MODULE-1

RECOGNITION OF STROKE, RISK FACTORS AND STROKE MIMICS
The **core purpose**
To upgrade practising physicians in the management of **Stroke** with the help of eminent Neurologists and to build a sustainable business relationship with the practising physicians of API.

**Registration Form**

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City: State:

Specialization:

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## STROKE MIMICS

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WHAT IS STROKE?

Strokes are a heterogeneous group of disorders involving sudden, focal interruption of cerebral blood flow that causes neurologic deficit.

**Strokes can be classified as:**
- Ischemic (80%), typically resulting from thrombosis or embolism
- Hemorrhagic (20%), resulting from vascular rupture (e.g. subarachnoid hemorrhage, intracerebral hemorrhage)

**Figure 1: Ischemic and Hemorrhagic stroke**

In cerebrovascular emergencies, is survival a mere STROKE of luck?
In stroke, every minute matters i.e. "time is brain"

"My opinions are founded on knowledge but modified by experience."
"Expert is one who limits himself to his chosen mode of ignorance.”
The key diagnostic principles include:
- Perceptual Sense (Observation)
- Word Sense (Recording)
- Common Sense (Thinking)
  - leading to clinical Sense

There are many mind boggling facts associated with cerebrovascular disease (CVD).

The worldwide incidence of CVD has been estimated to be 2/1000 population per year with an incidence of about 4/1000 amongst people in the age group of 45-84 years.

According to a study conducted in Calcutta, CVD incidence in India was found to be 36/1,00,000 in the year 1998-1999. According to the data from the India:WHO study, the incidence of mortality due to stroke was estimated to be 73/1,00,000 per year.

CVD is one of the most disabling of all neurologic diseases. Approximately 50% of survivors have a residual neurologic deficit and greater than 25% of the patients require chronic care.

“He who cannot forgive others destroys the bridge over which he himself must pass.” - George Herbert

“Whether you think you can, or you think you can’t—you’re right.” - Henry Ford

**Table 1: Annual risk of CVD, MI, vascular death following TIA, minor CVD**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Annual risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD</td>
<td>6.7%</td>
</tr>
<tr>
<td>MI</td>
<td>2.5%</td>
</tr>
<tr>
<td>Death</td>
<td>7.2%</td>
</tr>
<tr>
<td>CVD, MI, vascular death</td>
<td>8.6%</td>
</tr>
<tr>
<td>CVD, MI, death</td>
<td>10.3%</td>
</tr>
</tbody>
</table>

CVD - Cerebrovascular Disease, MI - Myocardial Infarction, TIA - Transient Ischemic Attack

In India, stroke is responsible for 1,880 deaths/day which is equal to 6 Boeings 737 crashes every day.

Also the number of deaths due to stroke in India are almost equal to those caused by ischemic heart disease (IHD). On the other hand, stroke deaths occur:
- 22 times more than those caused by malaria,
- 1.4 times more than those due to tuberculosis and
- 4 times more than those attributed to rheumatic heart disease

Experience can be defined as yesterday’s answer to today’s problems.
INDIANS ARE MORE VULNERABLE

- The age-adjusted stroke mortality among Indians is 2 to 3 times higher compared to other countries with established market economies
- Indian immigrants to England have higher risk of dying due to stroke than local population
- Stroke mortality has declined in US since 1940 while it is likely to increase in India due to increased life expectancy (aging population) and urbanization

STROKE - TYPES AND COMMON SIGNS

Types of stroke
As mentioned previously, stroke is mainly of 2 types:
- Hemorrhagic stroke
- Ischemic stroke

Signs of stroke
The most common signs of stroke are:
- Onset of numbness or weakness of the face, arm or leg, especially on one side of the body
- Confusion or trouble speaking or understanding
- Trouble seeing with one or both eyes
- Problems with walking, loss of balance or coordination
- Inability to understand what someone is saying
- Sudden, severe headache with no known cause
Recognizing the early signs of a stroke is very important. Thankfully, they are fairly easy to learn and identify with the acronym BEFAST

