433 Teams

MEDICINE

16| Stroke

433medicine.team@gmail.com

جامعة الملك سعود
King Saud University

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Objectives:

1. know the list common modifiable and non-modifiable stroke risk factors
2. Differentiate between TIA and stroke
3. Recognize common stroke presentation based on arterial distribution
4. Familiarize with guidelines re: Acute stroke therapies
5. Recognize common stroke complication and associated morbidities like aspiration pneumonia, DVT, and UTI
6. Familiarize with primary and secondary stroke prevention
7. Know common types of intracerebral haemorrhage
8. Know common causes for intracerebral haemorrhage
9. Familiarize with management of drug induced intracerebral haemorrhage
10. Know indication for surgical Rx in pts with intracerebral haemorrhage

The lecture was focusing on management and risk factors, other objectives from the department.

SIADH	Syndrome of Inappropriate Antidiuretic Hormone Secretion
MRS	Modified Rankin Score
rt-PA	Recombinant Tissue Plasminogen Activator
(r-pro-UK)	Recombinant pro-urokinase

Introduction

A. The High Socioeconomic Cost of Stroke

- ✓ A leading cause of serious, longterm disability
- ✓ A second to only heart disease in causing death world-wide.
- ✓ According to the WHO 15 million people worldwide suffer a stroke each year
- ✓ 30-day mortality is 8-12%
- ✓ For survivors aged > 65 years:
  - 50% have hemiparesis
  - 30% are unable to ambulate
  - 19% are aphasic
  - 35% are depressed
  - 26% resides in nursing home
- ✓ Stroke risk and mortality increase with age
- ✓ The increase in life expectancy will increase the incidence of stroke
- ✓ In the US, total direct and indirect costs are $56.8 billion annually
- ✓ The mean lifetime cost of ischemic stroke is estimated at $140,048
- ✓ Stroke was wrongly named Cerebrovascular Accident (CVA)
- ✓ Prior to two decades ago, no treatment was offered for acute stroke victims because of the misconception that arterial occlusion in the brain leads to irreversible necrosis and dead tissue within minutes.
- ✓ Stroke care was focused on supportive care, stroke prevention and rehabilitation

B. Penumbra

Penumbra is zone of reversible ischemia around core of irreversible infarction salvageable in first few hours after ischemic stroke onset. *"TIME IS BRAIN: SAVE THE PENUMBRA"* (Figure1)

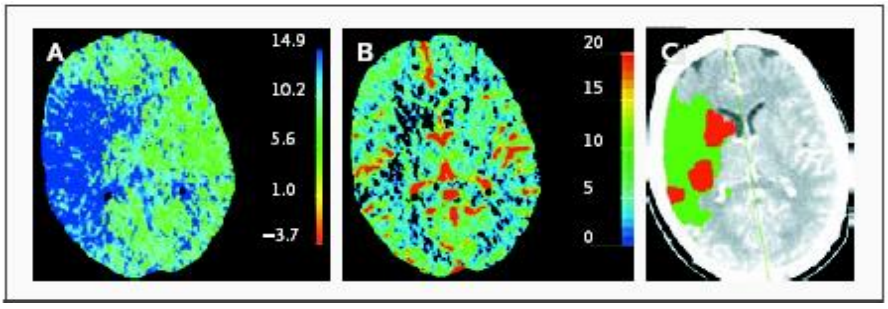


Figure1: **Perfusion CT Scans Obtained 1 Hour 45 Minutes after the Onset of Ischemia in the Territory of the Right Middle Cerebral Artery**. A large area shows prolongation of the mean transit time (in seconds) (Panel A), and a smaller area shows a reduction in cerebral blood volume (in ml per 100 g) (Panel B). These two maps suggest a large penumbra and a small infarct core (Panel C, with the penumbra shown in green and the suggested infarct core in red).

