

Intracerebral Hemorrhage: Epidemiology, Causes and Clinical Outcomes

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Basic Epidemiology

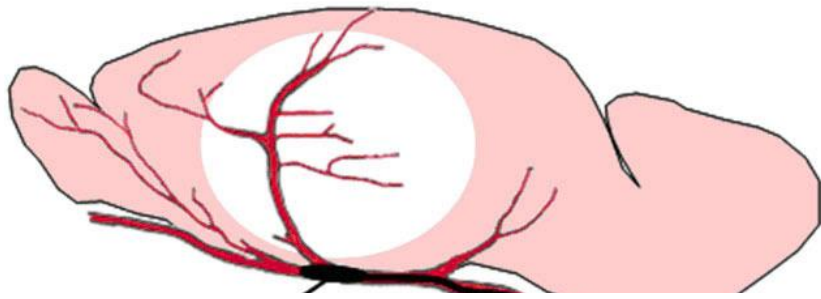
- Primary Spontaneous ICH
- Accounts for roughly 10-15% of all strokes
- 40-50% mortality rate
- Over 70% of survivors with significant morbidity/disability
- Half of the mortality occurs in the first two days after stroke

Branching

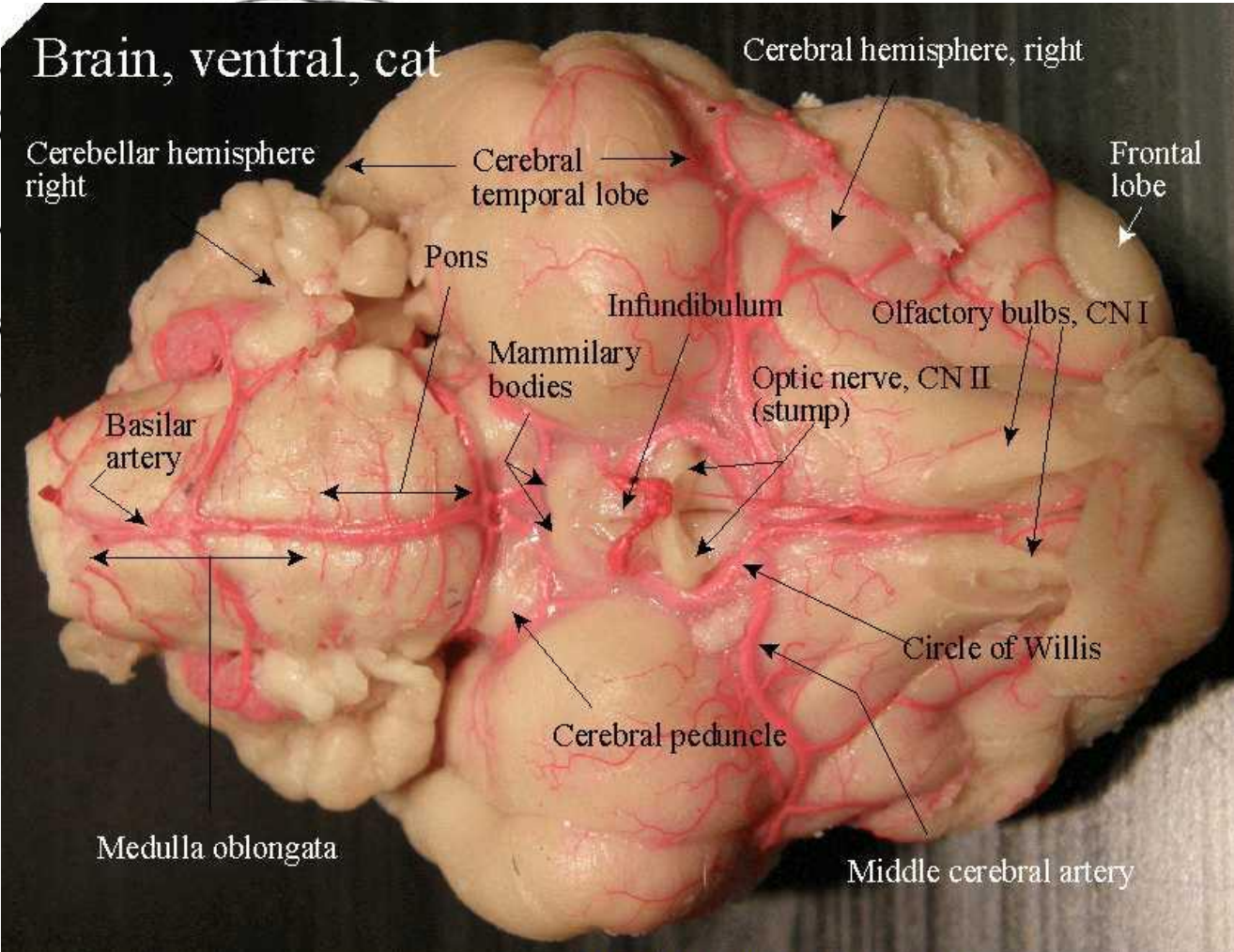
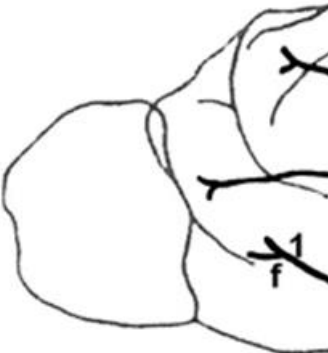
- In most vertebrates, the large medium-sized arteries and arterioles branch into smaller
- Arterioles that branch into capillaries that blood
- Thus, the capillary bed is distributed



