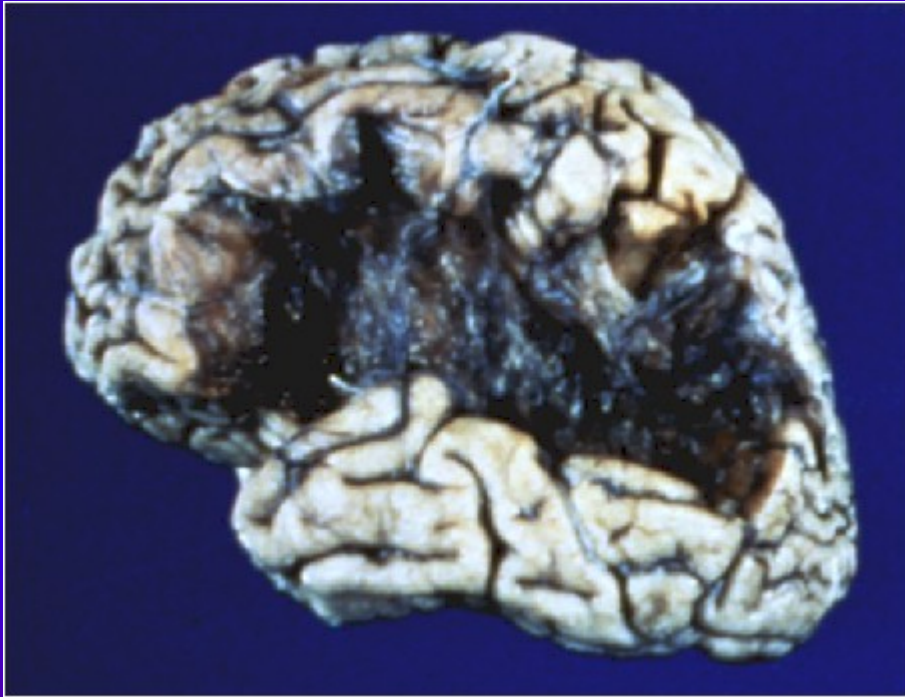


# *Stroke: Incidence and Cost in the United States*



- ◆ 700,000 new cases yearly
- ◆ #3 cause of death
- ◆ \$43 billion annual health cost (1998)
- ◆ 4,400,000 stroke survivors at high risk for recurrence

***Most strokes can be prevented***

# *Cost of Stroke*

- ◆ Stroke severity includes a broad range; about half of survivors unable to walk unaided.
- ◆ Acute inpatient costs average \$38,000 but are only a fraction of total economic burden (including rehab, long-term care).
- ◆ Average lifetime cost of stroke in the U.S. estimated to be \$60,000.

# *Race and Stroke Risk*

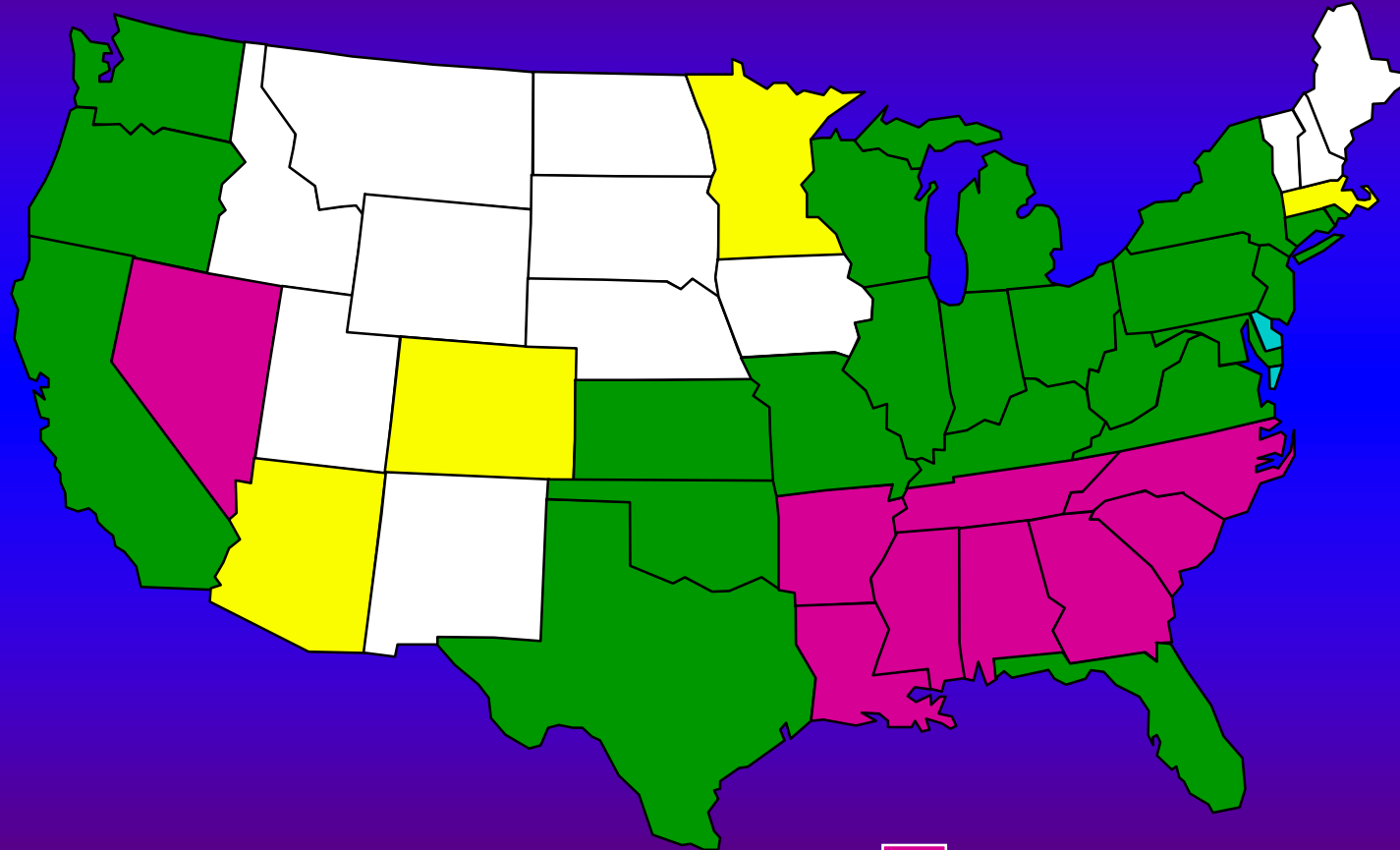
## African -Americans

- ◆ Stroke risk increased 1.5-2.5 times.
- ◆ Higher prevalence of hypertension.

## Hispanic - Americans

- ◆ Stroke occurs at younger age (about 6 years earlier than in whites).
- ◆ Small subcortical “lacunar” strokes are more frequent.
- ◆ Diabetes is an important risk factor.

# *The Stroke Belt: Stroke Mortality in Black Men*



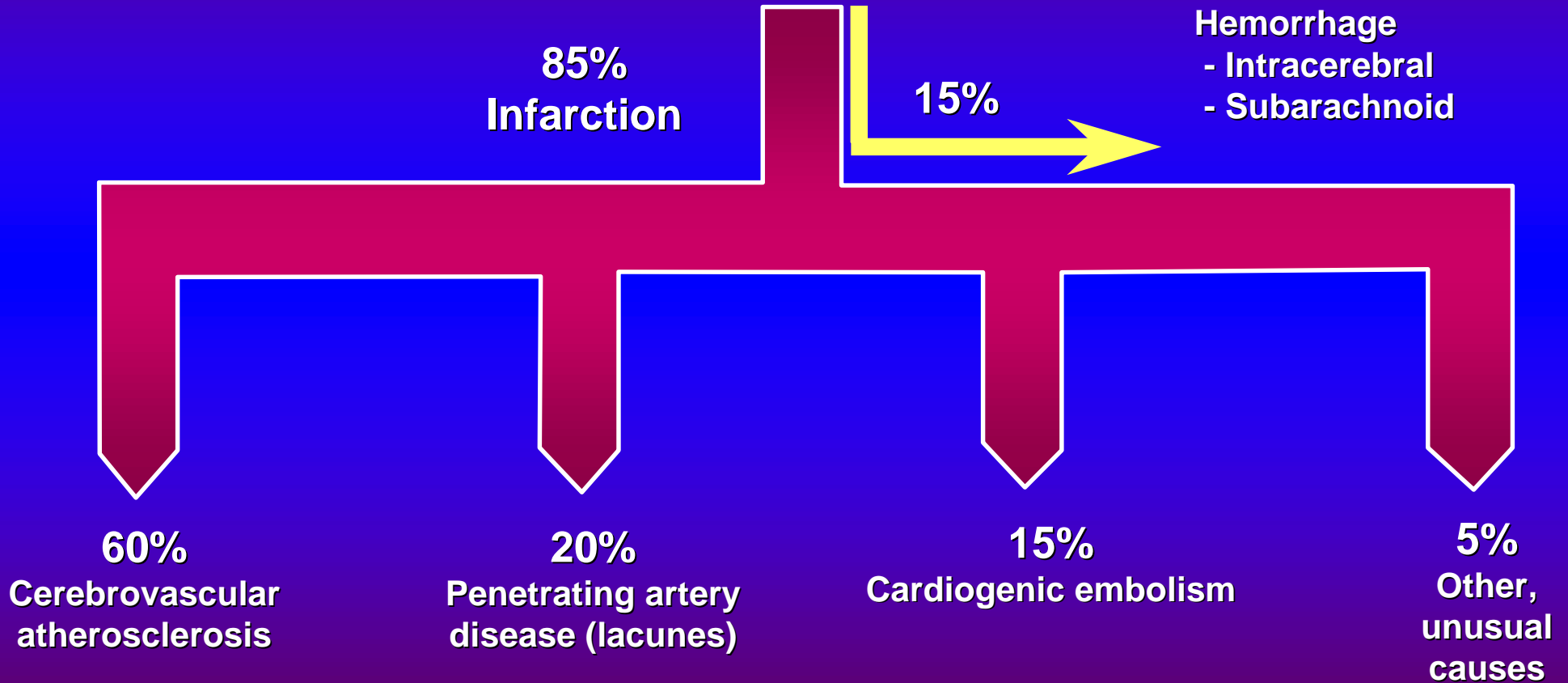
Yellow: Fewer than 80 deaths per 100,000 people

