UNIVERSITY OF NAIROBI
NEUROSURGERY CLINICAL TEACHING PROGRAM
PROF NJM MWANG'OMBE MBCHB, MMED, PHD (LOND)

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| Monday:<br>8:00 AM – 11:00 AM<br>WR/PG Teaching; PW, PM,DO,MQ | Monday:<br>2:00PM- 5:00 PM<br>NSOPC (No. 24)<br>MBChB 5-Clinical Teaching<br>NJM, JK, PA, CM, PM |
| Tuesday:<br>8:00 AM-11:00 AM<br>MBChB 5-Wd Teaching: (JK).<br>WR/PG teaching; JK<br>Theatre whole day: NJM, PA, PM | Tuesday:<br>2:00 PM-5:00 PM<br>NSOPC (No. 24)<br>DO, PW, PL,<br>Theatre whole day: NJM,PA, PM |
| Wednesday:<br>8.00 AM-9.00 AM:<br>PGyr 2 PoS, (NJM).<br>9:00 AM – 10:00 AM:<br>MBChB 3-lecture: (NJM)<br>10:00 AM-11:00 AM:<br>MBChB 3-wd teaching (PA/DO)<br>WR/PG teaching; PA/DO<br>Theatre-whole day: DO,PW,<br>Theatre Matta Hospital (CKM/Spinal) | Wednesday:<br>Theatre-whole day: DO, PW,<br>2:00 PM-5:00PM Mentorship |
| Thursday: Academic Day<br>8:00 AM-9:00 AM<br>Neuroradiology Conference (Rad. Dept.)<br>9:00 AM-11:00 AM Grand Round (NJM)<br>MBChB 5-wd teaching (CM)<br>11 AM-1 PM: Neurosurgery lectures, Journal Club/ M&M conference (Surg Dept) | Thursday: Academic Day<br>2:00 PM-3:00 PM<br>Surgical Grand Round<br>3:00 PM-5 PM: Mentorship |
| Friday:<br>7.00 AM-8.00 AM<br>Neuropathology Conference<br>(Dept. Path)<br>Theatre-whole day ( PL, CM, JK) | Friday:<br>Theatre-whole day (PL, CM, JK)<br>2:00 PM-5:00 PM Mentorship |

WR; ward round. PG; post graduate. M&M; mortality and morbidity. wd; ward. PoS; principles of surgery. PGyr; post grad year.
NM; Prof Mwang'ombe. PA; Dr. Akuku. CM; Dr. Musau. DO; Mr. Olunya. JK; Dr. Kiboi. PL; Dr. Lubanga. PW; Dr. wanyoike. PM; Dr. Mwangi.
Neurosurgery 3rd Year Clinical Lectures: 1. Management of Head Injuries/Brain Death. 2 Management of Brain Tumours & Stroke. 3. Management of Spinal Cord Tumours & Degenerative Conditions. 4 Congenital Malformations of the CNS. 5. Surgical Infections of the CNS 6. Spinal Cord Injury. Pain Management. Functional Neurosurgery

# NEUROLOGICAL HISTORY AND PHYSICAL EXAMINATION

**Prof. N J M Mwang'ombe MBChB, MMed, PhD (Lond)**

## Examination of the Higher Functions

**Higher functions include gait, speech, and mental status**. These are referred to as higher functions because human bipedal gait, receptive and expressive speech, and cognitive function are more sophisticated than similar functions of any other member of the animal kingdom.

Gait

Gait is the attitude of a person in the upright position. Abnormal types are described below.

**Hemiparetic gait**

In hemiparesis, facial paresis may not be obvious. In mild cases, subtle features of facial paralysis (eg, flattening of the nasolabial fold on 1 side compared to the other, mild asymmetry

of the palpebral fissures or of the face as the patient smiles) may be sought. The shoulder is adducted; the elbow is flexed; the forearm is pronated, and the wrist and fingers are flexed. In the lower extremities, the only indication of paresis may be that the ball of the patient's shoe may be worn more on the affected side.

In severe cases, the hand may be clenched; the knee is held in extension and the ankle is plantar flexed, making the paralyzed leg functionally longer than the other. The patient therefore has to circumduct the affected leg to ambulate.

In hemiplegic patients in whom all the paralysis is on the same side of the body, the lesion is of the contralateral upper motor neuron. In most cases, the lesion lies in the cortical, subcortical, or capsular region (therefore above the brainstem). In the alternating or crossed hemiplegias, CN paralysis is ipsilateral to the lesion, and body paralysis is contralateral. In such cases, CN paralysis is of the lower motor neuron type, and the location of the affected CN helps determine the level of the lesion in the brainstem. Therefore, paralysis of CN III on the right side and body paralysis on the left (Weber syndrome) indicates a midbrain lesion, whereas a lesion of CN VII with crossed hemiplegia (Millard-Gubler syndrome) indicates a pontine lesion, and CN XII paralysis with crossed hemiplegia (Jackson syndrome) indicates a lower medullary lesion.

**Ataxic gait**

In ataxia, the patient spreads his or her legs apart to widen the base of support to compensate for the imbalance while standing or walking. In severe cases, patients stagger as they walk. The heel-to-toe or tandem walking maneuvers and standing on 1 leg uncover subtle forms of ataxia. Ataxia results from midline lesions of the cerebellum and may be isolated or associated with other cerebellar findings (see Cerebellar signs). When the lesion is unilateral, the patient may veer to the side of the lesion. With bilateral cerebellar involvement, the patient may fall to either side.

**Shuffling gait**

The individual takes short steps to the point of practically not moving forward or making little progress. In other words, the patient appears to shuffle his or her legs rather than put them forward. In some patients, the steps (albeit short) and pace may vary with a tendency for the patient to accelerate (festinating gait) as he or she walks. Both types are seen in Parkinson disease and may be associated with other extrapyramidal signs.

**Steppage gait**

In steppage (high-stepping, slapping), the individual takes high steps as if climbing a flight of stairs while walking on a level surface. This peculiar gait pattern results from the patient trying to avoid injury to the feet (from dragging them) by stepping high. However, as the patient puts the feet down 1 by 1, they slap the ground, hence the description of a foot-slapping gait. This is 1 condition that can be diagnosed even before the patient enters the room because the sound is so characteristic.

Steppage gait is seen in chronic peripheral neuropathies and can be the result of the functional elongation of the legs due to bilateral drop foot.

**Spastic or scissor gait**

In this condition, the legs are held in adduction at the hip and the thighs rub against each other as the patient walks. Spasm of the inner thigh muscles also occurs. If the spasm is severe, with each advancing step the knees tend to slide over each other like the blades of a pair of scissors. This is typically seen in cerebral diplegia, a form of cerebral palsy.

**Antalgic gait**

Patient favors the affected painful (usually lower) extremity and walks, putting weight on the normal leg. The hand held over hip on the affected side is typical in patients with radicular pain.

**Speech**

Speech enables communication between individuals. Abnormalities include dysphonia, dysarthria, and dysphasia or aphasia.

**Dysphonia or aphonia**

Dysphonia is the impairment or inability to phonate. As a result, the voice becomes hoarse. In extreme cases, it is absent, and the patient is mute.

The most frequent cause of this problem is the common cold, which results in dysphonia due to inflammation of the larynx. Dysphonia may also occur in patients with hypothyroidism, as a result of thickening of the vocal cords from amyloid deposits. Neurologic causes include unilateral recurrent laryngeal nerve paralysis and lesions of the vagus nerve. Intermittent hoarseness may affect patients with vagus nerve stimulator implants, which are used for the treatment of certain medically intractable forms of epilepsy (MIE) and pharmacoresistent depression (PRD).

**Dysarthria or anarthria**

Dysarthria is the inability to articulate spoken words. The quality of oration is impaired, but the content remains intact (eg, slurred speech). The patient's ability to understand and synthesize speech remains intact. It results from paralysis of pharyngeal, palatal, lingual, or facial musculature. It also is observed with cerebellar lesions and/or disease (eg, scanning or staccato speech).

**Dysphasia or aphasia**

In dysphasia, the ability to process language is impaired, resulting in an inability to understand (ie, receptive or sensory or Wernicke aphasia), transfer signals from the Wernicke to the Broca area (ie, conduction aphasia), or properly execute speech (ie, expressive, motor, or Broca aphasia). The combination of Broca and Wernicke aphasias is referred to as global aphasia.

**Mental status**

Mental status evaluation includes testing of memory, orientation, intelligence, and the other aspects of the patient's psychic state. Only the first 3 are discussed here. When overt symptoms or signs of a psychic disturbance are present, psychiatric evaluation should be considered.

**Memory**

Memory is the ability to register and recall prior sensory input. Recent and remote memory functions are differently affected depending on the disease process. Remote memory is relatively

preserved in chronic dementing processes, with major disturbances in the attention span and recent memory. On the contrary, all aspects of memory are impaired in acute encephalopathies.

**Orientation**

Orientation is an individual's cognitive sense of his status in time, place, and person. These functions are affected in the same order as they are in organic disease. In other words, the sense of time is first to be impaired in organic dysfunction, and the sense of person is the last to be lost. However, the order may be disturbed in psychological dysfunction.

A patient who does not know who he or she is, but at the same time can tell the time and is oriented in place, is more likely to have a psychological disturbance than to have an organic etiology for the condition. Nonetheless, rare cases of isolated amnesia have been reported.

**Intelligence**

Intelligence is the ability to quickly and successfully apply previous knowledge to a new situation and to use reason in solving problems. Vocabulary, fund of knowledge, calculations (eg, serial-7 calculations), abstraction (eg, use of proverbs), and judgment (eg, what to do with a found wallet) are good indicators of intelligence.

**Psychological disturbances**

A brief survey of the other aspects of psychological function may be helpful in revealing abnormalities of thought process (eg, circumstantiality and tangentiality); of perception (eg, illusions and hallucination); or of thought content (eg, delusions of grandeur). Patients with these findings should be referred for appropriate evaluation.

**Examination of the Cranial Nerves**

Of the 12 CNs, some are named according to their function. Examples of these are the olfactory (smell), optic (vision), oculomotor (eye movements), abducens (abduction of the eye), facial (facial expression), and vestibulocochlear or statoacoustic (hearing and balance) nerves. Others are named for their relationship to neighboring structures (trochlear nerve), appearance (trigeminal nerve), extent of distribution (vagus nerve), composition (spinal accessory nerve), or location (hypoglossal nerve).

Trochlear: Its midsection extends over a trochlea or pulley to reach its insertion on the inferior aspect of the globe.

Trigeminal: The nerve divides into 3 divisions distal to the Gasserian ganglion.

Vagus: The vagabond or wanderer, it travels long distances in the body.

Spinal accessory: This nerve is composed of rootlets from the spinal cord in addition to its medullary component.

Hypoglossal: Its course is sublingual in the neck.

Knowing the names of the CNs makes it easy to remember their function, thereby making their examination self-evident. The following mnemonic is helpful in recalling the names of the CNs: Oh, oh, oh; to trek and feel a great valley; ah! ha! Another is this: On old Olympus towering tops, a Finn and German viewed some hops.

**Olfactory nerve - CN I**

The olfactory nerves consist of small unmyelinated axons that originate in the olfactory epithelium in the roof of the nasal cavity; they pierce the cribriform plate of the ethmoid and terminate in the olfactory bulb. Lesions of the nerve result in parosmia (altered sense of smell) or anosmia (loss of smell).

The common cold is the most frequent cause of dysfunction. Dysfunction can be associated with fractures of the cribriform plate of the ethmoid bone. Frontal lobe tumors may compress the olfactory bulb and/or tracts and cause anosmia, but this is rare occurrence.

Olfactory function is tested easily by having the patient smell common objects such as coffee or perfume. Commercially available scented scratch papers may also be used.

**Optic nerve - CN II**

The optic nerve is a collection of axons that relay information from the rods and cones of the retina. The temporal derivations reach the ipsilateral and the nasal derivations the contralateral superior colliculi and the lateral geniculate bodies. From there, axons extend to the calcarine cortex by means of the optic radiation, traversing the temporal (Myer loop) and parietal lobes. Fibers responsible for the pupillary light reflex bypass the geniculate body and reach the pretectal area, from where they innervate the parasympathetic (midline) portion of the third-nerve nucleus, enabling the consensual pupillary reflex.

The following testing is appropriate:

Acuity, by using the Snellen chart (near and distant vision)

Visual fields, by means of confrontation or perimetry if indicated

Color, with use of an Ishihara chart or by using common objects, such as a multicolored tie or color accent markers

Funduscopy

Lesions of the visual pathways result in blindness and pupillary abnormalities, such as the Marcus-Gunn pupil (retinal or optic nerve disease), scotomata, quadrant or hemianopsias (optic tract and radiation), and hemianopsias with macular sparing (calcarine cortex).

**Oculomotor nerve - CN III**

The oculomotor nucleus of the nerve is located in the midbrain and innervates the pupillary constrictors; the levator palpebrae superioris; the superior, inferior, and medial recti; and the inferior oblique muscles. Lesions of CN III result in paralysis of the ipsilateral upper eyelid and pupil, leaving the patient unable to adduct and look up or down. The eye is frequently turned out (exotropia). In subtle cases, patients complain of only diplopia or blurred vision. Lesions at the nucleus of the third nerve cause bilateral ptosis, in addition to the findings mentioned above. The exotropia seen in CN III paralysis can be distinguished from that in internuclear ophthalmoplegia because in the latter convergence is preserved.

Paralysis of CN III is the only ocular motor nerve lesion that results in diplopia in more than 1 direction, distinguishing itself from CN IV paralysis (which also can result in exotropia).

Pupillary involvement is an additional clue to involvement of CN III. Pupil-sparing CN III

paralysis occurs in diabetes mellitus, vasculitides of various etiologies, and certain brainstem lesions such as due to multiple sclerosis.

**Trochlear nerve - CN IV**

The nucleus of the nerve is located in the midbrain. It innervates the superior oblique muscle, which incycloducts and infraducts the eye. Trochlear nerve typically allows a person to view the tip of his or her nose.

An isolated right superior oblique paralysis results in exotropia to the right (R), double vision that increases on looking to the (L), and head tilt to the right (R). The mnemonic is R, L, R (ie, the marching rule). The rule is L, R, L for left superior oblique paralysis. This rule and the lack of ptosis and/or pupillary involvement allow easy distinction of the exotropia of CN IV paralysis from that seen in CN III paralysis.

**Trigeminal nerve - CN V**

The nucleus of the nerve stretches from the midbrain (ie, mesencephalic nerve) through the pons (ie, main sensory nucleus and motor nucleus) to the cervical region (ie, spinal tract of the trigeminal nerve). It provides sensory innervation for the face and supplies the muscles of mastication.

