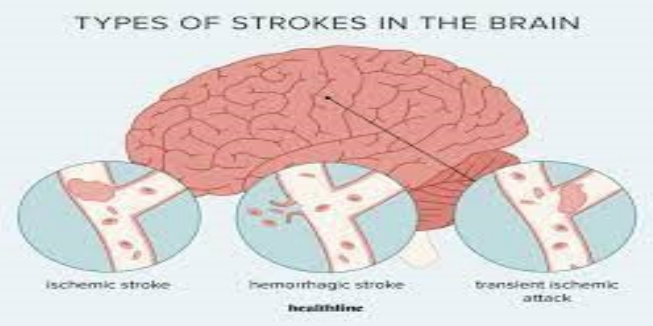

PATHOPHYSIOLOGY OF STROKE

Cerebral Vascular Accidents (CVA)

Course Name: Pathophysiology

Course Code: 0520300

Lecturer: Ms. Asma El-Shara'. MPH

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Philadelphia University-Jordan

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Introduction

- Stroke is one of the leading killers of individuals worldwide.

- **A stroke** is defined as the clinical syndrome of rapid onset of cerebral deficit lasting more than 24 hours or leading to death with no apparent cause other than a vascular one.
- A stroke is a rapid loss of brain function due to the disturbance in the blood supply to brain.
- Stroke is so called because of the way it strikes people down.

Introduction

- Stroke carries a high risk of death.
- Survivors can experience loss of vision and/or speech, paralysis and confusion.
- The risk of **further episodes** is significantly increased for people having experienced a previous stroke.
- The risk of death depends on the type of stroke.
- Transient ischaemic attacks or TIA – where symptoms resolve in less than 24 hours – have the best outcome, followed by stroke caused by carotid stenosis (narrowing of the artery in the neck that supplies blood to the brain). Blockage of an artery is *more dangerous, with rupture* of a cerebral blood vessel the most dangerous of all.

Risk Factors For Stroke

Nonmodifiable

- Age
- Gender
- Race
- Family history of stroke
- Low birth weigh

Potentially modifiable, less-well documented

- Oral contraceptives
- Migraine
- Drug and alcohol abuse
- Hemostatic and inflammatory factors—fibrinogen linked to increased risk
- Homocysteine
- Sleep disordered breathing

Modifiable

- **Hypertension—single most important risk factor for ischemic stroke**
- **Atrial fibrillation**—most important and treatable cardiac cause of stroke
- Other cardiac diseases
- Diabetes—independent risk factor
- Dyslipidemia
- Cigarette smoking
- Alcohol
- Sickle cell disease
- Asymptomatic carotid stenosis
- Postmenopausal hormone therapy
- Lifestyle factors—associated with stroke risk
  - ✓Obesity
  - ✓Physical inactivity
  - ✓Diet

ATRIAL FIBRILLATION AND STROKE RISK

- The abnormal atrial contractions that accompany this condition can lead to pooling of blood in the atria, where it can form a clot.

- If this clot is ejected from the heart, it can travel through the circulation and lodge in the cerebral vasculature to cause an occlusive stroke

ETIOLOGY AND CLASSIFICATION

1- **"Occlusive" or "ischemic" stroke,** which is caused by a **blockage** of blood flow to the brain

→ The most common form of stroke (87%)