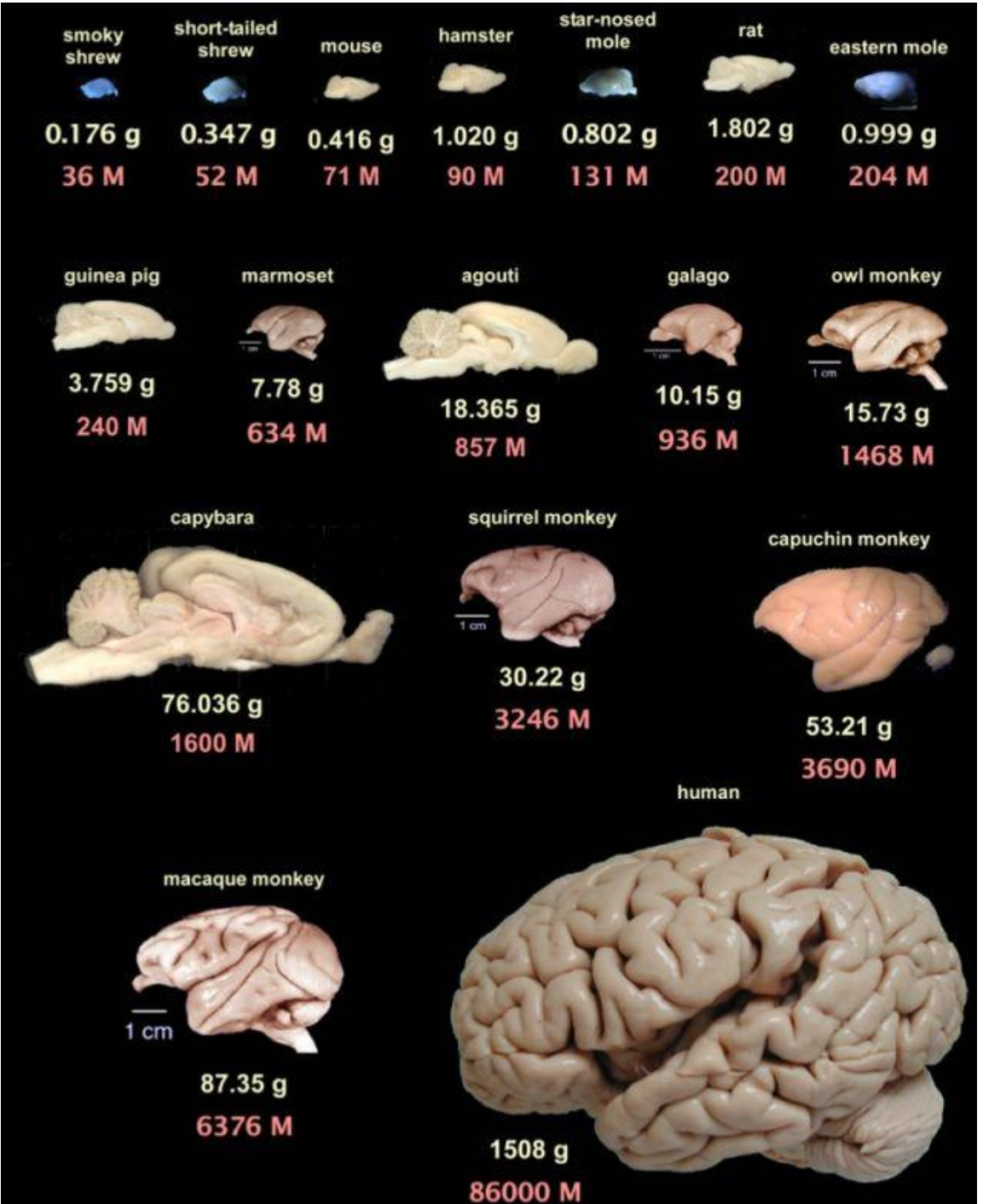
branch into
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MCA Branche:

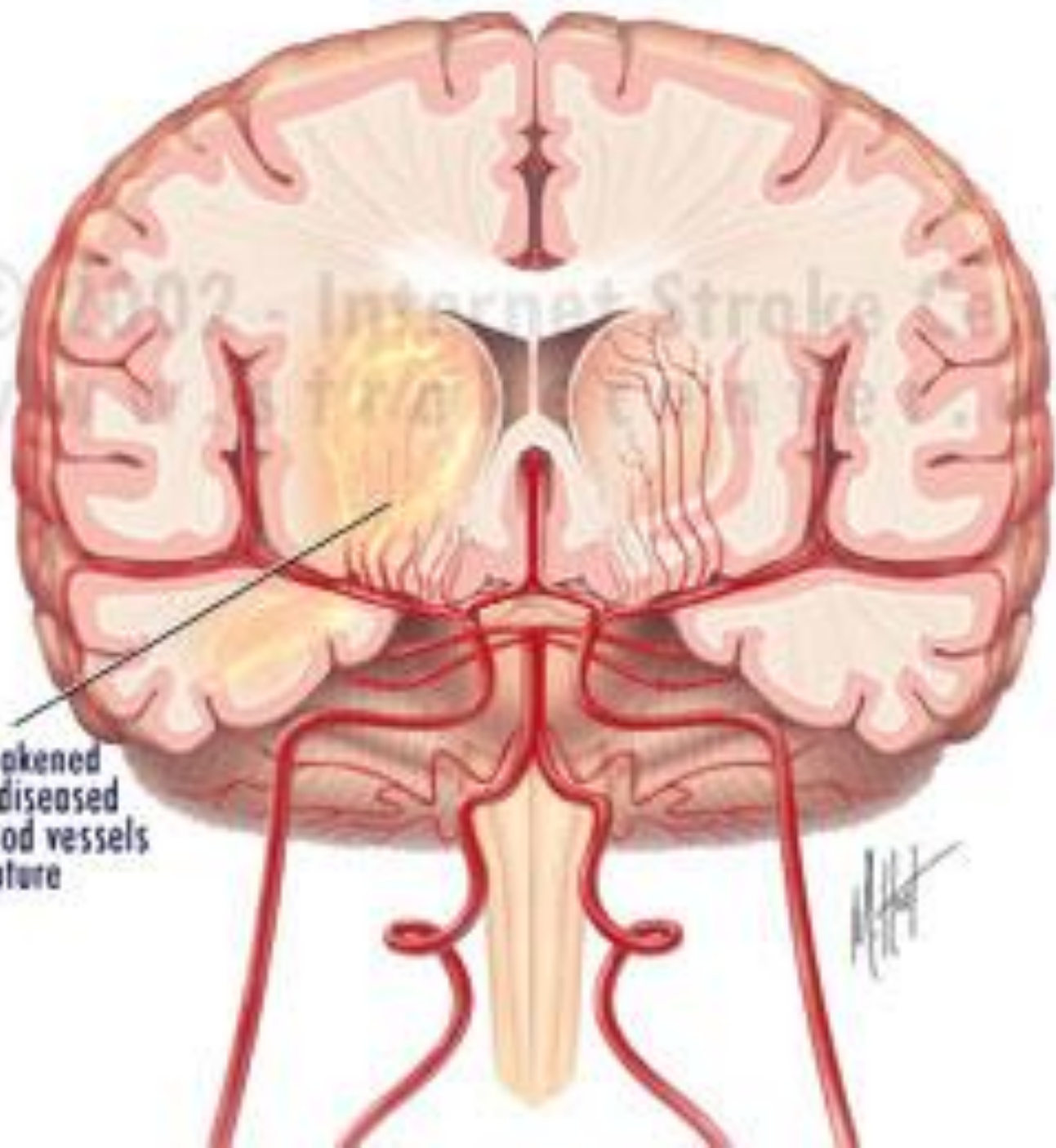


Vascular Anatomy - Cat



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Weakened
or diseased
blood vessels
rupture



