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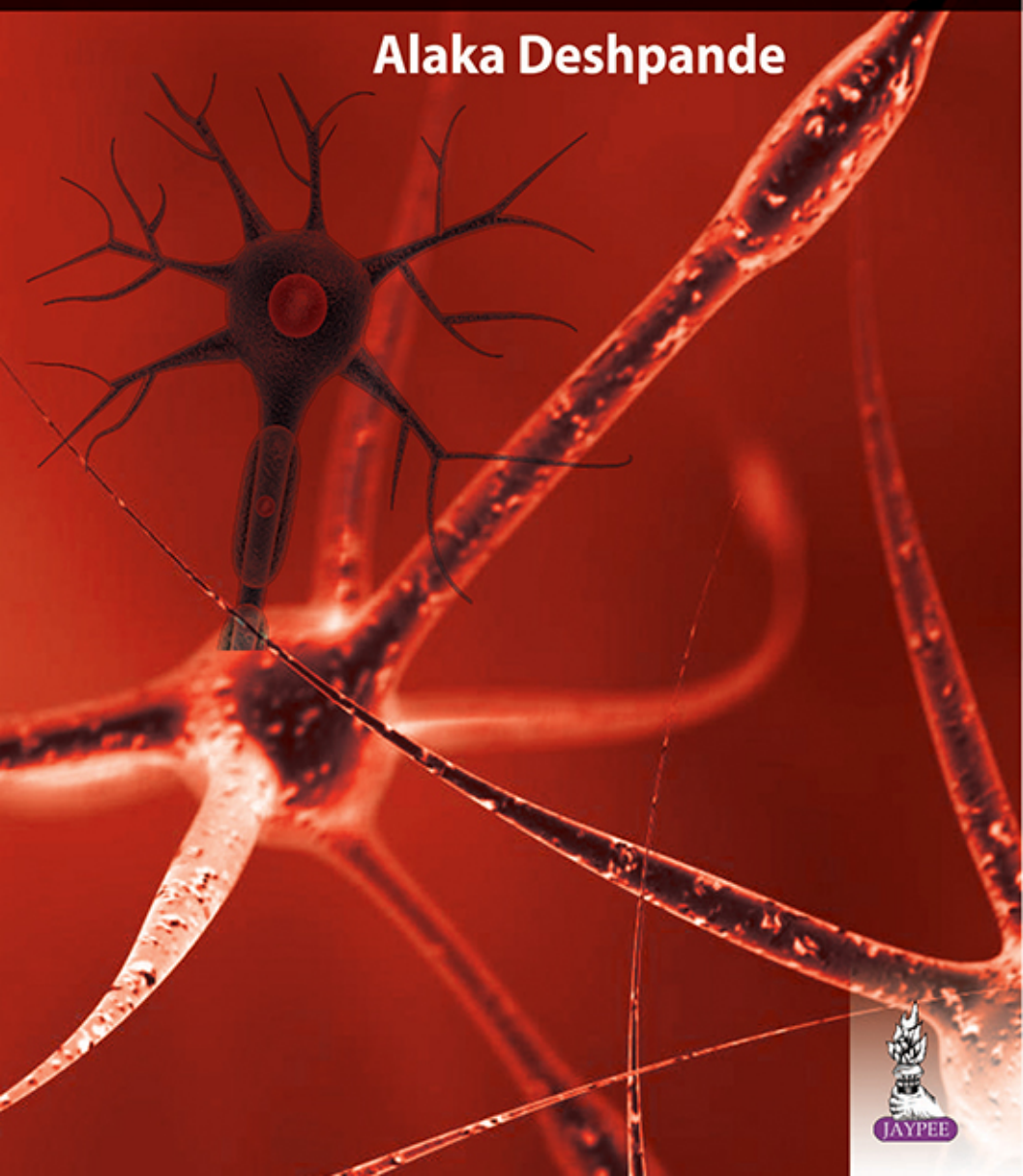
Clinics in NEUROLOGY

Alaka Deshpande



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CHAPTER

3

Cerebrovascular Disorders

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DEFINITION

Cerebrovascular diseases denote any abnormality or impairment of cerebral circulation resulting into a neurodeficit which is acute or abrupt.

Stroke is the term used synonymously with cerebrovascular accidents (CVAs). Stroke and accident both words connote the unexpected abruptness as if something has struck from the blue.

