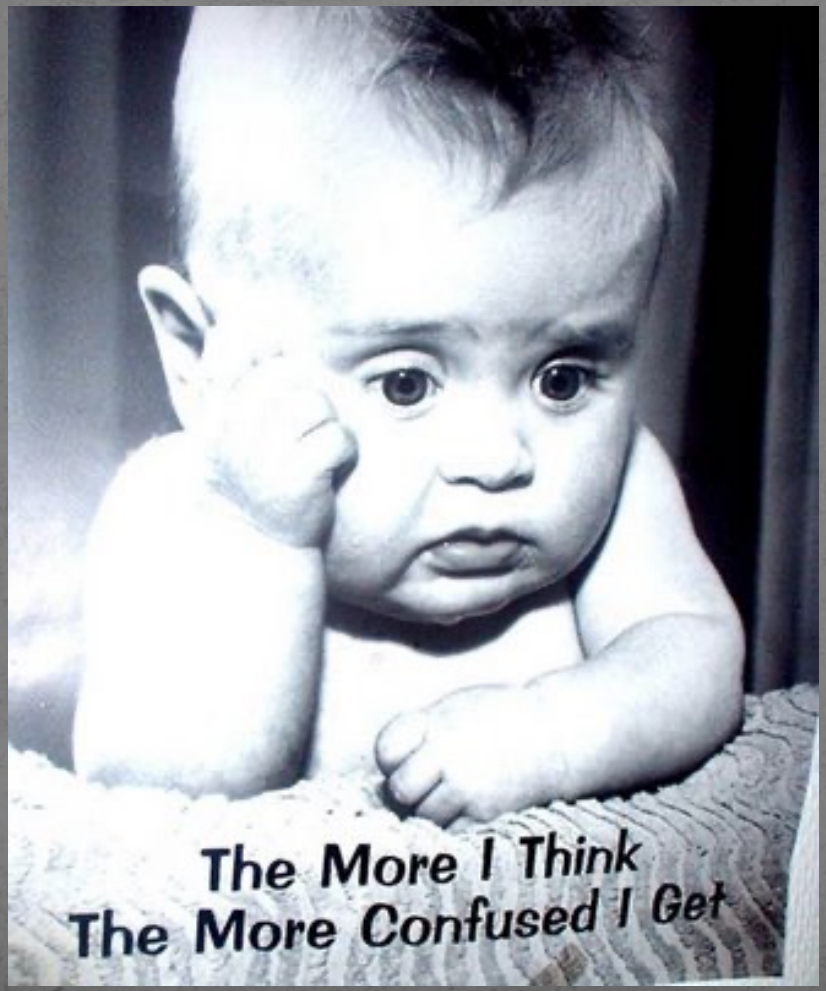
Overview

- Coma is very broad in all aspects
- Vague in presentation
- Vague in approach
- Long list of differentials
- Needs very meticulous examination
- Neurological assessment is vital to the diagnosis

Definitions

- **Confusion**: an inability to think with customary speed, clarity, and coherence.
- All states of confusion are marked by some degree of inattentiveness and disorientation.


The More I Think
The More Confused I Get

- **Mild degree**: roughly oriented as to time and place, with only occasional irrelevant remarks betraying an incoherence of thinking.

Moderately confused

- Carry on a simple conversation for short periods of time, with slow thinking and incoherent, responses are inconsistent, attention span is reduced.
- Unable to stay on one topic and to inhibit inappropriate responses.
- Usually they are variably disoriented in time and place.
- Distractible with any stimulus.
- Movements are often tremulous, jerky, and ineffectual. Sequences of movement reveal impersistence

Severely confused

- Inattentive persons are usually unable to do more than simplest commands.
- Speech is usually limited to a few words or phrases
- Disoriented in time and place.
- Illusions may lead to fear or agitation. Occasionally, hallucinatory or delusional experiences impart a psychosis.

Drowsiness

- Inability to sustain a wakeful state without the application of external stimuli.
- Inattentiveness and mild confusion are the rule, both improving with arousal.
- The lids droop without closing completely; there may be snoring, the jaw and limb muscles are slack, and the limbs are relaxed.

