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the SQUARE Healthcare bulletin

- Parkinson's disease
- Palliative care
- Migraine
- Dengue complications

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the SQUARE
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Editorial

Dear Doctor,

Welcome to this edition of *"the SQUARE"* !

We hope all of you are in good health!

Firstly, we express our heartiest appreciation for your encouraging response regarding *"the SQUARE"* !

In this issue we have published a special feature on "Parkinson's Disease", a neurodegenerative brain disorder that progresses slowly in most people. It is itself is not fatal. However, complications from the disease are serious. As "Parkinson's Disease" is vast to describe, we have designed to publish this in two successive issues.

We also bring you all the details on "Palliative care", a specialized medical care for people with serious illness that focuses on the best quality of life for both the patient and his or her family.

You will also find an article on "Migraine" which is an extraordinarily prevalent neurological disease, affecting 38 million men, women and children in the U.S. and 1 billion worldwide. Migraine is the 3rd most prevalent and 6th most disabling disease in the world.

Moreover, we have focused on "Dengue Complications". When treated, dengue hemorrhagic fever has a mortality rate of 2-5%, but when left untreated, the mortality rate is as high as 50%.

In addition, our regular feature includes a "Product Profile".

Every effort has been made to make this issue interesting and we are quite sure that you will enjoy this issue as well.

On behalf of the management of *SQUARE*, we wish you all a very blissful, healthy and successful life!

Thank You!

Omar Akramur Rab

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Key title: The square (Dhaka)
Abbreviated key title: Square (Dhaka)

Parkinson's disease is predominantly a disorder of the basal ganglia, which are a group of nuclei situated at the base of the forebrain. The striatum, composed of the caudate and putamen, is the largest nuclear complex of the basal ganglia. The striatum receives excitatory input from several areas of the cerebral cortex, as well as inhibitory and excitatory input from the dopaminergic cells of the substantia nigra pars compacta (SNc).

Pathophysiology

No specific, standard criteria exist for the neuropathologic diagnosis of Parkinson's disease, as the specificity and sensitivity of its characteristic findings have not been clearly established. However, the following are the 2 major neuropathologic findings in Parkinson's disease:

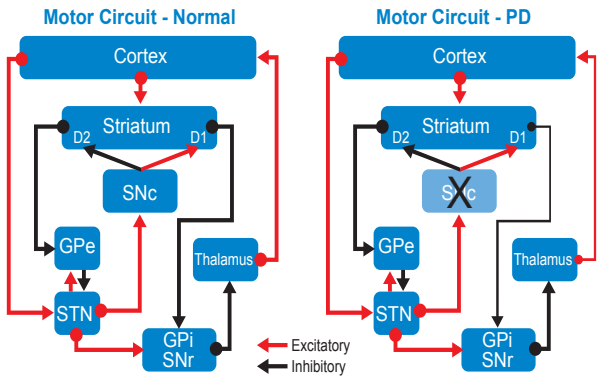
- Loss of pigmented dopaminergic neurons of the substantia nigra pars compacta.
- The presence of Lewy bodies and Lewy neurites.

The loss of dopamine neurons occurs most prominently in the ventral lateral substantia nigra. Approximately 60-80% of dopaminergic neurons are lost before the motor signs of Parkinson's disease emerge.

Some individuals who were thought to be normal neurologically at the time of their deaths are found to have Lewy bodies on autopsy examination. These incidental Lewy bodies have been hypothesized to represent the presymptomatic phase of Parkinson's disease. The prevalence of incidental Lewy bodies increases with age. Note that Lewy bodies are not specific to Parkinson's disease, as they are found in some cases of atypical parkinsonism, Hallervorden-Spatz disease and other disorders. Nonetheless, they are a characteristic pathology finding of Parkinson's disease.

Motor circuit in Parkinson's disease

The basal ganglia motor circuit modulates the cortical output necessary for normal Movement. Signals from the cerebral cortex are processed through the basal ganglia-thalamocortical motor circuit and return to the same area via a feedback pathway. Output from the motor circuit is directed through the internal segment of the globus pallidus (GPi) and the substantia nigra pars reticulata (SNr). This inhibitory output is directed to the thalamocortical pathway and suppresses movement.



Thick lines indicate increased output and thin arrows indicate decreased output patterns present in Parkinson's disease. Black lines indicate inhibitory actions and lines in red indicate excitatory actions.

Two pathways exist within the basal ganglia circuit, the direct and indirect pathways, as follows:

- In the direct pathway, outflow from the striatum directly inhibits the GPi and SNr; striatal neurons containing D1 receptors constitute the direct path-way and project to the GPi/SNr.
- The indirect pathway contains inhibitory connections between the striatum and the external segment of the globus pallidus (GPe) and between the GPe and the subthalamic nucleus (STN); striatal neurons with D2 receptors are part of the indirect pathway and project to the GPe.

The STN exerts an excitatory influence on the GPi and SNr. The GPi/SNr sends inhibitory output to the ventral lateral nucleus (VL) of the thalamus. Dopamine is released from nigrostriatal (substantia nigra pars compacta [SNpc]) neurons to activate the direct pathway and inhibit the indirect pathway. In Parkinson's disease, decreased striatal dopamine causes increased inhibitory output from the GPi/SNr via both the direct and indirect pathways.

The increased inhibition of the thalamocortical pathway suppresses movement. Via the direct pathway, decreased striatal dopamine stimulation causes decreased inhibition of the GPi/SNr. Via the indirect pathway, decreased dopamine inhibition causes increased inhibition of the GPe, resulting in disinhibition of the STN. Increased STN output increases GPi/SNr inhibitory output to the thalamus.

Etiology

Although the etiology of Parkinson's disease is still unclear, most cases are hypothesized to be due to a combination of genetic and environmental factors. Currently known genetic causes of Parkinson's disease account for approximately 10% of cases.

Environmental causes

Environmental risk factors commonly associated with the development of Parkinson's disease include use of pesticides, living in a rural environment, consumption of well water, exposure to herbicides, and proximity to industrial plants or quarries.

Higher caffeine intake was associated with lower risk of Parkinson's disease in both men and women. A similar association was found for smoking and Parkinson's disease risk.

MPTP interference with mitochondrial function

Several individuals were identified who developed parkinsonism after self-injection of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). These patients developed bradykinesia, rigidity and tremor, which progressed over several weeks and improved with dopamine replacement therapy.

Oxidation hypothesis

The oxidation hypothesis suggests that free radical damage, resulting from hydrogen peroxide produced by dopamine's oxidative metabolism, plays a role in the development or progression of Parkinson's disease. This hypothesis has raised concern that increased dopamine turnover due to levodopa administration could increase oxidative damage and accelerate loss of dopamine neurons.

Genetic factors

Genetic factors in Parkinson's disease appear to be very important when the disease begins at or before age 50 years.

A total of 18 loci in various genes have now been proposed for Parkinson's disease. Mutations within 6 of these loci (SNCA, LRRK2, PRKN, DJ1, PINK1, and ATP 13A2) are well-validated causes of familial parkinsonism. Inheritance is autosomal dominant for SNCA and LRRK2 (although LRRK2 mutations exhibit variable penetrance). Inheritance is autosomal recessive for PRKN, DJ1, PINK1 and ATP13A2. In addition, polymorphisms within SNCA and LRRK2, as well as variations in MAPT and GBA, are risk factors for Parkinson's disease.

Although the mechanisms by which genetic mutations cause Parkinson's disease is not known, evidence to date converges on mechanisms related to abnormal protein aggregation, defective ubiquitin-mediated protein degradation, mitochondrial dysfunction and oxidative damage.

Alpha-synuclein conformational changes and aggregation

Abnormally aggregated alpha-synuclein is the major component of Lewy bodies and Lewy neurites, which are characteristic pathologic findings in Parkinson's disease. Missense mutations and multiplications in the SNCA gene that encodes alpha-synuclein, although rare, cause autosomal dominant Parkinson's disease. However, genome-wide association studies have also demonstrated a link between SNCA and sporadic Parkinson's disease.

