CHAPTER 9

CENTRAL NERVOUS SYSTEM DISEASES

MIGRAINE

Benign and recurring syndrome of headache, nausea, vomiting and other neurological symptoms in various admixtures.

SALIENT FEATURES

A. At least 5 attacks fulfilling criteria B-D.

B. Headache attacks lasting 4-72 h (untreated or unsuccessfully treated)

C. Headache has at least two of the following characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain
   4. Aggravation by or avoidance of routine physical activity.

D. During attack at least one and the following
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia

E. Not attributed to another disorder.

- Migraine may also be preceded by focal neurological phenomenon called "aura" most commonly experienced as visual alteration (flickering lights, spots; loss of vision) but it may involve sensory symptoms (pins and needles numbers) or fully reversible dysphasic speech disturbance.
- May be mild (nondescript-tight band like discomfort often involving the entire head) or severe throbbing headache associated with vomiting, scalp tenderness with or without other neurological features.

Treatment

Nonpharmacological

Identify and avoid trigger factors such as alcohol, foods (chocolate, cheese), irregular sleep patterns and stress levels. Also assess menstrual cycle relationships in female patients.

Pharmacological

A staged approach to migraine pharmacotherapy

1. **In case of mild migraine,** i.e. occasional throbbing headaches, no major impairment of functioning.
   Tab. Aspirin 650 mg stat; if required can be repeated after 4 hours.
   Or
   Tab. Ibuprofen 400-800 mg stat; if required can be repeated after 6 hours; maximum 3 times/day.
   Or
   Tab. Paracetamol 1000 mg stat; if required can be repeated after 4 hours.
   Or
   Cap. Indomethacin 50 mg stat; if required can be administered 3 times a day.
   If associated nausea and vomiting, Tab. Metoclopramide 10 mg stat.
2. **In case of moderate to severe headache,** i.e. three severe attacks of headache a month with significant impairment of functioning and marked nausea or vomiting.
   Tab. Ergotamine 2 mg sublingual at onset and after half an hour (maximum 6/day, 10/week).
   Or
   Tab. Ergotamine (1 mg) + Caffeine (100 mg) 1/2 tab at onset, then 1 tab half hourly (maximum 6/day, 10/week).
   Or
   Tab. Ergotamine (2 mg) + Caffeine (100 mg) suppository; 1 suppository at onset (max 6/day, 10/week).
   (A subnauseating dose should be determined preferably during headache free period).
   Or
   Tab. Sumatriptan 25-100 mg orally at onset.
   Or
   Inj. Sumatriptan 6 mg SC at onset (may repeat once in 24 hours).
   (**Caution:** Contraindicated in ischaemic heart disease and hypertension).
   Or
   Inj. Diclofenac 75 mg IM at onset.
   Refer patient with severe migraine to hospital, if attack is not controlled by above and if the patient is dehydrated. Also consider prophylactic medications.

Hospital management of acute migraine

1. Inj. Metoclopramide 10 mg IV.
2. Inj. Sumatriptan 6 mg SC (may repeat once in 24 hours).
   (**Caution**: Contraindicated in ischaemic heart disease and hypertension).
   Or
   Inj. Prochlorperazine 12.5 mg in 25-50 ml saline slow push over 2 minutes can be given twice or thrice a day.
   Or

Inj. Chlorpromazine 7.5-20 mg in 25-50 ml saline slow push over 2 minutes can be given twice or thrice a day.
(**Caution:** Monitor carefully for orthostatic hypotension. Administer IV diphenhydramine, if acute dystonic reaction occurs).

3. In severe headache unresponsive to other drugs, Inj. Pethidine 50-100 mg IM as a single dose.
4. Status migranous (A debilitating migraine attack lasting for more than 72 hours)
   Inj. Dexamethsaone 4 mg/ml 2 ml IV 8 hourly for 2 days.
   Or
   Inj. Sodium Valproate 500 mg IV 8 hourly for 2 days.

Prophylaxis

Consider prophylactic treatment, if number of attacks is two or more attacks per month or each attack is very severe necessitating loss of work time. Frequent headaches (more than two a week) or a pattern of increasing attacks with risk of developing medication overuse headache or failure of, contraindication to, troublesome side effects from acute medications.

Prophylaxis treatment

In addition to the above nonpharmacological and pharmacological treatment of the acute episode, consider following depending on co-morbidity:

Tab. Atenolol 80-320 mg daily.
Or
Tab. Metoprolol 100-450 mg daily.
Or
Tab. Propranolol 80-320 mg daily.
Or
Tab. Amitriptyline 10-50 mg at bed time.
Or
Tab. Cyproheptadine 4-16 mg daily in children.
Or
Tab. Flunarizine 5-10 mg daily.
Or
Tab. Topiramate 50-200 mg daily for obese patients
Or
Tab. Sodium Valproate 50-100 mg/day for obese patients

The goals of preventive therapy are as follows: reduce attack frequency, severity, and/or duration, improve responsiveness to acute attacks, and reduce disability. Start the chosen drug at a low dose and increase it slowly until therapeutic effect or side effects develop. Give each treatment an adequate trial. A full therapeutic trial may take 2-6 months. If found to be effective, it should be continued for at least 6 months and then slowly tapered to assess its continued need. If headache recurs after discontinuation of prophylactic therapy, the medication regime should be reinstated for another 6 months trial.

