UNIT 5 INFECTIONS OF THE CENTRAL NERVOUS SYSTEM, SLEEP DISORDERS AND COMA

Structure

5.0 OBJECTIVES

After reading this unit, you will be able to:

- diagnose common infections of central nervous system in the elderly;
- appreciate types of infections and their mode of presentations;
- investigate and manage different types of infections;
- diagnose and treat sleep disorders; and
- list common cause of coma and manage comatose patients.

5.1 INTRODUCTION

In the previous unit, you have learnt about neuro degenerative order. As you know in this unit, we shall touching CNS with sleep disorders and coma. Infections of the Central nervous system that occur by invasion of Bacteria poses major challenge to geriatrician. Most of the bacterial infection have great impact on the elderly and have higher mortality and morbidity than in the younger adults. These infections are mostly preventable and curable and need good understanding of the diagnosis, treatment and prevention in the aged.

The mortality rate due to the bacterial meningitis is three times in elderly than compared to young. The risk and severity of infection are directly related to the virulence and inoculum of the bacteria and depend on the integrity of the host defense. In the present publications as well as all previous studies reported 56% of community-acquired meningitis occurred in over 50 years of age and have higher mortality rate. (10%). Noso-comial meningitis related to neurosurgical procedures has also a cause of increase incidence of meningitis in the aged.

The diagnosis and clinical features are more subtle than in the young adults and poses challenges to make interpretation of clinical signs and symptoms more difficult. They

have more mental status abnormalities, and are more likely to have convulsions, neurologic deficits and hydrocephalus. Elderly with meningitis may not high fever and at times remain afebrile. It has been seen that CSF findings in elderly patients are the same as seen in young adults with meningitis. The treatment of bacteial meningitis requires immediate initiation of antibiotic therapy to prevent high morbidity and mortality of the infections. Other infections which may affect the central nervous systems are Tuberculosis, viral and fungal and can present with varied clinical manifestations and will be discussed briefly. Sometimes brain abscess often presents with focal neurological deficit. Headache, change of mental status may be misdiagnosed as cerebral tumours or CVA. Besides we will also discuss about sleep disorders and strategies to treat them. There are many causes of coma and brief account will emphasise on general management will be touched upon.

5.2 MENINGITIS

Infections of the meninges by pathogenic organisms results in inflammation of the brain and is called meningitis. The term aseptic meningitis refers to the form of meningitis where the cerebrospinal fluid is bacteriologically sterile and accompanied by a lymphocytic pleocytosis. Viral meningitis is the most common cause of Aseptic Meningitis. The term Meningitis refers to stiffness of the neck and irritability of the meninges. It occurs in situations such as sub-arachnoid haemorrhage, enteric fever, pneumonia and tonsillitis etc. Meningitis present with characteristic combination of pyrexia, headache and neck stiffness, the severity of these features varies according to the causative organisms. The abnormalities in CSF are very helpful in distinguishing the cause of meningitis.

5.2.1 Pathogenesis

Bacteria may reach subarachnoid space of the elderly patient by several different mechanisms. 1. Via the blood stream following bacteraemic illness. 2. By way of direct inoculation from adjacent foci of infection as in patients with otitis media, sinusitis, or mastoiditis. Most cases of head trauma or after a neurosurgical procedure develop meningitis. 3. Infections may also occur iatrogenically following lumbar puncture, ENT Surgery.

5.2.2 Aetiological Agents

Streptococcus pneumonia is the most common organism responsible for more than one half of all cases of meningitis reported in several studies (Table 5.1). Gram negative bacilli cause meningitis both by bacteremic spread of infection and as a nosocomial infection after neurosurgery. E.coli is the most common organism cause meninigitis secondary to pneumonia or U.T.I. E.coli and Klebsiella pneumonia are the common organisms found after surgical procedure. More unusual organisms such as Acinetobacter have also been reported.

Table 5.1: Aetiology of Bacterial Meningitis

Aetiologic Organism	Percentage(%)	Possible Source of Infection
1) Streptococcus pneumoniae	54	Pneumonia, otitis media, skull fracture, mastoiditis.
2) Neisseria meningitis	16	Pharyngitis
3) Gram- negative bacilli	8	Head trauma, neurosurgery, urinary tract manipulation, osteomyelitis, decubitus ulcer pneumonia.
4) Staphylococcus aureus	6	Acute bacterial endocarditis pneumonia, neurosurgery.
5) Streptococci	4	Subacute endocarditis, nerurosurgery.
6) Hemophilus influenza	2	Ottitis media, pneumonia.
7) Unknown	3	Not kmown.
8) Listeria monocytogenes	7	Not seen in India.

Neisseria meningitidis is a common cause of bacterial meningitis in adult but does occur in the elderly (16%). The spread is by air borne route and epidemics occur particularly in cramped living conditions. The organisms invades through the naso-pharynx producing septicaemia leading to involvement of meninges.

Meningococcal meningitis is the most common form of meningitis seen in adults, but less common in the elderly. Outbreaks have occurred in nursing homes and hospitals conditions like acute or chronic otitis media, diabetes, alcoholism and splenectomy predispose to this form of meningitis. Presence of meningeal signs and petechial or macular rash point towards the diagnosis of Meningococcal meningitis. Haemophilus influenzae does occur in older but usually associated with non capsulated organism where as in children, the type β encapsulated causes infections.

5.3 CLINICAL FEATURES

Headache, fever and neck stiffness are the classical presenting features of the meningitis but these features in elderly are more subtle. Sometimes older patients often have cervical spine disease and poor mobility of neck. This makes the interpretation of these signs more difficult.

Alteration in mental status such as drowsiness lethargy or coma associated with seizures, neurologic deficits and hydrocephalus have been reported. Nausea, vomitting, photophobias are also common complaints observed in the elderly. Fever is sometimes not recorded and at times patient is afebrile. Patients with contagious spread of infection usually complaint of ear or facial pain. A diffuse encephalopathy may occur and sign of papilloedema as a result of increased intracranial pressure may occur.