Green: 80 to 129.9 per 100,000

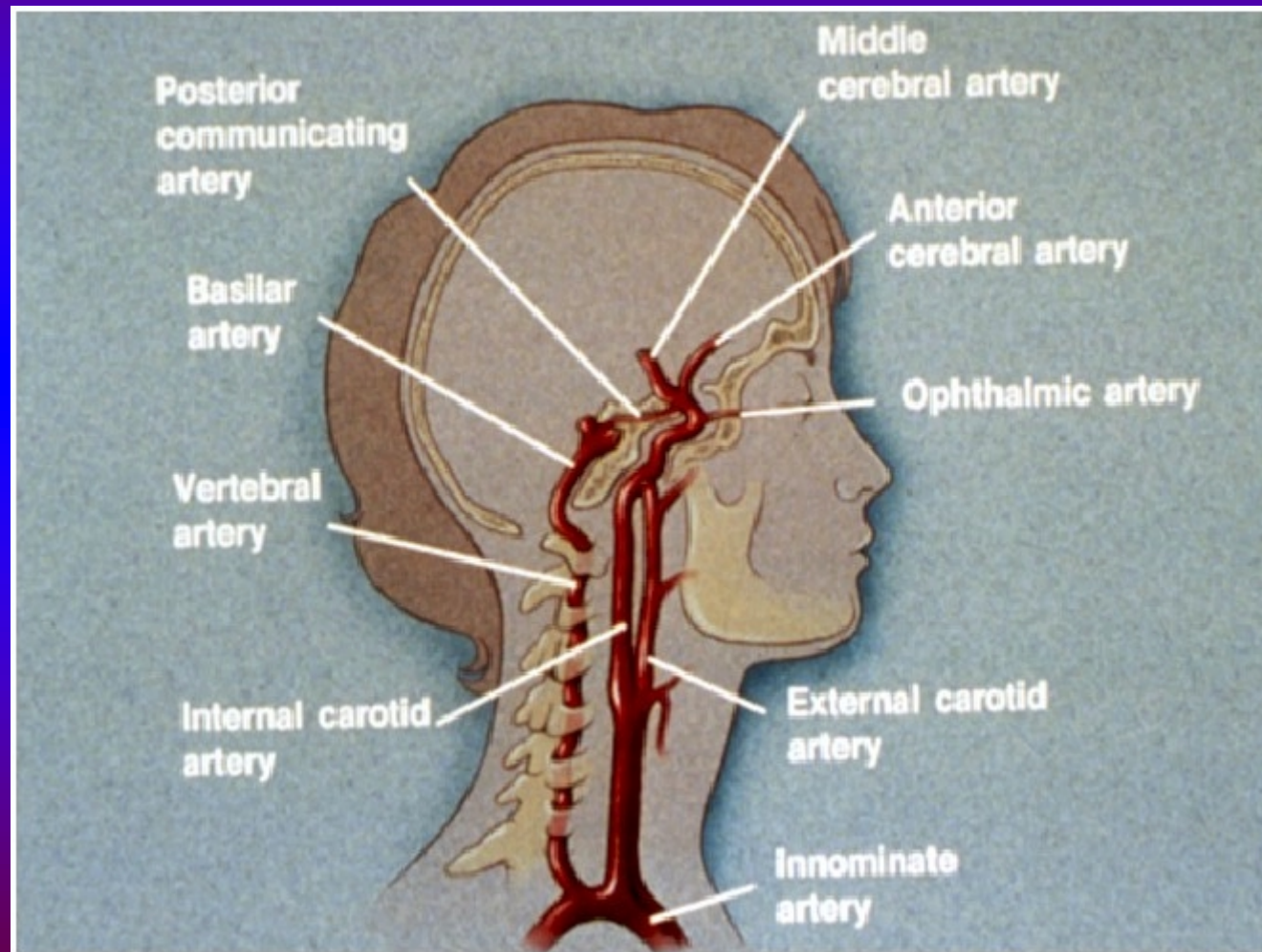
Pink: 130 or more per 100,000

White: No data or data unreliable

# *Causes of Stroke*

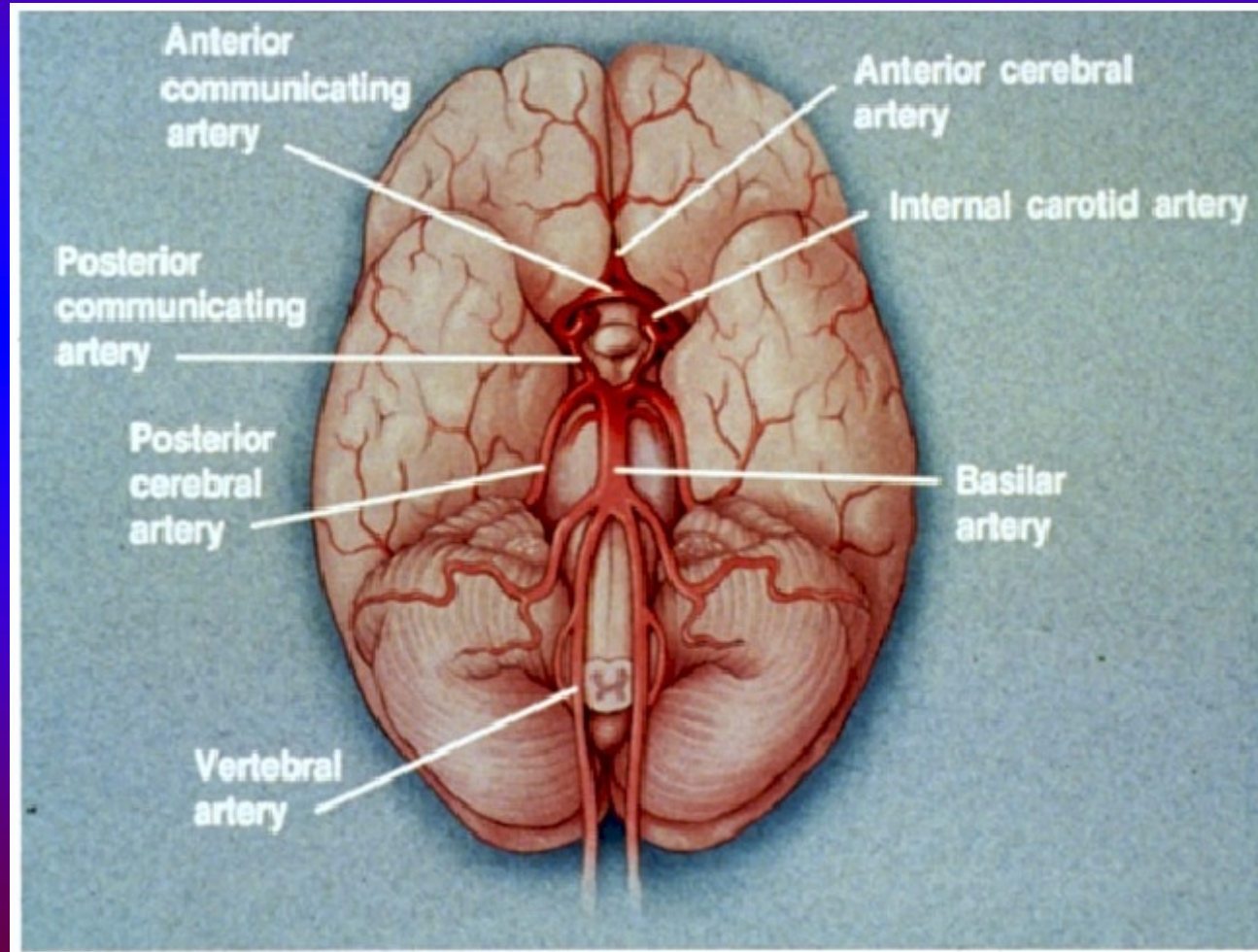


# *Cervical Carotid and Vertebral Arteries*

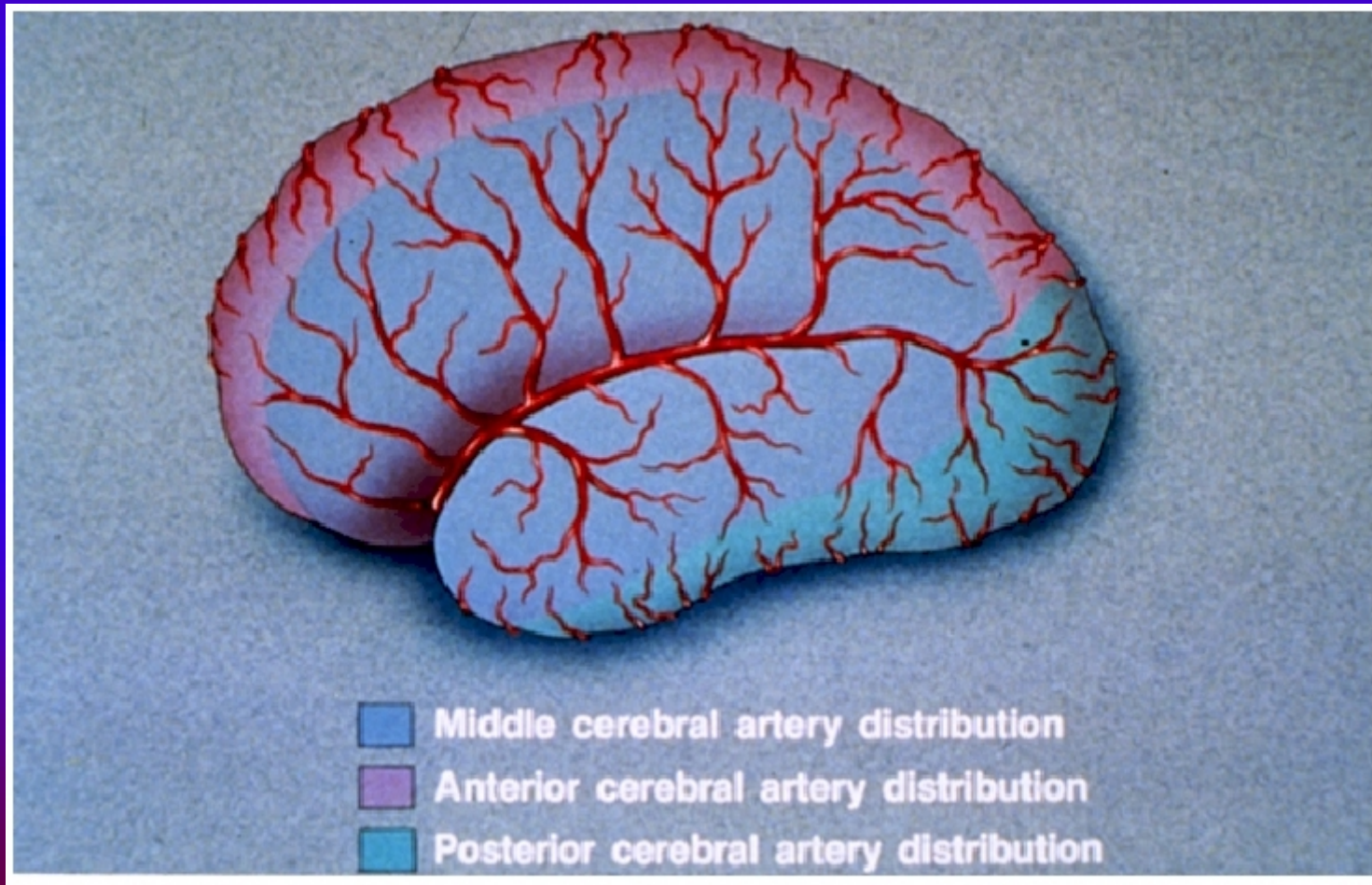




# *Circle of Willis: Key Collateral Circulation*

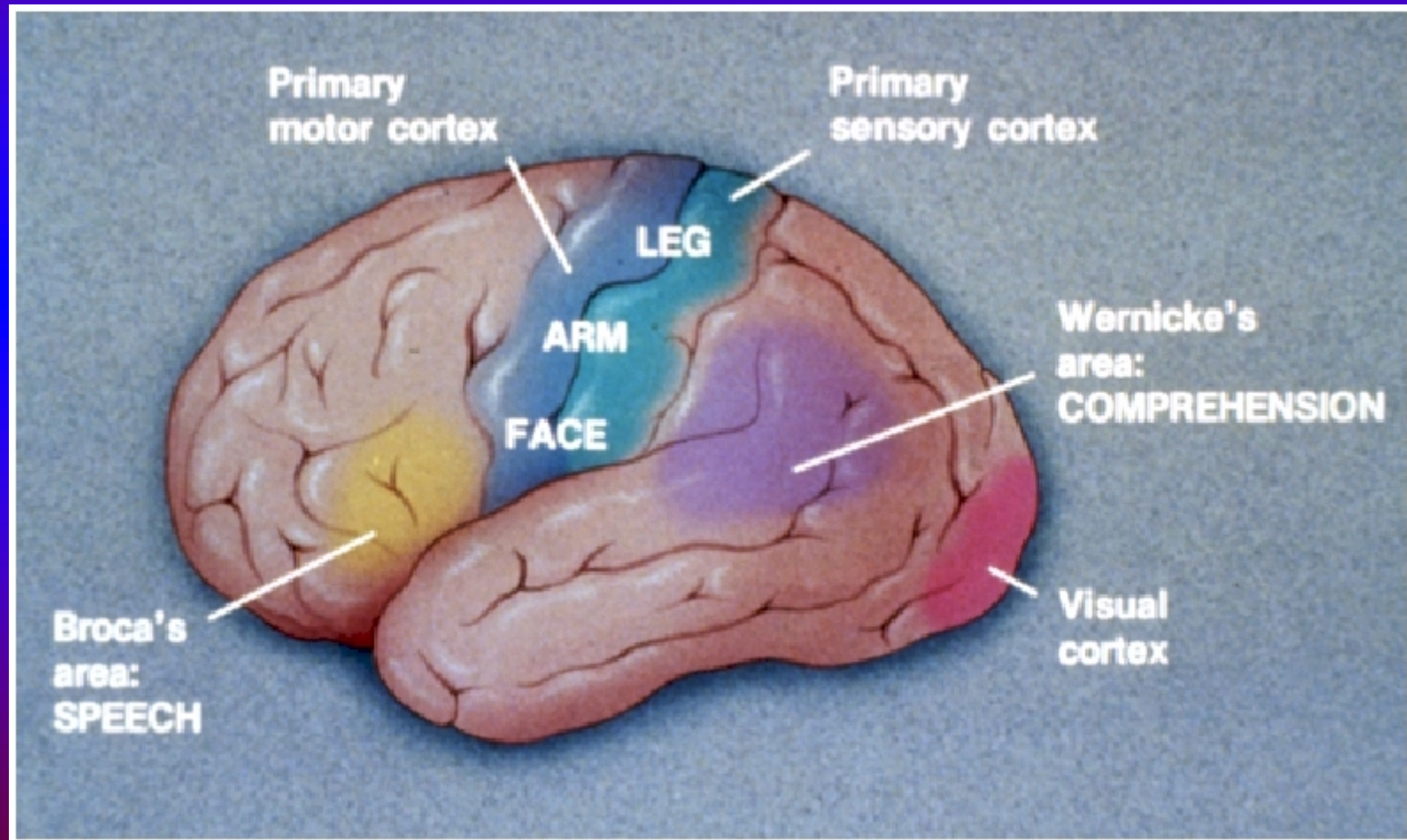


# *Vascular Territories of the Cerebral Hemisphere*

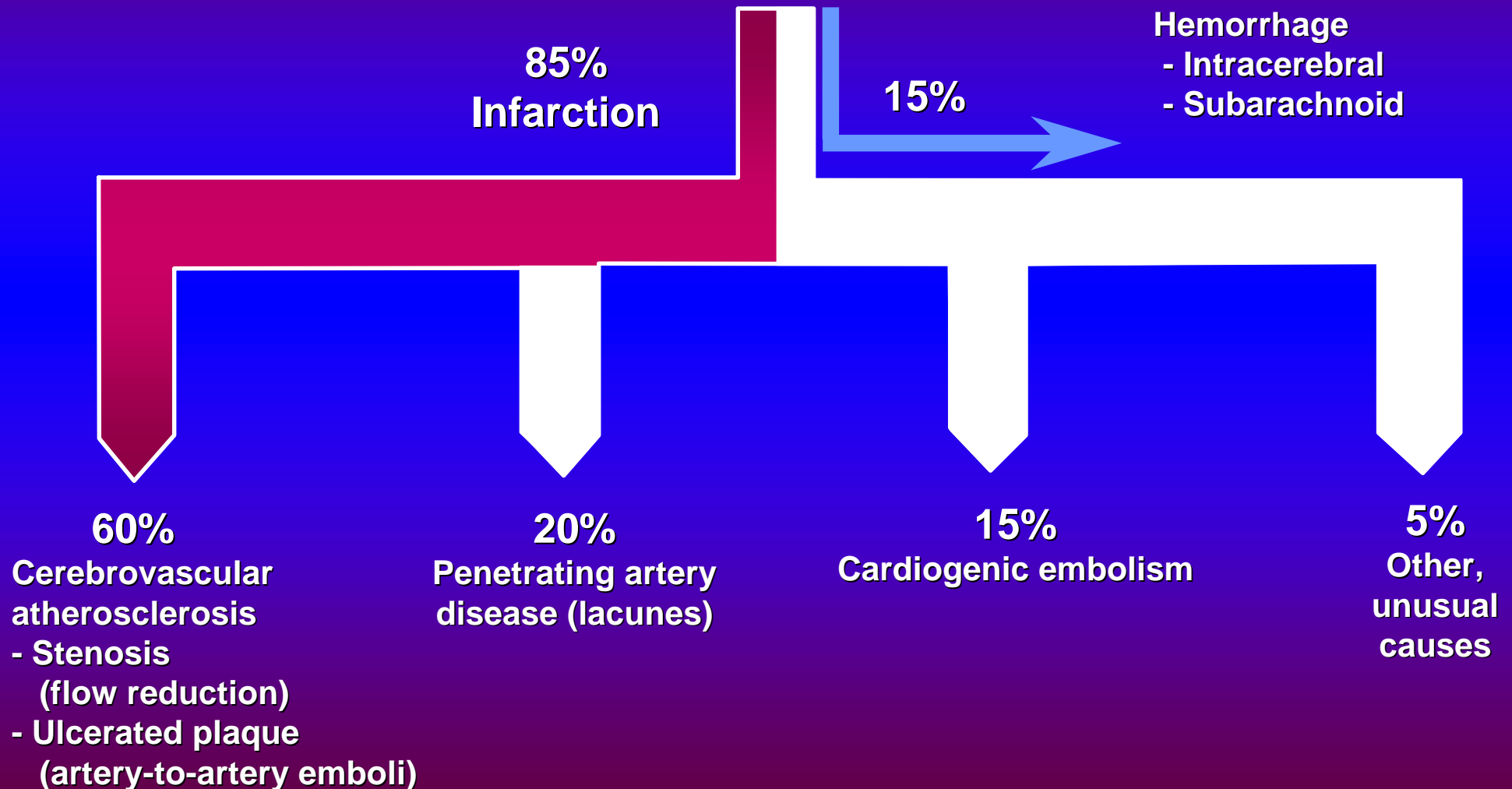




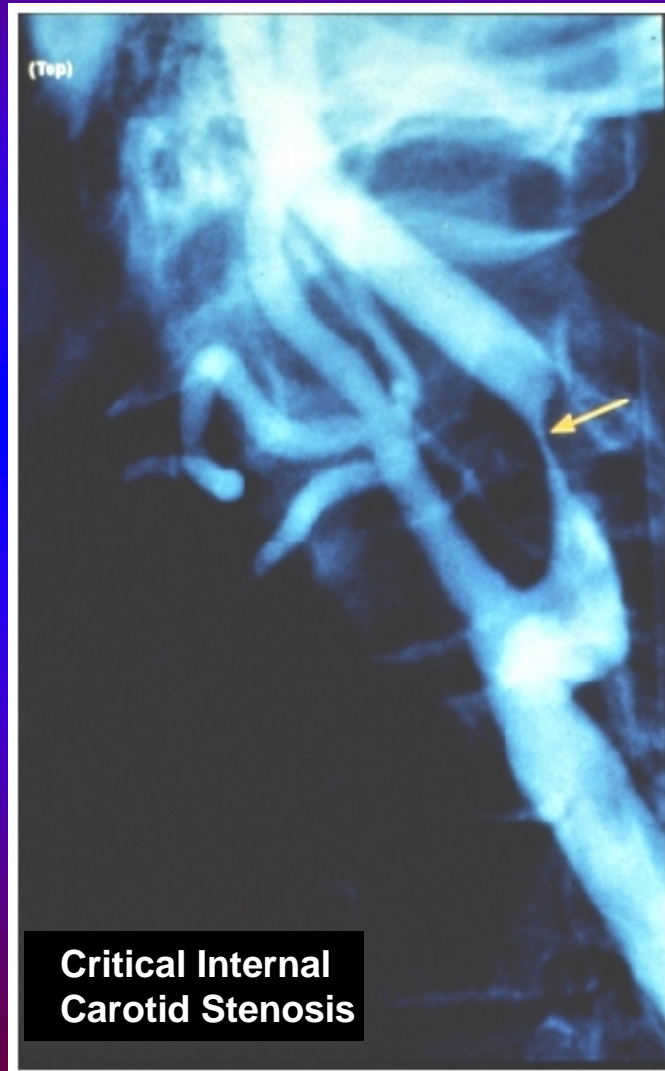
# *Functional Anatomy*



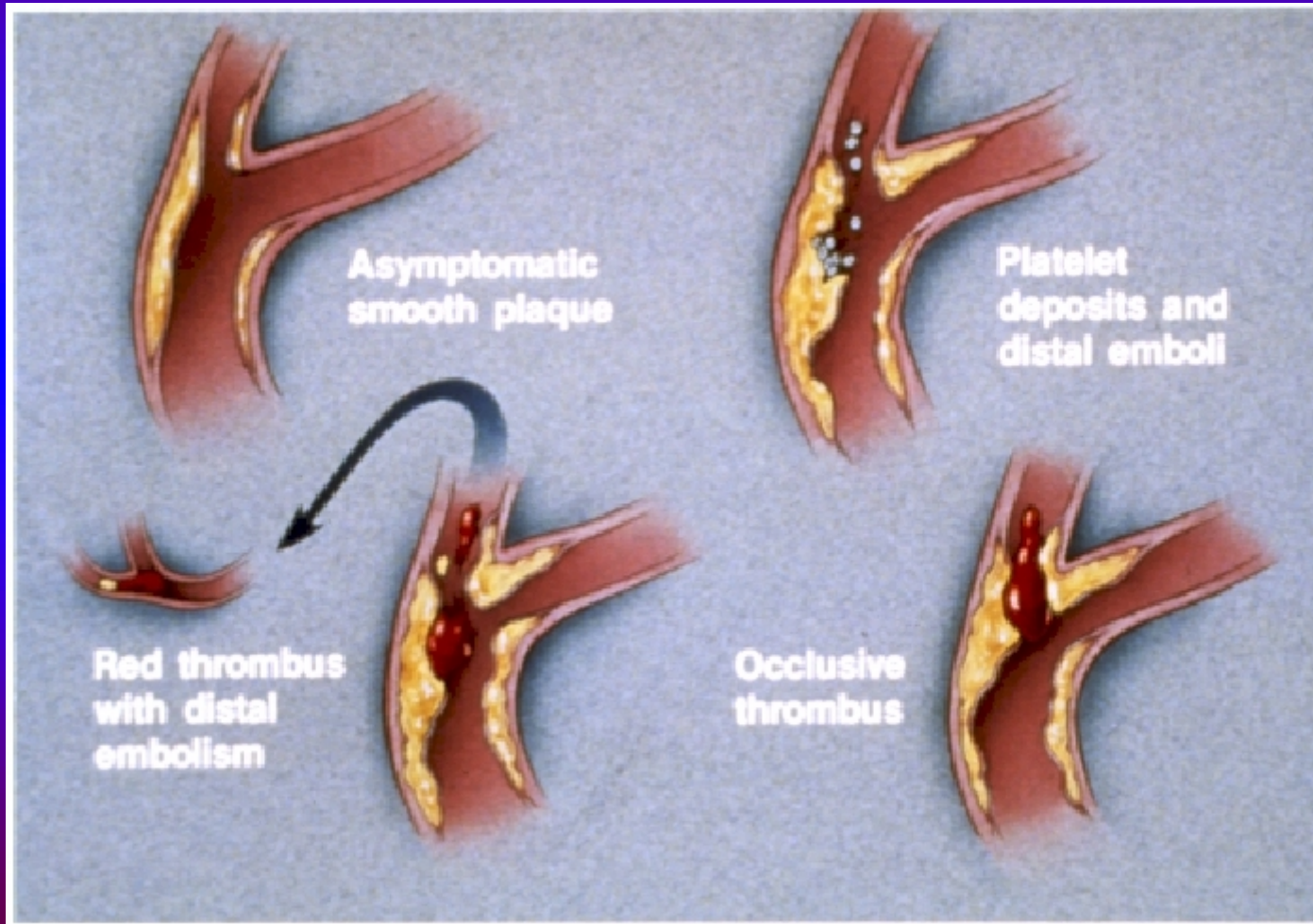
# *Causes of Stroke: Cerebrovascular Atherosclerosis*