- ✓ In every ischemic stroke there is ischemic core and penumbra. (Figure2)
- ✓ Penumbra is the region of tissue at risk of being recruited into the ischemic core
- ✓ Ischemic Penumbra presents a Window of Opportunity

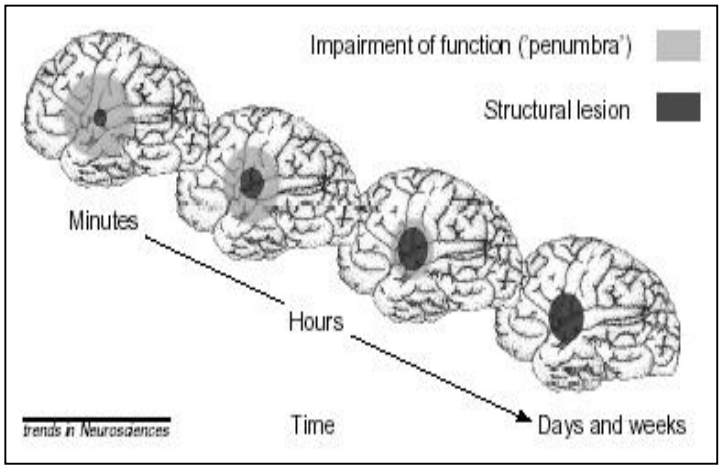


Figure2: Ischemic core and penumbra

Objective 1: Know the list common modifiable and non-modifiable stroke risk factors

A. Non-modifiable Risk Factors

1. *Age*	**The risk of stroke doubles in each successive decade after 55 years of age**
2. *Sex*	Men have higher age-specific stroke incidence rates than women, except in 35-44 year olds and in those over 85 years of age. Stroke related case-fatality rates are higher in women than men.
3. *Race*	Blacks and some Hispanic Americans, have high stroke incidence and mortality rates compared with whites (Blacks have 38% greater incidence of stroke than whites.
4. *Family History*	Both paternal and maternal history of stroke may be associated with increased stroke risk (RR paternal history: 2.4 and RR maternal history: 1.4.
5. *Birth weight*	Birth weight is inversely associated with incident of stroke.

B. Modifiable Risk Factors

Well-Documented Modifiable Risk Factors

1. *Hypertension*	✓ It is a major risk factor for stroke. ✓ Both systolic and diastolic hypertension are important risk factors for stroke ✓ Isolated systolic hypertension is an important risk factor for stroke in the elderly ✓ There is compelling evidence for more than 30 years that the control of high blood pressure contributes to the prevention of stroke. ✓ Unfortunately, a significant proportion of the population has undiagnosed or inadequately treated hypertension, especially in high-risk race/ethnic groups. ✓ Regular screening for hypertension (at least every 2 years in adults). Management should include both life style modification and antihypertensive medications.
2. *Smoking*	✓ 25% of adults are active smokers ✓ A prospective estimate of a 1.8 fold increase in stroke risk associated with smoking from the Framingham Heart Study. ✓ Former smoking also place individuals at increased risk for stroke (RR 1.34). ✓ Exposure to environmental tobacco also increases the risk of stroke. ✓ Patient and family should be encouraged to stop smoking (counseling, nicotine replacement etc..)
3. *Diabetes*	✓ It is an independent risk for stroke (RR 1.8 to 6). ✓ High BP is common in patients with type 2 diabetes, with a prevalence of 40 to 0% in adults. ✓ Tight BP control resulted in a convincing 44% relative risk reduction. ✓ Glycemic control is recommended to reduce microvascular complications.
4. *Hyperlipidemia*	✓ There is an association between serum cholesterol and an increasing risk of stroke (1.8 to 2.6) ✓ An inverse relationship between HDL and stroke was demonstrated ✓ SPARCL Trial: 80 mg of Atrovastatin per day reduced the overall incidence of strokes and cardiovascular events, despite a small increase in the incidence of hemorrhagic stroke
5. *Asymptomatic Carotid Stenosis* 6. *Sickle Cell Disease* 7. *Atrial Fibrillation*	

Potentially Modifiable Risk Factors

1. *Obesity*	✓ ABMI >30 kg/m2 predisposes to cardiovascular disease in general and stroke in particular ✓ Recent evidence support abdominal obesity in men and obesity in women as independent risk factors for stroke ✓ Weight reduction in overweight persons is recommended on the basis of the associated increase in comorbid conditions. Reduction in stroke risk with weight loss has not been established