Physical examination is being carried out to evaluate the presence of neck rigidity which is seen in 56-92% cases. Cranial nerve examination and funduscopy are also carried out to find out the presence of increased Intracranial pressure or brain abscess. Mental status should be carefully assessed and followed. Examination of head should include search for any fracture, haematoma, otitis media and examination of respiratory system to rule out pneumonia, and examination of CVS to detect underlying valvular heart diseases and endocarditis. Further, the examination of costovertebrae tenderness, petechial lesions and pressure sores will provide important clue about source of infections in arriving at diagnosis of meningitis.

5.4 INVESTIGATIONS

Performance of lumber puncture (LP) without delay is advised in both old and the young. About 35% patients present with focal neurologic findings and fundus examination is mandatory before the lumbar puncture is done as it is contraindicated in patients with brain abscess and increased intracranial pressure. Hence, computrised tomography (CT) or MRI is advised before this procedure is carried out. The CSF findings in bacterial meningitis is summarised in Table 5.2. Lumbar puncture will show prulent fluid with WBC count between 500-10,000/cumm. Polymorphonuclear leukocytes accounts for 90% of the total count. Mono-nuclear cell has been found high in Listeria monocytogenes meningitis. However, lack of cellular response in CSF has been reported in majority of the cases. Blood glucose level are usually low and serum glucose and CSF glucose ratio is usually less than 50% Protein level is elevated above 50mg/dl. If protein levels are very high than point towards poor prognosis.

Gram staining is usually positive in 60-90% cases, if Gram stain is negative than latex fixation, coaggulatination and counter immuno electrophoresis are done to demonstrate bacterial antigen. Other tests such as lactic acid levels and C-reactive proteins measurement have been found useful in differentiating bacterial from viral meningitis. Blood and CSF cultures are to be done in all suspected cases of bacterial meningitis. In addition, sputum, urine and wound cultures may be helpful in determining the causative agents and also the source of infections.

Table 5.2: CSF Findings in Bacterial Meningitis

Opening Pressure	>180mm H_2O
W.B.C.	500-10,000 cu/mm Neutrophils predominate more than 90% of total count
Glucose	<40 mg/dl.
CSF/ serum glucose ratio	< 0.40
Proteins	> 50 mg/dl.
Gram's stain	+ve in 60-90%
Culture	+ve in 80% cases
Latex agglutination	Specific for antigens of S. Pneumoniae, N. Meningitidis, E.coli, H. Influenzae
Limbus amebocyte lysate assay	+ve in gram negative meningitis.
PCR for bacterial DNA	Specificity and sensitivity unknown.

5.5 TREATMENT

Appropriate antibiotic therapy to be started immediately. The combination of ampicillin and 3rd generation cephalosporin are normally recommended to cover all pathogens likely to cause meningitis. After CSF findings and gram stain and culture report available, then appropriate antibiotics should be chosen, to be a, bactericidal for causative agents and able to diffuse across the Blood brain barrier. (Table 5.3). Role of corticosteroids in elderly is yet to be established. Dehydrated or volume depeleted patients are treated with colloid or crystalloid to improve blood pressure and urine output. Septic shock may sometime develop and is treated by parenteral fluid and dopamine administration.

Specialised care should be given to a comatose patients and frequent suctioning and frequent change in posture to prevent bed sores are carried out. A condom catheter is preferred to a Foleys unless urinary retention develops. A repeat lumbar puncture is necessary in patients who do not respond to the therapy.

Table 5.3: Antibiotic of Choice for Bacterial Meningitis

1) Neisseria meningitis	Penicillin sensitive	Pencicillin G or Ampicillin
	Penicillin resistant	Ceftriaxone or Cefotaxime
2) Streptococcus Pneumoniae	Penicillin sensitive Penicillin resistant	Penicillin G Vancomycin+ Ceftriaxone/Cefotaxime.
3) Gram-negative bacilli Cephalosporin	3rd Generation Cephalosporin	Ceftriaxone or Cefotaxime.
4) Staphylococcus aureus	Methicillin sensitive	Nafcillin or oxacillin
5) Staphylococcus aureus	Methicillin resistant	Vancomycin
6) Pseudomonas aerogenosa		Ceftazidine
7) β heamolytic streptococci		Penicillin
8) Listeria monocytogenes		Ampicillin
9) Hemophilus Influenzae		Ceftriaxone or Cefotaxime.

5.6 PREVENTION

Although there are no data available to support the prevention of pneumoccal meningitis but it is found that pneumococcal vaccine does decrease the severity of pneumoccocal respiratory infections. Hence, currently available pneumococcal vaccine has been routinely recommended in all patients above 65 years of age which may be of some benefit to older patients.

Check Your Progress 1

1) What is Meningitis?

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2) Enumerate two common causes of meningitis in old age?

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3) Describe CSF findings in acute Bacterial Pyogenic meningitis.

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4) Name antibiotics effective against Streptococcal pneumonae meningitis.

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5.7 TUBERCULAR MENINGITIS

In elderly, tuberculosis of meninges, is a serious disorder and is nearly always due to the human type of tubercle bacilli. A few isolated cases of meningitis due to a typical mycobacteria can occur. It is often an insiduous disease and presents with non-specific symptoms of fatigue, anorexia, nausea and an altered mental status presenting as dementia in an elderly. A miliary mottling in the X-ray Chest may be the only feature which differentiates tubercular meningitis from cryptococcal meningitis. Duration of symptoms range from two days to six months. Meningeal signs are present in less than half of the cases. Evidence of raised intracraneal pressure such as papillooedema, brady cardia, hypotension may be present. Occular palsies, particularly sixth nerve involvement has been seen in 30-70% of cases. Sensorial disturbances include confusion, disorientation, drowsiness and varying grades of unconsciousness has been seen along with focal neurological deficit. Convulsions are observed in 50% of the patients. Untreated patients progress to comatose state, metabolic disturbances, irregular respiration, and generalized seizures.