Patient education

- Avoid precipitating factors like lack of sleep, glare, anxiety, hunger, foods like processed cheese, banana, chocolates, wine, etc.
- Avoid overdose or frequent use of ergot preparation as these can cause hypertension and precipitate vascular disease.
- Drug for acute migraine should be taken as early as possible at the onset.
- Regular, more than twice a week, or increasing consumption of analgesics over time are alarms that require attention.
- Behavioural intervention relaxation techniques and stress management techniques.

References

1. Headache Classification Committee of the International Headache Society. Classification and Diagnostic Criteria for Headache Disorders, Cranial Neuralgias and Facial Pain. Cephalalgia 2004; 24 (Suppl 1): 1-195.
2. Campbell JK, Penzien DB, Wall EM. Evidence-based Guidelines for Migraine Headache: Behavioural and Physical Treatments available at www.aan.com/professionals/practice/guidelines/index.cfm accessed on July 2007.
3. Headache. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 112-128.

NEUROCYSTICERCOSIS

This is the most common parasitic disease of CNS worldwide produced by invasion of the CNS by the cystic stage (cysticercus) of pork-tapeworm (*Taenia solium*). Human beings acquire the disease, when they ingest the food or water contaminated with the eggs of *T. solium*.

SALIENT FEATURES

- The clinical features depend upon site and number of cysts in the CNS, and the inflammatory response of the CNS. It can remain silent or present most commonly with seizures, encephalitis, meningitis, hydrocephalus, or increased intracranial pressure.
- Neurologic, cognitive or personality disorder may be the presenting features and decreased visual acuity may be seen in ocular cysticercosis.
- In spinal neurocysticercosis, cord compression, nerve root pain, transverse myelitis, or meningitis.
- Neuroimaging (CT/MRI) is the investigation of choice.

Treatment

The aim of therapy is to control symptoms, i.e. convulsions and hydrocephalus.

Pharmacological

Antiepileptic drugs (for control of seizure, see Epilepsy section in Chapter 1). If there is no calcification and the patient is free of seizures for 2 years, treatment can be gradually

discontinued. Cysticidal drugs accelerate the destruction of the parasites, resulting in faster resolution of the infection.

Refer the patient to a hospital (to a physician or neurologist) for supervised treatment with following:

Tab. Albendazole 15 mg/kg/day (max 800 mg/day) in 2 divided doses per day for 8 days, taken with fatty meals. Before administering a two to three days priming with Tab. Prednisolone 1 mg/kg for 3 days.

(**Caution**: Absolute contraindications are ocular cyst, or spinal medullary cysts, heavy cyst burden, increased intracranial pressure).

Surgical treatment is indicated in case of ocular cysticercosis, ventricular cyst or hydrocephalus.

Patient education

- Prolonged freezing or thorough cooking of pork to kill the parasite.
- Personal hygiene and thorough washing and avoiding unpeeled fruits and vegetables in areas endemic for *T. solium* helps prevent ingestion of eggs.
- All members of a family of an index case of cysticercosis should be examined for the presence of eggs or signs of disease.

References

1. Cysticercosis. In: Nelson's Textbook of Paediatrics. Behrman RE, Kliegman RM, Jenson HB (eds), 19th Edition, Harcourt Publishers International Company, 2011; pp. 1234-1237.
2. Infectious Focal CNS Lesions. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 2637-2638.
3. Neurocysticercosis. American Epilepsy Society. Epilepsy Curr 2004; 4: 107-111.

ACUTE BACTERIAL MENINGITIS

The three main pathogens, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis*, account for 75-80% of cases after the neonatal period. There has been a worldwide increase in infection with strains of *S. pneumoniae* resistant to penicillin and other beta-lactam antibiotics (second- and third-generation cephalosporins).

SALIENT FEATURES

- Fever with prominent headache, neck stiffness, photophobia, nausea, vomiting and altered mental status (lethargy to coma).
- Infants, elderly, and immunocompromised patients may show only mild behavioural changes with low-grade fever and little clinical evidence of meningeal inflammation.
- Approximately, 15% of all patients, and 40% of older patients, demonstrate focal cerebral findings, and 20-50% of patients develop seizures at some time during the course.

Diagnosis

Blood cultures, urgent lumbar puncture (LP). In case with focal findings or clinical evidence of raised intracranial pressure (ICP), contrast-enhanced cranial computed tomography (CECT) before LP.

CSF examination reveals elevated pressure (200-500 mm H_2O) and protein (100-500 mg/dl, normal 15-45 mg/dl), decreased glucose (<40% of serum glucose), and marked pleocytosis (100-10,000 white blood cells/µl, (normal <5) with 60% or greater polymorphonuclear leucocytes.

The CSF Gram's stain result is positive in at least 60% of cases, and CSF culture results are positive in approximately 75%. The likelihood of finding Gram's stain or culture-positive CSF may decrease, if antibiotics are administered before doing LP. Early in disease, 10-20% of patients have CSF cell counts less than 1,000 cells/µl. Otherwise, cell counts below 1,000 cells/µl in a patient with a compatible clinical syndrome indicate partially treated meningitis, concurrent immunosuppression, or a nonbacterial cause. Petechial or purpuric rash suggests *N. meningitidis*, or, less often, *Staphylococcus aureus*, *Pneumococcus*, or the *Rickettsiae*.