Hypertension and Cerebral Small Vessel Disease

- Theoretically, the pressure on lenticulostriates and small capillaries branching off of the MCA and Basilar artery without an intervening resistance bed is very high
- Population attributable risk is proportion of disease that would have been prevented if the risk factor did not exist

Univariate Attributable Risk for ICH, Lobar ICH, and Nonlobar ICH

	Risk (95% CI)		
	All ICH (n=188)	Lobar ICH (n=67)	Nonlobar ICH (n=121)
First-degree relative with ICH	0.05 (0.02-0.08)	0.05 (0.0-0.16)	0.04 (0.005-0.08)
Previous ischemic stroke	0.13 (0.09-0.18)	0.09 (0.02-0.16)	0.14 (0.08-0.20)
Frequent alcohol u	0.05 (0.02-0.08)	0.05 (0.0-0.16)	0.04 (0.005-0.08)

Table 2.

Attributable Risk in Percentages: Univariate Analysis¹

Risk Factor	Type of Stroke	Odds Ratio	Attributable Risk, %	95% CI
Hypertension	All ischemic	1.7	27	7-43
Diabetes	All ischemic	2.7	21	11-29
History of MI	All ischemic	2.1	9	2-16
Hypertension	Small vessel	5.0	68	31-85
Diabetes	Small vessel	4.4	30	10-45
Diabetes	Cardioembolic	3.1	25	4-40
History of MI	Cardioembolic	3.6	21	4-35

Importance of Location

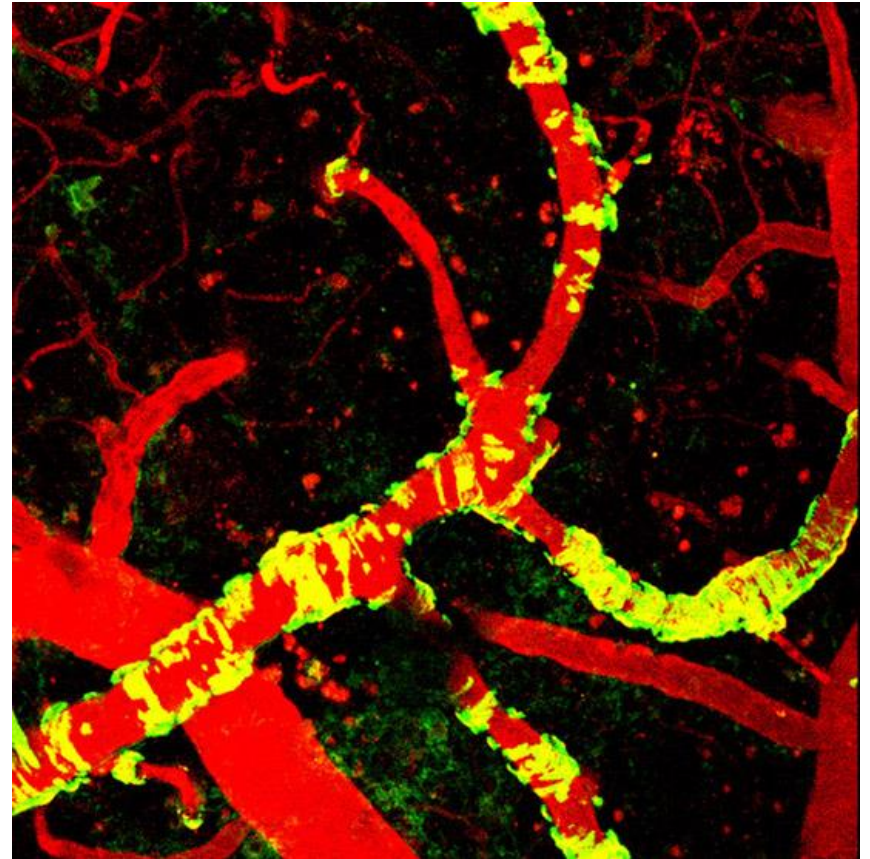
- At one time, hypertension was felt to be the cause of ICH in all locations and cerebral amyloid angiopathy to be a rare cause of ICH
- Population-based studies –
 - To determine the attributable risk of each risk factor
 - To control for regional differences in risk factor

