CEREBRAL COMPLICATIONS OF HTN

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HTN&NEUROLOGICAL COMPLICATIONS

- Hypertension (HTN) is a major cause of morbidity and mortality because of its complication like neuronal disease, coronary heart disease, cerebrovascular disease and renal disease.
- It is also known for the second most common cause of death after diabetes in adults worldwide. This topic is mainly focus on neurological complications due to HTN

Worldwide burden of hypertension

Global Health Observatory (GHO) data

Brain is one of the target organs in HTN complication

- HTN is the biggest risk factor for stroke
- Leading risk factor for vascular cognitive impairment as well as Alzheimer disease
- Most common cause of dementia in the elderly

- Thus , HTN is involved in the pathogenesis of 2 major brain diseases: stroke and dementia

- ✓ **Acute hypertension is associated with hypertensive encephalopathy and eclampsia.**

- ✓ **Chronic hypertension is a key risk factor for all stroke subtypes, including ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage.**

- ✓ **Hypertension can lead to carotid artery stenosis, intracranial atherosclerosis, and aortic arch atherosclerosis, which are important causes of ischemic stroke.**

Hypertension affects more than one in four adults.

Many hypertensive emergencies may also have a neurological presentation, such as hypertensive encephalopathy, haemorrhagic stroke or pre-eclampsia. Here we highlight the importance of blood pressure in maintaining brain health and the brain's role in controlling blood pressure.

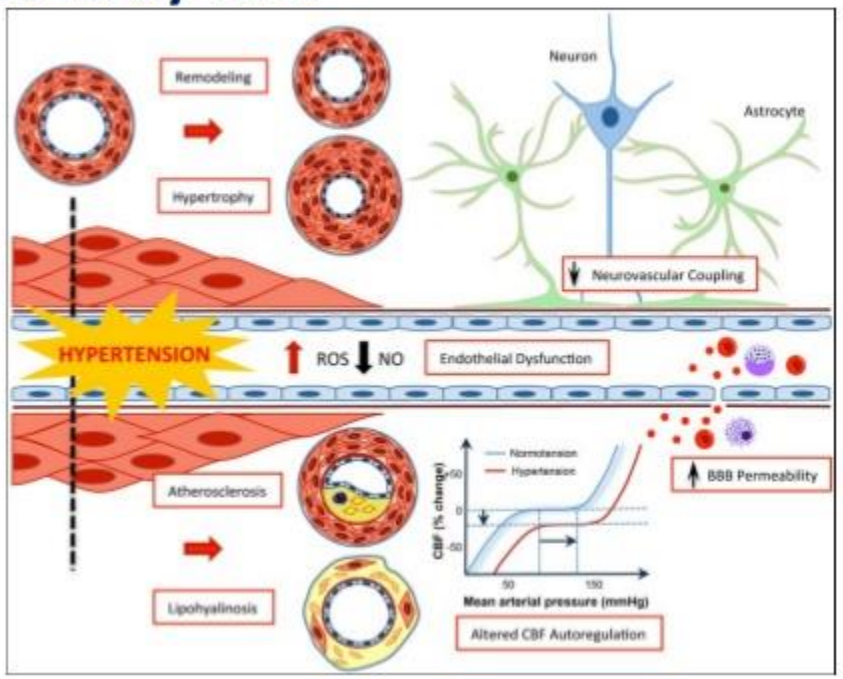
Complications:
Central nervous system

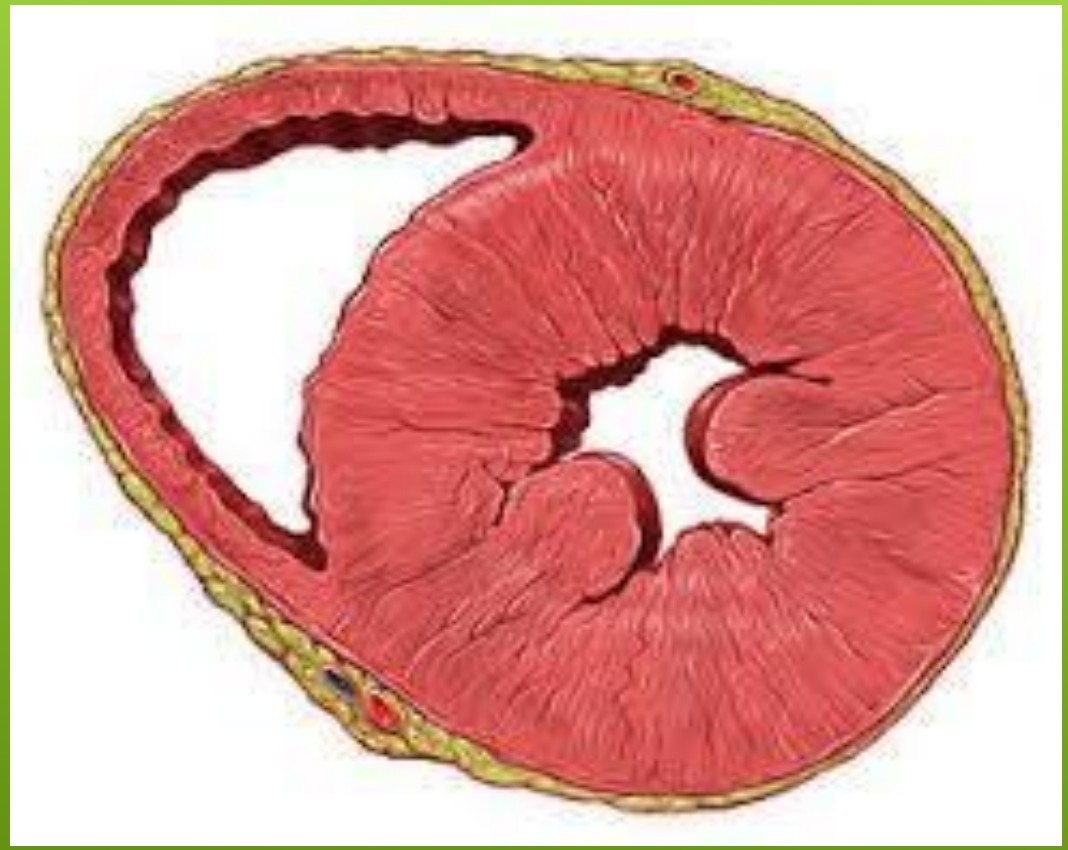
- **Stroke** most common complication
  - Cerebral haemorrhage or infarction
- **Subarachnoid haemorrhage**
- **Hypertensive encephalopathy** – rare conditions
  - High BP
  - **Neurological symptoms:** transient disturbances of speech or vision, paraesthesiae, disorientation, fits and loss of consciousness.
- **Neurological deficit -** usually reversible if the hypertension is properly controlled