Dysfunction of alpha-synuclein appears to play a central role in the pathogenesis of Parkinson's disease. Normally, alpha-synuclein is found mainly in neuronal presynaptic terminals and may play a role in assembly and function of SNARE (soluble N-ethylmaleimide-sensitive factor activating protein receptor) proteins that are involved in neurotrans-mitter release.

Under certain conditions, alpha-synuclein aggregates into oligomers that are gradually converted to the beta-sheet-rich fibrillary structures that form Lewy bodies and neurites in Parkinson's disease. Most evidence currently suggests that it is the intermediate soluble oligomers that are toxic to neurons.

Elevated levels of alpha-synuclein promote abnormal aggregation. SNCA multiplications lead to increased synthesis of alpha-synuclein and can cause Parkinson's disease.

Alpha-synuclein appears to be degraded by the ubiquitin proteasome system and the autophagy-lysosome pathway. Several genetic mutations associated with Parkinson's disease may lead to decreased alpha-synuclein degradation.

Epidemiology

Parkinson's disease is recognized as one of the most common neurologic disorders, affecting approximately 1% of individuals older than 60 years. The incidence and prevalence increase with age, and the average age of onset is approximately 60 years. Onset in persons younger than 40 years is relatively uncommon. Parkinson's disease is about 1.5 times more common in men than in women.

Prognosis

Before the introduction of levodopa, Parkinson's disease caused severe disability or death in 25% of patients within 5 years of onset, 65% within 10 years and 89% within 15 years. With the introduction of levodopa, the mortality rate dropped approximately 50%, and longevity was extended by many years.

The American Academy of Neurology notes that the following clinical features may help predict the rate of progression of Parkinson's disease:

- Older age at onset and initial rigidity/hypokinesia can be used to predict (1) a more rapid rate of motor progression in those with newly diagnosed Parkinson's disease and (2) earlier development of cognitive decline and dementia-however, initially presenting with tremor may predict a more benign disease course and longer therapeutic benefit from levodopa
- A faster rate of motor progression may also be predicted if the patient is male, has associated comorbidities and has postural instability/gait difficulty (PIGD)
- Older age at onset, dementia and decreased responsiveness to dopaminergic therapy may predict earlier nursing home placement and decreased survival

History

Onset of motor signs in Parkinson's disease is typically asymmetric, with the most common initial finding being an asymmetric resting tremor in an upper extremity. Over time, patients notice symptoms related to progressive bradykinesia, rigidity and gait difficulty. The first affected arm may not swing fully when walking and the foot on the same side may scrape the floor. Over time, axial posture becomes progressively flexed and strides become shorter.

Some nonmotor symptoms commonly precede motor signs in Parkinson's disease. Initial clinical symptoms in Parkinson's disease include the following:

- Tremor
- A subtle decrease in dexterity; for example, a lack of coordination with activities such as playing golf or dressing (about 20% of patients first experience clumsiness in one hand)
- Decreased arm swing on the first-involved side
- Soft voice
- Decreased facial expression
- Sleep disturbances
- RBD (Rapid eye movement (REM) Behavior Disorder), in which there is a loss of normal atonia during REM sleep: patients "act out their dreams" and may kick, hit, talk or cry out in their sleep
- Decreased sense of smell
- Symptoms of autonomic dysfunction, including constipation, sweating abnormalities, sexual dysfunction and seborrheic dermatitis
- A general feeling of weakness, malaise or lassitude
- Depression or anhedonia
- Slowness in thinking

Common early motor signs of Parkinson's disease include tremor, bradykinesia, rigidity and dystonia.

Tremor

Although tremor is the most common initial symptom in Parkinson's disease, occurring in approximately 70% of patients, it does not have to be present to make the diagnosis. Tremor is most often described by patients as shakiness or nervousness and usually begins in one upper extremity and initially may be intermittent.

Upper extremity tremor generally begins in the fingers or thumb, but it can also start in the forearm or wrist. After several months or years, the tremor may spread to the ipsilateral lower extremity or the contralateral upper extremity before becoming more generalized; however, asymmetry is usually maintained. Tremor can vary considerably, emerging only with stress, anxiety or fatigue. Classically, the tremor of Parkinson's disease is a resting tremor (occurring with the limb in a resting position) and disappears with action or use of the limb.

Bradykinesia

Bradykinesia refers to slowness of movement. Symptoms of bradykinesia are varied and can be described by patients in different ways. Facial bradykinesia is characterized by decreased blink rate and facial expression. Speech may become softer, less distinct or more monotonal. Truncal bradykinesia results in slowness or difficulty in rising from a chair, turning in bed or walking.

In the upper extremities, bradykinesia can cause small, effortful handwriting (ie, micrographia) and difficulty using the hand for fine dexterous activities such as using a key or kitchen utensils.

In the lower extremities, unilateral bradykinesia commonly causes scuffing of that foot on the ground, as it is not picked up during leg swing. This may also be described as dragging of one leg.

Rigidity

Some patients may describe stiffness in the limbs, but this may reflect bradykinesia more than rigidity. Occasionally, individuals may describe a feeling of ratchety stiffness when moving a limb, which may be a manifestation of cogwheel rigidity.

Dystonia

Dystonia is a common initial symptom in young-onset Parkinson's disease, which is defined as symptom onset before age 40 years.

Dystonia in Parkinson's disease commonly consists of a foot involuntary turning in (inversion) or down (plantar flexion), often associated with cramping or aching in the leg. Dorsiflexion of the big toe may also occur. Another common dystonia in Parkinson's disease is adduction of the arm and elbow, causing the hand to rest in front of the abdomen or chest. Dystonic postures can wax and wane, occurring with fatigue or exertion.

Physical Examination

There are 4 cardinal signs of Parkinson's disease, with 2 of the first 3 listed below required to make the clinical diagnosis. The fourth cardinal sign, postural instability, emerges late in the disease, usually after 8 years or more.

- ❏ Resting tremor
- ❏ Rigidity
- ❏ Bradykinesia
- ❏ Postural instability

Resting tremor

Resting tremor is assessed by having patients relax their arms in their lap while in a seated position. Having patients count aloud backward from 10 may help bring out the tremor. The arms should also be observed in an outstretched position to assess postural tremor and kinetic tremor can be observed during the finger-to-nose test.

Rigidity

The resistance can be either smooth (lead pipe) or oscillating (cogwheeling). Rigidity is usually tested by flexing and extending the patient's relaxed wrist and can be made more obvious by having the patient perform voluntary movements, such as tapping, with the contralateral limb.

Bradykinesia

Bradykinesia refers to slowness of movement but expressed as micrographia (small handwriting), hypomimia (decreased facial expression), decreased blink rate and hypophonia (soft speech). Thus, the patient's blink rate and facial expression should be observed.

In addition, speed and amplitude of movements are assessed by having the patient open his or her hand (each limb is assessed individually) and tap his or her thumb and index finger repetitively, trying to perform the movement as big and as fast as possible. Similarly, the patient should be asked to tap the toes of each foot as big and as fast as possible.

Finally, the patient should be asked to arise from a seated position with the arms crossed to assess the ability to arise from a chair. The patient is then observed while walking to assess stride length and speed, as well as arm swing.

Postural instability

Postural stability is typically assessed by having patients stand with their eyes open and then pulling their shoulders back toward the examiner. Patients are told to be ready for the displacement and to regain their balance as quickly as possible. Taking 1 or 2 steps backward to regain balance is considered normal. The examiner should be ready to catch patients if they are unable to regain balance.

Laryngeal dysfunction and dysphagia

As the patient is speaking, the vocal loudness, intonation and quality, including fluidity of speech and articulation, should be assessed. Sustaining vowel phonation (eg, "ah") for maximum duration, counting to 50 and reading a passage that tests articulation (eg, the rainbow passage) provide reasonable speech samples. Closely listening for reduced or diminishing loudness and intonation and increasing breathiness and hoarseness helps differentiate Parkinson's disease from hyperkinetic disorders such as spasmodic dysphonia.