Stupor

- Patient can be roused only by vigorous and repeated stimuli, and does not appear to be unconscious;
- Response to spoken commands is either absent or slow and inadequate.
- Restless or stereotyped motor activity is common with reduction in the natural shifting of positions.
- When left unstimulated, patients quickly drift back into a sleep-like state.
- The eyes move outward and upward, a feature that is shared with sleep
- Tendon and plantar reflexes and breathing pattern may or may not be altered.

Coma

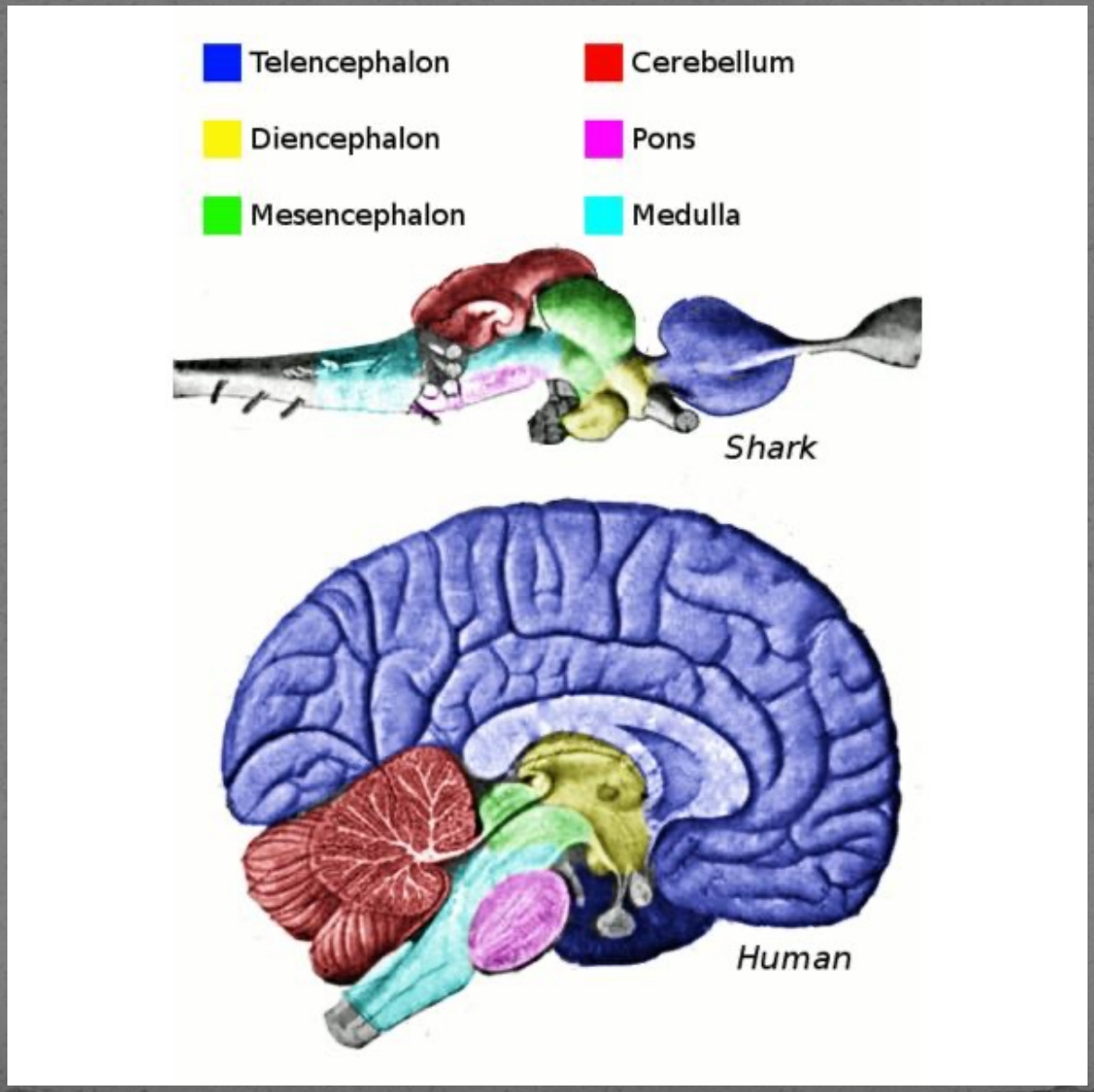
- Incapable of being aroused by external stimuli
- Pupillary reactions, reflex ocular movements, and corneal and brainstem reflexes are preserved in varying degree, muscle tone in the limbs may be increased
- Respiration may be slow or rapid, periodic, or deranged in other ways
- Vigorous stimulation of the patient or distention of the bladder may cause a stirring or moaning and a quickening of respiration.
- These physical signs vary somewhat depending on the cause of coma