Investigations

CSF findings usually reveal elevated protein levels above 50 mg/dl and low glucose below 40 mg/ dl. Mononuclear cells predominate except in early infection, there may be polymorphonuclear cells. Acid-fast positivity varies and range from 10-80% cases. Adenosine deaminase activity has been reported in the CSF and value of 9 units/L or greater suggests tubercular meningitis. Radioimmunoassay has been used for detecting tubercular antigen which becomes negative after therapy. Tuberculostearic acid, a structural component of mycobacterium tuberculosis can be detected by gas-liquid chromatography. PCR testing and immunomagnetic enrichment may also give evidence of tubercular meningitis.

Prognosis depends on age, duration of symptoms and neurologic deficits. Mortality is greatest in patients older than 50(60%). Clinical staging has been utilized to treat meningitis based on neurological status:

Stage I : Cational, no Focal neurologic signs or hydrocephalus.

Stage II : Confusion, depression or focal neurologic deficits.

Stage III : Stuporous or dense paraplegia or hemiplegia.

With the early diagnosis and treatment, cure is seen in 80-90% cases. However, patients usually present late and with complication and hence treatment of the diseases is unsatisfactory. About 20-30% cases are left with residual physical or mental defects such as mental retardation, visual and hearing defects, motor deficits, metabolic and endocrinal abnormalities.

Treatment

Antitubercular drugs like rifampicin, isoniazid (INH) and Pyrazinamide (PZA) penetrate the blood brain barrier to achieve adequate CSF concentrations. Streptomycin is not recommended as it causes otoxicity and Nephrotoxicity. Several studies suggest the adjunctive use of cortico-steroids for Stage II and Stage III patients, starting with dose of prednisone at 80mg/ day, which may be gradually reduce over 4 to 6 weeks, as guided by the patients symptoms. If hydrocephalus is present, ventricular shunting procedures has been found beneficial. Multidrug resistant tuberculosis needs several drugs include quinolone, amikacin, kanamycin, capreomycin and PAS.

Check Your Progress 2

1) Describe symptoms of TB Meningitis.

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2) Which is most common nerve involvement in TB Meningitis.

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3) Describe CSF findings in Tubercular meningitis.

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4) Describe clinical staging based on neurological status.

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5.8 FUNGAL AND VIRAL INFECTIONS

1) **Fungal Meningitis**

Usually occurs in patients who are immuno comprised and is a recognised complication of human immuno-deficiency virus (HIV) in 20-50% cases. It is caused by cryptococcus and candida and cause inflammation of meninges in a manner very similar to Tuberculosis.

Diagnosis is based on CSF findings which are similar to that of tuberculosis. There is lymphocyte predominance and India ink is positive in 50% or more of cases. A cryptococcal antigen is positive in 90% of cases. MRI and CT Scan helpful to rule out basal meningitis which occurs in tuberculosis and presence of hydrocephalus which at times seen in some of cases of cryptococcal meningitis.

High CSF opening pressure, along with low CSF glucose, fewer than 20 white cells in the CSF, high titre of cryptococcal antigen and presence of HIV disease point towards the poor prognosis.

Treatment

Amphotericin B is the drug of choice but Flucytosine and Fluconazole have also been found useful in the treatement of cryptococcal meningitis. Recently, a new liposomal Amphotericin B have been added to treat meningitis. A combination with flucytocine and fluconazole has been explored in patients with acquired immuno deficiency disease (HIV).

2) **Viral Meningitis**

Viral Meningitis refers to inflammation of the meninges and has sudden onset and a short course over days to week. The majority of the viruses enters the CNS via haemato-genous route. It is a beningn self limiting illness.

Aetiology

A large number of viruses have been implicated include: 1. Enteroviruses 2. Mumps

3. Arena 4. Herpes viruses 5. Retroviruses (HIV) 6. Others include influenza, adenovirus and arboviruses.

Clinical Features

Mostly seen in adult but do occur in elderly. It is often preceded by a prodormal phase consisting of non specific symptoms such as fever, headache, weakness and malaise. The sensorium is clear and focal neurological signs are rare. Symptoms usually reach a maximum within one week and subsides within two weeks.

Investigations

CSF findings show normal glucose and protein levels and an excess of lymphocytes. The virus can be identified by increase in specific antibody titres.

Treatment

There is no specific treatement as the disease is usually benign and self limiting. The patient is treated symptomatically. Majority of the patients recover without any sequaele.

3) **Herpes Simplex Encephalitis**

It is a serious infection of the CNS and is caused by herpes simplex virus type I. It occurs in both sexes and has no seasonal association. High Mortality- (60-80%) has been reported in patients over 50 years of age. However, 5-10 % cases recover without any neurologic sequelae.

Clinical Features

There is an abrupt onset of personality change, altered sensorium, fever and Headache. There occur some localizing signs such as speech deficits, temporal lobe seizueres, hemiparesis, olfactory hallucinations and nasal field defects.

Diagnosis

The spinal fluid findings are non- specific with an slightly elevated number of lymphocytes. However, increase in leukocytes may be found in the early course of the disease. The EEG (Electroencephalogram) may show slow wave complexes at regular to 2-3 second intervals, usually localized to the temporal lobe. CT Scan demonstrate abnormality in 70% cases but MRI is more sensitive and positive in the early course of the disease. Newly PCR technology done in CSF fluid is helpful in making the diagnosis. Definitive diagnosis is usually made by brain biopsy by appropriate culture and histology.

Treatment

Effective therapy consists of acyclovir at a dose of 10mg/kg every 3 hours for 10-12 days. If patients show renal insufficiency then dose has to be adjusted according to creatinine clearance. Dehydration is to be avoided.

Prognosis depends on the level of consciousness at the start of the therapy. If treatment is delayed or patient is comatosed then these patients develop neurologic sequelae.

5.9 BRAIN ABSCESS

It is collection of pus in the brain and presents a mass lesion with focal neurologic deficits. Infections spread through ear and sinus infection appear to be more common in younger adults than the older than 60 years of age. Mean duration of symptoms is usually 10-15 days. Mortality usually ranges between 30-50% and with the advent of CT scan, early diagnosis is possible. This has decreased mortality to 4-20%.