Paralysis of the first division (ophthalmic; V1) is usually seen in the superior orbital fissure syndrome and results in sensory loss over the forehead along with paralysis of CN III and CN IV. Paralysis of the second division (maxillary; V2) results in loss of sensation over the cheek and is due to lesions of the cavernous sinus; it also results in additional paralysis of V1, CN III and CN IV. Isolated V2 lesions result from fractures of the maxilla. Complete paralysis of CN V results in sensory loss over the ipsilateral face and weakness of the muscles of mastication. Attempted opening of the mouth results in deviation of the jaw to the paralyzed side.

**Abducens nerve - CN VI**

The nucleus of the nerve is located in the paramedian pontine region in the floor of the fourth ventricle. It innervates the lateral rectus, which abducts the eye. Isolated paralysis results in esotropia and inability to abduct the eye to the side of the lesion. Patients complain of double vision on horizontal gaze only. This finding is referred to as horizontal homonymous diplopia, which is the sine qua non of isolated CN VI paralysis. Paralysis of CN VI may result from increased intra cranial pressure without any lesion in the neuraxis, and it may result in false localization if one is not aware of it.

**Facial nerve - CN VII**

The nucleus of the nerve lies ventral, lateral, and caudal to the CN VI nucleus; its fibers elevate the floor of the fourth ventricle (facial colliculus) as they wind around the CN VI nucleus. The nerve leaves the cranial cavity through the stylomastoid foramen and innervates the muscles of facial expression and the stapedius.

Although it is considered a pure motor nerve, it also innervates a small strip of skin of the posteromedial aspect of the pinna and around the external auditory canal. The nervus intermedius of Wrisberg conducts taste sensation from the anterior two thirds of the tongue and supplies

autonomic fibers to the submaxillary and sphenopalatine ganglia, which innervate the salivary and lacrimal glands.
A lower-motor-neuron lesion of the nerve, also known as peripheral facial paralysis, results in complete ipsilateral facial paralysis; the face draws to the opposite side as the patient smiles. Eye closure is impaired, and the ipsilateral palpebral fissure is wider. In an upper motor neuron lesion, also known as central facial paralysis, only the lower half of the face is paralyzed. Eye closure is usually preserved. In peripheral facial paralysis, different types of clinical presentations are seen with nerve lesions at 4 levels, as described below.
Lesions of the meatal or canalicular segment: Facial paralysis with hearing loss (without hyperacusis) and loss of taste in the anterior two thirds of the tongue imply lesions in the internal auditory canal from fracture of the temporal bone or at the cerebellopontine angle from compression by a tumor.
Lesions of the labyrinthine or fallopian segment
Lesions that spare hearing (with hyperacusis) indicate lesions further down the course of the nerve.
Loss of taste in the anterior two thirds of the tongue and loss of tearing imply lesions that involve the chorda tympani and the secretomotor fibers to the sphenopalatine ganglion in the labyrinthine segment, proximal to the greater superficial petrosal nerve.
With lesions distal to the greater superficial petrosal nerve, lacrimation is normal but hyperacusis is still present. Geniculate lesions in this segment cause pain in the face.
Lesions of the horizontal or tympanic segment: The lesion is proximal to the departure of the nerve to the stapedius and results in hyperacusis, loss of taste in the anterior two thirds of the tongue, and facial motor weakness.
Lesions of the mastoid or vertical segment: Hyperacusis is present if the lesion is proximal to the nerve to the stapedius. It is absent if the lesion is distal to the nerve to the stapedius, and only loss of taste and facial paralysis occur. If the lesion is beyond the chorda tympani in the vertical segment (as in lesions of the stylomastoid foramen), taste is spared and only facial motor paralysis is seen.

**Vestibulocochlear nerve - CN VIII**

The vestibulocochlear or statoacoustic nerve enters the brainstem at the pontomedullary junction and contains the incoming fibers from the cochlea and the vestibular apparatus, forming the eighth CN. It serves hearing and vestibular functions, each of which is described separately.
Hearing loss may be conductive or sensorineural. Three tests help in evaluating the auditory component of the nerve.
The Weber test involves holding a vibrating tuning fork against the forehead in the midline. The vibrations are normally perceived equally in both ears because bone conduction is equal. In conductive hearing loss, the sound is louder in the abnormal ear than in the normal ear. In sensorineural hearing loss, lateralization occurs to the normal ear. The sensitivity of the test can

be increased (up to 5 dB) by having the patient block his or her external ear canals by simultaneously pressing the index fingers at the introit.
To perform the Rinne test, the vibrating tuning fork is placed over the mastoid region until the sound is no longer heard. It is then held at the opening of the ear canal on the same side. A patient with normal hearing should continue to hear the sound. In conductive hearing loss, the patient does not continue to hear the sound, since bone conduction in that case is better than air conduction. In sensorineural hearing loss, both air conduction and bone conduction are decreased to a similar extent.
In the Schwabach test, the patient's hearing by bone conduction is compared with the examiner's hearing by placing the vibrating tuning fork against the patient's mastoid process and then to the examiner's. If the examiner can hear the sound after the patient has stopped hearing it, then hearing loss is suspected.
The vestibular portion of the nerve enters the brainstem along with the cochlear portion. It transmits information about linear and angular accelerations of the head from the utricle, saccule, and semicircular canals of the membranous labyrinth to the vestibular nucleus. Linear acceleration is monitored by the macules in the utricles and saccules; angular acceleration is monitored by the cristae contained in the ampullae in the semicircular canals. These signals reach the superior (Bechterew), lateral (Deiters), medial (Schwalbe), and inferior (Roller) nuclei and project to the pontine gaze center through the medial longitudinal fasciculus; to the cervical and upper thoracic levels of the spinal cord through the medial vestibulospinal tract; to the cervical, thoracic, and lumbosacral regions of the ipsilateral spinal cord through the lateral vestibulospinal tract; and to the ipsilateral flocculonodular lobe, uvula, and fastigial nucleus of the cerebellum through the vestibulocerebellar tract.
The Romberg test is performed to evaluate vestibular control of balance and movement. When standing with feet placed together and eyes closed, the patient tends to fall toward the side of vestibular hypofunction. When asked to take steps forward and backward, the patient progressively deviates to the side of the lesion. Results of the Romberg test may also be positive in patients with polyneuropathies, and diseases of the dorsal columns, but these individuals do not fall consistently to 1 side as do patients with vestibular dysfunction.
Another test is to ask the patient to touch the examiner's finger with the patient's hand above the head. Consistent past pointing occurs to the side of the lesion. Provocative tests include the Nylen-Bárány test and caloric testing (see Ancillary signs).

**Glossopharyngeal nerve - CN IX**

The nucleus of the nerve lies in the medulla and is anatomically indistinguishable from the CN X and CN XI nuclei (nucleus ambiguous). Its main function is sensory innervation of the posterior third of the tongue and the pharynx. It also innervates the pharyngeal musculature, particularly the stylopharyngeus, in concert with the vagus nerve.
Vascular stretch afferents from the aortic arch and carotid sinus, as well as chemoreceptor signals from the latter, travel in the nerve of Herring to join the glossopharyngeal nerve; they

reach the nucleus solitarius, which in turn is connected to the dorsal motor nucleus of the vagus and plays a part in the neural control of blood pressure.

Lesions affecting the glossopharyngeal nerve result in loss of taste in the posterior third of the tongue and loss of pain and touch sensations in the same area, soft palate, and pharyngeal walls. CN IX and CN X travel together, and their clinical testing is not entirely separable. Therefore, examination of CN IX is discussed with that of the vagus nerve.

**Vagus nerve - CN X**

Starting in the nucleus ambiguous, the vagus nerve has a long and tortuous course providing motor supply to the pharyngeal muscles (except the stylopharyngeus and the tensor veli palati), palatoglossus, and larynx. Somatic sensation is carried from the back of the ear, the external auditory canal, and parts of the tympanic membrane, pharynx, larynx, and the dura of the posterior fossa. It innervates the smooth muscles of the tracheobronchial tree, esophagus, and GI tract up to the junction between the middle and distal third of the transverse colon.

The vagus provides secretomotor fibers to the glands in the same region and inhibits the sphincters of the upper GI tract. Along with visceral sensation from the same region, the nerve participates in vasomotor regulation of blood pressure by carrying the fibers of the stretch receptors and chemoreceptors (ie, aortic bodies) of the aorta and providing parasympathetic innervation to the heart.

The pharyngeal gag reflex (ie, tongue retraction and elevation and constriction of the pharyngeal musculature in response to touching the posterior wall of the pharynx, tonsillar area, or base of the tongue) and the palatal reflex (ie, elevation of the soft palate and ipsilateral deviation of the uvula on stimulation of the soft palate) are decreased in paralysis of CN IX and CN X. In unilateral CN IX and CN X paralysis, touching these areas results in deviation of the uvula to the normal side.

Unilateral paralysis of the recurrent laryngeal branch of CN X results in hoarseness of voice. Bilateral paralysis results in stridor and requires immediate attention to prevent aspiration and its attendant complications.

**Spinal accessory nerve - CN XI**

From the nucleus ambiguous, the spinal accessory nerve joins the vagus nerve in forming the recurrent laryngeal nerve to innervate the intrinsic muscles of the larynx. The spinal portion of the nerve arises from the motor nuclei in the upper 5 or 6 cervical segments, enters the cranial cavity through the foramen magnum, and exits through the jugular foramen, and provides motor innervation to the sternocleidomastoid (SCM) and the mid and upper thirds of the trapezius.

In testing, functional symmetry of the SCM and the trapezius muscles should be evaluated. Have the patient push the face against resistance to the right and to the left. When the right SCM is weak, pushing to the opposite (ie, left) side is impaired, and vice versa. Shrugging of the shoulder is impaired ipsilaterally when the trapezius is weak.

**Hypoglossal nerve - CN XII**

The nucleus of this nerve lies in the lower medulla, and the nerve itself leaves the cranial cavity through the hypoglossal canal (anterior condylar foramen). It provides motor innervation for all the extrinsic and intrinsic muscles of the tongue except the palatoglossus. To test the hypoglossal nerve, have the patient protrude the tongue; when paralyzed on 1 side, the tongue deviates to the side of paralysis on protrusion.

Examination of the Sensory and Motor Systems

Sensory system

**Noncortical sensory system**

This is constituted by the peripheral nerves with their central pathways to the thalamus. Light touch, pain, heat, cold, and vibration sensations can be included in this group.

Light touch is tested by touching the skin with a wisp of cotton or tissue. Pain is tested by using a sharp object such as an open safety pin. Temperature can be tested by touching the patient's skin with 2 test tubes, 1 with warm water and the other with cold water. Compare the 2 sides and also to a benchmark, such as the patient's own forehead (assuming sensation there is normal).

Vibration is tested with a tuning fork, preferably with a frequency of 128 Hz. Compare findings on the 2 sides, and also compare findings with those in the same body part of the examiner.

**Cortical sensory system**

The cortical sensory system includes the somatosensory cortex and its central connections. This system enables the detection of the position and movement of the extremities in space (ie, kinesthetic sensation), size and shape of objects (ie, stereognosis), tactile sensations of written patterns on the skin (ie, graphesthesia), and tactile localization and tactile discrimination on the same side or both sides of the body.

Position sensation is tested with the patient's eyes closed. The examiner moves various joints, being sure to hold the body part in such a way that the patient may not recognize movement simply from the direction in which the patient may feel the pressure from the examiner's hand.

Stereognosis is tested by placing some familiar object (eg, ball, cube, coin) in the patient's hand while his or her eyes are closed and asking the patient to identify the object. Inability to recognize the size or shape is referred to as astereognosis. Agraphesthesia is the inability to recognize letters or numbers written on the patient's skin. These abilities are impaired in lesions of the right parietal region.

Motor system

**Trophic state**

Assess the 3 *S* s: size, shape, and symmetry of a muscle. Atrophy, hypertrophy, or abnormal bulging or depression in a muscle is an important diagnostic finding in the presence of different muscle diseases or abnormalities. Hypertrophy occurs with commensurate strength from use and exercise; on the other hand, hypertrophy with weakness is seen commonly in Duchenne muscular dystrophy. The shape may also be altered when the muscle or tendon is ruptured.

**Muscle tone**

Muscle tone is the permanent state of partial contraction of a muscle and is assessed by passive movement. The muscle may be hypotonic or hypertonic. Hypotonia is defined as decreased tone and may be seen in lower motor neuron lesions, spinal shock, and some cerebellar lesions. Hypertonia may manifest as spasticity or rigidity.

Pyramidal lesions result in spasticity that may manifest as a clasp-knife phenomenon (ie, resistance to passive movement with sudden giving way, usually toward the completion of joint flexion or extension). Bilateral frontal lobe lesions may result in paratonia or *gegenhalten* (German for against-stop), in which resistance increases throughout flexion and extension. Rigidity refers to increased tone associated with extrapyramidal lesions; it may result in a cogwheel (stepwise) or lead-pipe (uniform) resistance to passive movement.

**Muscle strength**

Use this muscle-strength scale when assessing and documenting muscle strength

Muscle-Strength Scale

| Score | Description |
|---|---|
| 0 | Absent voluntary contraction |
| 1 | Feeble contractions that are unable to move a joint |
| 2 | Movement with gravity eliminated |
| 3 | Movement against gravity |
| 4 | Movement against partial resistance |
| 5 | Full strength |

**Involuntary movements**

Involuntary movements include fibrillations, fasciculations, asterixis, tics, myoclonus, dystonias, chorea, athetosis, hemiballismus, and seizures.

Fibrillations are not visible to the naked eye except possibly those in the tongue.

Fasciculations may be seen under the skin as quivering of the muscle. Although fasciculations are typically benign (particularly when they occur in the calf), if widespread, they can be associated with neuromuscular disease, including amyotrophic lateral sclerosis (ALS).

Asterixis can be elicited by having the patient extend both arms with the wrists dorsiflexed and palms facing forward and eyes closed. Brief jerky downward movements of the wrist are considered a positive sign. Asterixis is commonly seen with metabolic encephalopathies.

Tics are involuntary contractions of single muscles or groups of muscles that result in stereotyped movements. Gilles de la Tourette syndrome can manifest with multiple tics and elaborate, complex movements and vocalizations.

Myoclonus, as the word implies, is a muscle jerk; it is a brief (<0.25 seconds), generalized body-jerk, which is sometimes asymmetric. These occur alone or in association with various primarily generalized epilepsies.

Dystonias are muscle contractions that are more prolonged than myoclonus and result in spasms. Examples include blepharospasm, spasmodic torticollis, oromandibular dystonia, spasmodic dysphonia, and writer's cramp.

