STROKE (cerebrovascular accident):
- Blood stops flowing to any part of your brain
- This interruption causes damage to the brain cells which cannot be repaired or replaced
- The effects of a stroke depend on the part of the brain that was damaged and the amount of damage done

LABORATORY TESTS:

At ER	CBC, platelets, INR/PTT, electrolytes, random glucose, SCr, Egfr, BUN, troponin
Select pts	• Blood and/or urine screen (if indicated) • Pregnancy test
Additional	Fasting lipid profile, HbA1C, fasting glucose, ALT/ AST/ALP/GGT, albumin
Immunological tests (if clinical suspicion)	ESR, CRP, ANA, C and p-ANCA, C3/C4, ENA
Coagulopathy screen (if indicated)	Antiphospholipid antibody, lupus anticoagulant, sickle cell screen, anti-beta-2-glycoprotein type 1
Special considerations	Pediatric patients, young adults, or clinical suspicion of rare cause of stroke: • LP for CSF analysis • Genetic testes (CADASIL, Fabry's, MELAS) • Brain biopsy

SCORING SYSTEMS:

NIHSS	Tool used to objectively quantify impairment caused by a stroke
Modified Rankin Score	Commonly used scale for measuring the degree of disability or dependence in daily activities in stroke patients

GOALS OF THERAPY:
- Reduce the ongoing neurological injury
- Restore quality of life and function
- Prevent complications secondary to immobility and neurological dysfunction
- Decrease mortality
- Prevent stroke recurrence

STROKE TYPES:

Ischemic (88%)	Definition	Blood flow to brain is compromised due to • Atherosclerosis of cerebral vessels • Embolus to cerebral arteries from distant clot
	Etiology (TOAST classification)	• Large-artery atherosclerosis • Cardioembolism (AFIB, valve disease, ischemic heart disease, infective endocarditis) • Small-vessel occlusion (lacune) • Stroke of other determined etiology (prothrombotic state, dissections, drug abuse) • Stroke of undetermined etiology
Intracerebral hemorrhage	Definition	• Bleed occurring w/in brain parenchyma (tissue) • Escape of blood from blood vessels into brain & surrounding structures • Results in direct irritant effects of blood that is in contact with brain tissue
	Etiology	• Primary: spontaneous (80%) o HTN, cerebral amyloid angiopathy • Secondary (20%): arteriovenous malformation, hemorrhagic transformation of ischemic stroke, neoplasms

DIFFERENTIAL DIAGNOSIS: clinical situations that mimic stroke

Psychogenic	Lack of objective cranial nerve findings, neurological findings in a non-fascicular distribution, inconsistent examination
Seizures	Hx of seizures, witnessed seizure activity, postictal period
Hypoglycemia	Hx of diabetes, low serum glucose, decreased LOC
Migraine with aura	Hx of similar events, preceding aura, headache
Wernicke's encephalopathy	Hx of alcohol abuse, ataxia, ophthalmoplegia, confusion
CNS abscess	Hx of drug abuse, endocarditis, medical device implant w/ fever
CNS Tumor	Gradual progression of sx, other malignancy, seizure at onset
Drug toxicity	Lithium, phenytoin, carbamazepine

DIAGNOSTIC TESTS:

Head CT	• Identifies ischemia & arterial occlusions • Most commonly used imaging test
CTA (angiogram)	• Focuses on blood vessels
MRI	• More sensitive than CT in detecting ischemic changes, and acute vs. chronic origin • Greater spatial resolution • Expensive, limited availability • CI: pacemakers, metal implants, claustrophobia, pt confusion
MRA	• Detects intracranial stenosis, vessel occlusion
Transcranial Doppler	• Identification of intracranial stenosis
ECG	• Baseline CV assessment, detection of arrhythmia, concurrent MI
Holter monitor	• To detect arrhythmia
TTE/TEE	• To examine if there are any clots in the heart

ISCHEMIC STROKE:

PATHOPHYSIOLOGY:

- Normal cerebral blood flow 50 mL/100g/minute
  - Maintained by cerebral autoregulation
- Reduced blood flow (<20 mL/100g/min) to brain (=ischemia) by:
  - Carotid atherosclerosis/plaques: leads to plaque rupture and resulting clot formation & occlusion
  - Cardiogenic embolism: caused by stasis of blood in atria or ventricles due to AFIB
- Further reduced blood flow to <12mL/100g/min
  - Decreased ATP, electrolyte imbalances, lysis
  - Increased Ca levels to enzyme activation → irreversible tissue damage (infarct)
    - Tissue surrounding infarct = penumbra (potentially viable tissue)