Clinical Features

Fever is usually absent in 40-50% patients and common symptoms such as headache, change of mental status, focal neurologic deficits, are some times misdiagnosed as cerebral tumour or cerebrovascular accidents which are very common in elderly. The single abscess is generally localized in frontal lobe or parietal lobe rather than occipital or temporal region. Generalized seizures can prompt hospitalization and about 50% of patients may present focal neurologic signs (such as hemiparesis or focal seizure. These patients may go into diffuse neurologic dysfunction and became comatosed. They may also have neuropsychiatric manifestations. Fundus examination reveals papilledema.

Pus culture from brain abscess will show same organisms as seen in the adult patients. Often Viridans Streptococcus and Streptococcus milleri are the common pathogens. Fusobacterium and other anaerobes were also isolated from pus culture.

A lumbar puncture, which reveal slightly elevated WBC count may be dangerous particularly with focal neurolgic signs and raised Intracranial pressure. Hence, it should be avoided, 70% patients show show more than 500 WBC count suggesting a bacterial meningitis and spinal fluid culture is usually sterile.

Majority of cases with abscess demonstrate radiologic appearance of "dough nut ring". This may be seen in lesions with necrotic tumours and cerebral infarct. MRI and CT Scan are helpful in making the diagnosis.

Treatment

Medical therapy is recommended in cases where abscess is less than 2 cm in diamet er along with high density which is suggestive of cerebritis. A combination of a β–lactam agent with chloramphenicol or metronidazole or Tinidazole has been advised. Microbiologic culture obtained through Stereotaxic biopsy will guide the appropriate antibiotic therapy. Parenteral ceftriaxone or cefotaxime has also been found useful in the treatment of brain abscess. The duration of treatment has been variable and majority of authors recommend approximately 4-6 weeks of antibiotics which includes the combination of parenteral and oral agents.

Surgery is the only option if abscess is big and culture of the aspirated material help administration of appropriate antibiotics in curing the disease. 46% cases still have neurologic sequelae inspite of appropriate antibiotics given.

5.10 SLEEP DISORDERS

Sleep is the process that allows functioning throughout the day without feeling drowsy and impairment in concentration, memory and the performance. A person normally sleep approximately 1/3rd of the day (8 hr). Changes in structure and quality have long been associated as a feature of the aging process. Development in research methodology, especially polysomnography have demonstrated changes in sleep pattern with advancing age and there is increase incidence of insomnia in general population. Insomnia has been defined as inadequate or poor quality sleep characterised by one or more of the following:

1) Difficulty in falling asleep

2) Difficulty in maintaining sleep

3) Waking up too early in the morning and

4) Non- Refreshing sleep.

The understanding in sleep and its disorders is important in knowing the risks involved in deterioration in quality of life, the development of emotional problems such as depression, the worsening of the cognitive impairment and the risk for motor vehicle accident and for mortality which may be adversely affected by too much sleep (more than nine hours) as mediated by sleep apnea or too little sleep (less than 5 hours out of 24) and hence quality of sleep affect the quality of life and death.

Before discussing the sleep disorders, we would like to aprise you about the changes that occur in the elderly. Sleep becomes 'shallow' i.e. the auditory threshold for awakening diminishes which is manifested by reduction in slow wave sleep the deepest level of non rapid eye movement sleep (non-REM). There is increase in intermittent wakefulnes during the night as the age advances. Both long and short arousal, are observed mostly in second half of the night and results in fragmented nocternal sleep. There is evidence of frequent napping in day-time and older persons spend more time in bed often not asleep. The 24-hour sleep-wake patterns become polyphasic. Gradually as age increases, the prevalence of both sleep disorded breathing and periodic limb movements are seen in about 25% cases. This accounts for decreasing physiological ability to deep sleep and involved in day-time sleepiness. The sleep disorder is 1.5 times more common in persons aged > 65 years compared to younger counterparts and incidence in women is 1.3 times greater than in men.

Clinical Manifestation

Elderly presents with sleep onset problems (i.e. trouble getting to sleep), sleep maintainence problems (i.e. trouble staying asleep) and early morning awakening (EMA). These symptoms

may be present singly or in combination and may be transient or chronic (long-term). According to 1. CD-10 sleep disorders is divided into organic and non-organic. The non-organic include dysomnias (the disturbances of the amount, quality, or the timing of sleep) and the parasomnias (abnormal episodic events occuring during sleep).

Non-organic insomnia is a dysomnia characterised by persistent difficulty in getting to sleep or staying asleep. It should be atleast 3 times a week for atleast one month. It markedly interferes with social or occupational functioning.

The prevalence of insomnia increases steadily with age and reported by upto one in 3 people aged 65 years and above. It is more common in women than men (Table 5.4). Changes in both nature and the duration of sleep is affected by increasing age and complaints of early morning awakening (EMA) is also affected as age increases. The common causes of insomnia are listed in Table 5.5.

Table 5.4: Prevalence of Insomnia in Elderly

Location	Age	Prevalance overall (%)	Women	Men	EMA
Florida(US)	60-69 70+	20.9 25.9	22.6 29.4	18.3 20.0	4.0 3.3
Nottingham (UK)	65+	22.5	27.7	14.6	33.6
Paris (France)	55+	31.0	42.5	22.5	NR
Mannhein (Germany)	66-92	23.0	29.1	7.9	NR
East Boston (US)	65+	33.7	36.4	29.4	26.0
Iowa (US)	65+	23.2	25.4	19.5	15.0

Table 5.5: Causes of insomnia

- Transient/acute/Intermittent
  1) Stress
  2) Unfamiliar sleep environment
  3) Sleep/wake schedule problem (Jet leg, shift work).
  4) Non conducive sleep environment (excessive noise, extreme temperature).
  5) Drugs (Benzodiazepine withdrawl induced rebound insomnia).
- Chronic Insomnia
  1) Menopause
  2) Medical disorders (COPD, GERD, CHF, Muscoskeletal pains (Arthritis), diabetes, hyperthyroidism, prostatic problems, cancer etc.)
  3) Psychiatric disorders (depression, anxiety, menicets).
  4) Medication side-effects
  5) Behavioural conditioning (learned insomnia)
  6) Sleep related breathing disorder. (Obstructive sleep apnoea syndrome).
  7) Sleep related movement disorders (restless legs syndrome, periodical disorder).
  8) Delay: sleep phase disorder (circadian rhythm disorder).