In athetosis, the spasms have a slow writhing character and occur along the long axis of the limbs or the body itself; the patient may assume different and often peculiar postures.

The term chorea means dance. Quasi-purposeful movements affect multiple joints with a distal preponderance.

Hemiballismus is a violent flinging movement of half of the body. It is associated with lesions of the subthalamic nucleus (ie, body of Louis).

Seizures may result in orofacial or appendicular automatisms, repeated eye blinks, or tonic or clonic motor activity.

**Examination of Reflexes, Cerebellum, and Meninges**

**Reflexes**

The different reflex responses may be grouped into 3 categories on the basis of their clinical significance.

**Primitive reflexes**

These include the glabellar tap, rooting, snout, sucking, and palmomental reflexes. As a rule, these signs are generally absent in adults. When present in the adult, these signs signify diffuse cerebral damage, particularly of the frontal lobes (hence the term frontal-lobe release signs).

**Superficial reflexes**

These are segmental reflex responses that indicate the integrity of cutaneous innervation and the corresponding motor outflow. These include the corneal, conjunctival, abdominal, cremasteric, anal wink, and plantar (Babinski) reflexes.

The corneal and conjunctival reflexes may be elicited by gently touching the appropriate structure with a sterile wisp of cotton. The normal response is bilateral winking. Absence of such a response implies CN V paralysis. Blinking of only 1 eye suggests weakness of CN VII on the side that does not wink.

The abdominal reflex can be elicited by drawing a line away from the umbilicus along the diagonals of the 4 abdominal quadrants. A normal reflex draws the umbilicus toward the direction of the line that is drawn.

The cremasteric reflex is elicited by drawing a line along the medial thigh and watching the movement of the scrotum in the male. A normal reflex results in elevation of the ipsilateral testis.

The anal wink reflex is elicited by gently stroking the perianal skin with a safety pin. It results in puckering of the rectal orifice owing to contraction of the corrugator-cutis-ani muscle.

The best known of this group of reflexes is the plantar reflex. This reflex may be elicited in several ways, each with a different eponym. The most commonly performed maneuver is stroking the lateral aspect of the sole with a sharp object. The normal response is plantar flexion of the great toe, which is considered an absent (negative) Babinski sign. Dorsiflexion of the great toe (Babinski sign present) suggests an upper motor neuron lesion and also is referred to as a

positive Babinski sign. Dorsiflexion of the big toe also may be associated with fanning out of the other toes, as detailed in Babinski's original description, but most neurologists consider this an unnecessary accompaniment of an abnormal response.

Flexion of the knee and hip may occur in the paretic leg with urinary and fecal incontinence. This is referred to as the en-mass reflex. Lack of either response may indicate absence of cutaneous innervation in the S1 segment or loss of motor innervation in the L5 segment ipsilaterally.

**Deep tendon reflexes**

These are monosynaptic spinal segmental reflexes. When they are intact, integrity of the following is confirmed: cutaneous innervation, motor supply, and cortical input to the corresponding spinal segment.

These reflexes include the biceps, brachioradialis, triceps, patellar, and ankle jerks. The musculocutaneous nerve supplies the biceps muscle. The radial nerve supplies the brachioradialis and triceps. The femoral nerve supplies the quadriceps femoris, which enables the knee jerk, and the tibial nerve supplies the gastrocnemius and the soleus.

Spinal roots that subserve these reflexes are listed below.

Muscles and Spinal Roots

| Muscle | Spinal Roots |
|---|---|
| Biceps | C5,6 |
| Brachioradialis | C6 |
| Triceps | C7 |
| Patellar | L2-4 |
| Achilles | S4 |

On occasion, these root numbers are offset by 1 when the cervical and/or lumbosacral plexuses are prefixed or postfixed.

Several systems for reflex grading exist. An example is provided below.

Reflex-Grading System

| Score | Reflexes |
|---|---|
| 0 | Absent |
| 1 | Hypoactive or present only with reinforcement |
| 2 | Readily elicited with a normal response |
| 3 | Brisk with or without evidence of spread to the neighbouring roots |
| 4 | Associated with a few beats of unsustained clonus |
| 5 | Sustained clonus |

**Cerebellar signs**

The cerebellum provides an important feedback loop for coordination of muscle activity by integrating the functions of the cortex, basal ganglia, vestibular apparatus, and spinal cord. Midline cerebellar dysfunction results in ataxia of gait, difficulty in maintenance of upright posture, and truncal ataxia. Acute neocerebellar hemispheric lesions result in additional signs.
The following are various cerebellar signs:
Ataxia, atonia, and asthenia
Intention tremor
Dyssynergia (incoordination)
Dysmetria
Dysrhythmia
Dysdiadochokinesis
Dysarthria (staccato or scanning speech)
Gait is tested by having the patient walk normally and in tandem. In the latter, the patient is asked to walk with 1 foot immediately in front of the other (ie, heel to toe). A tendency to sway or fall to 1 side indicates ataxia, suggesting ipsilateral cerebellar dysfunction. Atonia and asthenia can occur in other lesions of the nervous system and are not specific to the cerebellum; their testing is described elsewhere.
Intention tremor refers to an oscillating tremor that accelerates in pace on approaching the target.
Dyssynergia or incoordination results in loss of smoothness of execution of a motor activity.
Dysmetria results in overshooting or undershooting of a target while attempting to reach an object. All 3 of these can be elicited by having the patient attempt to touch alternately his or her nose and the examiner's finger.
Dysrhythmia refers to the inability to tap and keep a rhythm. It can be tested by tapping the table with a hand (or the floor with a foot) and asking the patient to repeat the maneuver.
Dysdiadochokinesis is the inability to perform rapid alternating movements; it can be tested by asking the patient to tap 1 hand on the other (or on the thigh) repeatedly while simultaneously pronating and supinating the hand. Various combinations of the above signs appear, depending on the extent and location of the lesion in the cerebellum.
Dysarthria is usually a sign of diffuse involvement of the cerebellum. It is characterized by poor modulation of the volume and pitch of the speech, causing oscillations of these 2 qualities.

**Meningeal signs**

Signs of meningeal irritation indicate inflammation of the dura; these signs are described below.
Nuchal rigidity or neck stiffness is tested by placing the examiner's hand under the patient's head and gently trying to flex the neck. Undue resistance implies diffuse irritation of the cervical nerve roots from meningeal inflammation.
The Brudzinski sign is flexion of both knees during the maneuver to test nuchal rigidity. This indicates diffuse meningeal irritation in the spinal nerve roots.
The Kernig sign is elicited by flexing the hip and knee on 1 side while the patient is supine, then extending the knee with the hip still flexed. Hamstring spasm results in pain in the posterior

thigh muscle and difficulty with knee extension. With severe meningeal inflammation, the opposite knee may flex during the test.

The Lasègue or straight-leg raising (SLR) sign is elicited by passively flexing the hip with the knee straight while the patient is in the supine position. Limitation of flexion due to hamstring spasm and/or pain indicates local irritation of the lower lumbar nerve roots. Reverse SLR is elicited by passively hyperextending the hip with the knee straight while the patient is in the prone position. Limitation of extension due to spasm and/or pain in the anterior thigh muscles indicates local irritation of the upper lumbar-nerve roots.

System Survey and Ancillary Signs

System survey

**Autonomic nervous system**

Autonomic dysfunction results in abnormalities in the following: sweating, skin temperature, cyanosis or pallor, trophic changes of skin or nails, and postural changes in blood pressure. Observation (and any necessary additional testing) easily demonstrates the presence or absence of these signs. Understanding these signs helps the examiner assess the patient's neurologic condition.

**Neurovascular system**

The following may be tested by palpation of the pulses and use of appropriate instruments:

Brachial plexus and bilateral blood pressures

Cranial and peripheral pulses

Arterial bruits

**Neurocutaneous system**

Several neurologic conditions have telltale cutaneous stigmata. Evaluation for the following can provide valuable diagnostic clues: loss of skin pigmentation as in vitiligo, white hair-lock in Vogt-Harada-Koyanagi disease, cutaneous tumors or ash-leaf spots in tuberous sclerosis, and cutaneous eruptions over a dermatome which may signify herpes zoster.

Coffee-brown pigmented (ie, caf é; au lait) spots of varying sizes, usually greater than 1.5 cm in diameter, and axillary freckling are seen in neurofibromatosis. These are observed in addition to or in the absence of the characteristic blubbery subcutaneous tumors that give the condition its name.

Tufts of hair (satyr's tail), dimples, and large moles along the spine may indicate spina bifida occulta or diastematomyelia of the spinal column.

**Skeletal system - Cranium, spine, bones, joints**

Palpation of the skull can reveal congenital anomalies that may indicate underlying abnormalities of the brain. In cephaloplegia, one half of the skull may be smaller than the other, possibly signifying asymmetric brain development. Microcephaly or macrocephaly may be detected by measuring the circumference of the head. Observation of the spine may reveal the presence of myelomeningocele, scoliosis, and/or kyphosis. In cases of prenatal brain injuries, the length of the long bones may be reduced on the side opposite the cephaloplegia.

Trophic changes in the joints can be associated with denervation in tabes dorsalis or Charcot-Marie-Tooth (CMT) disease. The distal muscular atrophy seen in CMT disease gives the legs the appearance of inverted champagne bottles. Muscular atrophy seen in the region of the temporalis muscles and facial musculature associated with frontal balding is typical of myotonic dystrophy. Pes cavus deformity can be associated with spina bifida and other spinal dysraphisms. A young person with mental retardation, genu valgum, pes cavus, and stroke may have homocystinuria, an inborn error of metabolism typically associated with mental retardation (usually severe) and intimal thickening and necrosis of the media of blood vessels, resulting in strokes and coronary artery disease.

Ancillary signs

**Anisocoria**

This refers to pupillary asymmetry, which may result from sympathetic or parasympathetic dysfunction. Sympathetic dysfunction results in Horner syndrome, in which the pupil is small but reacts to light. Hippus, a series of oscillating pupillary contractions seen in response to light, is a benign condition. Argyll-Robertson pupil, seen in neurosyphilis, is irregular and small; it does not react to light, but does accommodate.

In parasympathetic paralysis, the affected pupil is larger and reacts poorly or not at all to light. Injury to the ciliary ganglion or short ciliary nerves results in a tonic pupil, which is large and has slow or absent reaction to light. A benign form of tonic pupil is seen in Adie syndrome, Holmes-Adie syndrome (ie, tonic pupil with absent patellar and Achilles reflexes), and Ross syndrome (ie, tonic pupil with hyporeflexia and progressive segmental hypohidrosis).

**Anosognosia**

This refers to denial of illness and typically is seen in patients with right frontoparietal lesions, resulting in left hemiplegia that the patient denies. A form of visual anosognosia (Anton syndrome) is seen in patients with bilateral occipital lobe infarctions; these patients with double hemianopsia (bilateral cortical blindness) deny that they are blind.

**Asterixis**

This is seen in patients with metabolic encephalopathies. Momentary loss of tone and flapping of the hand are seen when the patient extends his arms in front with the wrists dorsiflexed.

**Ataxia**

Heel-to-toe tandem gait is tested by asking the patient to walk with 1 foot directly in front of the other. Ataxia can be demonstrated in this manner.

**Beevor sign**

This is seen with bilateral lower abdominal paralysis that results in upward deviation of the umbilicus when the patient tries to raise his head and sit up from the supine, recumbent position.

**Benediction hand**

This is seen with lesions of the median nerve in the axilla and upper arm. When present, the index finger remains straight and the middle finger partially flexes when the patient tries to make a fist (assuming the position of the hand of a clergyman while saying the benediction).

**Bielschowsky sign**
This refers to increasing separation of the images seen when a patient's head is tilted toward the side of a superior oblique (trochlear nerve) paralysis. This sign by itself is not diagnostic and should be used only as a supplement to other tests in suspected CN IV paralysis.
**Chvostek sign**
This is seen in hypocalcemia. Tapping the cheek at the angle of the jaw precipitates tetanic facial contractions.
**Cogan sign**
This is seen in myasthenia gravis. It refers to transient baring of the sclerae above the cornea as the patient resumes the primary eye position after looking down.
**Dalrymple sign**
This refers to the upper-lid retraction seen in thyroid ophthalmopathy.
**Doll's-eye maneuver**
This refers to turning the head passively with the patient awake and fixated or when the patient is in a coma. In the former, the eyes remain fixated at the original focus when all gaze pathways are normal; in the latter, the eyes deviate in the opposite direction when the brainstem is intact.
**Gower sign**
This sign, seen in severe myopathies, occurs when the patient attempts to stand up from the floor. Patients first sit up, then assume a quadrupedic position, and then climb up their own legs by using their arms to push themselves up.
**Heterochromia iridis**
This term refers to the difference in color of the 2 irides. It indicates early injury to the sympathetic system. Ipsilateral to the injury the iris is blue or green, while the contralateral iris is darker.
**Jaw jerk**
This is elicited by placing the examiner's index finger on the patient's lower jaw and then striking it with the reflex hammer. An exaggerated reflex indicates the presence of a pontine lesion. When the rest of the examination findings are normal, it may indicate physiologic hyperreflexia.
**Kayser-Fleischer ring**
This is a brownish ring around the limbus of the cornea. It is best demonstrated during an ophthalmologic slitlamp examination.
**Lhermitte sign**
This refers to the sensation of electricity associated with cervical spinal cord lesions during passive or active flexion and extension of the neck. Once considered pathognomonic of multiple sclerosis, it simply is the result of electricity generation by the hypersensitive, demyelinated, or injured spinal cord; this sign can be associated with any lesion in or around the cord.
**Marcus-Gunn pupil**
This sign requires a swinging-flashlight test to assess. As the flashlight swings from 1 eye to the other, the abnormal pupil dilates as the light swings back from the normal side. No anisocoria is

seen. The phenomenon is also called a paradoxical pupillary reflex and indicates an afferent (optic nerve) pupillary defect.

**Milkmaid's grip**

This refers to the inability to maintain a sustained grip commonly seen in patients with chorea.

**Moebius sign**

This refers to weakness of ocular convergence (associated with proptosis) seen in dysthyroid ophthalmopathy.

**Myerson sign**

Patients with Parkinson disease, particularly those with bilateral frontal lobe dysfunction, continue to blink with repeated glabellar taps.

**Nylen-Bárány sign**

This is elicited by having the patient quickly lie down from the sitting position with the head turned to 1 side and hanging down $30^{o}$ below the horizontal over the edge of the examining table. The procedure is then repeated with the head turned to the other side.