Cerebral Amyloid Angiopathy

- Amyloid plaques made of beta-sheets of proteins, make blood vessels more rigid and fragile.
- CAA occurs in 70% of Alzheimer's disease patients
- In less than 10% of people less than 70 years of age but more than 50% of people age >90 years
- Occurs almost exclusively in the lobar regions of the brain and cerebellum

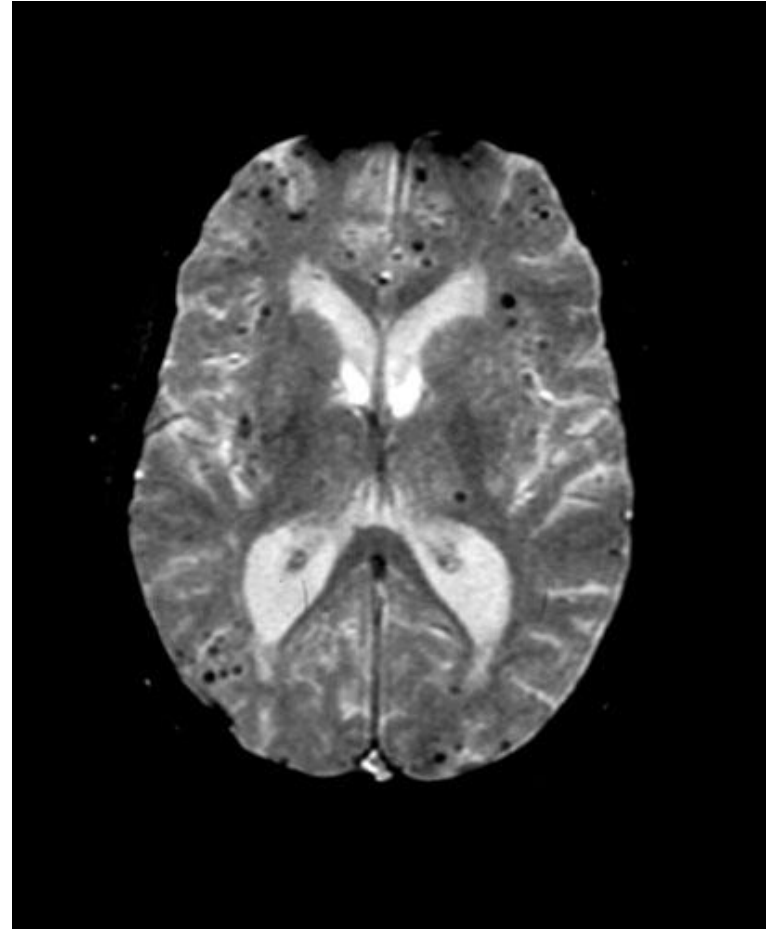
Cerebral Amyloid Angiopathy

- Disease of the elderly (~50% of ICH in >80)
- Deposition of amyloid protein in media/adventitia of small cortical arteries, arterioles and capillaries
- Cortex and cerebellum



Cerebral Amyloid Angiopathy

- Pathology
 - Destruction of normal cortical vasculature
- Microbleeds on MRI GRE sequences
 - More common in blacks with ICH?*
 - (Microbleeds also caused by HTN)
- Lobar ICH
- Association with Apo E2/E4



*(Kidwell) Neurology 2008;71:1176-1182.