History taking and diagnosis

Insomnia is often unrecognised and untreated because of non-reporting by the elderly to the doctor. The doctor should follow the diagnostic algorithm for insomnia (Table 5.6). The first step is to ascertain whether insomnia is related to patient's medical condition and or its treatment. It is often associated with pain, limitation of mobility, frequent urination and breathing difficulty. The second step is to see whether insomnia is associated with self medication or by a substance abuse disorder like consumption of alcohol, nicotine or caffeine. The third step is to differentiate it from psychiatric disorder like mood disorder (depression or anxiety) or related with neurodegenerative conditions like parkinsonism and delerium. The fourth step is to rule out the possibility of circadian rhythm sleep disorder. The fifth step is to find out whether elderly have primary sleep disorder such as restless legs or sleep-disordered breathing. Finally, if these more specific sleep disorders have been ruled out, then patients represent a primary or idiopathic form of insomnia. In this form of insomnia, the patient worries obsessively about

not sleeping and gets into a vicious cycle that is called "Conditional insomnia".

Table 5.6: Diagnostic Algorithm for Insomnia

1)	Its duration of insomnia is less than one month. If so search for acute and recent precipitant like adverse life event. If more than one month, consider the following additional diagnostic possibility.
2)	Can the complaint be adequately explained by concurrent medical disorders and/or their treatment i.e. nocturnal cardiac ischemia, chronic obstructive airway disease, gastrooesophageal reflux disease.
3)	Self medication and or/ substance abuse like alcohol abuse.
4)	Mental or neuropsychiatric disorder (depression and anxiety), breavement, dementia, delerium.
5)	Circadian rhythm sleep disorder.
6)	Breathing related sleep disorder.
7)	Primary or conditioned insomnia.

Lab Studies

Polysomnography is used to study the formal sleep, consist of overnight monitoring of sleep done in laboratory by EEG (Electroencephalogram) EOG (Electro-oculogram) and chin electromyogram (EMG) and of respiration, ECG and anterior tibialil EMG. Two consecutive nights may be required in the evaluation of patients not responding to routine intervention. It is not used routinely and usually preferred when clinician suspects sleep disordered breathing (sleep apnoea syndrome) or other abnormal events observed during sleep like marked behavioural disturbances, periodic limb movement disorder, seizure or cardiac arrythmia. The formal sleep studies is also undertaking in patients with excessive day-time sleepiness and narcolepsy. The differential diagnosis of excessive day-time sleepiness is summarised in Table 5.7.

Table 5.7: Differential Diagnosis of Excessive Sleepiness

1)	Inadequate sleep at night (secondary to medical disorders or inadequate sleep hygiene).
2)	Iatrogenic cases (long acting sedative hympnoties)
3)	Circulation rhythm sleep disorder.
4)	Breathing related sleep disorder (i.e. suggested by loud snoring and obesity).
5)	Narcolepsy-Cataplepsy.
6)	Sleep disorder related to mental disorder.
7)	Periodic limb movement disorder or restless leg syndrome.

Management of Insomnia

Primary idiopathic insomnia is best treated by behavioural intervention and it has been shown that sleep hygiene education is not effective when used alone but stimulus control and sleep restriction approaches have been found most effective and does require skill, time and energy. (Table 5.8). If non- pharmacological techniques are not sufficient then short-term therapy with an adjunctive benzodiazapine sedative hyniotics or with zolpidem is quite reasonable (Table 5.9).

There is now widespread agreement that hypnotic medication should not be the mainstay of the treatment for majority of causes of disturbed sleep. Benzodiazapine is preferred, in acute insomnia following a major life event such as bereavement or admissin to I..C.U. and lorazepam with short elimination half lives in the doses of 0.5-1.0 mg, oxazepam 15 mg or temazeapam 7.5-15 mg at bed time. They are less likely to cause day time sedation than drugs with longer elimination half-lives (flurazepam). Zolpidem 5 mg at bed-time is also good hypnotic sedative and offer additional advantage of no loss of efficacy over 35 days and absence of rebound insomnia or drug related impairment of memory.

The management of chronic insomnia is based on elimination of any psychiatric casuse. Low-dose trazodone or trimipramine have been found a useful intervention in the management of chronic insomnia associated with mood disorder and when given along with a program of good sleep hygiene, appropriate restriction of time in bed and stimulus control. Diphen hydramine is a mild drug for insomnia and has been widely prescribed but have side effects in elderly who are cholinergically brittle. Therefore, more safe and efficacious agents among the benzodiazepines or with Zolpidem are usually preferred.

Treatment options include non-pharmacological methods (Table 5.8) and pharmacological therapies (Table 5.9).

Table 5.8: Non-Pharmacololical Methods

1) Sleep hygiene instructions:
   - Maintain a regular sleep/wake schedule.
   - Participate in a relaxing activity until tired and go to bed when sleepy.
   - Use the bed and bedroom only for sleep.
   - Avoid day-time and mid-after-noon naps.
   - Avoid stimulants such as caffeine or nicotine and alcohol before bed-times.
2) Stimulus control;
   - Prepare a set of instructions designed to establish the bed-room as cues for steep instead of wakefulness.
3) Sleep Restriction:
   - Limit the length of time spent in bed, creating partial sleep deprivation, which results in deeper and more continous sleep.
   - Improves sleep efficiency (total sleep time/time spent in bed) and helps consolidate sleep.
4) Relaxing training
   - Biofeed back: teaches relaxation by conditioning specific muscular and EEG activity.
   - Autogenic training : teaches relaxation by associating pleasant visual images with relaxing sensations.
   - Progressive muscular relaxation: teaches relaxation by tensing and relaxing muscle groups.
   - Hypnosis.
5) Cognitive therapy
   - Psychotherapy aimed at changing the patient's assumptions and perceptions about the insomnia.