The test is positive when the patient experiences vertiginous discomfort and exhibits nystagmus after a latency period of about 10 seconds. The nystagmus increases for about 10 seconds then fatigues in peripheral vestibular disease. In central lesions, nystagmus may occur with the head turned to either side, without discomfort to the patient, and without latency of onset or fatigue.

**Ondine curse**

This refers to the failure of autonomic control of breathing when the patient falls asleep.

**Oommen sign**

Have the patient close the eyes and place a pebble the size of an M&M candy on the palm of the examiner's left hand. Cross the patient's middle finger over the index finger on its dorsal aspect. With the examiner's right hand, hold the patient's crossed fingers and have the patient's 2 (crossed) fingertips touch the pebble at the same time. Ask the patient how many pebbles are in the examiner's hand. With normal stereognosis, the patient should answer that there are 2 pebbles. In cases of astereognosis, the patient reports feeling only 1 pebble.

**Opsoclonus**

This refers to large-amplitude saccadic oscillations of the eyes in all directions, often exacerbated by refixation. They persist during sleep and are associated with brainstem and cerebellar lesions as well as a remote effect of certain carcinomas.

**Optokinetic nystagmus**

This is elicited by using a rotating, striped drum or a moving, striped piece of cloth. As the patient's eyes fixate on a stripe, nystagmus seen in healthy individuals is due to the optokinetic reflex. Lesions in the anterior aspects of the visual pathways decrease the response, and lesions of the vestibular system result in a directional preponderance to the elicited nystagmus.

**Phalen sign**

This refers to the aggravation of paresthesia and pain when the wrist is held in flexion (in patients with carpal tunnel syndrome).

**Roger sign**
This is numbness of the chin in patients with lymphoreticular (and other types of) malignancies.
**Stellwag sign**
This refers to decreased blinking frequency seen in thyroid ophthalmopathy.
**Summerskill sign**
This refers to the bilateral upper- and lower-lid retraction associated with severe liver disease.
**Tinel sign**
This refers to the tingling sensation elicited by tapping along the path of a regenerating nerve following injury. It helps to delineate the extent of nerve regeneration. The Tinel sign also can be observed in tardy ulnar palsy (palpation at the elbow) and carpal tunnel syndrome (tapping at the wrist).
**Trendelenburg sign**
This refers to the pelvic tilt toward the side of the unaffected raised leg when walking in patients with lesions of the superior gluteal nerve.
**Trombone tongue**
This is seen in patients with chorea. It refers to the unsteadiness of the tongue when the patient tries to protrude it outside the mouth.
**Tullio phenomenon**
This refers to the induction of vertigo and nystagmus with acoustic stimuli in patients with labyrinthine disease.
**von Graefe sign**
This refers to the lid lag on down gaze in patients with thyroid ophthalmopathy.
**Definition of Terms**
Apoplexy - Stroke (see definition of Stroke)
Cataplexy - Sudden fall, usually due to loss of muscle tone; may be precipitated by sudden changes in affect or mood in narcolepsy (see definition of Narcolepsy)
Cerebritis - Inflammation of the cerebral hemispheres
Encephalitis - Inflammation of the brain and brainstem structures
Encephalopathy - Dysfunction of the brain
Epilepsy - Recurrent seizures (see definition of Seizure)
Mononeuropathy - Dysfunction of individual nerves
Mononeuritis multiplex - Dysfunction of multiple single nerves
Myelitis - Inflammation of the spinal cord
Myelopathy - Dysfunction of the spinal cord
Myopathy - Primary muscle disease
Myositis - Inflammation of the muscles
Narcolepsy - Sudden attacks manifesting as an uncontrollable urge to sleep
Neuronopathy - Dysfunction of the cortical, cranial, or spinal neurons
Neuropathy - Dysfunction of the cranial or spinal nerves

Polyneuropathy - Bilateral symmetric ascending (stocking and glove) or descending dysfunction of the peripheral nerves
Radiculopathy - Dysfunction of the nerve roots
Seizure - Subjective or objective behavioral manifestation of an abnormal and excessive electrical discharge in the CNS
Stroke - Sudden onset of a neurological deficit, also known as a cerebrovascular accident

**TUMOURS OF THE CENTRAL NERVOUS SYSTEM**
**Prof. N J M Mwang'ombe MBChB, MMed, PhD (Lond)**

BRAIN TUMOURS
Classification of brain tumors
The new WHO Classification of Tumors affecting the Central Nervous System:
In 1993 the WHO ratified a new comprehensive classification of neoplasms affecting the central nervous system. The classification of brain tumors is based on the premise that each type of tumor results from the abnormal growth of a specific cell type. To the extent that the behavior of a tumor correlates with basic cell type, tumor classification dictates the choice of therapy and predicts prognosis. The new WHO system is particularly useful in this regard with only a few notable exceptions (for example all or almost all gemistocytic astrocytomas are actually anaplastic and hence grade III or even IV rather than grade II as designated by the WHO system). The WHO classification also provides a parallel grading system for each type of tumor. In this grading sytem most named tumors are of a single defined grade. The new WHO classification provides the standard for communication between different centers around the world. An outline of this classification is provided below.
1. Neuroepithelial Tumors of the CNS
A. Astrocytic tumors [glial tumors--categories I-V, below--may also be subclassified as invasive or non-invasive.
(i) Pilocytic astrocytoma [non-invasive, WHO grade I]
hemispheric
diencephalic
optic
brain stem
cerebellar
Subependymal giant cell astrocytoma [non-invasive, WHO grade I]
Pleomorphic xanthoastrocytoma [non-invasive, WHO grade I]
(ii) Astrocytoma (WHO grade II)
variants: protoplasmic, gemistocytic, fibrillary, mixed
(iii) Anaplastic (malignant) astrocytoma (WHO grade III)
hemispheric

diencephalic
optic
brain stem
cerebellar
(iv) Glioblastoma multiforme (WHO grade IV)
variants: giant cell glioblastoma, gliosarcoma
B. Oligodendroglial tumors
(i) Oligodendroglioma (WHO grade II)
(ii) Anaplastic (malignant) oligodendroglioma (WHO grade III)
C. Ependymal cell tumors
(i). Subependymoma (WHO grade I)
(ii) Ependymoma (WHO grade II)
variants: cellular, papillary, epithelial, clear cell, mixed
(iii) Anaplastic ependymoma (WHO grade III)
(iv) Myxopapillary ependymoma
D. Mixed gliomas
(i) Mixed oligoastrocytoma (WHO grade II)
(ii) Anaplastic (malignant) oligoastrocytoma (WHO grade III)
(iii) Others (e.g. ependymo-astrocytomas)
E. Neuroepithelial tumors of uncertain origin
(i) Polar spongioblastoma (WHO grade IV)
(ii) Astroblastoma (WHO grade IV)
(iii) Gliomatosis cerebri (WHO grade IV)
2. Tumors of the choroid plexus
(i) Choroid plexus papilloma
(ii) Choroid plexus carcinoma (anaplastic choroid plexus papilloma)
3. Neuronal and mixed neuronal-glial tumors
(i) Gangliocytoma
(ii) Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
(iii) Ganglioglioma
(iv) Anaplastic (malignant) ganglioglioma
(v) Desmoplastic infantile ganglioglioma
(vi) desmoplastic infantile astrocytoma
(vii) Central neurocytoma
(viii) Dysembryoplastic neuroepithelial tumor
(ix) Olfactory neuroblastoma (esthesioneuroblastoma)
variant: olfactory neuroepithelioma
4. Pineal Parenchyma Tumors
(i) Pineocytoma

(ii) Pineoblastoma
(iii) Mixed pineocytoma/pineoblastoma

5. Tumors with neuroblastic or glioblastic elements (embryonal tumors)

(i) Medulloepithelioma
(ii) Primitive neuroectodermal tumors with multipotent differentiation
(iii) medulloblastoma
variants: medullomyoblastoma, melanocytic medulloblastoma, desmoplastic medulloblastoma
(iv) cerebral primitive neuroectodermal tumor
(v) Neuroblastoma
variant: ganglioneuroblastoma
(vi) Retinoblastoma
(vii) Ependymoblastoma

6. Other CNS Neoplasms

A. Tumors of the Sellar Region

(i) Pituitary adenoma
(ii) Pituitary carcinoma
(iii) Craniopharyngioma

B. Hematopoietic tumors

(i) Primary malignant lymphomas
(ii) Plasmacytoma
(iii) Granulocytic sarcoma
(iv) Others; haemangioblastoma

C. Germ Cell Tumors

(i) Germinoma
(ii) Embryonal carcinoma
(iii) Yolk sac tumor (endodermal sinus tumor)
(iv) Choriocarcinoma
(v) Teratoma
(vi) Mixed germ cell tumors

D. Tumors of the Meninges

(i) Meningioma
variants: meningothelial, fibrous (fibroblastic), transitional (mixed), psammomatous, angiomatous, microcystic, secretory, clear cell, chordoid, lymphoplasmacyte-rich, and metaplastic subtypes
(ii) Atypical meningioma
(iii) Anaplastic (malignant) meningioma
(iv) Non-menigothelial tumors of the meninges

E. Benign Mesenchymal

(i) osteocartilaginous tumors

(ii) lipoma
(iii) fibrous histiocytoma
(iv) others
F. Malignant Mesenchymal
(i) chondrosarcoma
(ii) hemangiopericytoma
(iii) rhabdomyosarcoma
(iv) meningeal sarcomatosis
(v) others
G. Primary Melanocytic Lesions
(i) diffuse melanosis
(ii) melanocytoma
(iii) maliganant melanoma
(iv) variant meningeal melanomatosis
H. Tumors of Cranial and Spinal Nerves
(i) Schwannoma (neurinoma, neurilemoma)
cellular, plexiform, and melanotic subtypes
(ii) Neurofibroma
circumscribed (solitary) neurofibroma
plexiform neurofibroma
(iii) Malignant peripheral nerve sheath tumor (Malignant schwannoma)
epithelioid
divergent mesenchymal or epithelial differentiation
melanotic
I. Local Extensions from Regional Tumors
(i) Paraganglioma (chemodectoma)
(ii) Chordoma
(iii) Chondroma
(iv) Chondrosarcoma
J. Carcinoma
Metastatic tumours
K. Unclassified Tumors
1. Cysts and Tumor-like Lesions
(i) Rathke cleft cyst
(ii) Epidermoid
(iii) Dermoid
(iv) Colloid cyst of the third ventricle
(v) Enterogenous cyst
(vi) Neuroglial cyst

2. Granular cell tumor (choristoma, pituicytoma)
(i) hypothalamic neuronal hamartoma
(ii) nasal glial herterotopia
(iii) plasma cell granuloma

Table 1. WHO Grading Scheme for astrocytoma

| WHO Grade | Histological designation | Histological features |
|---|---|---|
| I | Pilocytic astrocytoma | Circumscribed tumour with bipolar astrocytic cells in a biphasic solid/cystic pattern |
| II | Diffuse astrocytoma | Diffusely infiltrating astrocytic cells with pleomorphism |
| III | Anaplastic astrocytoma | As above + mitotic activity |
| IV | Glioblastoma | As above + vascular proliferation +/or necrosis |

Table 2. Classification of Gliomas

| Gliomas | WHO Grade | Grouping |
|---|---|---|
| • Astrocytic tumours | | |
| Diffuse astrocytoma | 2 | LGG |
| Anaplastic astrocytoma | 3 | HGG |
| Glioblastoma | 4 | HGG |
| Pilocytic astrocytoma | 1 | LGG |
| Pleomorphic xanthroastrocytoma | 2 | LGG |
| Subependymal Giant Cell Astrocytoma | 1 | LGG |
| • Oligodendroglial Tumours | | |
| Oligodendroglioma | 2 | LGG |
| Anaplastic oligodendroglioma | 3 | HGG |
| • Mixed Gliomas | | |
| Oligoastrocytoma | 2 | LGG |
| Anaplastic oligoastrocytoma | 3 | HGG |
| • Ependymal Tumours | | |
| Ependymoma | 2 | n/a |
| Anaplastic ependymoma | 3 | n/a |
| Myxopapillary ependymoma | 1 | n/a |
| Subependymoma | 1 | n/a |

LGG; low grade glioma, HGG; high grade glioma, n/a; not applicable

LGG; low grade glioma, HGG; high grade glioma, n/a; not applicable

Factors associated with poor prognosis for survival in patients with cerebral LGG: age 40 years and above, largest diameter of tumour 6 cm and above, tumour crossing midline, presence of neurological deficits, astrocytoma histology (compared with oligodendroglioma/mixed histology).

**Neuroepithelial tumors**

**Astrocytoma**

Astrocytomas, which arise from astrocytes, are the most common primary brain tumor. These tumors represent 50% of all primary intracranial neoplasms

The genesis of astrocytoma and glioblastoma entails a cascade of molecular events that involves several oncogenes and tumor suppressor genes and evolves over a period of years. The pivotal event in the transformation of normal to neoplastic astrocytes is mutation of the tumor supressor gene p53 on 17p.An important epigenetic alteration in low grade astrocytomas and oligodendrogliomas is silencing of the O6-Methylguanine-DNA Methyltransferase gene (MGMT) through hypermethylation. The MGMT gene encodes a DNA repair enzyme which counters the effects of chemotherapeutic agents. Its inactivation makes these tumors more sensitive to the action of temozolomide. Specialized diagnostic laboratories are set up to detect the chromosomal and molecular changes that underlie the development of astrocytoma and GBM. The results can be used for grading and patient management. The proliferative index, determined by Ki 67(MIB-1) immunohistochemistry, can help distinguish grade II from grade III astrocytoma. Even low-grade astrocytomas may be clinically malignant because their location and diffuse spread make surgical excision impossible, and they are not very susceptible to chemotherapy or radiation.

Astrocytomas are histologically graded based on cellularity, anaplasia, mitotic figures, endothelial proliferation and necrosis.

Well-differentiated astrocytomas (WDA) have mild hypercellularity and minimal nuclear pleomorphism. They typically occur in children and young adults who present with a seizure or headaches. On CT or MRI scan they usually appear as a non-enhancing mass lesion. Anaplastic Astrocytomas (AA) have moderate cellularity and nuclear pleomorphism with mitotic activity. Moderate endothelial proliferation can be present but no necrosis. These lesions are typically found in mid-life as enhancing lesions with mass effect. They often present with seizures, headaches and/or focal neurological findings. Glioblastoma multiforme (GBM) is characterized by hypercellularity, dramatic nuclear pleomorphism, endothelial proliferation, mitotic figures and necrosis. These patients are usually older adults who present with headaches, seizures or focal neurologic findings. On CT or MRI scan a GBM typically appears as an irregular ring-enhancing lesion with significant mass effect and edema.