Treatment

Nonpharmacological

- Hospitalize in a quiet place with no bright lights preferably in ICU.
- Maintain vitals, endotracheal intubation in patient with poor respiratory effort.
- Elevation of head to 30° and hyperventilation, if evidence of raised intracranial pressure.

Pharmacological

Empiric antimicrobial to be initiated based on the patients age and underlying disease status; once a bacterial pathogen is isolated, antimicrobial therapy can be modified for optimal treatment.

1. Inj. Ceftriaxone 4 g/day in 2 divided doses administered every 12 hours. It can also be administered as a single dose.
   Or
   Inj. Cefotaxime 8-12 g/day, in divided doses administered every 4 hours.
   If age is more than 50 years to cover *Listeria monocytogenes* and *Pseudomonas* or in immunocompromised patients.
   Inj. Ceftazidime 8 g/day in divided doses administered every 6 hours plus
   Inj. Ampicillin 10-12 g/day in divided doses every 4 hours.
   Or
   In case of resistant Gram-negative infection and are sensitive to Inj. Meropenem 1-2 g 8 hourly.
   Continue treatment for 10-14 days with antibiotics. Clinical response is observed within 24-48 hours. Repeat lumbar puncture after 48 hours especially if on dexamethasone.

2. In case of head trauma, CSF rhinorrhoea, intracranial shunt or history of neurosurgical intervention, when penicillin or cephalosporin resistant strains of *Streptococcus pneumoniae* are suspected, add
   Inj. Vancomycin 500 mg IV 6 hourly.
3. In *H. influenzae* type-B meningitis, pneumococcal meningitis in children and in children over 2 months of age with neurological sequelae
   Inj. Dexamethasone 0.15 mg/kg every 6 hour IV for 2 days. It should be started at the same time or shortly before, the first dose of antibiotic (not effective, if given after antibiotics).
4. In patient with papilloedema, altered sensorium, 6th nerve palsy, convulsions or decerbate posturing
   Inj. Mannitol 20% 1 g/kg stat followed by 0.5 g/kg every 4-6 hours.
5. Chemoprophylaxis for close contacts of patients with meningococcal meningitis
   Cap Rifampicin 600 mg twice a day 5 days
   Or
   Cap Ciprofloxacin 500 mg single dose
   Or
   Tab. Ofloxacin 400 mg single dose
   Or
   Inj. Ceftriaxone 250 mg IM single dose.

Note: Diagnosis and management of underlying cause, e.g. CSOM is important.

Patient education

Explain to the relative that in unconscious patient nothing should be administered orally until patient recovers his level of consciousness.

References

1. Bacterial Infections. In: Neurology in Clinical Practice. WG Bradley, RB Daroff, GM Fenichel et al (eds), Butterworth-Heinemann, Boston: 1996; pp. 1181-1243.
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4. Acute Bacterial Meningitis in Adults. In: Current Clinical Topics in Infectious Diseases. Leemington JS, Swartz MN (eds), Blackwell Sciences, 1999; pp. 215-239.

TUBERCULOUS MENINGITIS

SALIENT FEATURES

- TB meningitis should be staged depending on the clinical symptomatology.

Clinical staging of patients with tuberculous meningitis

Stage I (early): Nonspecific symptoms and signs, no clouding of consciousness, no neurologic deficits.

Stage II (intermediate): Lethargy or alteration in behaviour, meningeal irritation, minor neurologic deficits (cranial, nerve palsies).

Stage III (advanced): Abnormal movement, convulsions, stupor or coma, severe neurologic deficits (paresis).

- Typically, the CSF is clear or slightly opalescent. There is a moderate degree of pleocytosis (usually less than 500 cells), with a predominant lymphocyte response. Biochemical examination reveals raised protein, usually below 200 mg%. But in late cases and particularly when a spinal block develops the protein content may be as high as 1 to 1.5 g%. Sugar is reduced to 40 mg% or below. Smear-positivity has been reported in less than 10% of samples.
- A diagnosis of tuberculous meningitis is often made, if a clinical syndrome is accompanied by a consistent CSF profile, evidence of tuberculosis elsewhere in the body or response to specific antimycobacterial therapy in the absence of evidence for other diagnosis.

Treatment

Patient should be hospitalized.

1. Intermittent short course chemotherapy regimens of 6-9 months are recommended for all forms of extrapulmonary TB. In patients with poor or no response at 8 weeks of intensive phase may be given benefit of extension of IP for one more month. In case of TBM the continuation phase shall be extended by 3 months making the total duration of treatment to a total of 9 months. A further extension may be done for 3 more months in continuation phase (making the total duration of treatment to 12 months) on a case to case basis in case of delayed response and as per the discretion of the treating physician.
   (for details of therapy, see Tuberculosis in Chapter 1).
2. Corticosteroids are indicated in stage II or III disease or in case of the impending or established spinal block and are given for 3-6 weeks and tapered slowly over 2-4 weeks.
   Inj. Dexamethasone 8-16 mg/day in divided doses in adults.
   In children: 8 mg/day or 0.3-0.6 mg/kg/day.
   Or
   Tab. Prednisolone 60 mg/day or 1 mg/kg/day.
3. Urgent neurosurgical consultation and intervention (ventricular shunt) in case of hydrocephalus.
4. If signs and symptoms of increased intracranial pressure manage accordingly.
5. Seizures to be controlled with antiepileptic drugs (see section on Epilepsy in Chapter 1).