# *Critical Internal Carotid Stenosis*

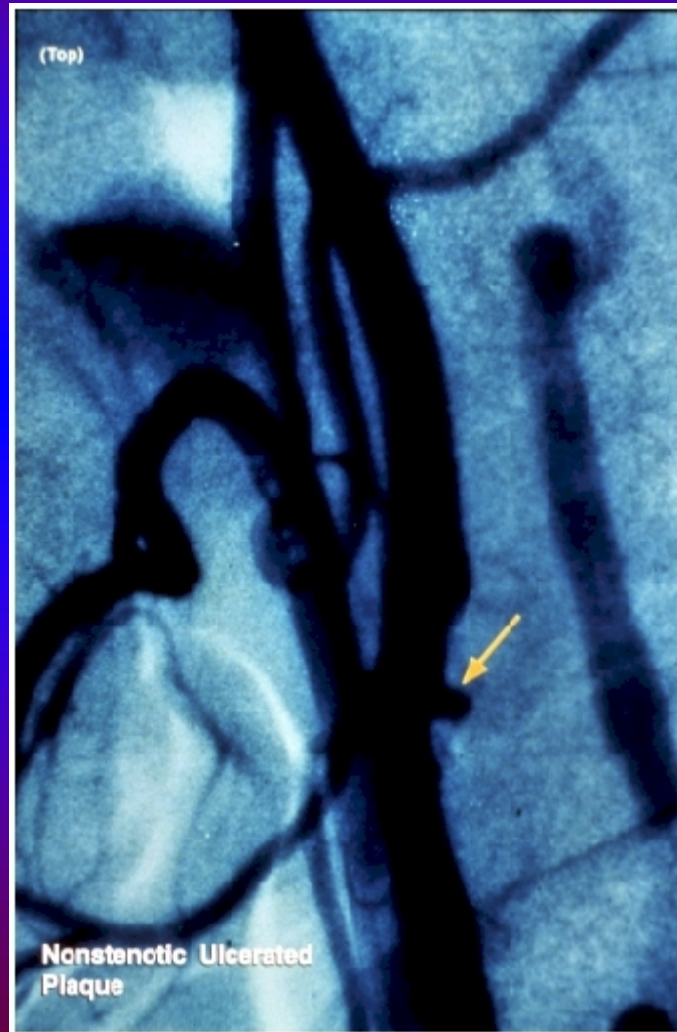


# *Mechanisms of Ischemia*

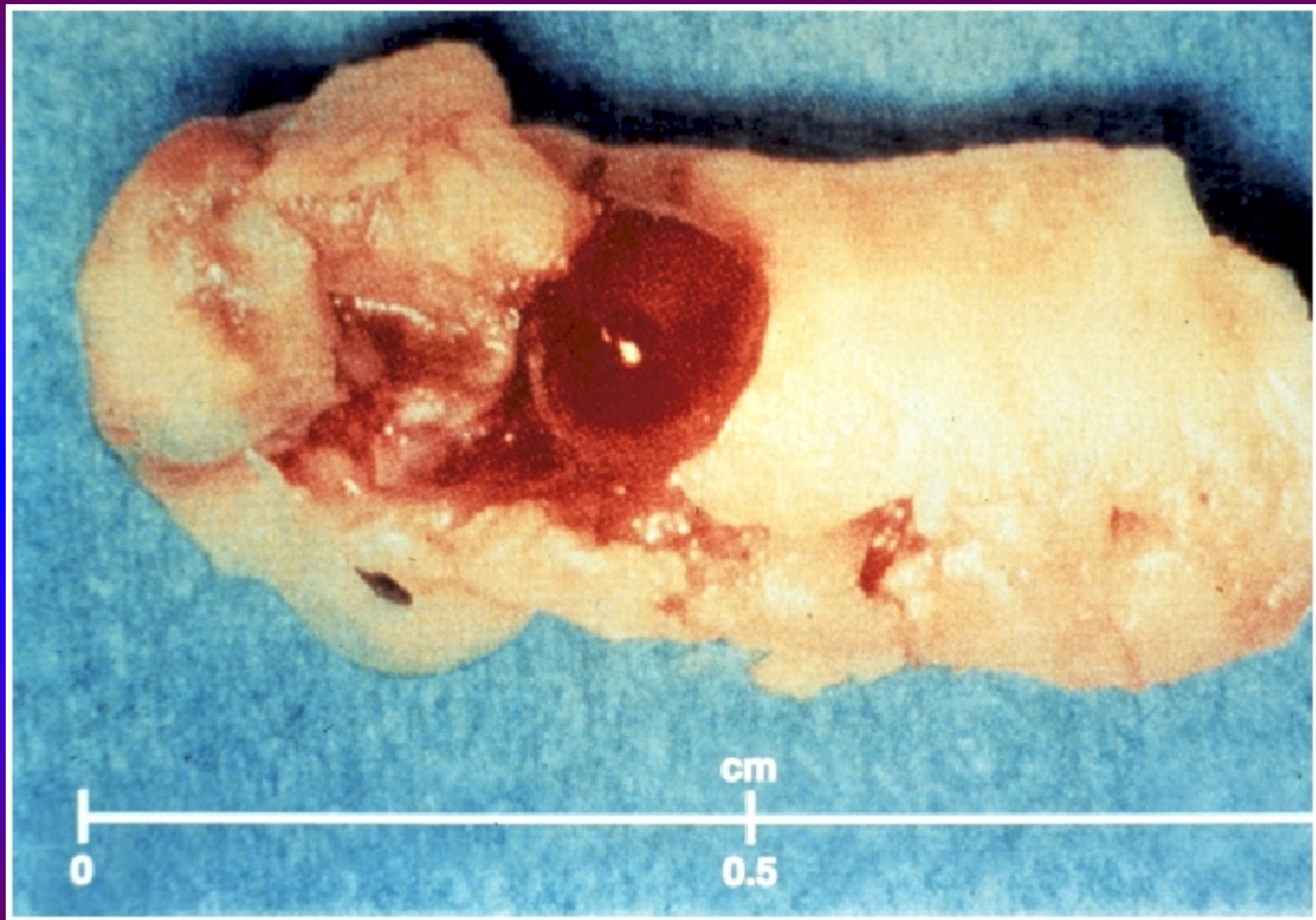




# *Nonstenotic Ulcerated Plaque*



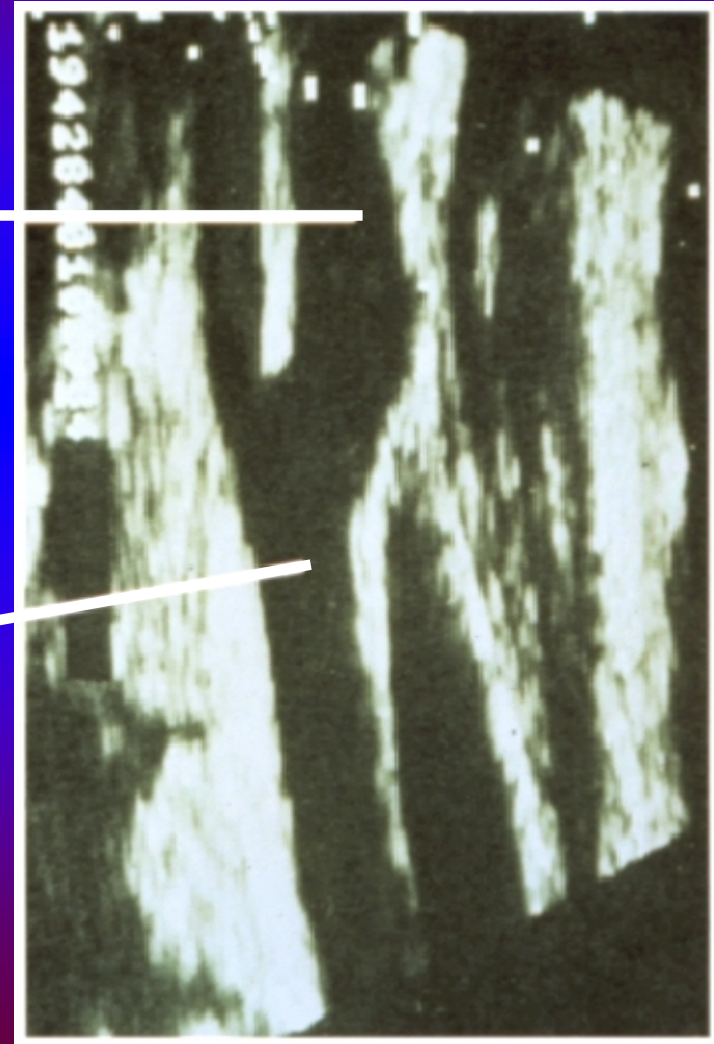




# *Carotid Ultrasound*

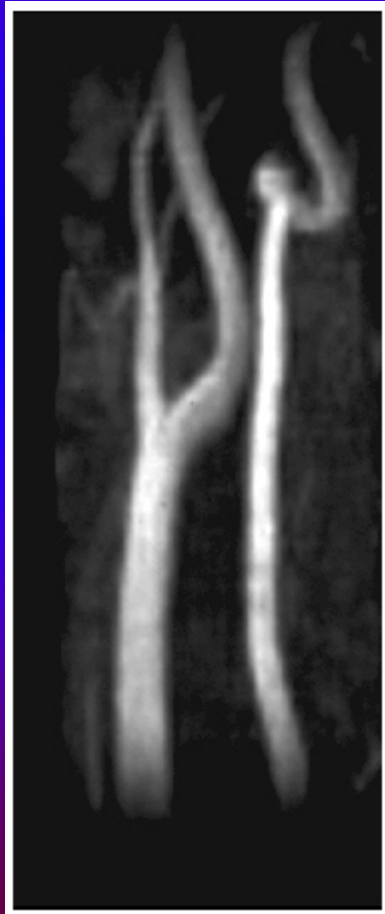
**Internal carotid  
artery**

**Common carotid  
artery**

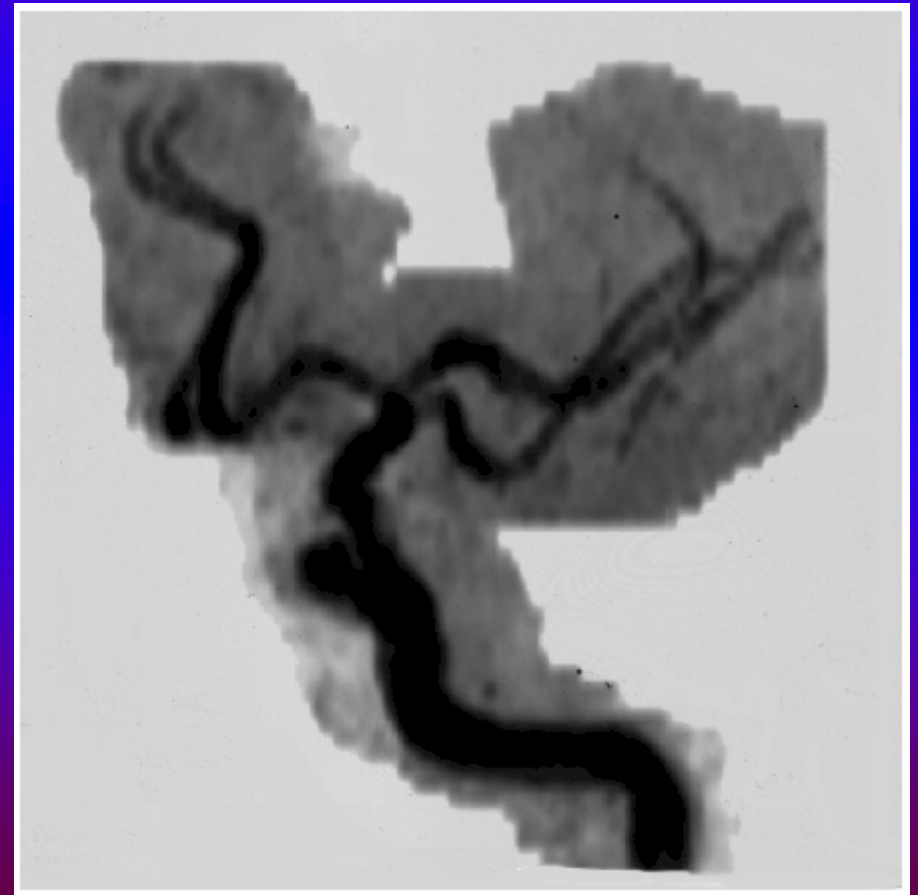


# *Magnetic Resonance Angiography (MRA)*

Cervical Carotid Artery



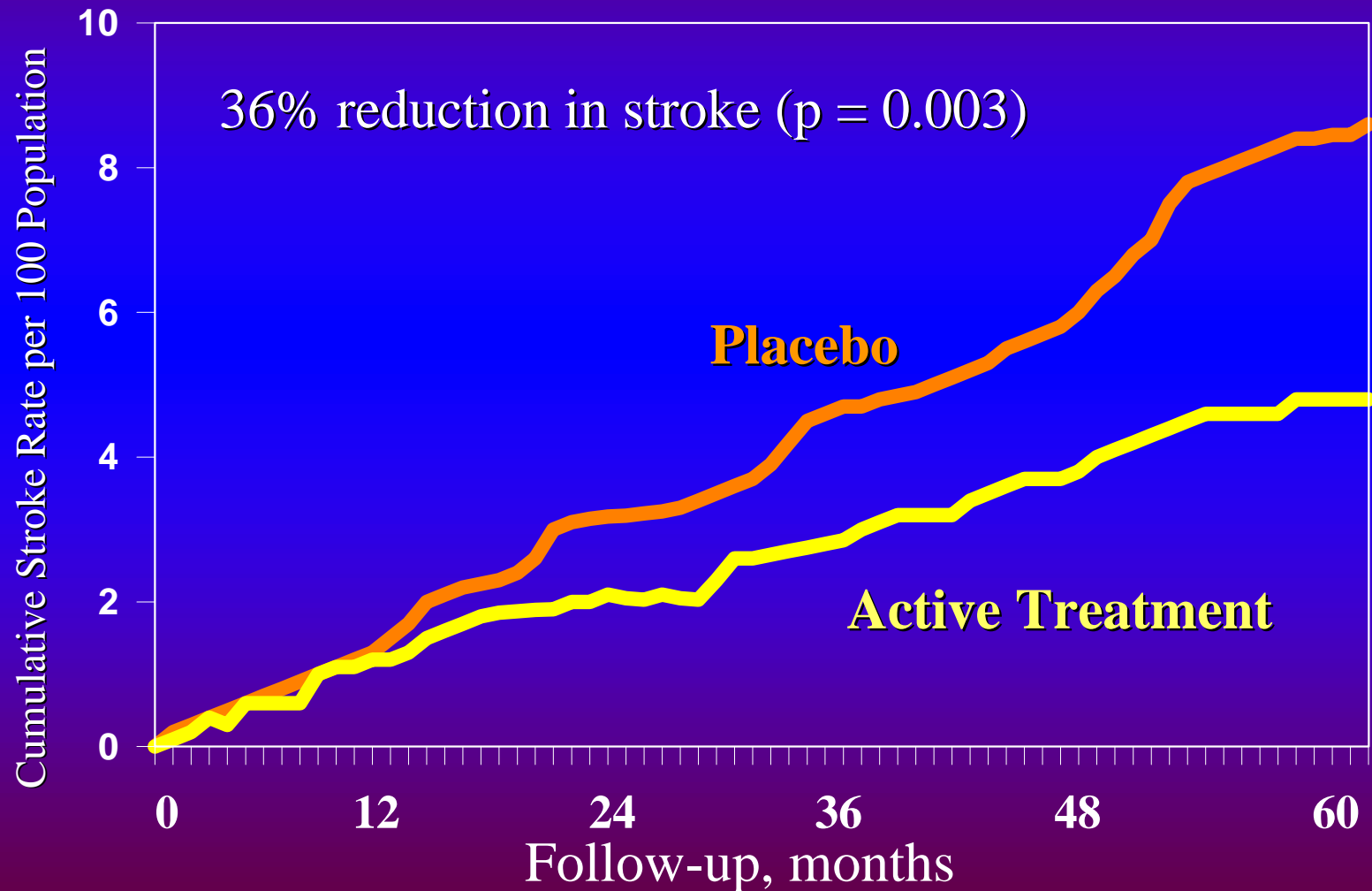
Middle Cerebral Artery



# *Major Risk Factors for Cerebrovascular Atherosclerosis*

<u>FACTOR</u>	<u>INCREASED RISK</u>
◆ Hypertension	X 5-10
◆ Smoking	X 2
◆ Diabetes	X 2
◆ Hyperlipidemia	X 1.5
◆ Obesity	X 1.5

