion (Tmax>6s) 129 ml

27 h Follow Up MRI

Infarct Volume 5 ml
100% Reperfusion
Small Core + Larger Perfusion defect
Malignant profile

Baseline CTP

- CBF (0.3 threshold) 182 ml
- Hypoperfusion (Tmax>6s) 215 ml

Non-Contrast CT at baseline

MRI at 48 h
A New Paradigm
What New Systems of Care Do We Need?

- CT scanners in ambulances to enable IV tPA en route?
- EMS/telestroke determination of LVO at the scene?
- Routing of LVO past PSC to CSC?
  - Does IVtPA on board improve outcome with EVT? Is the delay warranted?
- Does imaging predict which cases of LVO should have EVT? Dawn Trial halted early, and the answer was YES!
- How do we organize care in rural areas?