A soft, monotone voice, vocal tremor, poor articulation, variable speech rate, trouble with the initiation of speech and stuttering-like qualities are all characteristics of Parkinson's disease. Perhaps the most telling vocal symptom is the marked contrast between habitual vocal volume (soft and diminishing) and the patient's response to a request to increase loudness. A request to "say that again, twice as loud" often results in increased loudness, improved voice quality and a dramatic improvement in speech intelligibility.

Dysphagia is common, especially in advanced Parkinson's disease. Manifestations may range from drooling to aspiration.

An otolaryngologist can perform a more detailed assessment of laryngeal dysfunction in patients with Parkinson's disease, using neurolaryngeal examination and stroboscopy. Because distortion can occur when the tongue is held forward during rigid stroboscopy, the neurolaryngeal examination is best performed by viewing the larynx with a flexible laryngoscope.

The larynx is evaluated for vocal fold mobility, paresis or paralysis, coordination of movement, agility, fatigability, flexibility and use of accessory muscles during phonation while the patient says various phrases and syllables. Hyper-functional and hypofunctional disorders can often be differentiated by isolating the abductor and adductor muscle groups. The larynx is also visualized at rest.

Rigid stroboscopy plays a key role in the assessment of the vibratory characteristics of the vocal folds, including the presence of masses, lesions or scar and glottic configuration abnormalities, including an elliptical closure pattern, phase asymmetry and abnormal phase closure.

Stroboscopy and neurolaryngeal examination are complementary in the evaluation of the patient with Parkinson's disease. Common stroboscopy findings in Parkinson's disease include true vocal fold atrophy or other evidence of glottal incompetence, including a chasing wave or a shorter closed phase.

Pooling of secretions, decreased sensation and aspiration are also characterizations of the Parkinson's disease larynx. A paralyzed vocal fold suggests Parkinson-plus syndrome (PPS) as the etiology for the parkinsonism if other aspects of the diagnosis are present.

One study found that vocal tremor is present in 55% of patients with Parkinson's disease. Interestingly, only 35% of patients with Parkinson's disease exhibited a resting vocal cord tremor, whereas the remainder exhibited kinetic tremor. The tremor is primarily a vertical laryngeal movement. PPS was found to carry a higher incidence of vocal tremor (64%), with most tremors located in the arytenoids. The authors found no vertical laryngeal tremor in patients with PPS.

Autonomic dysfunction

Orthostatic hypotension often becomes a concern in late disease and impaired intestinal motility can lead to constipation and sometimes, vomiting or impaired absorption. Urinary symptoms, retention and bladder infection can occur and erectile dysfunction is not uncommon. In addition, many patients note episodes of sweating.

Cardiopulmonary impairment

The flexed posture of patients with Parkinson's disease can lead to kyphosis, cause a reduction in pulmonary capacity and produce a restrictive lung disease pattern.

Depression

Given the high prevalence of mood disorders in Parkinson's disease, these patients should be screened regularly for depression. Guilt and self-reproach are less prominent in depression in patients with Parkinson's disease, whereas anxiety and pessimism are more prominent.

Dementia

The prevalence of dementia in Parkinson's disease ranges from 20-40%, with the disease conferring a 2- to 6-fold increased risk compared with control populations. Many patients with Parkinson's disease have some executive function impairment, even early in the disease. Substantial cognitive impairment and dementia typically occur 8 years or more after the onset of motor features.

Dementia generally occurs late in Parkinson's disease; substantial cognitive dysfunction within 1 year of onset of motor features suggests a diagnosis of Lewy body disease. In the affected age group, comorbidity with other neurodegenerative disorders, particularly Alzheimer disease and cerebrovascular disease, is common. The relatively high prevalence of depression in patients with Parkinson's disease is another confounder in the diagnosis of Parkinson's disease dementia.

Executive function, short-term memory and visuospatial ability may be impaired in patients with Parkinson's disease dementia, but aphasia is not present. In a long-term Australian study investigators reported that dementia in parkinsonism appears to occur at about age 70 years regardless of the time of onset. However, although early and late dementia had similar effects in cognitive domains, individuals with early onset of parkinsonism had a preserved linguistic ability before the onset of dementia.

Atypical Parkinsonisms

Atypical parkinsonisms or Parkinson-plus syndromes, are primary neurodegenerative disorders that have parkinsonian features and are associated with complex clinical presentations that reflect degeneration in various neuronal systems. Patients with atypical parkinsonisms typically have a worse prognosis than those with Parkinson's disease, and atypical parkinsonisms respond poorly to standard anti-Parkinson's disease treatments.

Diagnostic Considerations

The most common tremor disorders are Parkinson's disease and essential tremor. When a patient presents with tremor, the clinician should pay particular attention to the body parts involved, positions/conditions in which the tremor occurs (ie, resting, postural, kinetic, intention) and the frequency of the tremor. It is also critical to look for potential associated signs. The patient should be examined for evidence of parkinsonism (bradykinesia, rigidity, postural instability), dystonia, and other neurologic signs.

An 8-12 Hz action (postural/kinetic) tremor of the upper extremities that is temporarily relieved by drinking alcohol is characteristic of essential tremor, whereas the presence of a pill-rolling rest tremor, bradykinesia and rigidity is consistent with Parkinson's disease and argues against essential tremor.

In patients with parkinsonism, careful attention to the history is necessary to exclude secondary causes such as medications, toxins or trauma. Medications that block striatal dopamine receptors, such as metoclopramide and neuroleptics, can cause drug-induced parkinsonism. Certain toxins such as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) and manganese (at high levels of exposure) can also cause parkinsonism.

Consider evaluating patients with parkinsonism for osteoporosis and osteopenia. Early clinical features that suggest an atypical parkinsonism rather than Parkinson's disease include the following :

- ❏ Falls at presentation or early in the disease
- ❏ Poor response to levodopa
- ❏ Symmetry at disease onset
- ❏ Rapid disease progression
- ❏ No tremor
- ❏ Dysautonomia (eg, urinary incontinence, fecal incontinence, catheterization for urinary retention, persistent erectile failure, prominent symptomatic orthostatic hypotension)

The atypical parkinsonisms are usually associated with little or no tremor, relatively early speech and balance difficulty and little or no response to dopaminergic medications. Multiple system atrophy (MSA) is relatively symmetric and characterized by parkinsonism, often with some combination of autonomic, corticospinal and cerebellar dysfunction.

Progressive supranuclear palsy (PSP) is relatively symmetric and characterized by parkinsonism with early falls (often in the first year) and a supranuclear gaze palsy in which the patient has difficulty with voluntary down-gaze.

Corticobasal ganglionic degeneration (CBD) is typically very asymmetric and characterized by both cortical (difficulty identifying objects, apraxias) and basal ganglionic (usually marked rigidity in an arm) features.

Lewy body disease is characterized by substantial cognitive dysfunction within 1 year of onset of parkinsonism. Hallucinations are common.

Patients with onset of parkinsonism before age 40 years should be tested for Wilson disease, starting with serum ceruloplasmin measurement and ophthalmologic evaluation for Kayser-Fleischer rings.

Differential Diagnoses

- ❏ Alzheimer Disease
- ❏ Cardioembolic Stroke
- ❏ Chorea in Adults
- ❏ Cortical Basal Ganglionic Degeneration
- ❏ Dementia With Lewy Bodies
- ❏ Dopamine-Responsive Dystonia
- ❏ Essential Tremor
- ❏ Hallervorden-Spatz Disease
- ❏ Huntington Disease
- ❏ Lacunar Syndrome
- ❏ Multiple System Atrophy
- ❏ Neuroacanthocytosis
- ❏ Neurological Manifestations of Vascular Dementia
- ❏ Normal Pressure Hydrocephalus
- ❏ Olivopontocerebellar Atrophy
- ❏ Parkinson-Plus Syndromes
- ❏ Progressive Supranuclear Palsy
- ❏ Striatonigral Degeneration

Work Up Considerations

Parkinson's disease is a clinical diagnosis. No laboratory biomarkers exist for the condition and findings on routine magnetic resonance imaging (MRI) and computed tomography (CT) scan are unremarkable. Positron emission tomography (PET) and single-photon emission CT (SPECT) may show findings consistent with Parkinson's disease and olfactory testing (for hyposmia) may provide evidence pointing toward Parkinson's disease, but these studies are not routinely needed.