2. *Physical Inactivity*	✓ Framingham Study and the Nurses Health Study demonstrated an inverse association between level of physical activity and stroke incidence ✓ NHANES and the Northern Mnhattan Study showed protective effects of leisure-time physical activity in Blacks and Hispanics ✓ Americans should exercise moderately for at least 30 minutes on most, and preferably all days of the week. For stroke, the benefits are apparent even for light to moderate activities such as walking
3. *Poor Diet /Nutrition*	✓ There is no evidence that the use of dietary vitamin E or C supplements reduces the risk of stroke ✓ Based on the nurses Health Study, there may be a protective relationship between stroke and consumption of fruits and vegetables, especially green leafy vegetables and citrus fruit and juice ✓ A healthy diet containing at least 5 daily servings of fruits and vegetables may decrease the risk of stroke
4. *Hormone Replacement Therapy*	✓ Framingham Heart Study: 2.6 fold increase in the relative risk of stroke among women receiving hormone replacement therapy compared with non-users ✓ Women Health Initiative Study: Increased risk of stroke, CHD, and pulmonary embolism in the arm receiving HRT
5. *Oral Contraceptive Use*	✓ A meta-analysis concluded that the risk of ischemic stroke is increased in oral contraceptive users but that the absolute increase in risk is small. ✓ Women who are cigarette smokers, are hypertensive, or have diabetes, migraine, or prior thromboembolic events may be at increased stroke risk if they use oral contraceptives ✓ Oral contraceptives should be avoided in women with additional risk factors (cigarette smoking, or prior thromboembolic events)
6. *Alcohol Abuse* 7. *Hyperhomocystenemia* 8. *Drug Abuse* 9. *Hypercoagulability* 10. *Inflammatory Processes*	

Objective 2: Differentiate between TIA and stroke

A. Types of strokes:

- ✓ Ischemic strokes (85%of cases)
- ✓ Hemorrhagic strokes (15% of cases)

B. Classes of ischemic stroke

1. Transient ischemic attack (TIA)
2. **Evolving stroke** is a stroke that is worsening.
3. **Completed stroke** is one in which the maximal deficit has occurred.

Transient ischemic attack (TIA)

- A neurologic deficit that lasts from a few minutes to no more than 24 hours (but usually lasts less than 30 minutes).
- Stroke may be indistinguishable from a TIA at the time of presentation: Duration of symptoms is the determining difference.
- The blockage in blood flow does not last long enough to cause permanent infarction.
- Usually embolic. However, transient hypotension in the presence of severe carotid stenosis (>75% occlusion) can lead to a TIA.
- Once a patient has a TIA, there is a high risk of stroke in subsequent months.

C. Causes of ischemic stroke

1. **Embolic stroke** is the most common etiology of TIA/CVA. Possible origins of an embolus include:
   - Heart (most common): Typically due to embolization of mural thrombus in patients with atrial fibrillation
   - Internal carotid artery
   - Aorta
   - Paradoxical: Emboli arise from blood clots in the peripheral veins, pass through septal defects (atrial septal defect, a patent foramen ovale, or a pulmonary AV fistula), and reach the brain.
2. **Thrombotic stroke**: Atherosclerotic lesions may be in the large arteries of the neck or in medium sized arteries in the brain (especially the middle cerebral artery [MCA]).
   - Most common location involves the middle cerebral artery results in contralateral weakness, sensory loss, and hyperreflexia.
3. **Lacunar stroke**: small vessel thrombotic disease
   - Causes approximately 20% of all strokes; usually affects subcortical structures and not the cerebral cortex.
   - Predisposing factor: A history of HTN is present in 80% to 90% of lacunar infarctions.
   - Diabetes is another important risk factor.
   - Narrowing of the arterial lumen is due to thickening of vessel wall (not by thrombosis).
   - The arteries affected include small branches of the MCA, the arteries that make up the circle of Willis, and the basilar and vertebral arteries.
   - When these small vessels occlude, small infarcts result; when they heal, they are called lacunes.

4. **Nonvascular causes**: Examples include low cardiac output and anoxia (may cause global ischemia and infarction).

Objective 3: Recognize common stroke presentation based on arterial distribution

A. Clinical features

Table3.1: Deficits seen in stroke

Distribution	Type of Deficiency
Anterior cerebral artery	Contralateral lower extremity and face
Middle cerebral artery (MCA)	✓ Contralateral hemiparesis and hemisensory loss ✓ Aphasia (if dominant hemisphere is involved)—for 90% of population this is left cerebral dominance ✓ Apraxia, contralateral body neglect, confusion (if nondominant hemisphere is involved)
Vertebral/basilar	✓ **Ipsilateral:** ataxia, diplopia, dysphagia, dysarthria, and vertigo. ✓ **Contralateral:** homonymous hemianopsia with basilar posterior cerebral artery (PCA) lesions
Lacunar	1) Pure motor lacunar stroke—if lesion involves the internal capsule. 2) Pure sensory lacunar stroke—if lesion involves the thalamus. 3) Ataxic hemiparesis—incoordination ipsilaterally. 4) Clumsy hand dysarthria