# *Reduction in Stroke in SHEP*

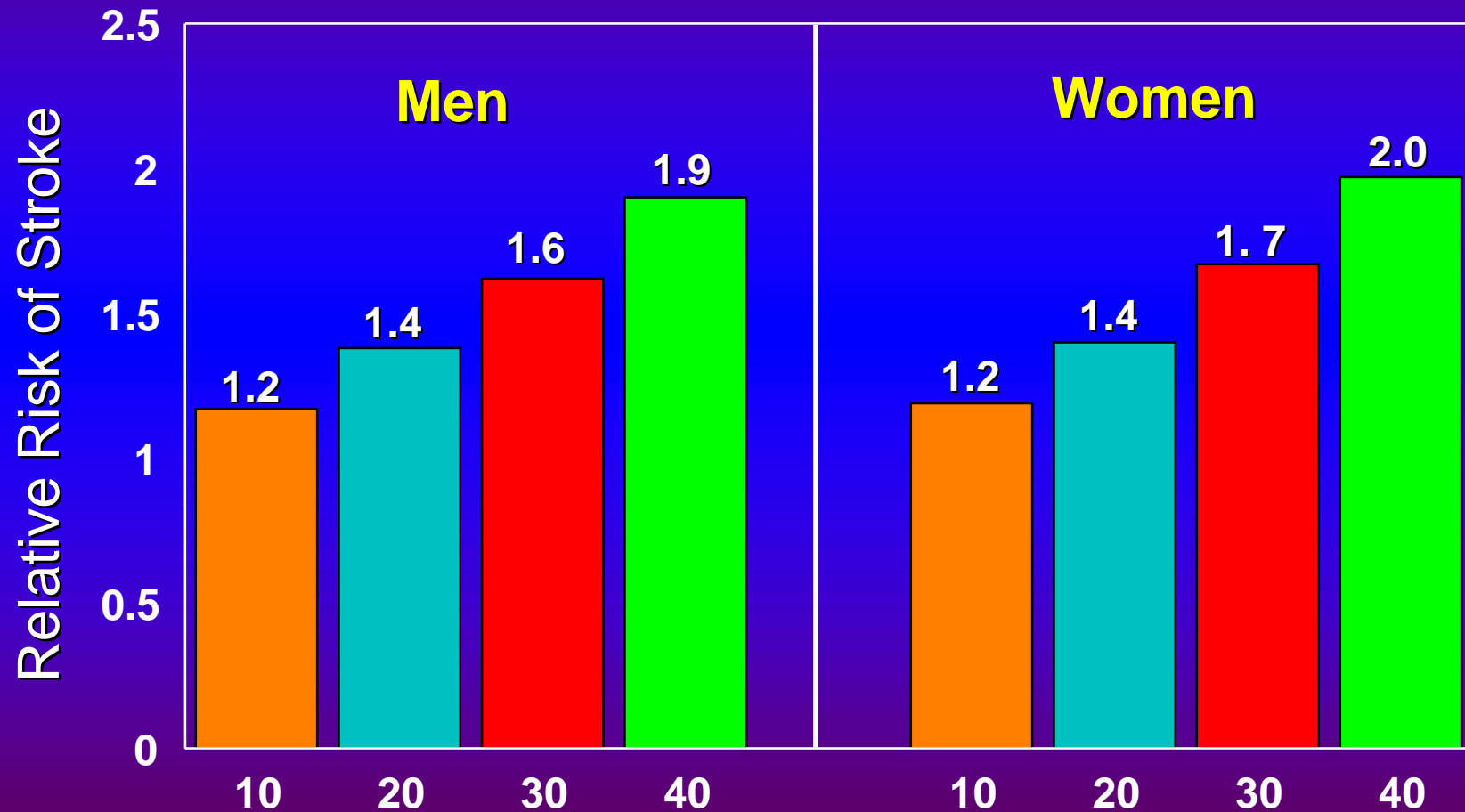




## *Therapeutic Goals for Antihypertensive Rx*

<u>Condition</u>	<u>Goal BP</u>
◆ Uncomplicated	140/90
◆ Diabetic	135/85
◆ African-American	135/85

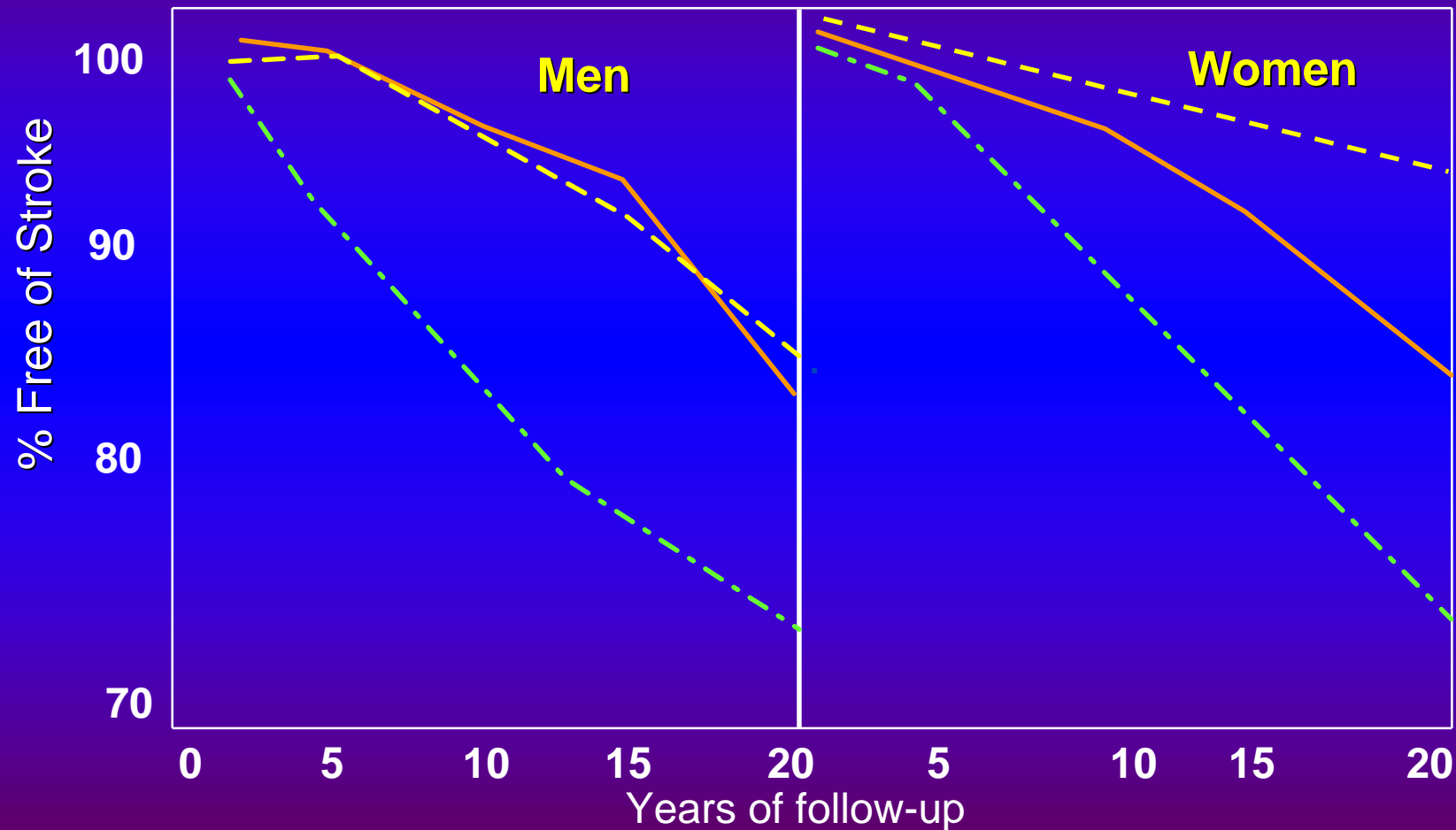
# *Stroke Risk in Smokers*



Framingham Data  
JAMA 259:1025, 1988

No. of Cigarettes Smoked/day

# *Stroke Free Survival in Smokers, Nonsmokers and Former Smokers*



Survival free of stroke in cigarette smokers (dotted line), nonsmokers (solid line), and former smokers (dashed line), aged 60 years, using Cox proportional hazard regression model, in men and women

## *Stroke Facts in Diabetes*

- ◆ Stroke risk 2 X higher
- ◆ Hypertension more prevalent in diabetics
- ◆ Strokes occur at younger age
- ◆ Risk of death after stroke 2 X higher
- ◆ Recovery from stroke less complete

# *Lipid Lowering and Stroke Prevention: Summary*

Recent clinical trials of “statins”:

- ◆ Reduces stroke by 30% in patients with MI and angina .
- ◆ Reversed progression of plaque by ultrasound in early asymptomatic carotid disease.
- ◆ Effective in “low-risk” (0.5%/yr stroke rate) patients with modestly elevated cholesterol; not yet tested in high risk patients.

Lipid lowering with “statins” seems sensible to reduce stroke for those with atherosclerotic cerebrovascular disease and LDL cholesterol >130 mg%.



# *Transient Ischemic Attack (TIA)*

- ◆ “Warning strokes:” transient focal ischemia
- ◆ Duration: <24 hrs (usually 5 to 10 minutes)
- ◆ May occur with any cause of ischemic stroke
- ◆ TIA patients have 10 times the risk of ischemic stroke:
  - Risk highest in first 3 months after TIA
  - 35% stroke risk with 3-5 years after TIA
- ◆ An opportunity to prevent stroke

# *Common Manifestations of TIA*

## Carotid system TIA

- ◆ Unilateral weakness
- ◆ Unilateral sensory symptoms
- ◆ Aphasia
- ◆ Monocular vision loss

## Vertebrobasilar system TIA

- ◆ Bilateral weakness
- ◆ Bilateral sensory symptoms

- ◆ Diplopia
  - ◆ Vertigo
  - ◆ Ataxia without weakness
  - ◆ Dysphagia
- only in combination; not as isolated symptoms

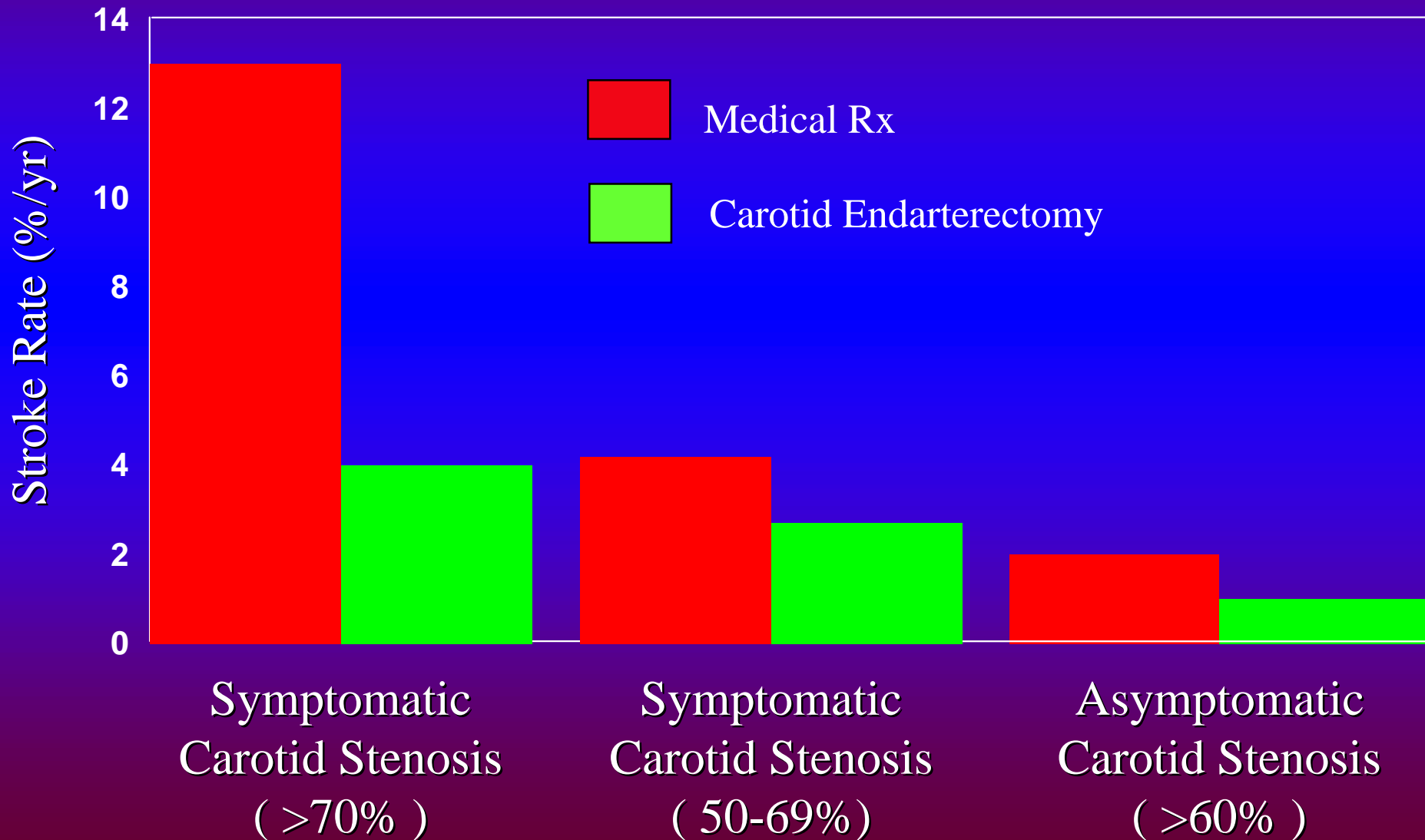
# *Established Therapies to Reduce Stroke Due to Cerebrovascular Atherosclerosis*

- ◆ Control of risk factors  
(especially hypertension, lipids, smoking)
- ◆ Antiplatelet agents
  - aspirin
  - ticlopidine / clopidogrel
- ◆ Carotid endarterectomy (selected patients)

## ***Antiplatelet Therapies for Stroke Prevention***

<b>Agent</b>	<b>Mechanism</b>	<b>Daily Dose</b>	<b>Comment</b>
Aspirin	Cyclo-oxygenase inhibition	50-1500 mg	25% stroke reduction
Ticlopidine	ADP receptor blockade	250 mg bid	35% stroke reduction; expensive, rash, diarrhea, leukopenia (1%)
Clopidogrel	ADP receptor blockade	75 mg	30% stroke reduction; non-toxic
Dipyridamole (with aspirin)	Phosphodiesterase inhibition	200 mg bid (25 mg bid)	35-40% stroke reduction; headache in 6%