References

1. Technical Guidelines for Tuberculosis Control. Central TB Division. Directorate General of Health Services, Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi, 2009.
2. Tuberculosis. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 1006-1020

HERPES SIMPLEX ENCEPHALITIS

Herpes simplex encephalitis (HSE) is the most common cause of fatal sporadic acute encephalitis having a mortality of 70-80%, and leaves many survivors severally disabled, without any significant predilection for age, sex, race or season.

SALIENT FEATURES

- The clinical hallmark of the HSE is acute/subacute onset of fever, headache, altered consciousness and focal neurologic symptoms/signs, especially personality/ behaviour changes suggestive of a temporal lobe/frontal involvement.
- CSF shows mononuclear pleocytosis (50-200 cell/mm^3), mildly raised protein and normal or mildly decreased sugar.
- The diagnosis is confirmed by CSF-PCR suggestive of HSV expression in CSF and contrast-enhanced MRI. EEG usually shows abnormality (slow waves/ PLEDS) localized to temporal/frontal lobes.

High index of suspicion is required and diagnosis should be considered in any patient with progressive deteriorating level of consciousness, fever, abnormal CSF and focal neurological signs in the absence of other causes.

Treatment

Hospitalize the patient preferably in a set-up with ICU facilities.

Nonpharmacological

In patients with signs of increased intracranial pressure, raise head end of patient by 30°, intracranial pressure monitoring, and hyperventilation in intensive care unit.

Maintain adequate hydration, however, in patients with syndrome of inappropriate ADH secretion (SIADH), restrict fluid intake.

(**Caution**: Prevent dehydration).

Pharmacological

For seizures (see section on Status Epilepticus).

1. Inj. Mannitol 20% 1 g/kg stat followed by 0.5 g/kg every 4-6 hours.
   Or
   Sol. Glycerol 30 ml 6 hourly orally.
2. Start empirical treatment with Acyclovir in all cases at a very early stage or suspected of HSE pending confirmation of the diagnosis.
   (Role of steroids is controversial).
   Inj. Acyclovir 10 mg/kg 8 hourly for 10 days. The drug should be diluted to a concentration not exceeding 7 mg/ml and infused slowly over 60 minutes (can cause local phlebitis, if extravasation occurs).
   If diagnosis of HSE is definite, give treatment for 21 days to prevent relapse.

However, in a stable patient without documented evidence of HSE including negative CSF-PCR and a normal MRI, acyclovir can be discontinued after 5 days of presumptive treatment.

Patient education

- Unlike most viral infections this is treatable and the drug used is quite safe.

Reference

1. Meningitis, Encephalitis, Brain Abscess and Empyema. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 3410-3434.
(For treatment of acute meningoencephalitis in children see Chapter – 19).

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) is an acute viral infection of the central nervous system caused by JE virus which is a flavivirus. The virus is transmitted by the bite of infected Culex mosquitoes. Culex tritaeniorhenchus is the principal vector of the disease in South East Asia. The mosquito becomes infected by feeding on pigs and wild birds infected with the JE virus. The infected mosquitoes then transmit the virus to human and animals during the feeding process. The transmission reaches its dead end in human. The disease is not directly transmitted from person-to-person. The incubation period is usually 6 to 16 days (usually 4-6 days).

SALIENT FEATURES

- Mild infections may occur without apparent symptoms other than fever with headache. More severe infection is marked by rapid onset, headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions (especially in infants) and paralysis. Case fatality rates range from 10 to 35%. Neurological-movement disorder (Parkinson's features, dystonia, dyskinesia), seizures, focal weakness or mental retardation, and psychiatric sequelae are common among survivors.
- Diagnosis of JE infections can be made by serological tests, such as haemagglutination-inhibition test, by demonstrating a fourfold rise in antibody (IgG) titres in paired sera or IgM antibody in serum and CSF.
- CT/MRI helps differentiating Japanese encephalitis from herpes simplex encephalitis and shows low density non-enhancing areas in thalamus, basal ganglia and brainstem.

Treatment

Treatment of JE is supportive and symptomatic with mannitol, steroids, antiepileptic drugs and IV fluids.

Patient education

- As JE is a mosquito-borne disease, measures should be taken to eliminate mosquito breeding sites and prevent mosquito bites.
- Vaccination is indicated mainly for person spending 30 days or more in a rural agricultural endemic area during the transmission season.
- For initial immunization, usually two doses of JE vaccine are administered at an interval of 1-2 weeks and single booster dose at 1 year. Immunity may take one month to develop. Revaccination is recommended at 3 years interval.
- Common reported side effects include local reactions at the injection site, and mild systemic symptoms such as headache, myalgia, gastrointestinal symptoms and fever.

Reference

1. Meningitis, Encephalitis, Brain Abscess and Empyema. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 3410-3434.

STROKE

Cerebrovascular disease (CVD)/stroke refers to rapidly developing clinical syndrome of focal or global loss of brain functions lasting for more than 24 hours or leading to death with no apparent cause other than that of vascular origin. Transient ischaemic attacks (TIAs) refer to when focal or global cerebral dysfunction disappears within 24 hours. Most TIAs last for less than 30 minutes. Stroke is not a homogeneous condition. There are clear pathological sub-types—cerebral infarction, primary intracerebral haemorrhage and subarachnoid haemorrhage with over 100 potential underlying causes. Pre-hosptial stroke identification and prompt transfer of patient to a center well equipped with stroke management is very important.