B. Diagnostic tests of stroke

- ✓ The best initial test in any kind of stroke is a CT scan of the head without contrast.
- ✓ Positive in hemorrhagic stroke.
- ✓ The most accurate test is an MRI.
- ✓ Evidence of ischemia may not become apparent until 48 to 72 hours.
- ✓ CT scan is done first, not because it is the most sensitive test for stroke, but in order to exclude hemorrhage as a cause of the stroke prior to initiating treatment.
- ✓ CT scan needs 4 to 5 days to reach greater than 95% sensitivity. MRI needs only 24 to 48 hours to reach greater than 95% sensitivity.

Objective 4: Familiarize with guidelines: Acute stroke therapies

Pharmacological re-canalization

A. National Institute of Neurological Disorders and Stroke (NINDS) Trial

Trial Design	**624 acute stroke patients were randomized to either Placebo or 0.9mg/kg of IV rt-PA within 3 hours from the stroke onset.**
Results	✓ Those treated with IV rt-PA were 30% more likely to have no or only minor disability at 3 months post stroke ✓ Absolute risk reduction of poor outcome in the t-PA patients is 13% ✓ OR for favorable outcome (MRS 0-1) in the t-PA patients 1.9 ✓ No difference in mortality between the two groups ✓ 6.4% symptomatic hemorrhage in the t-PA group compared to 0.6% in the Placebo group
Primary outcome:	Complete or nearly complete neurological recovery at 3 months after stroke
CONCLUSTION	FDA in 1996 approved IV t-PA for the treatment of acute ischemic stroke within 3 hours from stroke onset.

B. European Cooperative Acute Stroke Study (ECASS II):

Trial Design	**Acute stroke patients were treated with either 0.9 mg/kg rt-PA or Placebo within 6 hours after stroke onset**
Results	Results showed increase intracerebral hemorrhage in the t-PA group.

C. European Cooperative Acute Stroke Study (ECASS III)

Trial Design	**A total of 821 acute stroke patients were treated with either 0.9 mg/kg rt-PA or Placebo within 4.5 hours of the stroke symptoms onset** • **Additional exclusion criteria to the NINDS trial include age >80, oral anticoagulant, NIHSS > 25, CT showing > 1/3 MCA infarct, and history of both stroke and diabetes**
Results	Absolute risk reduction of poor outcome is 7%
CONCLUSTION	The AHA,ASA, and ESA endorsed the use of alteplase within 4.5 hours of the symptoms onset

Tissue Plasminogen Activator (t-PA)

- ✓ t-PA, which is clot specific, degrades the Plasminogen to Plasmin which in turn break apart the fibrin and the clot dissolves.
- ✓ T-PA produces economic benefit by reducing societal and health care costs.
- ✓ Despite supporting data on the efficacy and safety of IV t-PA, it remains substantially underutilized:
  - Only <1% of acute stroke patients receive thrombolysis in U.S in 2006 *(Mohammad et al. ISC)*

Main reason for under utilization, patients present beyond 3 hours from symptoms onset

- Challenges to the utilization of t-PA include:
  - ✓ Narrow eligibility and treatment window
  - ✓ Risk of hemorrhage
  - ✓ Perceived lack of efficacy in large vessel occlusion
    - Large vessel occlusion predicts large infarct size and is associated with poor outcome (46%)
    - Patients with hyperdense which is indicative of large vessel occlusion respond poorly to IV t-PA (70-84% Have poor outcome)
  - ✓ Limited pool of stroke expertise in the community

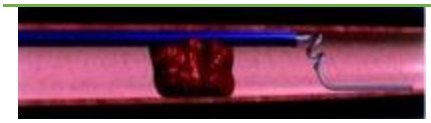
D. PROACT (Prolyse in Acute Cerebral Thromboembolism) Trial:

Trial Design	**180 acute stroke patients who presented with middle cerebral artery occlusion were randomized to either Heparin or Intra-arterial r- ProUK within 6 hours from stroke onset.**
Outcome	Minimal or no neurological disability at 3 months.