# *Effect of Carotid Endarterectomy in Carotid Stenosis: Symptomatic vs. Asymptomatic*



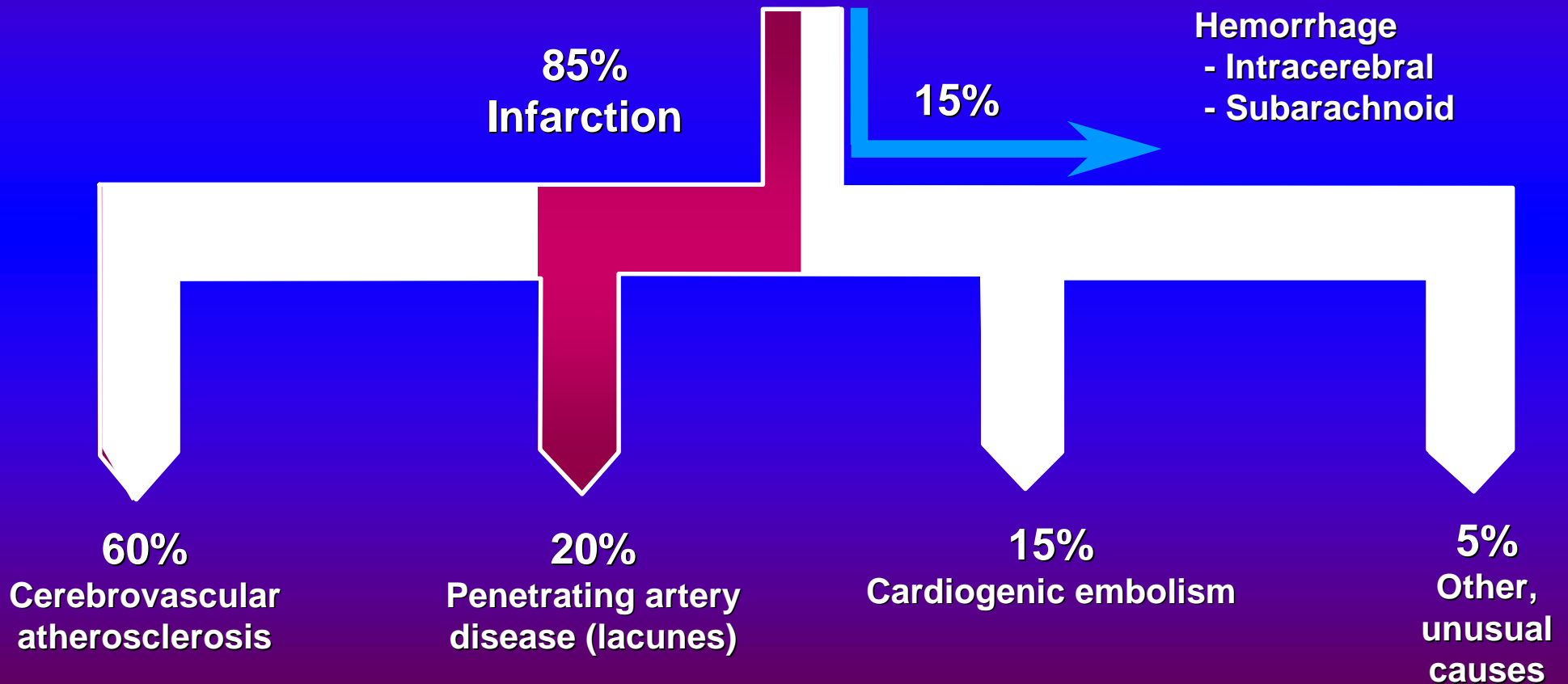


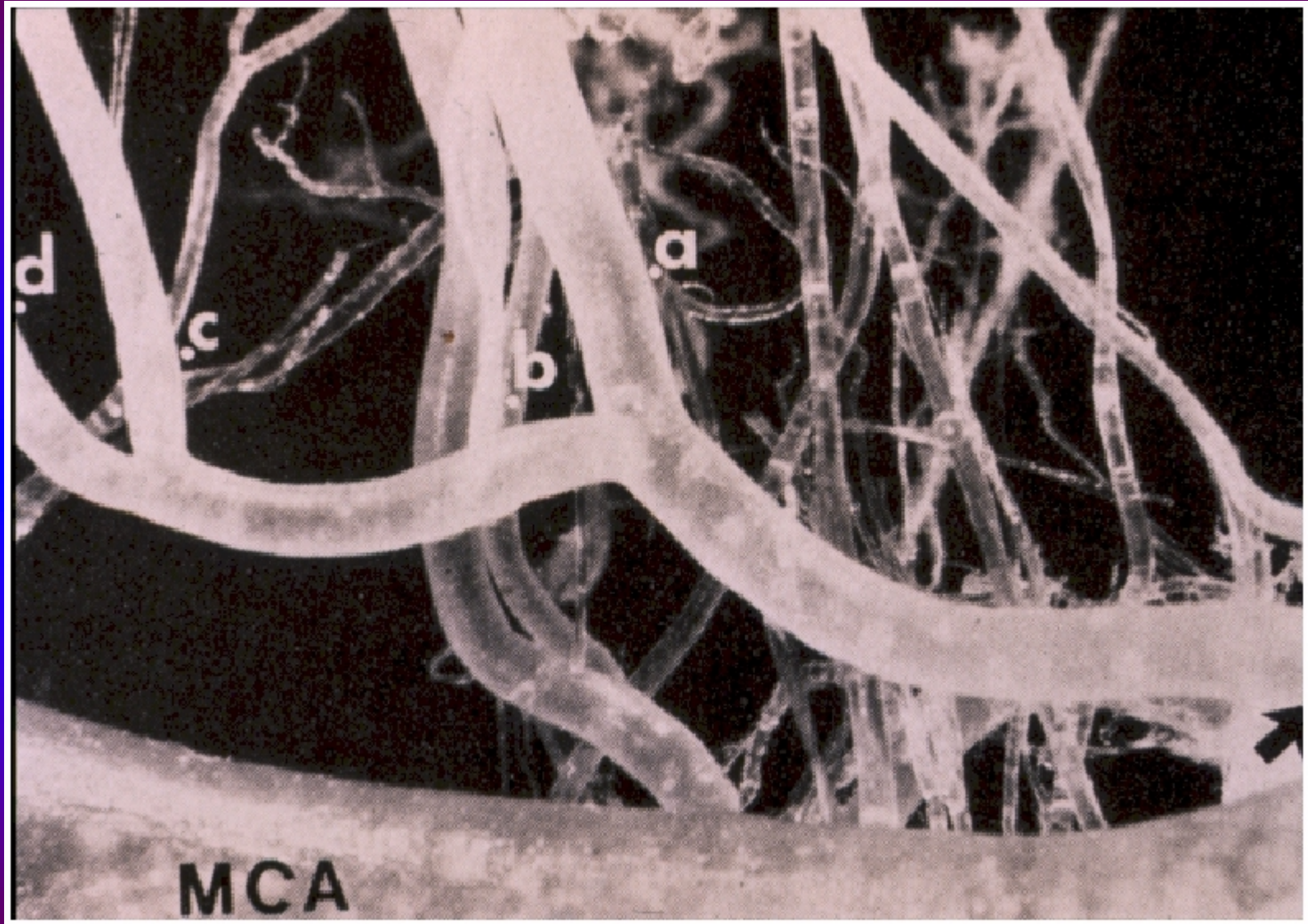
# *Carotid Endarterectomy for Stroke*

## *Prevention: Summary*

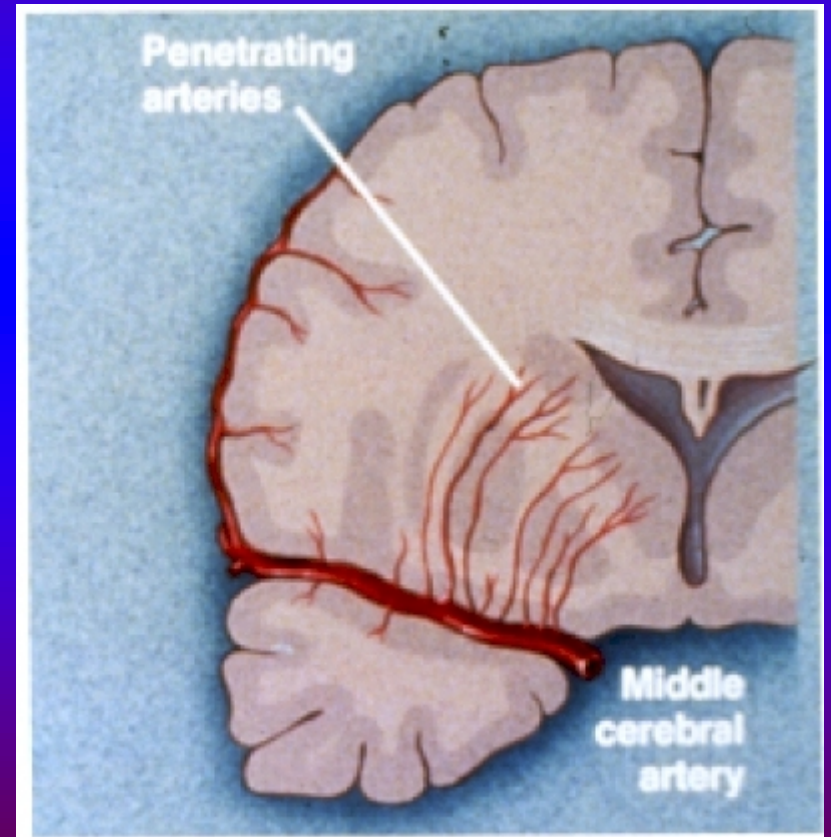
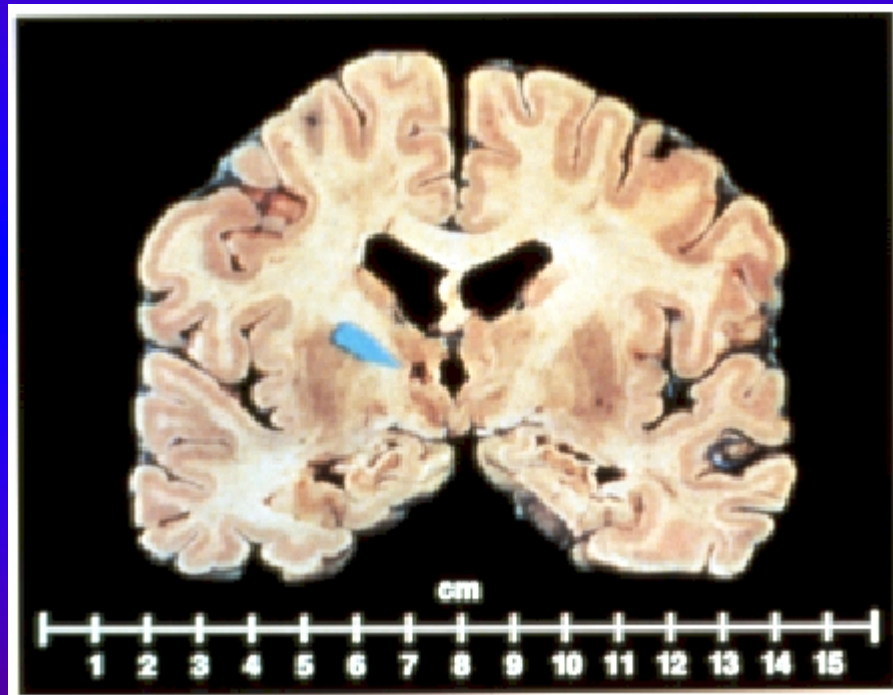
- ◆ Benefit is established for high-grade ( $\geq 70\%$ ) symptomatic carotid stenosis.
- ◆ Value in moderate (50-69%) symptomatic stenosis is modest and similar to that for asymptomatic carotid stenosis.
- ◆ Reduces stroke in asymptomatic carotid stenosis, but magnitude of benefit is small (1%/yr).
- ◆ Whether catheter arteriography should routinely precede endarterectomy is controversial.
- ◆ Role of carotid angioplasty/stenting undergoing evaluation in trials.

# *Causes of Stroke:* *Penetrating Artery Disease (Lacunes)*

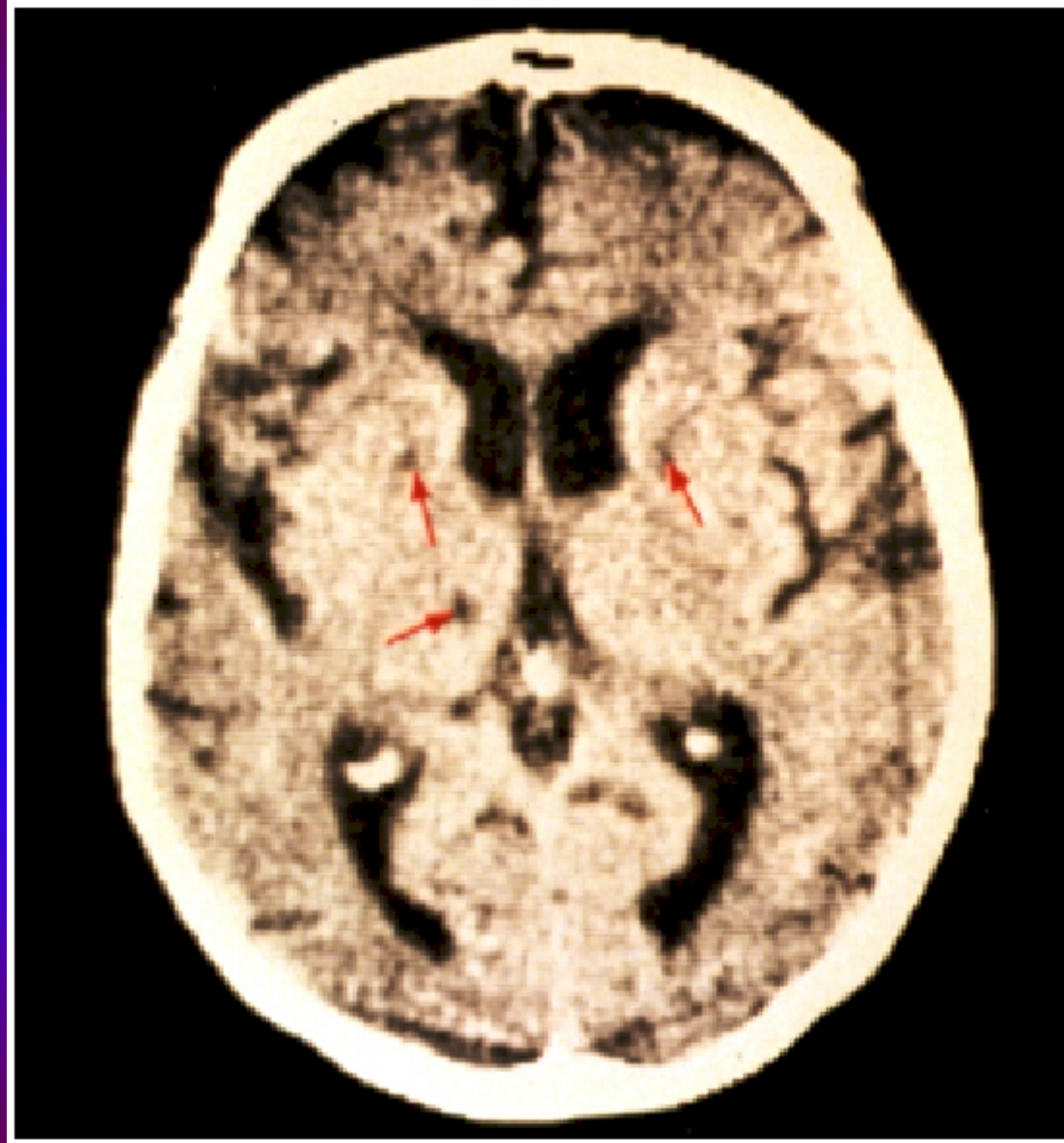




# *Lacunar Stroke*





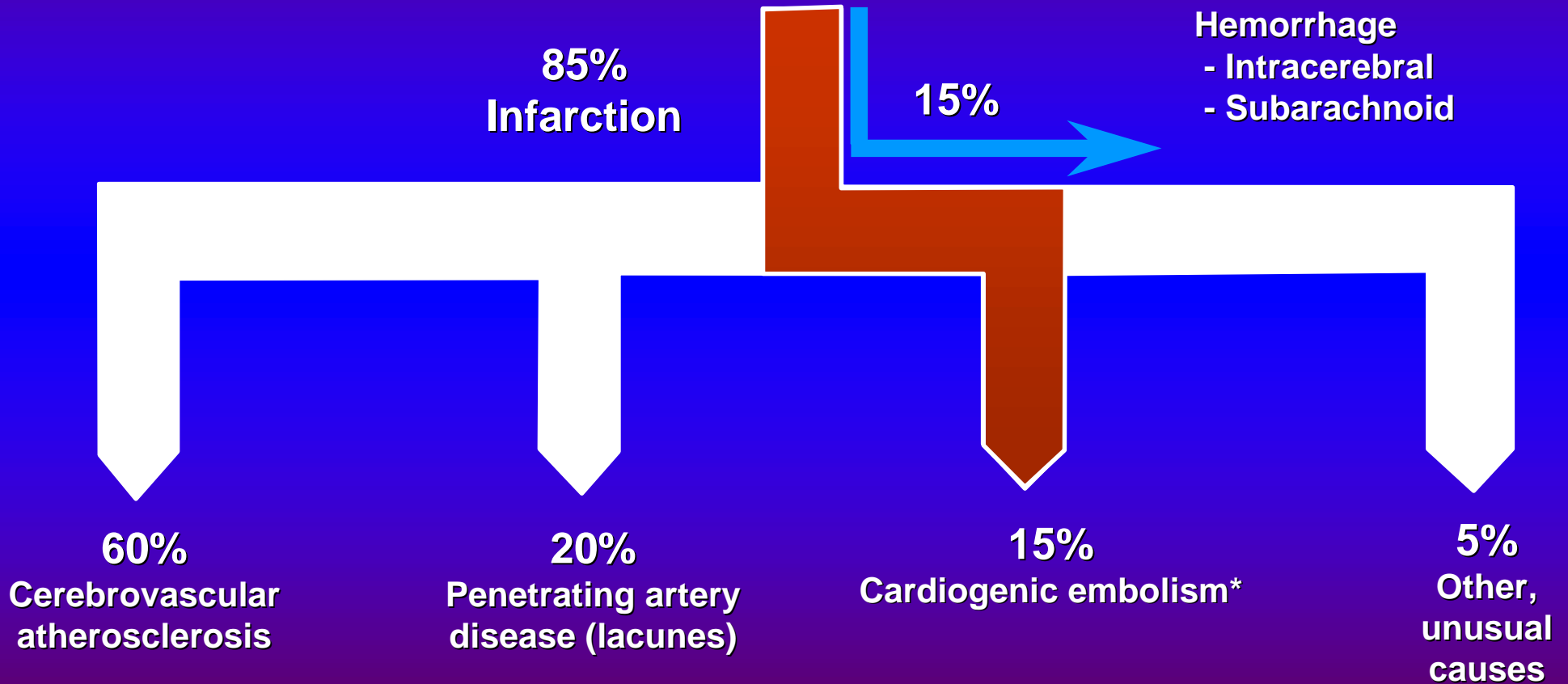




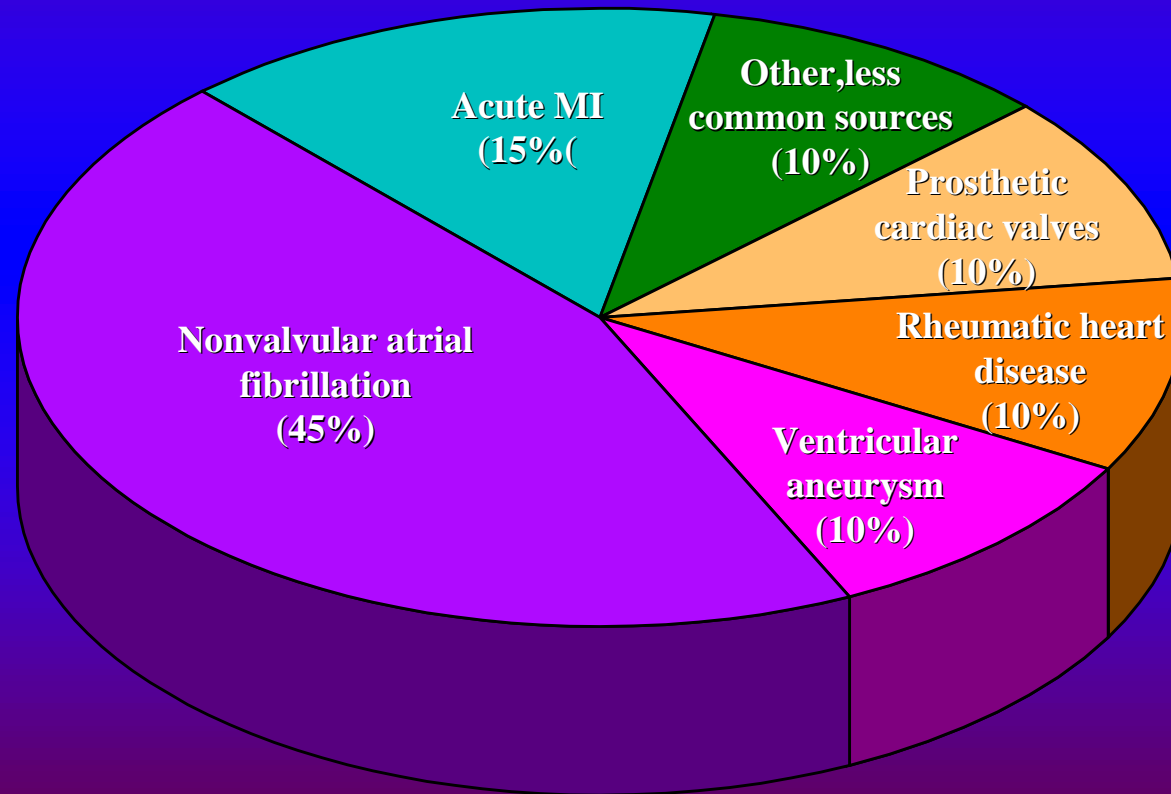
## *Lacunar Infarcts (Small Subcortical Strokes): Summary*