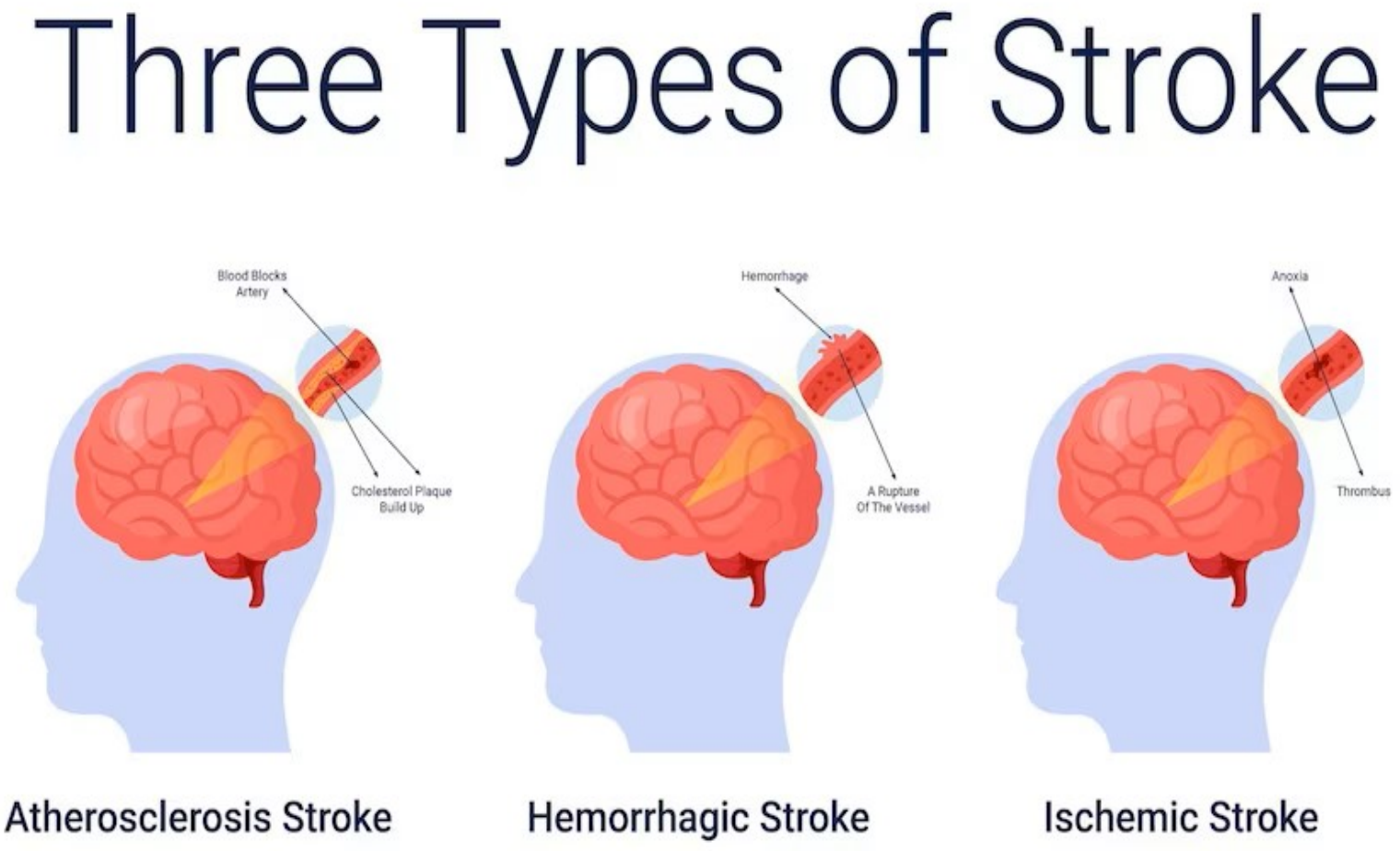
→ *Occlusive strokes may result from an **embolism** that lodges in the cerebral vasculature of from a **thrombus** that forms in situ. Complete occlusion of cerebral blood vessels will lead to injury and death of neuronal tissue.*

2- **Transient ischemic attacks (TIAs)** or "mini-strokes" lasting several minutes may also occur as a result of a developing thrombus or transient occlusion by thrombotic particle.

3- **Hemorrhagic stroke ,** meaning they are caused by bleeding into the brain.

→ Causes of hemorrhagic stroke include a ruptured cerebral aneurysm or damage to blood vessels.

To be more easy!!