**B - BALANCE:** A sudden loss of balance or coordination, such as not being able to walk a straight line or touch a finger to the nose

**E - EYES:** Sudden vision changes, such as double vision or blindness in one eye

**F - FACE DROPPING:** Droopiness or numbness on one side of the face, such as an uneven smile

**A - ARM WEAKNESS:** Weakness in one arm, such as not being able to raise both arms

**S - SPEECH DIFFICULTY:** Slurred speech or speech that is difficult to understand

**T - TIME TO CALL 911:** If any of the above symptoms are present, it’s important to call emergency responders or go to the emergency room right away, even if symptoms seem to disappear. Be sure to record the time when symptoms started.

A TIA is focal brain ischemia that causes sudden, transient neurologic deficits and is not accompanied by permanent brain infarction (e.g., negative results on diffusion-weighted magnetic resonance imaging). Diagnosis is clinical. Carotid endarterectomy or stenting, antiplatelet drugs and anticoagulants decrease risk of stroke after certain types of TIA. Since it doesn’t cause permanent damage, it might seem like no big deal. But ignoring it is a big mistake as TIA may signal a full-blown stroke ahead.

**Transient ischemic attack are warning strokes.** They are often labelled as “mini-strokes,” because they can be relatively benign in terms of immediate consequences. The term “warning stroke” is more appropriate for these temporary episodes, since they can indicate the likelihood of a coming stroke. 40% of people who get TIA’s eventually have a stroke.

The U.S. Preventive Services Task Force discourages routine ultrasounds of the carotid arteries. The reasons for this are as follows:

- Only about 1% of the general population has significant narrowing of these carotid arteries
- Less than 10% of first-time strokes are associated with such narrowing of the carotid artery
- Approximately 8 in every 100 ultrasounds produces a false positive result (a result that indicates the presence of significant narrowing that isn’t really there)
- False positive results lead to unnecessary tests and possibly unnecessary treatment
THE INJURED BRAIN

Amongst adults aged between 45 to 85 years, stroke occurs in 25% of men and 20% of women. Therefore, guidelines for stroke management for 24 hours is mandatory.

Level of evidence:
- Level A: Based on RCT or meta analysis of RCT
- Level B: Based on robust experiments or observational studies
- Level C: Based on expert opinion

Figure 4: The WHO model: The International Classification of functioning, disability and health

The doctor’s assessment of handicap may not coincide with patients assessment. The neurologist depends on physiotherapy, occupational therapy and speech therapy in rehabilitating the stroke patients.

“The True Art of Memory is The Art of Attention” - S. Johnson

NEUROLOGIC PREDICTORS

- Flaccid paralysis for more than 96 hrs
- Recovery of tendon reflexes without return of voluntary movement - prognosis poor
- Senses recover, though to a lesser degree than usual e.g. position sense recovers but not that for pain and temperature
- Recovery from dysphasia is incomplete
- Dysarthria usually improves whereas dysphagia doesn’t
- Diplopia due to brainstem stroke is usually permanent
- Conjugate gaze recovers
- Vertigo improves, though loss of hearing is permanent
- Pseudobulbar palsy is permanent

The stroke timeline

“*The art of medicine is caring for the heart of the patient***
Risk factors for stroke

- Uncontrollable (Non-modifiable)
- Controllable (Modifiable)