Survival correlates with grade: WDA 5-10 years, AA 2-3 years and GBM 1-1.5 year.

Astrocytomas can initially present as a low-grade tumor and subsequently convert to a higher grade. De novo AA and GBM tumors occur as well.

Treatment is based on grade. Controversy exists for the optimal treatment of WDA. Most agree that a WDA in non-eloquent brain with mass effect should be resected. A stereotactic brain biopsy for diagnosis is an option for symptomatic lesions in areas of the brain where open surgery carries an increased risk of causing a deficit. Radiation is controversial in stable tumors but is often used if growth is demonstrated. AA and GBM are typically treated by surgical resection followed by radiation and BCNU chemotherapy. Surgery is indicated for diagnosis, to relieve mass effect, and, possibly, to decrease the "tumor burden". AA or GBM in the motor strip, language areas or other eloquent brain regions are often biopsied rather than resected because of the high risk of surgery in these areas. It has been difficult to prove that the extent of tumor resection has an effect on patient survival. As a rule, surgery is never curative. BCNU impregnated wafers implanted in the tumor bed after resection of a recurrent AA or GBM have proven to be efficacious. Recurrence within a centimeter or two of the resection site is typical regardless of the treatment given after surgical resection. Surgery for recurrent AA and GBM is controversial. Most surgeons agree that reoperation is indicated for the relief of headaches or neurological deficits due to mass effect.

Pathologically, several types of astrocytomas exist, such as fibrillary, protoplasmic and gemistocytic astrocytomas. Glioblastomas also have giant cell and gliosarcoma variants.

A separate group of astrocytoma is the juvenile pilocytic astrocytoma (JPA). This group is either not graded or considered Grade 0. JPA are distinct because they behave in a more benign fashion and when completely resected can be cured by surgery alone. The are typically discrete cystic lesions with an enhancing mural nodule. Histologically, JPA are composed of loose and dense regions of stellate astrocytes. These have Rosenthal fibers that indicate slow growth. JPA are typically found in children and young adults. They tend to occur in the cerebellar hemisphere, optic nerve, hypothalamus and brainstem. Cerebellar JPA often present with signs of increased intracranial pressure (headache, nausea, vomiting) due to hydrocephalus. JPA also can present with cerebellar dysfunction such as gait ataxia or ipsilateral extremity dysmetria. Rarely, JPA can undergo malignant degeneration. Subarachnoid seeding does occur rarely with JPA and probably carries a poorer prognosis. This has been seen with hypothalamic tumors. Optic nerve JPA and WDA tumors are associated with neurofibromatosis type II.

Pleomorphic xanthoastrocytomas are astrocytic neoplasms found in young adults with a long history of seizures. They are usually superficial in the cerebral cortex and may consist of a mural nodule associated with a cyst. They are typically slow growing but malignant transformation does occur. Subependymal giant cell astrocytomas are typically found at the foramen of Monro in patients with tuberous sclerosis.

Gliomatosis cerebri is a condition where there is diffuse infiltration of the entire brain with an astrocytic tumor.

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**WHO Grade I. Pilocytic astrocytoma**

Pilocytic astrocytoma is a biologically and histologically distinct form of astrocytoma of children and young adults. Most pilocytic astrocytomas arise in the cerebellum and hypothalamus. Some arise in the cerebral hemispheres and other locations.

Grossly, pilocytic astrocytomas are circumscribed and often cystic. Histologically, they are sparsely cellular tumors without anaplasia or mitoses. They show a biphasic pattern, consisting of cellular and fibrillary perivascular areas, alternating with loose microcystic zones. The tumor cells often contain Rosenthal fibers and **granular eosinophilic droplets.** The word pilocytic (hair cell) refers to the fiber-like appearance of the tumor cells and their fibrillary stroma, but large parts of these tumors, especially in the loose areas, do not fit this description. Pilocytic astrocytomas are highly vascular and enhance with contrast injection. Most PAs are biologically low grade, probably benign, and do not evolve into more malignant tumors. Surgical excision of cerebellar PA alone (even partial resection in some instances) sometimes results in permanent cure. Cerebellar pilocytic astroctomas and medulloblastoma are the most frequent brain tumours in children.

Cerebellar juvenile pilocytic astrocytomas are the most common infratentorial neoplasm in the pediatric age group. Although they commonly form well-defined lobular masses which contain cysts and a vascular mural nodule, they may occasionally present a solid mass without a cystic component and may simulate other pediatric posterior fossa masses.

Juvenile pilocytic astrocytomas are one of the most benign tumors of glial origin. They have an increased incidence in type I neurofibromatosis. They have an excellent prognosis following complete resection. However, 15% of cerebellar astrocytomas are of the fibrillary type (85% are of the pilocytic type) and carry a worse prognosis due to infiltration. Fibrillary type of astrocytoma is the predominate histological type in brainstem gliomas.

The differential diagnosis includes medulloblastoma and ependymoma in a child. Hemangioblastomas are more often seen in adults and show flow voids on MR due to hypervascularity.

The differential diagnosis for posterior fossa tumors in children include juvenile pilocytic astrocytoma, medulloblastoma as well as ependymomas. Astrocytomas and medulloblastomas account for approximately two thirds of posterior fossa tumors in the pediatric population. Pilocytic astrocytomas usually present within the first two decades of life with a peak age of presentation at ten years old. Patients present with headache, nausea and vomiting.

The typical radiographic appearance is that of an enhancing mural nodule as well as a nonenhancing cystic component. Approximately 85% of posterior fossa juvenile pilocytic astrocytomas arise from the cerebellar vermis. Other common locations include the optic chiasm and hypothalmus as well as around the third ventricle. When occurring in the region of the vermis, obstructive hydrocephalus occurs relatively early.

When completely removed, there is a greater than 90% five year survival rate. Surgery is usually curative, but prognosis does depend on cellular morphology.

**WHO Grade II. Low grade astrocytomas. (Gemistocytic)**

Well-differentiated astrocytomas (WDA-low grade astrocytomas) have mild hypercellularity and minimal nuclear pleomorphism. They typically occur in children and young adults who present with a seizure or headaches. On CT or MRI scan they usually appear as a non-enhancing mass lesion. They arise anywhere in the CNS, but are most frequent in the cerebral hemispheres. Most low grade astrocytomas are poorly demarcated and it is difficult to determine, by imaging, direct observation during surgery or by gross pathological examination where the tumor ends and normal tissue begins. All that is seen may be an enlargement of the involved portion of the brain and blurring of anatomical landmarks. Some astrocytomas involve a large part of the brain or the entire CNS in a diffuse fashion (gliomatosis cerebri). Most pontine and medullary astrocytomas are diffuse. Histologically, the tumor cells can be stellate, spindle-shaped with fiber like processes, or plump with a large eosinophilic cytoplasmic mass (gemistocytic astrocytomas). They spread in a diffuse fashion but may also form microcysts and other tissue patterns.

**WHO Grade III. Anaplastic astrocytomas.**

Anaplastic Astrocytomas (AA) have moderate cellularity and nuclear pleomorphism with mitotic activity. Moderate endothelial proliferation can be present but no necrosis. These lesions are typically found in mid-life as enhancing lesions with mass effect. They often present with seizures, headaches and/or focal neurological findings.

**WHO Grade IV. Glioblastoma multiforme.**

Glioblastoma multiforme (GBM-Grade IV) is the most malignant glioma. It is characterized by hypercellularity, dramatic nuclear pleomorphism, endothelial proliferation, mitotic figures and necrosis.

It occurs most frequently in middle aged adults and presents with headaches, seizures or focal neurologic findings. Its most common sites are the frontal and temporal lobes, but it may occur at any age and involve any part of the CNS. On CT or MRI scan a GBM typically appears as an irregular ring-enhancing lesion with significant mass effect and edema. GBM arises most commonly de novo (primary GBM). Some GBMs arise by malignant transformation of low-grade astrocytomas (secondary GBM). Primary GBMs are more common in older patients and are more aggressive. Survival from glioblastoma rarely exceeds one year. Postoperative irradiation and chemotherapy prolong survival minimally.

Imaging shows a large irregular mass of variable density with cavitation, surrounded by a large area of edema**.** Vascularity accounts for the contrast-enhancing properties of GBM. Contrast enhancing should not be equated with malignancy. Pilocytic astrocytoma also enhances. On naked eye examination, GBM is a poorly defined mass with variegated (multiform) appearance due to necrosis and hemorrhage. If the tumor is near the center of the cerebrum, it may spread from one hemisphere to the other through the corpus callosum. Other malignant brain tumours can have the same pattern. Also, large MS lesions, especially Schilder's disease, may involve both hemispheres and be confused with GBM.

Microscopically, GBM shows high cellularity, cellular and nuclear anaplasia which is the basis of the designation "multiforme", mitoses, microvascular proliferation, and necrosis.
Densely cellular arrays of tumor cells are often arranged in a perpendicular (pseudopalisading) fashion around serpiginous necrotic areas. It has been proposed that these tumor cells are migrating away from a central hypoxic area. Thrombosed vessels are often seen in the central necrotic area while microvascular proliferation in adjacent areas sustains tumor growth. GBM is one of the most highly vascular solid tumors. Angiogenesis in GBM is a complex molecular process. Hypoxia, which develops as GBM outgrows its vascular supply, induces upregulation of hypoxia inducible factor 1 (HIF-1), which, in turn, stimulates the expression of vascular endothelial growth factor (VEGF). Overexpression of these genes in GBM induces formation of new vessels, which allow continuing tumor growth. The new vessels are often arranged in glomeruloid formations, and lack a blood-brain barrier. The latter property contributes to cerebral edema, a clinically important feature of GBM. Primary GBMs are often composed of small undifferentiated cells (small cell glioblastoma) and show extensive ischemic necrosis and a higher proliferative index. Secondary GBMs are composed of larger cells with astrocytic differentiation.
Losses of chromosome 10 involving the tumor suppressor PTEN (Phosphatase and Tensin Homologue Deleted in Cromosome Ten) and other chromosomal loci convert low-grade astrocytoma to anaplastic astrocytoma and GBM. Overexpression of the Epidermal Growth Factor Receptor (EGFR) gene on 7p characterizes GBMs that arise de novo (primary GBMs) and provides a potential target for EGFR inhibitors. The status of expression of these genes and others that interact with them determines the response of GBM to tyrosine kinase inhibitors and temozolomide, which are used in GBM chemotherapy.
GBM tumors are treated with surgical resection and post-operative radiation. Nonetheless, this malignant process has a poor prognosis with the median survival being 8-10 months. The 1, 2, and 5-year survival rates are 30-44%, 8-12%, and 2.5-5%. The most common cause of death is reoccurrence of tumor at the original site.
Butterfly Lesion
A butterfly lesion is a lesion which infiltrates across the corpus callosum. Thus this pathological process spreads from one hemisphere to another. The differential diagnosis of a butterfly lesion includes: glioblastoma multiforme (GBM), lymphoma, and demyelinating process. Symptoms can range from seizures to focal neurologic deficits to symptoms associated with increased intracranial pressure (headaches, nausea, vomiting, decreased visual acuity). Once a mass lesion is suspected, then an MRI with Gadolinium should be performed. This will usually show the classic ring enhancing (associated with angiogenesis occurring at the periphery of the tumor) lesion. However, definitive diagnosis is based on surgical biopsy.

**Oligodendroglial tumors**

The majority of oligodendrogliomas present in young adulthood with the onset of seizures. Radiographically, calcifications are typical. The classic histologic appearance is of

homogeneously appearing cells with a "fried egg" appearance and "chicken wire" vessel pattern. Similar to WDA, patients can have long term survival. Malignant transformation does occur; these tumors are called anaplastic oligodendrogliomas. In general, surgical resection is recommended when possible for diagnosis, to relieve mass effect, and resect as much tumor as safely as possible. Radiation therapy is controversial, but is probably beneficial. PCV (procarbazine, CNU, & vincristine) chemotherapy has been shown to be beneficial in the treatment of oligodendrogliomas.

**Ependymal tumors**

Ependymomas typically arise from the lining of the ventricular system and usually occur in children and young adults. The floor of the fourth ventricle is a common location. Ependymomas typically present with hydrocephalus and increased ICP. Presenting symptoms include nausea, vomiting, headache, gait ataxia, diplopia and vertigo. Ependymomas have a significant potential for CSF seeding and thus "drop metastasis". Complete surgical resection has been shown to improve survival and should be attempted if there is minimal brainstem invasion. Postoperative radiation and chemotherapy is usually administered. No clear consensus exists for grading ependymomas but the term anaplastic ependymoma is sometimes used for more malignant appearing tumors. Paradoxically, intramedullary spinal cord ependymomas, which are histologically identical, may be cured by surgery alone.

Myxopapillary ependymomas are a variant of ependymomas. This tumor occurs in the conus or filum terminale of the spinal cord. Complete resection is probably curative. Subependymomas occur in anterior lateral ventricles or posterior fourth ventricle. They are benign slow growing tumors that are typically found incidentally at autopsy. However subependymomas can cause hydrocephalus from obstruction of cerebrospinal fluid pathways. Symptomatic or enlarging tumors should be removed. In elderly patients insertion of a VP shunt is a viable option if obstruction of CSF pathways is present.

**Mixed gliomas**

Mixed gliomas occur and appear histologically as a combination of neoplastic oligodendrocytes and astrocytes. These tumors are referred to as oligo-astrocytomas or anaplastic oligo-astrocytomas. Often the name is shortened to the dominant cell type only.

**Choroid plexus tumors**

Tumors of the choroid plexus are called choroid plexus papillomas (CPP). In children less than 2 years of age, they usually are located in the lateral ventricle and present with hydrocephalus. In adults CPP usually occur in the fourth ventricle, foramen of Luschka or cerebellopontine angle. The treatment is surgical resection, though elderly patients with an asymptomatic cerebellopontine angle tumor may be followed with serial imaging studies. Recurrence should be treated aggressively with reoperation, when possible, due to a favorable prognosis. One or two percent of choroid plexus tumors are carcinomatous. Choroid plexus carcinoma carries a poor prognosis.

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**Neuronal and mixed Neuronal-glial tumors**

Gangliocytoma is a tumor composed of large abnormal mature neurons. They are primarily supratentorial with the most common location being the temporal lobe. The majority of patients are in their first two decades of life. Surgical resection, when complete, is curative. Variable radiographic features occur, ranging from an enhancing mural nodule to a ring enhancing mass with calcifications.