No laboratory or imaging study is required in patients with a typical presentation. Such patients are aged 55 years or older and have a slowly progressive and asymmetric parkinsonism with resting tremor and bradykinesia or rigidity. Patients who do not have tremor should generally be considered for MRI evaluation to exclude brain lesions such as stroke, tumor or demyelination.

In patients with an unusual presentation, diagnostic testing may be indicated to exclude other disorders in the differential diagnosis. Such tests may include serum ceruloplasmin, sphincter electromyography or lumbar puncture.

Serum ceruloplasmin concentration is obtained as a screening test for Wilson disease in patients younger than 40 years who present with parkinsonian signs. If the ceruloplasmin level is low, measurement of 24-hour urinary copper excretion and slit-lamp examination for Kayser-Fleischer rings must be performed. Abnormal results on urinary sphincter electromyography have been noted in patients with multiple system atrophy (MSA).

A substantial and sustained response to dopamine medications (dopamine agonists or levodopa) helps confirm a diagnosis of Parkinson's disease. It is unclear whether acute levodopa or apomorphine challenge has any advantage over clinical diagnostic criteria. Over time, diagnostic accuracy improves as the progression of signs and symptoms and response to medications unfolds.

In the general community, there is a high diagnosis error rate between Parkinson disease and essential tremor. For movement disorder neurologists, when an erroneous diagnosis of Parkinson's disease is made, the most likely correct diagnoses are the atypical parkinsonisms (MSA, progressive supranuclear palsy [PSP], corticobasal ganglionic degeneration [CBD]). Early in the disease course, it may be very difficult to distinguish between Parkinson's disease and the atypical parkinsonisms. These disorders also do not have laboratory biomarkers and therefore, distinguishing among them is based on clinical criteria. Olfactory testing may help differentiate Parkinson's disease from PSP and CBD, but olfaction is also reduced in MSA.

Radiologic Studies

Magnetic resonance imaging

Magnetic resonance imaging (MRI) is useful to exclude strokes, tumors, multi-infarct state, hydrocephalus, and the lesions of Wilson disease.

MRI should be obtained in patients whose clinical presentation does not allow a high degree of diagnostic certainty, including those who lack tremor, have an acute or stepwise progression or are younger than 55 years.

PET and SPECT scanning

Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) scanning are useful diagnostic imaging studies, but these are not routinely required. Different radioligands permit imaging of different components or abnormalities within the brain.

At the onset of motor signs, patients with Parkinson's disease show an approximately 30% decrease in ^{18}F-dopa (fluorodopa) uptake on PET imaging in the contralateral putamen. However, this study is not widely available and is currently generally considered a research tool.

Carbon-11 (^{11}C)-nomifensine and cocaine analogues such as ^{123}I-beta-CIT (iodine-123-labeled carboxymethoxy-3beta-4-iodophenyl-nortropane) and ^{123}I-FP-CIT (fluoropropyl-CIT) bind to dopamine reuptake sites on nigrostriatal terminals and provide an index of the remaining dopamine neurons. Ioflupane (^{123}I) (DaTscan) is a radiopharmaceutical agent that is indicated for striatal dopamine transporter visualization using SPECT brain imaging to assist in the evaluation of adults with suspected Parkinsonian syndromes (PSs). This agent may be used to help differentiate essential tremor from tremor due to PSs (idiopathic Parkinson's disease [IPD] and Parkinson-plus syndromes [PPS]).

Deficits on ^{123}I SPECT scans indicate a dopamine deficiency syndrome but do not differentiate Parkinson's disease from atypical parkinsonisms, including multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). Ioflupane SPECT imaging reveals a dopamine deficiency in Parkinson's disease, MSA, PSP, corticobasal ganglionic degeneration and Lewy body disease. This study is normal in essential tremor, dystonic tremor, medication-induced parkinsonism or tremor, psychogenic disorders and in normal individuals.

Histologic Findings

Classic pathologic findings in Parkinson's disease incl-ude degeneration of the neurons containing neuro-melanin, especially in the substantia nigra and the locus ceruleus. Surviving neurons often contain eosi-nophilic cytoplasmic inclusions called Lewy bodies. The primary biochemical defects are loss of striatal dopamine, which results from degeneration of dopamine-producing cells in the substantia nigra, as well as hyperactivity of the cholinergic neurons in the caudate nucleus.

Alpha-synuclein is a major structural component of Lewy bodies; all Lewy bodies stain for alpha-synuclein and most also stain for ubiquitin. Lewy bodies are concentric, eosinophilic, cytoplasmic inclusions with peripheral halos and dense cores. The presence of Lewy bodies within pigmented neurons of the substantia nigra is characteristic, but not pathognomonic, of Parkinson's disease. Lewy bodies are also found in the cortex, nucleus basalis, locus ceruleus, intermediolateral column of the spinal cord and other areas.

Lumbar Puncture

Lumbar puncture should be considered if signs of normal-pressure hydrocephalus (NPH) are observed (eg, incontinence, ataxia, dementia). In NPH, clinical signs characteristically improve after removal of about 20 mL of cerebrospinal fluid.

References:

❏ emedicine.medscape.com
❏ neuroendoimmune.wordpress.com

Management of Parkinson's Disease will be discussed in the next issue.

Palliative Care

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment. Palliative care is provided by a specially-trained team of doctors, nurses, social workers and other specialists who work together to provide an extra layer of support.

It is appropriate at any age and at any stage in a serious illness and can be provided along with curative treatment. Palliative care teams specialize in treating people suffering from the symptoms and stress of serious illnesses such as Stroke, Cancer, Congestive Heart Failure (CHF), Chronic Obstructive Pulmonary Disease (COPD), kidney disease, Alzheimer's, Parkinson's, Amyotrophic Lateral Sclerosis (ALS) and many more. Symptoms may include depression, pain, shortness of breath, fatigue, constipation, nausea, loss of appetite, difficulty sleeping and much more.

Benefits of Palliative care

- Improves quality of life.
- Provides relief from pain and other distressing symptoms.
- Supports life and regards dying as a normal process.
- Doesn't quicken or postpone death.
- Combines psychological and spiritual aspects of care.
- Offers a support system to help people live as actively as possible until death.
- Offers a support system to help the family cope during a person's illness and in bereavement.
- Uses a team approach to address the needs of the person who is ill and their families.
- Also applies to the earlier stages of illness, alongside other therapies that are aimed at prolonging life.

Palliative care providers

General care

This is type of palliative care which includes day-to-day care to people with advanced illness and may be their family and friends and provided by GP, community nurses or others.

General Palliative care team includes

- GP (General Physician)
- Community nurses
- Social workers
- Care workers
- Spiritual care professionals

These professionals should be able to assess patients care needs. They should meet those needs where possible and know when to seek specialist advice. The aim of general palliative care is to provide:

- Information for all (Person who needed it most, friends and family etc.).
- Accurate and all-round assessment of needs.
- Coordination of care teams in and out of hours.
- Basic levels of symptom control.
- Psychological, social, spiritual and practical support.
- Good communication with needed person and with the specialist for providing better care.

Specialist care

Specialist palliative care services manage more complex patient care problems that cannot be dealt by generalist services. Palliative care specialists usually work in teams to provide joined-up care.

Specialist teams include:

- Doctors and nurses
- Counsellors
- Specialist allied health professionals, such as physiotherapists, occupational therapists, dieticians and social workers.