♁Mechanical Recanalization

E. Mechanical Embolus Removal in Cerebral Ischemia (MERCI) Trial:

Trial Design	Non-randomized study that evaluated the safety and efficacy of clot removal by the MERCI retriever. 141 patients with intracranial large vessel occlusion treated within 8 hours



After the microcatheter transverses the thrombus, the first loops of the Merci Retriever are delivered distal to the occlusion site

The Merci Retriever is pulled back at the contact of the thrombus, additional loops are delivered within the thrombus, and the Merci Retriever is torqued to ensnare the thrombus

The balloon of the balloon guide catheter (BGC) (insert) is inflated to control antegrade flow, and the Merci Retriever is pulled back with the ensnared thrombus toward the tip of the BGC where it is aspirated

Results	✓ Recanalization: 48% (19% PROACT control) ✓ Complications: 7% (emboli, dissection, SAH) ✓ Good outcome: 28% (46% recanalized, 10% occluded) ✓ Mortality: 43% (32 recanalized, 54% occluded) ✓ Symptomatic hemorrhage occurred in 5%.
Outcome	Embolectomy performed using a MERCI retriever device can also result in successful recanalization. The patient presented here had significant clinical improvement following MERCI assisted embolectomy.
CONCLUSTION	The FDA in 2005 approved the MERCI retriever for removing clot within 8 hours of stroke symptoms.

F. Penumbra microcatheters, with separator wires

This device uses aspiration assisted by a separator wire to suction out thrombus.

Figure3

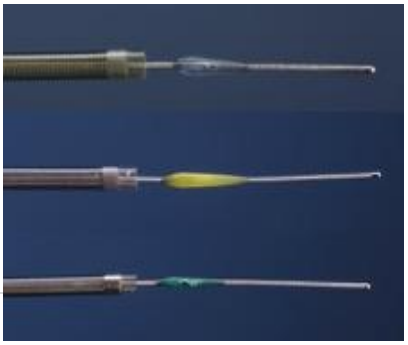


Figure3: Penumbra microcatheters

ADVANTAGES

- ✓ Can be used in some patients with contraindications to thrombolysis
- ✓ 8-hour window
- ✓ Initial data indicates higher revascularizton rates relative to other methods.
- ✓ Preliminary data shows better outcome at 90 days relative to other devices show

DISADVANTAGES

- ✓ Vessel tortuosity precludes use
- ✓ Distal vessels not reachable
- ✓ Operator experience
- ✓ Higher rate of symptomatic intra-cerebral hemorrhage

Trial Design	Enrolled 125 patients at 24 international centers. Patients in the trial presented within 8 hours from symptoms onset, had an NIHSS >8 and had complete occlusion of a large intracranial vessel.
Results	Recanalization: 81.6 % Hemorrhage: 11.2% Mortality: 26%

G. Phenox Clot Retriever

It has a system with a highly flexible core wire compound resembling a pipe cleaner. Figure 4

H. Stent Placement in Acute Stroke

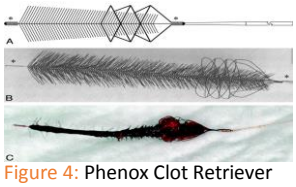


Figure 4: Phenox Clot Retriever

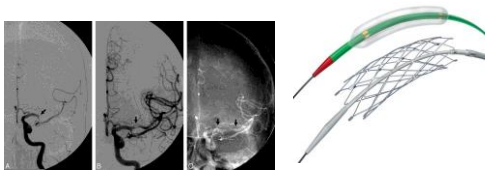


Figure 5: Stent Placement in Acute Stroke

Summary for Acute Stroke Treatment

- ✓ IV t-PA was effective and is FDA approved for acute stroke treatment within 3 hours of stroke onset
- ✓ IV t-PA effective within 4.5 hours
- ✓ Intra-arterial thrombolysis was effective, within six from the symptoms onset, in improving outcome in a large open label study.
- ✓ MERCI retriever proven effective within Eight hours from Stroke Symptoms and FDA Approved.
- ✓ Penumbra proven effective within eight hours from stoke symptoms and FDA approved

I. The best initial therapy for a nonhemorrhagic (Ischemic) stroke is:

- ✓ Less than 3hours since onset of stroke: thrombolytic
- ✓ More than 3hours since onset of stroke: aspirin
- ✓ Hemorrhagic stroke: nothing
- ✓ If the patient is already on aspirin at the time of the stroke?
  - Add dipyridamole OR Switch to dopidogrel
- ✓ Treatment for prevention of a stroke is with either aspirin or clopidogrel. DO NOT COMBINE THEM. It causes bleeding. You cab combine dipyridamole with aspirin as an equivalent of clopidogrel.