Brain death

- Complete unresponsiveness to all modes of stimulation, respiratory arrest, and absence of all EEG activity for 24 h.
- The central considerations in the diagnosis of brain death are
  (1) absence of cerebral functions;
  (2) absence of brainstem functions, including spontaneous respiration
  (3) irreversibility of the state such as drug overdose.

The Anatomy and Neurophysiology of Alertness and Coma

- Paramedian upper brainstem tegmentum and lower diencephalon are the alerting systems of the brain.
- The anatomic boundaries of the upper brainstem reticular activating system are the paramedian regions of the upper (rostral) pontine and midbrain tegmentum.
- At the thalamic level, it includes the functionally related posterior paramedian, parafascicular, and medial portions of the centromedian and adjacent intralaminar nuclei.


Telencephalon
Diencephalon
Mesencephalon
Cerebellum
Pons
Medulla
Shark
Human

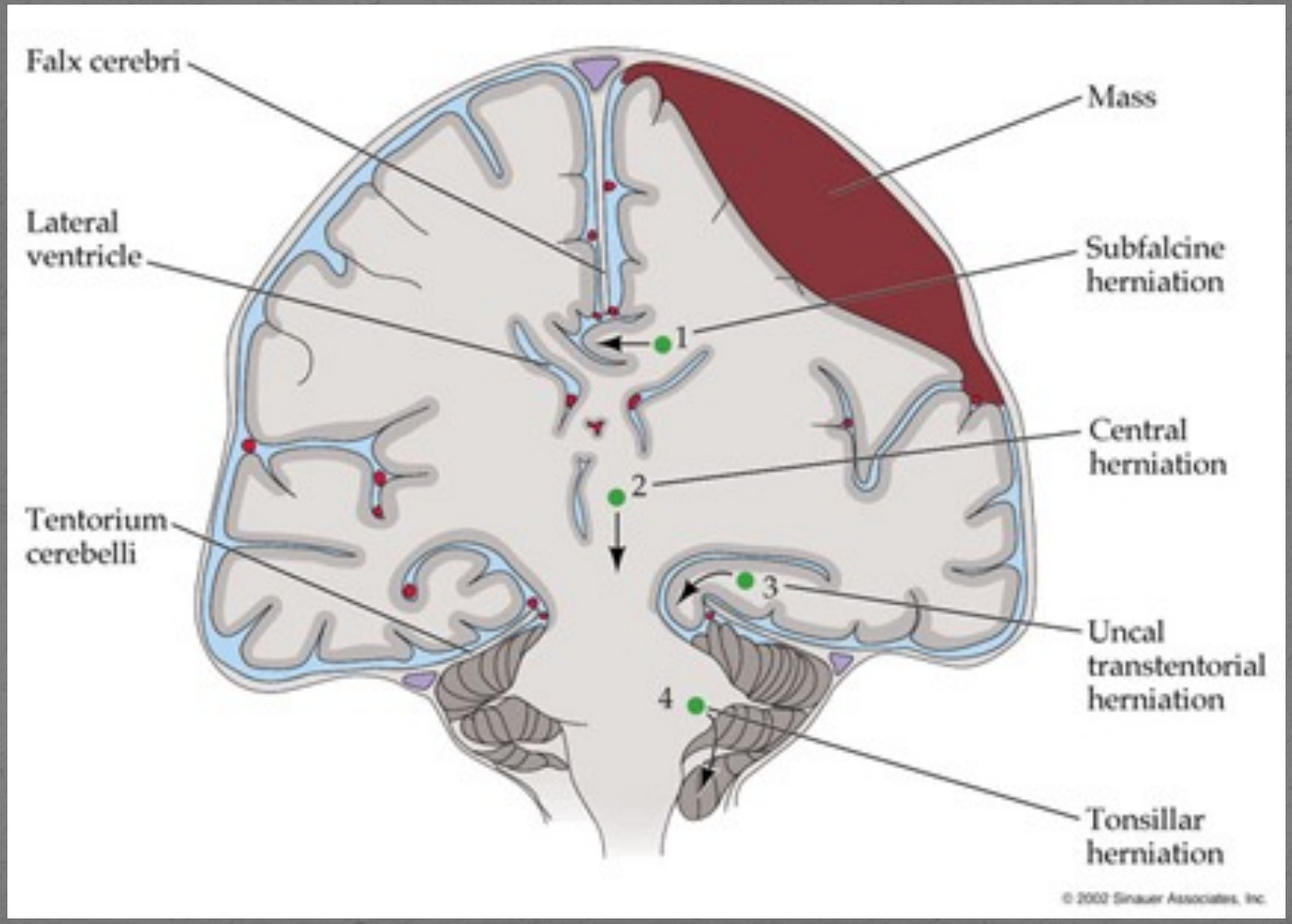
- In the brainstem, nuclei of the reticular formation receive collaterals from the spinothalamic and trigeminal-thalamic pathways and project not just to the sensory cortex of the parietal lobe,, but to the whole of the cerebral cortex.
- It has become apparent that during wakefulness, there is also a widespread low-voltage fast rhythm (a gamma rhythm that has a frequency of 30 to 60 Hz). This activity, coordinated by the thalamus, has been theorized to synchronize widespread cortical activity and to account perhaps for the unification of modular aspects of experience (color, shape, motion) that are processed in different cortical regions.