Specialist Palliative Care Level 1

Capability

Provide palliative care for patients, primary carers and families whose needs exceed the capability of primary care providers. Provides assessment and care consistent with needs and provides consultative support, information and advice to primary care providers. Has formal links to primary care providers and level 2 and/or level 3 Specialist Palliative Care providers to meet the needs of patients, carers and families with complex problems. Has quality and audit programme.

Resource Team

Multidisciplinary team including

- ❏ Medical practitioner with skills and experience in palliative care
- ❏ Clinical nurse specialist/consultant
- ❏ Allied health staff
- ❏ Pastoral care and volunteers.
- ❏ A designated staff member if available coordinates a volunteer service.

Specialist Palliative Care Level 2

Capability

Able to support higher resource level due to population base (e.g. regional area). Provides formal education programs to primary care and level 1 providers and the community. Has formal links with primary care providers and level 3 Specialist. It ensures palliative Care Services for patients, primary carers and families with complex needs.

Resource Team

- ❏ Interdisciplinary team including medical practitioner and clinical nurse specialist/consultant with specialist qualifications.
- ❏ Includes designated allied health and pastoral care staff

Specialist Palliative Care Level 3

Capability

Provides comprehensive care for the needs of patients, primary carers and families with complex needs. Provides local support to primary care providers, regional level 1 and/or level 2 Services including education and formation of standards. Has a comprehensive research and teaching role. Has formal links with local primary care providers and with Specialist Palliative Care Providers level 1 and/or level 2 and relevant academic units including professorial chairs where available.

Resource Team

- ❏ Interdisciplinary team including a medical director and clinical nurse consultant/nurse practitioner and allied health staff with specialist qualifications in palliative care.

Specialist Palliative Care (SPC) activities

There should be 24 hour access to SPC advice, delivered by phone as a minimum. In addition, SPC:

- ❏ Undertakes detailed, specialized and holistic assessments of the needs of the patient across physical, psychological, social and spiritual domains.
- ❏ Provides expert management of complex symptoms.
- ❏ Provides advice in situations of ethical complexity.
- ❏ Delivers direct clinical care in partnership with colleagues in primary, secondary and social care.
- ❏ May provide care in any setting, including: hospital; community (including care homes); hospice inpatient units; hospital inpatient units; day therapy; outpatient clinics.
- ❏ May under take case management/case leadership (if this is not already and appropriately undertaken by another professional).
- ❏ Attends the range of multidisciplinary team meetings in secondary care (for example, lung and other specific cancer type meetings).
- ❏ Attends multidisciplinary community meetings (for example Gold Standards Framework meetings and in some areas, disease - specific meetings such as for COPD).
- ❏ Supports colleagues, patients and carers with advice and information on palliative care issues.
- ❏ Facilitates education and training across a variety of topics and according to local need, such as symptom control, advance care planning, support for the use of tools such as integrated care pathways for the last days of life, communication skills training, etc.

- Supports/undertakes research.

Referral criteria for Specialist Palliative Care

There are no nationally agreed criteria for accessing SPC but a good service should have written criteria which include the following

1. The patient has active, progressive advanced disease, a limited prognosis and the focus of care is on quality of life, for example:

- Potentially fatal conditions where treatment has changed from curative to palliative intent, e.g. cancer, multiple co-morbidities where curative treatment is no longer possible
- Complex symptom control issues during treatment
- Treatment available to prolong life but prognosis is uncertain, e.g. advanced chronic obstructive pulmonary disease, advanced heart failure
- Palliative treatment from the outset with no cure available, e.g. Motor neuron disease, multiple systems atrophy, advanced dementia.

2. The patient has unresolved complex needs that cannot be met by the caring team. These needs may be physical, psychological, social and /or spiritual. Examples may include complicated symptoms, difficult family situations or ethical issues regarding treatment decisions.
3. Patient consent for referral (where the patient has capacity for this consent).

How Palliative care works

Emotional and coping

Palliative care specialists can provide resources to help patients and families deal with the emotions that come with a disease diagnosis and treatment. Depression, anxiety and fear are only a few of the concerns that can be addressed through palliative care. Experts may provide counseling, recommend support groups, hold family meetings or make referrals to mental health professionals.

Practical

Patients may have financial and legal worries, insurance questions, employment concerns and concerns about completing advance directives. For many patients and families, the technical language and specific details of laws and forms are hard to understand. To ease the burden, the palliative care team may assist in coordinating the appropriate services. For example, the team may direct patients and families to resources that can help with financial counseling, understanding medical forms or legal advice or identifying local and national resources, such as transportation or housing agencies.

Spiritual

With a serious illness, patients and families often look more deeply for meaning in their lives. Some find the disease brings them more faith, whereas others question their faith as they struggle to understand why disease happened to them. An expert in palliative care can help people explore their beliefs and values so that they can find a sense of peace or reach a point of acceptance that is appropriate for their situation.

National and international recommendations about specialist palliative care provision

Although the most recent available in practice but these recommendations are already several years old and do not accommodate the changing demographics and patterns of death being experienced in the provision of health care. Nor do they take into account local variations which will influence the provision that needs to be commissioned, e.g. urban or rural factors, historical provision and balance of palliative care and end of life care provision available. The less end of life care provision there is in any setting, the more palliative care will be required

These recommendations also do not reflect the impact of changing expectations which are hard to measure at this stage These include: availability of seven day face to face assessments by palliative care clinicians, and capacity of palliative care to support care closer to home and dying in the person's usual place of residence.

In-patient specialist palliative care beds

- Between 16-18 in-patients SPC beds per 250,000 populations.
- Considering predominantly the needs of cancer patients: a minimum of 12.5 palliative care beds for 250,000 population i.e. one bed per 20,000 population. Considering the needs of both cancer

and non-cancer patients and the growing prevalence of advanced chronic diseases, a minimum of 20-25 palliative care beds for 250,000 populations.

- One consultant for each 20 specialist in-patient palliative care (hospice) beds, including outpatient and day care provision or at least 3 physicians (consultant and other grades) per every 20 specialis inpatient palliative care beds (with at least one whole time SPC physician for every 5-6 beds).
- One SPC nurse to oversee each 7.5 hospice beds, whether in-patient or Hospice At Home - note that additional nursing will be needed to provide the nursing care.
- Within palliative care units or hospices, nursing staff ratios for the provision of nursing care of at least 1 nurse per bed, but preferably 12 nurses per bed are recommended.

Community specialist palliative care

- At least 2 whole-time equivalent (WTE) community-based consultants in palliative medi-cine for 250,000 population.
- At least 5 SPC nurses per 250,000 populations.
- 10 to 12 full time professionals, including predominantly nursing and physician time and with social worker and administration support for every 250,000 population, with 24 hour and 7 day per week provision for support.

Specialist palliative care delivered by hospital advisory teams

- One consultant per 850 District General Hospital beds.
- One SPC nurse per 300 District General Hospital beds.
- At least one hospital palliative care support team (minimum one physician and one nurse, with SPC training) should be available for a hospital with 250 beds.
- Large secondary care hospitals and hospitals accepting tertiary referrals and management may need additional SPC professionals, including sub-specialization roles and provision of additional support and education.

Additional recommendations

Each consultant (whether community, hospital or hospice based) needs support from a minimum of one matching doctor, either trainee or staff grade or clinical assistant.

Pediatric Palliative Care

Pediatric Palliative care is specialized medical care for children with serious illnesses. It focuses on providing relief from the symptoms like pain and stresses of a serious illness-whatever the diagnosis. The goal is to improve quality of life for both the child and the family.

Pediatric palliative care is provided by a team of doctors, nurses and other specialists who work together with a child specialist as an extra layer of support. It is appropriate at any age and at any stage of an illness and can be provided along with treatment meant to cure.