RISK FACTORS:

Non-modifiable	Modifiable, well-documented	Potentially modifiable, less well documented
• Age • Gender • Race • Family hx • Low birth weight	• HTN • AFIB • Other CVD • Diabetes • Dyslipidemia • Smoking • Alcohol • Sickle cell disease • Asymptomatic carotid stenosis • Postmenopausal HRT • Obesity • Low physical activity • Poor diet	• Oral contraceptives • Migraine • Drug & alcohol abuse • Hemostatic & inflammatory factors • Sleep disordered breathing

SIGNS & SYMPTOMS:

CNS	• Headache • Vertigo • Altered LOC • Falling • Sudden numbness of leg, arm or face
HEENT	• Loss of vision (hemanopsia) • Double vision • Visual defects • Aphasia (inability to comprehend or produce language) • Dysarthria (slurred or slow speech)
MSK	• One sided weakness • Hemiparesis • Sudden issue with coordination

COMPLICATIONS OF IS:

- Brain edema
- Hemorrhagic transformation
- Pneumonia
- UTI
- Seizures
- Clinical depression
- DVT

TIA VS. ISCHEMIC STROKE:

- TIA = transient ischemic attack = abrupt-onset focal neurological deficit that lasts < 24h and usually <30 min
- TIAs may or may not result in infarction
- Treated as stroke until tissue damage is ruled out on imaging
- Highest risk of stroke after a TIA is in the first few days
  - $ABCD^2$ score predicts short-term risk of stroke after TIA

INTRACEREBRAL HEMORRHAGE (ICH):

RISK FACTORS:

Non-modifiable	Lifestyle	Concurrent disease
• Age • Male gender • 1st degree relative (genetic) • Japanese • Underlying vascular lesions	• Smoking • Excess alcohol • Drug abuse	• HTN • Coagulopathy • Diabetes • Central amyloid angiopathy

SYMPTOMS:

- Can overlap with ischemic stroke symptoms
- Altered LOC
- Symptoms of increased ICP or meningismus (neck stiffness, papilledema)
- Headache
- N, V
- Seizures
- Contralateral sensory-motor deficits
- Abnormalities indicating higher cortical level dysfunction (aphasia, neglect, gaze deviation)

DIAGNOSIS:

- Non-contrast CT = gold standard
- MRI = more sensitive for "microbleeds"
- CT angiography
  - Identifies "SPOT" sign (indicator of ICH growth)
  - Find secondary causes (AVM, vasculitis, neoplasms)

ICH MANAGEMENT

ABCs		
Review for surgical management		
Stop any causative agents	Stop antiplatelet/coagulants	
Reversal of anticoagulation	Vitamin K 10 mg slow IV infusion	• All pts • Target INR <1.4 within 30 min • Repeat INR to catch rebound increase
	Reversal agents	• Fresh frozen plasma • Prothrombin complex concentrate • Recombinant factors VIIs
Blood pressure stabilization	• Less aggressive with ICH BP targets for pts with moderate severity strokes and limited to no intraventricular extension and contained bleeds • Target SBP 140-160	
Resumption of antiplatelets	• Aspirin monotherapy can be restarted in days after ICH	
Resumption of anticoagulants	• High risk pts may need careful bridging with a reversible agent prior to initiating anticoagulation • Could resume within 7-14 days of ICH if benefit >>>>> risk and pt/family aggregable to resumption • If risk >>> benefit, anticoagulation may NEVER be restarted	

MANAGEMENT OF ISCHEMIC STROKE:

STAGE 1: HYPERACUTE < 6 HOURS:

Oxygen	Common causes of hypoxia	Partial airway obstruction; hypoventilation; aspiration; atelectasis; pneumonia	
	Supplemental oxygen	For patients with SaO_2 < 95% ; goal is to maintain SaO_2 > 92%	
	Positioning	• If not hypoxic, supine position may offer advantages in terms of cerebral perfusion • If pt is at risk of obstruction, aspiration or elevated intracranial pressure, elevate head of bed to 15-30°	
BP	Let BP remain high?	• Advantages: could improve cerebral perfusion of ischemic tissue • Disadvantages: could exacerbate edema & hemorrhagic transformation of ischemic tissue; also encephalopathy, cardiac complications and renal insufficiency	
	Eligible for thrombolytic therapy	• Treat to target < 180/105 (may reduce risk of intracranial hemorrhage)	
	Not eligible for thrombolytic therapy	• Only treat extreme BP elevation (SBP > 220 or DBP < 120) –reduce by 15% (max. 25%) over first 24 hours • D/C or holding BB therapy → rebound tachycardia or rapid AFIB (therefore not recommended) ○ Lower dose may be considered to meet BP targets • Consider holding pt's normal antihypertensive regimen • Re-assess BP regimen 48 h after stroke/TIA when pt is neurologically stable	
Volume Status	Consequences of hypovolemia	• Hypoperfusion, exacerbation of ischemia, renal impairment	
	Consequence of hypervolemia	• Increased brain edema, stress on myocardium	
	Volume replacement	• Hypotonic solutions (D5 ½ NS) may worsen edema because they distribute intracellularly • Use isotonic solutions (0.9% NS) because it distributes more evenly into extracellular spaces	
Glucose	Hyperglycemia	• Common during acute stroke (40% of pts) • Stress reaction → impaired glucose metabolism • Associated with increased infarct volume & increased risk of sICH	
	Hypoglycemia	• Rare but most likely related to antidiabetic medications • Can cause autonomic and neurological symptoms → stroke mimics and seizures	
	Target blood glucose	• 7.7 – 10 mmol/L for all hospitalized patients • tPA is contraindicated if BG < 2.7 or > 22 mmol/L	
Temp.	Hyperthermia	• 1/3rd of stroke pts will be hyperthermic within first hours of acute stroke onset • Associated with poor neurological outcomes: ↑ metabolic demands, ↑ release of NTs, ↑ free radical production	
	Recommendations	• Determine cause: may be secondary to cause of stroke (infective endocarditis) or a complication of stroke (pneumonia, UTI, sepsis) • Treat cause if identified: antipyretic meds to lower meds if >38 C ○ Insufficient evidence to support use of hypothermia	
Reperfusion strategies	Fibrinolysis	MOA	Recombinant tissue plasminogen activator (tPA) which binds fibrin; converts plasminogen to plasmin
		PK	• Onset < 1h • Duration: up to 1h after infusion terminated • Elimination: primarily hepatic ($t_{1/2}$ 5 mins)
		Dose	0.9 mg/kg (max 90 mg), 10% as bolus, 90% infused over 1h
		Indications	• Goal: door to needle time < 60 mins for tPA • Blood glucose is the only lab test that must precede tPA administration ○ Unless hx of anticoagulant use, abnormal bleeding
		Contraindications	• Too many (slides 45-46)

		Monitoring	• Vital signs q15 min x 2 h, then q30 min x 6h, then q1h until 24 h post tx
			• Neurovital signs q1h x 6h, then reassess
			• Signs of clinical deterioration: new HA, acute HTN, N, V, evidence of bleeding
			  ○ IF PRESENT: D/C tPA infusion, CT scan STAT, INR, fibrinogen, CBC
			• Angioedema
			  ○ IF PRESENT: D/C tPA infusion; manage airway; IV hydrocortisone 100 mg, diphenhydramine 50mg, ranitidine 50 mg
			  ▪ Epinephrine weighed against risk of sudden HTN & ICH
			• CT head – repeat 24 hours after tPA

		Precautions after dose	• No tooth brushing or shaving x 24h • Avoid central venous access and arterial punctures x 24h • Avoid placing indwelling catheter during infusion and at least 30 mins fter • Avoid insertion of a NG tube in first 24 h
	Endovascular therapy	Indication	• Patients > 18 years of age with functionally disabling stroke (NIHSS > 2, ASPECTS >6) • Can be performed +/- tPA treatment

		Imaging	• Small to moderate ischemic core
			• Intracranial artery occlusion in anterior circulation
			  ○ Moderate to good collateral circulation
			  ○ Rule out ICH

		Time to treatment	• Within 6h of symptom onset, up to 12 h • Must be transferred to a stroke centre with expertise in 2nd gen stent retrievers
		Exclusion	• BP > 185/110, IV tPA > 0.9 mg/kg, evidence of coagulation abnormalities

MANAGEMENT OF ISCHEMIC STROKE

STAGE 2: ACUTE ISCHEMIC STROKE MANAGEMENT (ACUTE > 24 HR)