Stroke is defined as a sudden, nonconvulsive focal neurological deficit which is attributable to a vascular cause. In its mildest form, it may be transient and does not warrant immediate medical attention while most severe form may be devastating as patient may develop hemiplegia or become comatose.

Several stroke syndromes have been described based on the site and size of the vascular insult. Stroke and hemiplegia are not synonymous, but the most common cause of hemiplegia is a CVA/stroke.

EPIDEMIOLOGY

Cerebrovascular accident is the third most common cause of death in United States. The manifestations are acute. The neurological deficit resulting from the CVA is determined by several factors like the site of the lesion, the size of the lesion, duration, comorbid conditions, status of the collateral circulation, etc. as discussed below.

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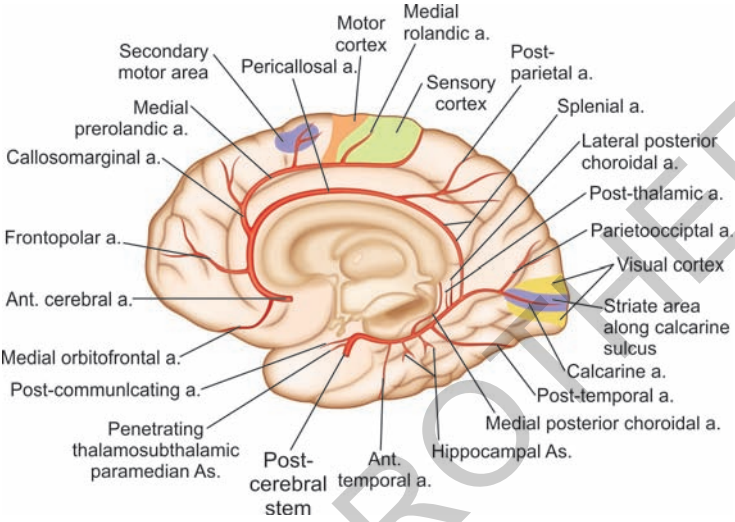
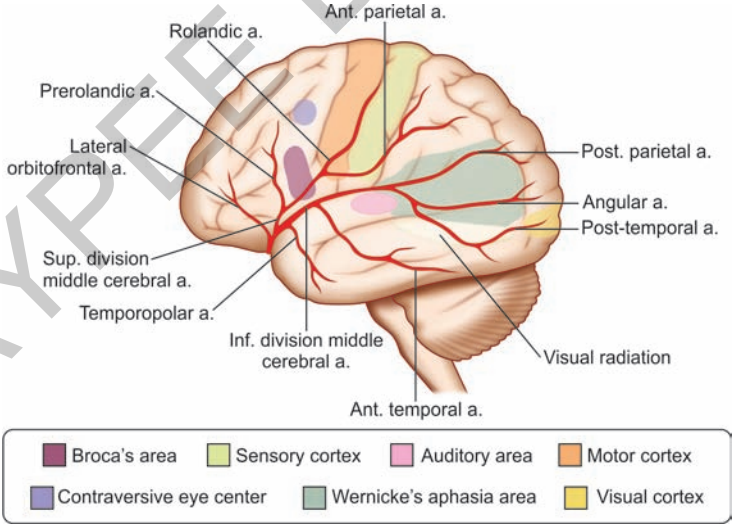
(A) Medial surface of the brain



(B) Lateral surface of the brain



Figs 1A and B: Vascular supply of cerebral hemisphere

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The brain is richly supplied by two internal carotid arteries and two vertebral arteries. There are extensive communications between carotid systems and vertebrobasilar system (circle of Willis). In addition, there are communications between internal and external carotid arteries.

Although cerebral arteries anastomose with one another on the surface of the brain, once they enter the brain substance no further anastomosis occur (end arteries).

HEMODYNAMICS

Brain is the highly evolved organ, uses only glucose as its substrate for energy. Glucose and oxygen reach the brain tissue by perfusion via circulation. The studies in the experimental animals have revealed that:

- Normal cerebral blood flow (CBF) is 55 mL/100 gm/min
- Critical threshold is CBF 23 mL/100 gm/min
- Cerebral infarction occurs at CBF less than 8–9 mL/100 gm/min regardless of its duration.