Key modifiable risk factors

- **Hypertension:** Hypertension is a major risk factor for heart attack and the most important risk factor for stroke.
- **Dyslipidemia:** Abnormal blood lipids such as high total cholesterol, low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels and low levels of high density lipoprotein cholesterol (HDL-C) increase risk of coronary heart disease and ischemic stroke.
- **Cigarette smoking:** Tobacco use increases risks of cardiovascular disease, especially in people who start young and in heavy smokers. Passive smoking is an additional risk.
- **Lack of physical activity:** Physical inactivity increases risk of heart disease and stroke by 50%.
- **Obesity:** Obesity, especially abdominal obesity, is a major risk for coronary heart disease (CHD) and diabetes.
- **Unhealthy diet:** Low fruit and vegetable intake is estimated to cause about 31% of CHD and 11% of stroke worldwide. High saturated fat intake increases the risk of heart disease and stroke through its effect on blood lipids and thrombosis.
- **Diabetes:** Diabetes mellitus is a major risk factor for coronary heart disease and stroke.

Other modifiable risk factors:

- **Low socioeconomic status:** It has shown consistent inverse relationship with risk of heart disease and stroke.
- **Mental ill-health:** Depression is associated with an increased risk of coronary heart disease.
- **Psychosocial stress:** Chronic life stress, social isolation and anxiety increase the risk of heart disease and stroke.
- **Alcoholism:** One to two drinks per day may lead to a 30% reduction in heart disease, but heavy drinking damages the heart muscle.
- **Use of certain medications:** Some oral contraceptives and hormone replacement therapy increase the risk of heart disease.
- **Lipoprotein(a):** Lipoprotein (a) increases the risk of heart attacks, especially in presence of high LDL-C.
- **Left ventricular hypertrophy (LVH):** LVH is a powerful marker of cardiovascular death.

Other modifiable risk factors:

- **Insulin resistance, heart disorders (particularly disorders that predispose to emboli, such as acute myocardial infarction (MI), infective endocarditis and atrial fibrillation), hypercoagulability (for thrombotic stroke only), intracranial aneurysms (for subarachnoid hemorrhage only), use of certain drugs (e.g., cocaine, amphetamines), vasculitis**

Unmodifiable risk factors:

- **Older age:** Advancing age is the most powerful independent risk factor for cardiovascular disease. The risk of stroke doubles every decade after the age of 55.
- **Heredity or family history of stroke:** The risk increases if a first-degree blood relative has had CHD or stroke before the age of 55 years (for a male relative) or 65 years (for a female relative).
- **Gender:** Higher rates of CHD are seen among men compared to women (who are premenopausal); the risk of stroke is similar for both men and women.
LIFESTYLE MODIFICATIONS FOR STROKE

- **Ethnicity or race**: The increased risk of stroke has been noted for Blacks, some Hispanic Americans, Chinese and Japanese populations. Increased cardiovascular disease deaths have been observed in South Asians and American Blacks in comparison with the whites population.

**“Novel” risk factors**

- **Hyperhomocysteinemia**: High levels of homocysteine in blood may be associated with an increase in cardiovascular risk. Homocysteine is a highly reactive amino acid toxic to vascular endothelium. It has prothrombotic and prothrombotic effect on blood vessels. It can potentiate the auto-oxidation of LDL. It is emerging as a potentially modifiable risk factor for atherosclerosis.

- **Inflammation**: Several inflammatory markers are associated with increased cardiovascular risk, e.g. elevated C-reactive protein (CRP).

- **Abnormal blood coagulation**: Elevated blood levels of fibrinogen and other markers of blood clotting increase the risk of cardiovascular complications.

- **Additional genetic factors**: Hemostatic and coagulation disorders.

- **Fast food restaurant abuse**: Increased trans fatty acid intake from foods fried in partially hydrogenated fats at fast food restaurants is also a risk factor. Partially hydrogenated fats contain trans-unsaturated fatty acids which raise LDL levels and decrease HDL levels leading to plaque build-up in the arteries.

- **Second hand smoke**: Second hand smoke also enhances stroke risk.