SALIENT FEATURES

- Presentation varies depending on the site of involvement – carotid circulation stroke presents with hemiplegia and/or aphasia. Vertebrobasilar insult produces dysphagia, dysarthria, diplopia, dizziness/crossed signs or coma.
- Diagnosis of stroke to be ascertained clinically supported by brain imaging (plain CT/MRI) within 48 hours and not later than 7 days but urgently, if: Level of consciousness is depressed; history of head trauma, severe headache at onset; history of fever, neck stiffness, papilloedema; indications for thrombolysis or anticoagulation or history of anticoagulation.
- Cardiac status for associated coronary artery disease.

Treatment

The overall goal is to minimize acute brain injury and maximize patient recovery. The guidelines for stroke also include the management of patients with TIAs. The term stroke should be understood to encompass to TIA.

The "D's of Stroke Care" remain the major steps in diagnosis and treatment of stroke and for identification of the key points at which delays can occur.

- Detection: Rapid recognition of stroke symptoms
- Dispatch: Early activation and dispatch of emergency medical services (EMS) system by calling 102
- Delivery: Rapid EMS identification, management, and transport
- Door: Appropriate triage to stroke centre
- Data: Rapid triage, evaluation, and management within the emergency department (ED)
- Decision: Stroke expertise and therapy selection
- Drug: Fibrinolytic therapy, intra-arterial strategies
- Disposition: Rapid admission …

(Stroke is best treated in specialized stroke unit).

Immediately following acute stroke

- Manage airway, breathing and circulation. Take precautions to avoid aspiration and ensure adequate oxygenation.
- Nil orally. A swallowing assessment should be undertaken at home or hospital before starting eating or drinking.
- Urgent neurosurgical assessment should be available for patients with large cerebellar infarcts with hydrocephalus, subarachnoid haemorrhage and for selected cases of cerebral haemorrhage.
- Establish time of symptom onset (last normal)
- For secondary prevention, identify and treat the underlying risk factors. Hypertension is the single most important modifiable risk factor for all types of strokes in both sexes and at all ages.
- Acute elevation of BP is often transient and decline spontaneously. Hypotension/ excissive BP reduction not recommended.
- Glucose levels should be kept below 150 mg% as hyperglycaemia may be deleterious to the brain cells. Dextrose containing fluids in nonhypoglycemics not recommended. Excessive intravenous fluids not recommended.
- Treat even mild fever as elevation of temperature consistently worsens the neurological outcome from ischaemic insults.
- Tab. Aspirin 650 mg within 48 hours of stroke after excluding intracerebral haemorrhage by brain imaging. Subcutaneous LMVH for preventing deep vein thrombosis in immobilized patients.

Elevated blood pressure not to be treated unless

- If systolic BP >220 mmHg or diastolic BP >120 mmHg on two readings 5 minutes apart, or if systolic BP is 180-220 mmHg, diastolic BP is 105-120 mmHg; or mean arterial BP is >130 mmHg on two readings 20 minutes apart. (If rt-PA is to be given BP should be <185/110).
- Patient has myocardial infarction/cardiac failure/dissection of aorta.

Patient otherwise eligible for acute reperfusion therapy except that blood pressure is >185/110 mmHg, Inj. Labetalol 10-20 mg IV over 1-2 minutes, may repeat once.

If systolic BP 180-230 mmHg or diastolic BP 105-120 mmHg: Inj. Labetalol 10 mg IV followed by continuous IV infusion 2-8 mg/min. If blood pressure not controlled or diastolic BP >140 mmHg, institute Nitroprusside 0.5-1.5 mcg/kg/min then increased in steps of 500 mg/kg/min every 5 minutes within a range of 0.5-0.8 mcg/kg/min. Stop, if response is unsatisfactory with maximum dose in 10 minutes.

If systolic BP is <180 mmHg and diastolic BP is <105 mmHg, defer antihypertensive therapy. Overzealous treatment can convert ischaemic penumbra into an infarct.

Monitor blood pressure every 15 minutes for 2 hours from the start of rt-PA therapy; then every 30 minutes for 6 hours; and then every hour for 16 hours.

Low blood pressure. Volume replenishment is the first line of approach. Isotonic saline or colloids can be used and monitored with the central venous pressure or pulmonary artery wedge pressure. If hypotension persists after correction of volume deficit, continuous infusions of pressors (Dopamine 2-20 mcg/kg/min) should be considered, particularly for low systolic blood pressure, such as systolic BP<90 mmHg.

Cerebral infarction

No therapy has yet been confirmed to limit the neuronal damage associated with acute cerebral infarction.

- Thrombolytic therapy with rt-PA in cerebral infarction demonstrates significant improvement in functional outcome in carefully selected patients treated in specialist units, if used within 4.5 hours of stroke onset. This should not yet be regarded as a routine therapy, particularly without specialist centres.
- No benefit has been demonstrated for heparin, corticosteroids, nimodipine or other calcium channel antagonists, barbiturates, plasma volume expanders or haemodilution techniques in mortality in patients with acute ischaemic attack.

Subarachnoid haemorrhage

Acute severe headache with vomiting, neck stiffness and altered sensorium and CT scan shows blood in the cisterns and CSFs uniformly blood stained.

Tab. Nimodipine 60 mg 4 hourly.

Treatment

Immediately transfer the patient to a tertiary care centre with a neurosurgery set-up after securing patent airway and blood pressure.