Atherosclerosis

- HTN is a leading risk factor for atherosclerosis
- A 10-mm Hg increase in arterial pressure increases by 43% the odds of complex aortic atherosclerosis , highly predictive of ischemic strokes
- Atherosclerotic lesions are also observed at sites of turbulent flow, such as the carotid bifurcation and the vertebrobasilar system, and less frequently in intracranial arteries

Alterations in cerebrovascular structure induced by HTN

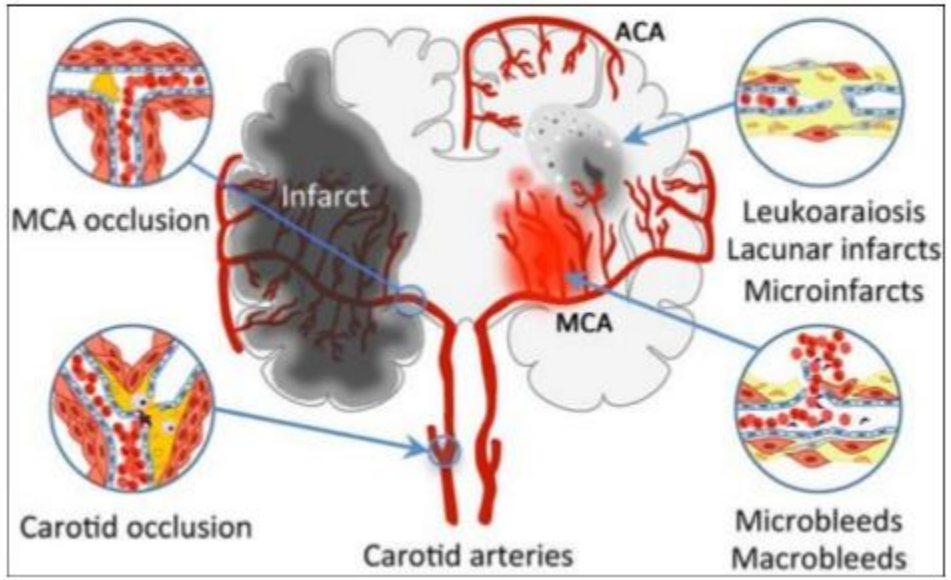


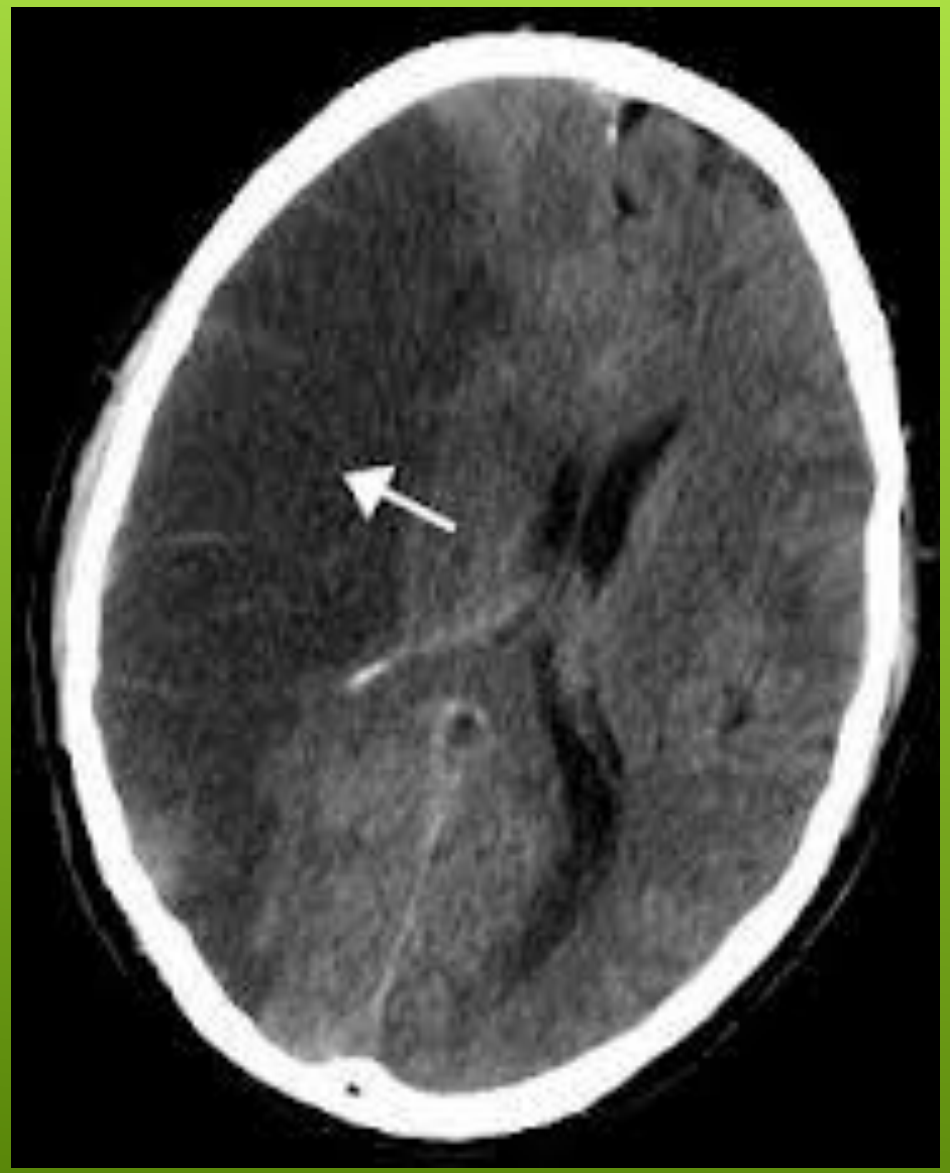


Alterations in cerebrovascular structure induced by HTN

- HTN induces atherosclerosis of major extracranial and intracranial arteries, which could lead to major infarcts
- HTN causes both microbleeds and macrobleeds and is main pathogenetic factor for small vessel disease responsible for lacunar infarcts, white matter lesions (leukoaraiosis), and microinfarcts
- Subcortical white matter at boundary between different vascular territories (middle cerebral artery and anterior cerebral artery) is particularly susceptible to damage