Objective 5: Recognize common stroke complication and associated morbidities

A. Complications of ischemic stroke

- ✓ Progression of neurologic insult
- ✓ Cerebral edema occurs within 1 to 2 days and can cause mass effects for up to 10 days. Hyperventilation and mannitol may be needed to lower intracranial pressure.
- ✓ Hemorrhage into the infarction (rare)
- ✓ Seizures (fewer than 5% of patients)

B. Complications of Hemorrhagic stroke

1. Intracerebral hemorrhage (ICH)

Increased ICP/Seizures / Rebleeding/ Vasospasm e/ Hydrocephalus/ SIADH

2. Subarachnoid hemorrhage (SAH)

- ✓ Rerupture: occurs in up to 30% of patients
- ✓ Vasospasm: occurs in up to 50% of patients (more often with aneurysmal SAH); can cause ischemia/infarction and therefore stroke
- ✓ Hydrocephalus (communicating): secondary to blood within the subarachnoid space hindering normal CSF flow
- ✓ Seizures may occur (blood acts as an irritant).

Objective 6: Familiarize with primary and secondary stroke prevention

A. Stroke Awareness

- ✓ Estimated that up to 80% of strokes could be prevented
- ✓ Many of the established risk factors for stroke, such as hypertension, diabetes, obesity, hyperlipidemia, and smoking can be controlled either through change in the life style or the use of medications
- ✓ Greater understanding and awareness of the stroke risk factor would enhance people's compliance with the physician visits and instructions

B. Stroke prevention

1. **Echocardiogram:**
   - ✓ Surgical replacement or repair of certain damaged valves
   - ✓ Thrombi: heparin followed by warfarin to an INR of 2to3
   - ✓ Patent foramen ovale (PFO)
2. **EKG:** Atrial fibrillation or flutter is treated with warfarin to an INR of 2 to 3 as long as the arrhythmia persists.
3. **Holter monitor (24 to 48 hour ambulatory EKG):** If the initial EKG is normal, a Holter monitor should be performed to detect atrial arrhythmias with greater sensitivity.
4. **Carotid duplex ultrasound:** Carotid stenosis is a frequent cause of emboli to the brain. If a patient has symptomatic cerebrovascular disease and more than 70% stenosis is

detected, surgical correction of the narrowing should be performed. Endarterectomy is superior to carotid angioplasty.

5. **Endarterectomy has no value for milder stenosis (under 50%).** It is unclear if endarterectomy will benefit moderate stenosis (50%-70%). If the stenosis is 100%, however, no intervention is needed. No point in opening a passage that is 100% occluded.

C. Stroke in Saudi Arabia

An interview survey of 21 questions, pertaining to stroke awareness (stroke symptoms, and signs and stroke risk factors), was distributed in malls, super markets, health clubs, mosques, universities and schools. Conclusion:

- ✓ There is an alarming deficit in the level of stroke awareness in the Saudi population.
- ✓ This calls for an urgent need to improve the knowledge and awareness levels of stroke.

Objective 7: Know common types of intracranial haemorrhage

A. Two Major categories of hemorrhagic stroke:

1. Intracerebral hemorrhage (ICH): bleeding into brain parenchyma.
   - ✓ ICH is associated with a high mortality rate (50% at 30 days). For those who survive, there is significant morbidity.
   - ✓ Hematoma formation and enlargement may lead to local injury and increase in intracerebral pressure.
2. Subarachnoid hemorrhage (SAH): bleeding into the CSF; outside brain parenchyma.
3. Epidural hematoma
4. Subdural hematoma

(3 & 4 under the types of intracranial haemorrhage)

Objective 8: Know common causes for intracerebral haemorrhage (ICH)

A. Causes of ICH:

1. HTN (particularly a sudden increase in BP) is the most common cause (50% to 60% of cases).
   - ✓ HTN causes a rupture of small vessels deep within the brain parenchyma. Chronic HTN causes degeneration of small arteries, leading to microaneurysms, which can rupture easily.
   - ✓ It is typically seen in older patients; risk increases with age.
2. Ischemic stroke may convert to a hemorrhagic stroke.
3. Other causes include amyloid angiopathy (10%), anticoagulant/antithrombolytic use (10%), brain tumors (5%), and Arteriovenous malformation (AVM) (5%).