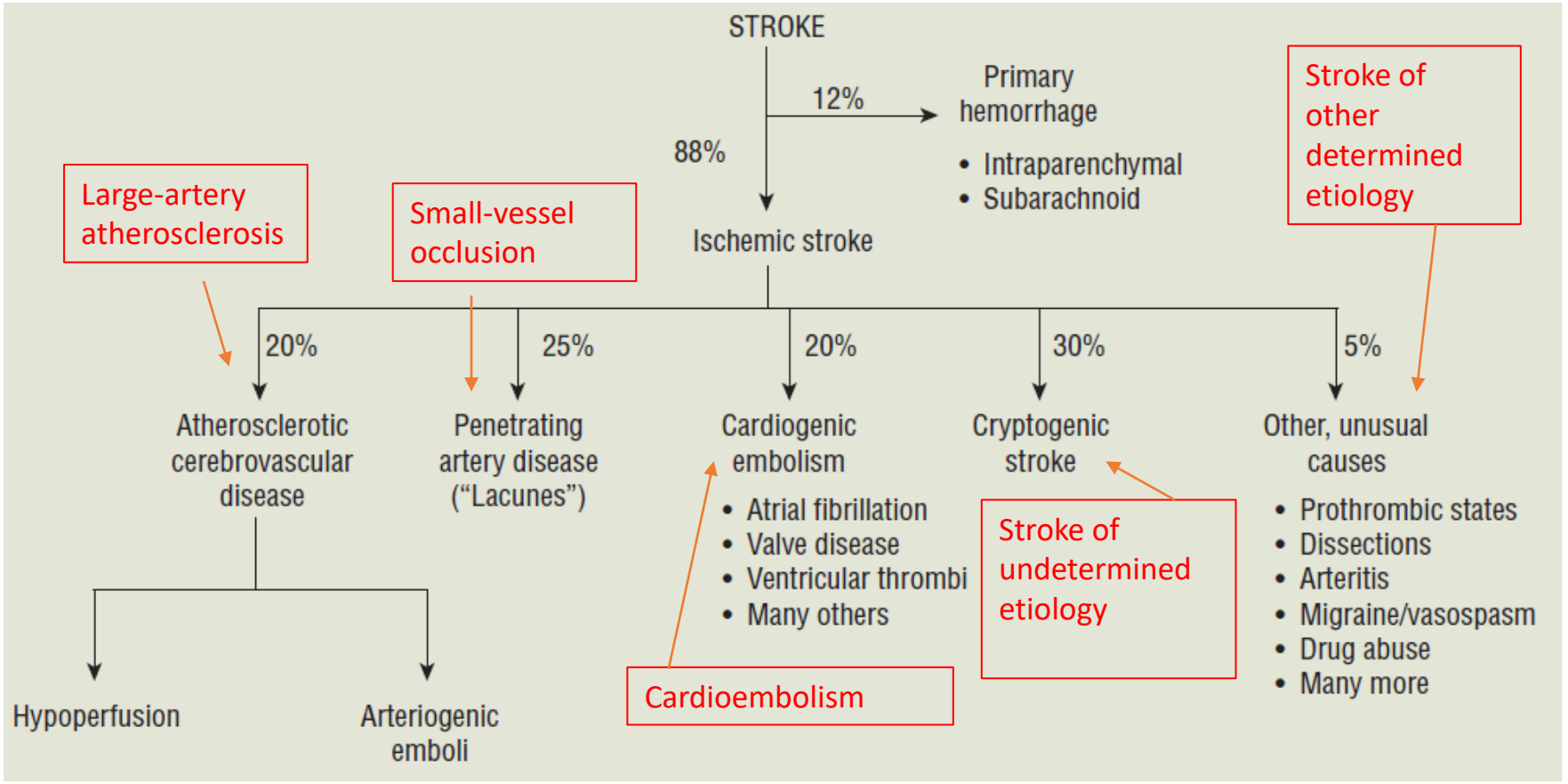


A more accurate sub-classification!!

Based on the aetiology of ischaemic stroke, a more accurate sub-classification is generally used:

- Large artery disease – atherosclerosis of large vessels, including the internal carotid artery, vertebral artery, basilar artery, and other major branches of the Circle of Willis.
- Small vessel disease – changes due to chronic disease, such as diabetes, hypertension, hyperlipidaemia, and smoking, that lead decreased compliance of the arterial walls and/or narrowing and occlusion of the lumen of smaller vessels.
- Embolic stroke – the most common cause of an embolic stroke is atrial fibrillation.
- Stroke of determined aetiology – such as inherited diseases, metabolic disorders, and coagulopathies.
- Stroke of undetermined aetiology – after exclusion of all of the above.

- A classification of stroke by mechanism with estimates of the frequency of various categories of abnormalities.
  → Approximately 30% of ischemic strokes are cryptogenic= Strokes without a known cause are called **cryptogenic**
  → **lacunes=** caused by occlusion of a single penetrating artery. The deep penetrating arteries are small, nonbranching end arteries (usually smaller than 500 µm in diameter)



PATHOPHYSIOLOGY of ISCHEMIC STROKE

https://pro.boehringer-ingelheim.com/strokeforum/overview/pathophysiology

- The common pathway of ischaemic stroke is ***lack of sufficient blood flow to perfuse cerebral tissue, due to narrowed or blocked arteries leading to or within the brain***.
- Ischaemic strokes can be broadly subdivided into thrombotic and embolic strokes.
- Narrowing is commonly the result of atherosclerosis – the occurrence of fatty plaques lining the blood vessels. As the plaques grow in size, the blood vessel becomes narrowed and the blood flow to the area beyond is reduced.
- Damaged areas of an atherosclerotic plaque can cause a blood clot to form, which blocks the blood vessel – **a thrombotic stroke**.
- In **an embolic stroke**, blood clots or debris from elsewhere in the body, typically the heart valves, travel through the circulatory system and block narrower blood vessels.