Dysplastic gangliocytoma of the cerebellum (Lhermite Duclos Disease) is a non-neoplastic mass of hypertrophic granular cell neurons which expands the cerebellar folia. These tumors can cause mass effect and hydrocephalus and typically occur in young adults. Resection (total or subtotal) and/or shunting are therapeutic options.

Dysembryoplastic neuroepithelial tumors (DNET) are a "hamartomatous", supratentorial, predominantly temporal lobe lesion composed primarily of glial cells. They usually present with seizures. Radiographically these tumors often lack edema and have a multinodular appearance. Inner table skull erosion or deformation may be present.

Gangliogliomas are tumors consisting of large mature neurons and a neoplastic glial component. This tumor affects patients of all ages with the majority diagnosed in young adults who often have a long history of seizures. Surgical resection even if subtotal can be curative. Surgery is recommended for diagnosis and, on occasion, for control of seizures.

**Pineal tumors**

Pineal tumors are tumors arising from pineocytes. The well-differentiated pineocytoma occurs in mid-life as a discrete contrast enhancing mass in the posterior third ventricle/pineal region. The poorly differentiated pineoblastoma has a similar location and enhances with contrast but shows signs of local invasion and is prone to CSF dissemination. The complex of pineoblastoma and bilateral retinoblastoma is called trilateral tumor. In general, pineocytomas have a good prognosis while pineoblastomas with subarachnoid spread are aggressive and carry a poor prognosis. Pineal tumors often present with hydrocephalus due to obstruction of the aqueduct of Sylvius. Compression of the dorsal midbrain by a pineal tumor can result in Parinaud's syndrome of pupillary mydriasis, paralysis of upgaze, and convergence retractorius.

**Embryonal tumors**

Neuroblastoma is a small cell neoplasm with neuroblastic differentiation arising in the deep cerebral hemispheres of young children (<5 yrs. of age). A variant is the ganglioneuroblastoma that has a preponderance of ganglion appearing cells.

The olfactory neuroblastoma (esthesioneuroblastoma) is a neuroblastic tumor arising from the nasal epithelium with cribiform plate involvement. There is a bimodal age distribution in adolescents and older adults. Patients present with nasal obstruction and or epistaxis. Complete surgical resection with combined cranio-facial resection is the treatment of choice, with a generally favorable prognosis. Adjuvant radiation therapy is generally recommended.

Ependymoblastoma is a rare small cell embryonal neoplasm with prominent ependymoblastic rosettes. It typically occurs in the cerebrum of children less than five years of age. Its propensity

for craniospinal dissemination often leads to death within a year.

Retinoblastoma is a retinal neoplasm that occurs in children < 3 years of age. Ophthalmoscopic exam is diagnostic, giving the characteristic white reflex. These tumors have both hereditary (earlier onset and bilateral) and sporadic forms. Surgical resection with or without radiation can be curative.

Medulloblastoma or primitive neuroectodermal tumor (PNET) of the cerebellum is a small cell neoplasm believed to arise from the external granular layer of the cerebellum. This tumor arises in the vermis of children and young adults although cases in older patients have been reported. Radiographically, these are homogeneously enhancing masses of the cerebellar vermis. CSF tumor seeding can produce drop metastases, even at the time of diagnosis. Surgical resection, combined with radiation and chemotherapy, may lead to significant long-term survivals. Rarely, metastasis to bone, lymph nodes and lung have been reported. Variants include desmoplastic medulloblastoma, medullomyoblastoma, and melanocytic medulloblastoma.

Medullomyoblastoma occurs in children, with a propensity for boys. Cerebral (supratentorial) and spinal PNET's occur, but with much less frequency.

**Mesenchymal tumours: Haemangioblastoma**

Hemangioblastomas are sporadic or familial. The latter are associated with the von Hippel Lindau disease. They occur in young to middle-aged adults. It is the most common primary intra-axial tumor of the posterior fossa in adults. About 20% are associated with Hippel-Lindau disease, and hereditary factors have been implicated in another 20%. Typically, they are found in the cerebellum as a mural nodule within a cyst. In von Hippel Lindau disease, there are multiple hemangioblastomas involving the retina, spinal cord, and brain. Hemangioblastoma is a benign tumor which consists of numerous delicate capillaries set in a background of clear foamy cells.

Hemangioblastomas are rare, benign, generally solitary tumors of the central nervous system most commonly identified within the posterior fossa. These lesions are most often found in the cerebellum, and although they may be solid, the majority are cystic. In addition, the majority of hemangioblastomas will demonstrate a densely enhancing peripheral nodule. In addition to the cerebellar hemispheres, the vermis and medulla are other potential sites of origin of hemangioblastomas. Between 4 and 20% of patients with hemangioblastomas of the cerebellum or spinal cord have von Hippel-Lindau disease. Histologically, these tumors are characterized by a fine hypervascularity mesh in a stroma of polygonal cells without evidence for mitotic activity. These lesions are always superficial in location most often located within the periphery of the cerebellar hemisphere. The nidus of the tumor always abuts the pial surface. The vascular supply to a hemangioma is derived from the pia. The characteristic radiologic findings of a hemangioblastoma on both CT and MR include a peripherally located cerebellar lesion with central cystic region with peripheral enhancing nodule. About 60% are cystic, so solid lesions are not uncommon. Calcification is rare. The signal intensity of the cystic portion of the hemangioma may be brighter than that of cerebral spinal fluid. In summary, the findings of a

peripheral cystic structure with bright signal intensity on T2 weighted images located within the posterior fossa with an associated densely enhancing mural nodule is virtually pathognomonic for hemangioblastoma. The tumor nodules are hypervascular and the vascular pedicle often produces a characteristic flow void on MR. Von Hippel-Lindau Disease is an autosomal dominant disease, associated with hemangioblastomas of the cerebellum and retina, cysts of the liver and pancreas, pheochromocytomas, and tumors of the kidneys. It is linked to VHL, a tumor suppressor gene on chromosome 3p. The product of this gene is involved in mRNA transcription.

**Von Hippel-Lindau Disease** is an autosomal dominant disease, associated with hemangioblastomas of the cerebellum and retina, cysts of the liver and pancreas, pheochromocytomas, and tumors of the kidneys. It is linked to VHL, a tumor suppressor gene on chromosome 3p. The product of this gene is involved in mRNA transcription.

**Tumors of cranial and spinal nerves**

**Schwannomas**

Schwannomas (neurinoma, neurilemmoma) are tumors composed of Schwann cells that arise along cranial or spinal nerves. The vestibular schwannoma (acoustic neuroma) is probably the most common schwannoma and arises typically from the superior vestibular nerve. Vestibular schwannomas typically present with tinnitus and sensori-neural hearing loss. Facial numbness follows when the tumor reaches approximately 2.5 cm. Ipsilateral coordination difficulties and mild facial nerve weakness typically do not occur until the tumor diameter is greater than 3 cm. Radiographically, these tumors enhance with contrast and extend into the internal auditory canal. Complete surgical resection is curative. Hearing and facial nerve preservation is dependent on tumor size and preoperative level of nerve function. In older patients or poor surgical candidates, stereotactic radiosurgery is an effective treatment for tumor size < 2.5cm. Some proponents of radiosurgery feel that it should be used as the primary treatment for all but the largest tumors. Bilateral vestibular schwannomas occur with neurofibromatosis type II.

**Neurofibromas**

Neurofibromas are a nerve sheath tumor composed of Schwann cells, fibroblasts and perineural cells. This tumor can occur in isolation or in associated with neurofibromatosis. This tumor may be solitary, plexiform or occur as a mixed neurofibroma/schwannoma. These tumors arise from nerves in the subcutaneous tissue or in the neuroforamena. Classic spinal tumors have a dumbbell appearance when they extend across the neuroforamena. Surgical resection is indicated in symptomatic lesions. Malignant transformation in neurofibromas is rare but should be suspected with increasing size or pain.

**Malignant peripheral nerve sheath tumors**

Malignant peripheral nerve sheath tumors: neurogenic sarcoma, anaplastic neurofibroma, and malignant schwannoma are rare malignant tumors arising from the non-neural elements of nerves. These have a poor prognosis with death resulting within the year. Complete resection is usually not feasible.

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**Tumors of the meninges**

Meningioma (subtypes: meningothelial, transitional, fibrous, psammomatous, angiomatous, microcystic, secretory, clear cell, choroid, lymphoplasmacyte-rich, metaplastic variants, atypical, anaplastic).

Meningiomas are typically solitary, benign, slow growing, extra-axial tumors arising from arachnoid cap cells in the cranium and spine. The most common locations are parasagittal, convexity, tuberculum sella and sphenoid ridge. A small percentage may be intraventricular. Meningiomas rarely occur in children but when they do there is a predilection for the posterior fossa and ventricle. Less than five percent of meningiomas are malignant, characterized by brain invasion and increased mitotic activity. Meningiomas are most common in middle age and elderly women. Common symptoms include headache, seizures, weakness, and mental status changes. Focal neurologic deficits on presentation depend on the site of origin of the tumor. Radiographically these tumors are well circumscribed, homogeneously enhancing lesions. There may be hyperostosis of the underlying skull. There is often a tail of dural enhancement at the edge of the tumor after contrast administration on imaging studies. The primary treatment of symptomatic surgically accessible tumors is surgical resection. Surgery if complete is often curative. Large lesions may require embolization of intra-operatively inaccessible vascular supply prior to surgical resection to decrease intraoperative bleeding. Small or asymptomatic meningiomas in older individuals can be followed and treatment recommended if growth is demonstrated. Radiation therapy and/or radiosurgery are treatment alternatives for recurrent tumors or if surgery carries an increased risk of complications. There is an association between meningiomas and neurofibromatosis type 2 and an abnormality in the long arm of chromosome 22.

**Cysts and tumor-like lesions**

Numerous cysts and tumor-like lesions can occur in the brain including Rathke's cleft cyst, epidermoid cyst, dermoid cyst, colloid cyst of the third ventricle, enterogenous cyst (neuroenteric cyst), neuroglial cyst, other cysts, lipoma, granular cell tumor (choristoma, pituicytoma), hypothalamic neuronal hamartoma, nasal glial heterotopias.

**Tumors of the anterior pituitary**

Pituitary adenomas are slow growing, benign tumors that arise in the anterior pituitary gland. Pituitary tumors are divided into hormone secreting tumors and non-secretors. Tumors less than 1 cm in diameter are referred to as microadenomas while tumors larger than 1 cm are called macroadenomas. Prolactinomas are pituitary adenomas that secrete the hormone prolactin. Prolactinomas often present with amenorrhea in women and loss of libido in men. The primary treatment for prolactinomas is medication, usually bromocryptine analogues. Bromocryptine often results in a decrease in tumor size but does not kill tumor cells. It usually must be continued for life or tumor recurrence is the rule. Adenomas that secrete growth hormone produce gigantism if present before puberty and acromegaly if present after puberty. ACTH secreting adenomas result in Cushing's disease. Hypercortisolism is characterized clinically by

centripetal obesity, moon facies, buffalo hump, glucose intolerance, hypertension and impaired wound healing. Non-secreting macroadenomas with suprasellar extension can compress the optic chiasm. Compression of the optic chiasm from below often produces a bitemporal hemianopsia. Spontaneous hemorrhage or infarction of a pituitary adenoma is referred to as pituitary apoplexy and can result in sudden visual loss or hypocortisolism. Emergent surgery is sometimes necessary for pituitary apoplexy.

The primary treatment for patients with secreting pituitary adenomas producing Cushing's disease, acromegaly, or symptomatic non-secreting tumors is surgical resection. Surgery is typically performed through the transsphenoidal route. Cavernous sinus invasion by adenoma cells often makes a surgical cure difficult. Recurrent tumors or those with cavernous sinus invasion can be treated with re-operation or radiation therapy.

**Metastasis**

Metastases are the most common brain tumor. Tumors that frequently spread to the brain, in order of decreasing incidence are: lung, breast, skin, colon, and kidney. Commonly, lung, thyroid, renal cell and melanoma metastases can become hemorrhagic. The treatment of solitary lesions is surgical resection followed by radiation therapy. For patients with multiple asymptomatic lesions, surgery is reserved for diagnosis only. For patients with controlled systemic disease but multiple brain metastases, a large symptomatic accessible lesion could be considered for resection. Whole brain radiation is generally given for multiple brain metastases.

**INCIDENCE/EPIDEMIOLOGY.**

The annual global age standardized incidence of primary malignant brain tumours is 3.7 per 100,000 for males and 2.6 per 100,000 for females (1). These rates are said to be higher in more developed countries (males 5.8 females 4.1 per 100,000) than in less developed countries (males 3.0 and females 2.1 per 100,000). Males generally have higher rates of primary malignant brain tumours while females have higher rates of non-malignant tumours, primarily meningiomas. Global age-standardized mortality for primary malignant brain tumours is 2.8 for males and 2.0 for females per 100,000, and estimated mortality is higher in developed countries than in less developed countries (2). These figures differ significantly in relation to histology and age; glioblastoma has a five year survival rate of approximately 30% while low grade gliomas such as pilocytic astrocytoma, oligodendroglioma and ependymoma have five year survival rates of over 70%. High grade gliomas and anaplastic astrocytomas have 5 year survival rates of less than 40%.There is no evidence that brain tumours can be prevented by lifestyle changes. Less developed countries have a lower incidence than more developed countries and there is evidence that in multicultural communities those of African and Asian descent have lower incidence than those of Caucasian descent (3). There are other non-occupational risk factors such as age, gender, inherited familial syndromes, irradiation and ethnicity. Studies of syndromes, familial aggregation, linkage and mutagen sensitivity in adults suggest genetic susceptibility to gliomas although the mechanisms are not clear (4). However, brain tumours aggregate in families and this may be as a result of multifactorial inheritance where genetic factors determine the degree of

risk from exposure to exogenous environmental factors such as irradiation (5). Imunnosuppression as a result of AIDS is a well recognized cause of cerebral lymphoma (6).

**RISK ASSESSMENT**

The risk of developing CNS tumours is dependent on age, gender, social status, high dose radiation; brain tumours are said to be more common in the affluent groups (7). Combined loss of chromosome 1p and 19q in oligodendrogliomas is a consistent favourable prognostic indicator (9).

**DIAGNOSIS/PRESENTING SIGNS & SYMPTOMS**

Signs and symptoms

Signs and symptoms may develop in patients with CNS tumours due to;

(a) initial presentation or recurrence
(b) following surgical biopsy/resection, bleed, infection
(c) after radiotherapy/chemotherapy (weeks)
(d) following reduction in steroids

The most frequent symptoms of brain tumors include:

- Headaches that tend to be worse in the morning and ease during the day
- Seizures or convulsions
- Nausea or vomiting
- Weakness or loss of feeling in the arms or legs
- Stumbling or lack of coordination in walking
- Abnormal eye movements or changes/loss in vision
- Drowsiness
- Changes in personality or memory
- Changes in speech

These symptoms may be caused by brain tumors or by other problems. Diagnostic tests should be be performed to determine if these symptoms are that of a brain tumor and if it is a primary or secondary one.