The state of hypoperfusion in between 8 mL and 23 mL/100 gm/min is called as "ischemic penumbra". The measures to restore perfusion at this stage may reverse the neurodeficit.

Cerebral blood flow of 6–8 mL/100 gm/min results into a marked depletion of adenosine triphosphate (ATP), increase in intracellular calcium (Ca^+), increase in extracellular potassium (K^+), cellular acidosis —all these changes finally culminating into signs of tissue necrosis as seen on histology.

The interventions during the stage of ischemic penumbra to restore perfusion are aimed at preventing/reducing infarction so as to limit neurodeficit.

PATHOLOGY

The CVA results into following major types of lesions:

- Cerebral ischemia
- Cerebral infarction
- Cerebral hemorrhage.

One must consider various components of cerebral circulation as the determinants of cerebral perfusion:

- Cerebral arteries
- Cerebral veins
- Condition of the blood circulating through these vessels
- Heart as the central pump.

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Diseases of the Cerebral Arteries

- Atherosclerosis
- Arteritis
  - Infective inflammation
    - Arteritis secondary to pyogenic and tuberculous (TB) meningitis
    - Malaria, schistosomiasis, typhus, mucormycosis
    - Human immunodeficiency virus (HIV)
    - Meningovascular syphilis
  - Noninfective inflammation/arteritis connective tissue diseases
    - Polyarteritis nodosa
    - Systemic lupus erythematosus (SLE)
    - Necrotizing arteritis
    - Giant cell arteritis
    - Takayasu disease
    - Wegener's arteritis
- Trauma to carotid artery
- Congenital or acquired aneurysms
- Dissecting aortic aneurysm
- Complication of arteriography
- Neurologic migraine (complicated).

Diseases of Cerebral Veins

- Cerebral venous thrombosis
  - Hypercoagulable disorders like protein S, protein C deficiency
  - Severe dehydration particularly in children
- Cerebral thrombophlebitis
  - Postpartum
  - Postoperative particularly after pelvic surgery
  - Meningitis
  - Subdural empyema.

Diseases of the Blood

- Polycythemia
- Thrombotic thrombocytopenia
- Sickle cell disease
- Severe anemia

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- Disseminated intravascular coagulation (DIC)
- Beta thalassemia
- Hypercoagulable disorders
- Dysproteinemia, e.g. multiple myeloma
- Protein S, protein C deficiency, factor V Leiden mutation, antithrombin III deficiency, antiphospholipid antibody syndrome, prothrombin gene mutation, nephrotic syndrome, homocysteinemia, systemic malignancy, inflammatory bowel disease (IBD), oral contraceptive pill use.

Diseases of the Heart

- Stokes-Adams syndrome
- Cardiac arrhythmias
- Myocardial infarction—mural thrombosis
- Valvular heart disease
- Congenital heart disease
- Prosthetic valves
- Infective endocarditis
- Dilated cardiomyopathy
- Systemic hypertension
- Systemic hypotension.

The major types of cerebrovascular diseases are:

- Cerebral ischemia
- Cerebral infarction:
  - due to cerebral embolism
  - due to cerebral thrombosis
- Cerebral hemorrhage.

Once the lesion is anatomically localized, its vascular territory can be identified which may be indicated in the diagnosis.

Salient features of different types of CVA are described here:

Transient Ischemic Attacks

As the name suggests, attacks are episodic.

- Transient ischemic attacks (TIAs): Short duration few seconds to less than 24 hours
- Ischemic attacks: Neurodeficit due to cerebral ischemia

These are brief/transient episodes of neurodeficit lasting from few seconds to minutes and recovering fully, caused by cerebral ischemia.

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Average duration of an attack is about 12 minutes. The attack ranges from a mere dysarthria, a spell of vertigo (as in vertebrobasilar insufficiency) or as great as a hemiparesis, all of which gets reversed within minutes to hours, maximum time being less than 24 hours.

The attacks are due to emboli coming from distant thrombus located in the heart, neck vessels, or in the cerebral vessels.

In most of the cases, TIAs are forerunners of full stroke. The risk of stroke after TIA is about 10% in first 3 months with most events occurring in first 48 hours.

Transient monocular blindness (amaurosis fugax) may occur in patients with carotid artery stenosis, because central retinal artery is the first branch of internal carotid artery intracranially.