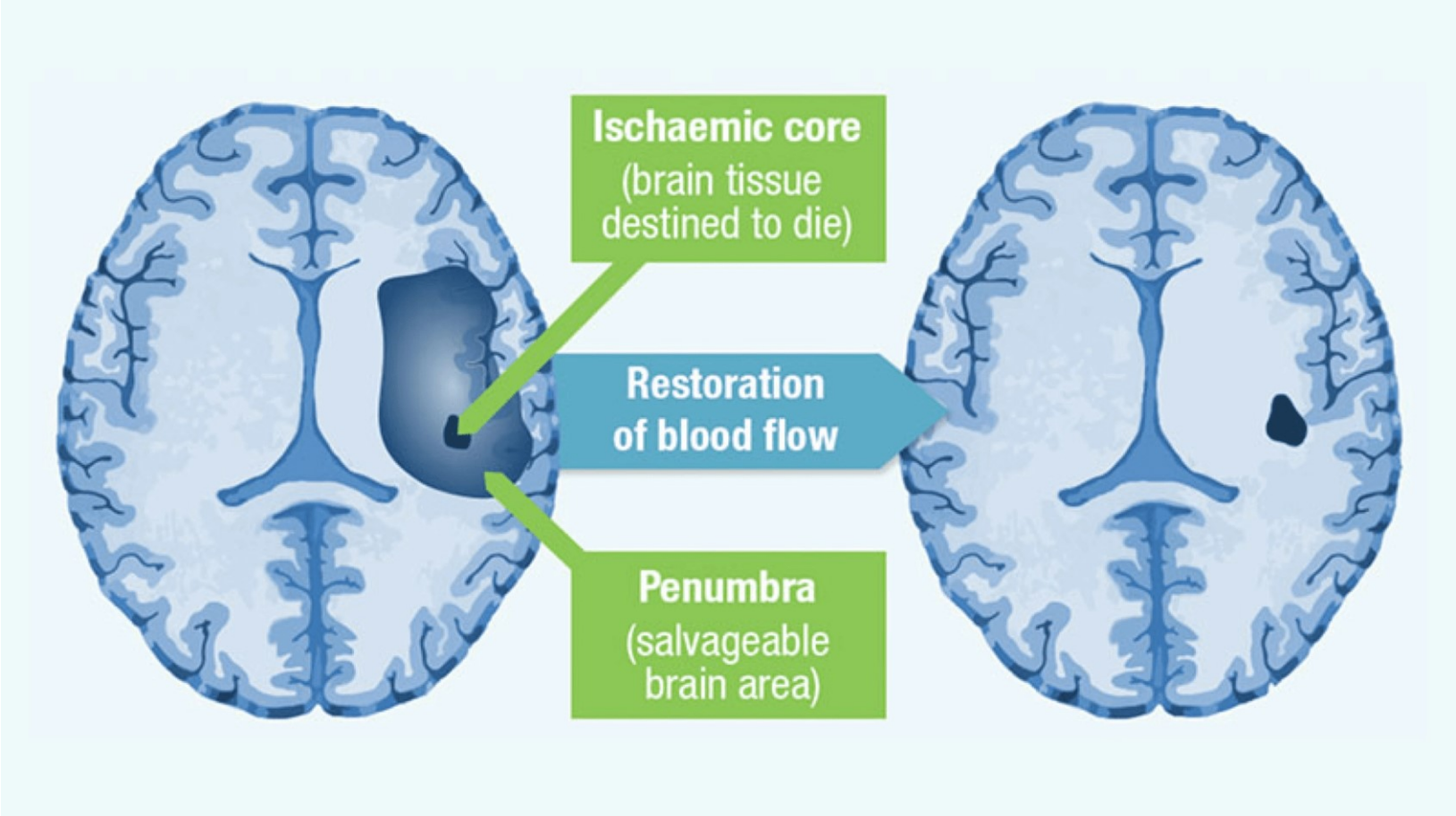
PATHOPHYSIOLOGY of ISCHEMIC STROKE (continued)

→ **Ischaemic penumbra**

- The tissue in the region bordering the infarct core, known as the **ischaemic penumbra**, is less severely affected.

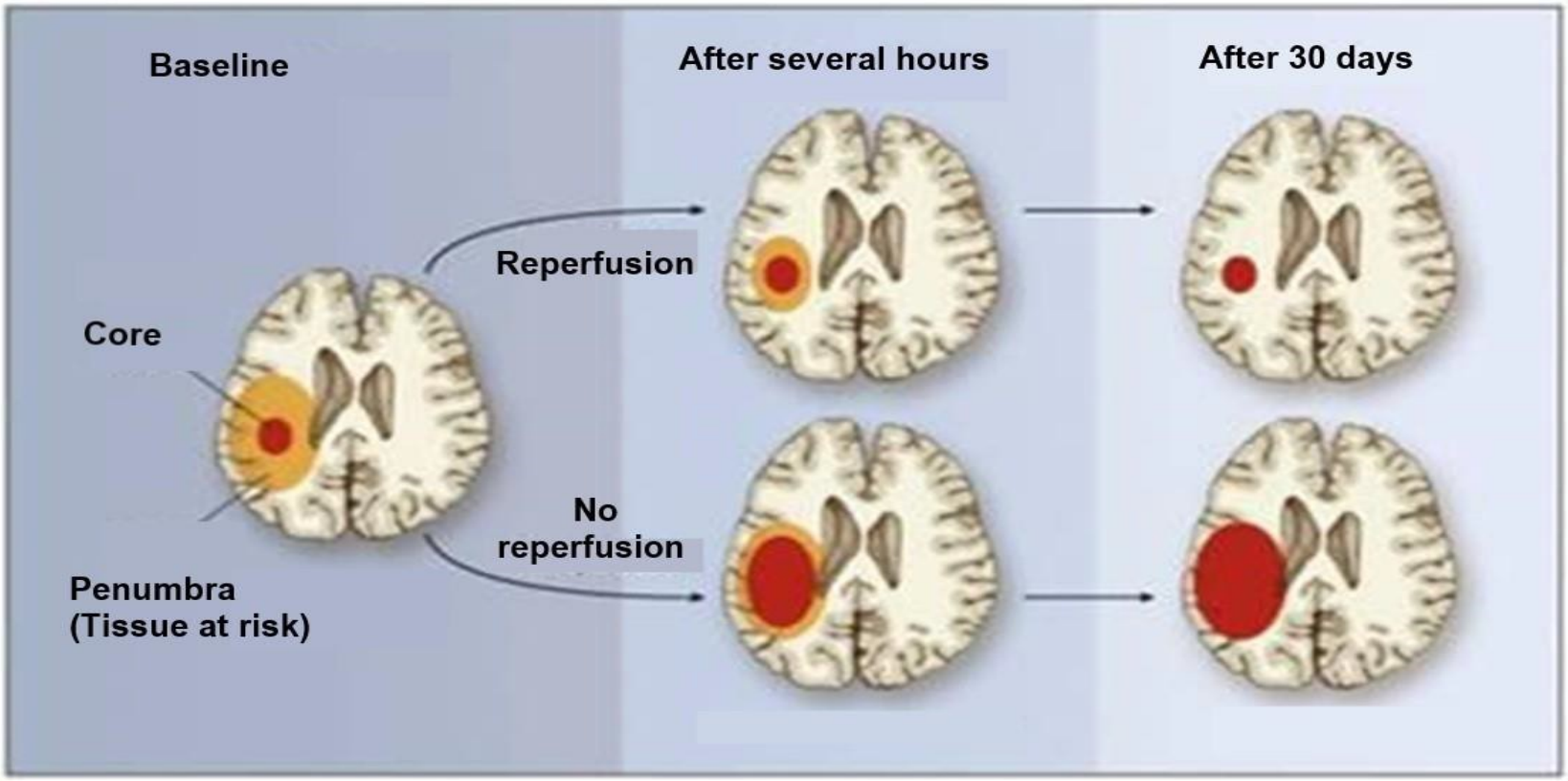
- This region is rendered functionally silent by reduced blood flow but remains metabolically active.
- Cells in this area are endangered but not yet irreversibly damaged.
- They may undergo apoptosis after several hours or days but if blood flow and oxygen delivery is restored shortly after the onset of stroke, they are potentially recoverable.