- **Don’t smoke and avoid second-hand smoke**

- **Improve eating habits. Eat foods low in saturated fat, trans fat, sodium and added sugars**

- **Be physically active**

- **Take medication as directed**

- ** Routinely check blood pressure and work with healthcare provider to manage high blood pressure**

- **Reach and maintain a healthy weight**

- **Decrease your stress level**

- **Seek emotional support when it’s needed**

- **Have regular medical check-ups**
STROKE MIMICS
STROKE MIMICS

Sometimes differentiation between stroke and its mimic becomes difficult. Moreover, stroke treatment is expensive and may harm the patient if the real cause is not determined.

Common stroke mimics with normal or non specific radiology are:
- Post ictal palsy
- Hypoglycemia
- Migraine aura
- Functional
- Drug overdosage

Common stroke mimics with radiology clues include:
- Brain tumour
- Brain abscess
- Subdural hematoma
- Encephalitis
- Demyelination

Some uncommon stroke mimics are:
- Hypertensive encephalopathy
- Posterior Reversible Encephalopathy Syndrome (PRESS)
- Reversible vasoconstriction syndrome
- Wernickes encephalopathy
- Handle
- Episodic ataxia
- Alternating hemiplegia of childhood
In this study, amongst 326 patients, 23 (7%) presented with stroke mimics (SM). As compared to patients with ischemic stroke, patients with SM presented with no oculomotor disturbance (0 vs. 37%), hemineglect (0 vs. 30%) and hemianopia (0 vs. 22%). Dysarthria (9 vs. 51%) and facial weakness (33 vs. 70%) were also observed less often with SM. On the other hand, global aphasia without hemiparesis was more prevalent in patients with SM (43 vs. 6%) as compared to those with ischemic stroke.

Case 1
- 70-year man with gradual left hemiplegia
- History of fall at home 1 week ago
- Mild drowsiness, headache since a week

Case 2
- 25-year old lady, was on oral contraceptives
- Acute onset weakness of right side of body
- Preceded by headache for three days
- One episode of seizure while in ER
- Drowsy, arousable, obeys a few commands
- Bilateral papilloedema
- Power grade 3/5 right UL, LL
Case 3
- 21-year man has right hemiplegia since 1 hour
- He is epileptic and had seizure at onset of weakness
- Conscious, confused, power grade 3/5 on right side
- CT Brain normal; patient recovered fully by evening

Case 4
- 55-year diabetic on Metformin and Glimepiride
- Sudden left hemiplegia for one hour
- Drowsy, not obeying commands, confused
- CT brain- normal; Blood sugar 30 mg/dl
- Recovered fully in few hours with IV dextrose
- 7% of stroke mimics are due to hypoglycemia and focal neurological symptoms can occur

Case 5
- 19-year old girl, looks toxic and sick
- Presented with acute onset right hemiplegia
- History of fever and headache since 1 week

Case 6
- Acute hemiplegia with drowsiness a week after fever

Figure 7: Post ictal or Todd’s palsy
Figure 8: Hypoglycemic hemiplegia
Figure 9: Brain abscess
Figure 10: Acute Disseminated Encephalomyelitis (ADEM)
STROKE MIMIC AND THROMBOLYSIS - Clinical evidence

Case 7
- Clumsiness of left hand and altered gait for 1 month
- Mild memory disturbances and confusion
- Dull persistent headache since 3 months

Chernyshev OV et al. determined the safety and outcome of IV thrombolysis within 3 hours of symptom onset in patients with SM and neuroimaging-negative cerebral ischemia. Among 512 patients treated with IV thrombolysis, 14% were SM (mean age 55 years). The etiologies of SM are shown in the figure 12. The most common etiologies in the SM group were seizures (38%), complicated migraine (37%) and conversion disorder (21%). There was no increase in bleeding complications.