Transient ischemic attacks need complete investigations to find out source of emboli. Institution of prompt treatment is necessary to prevent a stroke. Patient's risk profile can help in modification of lifestyle.

Cerebral Infarction

Cerebral infarction is caused by cerebral embolism or by cerebral thrombosis. The clinical profile in these two conditions may help in the diagnosis.

Infarct due to embolization: A small fragment of thrombus situated distantly is swept in the circulation which gets lodged in smaller cerebral arteries. Occlusion by this embolus results into instantaneous neurodeficit.

Majority of the cases are younger in this age group. The embolic episode occurs in a wakeful state. The onset is sudden; the maximum neurological deficit develops almost instantaneously.

As the embolus gets lysed, the recovery is rapid.

Causes of cerebral embolism:

- *Cardioembolism*: The source of emboli is a thrombus situated in the heart
  - Valvular heart disease: Thrombus most often is in the left atrial appendage
  - Congenital heart diseases
  - Infective endocarditis
  - Mural thrombosis on the scar of myocardial infarction
  - Arrhythmias with/without heart disease
  - Prosthetic valves

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  - Paradoxical embolization: Embolus originating from the venous circulation deep vein thrombosis (DVT) escapes from the right atrium to the left atrium via patent foramen ovale or small atrial septal defect (ASD), and gets lodged in systemic circulation.
- *Artery-to-artery embolic stroke*: Thrombus formation on atherosclerotic plaque in extracranial vessels or intracranial carotid vessel may embolize in cerebral circulation. Any diseased artery may be the source of artery-to-artery cerebral embolization but the most common sites are:
  - Carotid bifurcation
  - Aortic arch
  - Internal carotid artery
  - Carotid artery stenosis.
- *Rare emboli—fat, air and tumor*: Once a provisional diagnosis of cerebral embolic infarct is made, further examination is to be carried out to find out the source of emboli. History of risk factors such as smoking, tobacco chewing, heart disease, hypertension, diabetes mellitus, hyperlipidemia, drug abuse may be specifically elicited (phenylpropanolamine is implicated to cause hemorrhagic stroke and cocaine can lead to ischemic stroke).

General examination should specifically include:

- Palpation of the carotid arteries in the neck. Carotid arteries should be palpated one after the other and not both the carotids simultaneously. In case of partial occlusion of carotid, the bruit may be heard by auscultation over carotids in the neck or just behind the mastoid process or over the orbit with the eyes closed with the help of the bell of the stethoscope.
- Measurement of blood pressure (BP) on both sides.
- Ophthalmoscopic examination of retina may reveal visible embolic material in retinal vessels.

Careful examination of the cardiovascular system is necessary for evidence of cardiac murmurs and peripheral emboli as well.

Specific investigations include:

- Electrocardiogram (ECG)
- Computed tomography (CT) scan of brain
- Doppler study of carotids
- Echocardiography
- Magnetic resonance angiography (MRA).

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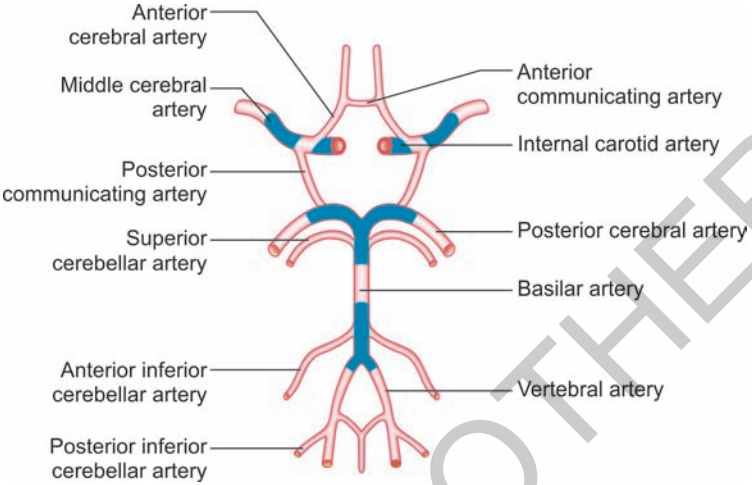

Fig. 2: Circle of Willis and the sites of predilection for atherosclerosis in the intracranial arterial circulation

Cerebral infarct due to cerebral thrombosis: Cerebral infarct due to cerebral thrombosis is common in the elderly age group. The most common cause is an atherosclerotic plaque on which thrombus formation takes place in cerebral vessel. As the thrombus increases in size, it occludes the vessel resulting into cerebral infarction. The onset is acute. The neurological deficit develops progressively (unlike embolic episode where it is instantaneous) over few hours as stroke in evolution, (step-ladder pattern). However, with advances in early diagnosis and therapeutic interventions, stroke in evolution is becoming a rarity.