Ischaemic penumbra – Potential to reverse neurologic impairment with post-stroke therapy



Ischemic Penumbra

- ✓ Brain tissue at risk of progressing to infarction but is still salvageable if re-perfused.
- ✓ Generally located around
- ✓ An infarct core which represents the tissue which has already infarcted or is going to infarct regardless of reperfusion.



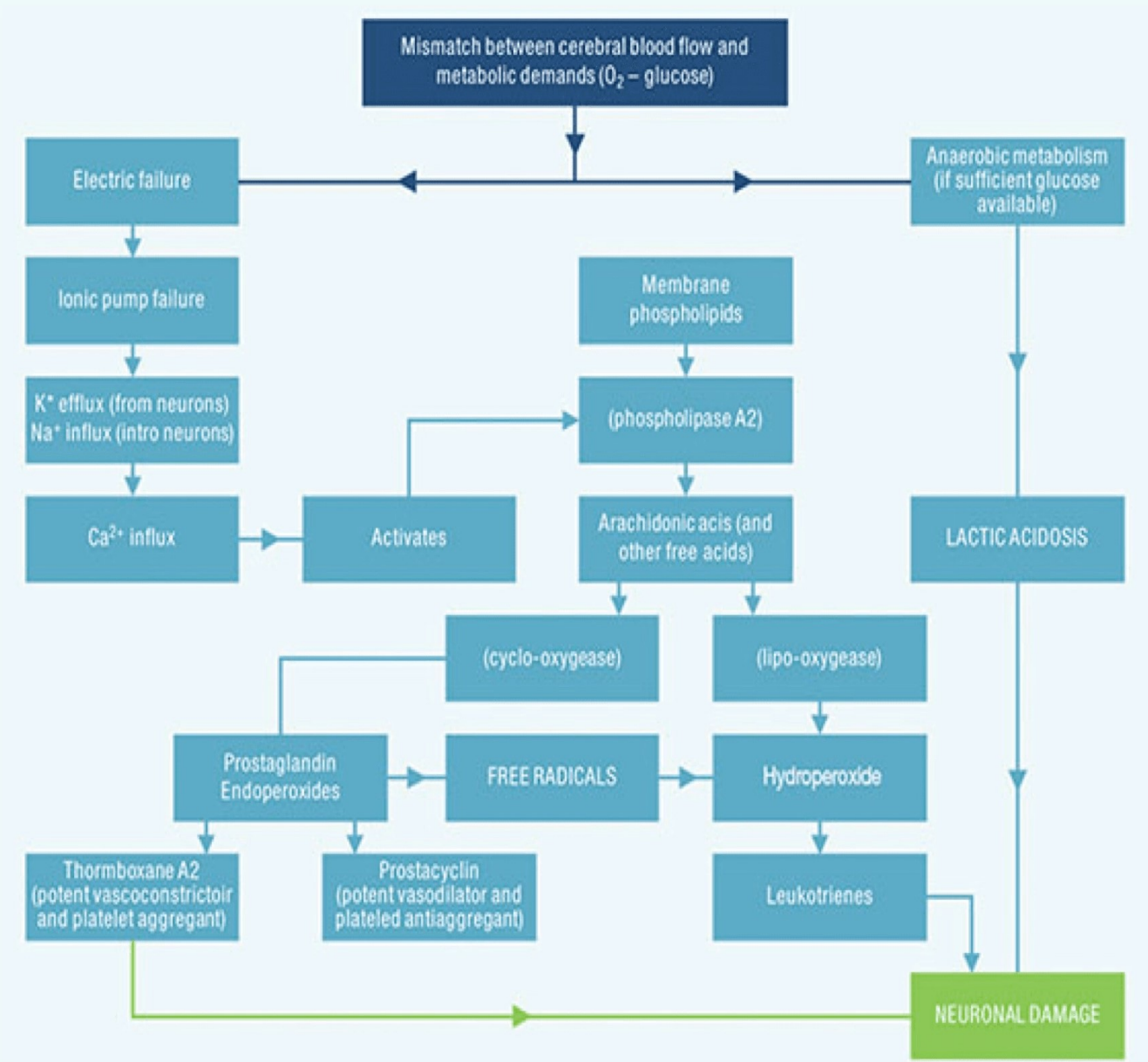
Important steps of the ischaemic cascade