Pathologic Anatomy of Coma

- Coma is produced by one of two broad groups of problems:
  - The first is clearly morphologic, consisting either of discrete lesions in the upper brainstem and lower diencephalon (which may be primary or secondary to compression) or of more widespread changes throughout the hemispheres.
  - The second is metabolic or submicroscopic, resulting in suppression of neuronal activity.

Three pathways

- (1) Discernible mass lesion, tumor, abscess, massive edematous infarct, or intracerebral, subarachnoid, subdural, or epidural hemorrhage.
- Usually the lesion involves only a portion of the cortex and white matter, leaving much of the cerebrum intact, and it distorts deeper structures.
  - Cause coma by a lateral displacement of deep central structures, sometimes with herniation of the temporal lobe into the tentorial opening, resulting in compression of the midbrain and subthalamic region of the RAS


Falx cerebri
Mass
Lateral ventricle
Subfalcine herniation
1
Central herniation
2
Tentorium cerebelli
3
Uncal transtentorial herniation
4
Tonsillar herniation
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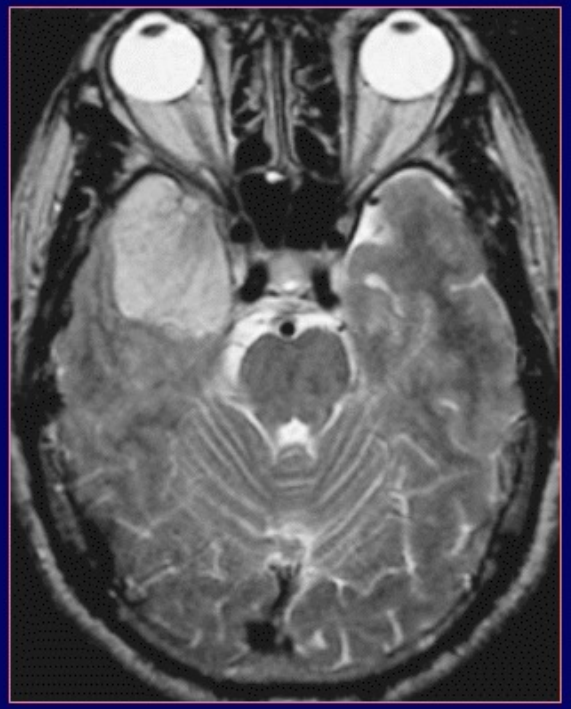
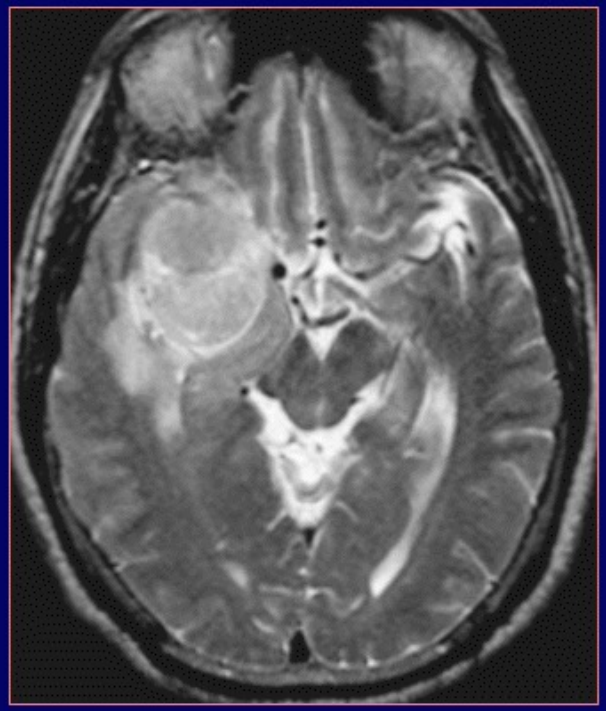
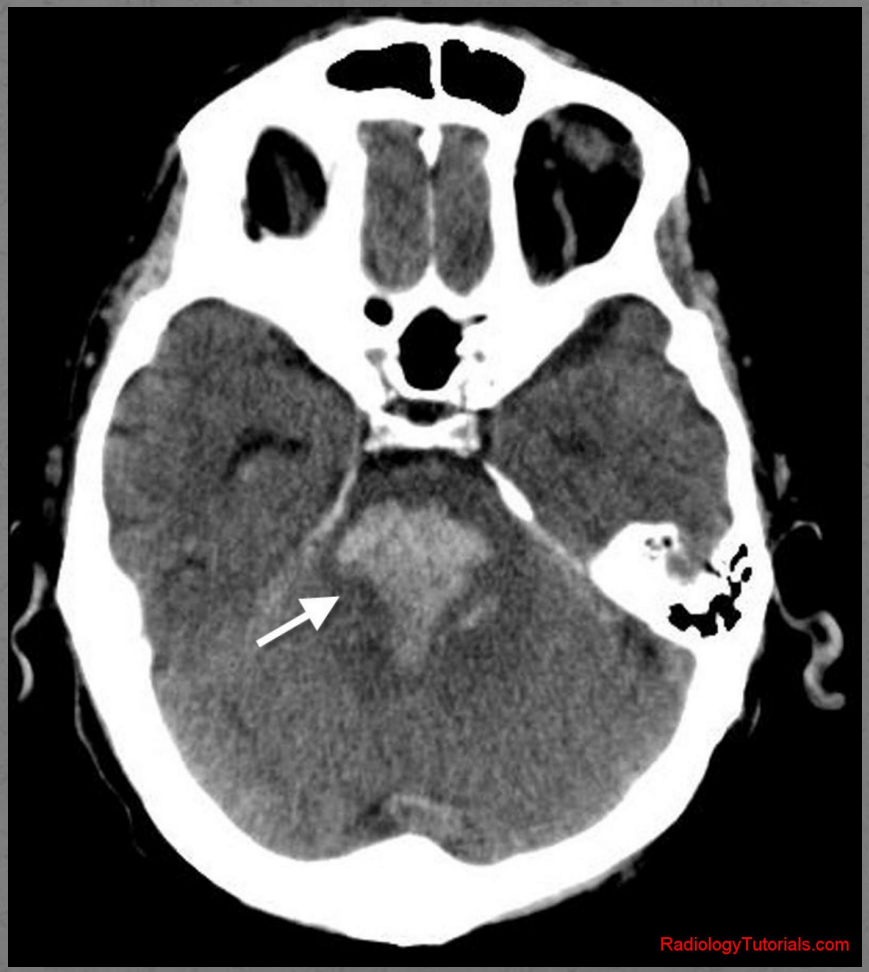