Figure 11: Brain tumour: Glioma

Figure 12: Etiologies of stroke mimics

Safety of intravenous thrombolysis in stroke mimics: Prospective 5 - year study and comprehensive meta-analysis
Georgios Tsivgoulis, Ramin Zand, Aristeidis H. Katsanos, Nitin Goyal, Ken Ichino, Jason Chang, Efthimios Dardiotis, Jukka Putaala, Anne W. Alexandrov, Marc D. Mallof, Andrei V. Alexandrov

Another prospective study by Tsivgoulis G et al. sought to determine the safety of IV thrombolysis (IVT) in SMs using prospective, single-center data and by conducting a comprehensive meta-analysis of reported case-series. Amongst 156 IVT consecutive patients studied over 5 years, 75 were SM cases. Symptomatic intracerebral hemorrhage occurred in 1 patient, whereas no cases of oro-lingual edema or major extracranial hemorrhagic complications were documented.
In the meta-analysis of 9 studies (8942 intravenous thrombolysis [IVT]-treated patients), the pooled rates of symptomatic intracerebral hemorrhage and orolingual edema among 392 patients with SM treated with IVT were 0.5% (95% confidence interval [CI], 0%–2%) and 0.3% (95% CI, 0%–2%), respectively. Patients with SM were found to have a significantly lower risk for symptomatic intracerebral hemorrhage compared with patients with acute ischemic stroke (risk ratio=0.33; 95% CI, 0.14–0.77; P=0.010), with no evidence of heterogeneity or publication bias.

Favorable functional outcome was almost 3-fold higher in patients with SM in comparison with patients with acute ischemic stroke (risk ratio=2.78; 95% CI, 2.07–3.73; P<0.00001). The pooled rate of favorable functional outcome for SM at hospital discharge was 84.5% (Table 2). Thus the study which included the prospective, single-center experience along with the findings of the comprehensive meta-analysis underscored the safety of IVT in SM.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n (Studies)</th>
<th>n (SM)</th>
<th>Pooled rates (95% CI)</th>
<th>I²</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>9</td>
<td>392</td>
<td>0.5% (0%–2%)</td>
<td>0%</td>
<td>0.941</td>
</tr>
<tr>
<td>Orolingual edema</td>
<td>7</td>
<td>315</td>
<td>0.3% (0%–2%)</td>
<td>0%</td>
<td>0.913</td>
</tr>
<tr>
<td>Favorable functional outcome</td>
<td>4</td>
<td>206</td>
<td>84.5% (63.8%–94.4%)</td>
<td>78.7%</td>
<td>0.003</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and SM, stroke mimics. Cochran Q statistic; *Defined as a modified Rankin Scale score of 0–1 at discharge.

In a multicenter observational cohort study containing 5581 consecutive patients treated with intravenous thrombolysis, Žinkašk SM et al. determined the frequency and the clinical characteristics of SM.

### Table 3: Safety end points and functional outcome after IVT in patients with ischemic strokes and stroke mimics

<table>
<thead>
<tr>
<th>Stroke Mimics</th>
<th>Stroke n=5418 (%)</th>
<th>Stroke n=5418 (%)</th>
<th>Stroke n=5418 (%)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SICHcoma</td>
<td>2/99 (2.0)</td>
<td>403/5077 (7.9)</td>
<td>7.2–8.7</td>
<td>0.030</td>
</tr>
<tr>
<td>SICHmicro</td>
<td>1/100 (1.0)</td>
<td>275/4995 (5.5)</td>
<td>4.9–6.1</td>
<td>0.049</td>
</tr>
<tr>
<td>Fatal ICH</td>
<td>0/99 (0.0)</td>
<td>125/4669 (2.7)</td>
<td>2.2–3.1</td>
<td>0.115</td>
</tr>
<tr>
<td>Mortality</td>
<td>2/96 (2.1)</td>
<td>766/5327 (14.4)</td>
<td>13.4–15.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mRS 0–1</td>
<td>72/96 (75.0)</td>
<td>2106/5327 (39.5)</td>
<td>38.2–40.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mRS 0–2</td>
<td>84/96 (87.5)</td>
<td>2958/5327 (55.5)</td>
<td>54.2–56.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Orolingual edema</td>
<td>0/49 (0.0)</td>
<td>25/2493 (1.0)</td>
<td>0.1–1.5</td>
<td>1.00</td>
</tr>
</tbody>
</table>