1. Without adequate blood supply and thus lack of oxygen, brain cells ***lose their ability to produce energy*** - particularly adenosine triphosphate (ATP).
2. Cells in the affected area switch to anaerobic metabolism, which leads to a lesser production of ATP but releases a by-product called ***lactic acid***.
3. Lactic acid is an irritant, which has the potential to ***destroy cells*** by disruption of the normal acid-base balance in the brain.
4. ATP-reliant ion transport pumps fail, causing the cell membrane to become depolarized; leading to a large ***influx of ions***, including ***calcium (Ca^{++}),*** and an ***efflux of potassium***.
5. Intracellular calcium levels become too high and trigger the release of the excitatory amino acid neurotransmitter ***glutamate***.
6. Glutamate stimulates AMPA receptors and Ca^{++}-permeable NMDA receptors, which leads to even ***more calcium influx into cells***.

Important steps of the ischaemic cascade (continued)

7. Excess calcium entry overexcites cells and activates ***proteases*** (enzymes which digest cell proteins), ***lipases*** (enzymes which digest cell membranes) and ***free radicals formed*** as a result of the ischaemic cascade in a process called ***excitotoxicity***.
8. As the cell's membrane is broken down by phospholipases, it becomes more permeable, and ***more ions and*** harmful chemicals enter the cell.
9. ***Mitochondria break down***, releasing toxins and apoptotic factors into the cell.
10. Cells experience ***apoptosis***.
11. If the cell dies through ***necrosis***, it releases glutamate and toxic chemicals into the environment around it. Toxins poison nearby neurons, and glutamate can overexcite them.
12. The loss of vascular structural integrity results in a ***breakdown of the protective blood brain barrier*** and contributes to cerebral ***oedema***, which can cause secondary progression of the brain injury.

The ischaemic cascade



PATHOPHYSIOLOGY of HAEMORRHAGIC STROKE

- Haemorrhagic strokes are due to the rupture of a blood vessels leading to compression of brain tissue from an expanding haematoma. This can distort and injure tissue.
- In addition, the pressure may lead to a loss of blood supply to affected tissue with resulting infarction, and the **blood** released by brain haemorrhage appears to have **direct toxic** effects on brain tissue and vasculature.
- **Intracerebral haemorrhage** – caused by rupture of a blood vessel and accumulation of blood within the brain. This is commonly the result of blood vessel damage from chronic hypertension, vascular malformations, or the use of medications associated with increased bleeding rates, such as anticoagulants, thrombolytics, and antiplatelet agents.
- **Subarachnoid haemorrhage** is the gradual collection of blood in the subarachnoid space of the brain dura, typically caused by trauma to the head or rupture of a cerebral aneurysm.

SYMPTOMS OF ***OCCLUSIVE*** STROKE

Symptoms develop progressively as the ischemia progresses

- Numbness on one side (hemiparesis)
- Confusion
- Difficulty speaking
- Blurred vision
- Loss of coordination
- Difficulty walking

SYMPTOMS OF ***HEMORRHAGIC*** STROKE

Symptoms develop rapidly

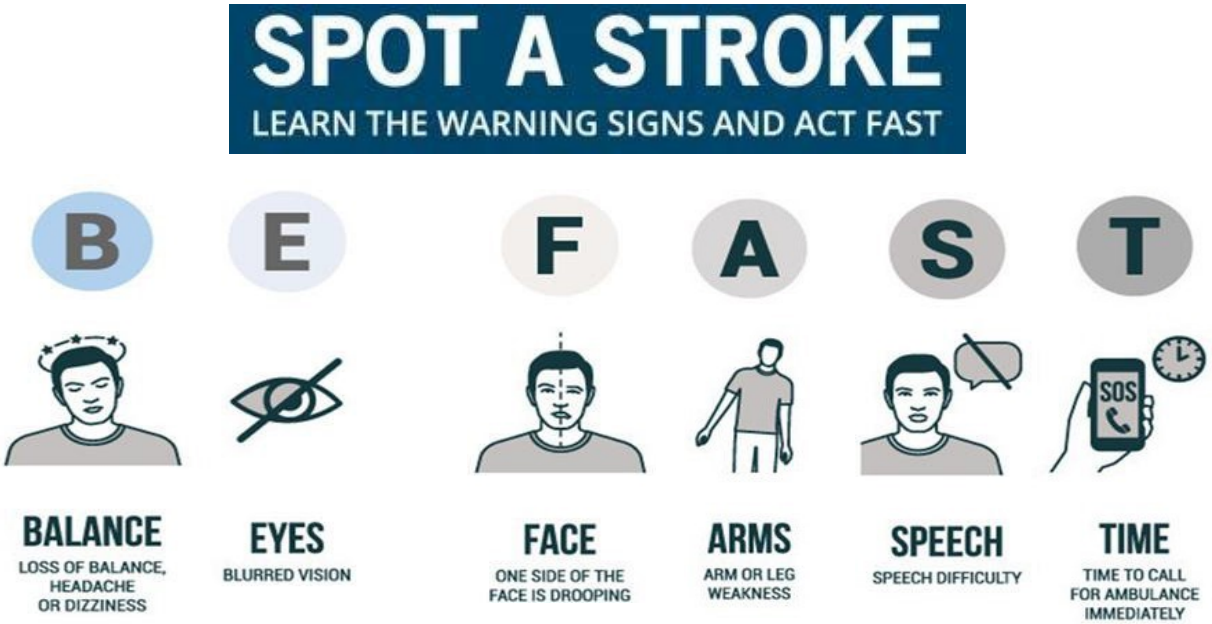
- Excruciating headache → worst headache the patient has ever had, due to increasing **intracranial pressure**