Figure 3 shows the common sites for cerebral thrombosis.

Causes of thrombotic occlusion of cerebral vessels:

- Atherosclerosis in aged
- Accelerated atherosclerosis in middle-aged due to:
  - Hypertension
  - Diabetes mellitus
  - Dyslipidemias
  - Smoking
  - Drug abuse

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- Arteritis
  - Infective arteritis
  - Noninfective (autoimmune) arteritis
  - Carotid artery dissection
- Hematological disorders
- Venous thrombosis.

A provisional clinical diagnosis is made after a detailed clinical examination regarding:

- The anatomical localization of the lesion with vascular territory
- The nature of the lesion
- The etiology of the lesion.

Management of the patient

- Investigations
- Management in first 6 hours
  - Medical
  - Surgical
- Long-term management
- Nursing care
- Physiotherapy and rehabilitation.

Investigations

Baseline:

- Complete blood count (CBC), erythrocyte sedimentation rate (ESR)
- Blood sugar
- Lipid profile
- Venereal Disease Research Laboratory (VDRL) test for blood
- Anti-HIV antibodies
- Electrocardiography
- Echocardiography, if indicated.

Specific investigations:

- Noncontrast CT/magnetic resonance imaging (MRI) of brain: It helps in differentiation between infarction and hemorrhage as the cause of the stroke. Hemorrhage is seen as a hyperdense lesion on noncontrast CT scan immediately. CT is the preferred modality as it is fast and sensitive in picking up bleeds or edema. In addition, it gives information regarding the site of the lesion, size of the lesion,

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Fig. 3: Noncontrast computed tomography (CT scan) of brain—cerebral hemorrhage

evidence of perilesional edema or presence of any other lesion resulting into a neurodeficit (Fig. 4)

- Magnetic resonance imaging may be superior to CT scan for early detection of the infarct, particularly in the brain stem or cerebellum and also for detecting venous thrombosis.
  Infarct may not be evident in the first 24 hours. But it is crucial to rule out hemorrhage before starting thrombolytic therapy. Aspirin can be started and tissue plasminogen activator (tPA) is considered only if there is NO evidence of hemorrhage on CT scan.
- *Carotid Doppler study*: It is a noninvasive investigation which delineates the sclerotic occlusion of the carotids in the neck. It also measures the blood flow velocity. Delineating the degree of stenosis is crucial to determine whether or not to perform a carotid endarterectomy (CEA) to remove the obstructing plaque.
  - *Indications for CEA*: Greater than 60% and 70% stenosis in symptomatic and asymptomatic cases respectively.
- *Magnetic resonance angiography*: It is a noninvasive technique, which has certain limitations, compared to conventional angiography. It is lower in spatial resolution, may not reliably differentiate between total and near total occlusion. Detection of small vessel details, e.g. vasculitis is difficult with MRA. However, being noninvasive technique with a very high resolution it is commonly employed.

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GOAL OF THERAPY

To prevent or limit the amount of tissue infarction, the management is:

- Medical
- Surgical.

The medical management is planned under following categories:

- Immediate support:
  - Thrombolysis
  - Anticoagulants
  - Antiplatelet agents
  - Neuroprotection.

Immediate Support

- Airway
- Breathing
- Circulation.

After stabilizing these parameters, the patient is subjected to neuroimaging. After confirmation of the lesion, the further specific management is instituted.

Thrombolysis

- The thrombolysis is achieved by recombinant tPA, (rTPA) given intravenously (IV).
- It is indicated in properly selected cases. The therapy is best given in an institution having an expert team for stroke management.
  - Recombinant tPA dose: 0.9 mg/kg (maximum dose 90 mg)
    - 10% is given as a bolus IV
    - 90% is given as an infusion over next 60 min.
- The thrombolysis is indicated within first 3 hours of the onset of *nonhemorrhagic stroke.*
- Symptomatic intracerebral hemorrhage is reported in 6% of cases after rTPA therapy.
- The risks and benefits have to be carefully weighed before giving tPA.