Table 5.9: Drug Therapy of Insomnia

Type of drug	Example	Mechanism/Comment
1) Non-barbiturate, non-benzodiazepines.	Chloralhydrate Glutethimide	• Prolonged use can lead to dependency.
2) Barbiturates	Amylobarbitone, Butobarbitone	• Depress action of CNS • Lethal in overdose.
3) Benzodiazepines	Nitrazepam, Flurazepam, oxazepam, lorazepam, temazepam.	• Binds to GABA receptors. • Act selectively in areas of brain involved and psychomotor functioning.
4) Non-benzodiazepines	Zolpidem, Zopicline,	• Bind selectively to GABAreceptors in CNS with calming effects.
5) Antidepressants	Amitryptyline, Tradozone, Nefazodone, Paroxetine	• Are hypnotics • Somehave serotinin like mode of action. • Useful for patients with depression.
6) Antihistamine	Diphenhydramine, Doxylamine.	• Antagonise central histamine-I receptors.
7) Others	Melatonin, Trytophan	• It regulates sleep onset via its receptors in CNS. • Regulates circadian clock via receptors in suprachiasmatic nucleus.

Check Your Progress 3

1) Define Insomnia.

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2) Name drug which causes insomnia.

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3) Enumerate lab investigations for insomnia.

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4) Name non-benzodiszepines used in the treatment of insomnia.

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5.11 COMA

As you know, coma is the severest form of medical alertness and responsiveness, a deep sleep like state from which the patient cannot be aroused by painful stimuli. It is different from ***Stupor,*** which is a lesser degree of unarousability state, where the patient can be briefly aroused by painful stimuli. You should also be familiar with the situation of drowiness, which simulates light sleep and is characterized by easy arousal and persistent alertness for short periods.

The principle factors responsible for coma are :

1) Damage of substantial protion of RAS

2) Destruction of major portions of cerebal hemispheres

3) Suppression of the thalmocerebral function

The main causes of coma are enlisted in Table 5.10.

Table 5.10: Causes of Coma

A)	**Metabolic**	
	1)	Drug overdose (Alcohol, sedative drugs, opiates etc.)
	2)	Hypoglycemia or Hyperglycemia
	3)	Renal Failure
	4)	Hepatic Failure
	5)	Hypothyroidism (Myxedema coma)
	6)	Cardiorespiratory Failure
	7)	Hypoxic Encephalopathy
	8)	Shock from any cause
	9)	Electrolye Imbalance (Hyponatremia, Hypernatremia, Hypercalcemia)
	10)	Profound Nutritional deficiency
B)	**Structural**	
	i)	**Diffuse**
		a) Meningitis
		b) Encephalitis
		c) Cerebral Malaria
		d) Sub-archanoid Haemorrhage
		e) Epilepsy
		f) Head Injury
		g) Hypertensive Encephalopathy
	ii)	**Focal**
	a)	***Supra-tentorial***
		1) Cerebral Haemorrhage
		2) Cerebral Infarction
		3) Subdural haematoma

4) Extra dural haematoma
5) Tumour
6) Cerebral abscess
7) Pituitary Apoplexy

b) ***Sub-tentorial***

1) Cerebellar haemorrhage
2) Ponitive haemorrhage
3) Brainstem infarction
4) Tumour
5) Cerebellar abscess
6) Transtentorial herniation

Establishing Coma

The first thing you should make sure is that the unresponsiveness is due to coma as it can be confused with the following :

1) Pseudo-coma which may occur in psychiatric states i.e. hysteria. It can be differentiated from coma as it is characterized by the presence of all motor reflexes. The patient avoids response to lifting and dropping of the arm and has active resistance to eye-lid elevation.

2) Locked-in-state, where the patient has no means of producing speech or voluntary limb, face and pharyngeal movements though vertical eye movements and lid elevation remain unaffected, allowing the patient to signal. Infarction or haemorrhage of the ventral pons is the usual cause.

3) Akinetic mutism is another clinical state, which may be interpreted as stupor or coma. Here a patient who is partially or fully awake, tries to make impressions and think, but remains immobile and mute, particularly when unstimulated. This state results from damage in the region of the medical thalamic nuclei, the frontal lobe or from hydrocephalous.

History and Physical Examination

The history is of great importance in arriving at a provisional diagnosis in the case of coma. A sudden onset of coma suggests a cerebro-vascular disorders, such as sub-arachnoid haemorrhage or stroke, trauma or seizures. A gradual deterioration, usually points towards a metabolic cause, tumour or infection. One should also inquire about a previous history of diabetes, hypertension, renal disease, hepatic dysfunction and cardiac disease.. History of drugs or toxic exposure is an important component to be asked for.

The examinations of vitals include temperature, pulse, respiratory rate and pattern and blood pressure. All these should be measured quickly. Fever suggests a sytemic infection, bacterial meningitis or encephalitis and is only rarely attributable to brain lesions. High body temperature (42-44 ^{o}C) associated with dry skin, should arouse the suspicion of heat stroke or anticholinergic drug intoxication. Tachypnea may indicate acidosis or pneumonia. Marked hypertension is a sign of hypertensive encephalopathy or rapid rise in intracranial pressure and it may also be acute after trauma or head injury. Hypotension is a characteristic feature of coma, associated with alcohol or barbiturate intoxication and internal haemorrhage. The fundoscopy examination is valuable to check raised intra-cranial pressure. Generalized cutaneous petechiae indicate thrombotic or bleeding diathesis.

Neurological Assessment

You should carry out the following examination.

i) Level of consciousness is assessed by Glasgow Coma Scale.