- Loss of consciousness


STROKE SYMPTOMS
LEARN THE WARNING SIGNS!
B E F A S T
BALANCE
EYES
FACE
ARMS
SPEECH
TIME

ACUTE STROKE IS A MEDICAL EMERGENCY

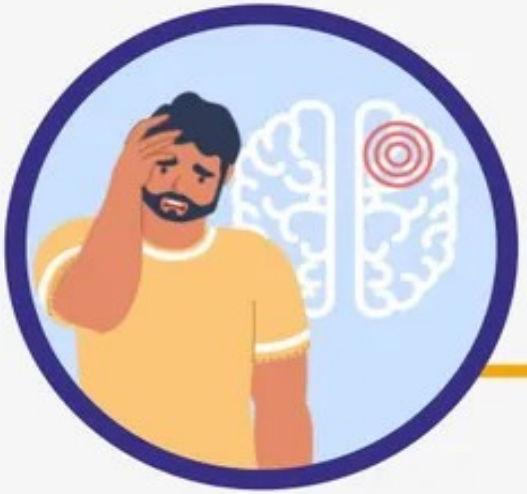
	Neurons Lost
Per Stroke	1.2 billion
Per Hour	120 million
Per Minute	1.9 million
Per Second	32 000



J.L.Saver, Time is Brain-Quantified, Stroke. 2006;37:263-266.

PACE HOSPITALS

State-of-the-art Liver and Kidney Transplant Centre



Symptoms of Brain Stroke

Face Dropping

Sudden Trouble Seeing

Arm Weakness

Loss of Co-ordination

Nausea

Fever

Trouble Speaking

Sudden Confusion

Hyderabad, Telangana, India 040 4848 6868 pacehospital.com

ACUTE STROKE MANAGEMENT

Target Response Times:

- **EMS recognition of stroke in the field** → hospital pre-notification that a stroke patient is en route
- **MD Evaluation**: <10 minutes
- **Stroke Team**: < 15 minutes
- **CT Initiation Time** : <15 minutes
- **Lab result** : <45 minutes ; only the assessment of blood glucose level must precede the administration of IV alteplase or IV tenecteplase unless there is a suspicion of abnormal hematologic or coagulation test.
- **IV thrombolytic administration** : <45 minutes
- **Mechanical Thrombectomy: First Pass** : < 60 minutes for Transfers and Mobile Stroke Unit;