Stroke prevention

- Treat isolated systolic hypertension.
- Intensive cholesterol lowering with statins reduces stroke risk and goal is an LDL-C level of < 100 mg/dl for very high-risk patients. Low HDL-C may be considered for treatment with niacin or gemfibrozil.

- Tab. Aspirin 50-325 mg once daily after ischaemic stroke/TIA should be prescribed as early as possible or Tab. Clopidogrel 75 mg once daily or extended release Dipyridamole 200 mg added to Aspirin 50 mg twice daily. For patients who have an ischaemic cerebrovascular event while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit.
- In patients with non-valvular atrial fibrillation and also after cardioembolic stroke from valvular heart disease and recent myocardial infarction.

  Tab. Warfarin 5 to 7.5 mg/day to keep patients (International Normalized Ratio (INR) between 2-2.5). Urgent anticoagulation is not recommended in view of no added benefit in preventing recurrence and for increased risk of serious intracranial haemorrhage in cases of moderate to large infarction.
- Carotid endarterectomy (by a specialist surgeon) for patients who had carotid or TIA/stroke but no major disability with 70-99% stenosis.

Long-term management

Management of hypertension – if hypertension persists for more than 2 weeks, treat hypertension and lifestyle modification (for details see section on Hypertension in Chapter 3).

Atrial fibrillation (Af). Aspirin in AF patients who have a clear contraindication to vitamin-K antagonist therapy but are able to tolerate antiplatelet therapy. The combination of clopidogrel plus aspirin carries a bleeding risk similar to warfarin and so is not recommended for those with a haemorrhagic contraindication to warfarin or patients with AF who are at high risk of recurrent stroke but who require temporary interruption of oral anticoagulation, bridging therapy with a low-molecular-weight heparin. Avoid long-term anticoagulation as treatment for nonvalvular atrial fibrillation.

Patient education

- Activation of emergency response team by patients or other members of the public speed treatment of stroke.
- Modification of lifestyle factors including physical activity, not smoking, avoiding environmental tobacco smoke, moderate alcohol consumption, maintaining a normal body weight, and eating a low-fat diet high in fruits and vegetables.
- Control of risk factors such as hypertension, diabetes mellitus, hyperlipidaemia and cessation of cigarette smoking.
- Cardiac features of metabolic syndrome improve with weight loss, which has also been shown to improve insulin sensitivity; lower plasma glucose, plasma LDL-C, and plasma triglycerides; raise HDL-C; lower BP; reduce inflammation; improve fibrinolysis; and improve endothelial function in patients with metabolic syndrome.

References

1. Pauline Anderson. AHA/ASA releases updated Secondary Stroke-Prevention Guidelines. 2010 . http://www.theheart.org/article/1140411.do accessed on September 5, 2012.
2. New Guidelines on Primary Stroke Prevention from AHA/ASA The Heart.org. September 05, 2012.
3. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage : A Guideline. Stroke. 2010;41:2108-2129.
4. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update. Circulation 2011; 124: 2458-2473.

ACUTE INFLAMMATORY DEMYELINATING NEUROPATHY/ GUILLAIN-BARRE SYNDROME (GBS)

GBS is an acute frequently severe fulminant polyradiculoneuropathy, usually presenting as ascending paralysis. GBS is presumed to have immune-mediated pathogenesis with lymphocytic infiltration of peripheral nerves and destruction of myelin for which no specific cause can be demonstrated, although it is commonly preceded by a viral or other infection—respiratory and gastrointestinal; it reaches a peak of disability within four weeks and follows a monophasic course with recovery. Several subtypes are recognized.

SALIENT FEATURES

- Diagnostic criteria for GBS are progressive motor weakness of more than one limb and partial or total areflexia.
- Involvement of ventilatory muscles is common and can be diagnosed by presence of respiratory distress/shallow respiration, weak voice, inability to cough effectively and decreased inability to count in single breath.
- Features strongly supportive of diagnosis are progression of symptoms up to 4 weeks, relative symmetry, mild sensory signs or symptoms, facial nerve (50%) or other cranial nerve involvement, transient or absent bladder involvement, recovery 2-4 weeks after nadir, autonomous dysfunction and absence of fever at the onset; CSF features are protein elevated after first week and cell count <10 mononuclear/mm; electrophysiological evidence of demyelination (prolonged F-wave, distal latencies, decreased conduction velocities, conduction block).

Treatment

Nonpharmacological

- Hospitalization is necessary for even mild cases for observation of progression of neurological deficit.
- General care includes: care of back, bowel and bladder, pressure points.

- Physiotherapy should be instituted early.
- Ventilatory support in impending respiratory failure (required in ~30% cases).

Pharmacological

Treatment should be started at the earliest and is not effective, if started after ~2 weeks of first motor symptoms.

Mild cases. No specific therapy is needed (corticosteroids have no role).

Severe cases. As indicated by progressive weakness requiring assistance for walking (power grade 3 or less), involvement of respiratory/bulbar muscles, swallowing difficulty.

Inj. Human immunoglobulins 400 mg/kg day for 5 days.

(**Caution:** Contraindicated in patients with IgA deficiency).

Or

If facilities are available, Plasmapheresis for a total of 4-5 exchanges over 7-10 days.

All patients to be closely monitored for: (a) progression of motor weakness, (b) involvement of respiratory/bulbar muscles, (c) autonomic disturbance, e.g. hypo/hypertension, cardiac arrhythmia.