Alterations in cerebrovascular structure induced by HTN

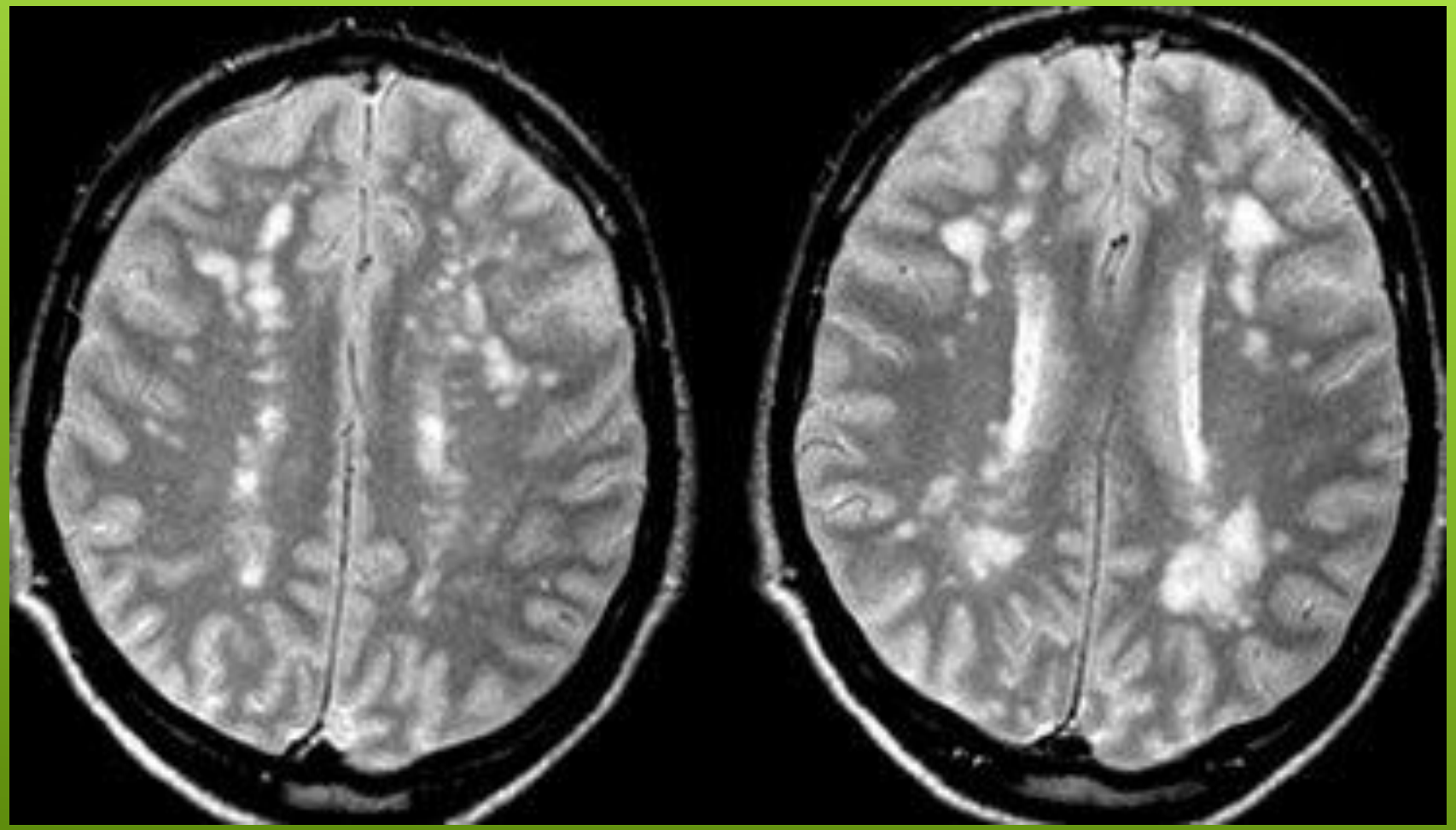




Lacunar infarcts

- Small (<20 mm in diameter) rounded lesion most commonly found in basal ganglia, are commonly associated with SVD and are a strong predictor of VCI

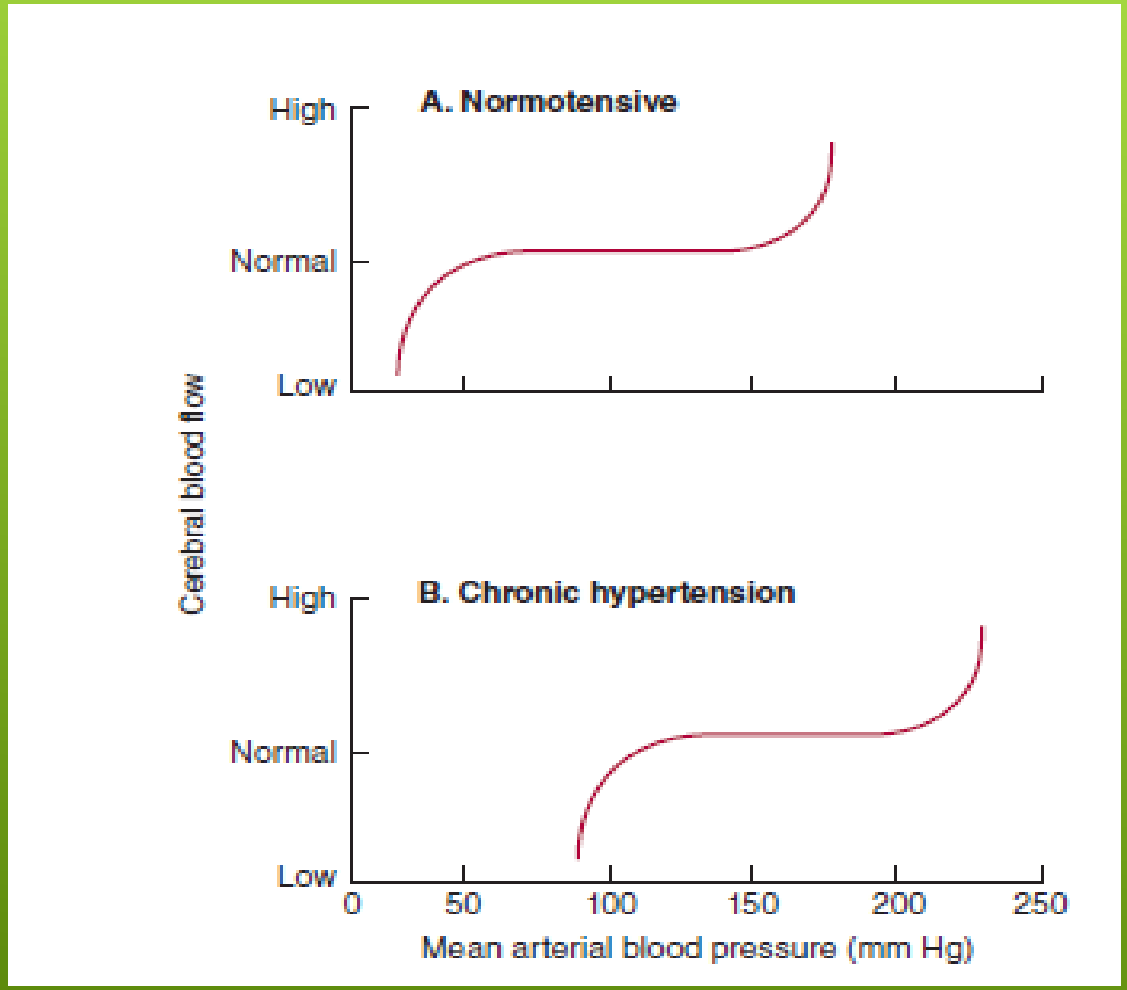
- They have been attributed to acute occlusion of small perforating cerebral arteries (40–200 µm diameter) because of SVD pathology or, less likely, embolism from upstream vessels