CI indicates confidence interval: ECASS-II, European Cooperative Acute Stroke Study II; ICH, intracerebral hemorrhage; mRS, modified Rankin Scale; NINDS, National Institutes of Neurological Diseases and Stroke; and SICH, symptomatic intracerebral hemorrhage. *χ² test unless stated otherwise. **Fisher exact test.**
One hundred SM patients were identified. Symptomatic intracranial haemorrhage (SICH) rate in SM was 1.0% (95% CI, 0.0–5.0) compared with 7.9% (95% CI, 7.2–8.7) in ischemic strokes. Compared with ischemic strokes, the rate of SICH (by any definition) was lower in SM. Fatal ICH did not reach statistical significance because no fatal ICH occurred in stroke mimics. Fatal intracranial haemorrhage (ICH) did not reach statistical significant since none occurred in SM. Oroplungal edema also did not occur in SM (Table 3).

**Bleeding is less in stroke mimics** since there is no friable infarcted tissue, no friable ischemic vessels, no reperfusion injury, no high blood pressure and no hyperglycemia.

---

**Figure 13: Symptomatic intracranial hemorrhage risk ratios between SM and confirmed acute ischemic stroke patients treated with and without IVT**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SM Events</th>
<th>AIS Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio (N, Randus, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1.1.1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Houston</td>
<td>69</td>
<td>69</td>
<td>5</td>
<td>486</td>
<td>23.7%</td>
</tr>
<tr>
<td>Memphis</td>
<td>66</td>
<td>75</td>
<td>160</td>
<td>515</td>
<td>25.1%</td>
</tr>
<tr>
<td>Phoenix</td>
<td>54</td>
<td>56</td>
<td>169</td>
<td>483</td>
<td>25.9%</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>280</td>
<td>1405</td>
<td>1645</td>
<td>743</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>160</td>
<td></td>
<td>41.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Forest plots** of the symptomatic intracranial hemorrhage (SICH) risk ratios between patients with stroke mimics (SM) and confirmed acute ischemic stroke (AIS) treated with intravenous (IV) thrombolysis with (A) and without (B) a continuity correction of 0.3 for studies with a zero cell (no SICH case in SM). CI indicates confidence interval.

In a study conducted by Tsivgoulis G et al. favourable functional outcome at discharge was almost 3-fold higher in patients with SM.

But don’t worry if one have thrombolysed a stroke mimic

If it was stroke, giving tissue plasminogen activator would be the right thing to do

If it was not stroke, giving tissue plasminogen activator would not do any harm
CONCLUSION

- Some diseases can sometimes mimic stroke
- Physicians should always use a checklist to rule out a stroke mimic
- Though thrombolysis is safe, one should think before thrombolysing a patient

MCQs

Q1. The worldwide incidences of CVD amongst people in the age group of 45 – 84 years are
   A. 2/1000  B. 1/1000  C. 7/1000  D. 4/1000

Q2. BEFAST stands for
   A. Balance, Eyes, Face, Arms, Speech, Time  B. Balance, Ear, Face, Arms, Speech, Time
   C. Balance, Eyes, Face, Arms, Sense, Time  D. Balance, Ear, Face, Arms, Sense, Touch

Q3. Which risk factor mentioned below is not unmodifiable risk factor?
   A. Age  B. Family History
   C. Diabetes  D. Gender

Q4. Which is the common stroke mimics?
   A. Postictal Palcy  B. Hypoglycemia
   C. Drug Overdose  D. All of the above

Q5. _______% of people who get TIAs eventually have a stroke.
   A. 40%  B. 20%
   C. 60%  D. 10%