**IMAGING GUIDELINES FOR BRAIN TUMOURS**

Indications:

(a) as part of initial diagnostic work-up: an unenhanced CT scan will exclude most intracranial mass lesions except (i) pituitary tumours (perform high resolution sagittal and coronal TIWI with contrast in selected cases eg Cushing's), (ii) vestibular schwannoma ( high resolution axial MRI, T2 or TI pre and post contrast), (iii) suspected brain metastases ( contrast enhanced CT/MRI), (iv) certain paediatric tumours eg optic glioma
(b) for surgical planning
(c) for follow up

After initial CT/MRI examination demonstrates an intracranial mass lesion, the following imaging protocols may be applied

1. Intra-axial supratentrial mass lesion

-give intravenous contrast and obtain post-contrast images
-for midline lesions (hypothalamus/chiasm, corpus callosum, pineal region) do sagittal contrast enhanced T1WI and T2WI
-for ring enhancing CT images do MRI DWI sequence to exclude abscess/tuberculoma (should not delay treatment)
-brain metastases; search for primary tumour by performing chest x-ray, chest and abdomen CT, and mammography before considering biopsy of intracranial lesion.
2. Intra-axial posterior fossa mass lesion
–give iv contrast material and obtain post-contrast images
-perform sagittal T2 and contrast enhanced T1WI to demonstrate brain stem invasion
-perform sagittal T1WI with contrast for whole spine
-if there is tumour with hydrocephalus perform sagittal high resolution T2WI to assess suitability for endoscopic third ventriculostomy (ETV)
-for enhancing posterior fossa mass in older adults, exclude metastases by imaging-search for primary tumour.
3. Extra-axial mass lesion
-cerebellopontine angle lesions; do high resolution T2WI to demonstrate relationship of tumour to cranial nerves
-if CSF density on CT or CSF signal on T1WI and T2WI, a DWI sequence should be performed to distinguish between an arachnoid cyst and an epidermoid cyst. If DWI is not available a FLAIR sequence should be performed.
–where MRI is not available do multiplanar reconstructions in axial, coronal and sagittal planes to obtain more anatomical information. Where bone invasion is suspected do bone algorithm reconstructions.
Note: For patients with GFR <30,gadolinium based MR contrast should be avoided.For patients with GFR of 30-100, use of contarast is determined on a case by case basis,based on instituional protocols.
Lumbar puncture is generally not useful, and staging of other organs is not needed

**MANAGEMENT/TREATMENT**

A. Initial review by primary Health Care Physician. Request for CT scan/MRI. Referral to Neuroscience Multidisciplinary Team
B. CT/MRI Report: malignant disease suspected; urgent neurosurgical review if emergency otherwise refer to Pre-Operative Multidisciplinary Team for review and surgical management planning (biopsy/debulk/resection).
C. Post-operative Multidisciplinary Team discussion
(i) Primary CNS Lymphoma; referral to haematology MDT
(ii) Non malignant lesion; follow up with surgical team
(iii) Malignant lesion; follow up at oncology clinic for chemoradiotherapy, chemotherapy, radiotherapy, palliative care and surveillance for low grade glioma

(iv) Clinical progression; MDT review for possible adjuvant chemotherapy, repeat surgery, and supportive/palliative care.

D. Low grade glioma on MRI; review by MDT for (i) possible surgery, pathology confirmation and oncology treatment (ii) surgery not indicated, surveillance

**EARLY/EMERGENCY MANAGEMENT**

1. Management of Acute Cerebral Oedema due to raised intracranial pressure: Commence dexamethasone 4-8mg bd, p.o/i.v ( 8am and 12 noon) with a proton pump inhibitor for gastric protection. Manittol may be used if immediately prior to surgery. If patient already on dexamethasone double the dose initially to a maximum of 24-30mg. Start anticonvulsants for new onset seizures, usually phenytoin (iv if rapid control is needed), carbamazepine or lamotrigine as first line treatment. Contact neurosurgical registrar on call if surgery is indicated. Contact oncology team for advice on further treatment.

2. Management of Seizures in Patients with Brain Tumours:

Start the patient on treatment; po/iv phenytoin ( 15mg/kg/24 hours) or sodium valproate. These two drugs can be given iv at the same dose as the patients usual oral dose for rapid response. For long term treatment, carbamazepine or lamotrigine may be used for focal onset seizures and sodium valproate or lamotrigine for primary generalized seizures.

Table 3 Summary of commonly used antiepileptic drugs

| Drug | Start dose/day | Common maintenance dose/day | Dosage interval | Interactions | Common side effects |
|---|---|---|---|---|---|
| Carbamazepine SR | 200 mg | 400-1200 mg | Bd | Enzyme inducer | Dizziness, diplopia, nausea, rash |
| Phenytoin | 200 mg | 250-450 mg | Od | Enzyme inducer | Rash, gum hypertrophy, hirsutism |
| Valproate | 600 mg | 600-2000 mg | Bd | Enzyme inhibitor | Weight gain, tremor, hairloss, platelet dysfunction |
| Lamotrigine | 25 mg (if patient on Valproate, use 25 mg on alternate day) | 100-400 mg | Bd | Probable enzyme inducer | If rash discontinue, fatigue, headache, dizziness, diplopia |

Enzyme inducers may reduce plasma concentration of other hepatically metabolized drugs e.g oral contraceptive pills, Enzyme inhibitors may increase concentration of other hepatically metabolized drugs ; valproate increases plasma concentration of temozolamide and lamotrgine, sodium valproate can cause platelet dysfunction and thrombocytopenia and platelet function tests should be performed prior to any surgery. Monitoring of drug levels is necessary for phenytoin because of rapid changes in serum levels that occur with small increase/decrease in doses leading to neurotoxicity ( nausea, ataxia, dysarthria, mental slowing and nystagmus) or decline in seizure control.

Note:Prophylactic antiepileptic therapy before or after surgery is not needed . After tumour resection, the indication for anti-seizure therapy should be revisited.

3. Emergency Surgical Intervention for Brain and CNS Tumours :

Perform patient examination, history taking, neurological examination and imaging using approved protocols and guidelines. For suspected metastatic disease perform CT chest, abdomen and pelvis and refer patient to MDT for review. Manage cerebral oedema. For primary brain tumour, contact neurosurgical registrar on call; consultant neurosurgeon on call to decide on admission/emergency surgery.

**TREATMENT GUIDELINES**

Rationale for radical resection;

(a) rapid reduction of tumour burden
(b) reduce sampling error associated with a small biopsy
(c) decrease intracranial hypertension
(d) improve neurological function
(e) potentiate adjuvant therapy such as radiation therapy and chemotherapy
(f) possibly improve survival and disease-free progression

Low grade glioma (LGG, WHO Grade 1 and 2):

It is important to identify those patients who will benefit from "watchful waiting" and those who will need early surgical intervention. The European Organization for Research and Treatment of Cancer Guidelines (EORTC) on factors associated with poor prognosis for survival in adult patients with cerebral LGG should be applied to identify patients at increased risk of deterioration who may benefit from early intervention. These factors are as follows; age 40 years and above, tumour diameter 6 cm and above, tumour crossing the midline, astrocytoma histology ( compared with oligodendrolglioma/mixed histology), presence of neurological deficit (8). The role of chemotherapy and radiotherapy in the initial management is uncertain.

High Grade Glioma ( HGG, WHO Grade 3, 4):

Includes glioblastoma, anaplastic astrocytoma, anaplastic oligodendroglioma and anaplastic ependymomas. Usually associated with a poor prognosis and other factors that influence this are age, performance status, co-morbidity factors, tumour type and grade, and presence or absence of seizures.

Based on above guidelines defined management will include any of the following; Urgent surgical intervention (emergency decompression or shunt insertion for hydrocephalus), elective surgery followed by management plan based on MDT review (radiotherapy), patient considered not fit for any surgical intervention.

Radical Radiotherapy without histological Diagnosis:

may be considered where Neuroscience MDT feels surgery would put the patient at unacceptable risk (e.g. brain stem glioma).Should be done only after obtaining informed consent .

Treatment at relapse:

Post therapy recurrence of malignant CNS tumor is a therapeutic challenge. Best supportive care is the recommended option.

Temozolamide may be considered or implantable intratumoural chemotherapy if available.

Metastases:

Metastases in the brain occur in 20-40 % of patients with other primary cancers and are usually associated with poor prognosis. Palliative management will usually include radiotherapy, chemotherapy or hormone therapy. Where cerebral metastasis is the first sign of malignant disease, surgery may be required to provide a diagnosis. Surgery may also be necessary where neuroradiological diagnosis is unclear. Surgery and postoperative radiotherapy should also be considered in physically fit patients with solitary metastases.

Radiotherapy:

The aim of radical treatment in high grade gliomas is to deliver a high dose of radiation with a margin such that the disease free interval and survival are extended compared to surgery alone with minimal post radiation sequelae.

Low grade gliomas are treated with radiotherapy or observation depending on the individual circumstances.

Primary CNS lymphoma (PCL) has a poor prognosis when associated with HIV infection and patients receive palliative irradiation only. Patients with sporadic PCL receive induction chemotherapy followed by irradiation. Patients not suitable for aggressive chemotherapy receive radiotherapy alone.

CNS involvement with systemic lymphoma or leukaemia is treated with craniospinal radiotherapy usually after systemic and CSF remission with chemotherapy.

Ependymoma is treated with involved-field radiotherapy unless there is clear evidence of spinal involvement when craniospinal irradiation should be considered. Primary subependymomas are offered a surveillance strategy independently of the resection status.

Cranial germ cell tumours

Localised germinoma in the pineal or suprasellar region has an excellent prognosis when treated with craniospinal radiotherapy.

Cranial non-germinomatous germ cell tumours (NGGCT's) are treated by primary chemotherapy followed by localised or craniospinal irradiation.

For pituitary tumours local radiotherapy is indicated following incomplete removal, recurrence

after surgery and to control endocrinopathy.
Incompletely excised and recurrent craniopharyngiomas are irradiated locally.
For meningiomas radiotherapy is indicated after incomplete excision, recurrence after surgery and in aggressive or malignant meningiomas.
Primitive neuroectodermal tumours (PNET) include medulloblastomas, pineoblastomas, ependymoblastoma and supratentorial PNET's. Patients, especially if children, are treated with craniospinal irradiation and a boost to the primary tumour site.
All primary spinal tumours receive involved field radiotherapy except completely excised myxopapillary ependymoma or low grade ependymoma.
Primary Paediatric CNS Tumours
Children with acute lymphocytic leukemia (ALL) receive cranial prophylaxis
Paediatric brain tumours are treated as their adult counterparts with dose reduction where appropriate unless otherwise specified in the paediatric radiotherapy guidelines.
CNS Metastases
Multiple brain metastases receive whole brain irradiation.
Solitary brain metastases may be treated with stereotactic radiotherapy or surgery.
Monitoring during radiotherapy
Full blood counts (FBC) weekly. Treatment should be interrupted if neutrophils < 0.5 x 109/l, or platelets < 50 x 109/l. The patient should be supported with platelet transfusions if platelets < 20 x 109/l. The decision to continue radiotherapy is individual.
Chemotherapy:
Exclusive chemotherapy with Temozolamide (TMZ) has been proposed for elderly patients. For high grade gliomas/glioblastomas, concomitant chemoradiotherapy is the standard of care. TMZ (at a low dose of 75 mg/m2) is administered daily (7 days/week),1–1.5 hours before radiotherapy from the first to the last day of radiotherapy (usually 40–49 days). Continuous daily administration of TMZ will induce profound lymphocytopenia with CD4 counts <200/mm3 and this is associated with an increased risk of opportunistic Pneumocystis pneumonia. Similarly, steroids will also lower the lymphocyte counts. Prophylactic administration of pentamidine inhalations or trimethoprim–sulfamethoxazole during concomitant chemoradiotherapy should be considered, but is not required during the adjuvant daily X5 schedule TMZ administration. The blood counts should be monitored weekly, and chemotherapy should be temporarily suspended in the case of thrombocytes <75.000/mm3 or a neutrophil count of <1500/mm3. During the maintenance phase TMZ (150–200 mg/m2) is administered on a daily x5 schedule every 28 days; blood counts should be checked on days 21 and 28. Temozolamide treatment has improved average survival of patients with high grade glioma to 12-14 months.