Patient education

- Explain the natural course of the disease. It can progress to involve all the four limbs, respiration and swallowing.
- Disability can be reduced with treatment and most patients achieve complete or nearly complete recovery.
- Prognosis is bad in old age, rapidly progressive weakness, axonal form of GBS and delay in onset of treatment.
- Role of physiotherapy to be stressed.
- Provide psychological support.

References

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2. Asbury AK, Comblath DR. Ann Neurol 1990; 27:521.

DEMENTIA

Dementia is a progressive and largely irrevocable clinical syndrome characterized by a wide-spread impairment of mental function. The essential features of dementia are an acquired and persistent compromise in multiple cognitive domains that are severe enough to interfere with every day functioning. Majority of dementias are degenerative and progressive. The deficiency of acetylcholine is the predominant neurochemical

defect in dementia. Vascular dementia is second most common cause of dementia after Alzheimer's disease.

SALIENT FEATURES

As condition progresses, patient can experience some or all of the following:

- Memory loss, language impairment, disorientation, changes in personality, difficulties with activities of daily living, self-neglect, psychiatric symptoms (e.g. apathy, depression or psychosis) and out-of-character behaviour (e.g. aggression, sleep disturbance or disinhibited sexual behaviour, although the later is not typically the presenting feature of dementia).
- A diagnosis of dementia should be made only after a comprehensive assessment including: history, cognitive and mental state examination; physical examination and other appropriate investigations; a review of medications in order to identify and minimise use of drugs that may adversely affect cognitive functioning.
- A basic dementia screen should be performed at the time of presentation: Routine haematology, biochemistry, thyroid function test, serum vitamin B_{12} and folate levels.
- Syphilis serology, HIV, CSF examination and EEG should not be performed as a routine investigation.
- MRI is preferred modality to assist with early diagnosis and detect subcortical vascular changes, although CT scanning could be used. Specialists advice should be taken, when interpreting scans in patients with learning disabilities.

Treatment

The treatable causes of dementia are to be ruled out before considering the diagnosis of degenerative dementia. The common treatable causes of dementias are alcoholic, endocrinal–hypothyroidism, metabolic, infective and dementia related to head trauma (subdural haematoma).

Dementias are not curable, but the progression of dementia can be slowed down and quality of life can be improved by available treatment modalities. For optimal results, multiple modalities should be utilized including pharmacotherapy, behaviour management, psychotherapy, psychosocial treatment, support and education of families.

Nonpharmacological

- Behavioural modification, scheduled toileting and prompt voiding reduces urinary incontinence.
- Reactivation occupational rehabilitation
  - Memory training
  - Maximal creative activity

  - Improving sensory motor function
  - Psychosocial functioning
- Graded assistance, practice, and positive reinforcement should be used to increase functional independence.
- Low lighting levels, music, and simulated nature sounds may improve eating behaviour for persons with dementia, and intensive multimodality group training may improve activities of daily living, but these approaches lack conclusive supporting data.

Pharmacological (to be given by a specialist)

For cognitive deficits. For mild to moderate dementia (Mini-Mental State Examination (MMSE) score between 10 and 20).

Tab. Rivastigmine 1.5-6 mg/day in 2 divided doses (maximum dose 12 mg/day).
Or
Tab. Donepezil – 5-10 mg/day as a single dose.
Start with lowest dose and titrate to maximum dose in 4-6 weeks time.

For severe dementia, add 2nd line drug:

Tab. Mementine hydrochloride 5-10 mg as a single dose. Start with 5 mg and increase to 10 mg after 4 weeks.

Review after every 6 months by MMSE score and global, functional and behavioural assessment. Carer's views on the patients condition at follow-up also should be sought.

For noncognitive neuropsychiatry disturbances. Treat agitation or psychosis with dementia and depression accordingly (for details see section on Acute Psychotic Disorder and Depression in Chapter 16).

Patient education

- Short-term programmes which are directed towards educating the family caregivers about dementia, should be offered to improve caregiver's satisfaction.
- Intensive long-term education and support services should be offered to caregivers of the patient with dementia to delay time to nursing home placement.

References

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2. NICE Clinical Guidelines. NHS National Institute for Health and Clinical Excellence. Dementia, November 2006. Amendment March 2011.

PARKINSON'S DISEASE

Parkinson's disease (PD) refers to the idiopathic form of Parkinsonism. It affects 1-2 per 1000 population above the age of 65 years. Pathologically, there is degeneration and depletion of the pigmented dopaminergic neurons in substantia nigra compacta.

SALIENT FEATURES

- The core features are rigidity, bradykinesia and rest tremors (pill rolling movements along with abnormal gait and posture, onset is asymmetric).
- Difficulty in performing fine co-ordinated movements like writing, using hand tools and kitchen utensils, grooming, doing and undoing buttons.
- Difficulty in rolling in bed and getting out of chairs or automobiles.
- Gait difficulty with slowing, stooped posture, decreased or loss of arm swing. Limb discomfort and stiffness may be an early symptom.
- Diagnosis of Parkinson's disease remains clinical. As such no role of investigations.

Treatment

Nonpharmacological

Exercise: Occupational and physiotherapy improves activities of daily living along with mood and mobility.

Nutrition: A balanced diet with fibre supplement to be taken.

Pharmacological

'Early disease' refers to PD in people who have disease <5 years and have not developed motor complications. 'Late disease' refers to PD in people on levodopa who have developed motor complications. Figure 9.1 shows the algorithm for management of PD.