However, less so for minorities

- When evaluating importance of risk factors for AA and Hispanic ICH cases versus controls
 - ApoE2 and E4 were not significant risk factors for lobar ICH
 - Hypertension was a significant risk factor for lobar ICH
 - Suggests that hypertensive lobar ICH occurs and thereby making causation difficult to establish

On the importance of Intraventricular Hemorrhage

- Rupture of hemorrhage into the ventricles is an independent risk factor for worse outcomes and death
- Ventricular hemorrhage may lead to hydrocephalus, may require management with ventriculostomy or thrombolytic agent into the ventricles
- Over 945 patients with deep basal ganglia hemorrhages, rates of IVH varied by location ($p < 0.0001$)
 - Caudate: 89%
 - Putamen: 23%
 - Thalamus 64%

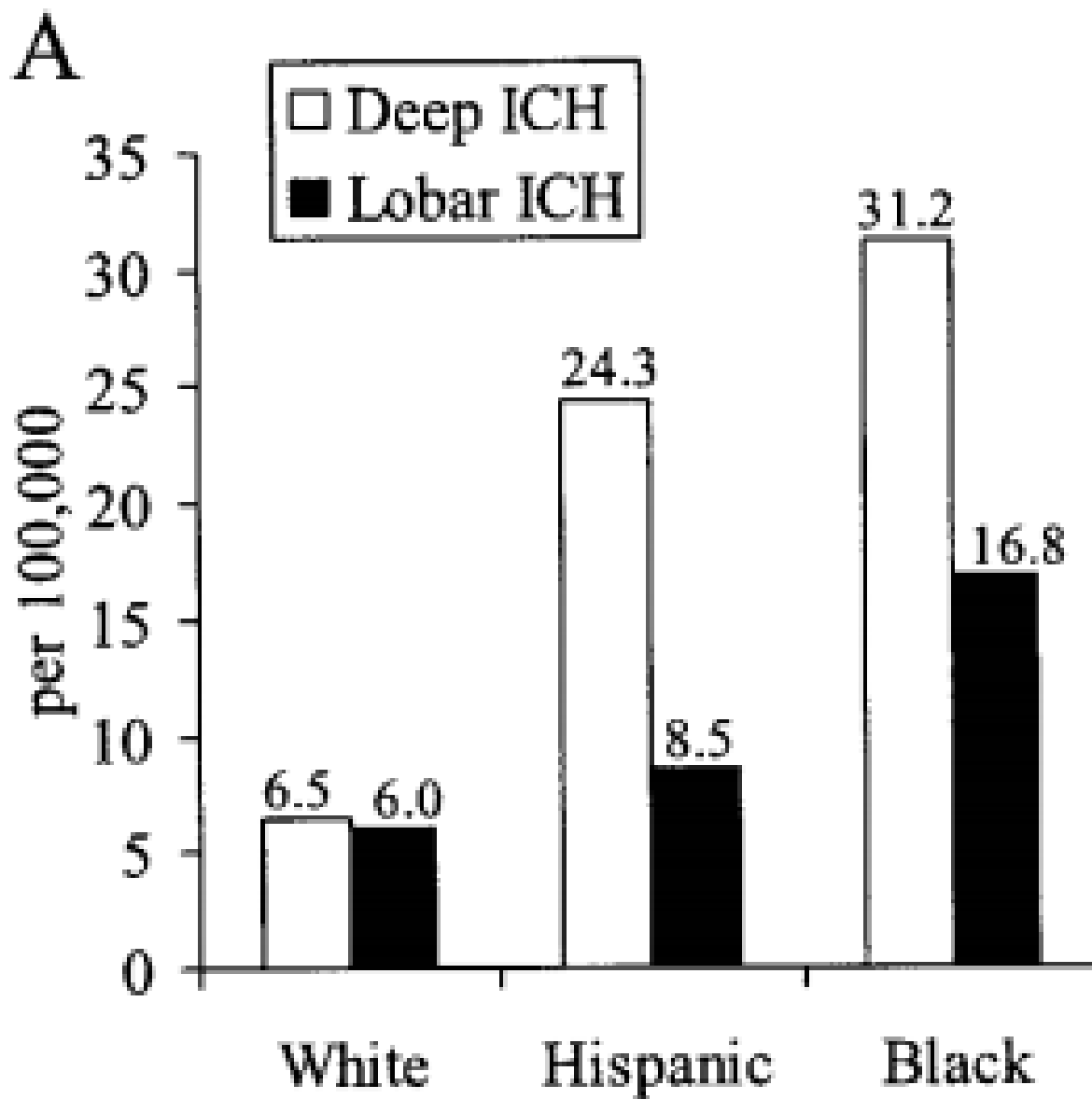
	GERFHS – Discovery Set				ERICH – Replication Set			
Variables	Incontinence		Dysmobility		Incontinence		Dysmobility	
	OR (CI)	p-value	OR (CI)	p-value	OR (CI)	p-value	OR (CI)	p-value