Diffuse white matter damage

- Another manifestation of SVD is diffuse white matter damage or leukoaraiosis, indicating a reduction in white matter density
- High systolic blood pressure precedes development of leukoaraiosis, and blood pressure lowering slows down its progression
- Often present in the periventricular white matter, leukoaraiosis could result from hypoxia-hypoperfusion
- The periventricular white matter is thought to be more susceptible to hypoperfusion because it is located at the boundary between separate arterial territories

CEREBRAL AUTOREGULATION



HTN alters cerebrovascular autoregulation

Mechanisms of effects of HTN on autoregulation

- Likely to include a combination of effects on myogenic tone and on changes in mechanical characteristics of cerebral blood vessels induced by remodeling and stiffening

- These changes are particularly damaging to periventricular white matter, which is located at boundary between different arterial territories and, as such, is most susceptible to hypoperfusion

Hypertension. 2013 Nov; 62(5): 10.1161/HYPERTENSIONAHA.113.01063.

Complications for rapid BP Reduction in Severe Hypertension

- Widening Neurologic Deficits
- Retinal ischemia and Blindness
- Acute MI
- Deteriorating renal function

HYPERTENSIVE ENCEPHALOPATHY

A sudden increase in blood pressure, with or without preexisting chronic hypertension, may result in encephalopathy
and headache, which develop over a period of hours to days.

Patients at risk include those with acute glomerulonephritis or eclampsia. Impaired autoregulation of cerebral
blood flow, vasospasm, and intravascular coagulation have all been proposed as contributing factors

Posterior Reversible Encephalopathy Syndrome (PRES) - Diagnosis

Clinical Features

Frequency > 50%

Altered mental status
Either lethargy, confusion, or agitation

Seizures
Generalized > focal

Frequency ≤ 50%

Headache
Typically constant, global, and refractory

Vision changes
↓ acuity, visual field deficits, hallucinations, cortical blindness

Risk Factors

- Hypertensive emergency
- Preelampsia / Eclampsia
- Immunosuppressive / Immunomodulatory meds
  - Cyclosporine
  - Cisplatin
  - Tacrolimus
  - VEGF inhibitors
- Renal failure
- Autoimmune disease

Diagnosis

Risk Factor

+

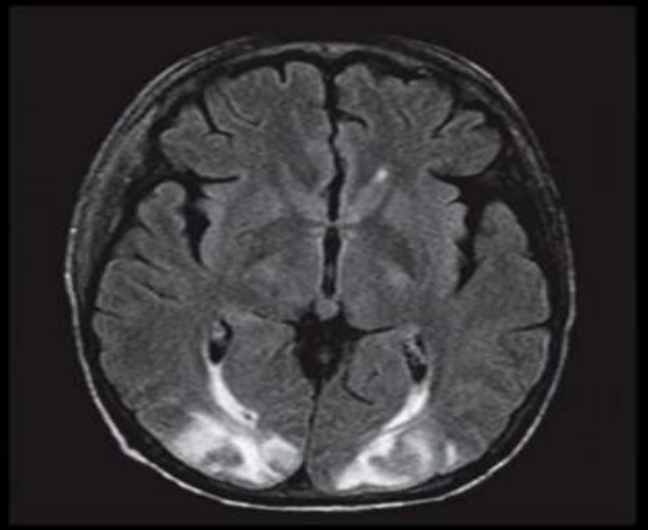
Clinical Features

+

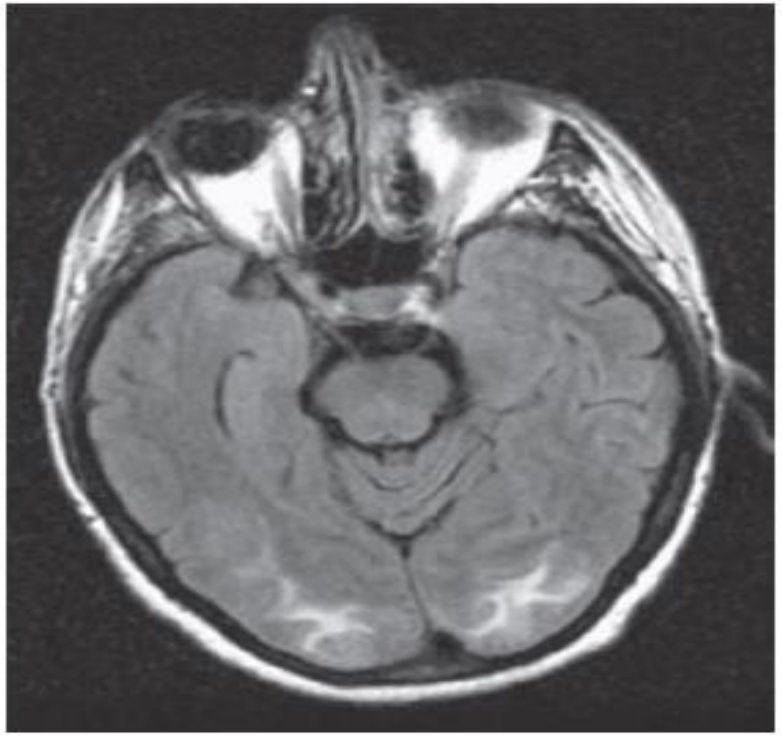
Neuroimaging

Classic MRI Finding:

Vasogenic edema in the subcortical white matter of the posterior cerebral hemispheres



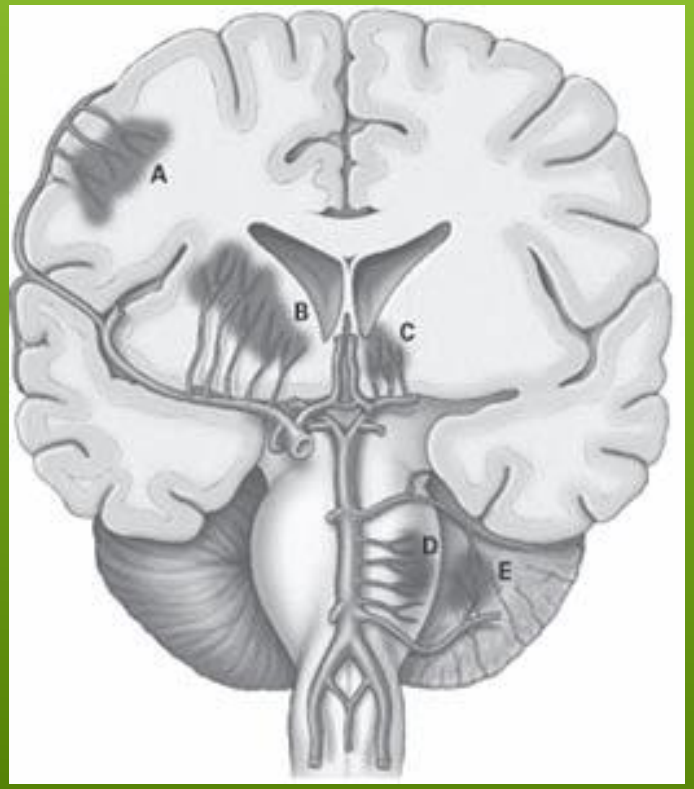
Axial T2 fluid-attenuated inversion recovery (FLAIR) sequence



▲ **Figure 4-23.** Axial FLAIR MRI in hypertensive encephalopathy showing increased signal (white) in the subcortical occipital white matter and occipital cortex bilaterally. These findings may represent reversible vasogenic edema.

INTRACEREBRAL HEMORRHAGE

- Spontaneous bleeding into the brain parenchyma or ventricles from a ruptured artery, vein, or other vascular structure



ETIOLOGY

Hypertension (most common)