1) Eye Opening

Spontaneous - 4
To speech - 3
To pain - 2
None - 1

2) Best Verbal Response

Oriented - 5

Confused	- 4
Inappropriate	- 3
Incomprehensible	- 2
None	- 1

3) Best Motor Response

Obeying	- 6
Localisting	- 5
Withdrawal	- 4
Flexing	- 3
Extending	- 2
None	- 1

(Interpretation : The Scale is based on an aggregate (sum total) of three types of responses. This range is from 15 (normal) to 3.

ii) Respiration :

Cheyne-stokes Respiration is characterised by periods of hyperventilation alternating with periods of aponea. This may be seen in bilateral deep hemispheric and basal ganglionic dysfunction. The upper brain stem may also be involved.

iii) Pupils :

Pupillary reactions are examined with a bright, diffused light. Normally reactive and round pupils essentially exclude mid-brain damaga. An unreactive or large pupil or one that is poorly reactive, signifies a compression or stretching of the 3rd nerve from the effect of mass. Unilaterally dilated and a fixed pupil, is usually sue to 3rd nerve palsy as a result of transtorial herniation.

iv) Occular movements :

Eye movements, are the second signs of importance in determining whether the brain stem has been affected. Spontaneous eye movements in coma, often take the form of conjugate horizontal roving and exclude the mid-brain and pons lesions. One should also see the occulocephatic reflexs and occulo-vestibular reflex, to rule out brain stem lesions.

v) Motor response :

Lack of restless movements on one side, or an outturned leg at rest indicates hemiplegia. Intermittent twitching movements of a face, foot or finger indicates a sign of convulsion and/ or seizures. Multifocal myoclonus almost, always indicates a metabolic disorder. Decorticate regidity and decerebrate rigidity, suggest severse bilateral damage to the mid-brain.

Laboratory Studies and Imaging

The following studies are useful in the diagnosis of confusional states and coma. These are : examination of blood and urine, CT or MRI, EEG and CSF examination. Arterial gas analysis is helpful in acid-base disorder and lung disease. The metabolic disorders commonly seen in clinical practices, require estimations of electrolytes, glucose, calcium, osmolarity and renal and hepatic function. Toxicological analysis is necessary in patients with coma, where diagnosis is not clear. CT and MRI have been found to be useful to rule out various causes of coma, that are radiologically detectable. The EEG is useful in metabolic or drug induced confusional states, but is rarely diagnostic, with the important exceptions of coma due to herpes virus encephalitis and Creuzfeldt-Jako disease. However, a majority of medical causes of coma, can be established without a neuroimaging study.

Management

Once coma has been confirmed, a complete medical examination is usually deferred, until the patient has been stabilized. Immediate therapeutic measures have to be initiated to prevent further neurological damage. Hypotension, hypoglycemia, hypercalcemia, hypoxia, hypercapnia and hyperthermia should be corrected rapidly.

A) ***Initial Management***

1) Establishment of an efficient airway

- If the patient is breathing normally, an oropharynegeal airway of adequate size is inserted and taped to prevent the tongue from obstructing the airway.
- If breathing is disturbed, then cuffed endotracheal tube is inserted and assisted ventilation is started.
- If intubation is required for more than 48-72 hours, a tracheostomy is preferable.
- Cervical injury should be ruled out in the case of trauma and if suspected, the neck should be immobilized with a hard collar.

2) A peripheral venous access is secured to administer fluid and drugs.

3) Blood is withdrawn for biochemical investigations and toxic screening.

4) Maintenance of blood pressure is ensured and hypotension is corrected with normal saline to ensure adequate cerebral, renal and cardiac perfusion.

5) Specific measures to be taken are as follows :

a) IV thiamine 100mg to prevent Wernicke's encephalopathy
b) 50 ml of 50% dextrose if hypoglycemia is suspected.
c) IV naloxone (2mg IV) if opiod intoxication suspected
d) IV atropine for organosphosphorous intoxication
e) IV physostigmine for anticholinergic poisoning.
f) IV chloroquine or quinine if cerebral malaria is suspected.
g) IV flumazenil if Benzodiazepines toxicity is suspected.

6) Management of seizures:

- IV Diazepam
- IV phenytoin
- IV Phenobarbitone
- IV Thiopentone

B) ***Management of Specific Purpose***

Trauma, sepsis, CNS infections, cerebrovasular accidents, tumours, metabolic derangements are treated accordingly, as you have learnt earlier in different units.

C) ***General Care of the Patient***

1) Prevention of aspiration of secretions by regular nasopharyngeal and oral cavity suction.

2) Prevention of bed sores : This has been discussed in detail earlier. However, the essential steps include :

- Patient has to be turned every two hours.
- The sheets should be dry and tightly drawn.
- Bony prominences should be padded.
- A water/air mattress should be used.
- The back should be regularly clearned with spirit.

3) Nutrition is provided by IV solutions initally and later by naso-gastric feeding after the condition becomes stable.

4) Bladder and bowel care:

- Condom catheter may be used in the males
- If an indwelling catheter becomes necessary, a three way catheter should be used with continuous irrigation with mild acetic acid solution, which acidifies the urine and prevents stone formation.
- Catheters should be clamped intermittently for bladder training
- Urine must be set regularly for routine and culture examination

5) Eyes : Corneal injury is prevented by taping the eyelids and using lubricant eye-drops.

6) Physiotherapy : Passive physiotherapy to prevent stiffness of joints.

D) **Management of Raised ICP**

1) IV Mannitol

2) Dexamethasone

3) Glycerol

Prognosis

Outcome of the coma, depends on the underlying cause, long-term care and medical resources. Metabolic and drug induced comas have good prognosis as compared to traumatic coma. Glasgow coma scale, is devised to predict the values in each case of brain trauma. For anoxic and metabolic coma, clinical signs such as pupillary and motor responses after 1st day, 3 rd day and 77th day have shown to have prognostic value. The absence of the cortical waves of the somatosensory evoked potential, suggests poor outcome of comatosed patient from any underlying aetiology.

Check Your Progress 4

1) Define coma.

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2) Name four important types of metabolic coma.

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3) What is pseudo coma?

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4) What is the cause of decorticate rigidity and decerebrate rigidity?

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5) Name the specific diseases which are diagnosed by EEG.