Treatment to be started once the Parkinsonian symptoms begin to impair the activities of daily living. Initiate treatment with levodopa in patients above 65 years of age; withhold Levodopa in younger patient. Treatment to be started with low dose and to be gradually increased until the benefit or side effects occur.

Early PD

There is no universal first-choice drug therapy. The choice of drug first prescribed should take into account clinical and life style characteristics and patient preference.

For tremors predominant PD

Tab. Trihexyphenidyl 6-20 mg in 3 divided doses.

Or

Tab. Benztropine 1-6 mg in 2-3 divided doses.

(**Caution**: Avoid anticholinergics in patients above 65 years of age).

Late PD

1. Trihexyphenidyl as above.
   Any of the following can be given as monotherapy or in combination.

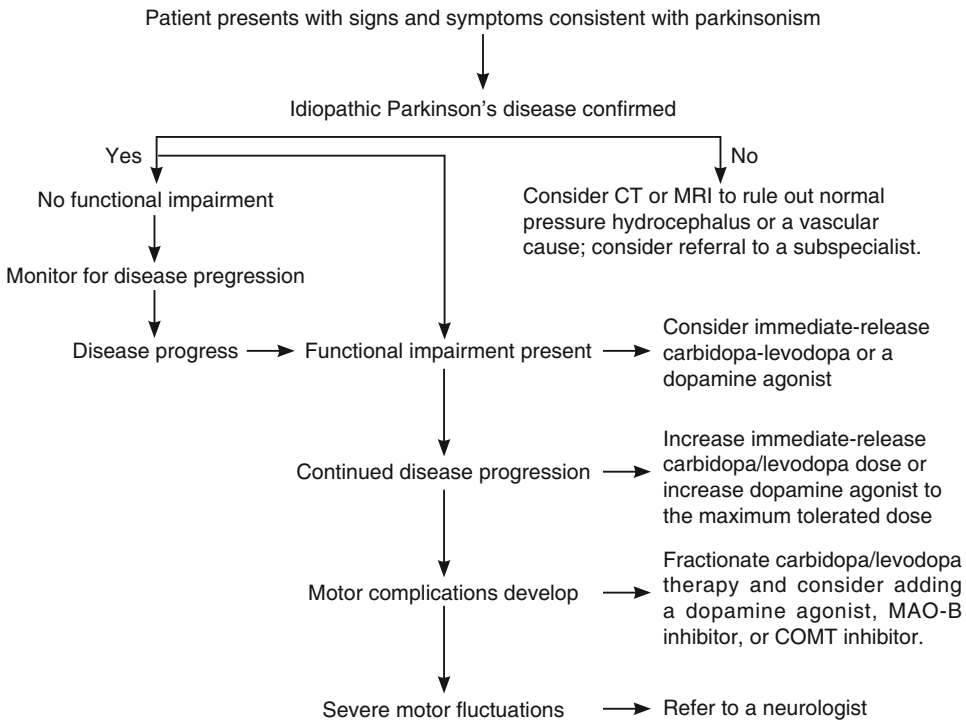

Fig. 9.1. Diagnosis and management of Parkinson's disease.

2. Tab. Bromocriptine 2.5-10 mg/day in 2-3 divided doses.
   Or
   Tab Pramipixol 0.375-4 mg per day in 3 divided doses.
   Or
   Tab. Ropinirole 6-24 mg /day in 3 divided doses.
   Or
   Tab. Peribidil 25-100 mg/day as single dose or 2 divided doses.
3. Tab. Levodopa plus carbidopa (100-250 mg Levodopa) in divided doses as per requirement (modified release levodopa preparations should not be used so as to delay the onset of motor complication in people with early PD).

The practice of withdrawing patients from their antiparkinsonian drugs (so-called drug holidays) to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome (NMS).

Selegiline, apomorphine and amantadine have limited role in treatment. **Dopamine agonists, MAO-B inhibitors,** co-enzyme Q_{10} and vitamin E should not be used as a neuroprotective therapy for people with PD except in context of clinical trial.

At present, there is no agent that slows down the progression of PD.

Most people with PD will develop, with time, motor complications and will eventually require levodopa therapy + Dopamine agonists/COMT inhibitors, triple combination—levodopa + carbidopa + entacapone and/or dopamine agonist.

Patient should be referred to neurologist, if drug-induced dyskinesias or motor fluctuations occur and Parkinson's plus syndrome (progressive supranuclear palsy, multisystem atrophy, etc.).

About 20-30% of patients with PD may also have dementia and around 40% of patients with PD have associated mild to moderate depression which has a major impact on quality of life, therefore, should be treated appropriately. ***For details of management, see section on Dementia and Depression***.

Patient education

- Provide all relevant information to patients and families regarding the disease, its prognosis and therapeutic options. Discussions should focus on therapeutic expectations, lifestyle modification and aids to overcome motor disability or limitation.
- Antiparkinsonian medication should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (e.g. gastroentritis, abdominal surgery) to avoid the potential for acute akinesia or nueroleptic maligant syndrome.

References

1. Parkinson's Disease. Diagnosis and Management in Primary and Secondary Care. NHS. National Institute for Health and Clinical Excellance. June 2006.
2. Rao SS, Hofmann LA, Shakil A. Parkinson's Disease. Diagnosis and Treatment 2006; 74: 2046-54.