**RESPONSE EVALUATION AND FOLLOW-UP**

Follow-up Imaging Protocols:
1. Request form should have following details: tumour site, histology (WHO Grade), previous treatment ( date of operation, type of surgery if total or partial resection or biopsy, if

radiotherapy/chemotherapy given and when finished, date of most recent scan.
2. Scan frequency: maybe 6 monthly for two years then annually until 5 years i.e from time of surgery or radiotherapy/chemotherapy if no surgery done and if no treatment given from time of diagnosis. 3. Case should be discussed at post-surgery multidisciplinary team meeting and imaging schedule arranged.
4. In case of a relapse, further imaging will depend on the proposed treatment plan
Table 4. Low grade glioma (WHO Grade)

| Clinical Imaging | Follow-up imaging frequency |
|---|---|
| Radiological diagnosis or biopsy/subtotal resection; watch and wait policy/radiotherapy for progression | Scan 6 monthly for two years, annually until 5 years then every 2 years |
| Complete resection; watch and wait policy/radiotherapy for resection | Scan at 6 months, 2 years and 4 years |
| Biopsy/resection and radiotherapy | Scan 3 months, 2 years, and 5 years after radiotherapy |

Table 5. Low grade glioma (WHO grade II)

| Clinical management | Follow up imaging frequency |
|---|---|
| Radiological diagnosis or biopsy, or resection followed by watch and wait policy and radiotherapy for progression | 6 monthly for two years then annually |
| Biopsy/resection and radiotherapy | 3 months after radiotherapy then annually for 5 years |

Table 6. High grade glioma (WHO Grade III, IV) and malignant skull base tumours

| Clinical management | Follow up imaging frequency |
|---|---|
| Biopsy/resection only | Poor status for radiotherapy, no imaging |
| Biopsy/resection and radiotherapy | 2 months after radiotherapy, 6 months after chemotherapy, then annual scans |

Table 7. Primitive neuroectodermal tumours, medulloblastoma, pineoblastoma, ependymoblastoma,germinoma, teratoma ( whole CNS imaging)

| Clinical management | Follow up imaging frequency |
|---|---|
| Biopsy/resection and craniospinal radiotherapy | 2 months after radiotherapy, annual scans for 5 years |

Table 8. Pituitary adenoma

| Clinical management | Follow up imaging frequency |
|---|---|
| Conservatively managed non-functioning adenomas | 6 months then annual for 6 years then bi-annual |
| Surgically managed non-functioning adenomas | 3 months post-surgery then annual for 6 years then bi-annual |
| Non functioning adenomas Surgically managed with radiotherapy | No further imaging except when relapse suspected from recurrence of symptoms |
| Prolactinoma treated with dopamine agonist | 3 months then yearly for two years |
| Functioning adenomas treated with surgery | Post operative imaging. Further imaging only done if there is biochemical evidence of relapse |

Table 9. Craniopharyngioma

| Clinical management | Follow up imaging |
|---|---|
| Surgery/with or without radiotherapy | 3 months on completion of treatment then annually for 5 years |

Table 10. Meningioma

| Clinical management | Follow up imaging |
|---|---|
| Radiological diagnosis with watch and wait policy | Annually for 5 years |
| Grade 1 with complete excision | 1 year post-op, 2 years post-op, 5 years post op<br>Residual diseases on 1 year scan; no radiotherapy |
| Grade 1 or 2, subtotal excision or residual disease on one year scan; no radiotherapy | Imaging at 6 months postop then annually for 5 years |
| Grade 1 or 2 post biopsy/resection and radiotherapy | Image at 6 months, 2 years and 5 years postradiotherapy |
| Grade 3 resection and radiotherapy | Image at 2 months then annually for 5 years |

Table 11. Vestibular schwannoma

| Clinical management | Followup imaging |
|---|---|
| Radiological diagnosis and medical management | Image at 6 months then annual for five years |
| Complete excision | Image at 6 months; if no disease then at 2 years, 5 years and stop |
| Subtotal excision/residual disease on 6 months scan | Image 6 months postop, two years, then two yearly scans for 10 years. |
| Following Radiosurgery | Scan at 1,3,5 and 10 years |

Table 12.Haemangioblastoma

| Clinical management | Followup imaging |
|---|---|
| Complete resection | 6 months, 2 years, 4 years |
| Incomplete resection/unresected tumours (eg VHL patient with multiple tumours) | 6 months then yearly |

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## SPINAL CORD COMPRESSION DUE TO TUMOURS

Incidence

Spinal cord tumours are rare. Figures available in the Western literature indicate that there are three to ten spinal cord tumours per hundred thousand population. They make up about 1/5 all the tumours of the Central Nervous System

Classification of Tumours of the Spine and Spinal Cord: (1) Extradural-55%. From vertebral bodies or extradural tissues; meningiomas (15% of spinal meningiomas are extradural), neurofibromas, metastatic ; i. Osteolytic- Lymphoma, lung, breast,prostate. ii) Osteoblastic-prostate, breast. Primary spinal tumours-rare- chordomas, neurofibromas, osteoid osteoma,osteoblastoma, aneurysmal bone cyst, chondrosarcoma, osteochondroma, chondroma, enchondroma, vertebral haemangioma, giant cell tumours of bone, osteogenic sarcoma-rare in spine. Miscellaneous; plasmacytoma, multiple myeloma, eosinophilic granuloma, Ewing's sarcoma, chloroma. (2) Intradural extramedullary-meningioma, neurofibroma, lipomas,

harmatomas, metastases. (3) Intramedullary spinal cord tumours (5%) arise in spinal cord substance; astrocytoma 30%, ependymoma 30%, miscellaneous 30% -malignant glioblastoma, dermoid, epidermoid, teratoma, lipoma, haemangioblastoma, neuroma, syringomyelia, lymphoma, oligodendroglioma, cholesteatoma, intramedullary metastases (rare)

Diagnosis/Presenting signs and symptoms

A patient with a spinal cord tumour may present at any of these stages;

1. Early Stage: In the early stages the patient presents with root and segmental sensory loss or motor disturbance.
2. Second Stage: Later, the patient presents with features of Brown-Sequard syndrome or incomplete transection syndrome.
3. Advanced Stage:In the late stages patients present with symptoms and signs of complete transection of the cord.

Clinical examination will reveal the following features:

a) Disturbances of motor function. This may be gradual in which case the patient presents with spastic paresis or rapid in which case the patient presents with flaccid paresis. Gradual onset is common in slow growing tumours i.e. meningiomas and neurilimomas. Rapid presentation is common in first growing tumours e.g. metastatic tumours. Patient will usually complain of progressive weakness of the extremitiesand tiredness.

(b) Disturbance of sensory long tracts (collectively or individual). This may involve the posterior column (vibration and positions sense are effected) or the antero-lateral tracts (loss of pain and temperature). Compression of the dorsal surface of the cord by meningiomas and neurilimomas will result in affection of all modalities of superficial sensation, position and vibration sense. This is common in extra medullary tumours. In intramedullary tumours the patient may present with paresthesias and numbness which may be associated with painful dysethesia.Patients with intra-medullary tumours may also present with bilateral dissociative sensory loss; loss of pain and temperature but touch and position intact.

c) Root symptoms. This may be unilateral pain at the level of the dermatome supplied by the root. The pain is worse at night and when the patient is supine or during Valsalva's manouvre. Other features which may be observed are fasciculations,paresis and amyotrophy.

Investigations

1. Plain radiography. The following features may suggest the presence of a spinal cord tumour; widening of the interpeduncular distance, widening of the neural foramina, scalloping of the vertebral bodies, loss of a pedicle, or evidence of bone destruction or blastic changes in the vertebral bodies (malignant extraduaral lesion).
2. Contrast MRI/CT
3. Myelography (optional):Lumbar puncture should not be done before myelography as it may cause cord shift and incarceration and collapse of subarachnoid space. Do Queckenstedt test, if there is free flow remove csf for analysis, if there is a block do Not remove (Froin's syndrome,

high protein and low cell count; suggestive of block Due to tumour). Features which may be observed during myelography and which are suggestive of spinal cord tumour are;

- Extradural tumours show features of paint brush appearance or hour glass deformity.
- Intradural tumours show cupping defect.
- Intramedullary tumours shows fusiform widening of the cord shadow

4. Spinal angiography.This is important where one suspects the presence of haemangioblastomas, arteriovenous malformations and occipital meningiomas. Treatment
The definitive treatment for spinal cord tumours is surgical excision through laminectomy. Total removal is possible for extradural and intradural extamedullary tumours. Total removal also may be possible in some intramedullary tumours.
Ependymoma:Most frequent intra-medullary spinal cord tumour in adult patients. MRI does not always differentiate between astrocytoma and ependymoma. Therefore surgery is always necessary so as to rule out ependymoma. Postsurgery radiotherapy not necessary (WHO Grade II).
Astrocytomas: These are less common than ependymomas. They may present as microcysts or large syrinxes. Treatment is decompression with aspiration of cysts followed by radiotherapy.
Neurilemomas/Neurofibroma: These are the most common tumours making up 30% of all spinal cord tumours. Male to female ratio is equal. 70% are intradural extramedullary and 15% are extradural. 14% are dumbbell and 1% are intramedullary. Thoracic site is the commonest followed by cervical, but rare in lumbar region. They are found mainly in the $4^{th}$ & $5^{th}$ decade.
Meningiomas: These are the second most common tumours making up approximately 20% of all spinal cord tumours. 80% are found in women and occur mainly in the $4^{th}$, $5^{th}$ and $6^{th}$ decade. Two thirds occur in the thoracic area. 85% are intradural/extramedullary. 15% are extradural.
Metastatic tumours: These are most common in patients over 50 years. Mainly from lung, breast, prostate, kidney, sarcomas and lymphomas. If the primary tumour is known and there is no motor weakness the patient is put on steroids and radiotherapy. In cases of prolonged paraplegia surgery is not helpful. Surgery is also of no benefit in patients in poor general condition with wide spread metastases. Treatment; aim at pain control, preservation of spinal stability, maintenance of sphincter control and ability to ambulate.

**TUMOURS OF THE SPINAL CORD IN CHILDREN**

Incidence: Same as in adults. Patients with Von Recklinghausens disease have an increased incidence of gliomas, neurinomas, and meningiomas. Commonly present between the ages of 3 and 5 years because of the high incidence of congenital neoplasms in childhood. Distribution of intraspinal tumours in children differs from that in adults and there is a greater number of intrinsic spinal cord neoplasms (intramedullary) especially astrocytomas (35 percent) and lesser incidence of intradural-extramedullary neoplasms such as neurinomas and meningiomas (30 percent) while extradural tumours make up 30 percent. (In adults intradural extramedullary, 60 percent, extradural 25 percent and intramedullary 15 percent). 40 percent of intraspinal tumours in children are found in the thoracic area and 60 percent evenly distributed in the cervical and

lumbosacral regions.

70 percent of intraspinal tumours in children are benign and slowly growing. The most common histological types are astrocytomas (25 percent), dermoids (15 percent), epidermoids (10 percent) and lipomas (5 percent). Secondary medulloblastomas that seed the spinal subarachnoid space are seen.

Symptoms and signs.

The symptoms and signs produced by these tumours may be observed in conditions such as cerebral palsy, congenital torticollis, idiopathic scoliosis, spina bifida occulta, transverse myelitis, Guillain Barre Syndrome, brain tumour, brachial plexus palsy, idiopathic enuresis, meningitis and appendicitis. Most common manifestation is motor weakness, (two thirds of the cases). This may present as increased fatigability while running or climbing stairs. Back or root pain may be seen in 40 to 50 percent of children. In older patients, it is accentuated by coughing, sneezing, flexion of the spine, or straight leg raising. Sensory disturbances and bladder and bowel dysfunction may be seen in 30 percent of children at the time of clinical presentation. Thorough sensory examination may be difficult in the very young subjects, but peri-anal anesthesia and segmental hypalgesia should be looked for. Delayed development of sphincter control or loss of established bladder or bowel control may be significant in the history. Tumours in the cervical and thoracic segments of the spinal cord produce a small spastic bladder. Patient voids in frequent small amounts. Tumours in the conus medullaris and cauda equina produce a large flaccid bladder with stress incontinence of urine and faeces.

Musculoskeletal deformities as a result of neuromuscular imbalance and somatic growth are seen in slowly growing neoplasms. These may be in the form of torticollis, scoliosis, kyphosis and foot deformities. Hydrocephalus may be seen in high cervical intramedullary gliomas. Recurrent meningitis may be seen where there is a connecting sinus tract. The organisms are usually Escherichia Coli and Staphylococcus aureus.

**MALIGNANT SPINAL CORD COMPRESSION**

Acute spinal cord compression:

Rapid loss of neurologic function below the level of the lesion due to vascular insult to the spinal cord. There is loss of position seen in the lower extremities from compression of posterolateral spinal arteries and ischaemia of posterior columns occurs due to involvement of anterior spinal artery leading to loss of motor and sensory function below the level of the lesion. It is usually associated with malignant extradural tumours. Treatment of spinal metastases is usually palliative in form of corticosteroids, decompressive laminectomy/vertebrectomy and radiation. Corticosteroids provide relief from pain. Recovery of neurologic function after emergency laminectomy is unlikely if the patient has been totally paraplegic for more than 6 hours. Indications for radiotherapy alone: Radiosensitive tumours (small cell lung carcinoma and myeloma), no instability, rapidly progressive neurological decline with limited life expectancy, the presence of significant co-morbidities. Indications for radiotherapy and surgery: Patients

who need a tissue diagnosis, patients who present with spinal instability, patients with radioresistant tumours.

**BRAIN ABSCESS**

**Prof. N J M Mwang'ombe MBChB, MMed, PhD (Lond)**

Brain abscesses arise by several mechanisms including hematogenous spread, penetrating trauma, surgery, or local spread from the paranasal sinuses, mastoid air cells or emissary veins. The peak incidence is in young men due to the occurrence of middle ear and paranasal sinus infections in addition to congenital heart disease. Other predisposing factors include Osler-Weber-Rendu syndrome with pulmonary arteriovenous fistulae, endocarditis, congenital heart disease, dental work and immunosuppression. Symptoms consist of headache, fever, seizures and/or neurological deficit. The majority of brain abscesses are solitary. Most patients present with signs of mass effect rather than those of infection. The clinical manifestation is also dependent on factors such as virulence of the organisms, patient immune status, and the location of the abscess.

Aerobic and anaerobic bacterial abscesses occur. Abscess cultures in one third of patients grow multiple organisms. Common organisms based on the site of origin include Streptococcus species from the frontal/ethmoid sinus; Bacteroides fragilis from chronic mastoiditis/otitis; Staph. aureus or enterobacteriacea following penetrating trauma or surgery; Strep. viridans and Strep. pneumonia in cases of congenital heart disease; Staph aureus and Strep. pneumonia in cases of endocarditis. In immunosuppressed patients, toxoplasma gondii, nocardia, mycobacteria, yeast and fungal abscesses occur. Outside the US, tuberculomas, cysticercosis, echinococcus, schistosomiasis and strongoloidiasis are more common.

In the first stage of brain infection, there is inflammation of the brain, termed early cerebritis. This stage occurs in the first 3-5 days after inoculation. The CT scan appearance of cerebritis is that of an ill-defined hypodense contrast enhancing area. This coalesces to a late cerebritis stage during days 4-13 with irregular rim enhancement. This is followed, at approximately day 14, by a collagen reticulum encapsulation with a necrotic center (early capsule stage) On CT scan or MRI scan this appears as a ring enhancing mass often with the abscess wall facing the ventricle appearing the thinnest. The final stage is the late capsule stage in which there is a three-layer capsule: an outer gliotic layer, a middle collagenous layer and an inner granulation layer. These can persist for months on imaging studies before ultimate resolution.

Antibiotics are the mainstay of treatment in all cases. Empiric treatment of a presumed bacterial abscess requires coverage for both aerobes and anaerobes. Surgery is usually indicated to confirm the diagnosis of an abscess and for culture and sensitivity of specific organisms. Stereotactic aspiration is the treatment of choice. Aspiration may need to be repeated before resolution occurs. Often two to three weeks of antibiotic treatment are needed before a size decrease is seen on imaging studies. In general 4 – 6 weeks of intravenous antibiotics are often used, followed by a period of oral antibiotics. Patients with nocardia abscesses, or patients in

whom treatment has failed after the third aspiration, should consider surgical resection when accessible. Often, aspiration alone can treat significant mass effect and prevent rupture of the abscess into the ventricular system. Ventricular rupture of a bacterial brain abscess is often fatal.