- (2) A destructive lesion in the thalamus or midbrain, in which case the neurons of the reticular activating are involved directly.
- This pathoanatomic pattern characterizes brainstem stroke from basilar artery occlusion, thalamic and upper brainstem hemorrhages, as well as some forms of traumatic damage.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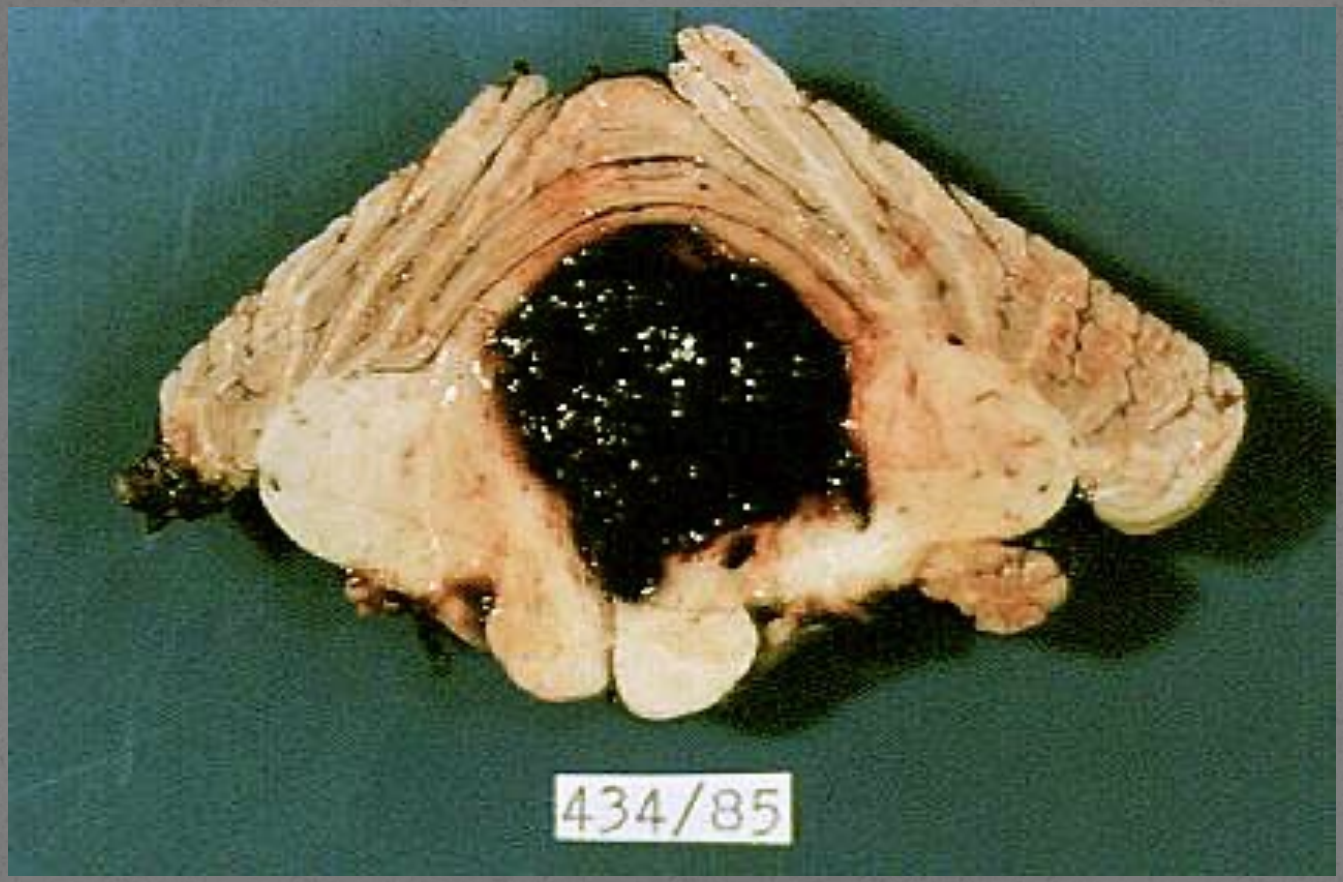