B. Causes of subarachnoid hemorrhage (SAH)

1. Ruptured berry (saccular) aneurysm is the most common cause (has higher morbidity and mortality than other causes). Polycystic kidney disease is associated with berry aneurysms.
2. Trauma is also a common cause.
3. AV malformation

Objective 10: Know indication for surgical Rx in patients with intracerebral haemorrhage

Hemorrhagic stroke has no treatment to reverse it. Surgical drainage will not help outside posterior fossa.

MCQs

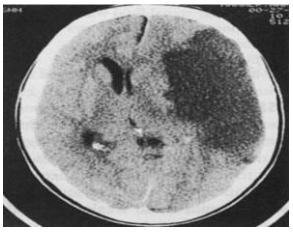
Question 1: A 71-year-old woman is brought to the emergency room by her daughter because of sudden onset of right-sided weakness and slurred speech. The patient, a recent immigrant from Southeast Asia, has not seen a doctor in two decades. Her symptoms began 75 minutes ago while she was eating breakfast. A stat noncontrast CT scan of the head is normal. Labs are normal. Physical examination reveals an anxious appearing woman with dense hemiplegia of the R upper and lower extremities. Deep tendon reflexes are not discernible on the R side and 2+ on the left. Aspirin has been given. What is the best next step in management of this patient?

A. Immediate intravenous unfractionated heparin
B. Immediate thrombolytic therapy
C. Immediate administration of interferon-beta
D. Emergent MRI/MRA of head
E. Emergent cardiac catheterization

Question2: A 65-year-old man presents with right-sided weakness and expressive aphasia that began suddenly 2 hours ago. He has a history of osteoarthritis, gout, and hypertension. He has no history of recent head trauma or surgery. Medications include lisinopril, allopurinol, and acetaminophen. On physical examination the patient is alert. His blood pressure is 164/90 and his pulse rate is 66. He has a dense right hemiparesis and is not able to speak. Complete blood count, platelet count, prothrombin time, glucose, and ECG are normal. CT of the head without IV contrast is normal. What is the next best step?

A. Urgent carotid ultrasonography.
B. Anticoagulation with heparin.
C. Discuss risks and benefits of thrombolysis with intravenous recombinant tissue-type plasminogen activator.
D. Aspirin 81 mg orally now. e. MRI scan of the brain.

Question 3: A 73-year-old man has had three episodes of visual loss in the right eye. The episodes last 20 to 30 minutes and resolve completely. He describes the sensation as like a window shade being pulled down in front of the eye. He has a history of hypertension and tobacco use. He denies dyspnea, chest pain, palpitations, or unilateral weakness or numbness. On examination the patient appears healthy; his vital signs are normal and the neurological examination is unremarkable. An ECG shows normal sinus rhythm without evidence of ischemia or hypertrophy. Initial laboratory studies are normal. Both noncontrast CT scan of the head and MR scan of the brain are normal. What is the best next step in this patient's management?



A. Begin anticoagulation with low-molecular-weight heparin and warfarin.
B. Obtain an echocardiogram.
C. Check for antiphospholipid antibodies and homocysteine levels.
D. Order a carotid duplex ultrasonogram and begin antiplatelet therapy.
E. Begin lamotrigine for probable nonconvulsive seizure.

Question 4: A 68-year-old man with a history of hypertension and coronary artery disease presents with right- sided weakness, sensory loss, and an expressive aphasia. Neuroimaging studies are shown here. In the emergency department the patient's blood pressure is persistently 160/95. Which of the following is the best next step in management of this patient's blood pressure?

A. Administer IV nitroprusside.
B. Administer clonidine 0.1 mg po until the blood pressure drops below 140/90.
C. Observe the blood pressure.
D. Administer IV mannitol. E. Administer IV labetolol.

Answer 1: The answer is b. This patient presents with an acute left middle cerebral artery stroke. Time is of the essence if thrombolytic therapy is to be beneficial. Intravenous thrombolytics may be administered up to 3 hours after the onset of symptoms. Recent studies have suggested expanding the window of opportunity to 4.5 hours. Fortunately, this patient was brought to the ER promptly. CT scan of the brain shows no evidence of bleed. Evidence of ischemia may not become apparent until 48 to 72 hours. A prior history of intracranial hemorrhage, recent surgery, bleeding diathesis, onset of symptoms greater than 3 to 4.5 hours prior to therapy, and unknown time of onset of symptoms are contraindications to thrombolytic therapy. This patient should be given intravenous tissue-type plasminogen activator (t- PA).