  < 90 minutes for patients presenting directly to ED

Diagnosis of stroke

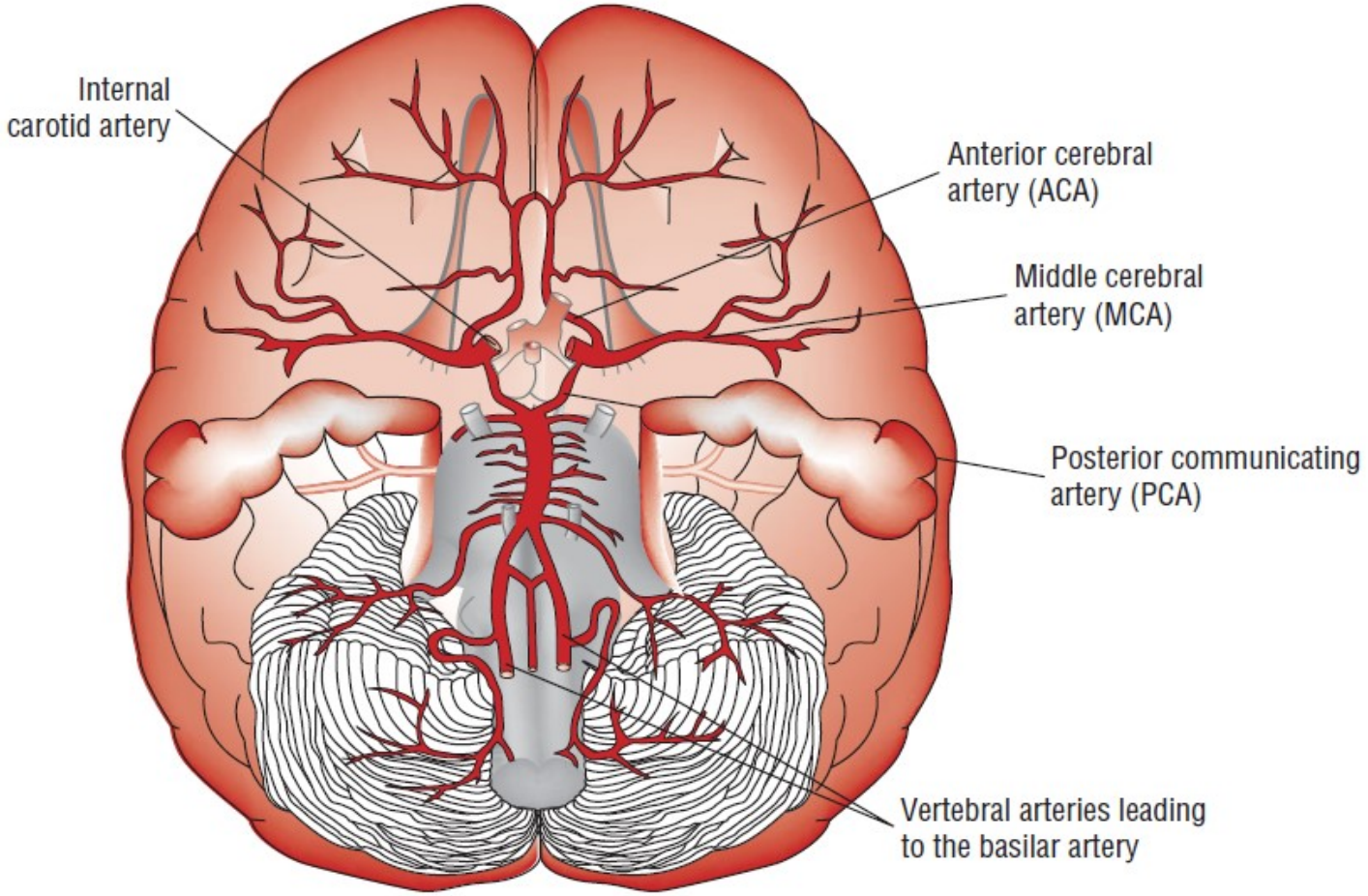
- Symptoms (clinical examination)
- CT scan
- MRI

DIAGNOSTIC CONSIDERATIONS

- *Stroke* is a term used to describe an abrupt-onset focal neurologic deficit that lasts at least 24 hours and is of presumed vascular origin.
- A TIA is the same but lasts less than 24 hours and usually less than 30 minutes.
- The abrupt onset and the duration of the symptoms are determined through the **history**.
- The use of sensitive imaging techniques (magnetic resonance imaging [MRI]) has revealed that symptoms lasting more than 1 hour and less than 24 hours, although technically TIAs, are associated with infarction, making TIA and minor stroke clinically indistinguishable.
- **The location of the central nervous system injury and its reference to a specific arterial distribution in the brain are determined through the neurologic examination and confirmed by imaging studies such as computed tomography (CT) scanning and MRI.**
- Further diagnostic tests are performed to identify the cause of the patient's stroke and to design appropriate therapeutic strategies to prevent further events.

→ The main arterial supply to the brain is illustrated in Fig. 22–2.

FIGURE 22-2. Main arterial blood supply to the brain.



DESIRED OUTCOME OF TREATMENT

The goals of treatment of acute stroke are

(1) To reduce the ongoing neurologic injury and decrease mortality and long-term disability

(2) Prevent complications secondary to immobility and neurologic dysfunction

(3) Prevent stroke recurrence

Rationale for rapid evaluation and treatment

- At the onset of stroke symptoms, the stroke is evolving
- Rapid clot lysis re-perfuses ischemic tissue limiting the eventual size of the infarct
- Timely restoration of blood flow in ischemic stroke patients is effective in reducing long-term morbidity.

TREATMENT OF STROKE

OCCLUSIVE STROKE, "time is brain." The more rapidly blood flow is restored, the greater the possibility of preserving brain function.

→ Fibrinolytic drugs such as tissue plasminogen activator (tPA) may be use (**ideally within 3 hours**) to dissolve any clots that may be present and restore blood flow

→Aspirin may be given immediately to inhibit platelet aggregation and prevent the formation of additional clots

HEMORRHAGIC STROKE must be ruled out before clot-dissolving drugs or aspirin are used.

→ For hemorrhagic stroke, drugs may be administered to lower intracranial pressure or blood pressure. Surgery may be required or surgical shunts implanted to remove accumulated blood and reduce intracranial pressure.

COMPLICATIONS OF STROKE

Disabilities caused by a stroke may be temporary or permanent and may include:

- ✓ Paralysis
- ✓ Difficulty talking
- ✓ Difficulty swallowing (dysphagia)
- ✓ Memory loss, cognitive difficulties
- ✓ Pain, paresthesia (Abnormal sensations such as prickling, tingling, itching, burning or cold, skin crawling. Paresthesia is usually felt in the hands, arms, legs, or feet, but can also occur in other parts of the body)
- ✓ Emotional changes