IVH Volume	1.50 (1.10, 2.06)	0.0117	1.58 (1.17, 2.15)	0.0031	1.42 (1.27, 1.60)	<.0001	1.40 (1.24, 1.57)	<.0001
Age (per year)	1.07 (1.04,1.10)	<.0001	1.06 (1.03, 1.09)	<.0001	1.04 (1.03, 1.05)	<.0001	1.04 (1.03, 1.05)	<.0001
ICH Volume	1.78 (1.25, 2.54)	.0015	1.85 (1.32, 2.60)	0.0004	1.77 (1.51, 2.06)	<.0001	2.22 (1.91, 2.58)	<.0001
Location								
-Lobar	0.33 (0.15,0.72)	.005	0.18 (0.09, 0.40)	<.0001	0.51 (0.36,0.72)	.0001	0.27 (0.19, 0.37)	<.0001
-Deep	REF	REF	REF	REF	REF	REF	REF	REF
-Brainstem	5.22 (1.05, 25.95)	.043	1.84 (0.35, 9.62)	.4712	3.39 (1.83, 6.29)	.0001	3.71 (2.06,6.69)	<.0001
-Cerebellar	1.73 (0.62, 4.83)	.30	1.48 (0.55, 3.99)	.4419	0.70 (0.41, 1.20)	.19	0.77 (0.48 1.24)	.28
-Primary IVH					1.72 (0.58, 5.03)	.33	1.54 (0.55, 4.32)	.42
GCS at presentation (per point)	0.89 (0.77 1.03)	.1198	0.88 (0.76, 1.03)	0.1020	0.90 (0.87, 0.94)	<.0001	0.88 (0.84, 0.93)	<.0001
mRS before ICH	1.65 (1.24, 2.18)	.0006	1.71 (1.29, 2.26)	.0002	1.62 (1.38, 1.91)	<.0001	1.45 (1.22, 1.71)	<.0001
Female	1.42 (0.79, 2.57)	0.2412	0.99 (0.56, 1.75)	0.9648	1.51 (1.15, 2.00)	0.0036	1.68 (1.29, 2.18)	0.0001