Contraindications to tPA

- Blood pressure greater than 185/110, despite treatment.
- Platelets less than 100,000/μL, hematocrit (HCT) less than 25%, glucose less than 50 mg/dL or greater than 400 mg/dL.

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- Heparin use, or prolonged partial thromboplastin time (PTT) or elevated international normalized ratio (INR).
- Prior stroke or head injury in the past 6 months, or any prior intracranial hemorrhage.
- Major surgery in past 2 weeks.

There is no significant difference in mortality.

Significant difference is noted in lessening the disability compared to placebo.

Antiplatelet Agents

Tablet aspirin 150 mg per day is an effective antiplatelet agent and the ONLY one with proven efficacy in acute ischemic stroke. The drugs acting at IIb/IIIa receptor are undergoing clinical trials. If successful, would be effective in first 6 hours of stroke.

Anticoagulants

The role of anticoagulants in thrombotic infarct is *uncertain*. It is not indicated in thrombotic infarct. As against in a stroke due to cardioembolism and TIAs it is indicated. Heparin is the drug of choice for acute anticoagulation. Injection heparin 5,000–10,000 unit IV is given as a bolus followed by continuous IV infusion of 1,000 units/hour. PTT is measured daily, heparin daily dose is adjusted to maintain PTT at about twice the pretreatment level. Oral anticoagulant tablet warfarin 5–15 mg/day is started simultaneously with heparin. After about 2 days, the prothrombin time (PT) reaches 1½ times the pretreatment level, thereafter heparin is discontinued. Warfarin is continued for about 3 months with careful monitoring of PT once in 2 weeks. The risk of intracerebral hemorrhage is high in elderly patients above 65 years of age and in hypertensive cases. Benefit may always be weighed against risk.

Warfarin prophylaxis is indicated in a patient of atrial fibrillation with a CHADS score of 2 or above. If the score is 0–1, give only aspirin (C, H, A and D, each parameter carries 1 point while S carries 2 points):

- C: Congestive heart failure
- H: Hypertension
- A: Age over 75 years
- D: Diabetes mellitus
- S: Prior stroke carries 2 points.

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Salient Features

- A concise yet comprehensive clinical approach to common neurological disorders
- Presents in simple and lucid language
- Supports the text with relevant tables, algorithms and boxes
- Colored, informative illustrations giving a lasting visual impression
- Focuses on practical approach, like a bedside clinic
- Deals with neuroanatomy, basic physiology, clinical profile and diagnosis, differential diagnosis, specific investigations and management
- Details of clinical examinations combined with relevant theoretical information
- Most useful for university students, national boards, family physicians and consultants of other disciplines.



Alaka Deshpande MBBS MD MAMS FIMSA FICP was formerly Head, Department of Medicine and Director, Center of Excellence in HIV Care, Grant Medical College, Sir JJ Group of Hospitals, Mumbai, Maharashtra, India. She has been teaching medicine to the undergraduate and postgraduate students for more than four decades. A great academician with large numbers of research publications to her credit, an astute clinician with a rich experience of managing thousands of patients in a tertiary care center, her lectures beautifully amalgamate both the knowledge and experience with a very lucid clinical approach. She is revered as one of the finest and the best teachers. She worked as a technical advisor on World Health Organization's Strategic and Technical Advisory Committee for HIV/AIDS. She was a technical expert on various committees of National AIDS Control Organization (NACO). As a member of various committees of Indian Council of Medical Research (ICMR), she has made significant contributions in the research carried out in the country. She is a member of the scientific advisory committee of National AIDS Research Institute (NARI).

Dr Alaka's popularity is reflected in her contribution as a faculty in innumerable medical seminars and CMEs. Many professional organizations have felicitated her as the best teacher in various scientific forums. Teaching is her passion. Medical care to the poorest of the poor is her dedication. Her medical services are acknowledged and appreciated by the Government of India by conferring on her the highest civilian honor of 'Padma Shri' in 2001.

Shelving
Recommendation
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