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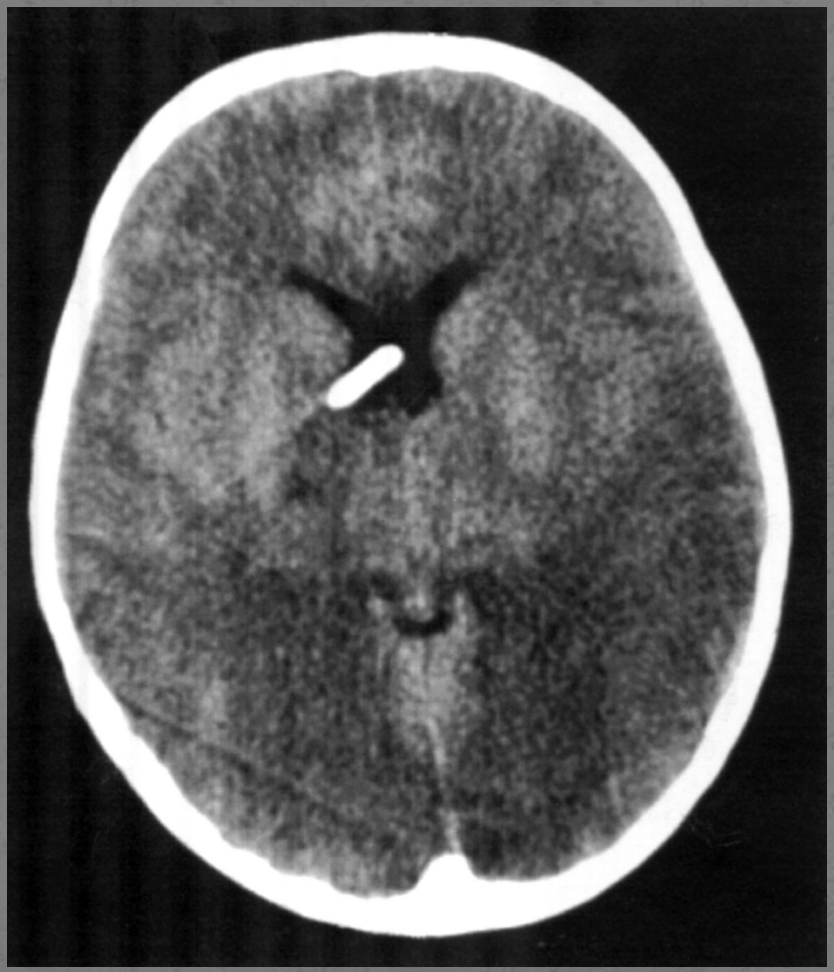
- (3) Widespread bilateral damage to the cortex and cerebral white matter as a result of traumatic damage (contusions, diffuse axonal injury), bilateral infarcts or hemorrhages, viral encephalitis, meningitis, hypoxia, or ischemia, as occurs after cardiac arrest.
  - The coma in these cases results from interruption of thalamocortical impulses or from generalized destruction of cortical neurons.