ICH among Blacks

- Annual incidence rate per 100,000
 - 48.9 for AAs vs. 26.6 for whites
 - Highest risk ages 35-44 years (OR=5.0)
- Is it all Hypertension?
 - Deep (OR=4.8 vs. whites)
 - Lobar (OR=2.8 vs. whites)

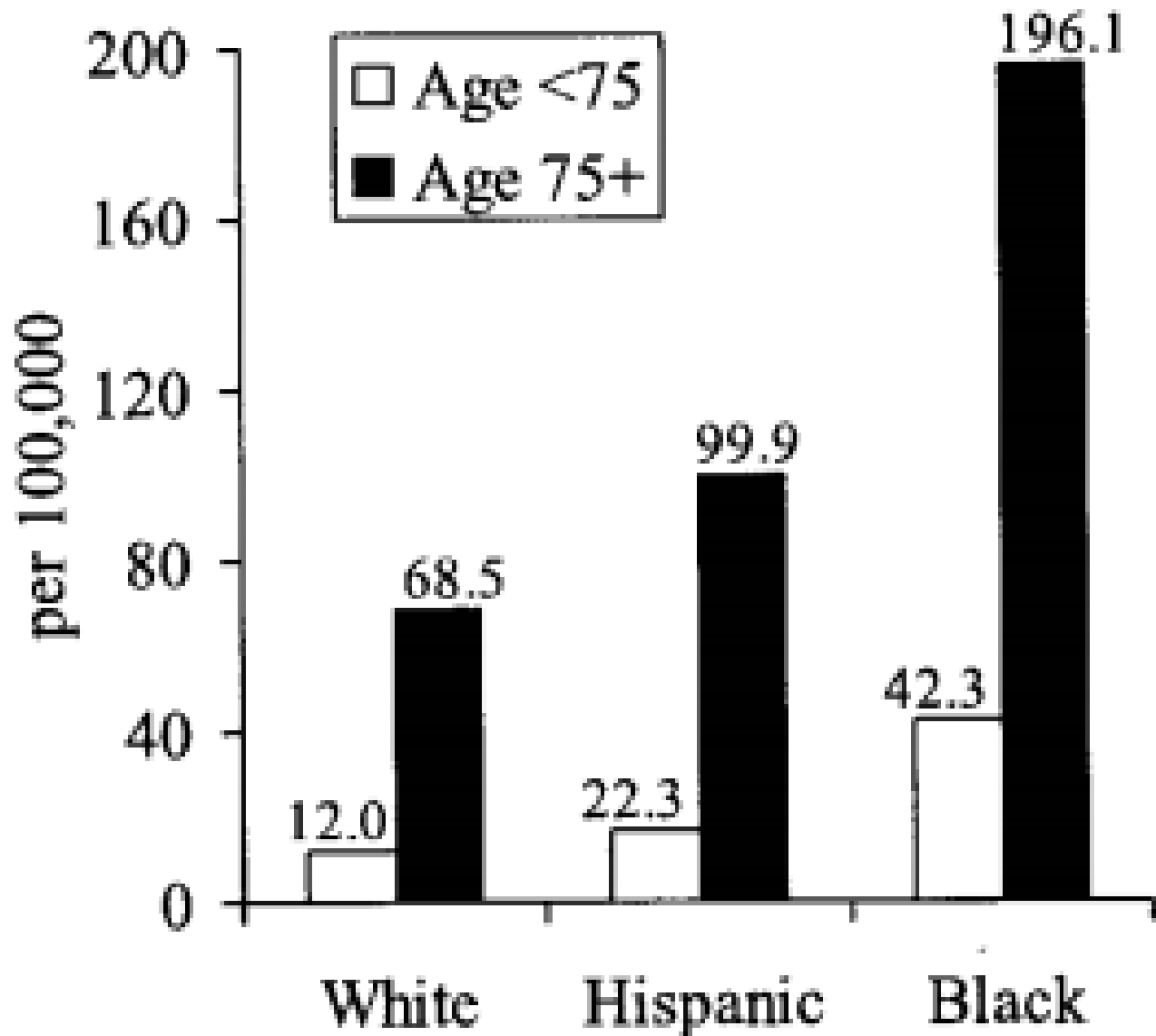
ICH among Hispanics

- Double the risk of ICH (OR=2.6; 1.4-6.1)
- Greatest for deep ICH (OR=3.7; 1.7-16.5)
- No increased rate for lobar ICH vs. whites
- Mortality rates higher for Hispanics compared to whites(Data conflicts with some other studies)



- Labovitz et al, Neurology 2005

B



Hypercholesterolemia and Intracerebral Hemorrhage

- 1976 – Konishi et al; Autopsy study in the Akita Prefecture found little arteriosclerotic change in cerebral blood vessels of hypertensive ICH patients; no risk from hypercholesterolemia
- 1988 – Ueda et al; Prospective population-based study; Higher serum cholesterol level associated with 50% reduction in rate of ICH.

Hypercholesterolemia and Intracerebral Hemorrhage

- 1989 – Honolulu Heart Program
- 1993 – Akita Pathology Study
- 1994 – MRFIT Study
- 1995 – Copenhagen Stroke Study
- 1996 - Kaiser Permanente Medical Care Study
- 1996 - Melbourne Risk Factor Study
- 1997 – Kim et al
- 1999 – Segal et al

Hypercholesterolemia and Intracerebral Hemorrhage

- 2001 – Korea medical insurance co. study
- 2002 – GERFHS - Cincinnati
- 2003 – Ariesen et al – Meta-analysis
- 2003 – Ko et al -
- 2004 – GERFHS – Statin and ICH
- 2007 – NOMAS
- 2012 – Martini et al

Brain and Cholesterol

- The brain is the largest repository of cholesterol in the human body (more so than even the liver)
- Largely in myelin sheaths but also essential to inflammation, neurovascular unit and vascular blood-brain barrier integrity
- 95% of all brain cholesterol is synthesized locally.
 - Minor uptake of serum cholesterol
 - Brain cholesterol is metabolized locally but synthesized using the same processes as liver

Mortality Rate vs. Case Fatality

- AA's have double the incidence of ICH than whites and because of the higher incidence, have a higher mortality rate on a population scale
- But on an individual case-by-case basis, AA's tend to have stroke at a younger age (10 years younger) and more deep ICH (which are smaller than lobar ICH) and thereby their case-fatality rate is actually better than white populations