Pediatric palliative care addresses serious medical conditions including genetic disorders, cancer, prematurity, neurologic disorders, heart and lung conditions and others. It relieves the symptoms such as pain, shortness of breath, fatigue, constipation, nausea, loss of appetite and difficulty sleeping. In short, it helps the child and the family, gain the strength to carry on with daily life. Above all, pediatric palliative care is family-centered. It helps with communication and coordination of care.

End of life care

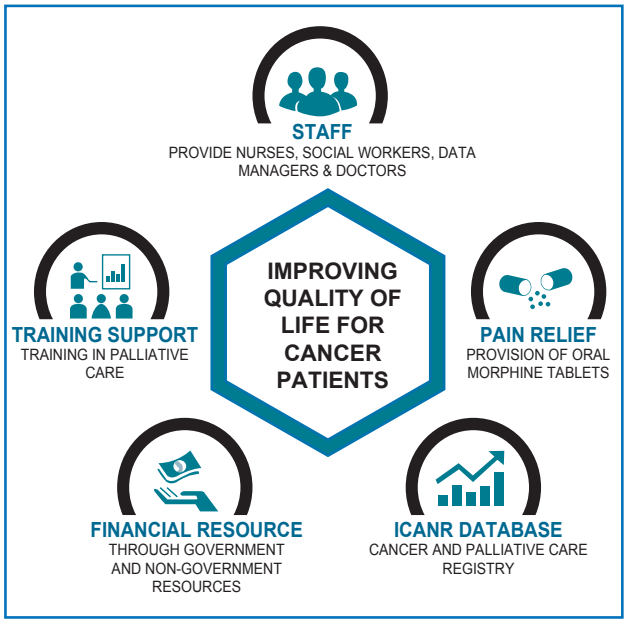
End of life care is an important part of palliative care for people who are nearing the end of life. End of life care aims to help people live as well as possible and to die with dignity. It also refers to care during this time and can include additional support, such as help with legal matters. End of life care continues for as long as anyone needs it.

Cancer and Palliative Care

Palliative care specialists can work in close partnership with oncologist. Any person, of any age, with any type or stage of cancer can benefit from palliative care-and the earlier, the better.

Palliative care teams understand that both the disease itself and the treatments for it can cause suffering.

Cancer symptoms might include pain, nausea, vomiting, fatigue, anxiety, depression, constipation, diarrhea, confusion or shortness of breath. The palliative care team not only specializes in relieving the symptoms of cancer, but they can also help with other situations, such as feeling overwhelmed by complicated medical information or confusion and worry about making important treatment decisions.



Palliative care specialists have both the time and the expertise to interpret the complex medical information receive from oncologist.

The good news is that because palliative care teams specialize in dealing with the full range of cancer symptoms, they can ensure that everyone enjoy the best quality of life possible. Palliative care providers help to figure out the best treatment choices. They'll help to sort out immediate concerns-like worrying about how chemotherapy or radiation might make feel or what impact surgery may have or if someone lose hair or what will happen if someone end treatment. And the best news is that, in a recent study, cancer patients receiving palliative care lived approximately three months longer than those who did not.

Stroke and Palliative Care

The most well-known stroke symptoms are paralysis and weakness on one side of the body. People with stroke may also experience trouble speaking or understanding speech, headaches, inappropriate behavior and loss of balance, memory difficulties, visual problems and emotional problems. Obtaining quick treatment when a stroke first begins can help to minimize long-term problems. Although palliative care is important at any stage of illness, it is best to involve the palliative care team sooner rather than later.

Palliative care team can help explain whether symptoms such as memory, speech or visual problems will be permanent, or whether they will improve over time. The palliative care specialists can use medicines and other therapies to help with depression or anger, which are common after a stroke. When someone living with stroke, people may also have problems with muscles and movement.

Someone may have spasms that cause pain. Palliative care specialists are experts in managing the symptoms of a serious illness like stroke. They can help to manage these symptoms through medicines that block nerve reactions and other treatments that help to live more comfortably overall. Palliative care team will be there for diseased person to talk about needs and expectations for the future at home. The specialists will help to understand what to expect physically and mentally and help to develop a realistic plan. They'll discuss whether someone might need home health care and the services of assisted living, skilled nursing or acute rehab. Palliative care specialists help to cope with the challenges of living with stroke-from the side effects of medical treatment to family caregiver stress. They will help to make tough decisions.

References:

- Commissioning Guidance for Specialist: Palliative Care (National Guideline Develop in Collaboration of Palliative Medicine Department of Great Britain and Ireland)
- Clinical Guidance for Quality Palliative Care (American Academy of Hospice and Palliative Medicine)
- Get Palliative Care : Center to Advance Palliative Care (CAPC)

Migraine is a complex disorder characterized by recurrent episodes of headache, most often unilateral and in some cases associated with visual or sensory symptoms-collectively known as an aura-that arise most often before the headache but that may occur during or afterward. However, it is much more; the International Headache Society diagnoses a migraine by its pain and number of attacks (at least 5, lasting 4-72 hours if untreated) and additional symptoms including nausea and/or vomiting or sensitivity to both light and sound. Migraine is three times more common in women than in men and affects more than 10 percent of people worldwide.

Roughly one-third of affected individuals can predict the onset of a migraine because it is preceded by an aura, visual disturbances that appear as flashing lights, zig-zag lines or a temporary loss of vision. People with migraine tend to have recurrent attacks triggered by a number of different factors, including stress, anxiety, hormonal changes, bright or flashing lights, lack of food or sleep and dietary substances. Migraine in some women may relate to changes in hormones and hormonal levels during their menstrual cycle. For many years, scientists believed that migraines were linked to the dilation and constriction of blood vessels in the head. Investigators now believe that migraine has a genetic cause.

Signs and symptoms

Typical symptoms of migraine include the following:

- Throbbing or pulsatile headache, with moderate to severe pain that intensifies with movement or physical activity
- Unilateral and localized pain in the frontotemporal and ocular area, but the pain may be felt anywhere around the head or neck
- Pain builds up over a period of 1-2 hours, progressing posteriorly and becoming diffuse
- Headache lasts 4-72 hours
- Nausea (80%) and vomiting (50%), including anorexia and food intolerance and light-headedness
- Sensitivity to light and sound

Features of migraine aura are as follows :

- May precede or accompany the headache phase or may occur in isolation
- Usually develops over 5-20 minutes and lasts less than 60 minutes
- Most commonly visual but can be sensory, motor, or any combination of these
- Visual symptoms may be positive or negative
- The most common positive visual phenomenon is the scintillating scotoma, an arc or band of absent vision with a shimmering or glittering zigzag border

Physical findings during a migraine headache may include the following :

- Cranial/cervical muscle tenderness
- Horner syndrome (ie, relative miosis with 1-2 mm of ptosis on the same side as the headache)
- Conjunctival injection
- Tachycardia or bradycardia
- Hypertension or hypotension
- Hemisensory or hemiparetic neurologic deficits (ie, complicated migraine)
- Adie-type pupil (ie, poor light reactivity, with near dissociation from light)

Pathophysiology

The cause of migraine is unknown but there is increasing evidence that the aura is due to dysfunction of ion channels causing a spreading front of cortical depolarization (excitation) followed by hyperpolarisation (depression of activity). This process spreads over the cortex at a rate of about 3 mm/minute, corresponding to the aura's symptomatic spread.

The headache phase is associated with vasodilatation of extra cranial vessels and may be relayed by hypothalamic activity. Activation of the trigeminovascular system is probably important. A Genetic contribution is implied by frequently positive family history and similar phenomena occurring in disorders such as CADASIL. The female preponderance and the frequency of migraine attacks at certain points in the menstrual cycle also suggest hormonal influences. Estrogen-containing oral contraception sometime exacerbates migraine and increases the small rusk of stroke in patients who suffer from migraine with aura.

Doctors and patients often over-estimate the role of dietary precipitants such as cheese, chocolate or red wine. When psychological factors contribute, the migraine attack often occurs after a period of stress, being more likely at the end of the working week or at the beginning of a holiday.