- ◆ Diagnosis: Clinical syndrome (e.g., pure motor or pure sensory) plus CT/MRI confirmation
- ◆ Risk factor management: Hypertension, diabetes
- ◆ Carotid stenosis: Present in only 10%
- ◆ Rate of occurrence: High (10% yr)
- ◆ Antiplatelet agents probably effective

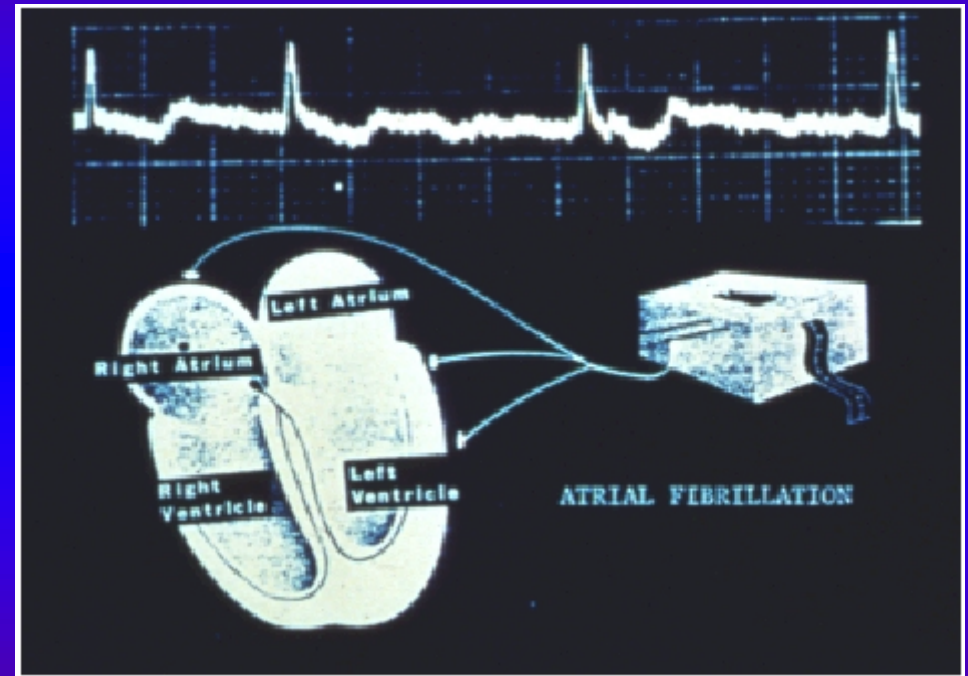
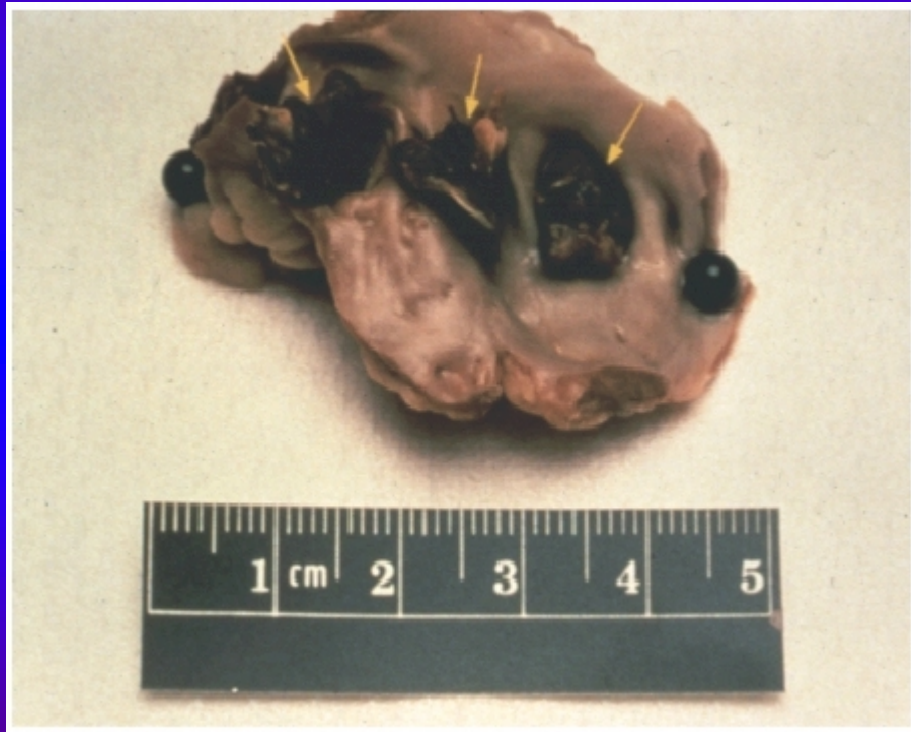
# *Causes of Stroke: Cardiogenic Embolism*



# *Sources of Cardiogenic Embolism*



# *Atrial Fibrillation (AF) Predisposes to Stroke*

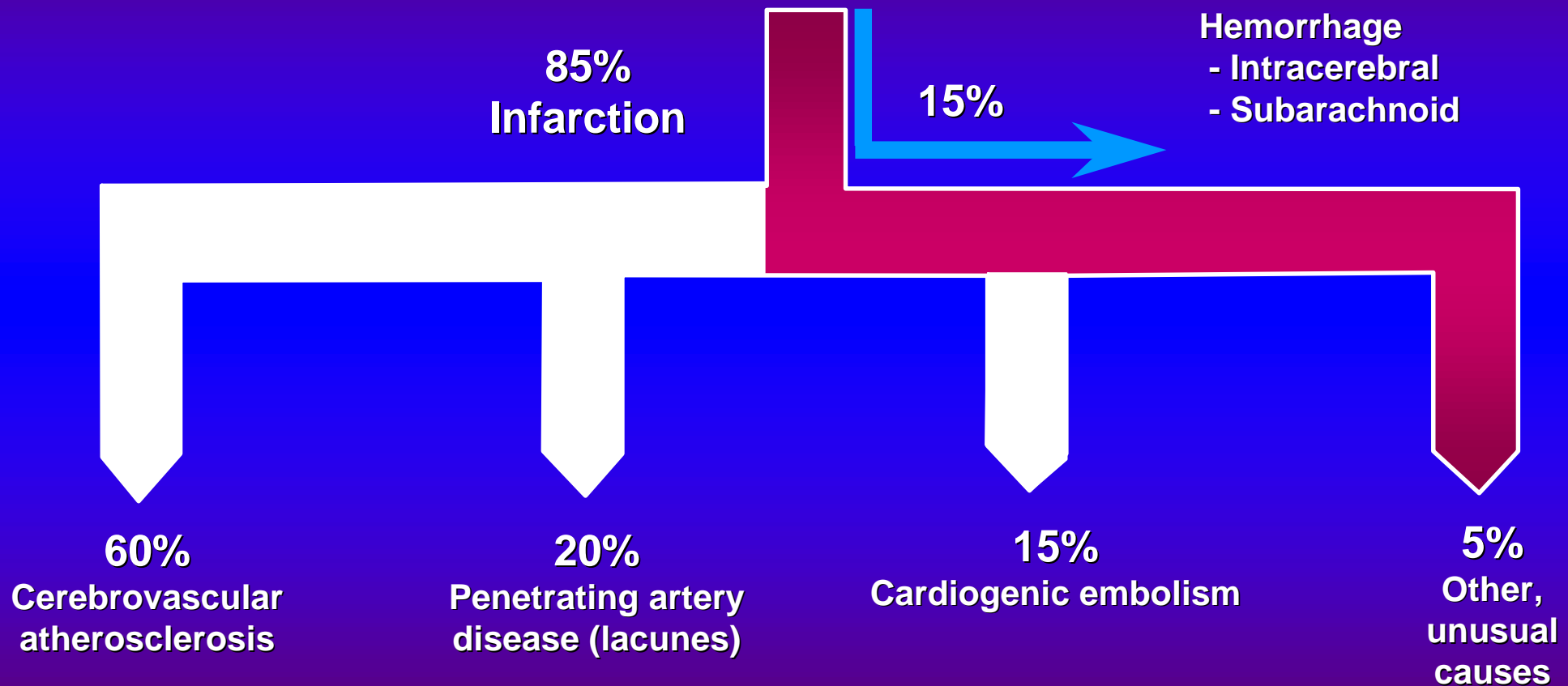


# *Stroke Prevention in Atrial Fibrillation*

- ◆ Mean Onset Age 64, > 2 Million People
- ◆ 35% Have Stroke During Lifetime
- ◆ 5% /Yr Stroke Rate
- ◆ >75,000 Strokes/Yr in U.S.

AF is a marker of 2 million Americans with a six-fold increased risk of stroke.

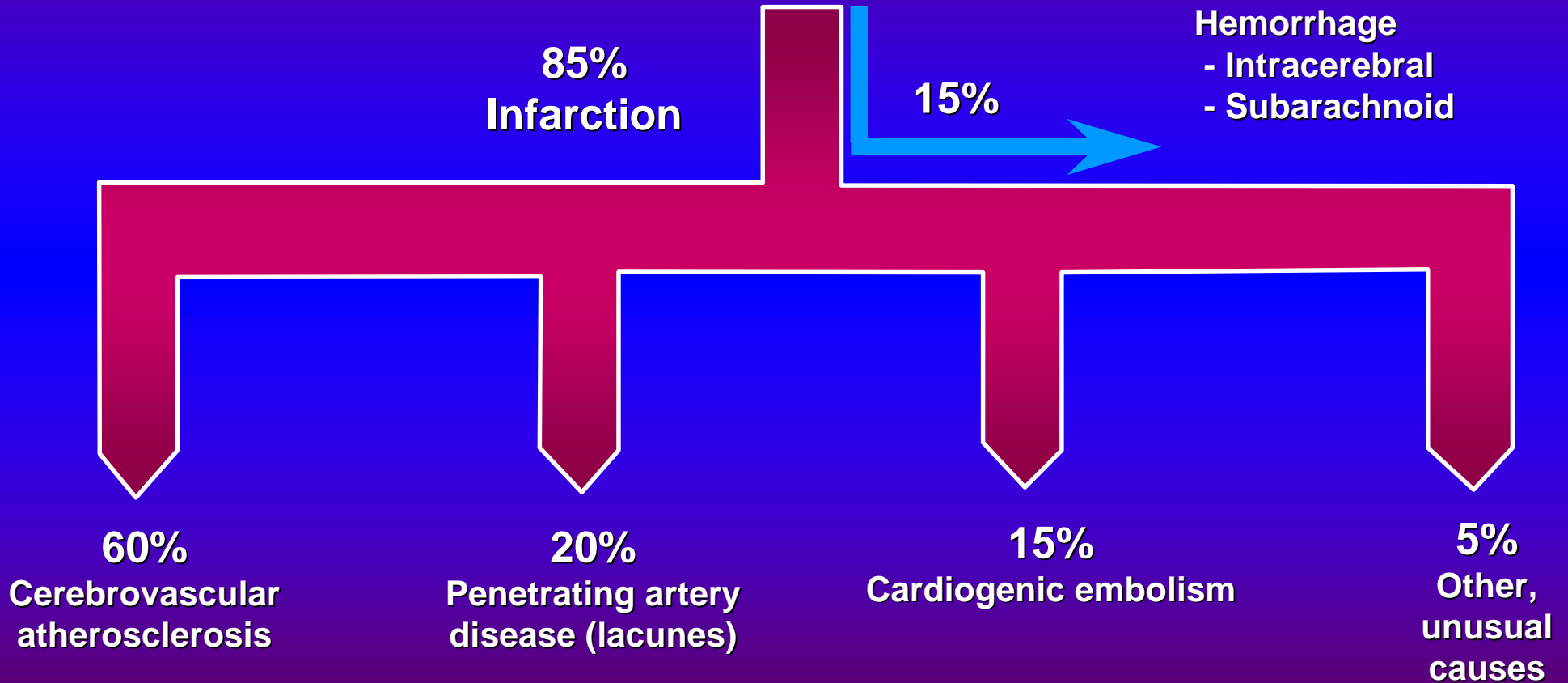
# *Stroke: Other, Unusual Causes*



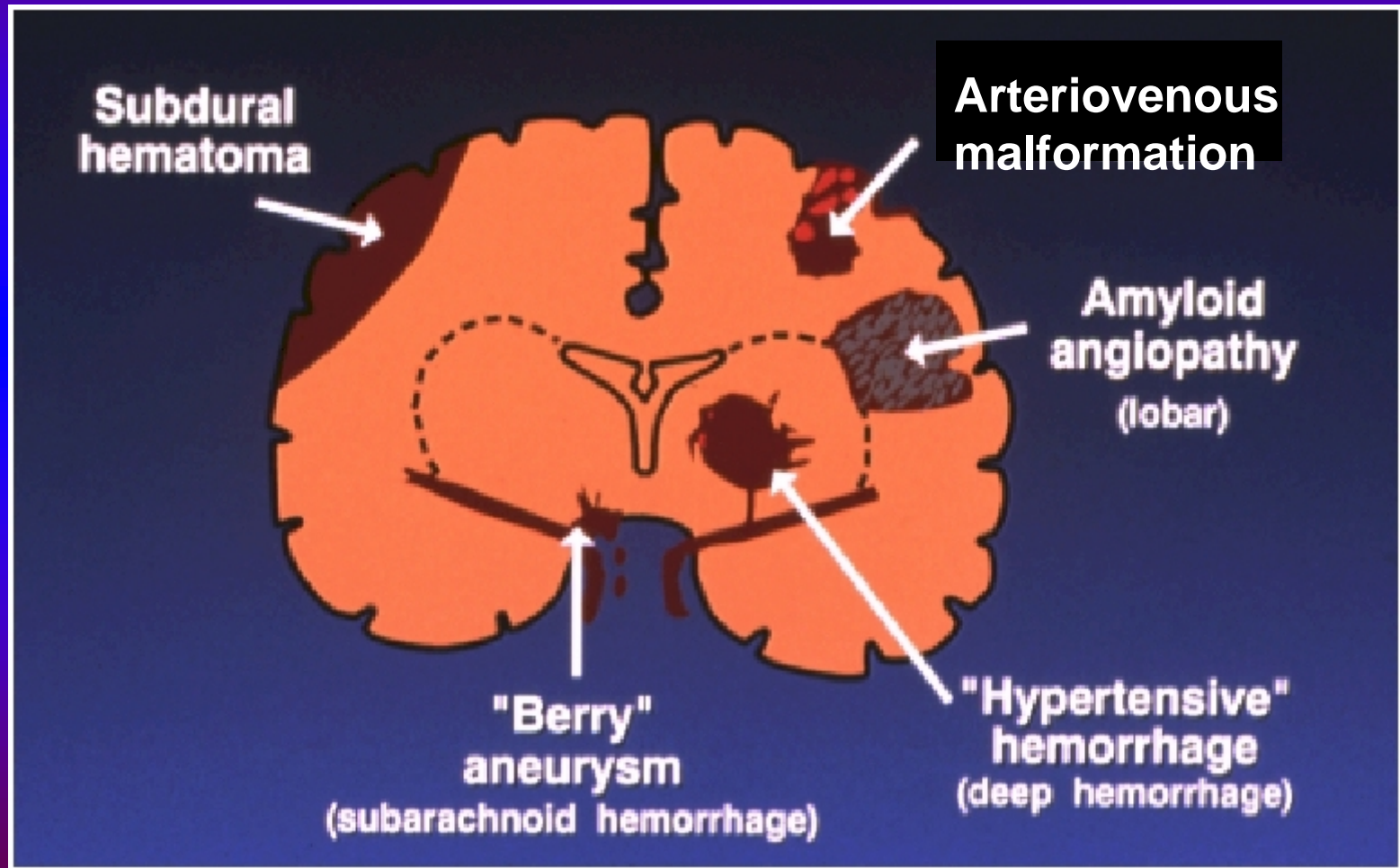
\*Dissection, migraine, oral contraceptive use in smokers, meningovascular syphilis, cocaine and amphetamine use, associated with prothrombotic states (e.g., sickle cell anemia)