Anticoagulation in acute stroke (answer a) is not currently recommended. In most trials of anticoagulation, any benefit of therapy is matched by an increase in hemorrhagic transformation. Interferon-beta (answer c) is used to treat multiple sclerosis, not ischemic stroke. Emergent scanning with MRI (answer d) wastes precious time and is not always available. Patients with acute stroke often have mild elevation in cardiac biomarkers. Cardiac catheterization (answer e) is unnecessary, and may very well prove harmful in the setting of a stroke.

Answer 2: The answer is c. This patient presents with a major middle cerebral artery territory stroke. Patients who present within 3 or 4 hours of onset of symptoms of ischemic stroke are candidates for thrombolysis, which has been shown to improve disability and decrease long-term neurologic deficit. In one study, 50% of patients treated with recombinant tissue-type plasminogen activator (r-TPA) had little or no neurologic deficit 6 months after the stroke, compared to 35% of controls. TPA is contraindicated in hemorrhagic strokes. Thus all patients who are candidates should have CT imaging to exclude a hemorrhagic stroke. CT scanning in acute ischemic stroke is frequently normal (as in this patient) and thus the diagnosis of stroke is made on clinical grounds. TPA use in acute ischemic stroke is associated with a 5% to 6 % risk of intracranial hemorrhage, and thus patients and/or their families should be carefully informed of the relative risks and benefits. Patients with intracranial hemorrhage on imaging, recent head trauma (within the last 90 days), surgery within the last two weeks, uncontrolled hypertension, coagulopathy, or who present with seizures are not candidates for TPA. Aspirin and heparin are to be avoided for 24 hours in patients who are given TPA. Extracranial cerebrovascular disease can be diagnosed with carotid ultrasonography, but carotid artery surgery is done to prevent a subsequent stroke and thus carotid ultrasonography can be done nonurgently. MRI scanning is more sensitive for diagnosing acute stroke, but does not need to be done to confirm a stroke in this patient who has clear cut symptoms and for whom urgent consideration of TPA therapy is the most pressing clinical issue.

Answer3: The answer is d.This patient has suffered several transient ischemic attacks with the classic description of amaurosis fugax. Although the traditional symptom duration of less than 24 hours is often cited, most TIAs last less than 1 hour, usually 15 or 20 minutes. Many patients whose symptoms last for several hours are found to have ischemic strokes on MRI imaging. TIAs carry a high risk of neurological morbidity and should be promptly evaluated and treated. Five percent of patients will have a full-blown stroke within the next 2 weeks. Assessing the extracranial carotid arteries for evidence of atherosclerosis is crucial in patients with anterior circulation TIAs. If a common or internal carotid stenosis of 70% or greater is found, carotid endarterectomy has been proven to decrease the risk of subsequent stroke. Carotid angioplasty with stenting is used in some centers, but has not been studied as rigorously as carotid endarterectomy. Lesions of the external carotid artery do not cause CNS symptoms. Cardiogenic sources of clots (ie, atrial fibrillation, mitral valve disease, intracardiac tumors) usually cause large vessel ischemic strokes rather than TIAs, so echocardiography would be less important in this patient. The use of anticoagulants in acute stroke has diminished greatly and is primarily used in cases of demonstrated cardiogenic emboli. For the typical atherosclerotic process, antiplatelet therapy is preferred. Testing for thrombophilia is rarely helpful in patients with TIA. These tests may be helpful in patients with large-vessel strokes and no identifiable source of the stroke. Amaurosis fugax would not be a manifestation of seizure disorder.

Answer4: The answer is c. Although hypertension is an important cause of stroke, it should not be aggressively treated in the setting of acute cerebral ischemia. Since cerebral autoregulation is disrupted in acute stroke, a drop in blood pressure can decrease perfusion and worsen the so-called ischemic penumbra. Generally, blood pressure elevation up to 185/110 is not treated. Some stroke specialists recommend more aggressive blood pressure control in acute intracranial hemorrhage, but this patient has an ischemic (not hemorrhagic) stroke. Mannitol is of minimal benefit in cerebral edema associated with acute stroke.

Done By:

Sara Alkharashi	
Amjad Albatli	Kholuod Aldossari
Faroq Abdulfattah	Areej Alwahaib