Types of Migraine

There are a number of different types of migraine, the most common being Migraine without Aura and Migraine with Aura. Other types of migraine include Basilar Migraine, Hemiplegic Migraine, Vestibular Migraine and Aura without Headache.

Migraine Without Aura

The majority of migraine sufferers have Migraine without Aura.

The most common symptoms of Migraine without Aura are

- Intense throbbing headache, usually on one side of the head, worsened by movement and lasting from 4-72 hours.
- Nausea, sometimes vomiting
- Sensitivity to light
- Sensitivity to noise
- Sensitivity to smells
- Stiffness of the neck and shoulders.
- Blurred vision

Migraine With Aura

- Migraine with Aura refers to a range of neurological disturbances that occur before the headache begins, usually lasting about 20-60 minutes.
- About 20% of people with migraine experience 'aura' in addition to some or all of the symptoms of 'Migraine Without Aura'.

The disturbances are usually visual e.g.

- Blind spots
- Flashing lights
- Zig-zag patterns

Aura can also present in other ways:

- Pins and needles on one side usually starting in the fingers/arm, sometimes spreading up into the face
- Slurring of speech
- Muscular weakness
- Loss of co-ordination
- Confusion

The other symptoms of migraine will usually follow the migraine aura. These are:

- Intense throbbing headache, usually on one side of the head, worsened by movement and lasting from 4-72 hours
- Nausea, sometimes vomiting
- Sensitivity to light
- Sensitivity to noise
- Sensitivity to smells
- Stiffness of the neck and shoulders
- Blurred vision

Migraine triggers

A history of migraine triggers may be elicited. Common triggers include the following:

- Hormonal changes (eg, those resulting from menstruation, ovulation, oral contraceptives or hormone replacement)
- Head trauma
- Lack of exercise
- Sleep changes
- Medications (eg, nitroglycerin, histamine, reserpine, hydralazine, ranitidine, estrogen)
- Stress

Family history

Approximately 70% of patients have a first-degree relative with a history of migraine. The risk of migraine is increased 4-fold in relatives of people who have migraine with aura. Migraine headache generally shows a multifactorial inheritance pattern, but the specific nature of the genetic influence is not yet completely understood.

Diagnosis

The diagnosis of migraine is based on patient history. International Headache Society diagnostic criteria are that patients must have had at least 5 headache attacks that lasted 4-72 hours (untreated or unsuccessfully treated) and that the headache must have had at least 2 of the following characteristics:

- ❏ Unilateral location
- ❏ Pulsating quality
- ❏ Moderate or severe pain intensity
- ❏ Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)

In addition, during the headache the patient must have had at least 1 of the following:

- ❏ Nausea and/or vomiting
- ❏ Photophobia and phonophobia

Investigation

Selection of laboratory and/or imaging studies to rule out conditions other than migraine headache is determined by the individual presentation (eg, erythrocyte sedimentation rate and C-reactive protein levels may be appropriate to exclude temporal/giant cell arteritis). Neuroimaging is not necessary in patients with a history of recurrent migraine headaches and a normal neurologic examination.

The American Headache Society released a list of 5 commonly performed tests or procedures that are not always necessary in the treatment of migraine and headache, as part of the American Board of Internal Medicine (ABIM) Foundation's Choosing Wisely campaign. The recommendations include:

- ❏ Don't perform neuroimaging studies in patients with stable headaches that meet criteria for migraine.
- ❏ Don't perform computed tomography imaging for headache when magnetic resonance imaging is available, except in emergency settings.
- ❏ Don't recommend surgical deactivation of migraine trigger points outside of a clinical trial.
- ❏ Don't prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders.
- ❏ Don't recommend prolonged or frequent use of over-the-counter pain medications for headache.

Treatment

There is no absolute cure for migraine since its pathophysiology has yet to be fully understood. There are two ways to approach the treatment of migraine headache with drugs: prevent the attacks or relieve the symptoms during the attacks. Prevention involves the use of medications and behavioral changes. Drugs originally developed for epilepsy, depression or high blood pressure to prevent future attacks have been shown to be extremely effective in treating migraine. Botulinum toxin A has been shown to be effective in prevention of chronic migraine.

Behaviorally, stress management strategies, such as exe-rcise, relaxation techniques, biofeedback mechanisms and other therapies designed to limit daily discomfort, may reduce the number and severity of migraine attacks. Making a log of personal triggers of migraine can also provide useful information for trigger-avoiding lifestyle changes, including dietary considerations, eating regularly scheduled meals with adequate hydration, stopping certain medications and establishing a consistent sleep schedule. Hormone therapy may help some women whose migraines seem to be linked to their menstrual cycle. A weight loss program is recommended for obese individuals with migraine.

Relief of symptoms or acute treatments, during attacks consists of sumatriptan, ergotamine drugs, and analgesics such as ibuprofen and aspirin. The sooner these treatments are administered, the more effective they are.

Prognosis

Responsive prevention and treatment of migraine is incredibly important. Evidence shows an increased sensitivity after each successive attack, eventually leading to chronic daily migraine in some individuals With proper combination of drugs for prevention and treatment of migraine attacks most individuals can overcome much of the discomfort from this debilitating disorder. Women whose migraine attacks occur in association with their menstrual cycle are likely to have fewer attacks and milder symptoms after menopause.

References :

- ❏ http://emedicine.medscape.com
- ❏ Davidson 22nd Edition
- ❏ NINDS

Dengue Complications

Dengue fever is one of the most common tropical illnesses worldwide. Dengue is a viral infection, spread by the female *Aedes* mosquitoes. These nearly always bite during the day, often the first half of the morning or second half of the afternoon. The incubation period is usually between 4 and 7 days. Dengue fever is a disease which has been rapidly spreading throughout the tropics. Around 2.5 billion people now live in areas where they might be affected. There are around 100 million cases a year globally, resulting in about 21,000 deaths.

A woman suffering from dengue fever lies under mosquito nets

Symptoms usually begin about four to seven days after the initial infection. In many cases, symptoms will be mild. They may be mistaken for symptoms of the flu or another infection. Young children and people who have never experienced infection may have a milder illness than older children and adults. Symptoms generally last for about 10 days and can include:

- sudden, high fever (up to 106˚F)
- severe headache
- swollen lymph glands
- severe joint and muscle pain
- skin rash (appearing between two and five days after the initial fever)
- mild to severe nausea
- mild to severe vomiting
- mild bleeding from the nose or gums
- mild bruising on the skin
- febrile convulsion

Sometimes blood tests should be done to check for viral antibodies or the presence of infection. There is no medication or treatment specifically for dengue infection. Patients should take rest and drink plenty of fluids and use only paracetamol to reduce fever, headache and joint pain. Aspirin and ibuprofen can cause more bleeding and should be avoided.

For the large majority of people infected with dengue fever viruses, the prognosis is excellent with complete recovery, although they are likely to feel very ill during the first one or two weeks of the acute illness and weak for about one month. Patients with underlying illness or immune suppression have a fair to good prognosis because they are more likely to get complications. Also, people who have been infected by one dengue virus type are still able to be infected by the remaining three types; a second infection increases the possibility that complications will develop, so patients with second-time dengue fever have a less optimal prognosis.

Dengue fever can result in the following complications:

- Dengue hemorrhagic fever
- Dengue shock syndrome

Dengue Hemorrhagic Fever (DHF) is caused by the same viruses and is characterized by increased vascular permeability, hypovolaemia and abnormal blood clotting mechanisms. Dengue hemorrhagic fever is a potentially deadly complication with symptoms similar to those of dengue fever, but after several days the patient becomes irritable, restless, and sweaty.