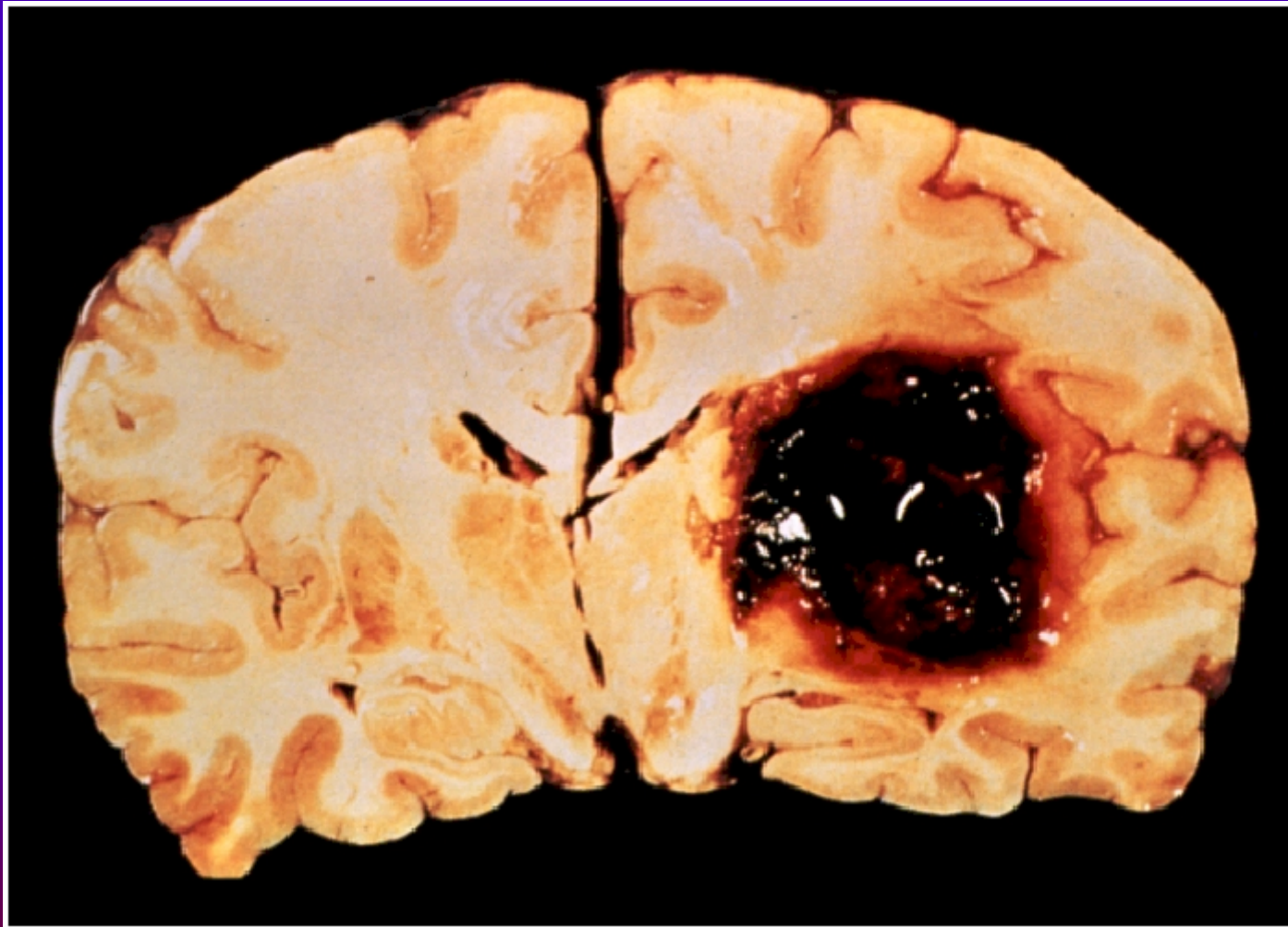
# *Hemorrhagic Stroke*



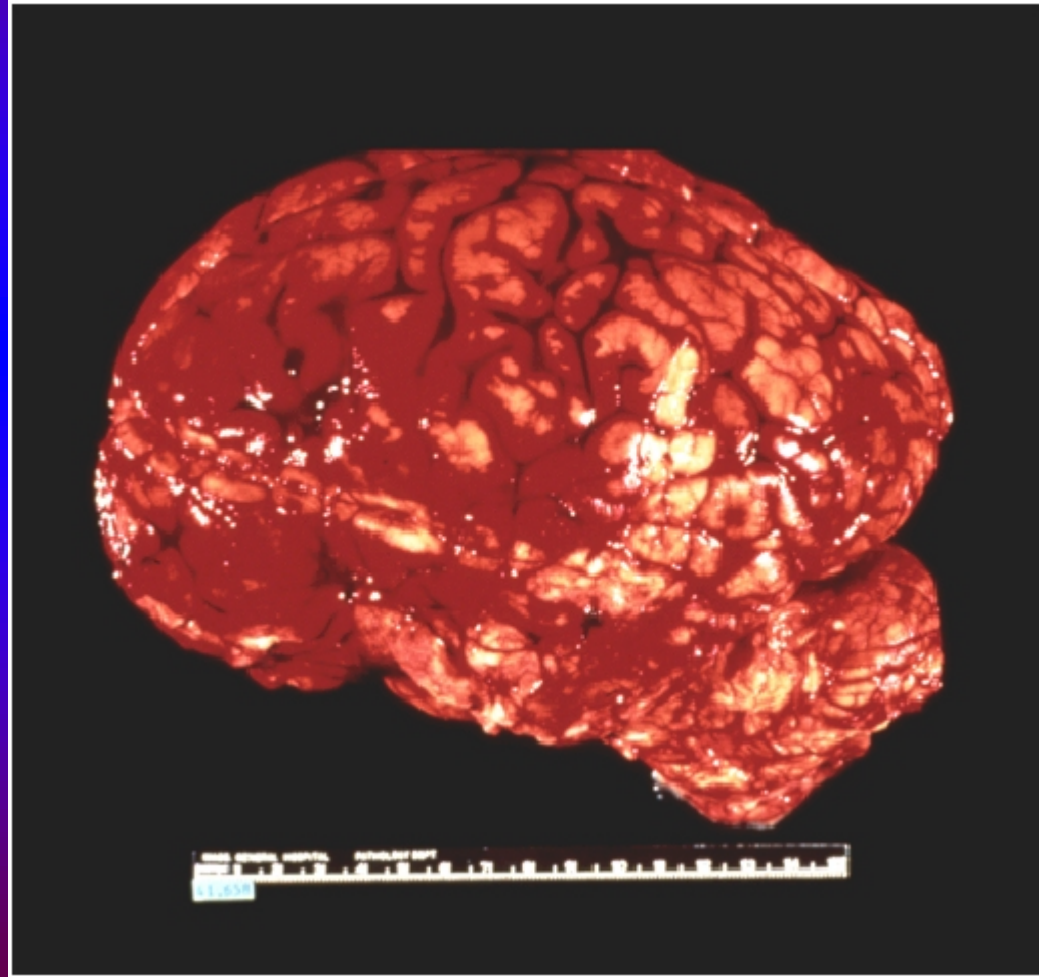
# *Types of CNS Hemorrhage*



# *Hypertensive Intracerebral Hemorrhage*



# *Aneurysmal Subarachnoid Hemorrhage*



# *Evaluation of TIA and Ischemic Stroke\**

## Step I:

- CBC, platelet count, PT, PTT, RPR
- Chemistry profile (glucose, cholesterol)
- ECG
- CT Scan

## Step II:

- Carotid ultrasound
- Echocardiography
- Rhythm (Holter) monitoring if suspicious symptoms

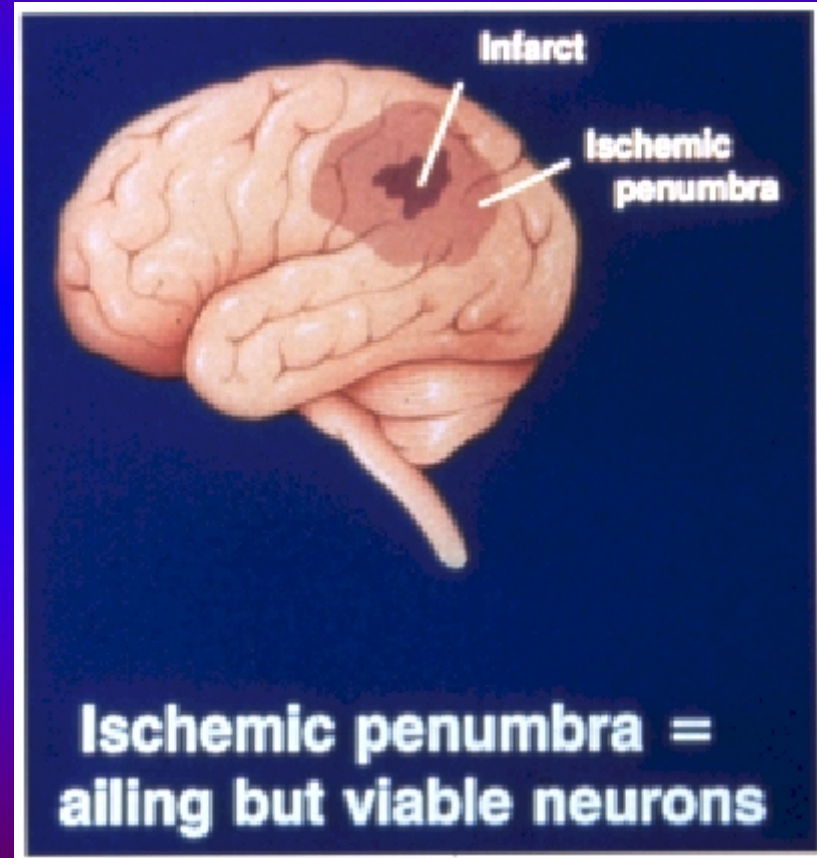
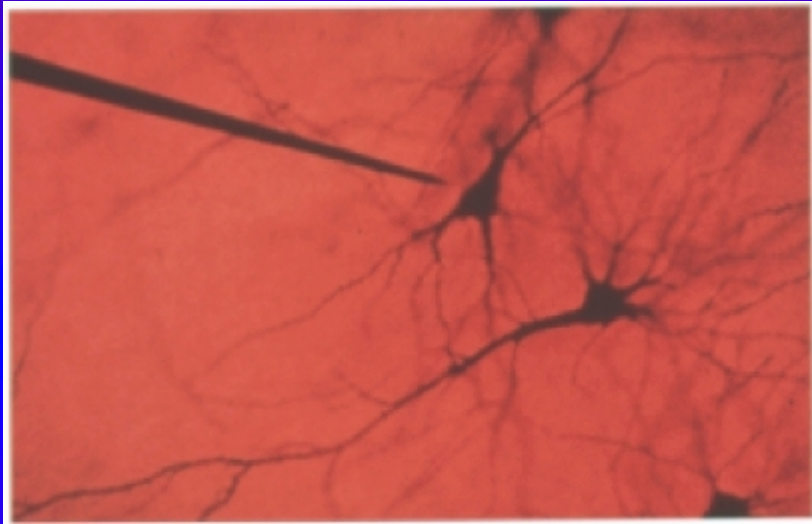
## Step III:

- Arteriography or MR angiography
- Magnetic resonance imaging
- Special coagulation testing
- Transesophageal echocardiography

\* for patients > 50 years old



# *Acute Stroke Treatment: Salvaging the Ischemic Penumbra*





*NINDS tPA Study*  
(*NEJM 1995: 333: 1581*)

- ◆ First proven effective intervention for acute stroke
- ◆ Double blind, randomized, 624 patients
- ◆ tPA 0.9 mg/kg (max 90mg) infused over 1 hour
- ◆ Treatment started <3hrs from stroke onset
- ◆ CT documenting absence of hemorrhage
- ◆ No anticoagulants or antiplatelet Rx for 24 hrs