Antiplatelet therapy	Use	• Acute aspirin therapy reduces risk of early recurrent ischemic stroke
	All pts not already on antiplatelet and not receiving tPA	• 160 mg of ASA immediately after imaging excludes ICH and dysphagia screening performed
	Pts treated with tPA	• Delay ASA until after 24h post-thrombolysis scan has excluded ICH
	All pts	• Continue ASA 81-325 mg daily indefinitely, or until alternative anti-thrombotic started
	Clopidogrel	• May be considered in patients on ASA prior to stroke or TIA (as an alternative)
	Dysphagic patients	• ASA 80 mg by enteral tube or 325 mg pr daily
VTE prophylaxis	Risk factors for VTE	• Ischemic stroke, immobility, paralysis
	Guidelines	• For pts with restricted mobility, recommended prophylactic low-dose SC heparin or LMWH (reduce risk by 60%) **within** 48 h after stroke onset • Restrict for 24h after administration of tPA therapy
	Intermittent pneumatic compression (IPC)	• No direct evidence to show pharmacological venous thromboembolism prophylaxis is superior over thigh-high IPC devices • Monitor: skin integrity daily, wound care consult if skin breakdown begins • IPC taken off when pt becomes mobile; at discharge from hospital; any AEs; after 30 days of use (whichever comes first)

STAGE 3: SECONDARY PREVENTION OF ISCHEMIC STROKE

Lifestyle and Risk Factor Management	Healthy balanced diet	• Mediterranean type diet: high in vegetables, fruit, whole grains, fish, nuts, olive oil • Sodium intake < 2000 mg/day
	Exercise	• Goal: 150 mins of moderate to vigorous activity per week, > 10 min per session • Physiotherapist involvement
	Weight	• BMI 18.5 – 24.9 kg/m^2 • Waist circumference < 88 cm (women), < 102 cm (men)

	Alcohol	• Avoid heavy alcohol use
		  o Women: max 10 drinks/wk and no more than 3 drinks on a single occasion
		  o Men: max 15 drinks/wk and no more than 4 drinks on a single occasion

	OC and HRT	• Should be discontinued, consider alternatives
	Recreational drug use	• Refer pts for support and resources for dealing with drug addiction
	Smoking cessation	• Offer assistance with the initiation of a smoking cessation attempt • Provide motivational intervention to enhance readiness to quit • Consider a combination of pharmacological therapy and behavioral therapy • Manage nicotine withdrawal in admitted stroke pts • Counsel pts, family members, and caregivers about harmful effects of 2nd hand smoke • Refer pts to BC Quit Now Program

	Sleep apnea	• Risk factor for stroke, also present in many patients following a stroke
		• Screen stroke/TIA patients for sleep apnea and refer to sleep specialist for management of OSA
		  o Avoidance of hypnotics, sedatives
		  o Weight loss
		  o Continuous positive airway pressure (CPAP)
		  o Dental appliances

Blood pressure	Secondary stroke prevention	• A 10/5 decrease in BP is associated with 30-40% decrease in risk of stroke • Optimal time to initiate antihypertensive post-stroke not defined; should be initiated or modified before discharge from hospital
	Evidence	• ACE-inhibitor or ARB alone = NSS reduction in secondary prevention • ACE-inhibitor + diuretic = reduced stroke in combo • SBP < 130 = NSS reduction in stroke compared to 130-149
	Target	• Stroke or TIA: < 140/90 • Diabetes (primary or secondary prevention): SBP < 130
Anti-platelet therapy	Secondary stroke prevention	• All patients with ischemic stroke or TIA unless there is indication for anticoagulation (ex// AFIB) • ASA (80 – 325 mg), ASA (25 mg) + ER dipyridamole (200mg) or clopidogrel (75 mg) • If on prior antiplatelet therapy (low-dose ASA) prior to stroke, no literate to support/refute switching to another antiplatelet
	DAPT	• Combo of ASA (81 mg) + clopidogrel (75 mg) uncertain benefit, should not be routinely used
Statins	Lipid level assessment	• All patients post ischemic stroke or TIA
	Lipid management	• Comprehensive approach including dietary modification
	Lipid target	• Target LDL of <2 mmol/L or 50% reduction in LDL baseline
	Statins	• Atorvastatin 80 mg or simvastatin 40 mg daily