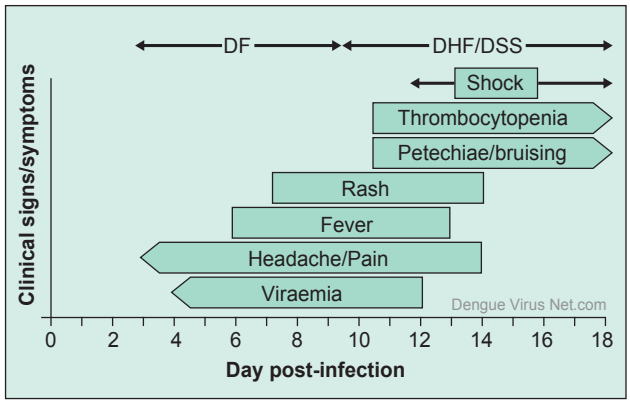
The illness often begins with a sudden rise in temperature accompanied by facial flush and other flu-like symptoms.

The fever usually continues for two to seven days and can be as high as 106˚F, possibly with convulsions and other complications.

In moderate Dengue hemorrhagic fever cases, all signs and symptoms abate after the fever subsides. In severe cases, the patient's condition may suddenly deteriorate after a few days of fever; the temperatures drops, followed by signs of circulatory failure and the patient may rapidly go into a critical state of shock.

The Dengue Shock Syndrome (DSS) is characterized by bleeding that may appear as tiny spots of blood on the skin (petechiae) and larger patches of blood under the skin (ecchymosis). Minor injuries may cause bleeding. Shock may cause death within 12 to 24 hours. Patients can recover following appropriate medical treatment.

The progress towards Dengue Hemorrhagic Fever (DHF) or The Dengue Shock Syndrome (DSS) occurs after 3-5 days of fever. At this time, fever has often come down. This may mislead many of us to believe that the patient is heading towards recovery. In fact, this is the most dangerous period that requires high vigilance.



Generalized time course of the events associated with DF, DHF and DSS. The incubation period before the development of signs of infection generally ranges from 4 to 7 days.

Recognition of Dengue Hemorrhagic Fever (DHF)

Symptoms similar to dengue fever plus, any one of the following:

- Severe and continuous pain in abdomen
- Bleeding from the nose, mouth and gums or skin bruising
- Frequent vomiting with or without blood
- Black stools, like coal tar
- Excessive thirst (dry mouth)
- Pale, cold skin
- Restlessness or sleepiness

Dengue Shock Syndrome is defined as Dengue Hemorrhagic Fever plus:

- Weak rapid pulse
- Narrow pulse pressure (less than 20 mm Hg)
- Cold, clammy skin and restlessness

Other complications that can occur in dengue infection include acalculous cholecystitis, associated with fever, right upper quadrant pain, abnormal liver tests, and a thickened gallbladder wall with absence of cholelithiasis at ultrasound. Cholecystectomy is not recommended or required in patients with dengue fever.

Clinical pancreatitis is a rare complication, although elevation of amylase and pancreatic enlargement has been observed in as many as 29% of cases.

Reye syndrome, acute parotitis, and diarrhea associated with high fever also have been noted.

References:

- http://www.medscape.com
- http://www.hse.ie
- http://www.emedicinehealth.com
- http://www.healthline.com
- http://www.denguevirusnet.com

Test Yourself - 41

Correct Answers :

1.	a	2.	c	3.	b	4.	c	5.	b	6.	d

CONGRATULATIONS!

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Test Yourself - 42

1. The followings are true for "Palliative Care" except :

a. Palliative care teams specialize in treating people suffering from symptoms and stress of serious illnesses except COPD, Stroke, CHF etc.
b. Specialist palliative care level 2 provides formal education programs to primary care and level 1 providers and the community.
c. Depression, anxiety and fear are only a few of the concerns that can be addressed through palliative care.
d. There should be 24 hour access to specialist palliative care advice, delivered by phone as a minimum.

2. All the followings are correct for "Migraine" except :

a. It is three times more common in women than in men and affects more than 10 percent of people worldwide.
b. The headache phase is associated with vasodilatation of extra cranial vessels and may be relayed by hypothalamic activity.
c. Estrogen - containing oral contraception never exacerbates migraine.
d. The majority of migraine sufferers have migraine without Aura.

3. All the below are true for "Parkinson's Disease" except:

a. About 60 - 80% of dopaminergic neurons are lost before the motor signs of this disease emerge.
b. Genetic causes of Parkinson's disease account for approximately 10% of cases.
c. With the introduction of levodopa, the mortality rate dropped about 50 percent.
d. The most common late motor signs of this disease include tremor, rigidity, dystonia and bradykinesia..

4. All the followings are correct for "Dengue Complications" except :

a. Symptoms usually begin about 4 - 7 days after the initial infection.
b. The progress towards Dengue Hemorrhagic Fever or Dengue Shock Syndrome occurs after 3 - 5 days of fever.
c. People who have been infected by one Dengue virus type are not in a chance to be infected by the other three types..
d. In severe Dengue Hemorrhagic Fever cases the patient's condition may suddenly deteriorate after a few days of fever..

5. The followings are right for "Parkinson's Disease" except :

a. The prevalence of dementia in Parkinson's disease ranges from 20 - 40 percent.
b. Metoclopramide and neuroleptics can cause drug induced Parkinsonism.
c. Parkinson-plus syndromes are secondary neurodegenerative disorders that have parkinsonian features and are associated with complex clinical presentation.
d. A substantial and sustained response to dopamine medications helps confirm a diagnosis of this disease.

6. All the followings are correct for "Migraine" except :

a. About 70 percent of patients have a first-degree relative with a history of migraine.
b. Botulinum toxin A has been shown to be effective in treatment of acute migraine.
c. Sumatriptan, ergotamine drugs and analgesics are used in acute treatment.
d. People with migraine tend to have recurring attacks triggered by a number of different factors.

Soon our officials will be visiting you with a token of our appreciation

Test Yourself - 41

Correct Answers :

1.	a	2.	c	3.	b	4.	c	5.	b	6.	d

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c. Depression, anxiety and fear are only a few of the concerns that can be addressed through palliative care.
d. There should be 24 hour access to specialist palliative care advice, delivered by phone as a minimum.

2. All the followings are correct for "Migraine" except :

a. It is three times more common in women than in men and affects more than 10 percent of people worldwide.
b. The headache phase is associated with vasodilatation of extra cranial vessels and may be relayed by hypothalamic activity.
c. Estrogen - containing oral contraception never exacerbates migraine.
d. The majority of migraine sufferers have migraine without Aura.

3. All the below are true for "Parkinson's Disease" except:

a. About 60 - 80% of dopaminergic neurons are lost before the motor signs of this disease emerge.
b. Genetic causes of Parkinson's disease account for approximately 10% of cases.
c. With the introduction of levodopa, the mortality rate dropped about 50 percent.
d. The most common late motor signs of this disease include tremor, rigidity, dystonia and bradykinesia..

4. All the followings are correct for "Dengue Complications" except :

a. Symptoms usually begin about 4 - 7 days after the initial infection.
b. The progress towards Dengue Hemorrhagic Fever or Dengue Shock Syndrome occurs after 3 - 5 days of fever.
c. People who have been infected by one Dengue virus type are not in a chance to be infected by the other three types..
d. In severe Dengue Hemorrhagic Fever cases the patient's condition may suddenly deteriorate after a few days of fever..

5. The followings are right for "Parkinson's Disease" except :

a. The prevalence of dementia in Parkinson's disease ranges from 20 - 40 percent.
b. Metoclopramide and neuroleptics can cause drug induced Parkinsonism.
c. Parkinson-plus syndromes are secondary neurodegenerative disorders that have parkinsonian features and are associated with complex clinical presentation.
d. A substantial and sustained response to dopamine medications helps confirm a diagnosis of this disease.

6. All the followings are correct for "Migraine" except :

a. About 70 percent of patients have a first-degree relative with a history of migraine.
b. Botulinum toxin A has been shown to be effective in treatment of acute migraine.
c. Sumatriptan, ergotamine drugs and analgesics are used in acute treatment.
d. People with migraine tend to have recurring attacks triggered by a number of different factors.

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