Amyloid angiopathy

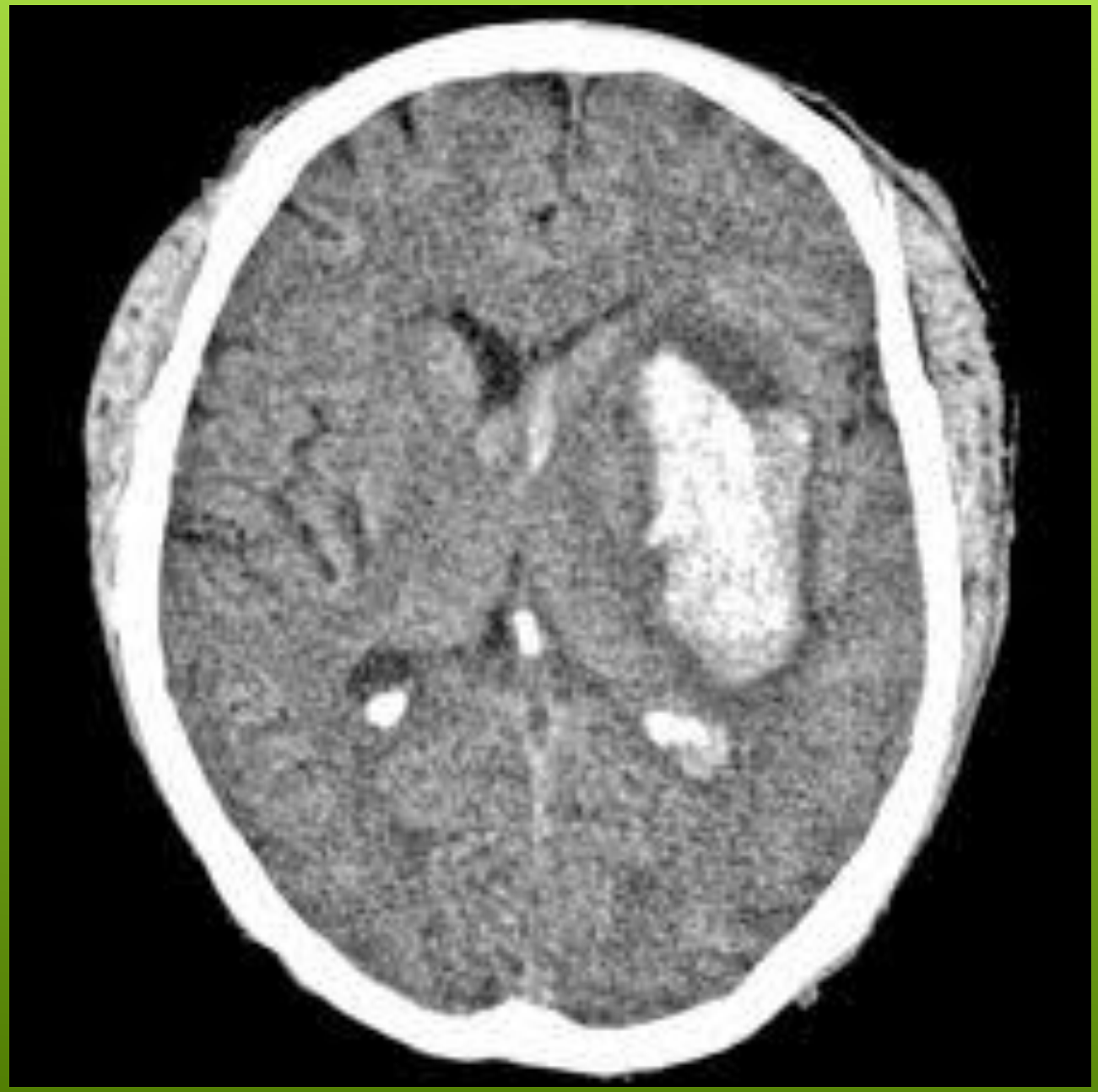
Drugs

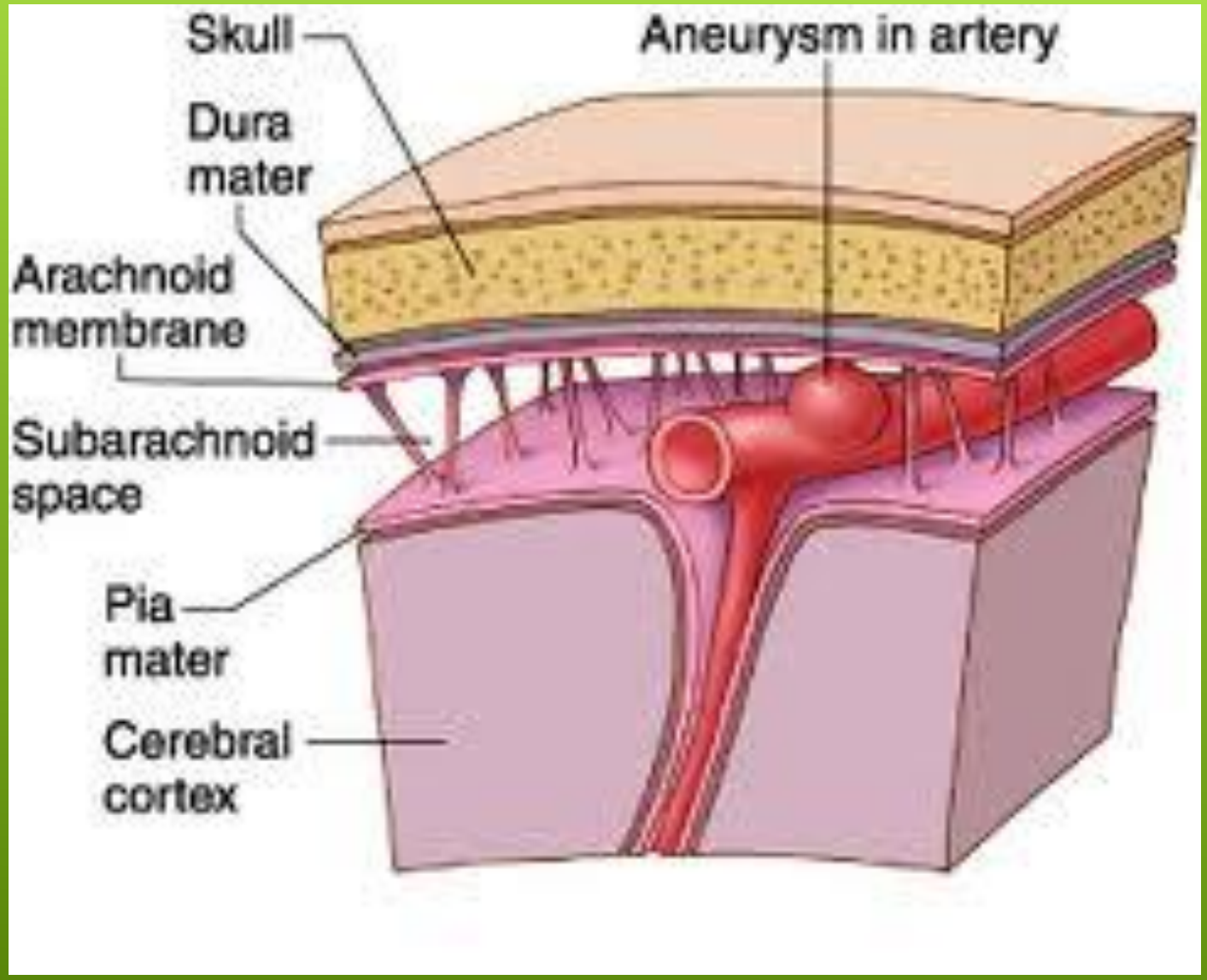
Vascular malformation

Cerebral vein thrombosis

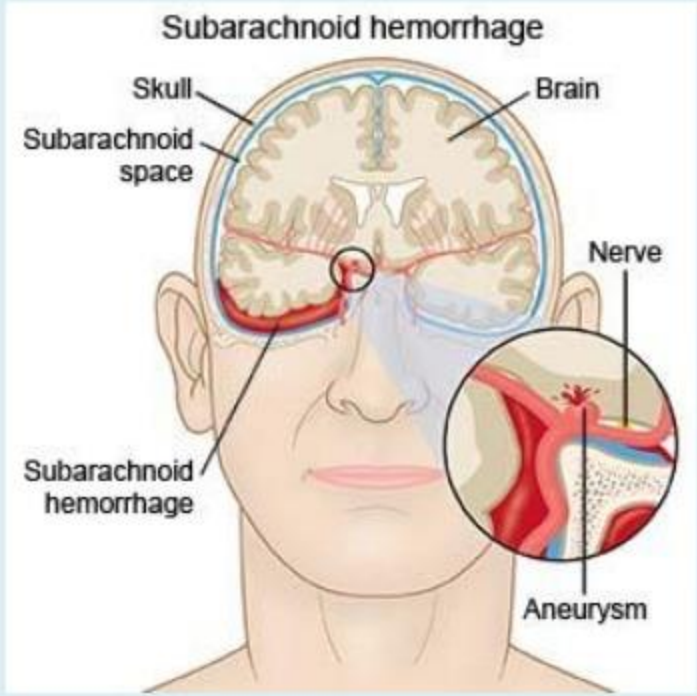
Tumor

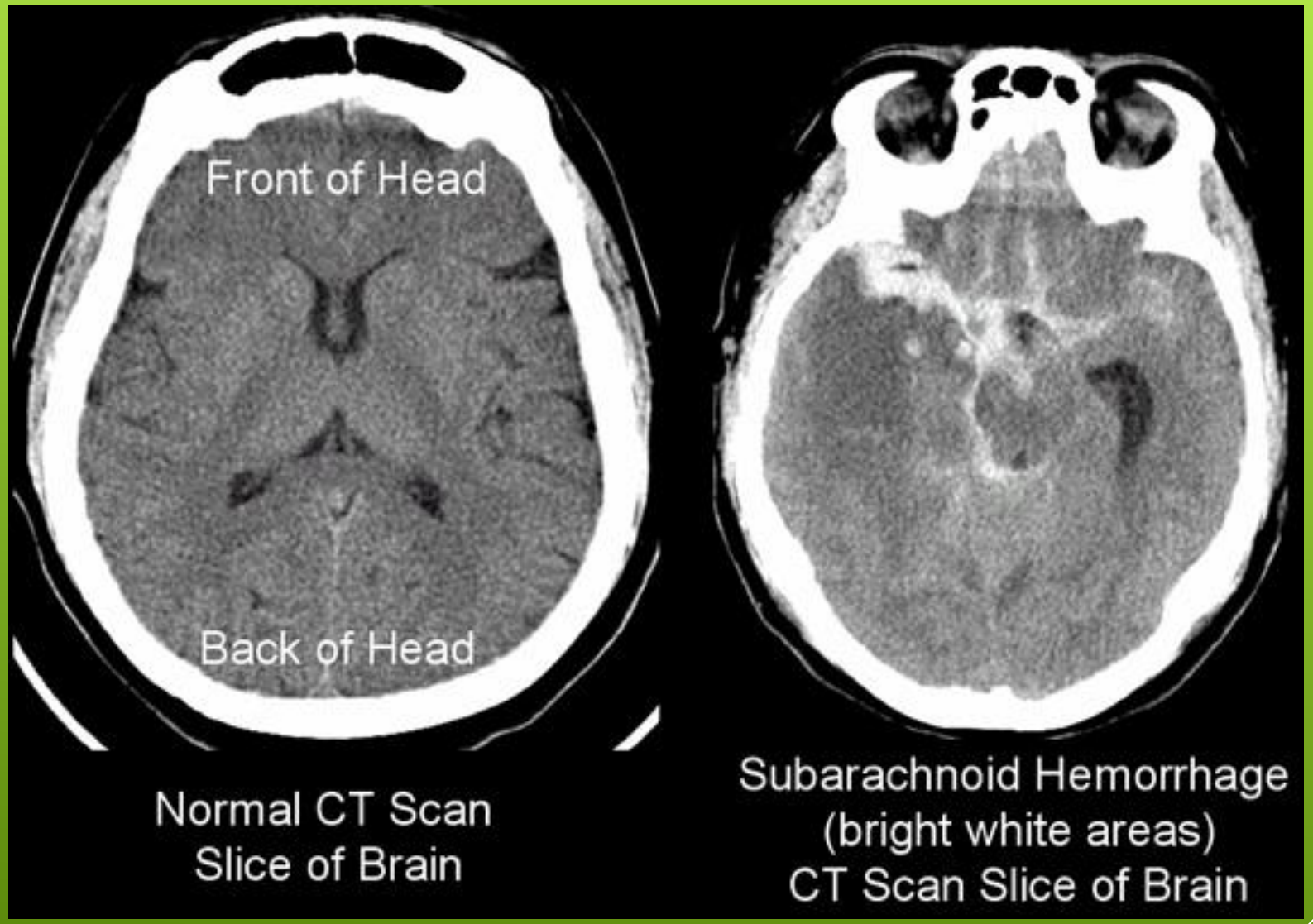
Trauma




Skull
Aneurysm in artery
Dura mater
Arachnoid membrane
Subarachnoid space
Pia mater
Cerebral cortex

Complications:
Central nervous system



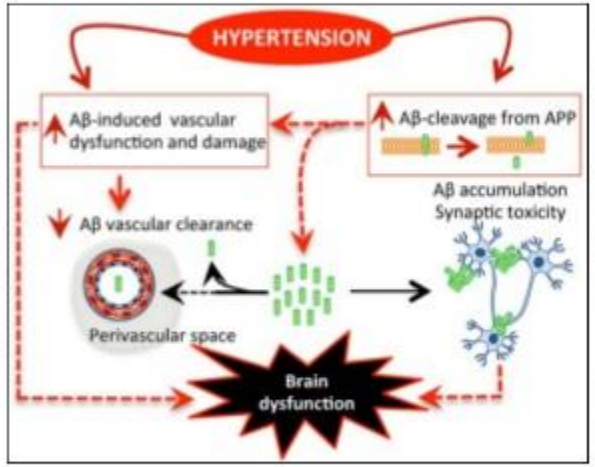

Front of Head
Back of Head
Normal CT Scan
Slice of Brain
Subarachnoid Hemorrhage
(bright white areas)
CT Scan Slice of Brain

Brain lesions underlying vascular cognitive impairment (VCI)

- A single stroke affecting a region important for cognition, like the thalamus or the frontal lobe, can lead to cognitive impairment (strategic-infarct dementia)

- VCI and dementia can also result from multiple strokes destroying large amounts of brain tissue (multi-infarct dementia)

Interaction between HTN and AD



- HTN increases deposition of β-amyloid (Aβ) and might aggravate cerebrovascular dysfunction induced by Aβ
- HTN could impair vascular clearance of Aβ and increase its cleavage from amyloid precursor protein (APP)
- This lead to increased Aβ concentration in brain parenchyma and blood vessels, aggravating attendant vascular and synaptic dysfunction

In addition, recent studies of hypertension and Alzheimer's biomarkers show that elevated blood pressure and pulse pressure are associated with the extent of brain beta amyloid (Aβ) deposition and altered cerebral spinal fluid profiles of Aβ and tau indicative of Alzheimer's pathology.

Malignant hypertension

- Also known as **accelerated hypertension**
- Blood pressure rises rapidly - diastolic blood pressure >120 mmHg
- **Characterized by**
  - accelerated **microvascular damage** with necrosis in the walls of small arteries and arterioles (**fibrinoid necrosis**)
  - Intravascular thrombosis.
- **Diagnosed by**
  - rapidly progressive end organ damage - retinopathy (grade 3 or 4)
  - renal dysfunction (especially proteinuria)
  - hypertensive encephalopathy
- Left ventricular failure may occur and, if this is untreated, death occurs within months

- **Computerized tomographic scans, magnetic resonance imaging, carotid duplex ultrasound, and catheter angiography play important roles in diagnosis.**
- **Antihypertensive treatment can substantially reduce the risk of these neurologic diseases. Antiplatelet agents, cholesterol reducing agents, and surgical and endovascular treatment of cerebral aneurysms and carotid stenosis also reduce burden of cerebrovascular disease.**

Management for Hypertension Associated with Neurological Complications

- Antihypertensive medications are recommended in addition to lifestyle measures for patients with blood pressure of 140/90 mmHg or higher,with a lower threshold of 130/80 mmHg or higher in those with diabetes and chronic kidney disease .