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5.12 LET US SUM UP

Bacterial infections in elderly have a great impact on mortality and morbidity including quality of life. It has become a more common problem in elderly over the past two decades which is preventable and curable and needs early diagnosis and prompt initiation of therapy. Clinical features are more subtle as compared to young adult. At times, triad of feature, fever, headache and neck stiffness are not present and only lumbar puncture gave the final diagnosis. The combination of ampicillin and 3rd generation cephalosporins has been recommended to cover all pathogens likey to cause meningitis. Streptococcus pneumoniae is the most common organism to cause meningitis in the elderly, outcome is excellent if appropriate antibiotic started immediately. Pneumococcal vaccines is now available and should be recommended in all patients over the age of 65 years, although no definite specific data is reported to support this.

Tubercular meningitis is a serious disorder in elderly and is often insidous and accompanied by confusion, disorientation, varying grades of unconsciousnes, focal neurological deficit, convulsions and nerve palsy. Diagnosis is made by lumbar puncture. Treatment usually cure the disease in 80-90%. About 20-30% are left with some some residual physical or mental defects. Hydrocephalus if present is treated surgically by ventricular shunt.

Inflammation of meninges by viruses and cryptococcus has also been seen in older people. It consists of non specific symptoms with normal sensorium and no focal neurological signs.

Diagnosis in cases of viral infection is based on normal glucose and protein levels with presence of predominant lymphocytes in CSF. Specific antibody titre to viruses may be increased. Fungal meningitis is difficult to differentiate from Tubercular meningitis. However, India ink is positive in 50% or more cases and cryptococcal antigen is seen in 90% cases. There is no specific treatment in cases of virus infection however, the fungal infection is treated by Amphotericin B, Flucytosive and new liposomal Amphotericin B. Herpes Simplex encephalitis carries high mortality in older people and accompanied by altered sensorium, localizing signs and nasal field defects. EEG changes and MRI including CT Scan help in arriving at diagnosis. Therapy with Acyclovir can improve the symptomatology in some of the cases.

Brain abscess presents with a mass lesion with focal neurologic deficit. Mortality is very high (30-50%) with advent of CT Scan & MRI, the early diagnosis has made significant contribution in reducing the mortality to 4-20%.

Advancing age as well as senescent changes directly influence the structure and quality of sleep. Problems related to disturbed sleep are multifactorial and require broad and flexible clinical approach. Therapeutic approaches have been well systamitized and special emphasis given to sleep assessments, health education and sleep hygiene and appropriate pharmacologic and psychologic strategies in treating complex sleep problems in the elderly.

Coma is a state unconsciousness from which a patient cannot be aroused by painful stimuli and all reflexes are lost. It can occur due to damage of substantial portion of RAS, cerebral hemispheres and suppression of thalamocerebral function. Diagnosis is established by meticulus history and neurological examination. Level of consciousness is assessed by Glasgow Coma Scale. Biochemical examination of blood and urine, CT or MRI, EEG and CSF examination and ABG analysis help in arriving at diagnosis of major causes of coma. The treatment is based on the establishment of an efficient airway, maintenance of vital functions and specific measures to treat underlying causes. Symptomatic treatment includes management of seizures, intracranial pressures, nutritional care, bladder and bowel care. The outcome of coma depends on the long term care as well as medical resources. Metabolic and drug induced coma have better prognosis as compared to traumatic coma. However the absence of the cortical waves of the somatosensory evoked potential indicate a poor outcome.

5.13 KEY WORD

Cheyne-Stokes Respiration : Periods of Hyper ventilation alternating with periods of Apnoea.

5.14 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Inflammation of meninges of the brain caused by pathogenic organism is called Meningitis.

2) Two common causes of meningitis are

   a) Streptococcal pneumoniae.

   b) Gram negative bacilli.

3) CSF findings are:

   a) Turbidity

   b) Polymorphs 500-10,000/ cumm.

   c) Glucose< 40 mg/dl.

   d) Proteins 0.5-2.g/dl.

   e) Gram stain +ve.

4) The antibiotics effective against streptococcal pneumonae meningites depends upon whether the organisms are pencillin sensitive or resistance.

   For pencillin sensitive–Pencillin G.

   For Pencillin resistant–Vancomycin + Ceftriaxone/Cefotaxime.

Check Your Progress 2

1) Tubercular meningites presents with non-specific symptoms of fatigue, anorexia, nausea, altered mental status, evidence of papilloelema, sixth cranial nerve palses and focal neurological deficits.

2) Most common nerve involvement is 6th nerve palsy.

3) CSF finding reveal 1. Elevated protein level above 50mg/dl. 2. Low glucose level below 40mg/dl. 3. Predominant mononuclear cells. 4. Raised Adenosine deaminase activity more than 9 units/L.5. Postive PCR in CSF fluid.

4) Clinical stages are:

   Stage I - Rational, no focal neurologic signs or hydrocephalus.

   Stage II - Confusion, depression, or focal neurologic deficits.

   Stage III - Stuporos or dense paraplegia or hemiplegia.

Check Your Progress 3

1) Insomnia has been defined as inadequate or poor quality sleep characterised by one or more of the situations like 1. difficulty in falling asleep. 2. Difficulty in maintaining sleep. 3. Waking up too early in the morning and 4. non refreshing sleep.

2) Benzodiazepine

3) Lab investigations include Polysomnography, EEG. EOG and chin EMG, ECG and anterior tibial EMG.

4) Non-benzodiazepines used in treatment of insomia include Zolpidem, Zopicline and Zolepon.

Check Your Progress 4

1) Coma is a state of reduced alertness and responsiveness from which a patient cannot be aroused by painful stimuli.

2) The four important causes are :

   a) Hypo or Hyper glycaemic coma

   b) Drug intoxication

   c) Hepatic Coma

   d) Uraemic Coma (Renal failure)

3) Pseudocoma is characterized by the presence of all motor reflexes. The patient avoids response to lifting and dropping of the arm and shows active resistance to eyelid elevation.

4) The cause of decorticate rigidity is a severe bilateral damage to the mid-brain.

5) There are two diseases namely Creutzfeldt-Jakob disease and Herpes virus encephalitis that are diagnosed by EEG.