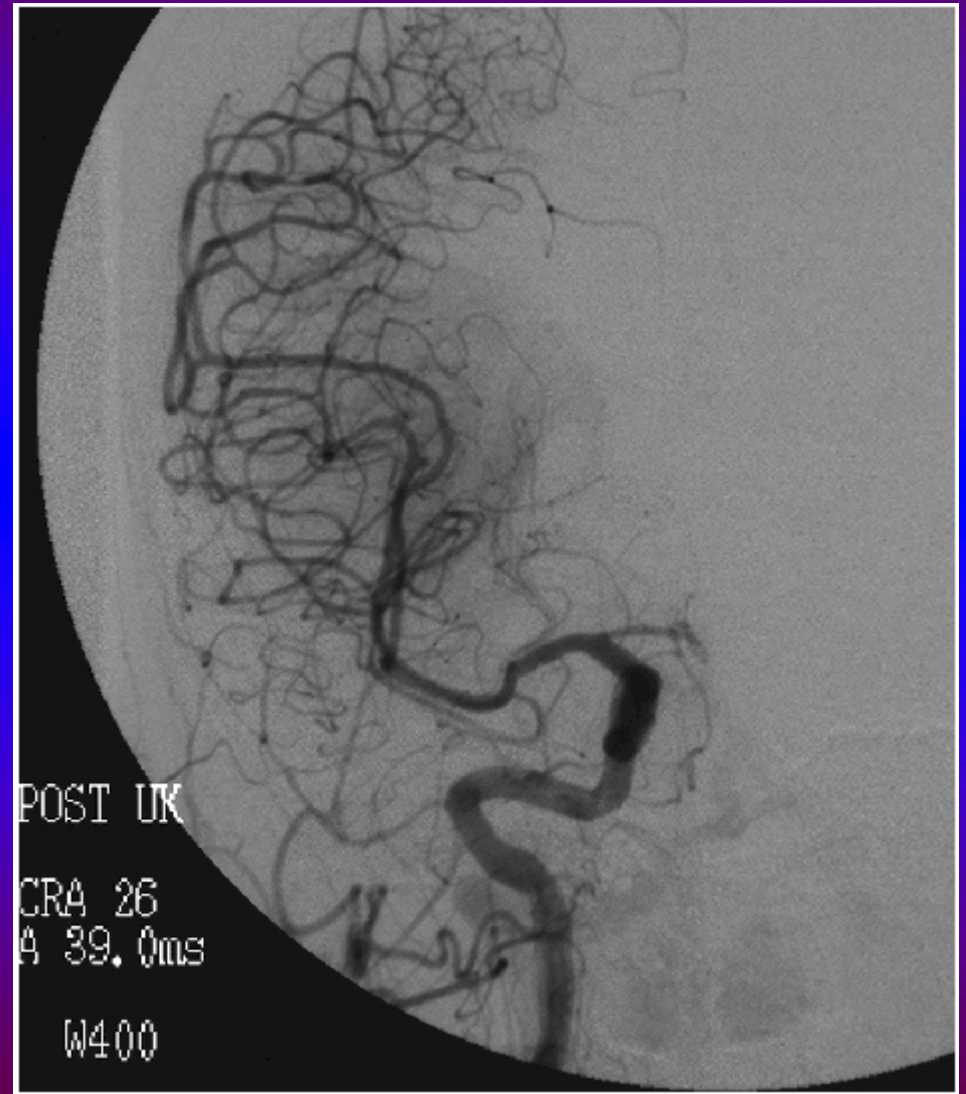
# *NINDS tPA Study*

## *Key Outcomes*

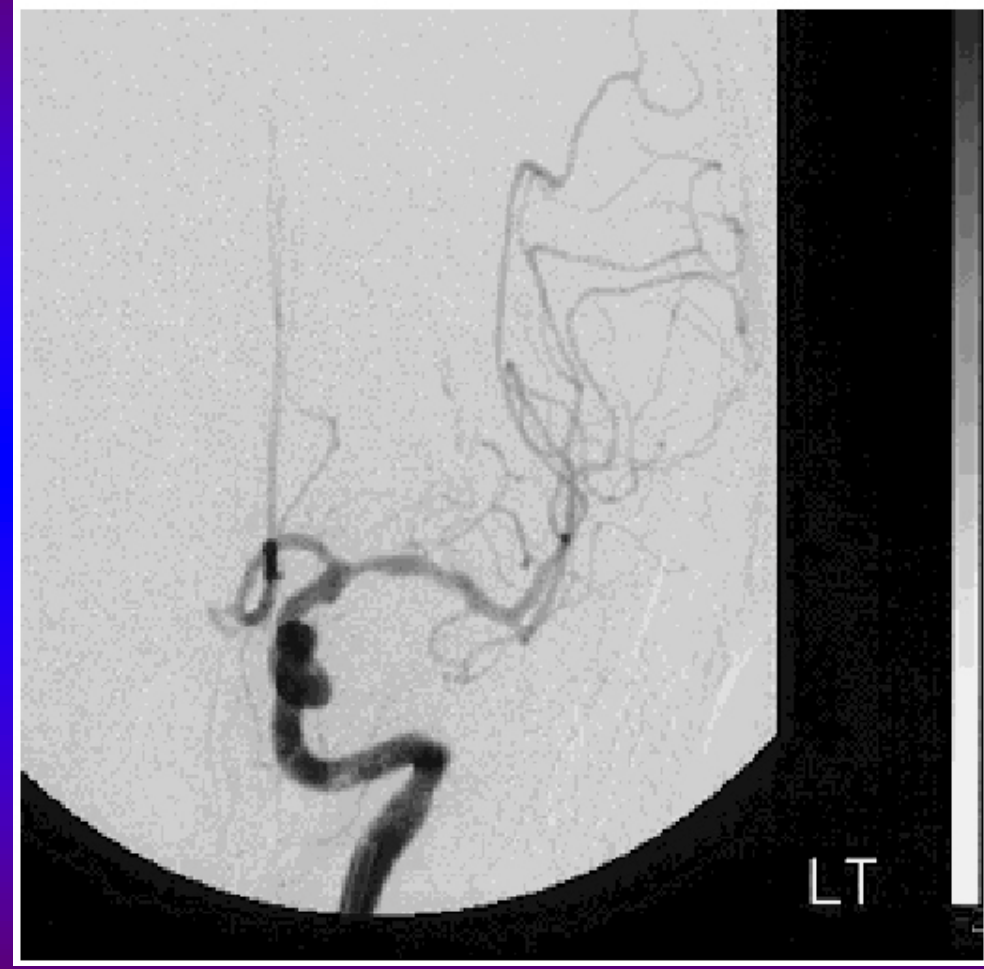
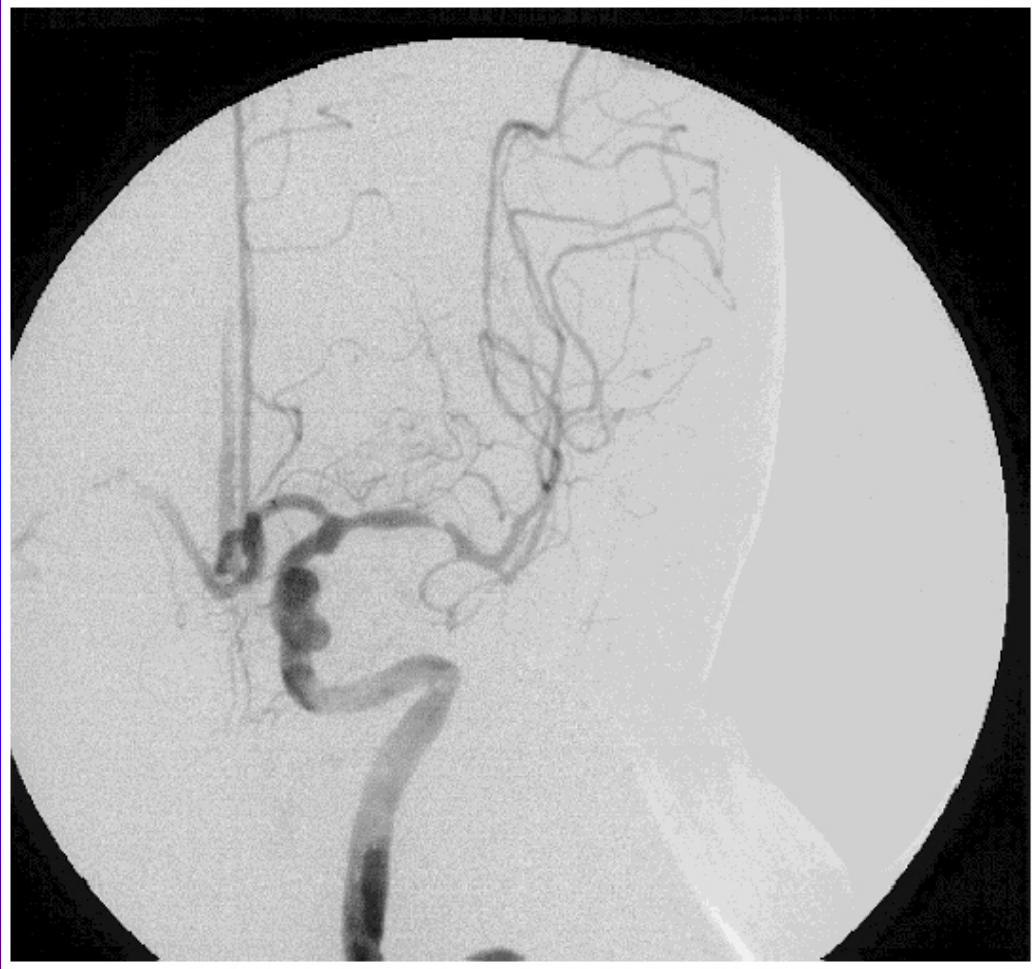
	<u>tPA</u>	<u>Placebo</u>	<u>Absolute Difference</u>
<u>Good Outcome</u>			
• Barthel 95-100	50%	38%	12% *
• Rankin 0,1	39%	26%	13%
<u>Death</u>			
• Brain hemorrhage	17%	21%	- 4%
	6%	1%	+5%

\* 12 extra pts./100 given tPA regained normal function

# *Thrombolytic Therapy*

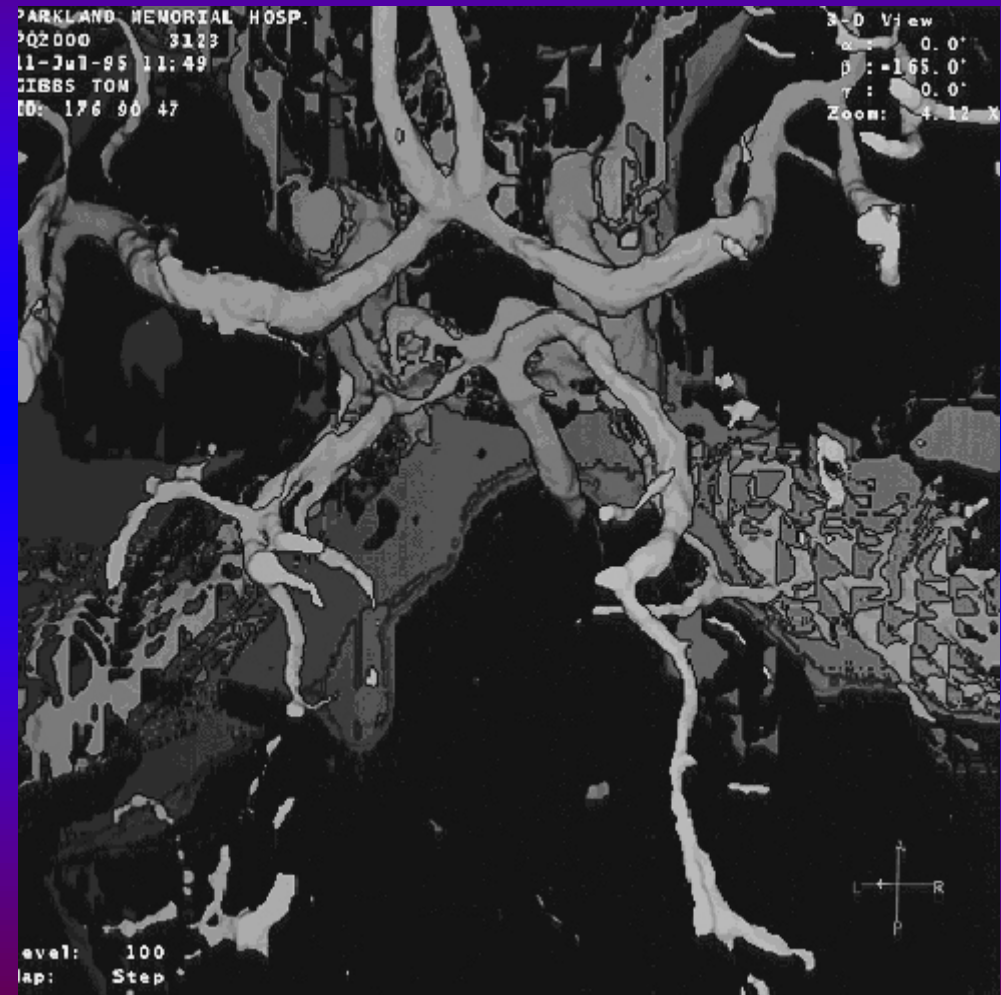


# *Angioplasty*





# *CT Angiography*



# *Initial Management of Acute Stroke*

- ◆ Determine ischemic vs. hemorrhagic by (CT)
- ◆ Consider thrombolytic Rx if <3 hrs from onset
- ◆ Assess stroke mechanism
- ◆ Systemic management issues:
  - blood pressure
  - oxygenation
  - glucose
  - dysphagia / aspiration precautions
  - D.V.T. prophylaxis
  - fluid status
  - seizures
- ◆ Consider aspirin if ischemic stroke, no contraindications

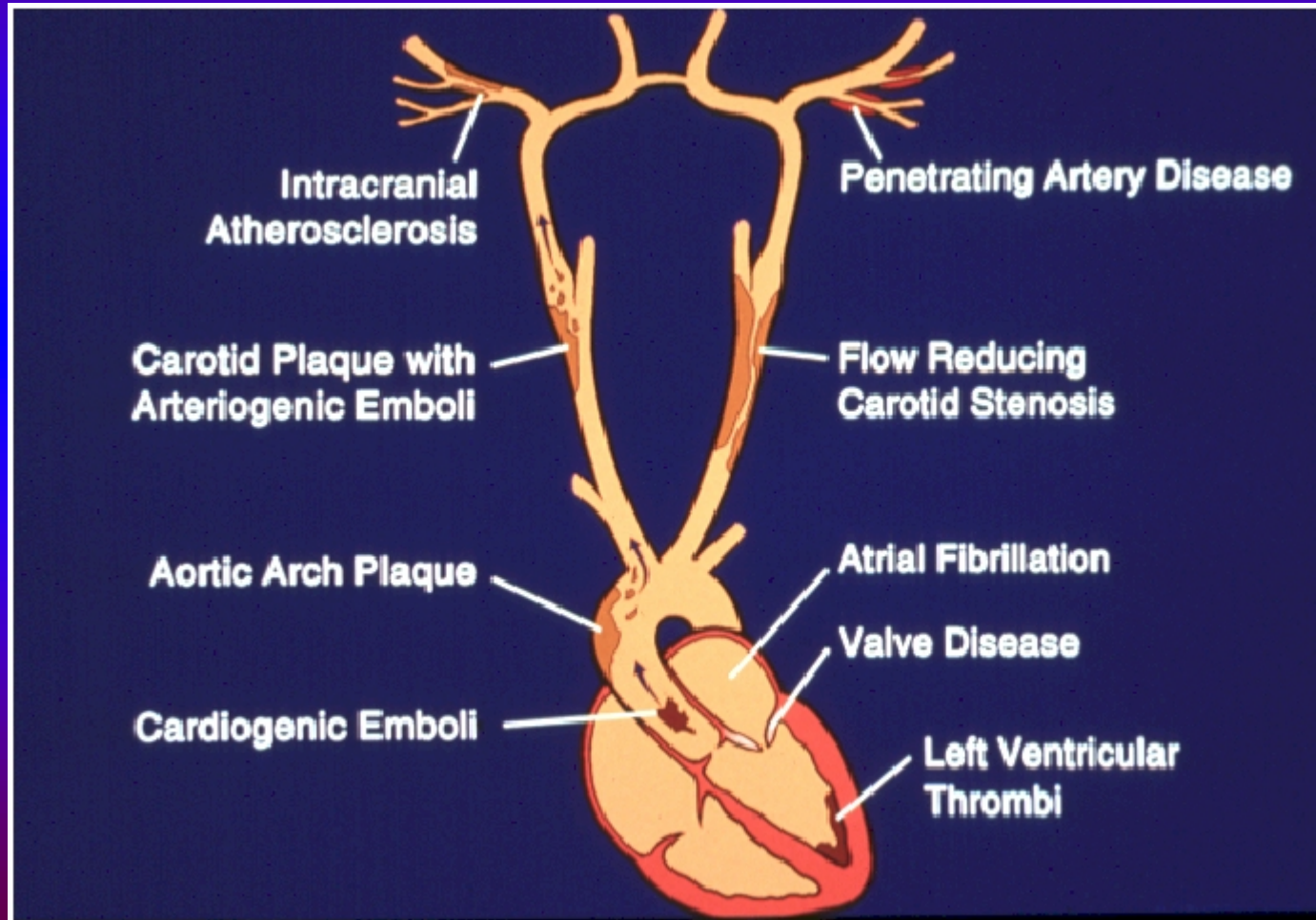


# *Stroke Prevention: High Risk Patients*

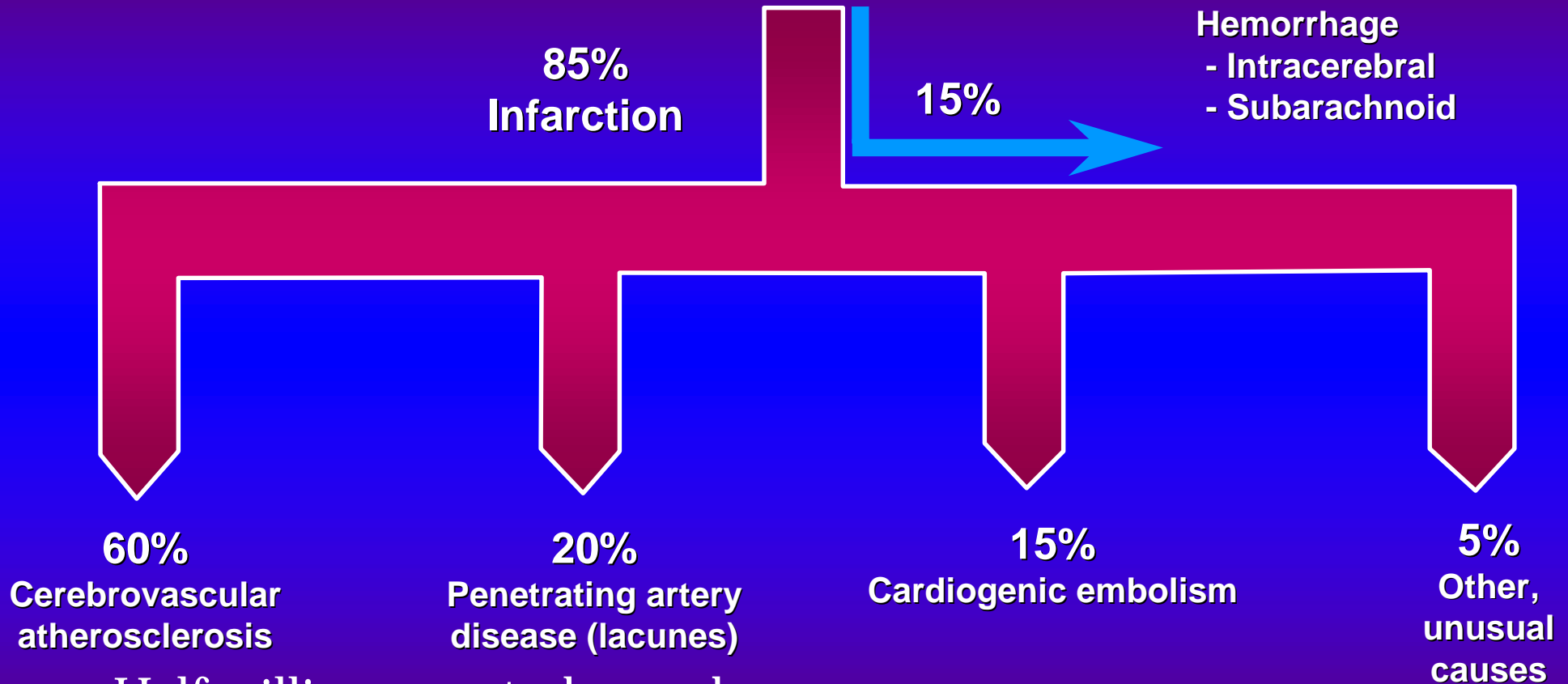
	<u>Relative Risk</u>
◆ Prior TIA or minor stroke	X 10
◆ Atrial Fibrillation	X 6
◆ Hypertension*	X 5-10
◆ Asymptomatic Stenosis	X 3
◆ Smoking*	X 2

\*Patients who have both uncontrolled hypertension and who smoke have a 10-20 fold risk!

# *Summary Diagram of Causes of Stroke*



# *Stroke Syndromes: Summary*



- Half million new strokes each year
- Effective preventive therapy available to prevent most strokes
- Emphasis must be on prevention

## *Established Therapies to Prevent Stroke*

- ◆ Risk factor control (hypertension, smoking, hyperlipidemia).
- ◆ Antiplatelet agents for cerebrovascular disease.
- ◆ Anticoagulation for atrial fibrillation and other selected heart diseases.
- ◆ Endarterectomy for high-grade symptomatic carotid stenosis (less benefit for moderate symptomatic and asymptomatic stenosis).

# *Antithrombotic Therapy for Stroke Prevention: Summary*

<u>Situation</u>	<u>Recommended</u>	<u>Reasonable Options</u>
<sup>o</sup> 1 Cerebrovascular diseases		
- TIA or stroke	ASA 50-1300 mg/d	Clopidogrel; Ticlopidine ASA + ER-DP
- TIA or stroke on ASA	Clopidogrel ASA + ER-DP	Ticlopidine Warfarin INR 1.5-2.5
Atrial Fibrillation		
- lone AF < 65 yr	ASA 325 mg/d	-
- low risk 65-75 yr	ASA 325 mg/d	Warfarin INR 2-3
- > 75 yr or high risk	Warfarin INR 2-3	ASA if warfarin is contraindicated

\*ASA=aspirin; ER-DP=Extended release Dipyridamole