- For patients without a history of cardiovascular disease or other compelling indication, initiating therapy with a thiazide diuretic such as chlorthalidone is generally recommended.

- When the BP is 160/100 mmHg or higher,initiating therapy with two-drug combinations is generally recommended

There is probably no single treatment strategy that covers all neurological hypertensive emergencies(stroke,ICH,SAH,hypertensive encephalopathy and RCVS).

Prompt diagnosis of the underlying disorder, recognition of its severity, and appropriate targeted treatment are required.

Agent	Mechanism of action	CBF	ICP	Autoregulation	Platelate activity	Cardiac Contractivity ++	Dose	Onset of action	Half life	Ischemic Strock	ICH
Labetalol	∞ and β-Andrenergic blocker	...	...	...	-	...	5-20 mg bolus every 15min up to 300 mg	5-10 min	3-6 h	SS, CS,[42] ES[87]	SS, CS, [82,88] ES[89]
Hydralazine	Direct relaxation of arteriolar smooth muscle	++	++	-	-	...	5-20 mg bolus every 15min	10-20 min	1-4 h	SS, ES[53]	SS, CS[82]
Nitroprusside	Releases nitiric oxide	++	++	-	-	...	Infusion of 0.2to 10 µg. Kg^{-1}. min^{-1}	Within Seconds	2-5 min	SS, CS,[42] ES [90]	SS, CS[82]
Nitroglycerine	Releases nitiric oxide	+	...	...	-	...	20 to 400µg min	1-2 min	3-5 min		SS, CS[91]
Nitropaste	Releases nitiric oxide	+	...	...	-	...	0.2-0.4mgh up to 0.8 mgh	1-2 min	3-5 min	SS, CS92	SS, CS92
Nicardipine	Calcium channel blocker	plus	...	-	-	...	5-15 mgh	5-10 min	0.54-4 h	SS, CS58	SS, CS81, 83
Esmolol +	β-Adrenergic blocker	...	...	...	Plus	-	250µg kg bolus followed by 25 to 300	5 min	9 min		SS
Enalapril*	ACE Inhibitor	...	...	plus	-	...	1.25-5 mg every 6 h	15 min	1-4 h	CS,93 ES 53	SS, ES94

Table 1: CBF: Cerebral Blood Flow; SS: Scientific Statement; CS: Clinical study; ES: Experimental Study; ACE: Angiotensin-Converting Enzyme; +: Increase or favorable effect; ++: Substantial increase or favorable effects; -: Decrease or negative effect; ...: No documented direct effect.

Different Blood Pressure Targets for Heart and Brain?

Blood pressure targets may need to be modified depending on the cardiovascular outcome for which the patient is most at risk, a new analysis of the ALLHAT trial suggests.

The results show that for a patient with a particular risk of stroke, more aggressive blood pressure lowering may be warranted than a patient with a particular risk for myocardial infarction (MI).

Results showed that for the composite outcome of all-cause mortality, MI, and heart failure, a U-shaped association was observed with both systolic and diastolic blood pressure, but the blood pressures associated with the lowest hazards differed for each outcome.

In contrast, the association of systolic and diastolic pressure and stroke was linear, with lower values of both measurements consistently linked to a lower risk of stroke.

"When we look at just cardiac events such as MI and heart failure, we see the traditional J-shaped curve with higher risks at both extremes. But we don't see that for stroke, where lower values are consistently better for both diastolic and systolic pressures,"

the idea that 'one size fits all' for BP targets is probably not appropriate.

There is no simple calculator for trying to figure out whether a patient is more at risk of a stroke or a cardiac event, and a lot of the risk factors are the same. But if someone has a history of stroke, that make us focus more on stroke as a future event [that] we are particularly trying to prevent, "And similarly, patients with a history of heart disease are probably at higher risk of a cardiac event. We have to use our clinical experience in this.

"For stroke prevention, therefore, the old blood pressure adage 'the lower the better' holds true,

"This is a pivotal take-home message for practicing cardiologists — were it not risky for the heart, the brain would prefer an optimally cerebroprotective systolic blood pressure of 110-120 mm Hg," the editorialists comment.

They point out that this fits in with the observation that because of autoregulation, the brain is able to maintain a relatively constant blood flow despite large fluctuations in perfusion pressure. But in contrast to the brain, perfusion of the heart predominantly occurs during diastole, so that an inappropriately low diastolic blood pressure is prone to compromise myocardial perfusion.

two large prospective randomized hypertension trials have both shown target organ heterogeneity (with optimally protective blood pressure differing for the risk of stroke and the risk of MI) causes clinicians to face an uncomfortable choice of aiming to prevent cardiac events at the expense of cerebrovascular events or vice versa.

When there is urgent need for low blood pressure in stable coronary artery disease patients because of cerebrovascular disease, should coronary arteries be revascularized prophylactically, even though this would go against the recent findings of the ISCHEMIA trial? This 2020 study suggested little benefit of revascularizing asymptomatic patients with stable coronary artery disease.

"Clearly this remains a complicated issue and it is unclear as to [whether] revascularization would improve tolerability of a lower diastolic blood pressure,"

conclusion:

the blood pressure management of patients with both stable coronary artery disease and cerebrovascular disease remains challenging and needs careful shared decision-making. "Questions remain as to if we should continue with medical therapy aimed at lowering blood pressure, or should we consider further options for increasing diastolic pressure leeway, to the point of prophylactic coronary artery revascularization."

CONCLUSION:

- As a conclusion, this topic highlights a serious situation as almost half of the people in the world aged more than 30 years have HTN.
- And of those, only half were aware of their hypertensive status, less than 40% were on treatment and few of them are controlled.
- Since HTN is a modifiable disease, it can be controlled and prevented. It is proven that neurological complications due to HTN, cause high mortality rate among people in the worldwide.
- Even though HTN can be controlled by antihypertensive drugs but the quality of life of a person is gone.

THANK YOU