Herniation patterns

PATHOLOGIC CHANGE	MECHANISM	CLINICAL DISORDERS
Injury to outer fibers of ipsilateral oculomotor nerve	Strangulation of nerve between herniating tissue and medial petroclinoid ligament; stretching of nerve over clivus from lateral displacement of midbrain; entrapment of nerve between posterior cerebral and superior cerebellar arteries from downward displacement of midbrain	Pupillary dilatation (Hutchinson pupil), ophthalmoplegia later
Creasing of contralateral cerebral peduncle (Kernohan's notch)	Pressure of laterally displaced midbrain against sharp edge of tentorium	Hemiplegia ipsilateral to herniation (*false localizing sign*) and bilateral corticospinal tract signs

Lateral flattening of midbrain and zones of necrosis and secondary hemorrhages in tegmentum and base of subthalamus, midbrain, and upper pons (Duret hemorrhages)	Crushing of midbrain between herniating temporal lobe and opposite leaf of tentorium and vascular occlusion (hemorrhages around arterioles and veins)	Cheyne-Stokes respirations; stupor-coma; bipyramidal signs; decerebration; dilated, fixed pupils and alterations of gaze (facilitated oculocephalic reflex movement giving way to loss of all response to head movement and labyrinthine stimulation)
Unilateral or bilateral infarction (hemorrhagic) of occipital lobes	Compression of posterior cerebral artery against the tentorium by herniating temporal lobe	Usually none detectable during coma; hemianopia (unilateral or bilateral) with recovery
Rising intracranial pressure and hydrocephalus	Lateral flattening of aqueduct and third ventricle and blockage of perimesencephalic SA space	Increasing coma, rising blood pressure, bradycardia

CLINICAL APPROACH TO THE COMATOSE PATIENT

- ABC
- IF trauma has occurred, one must check for bleeding from a wound or ruptured organ (e.g., spleen or liver), C-spine precaution
- Thiamine and glucose
- Drug screen and rule out drug intoxication

General Examination

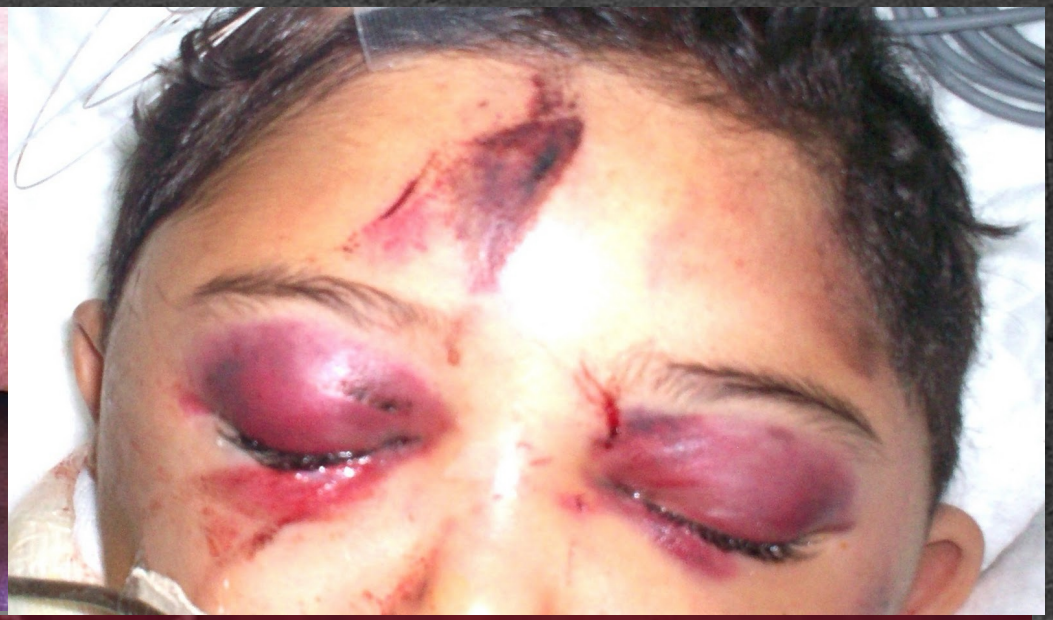
- Alterations in vital signs are important aids in diagnosis.
  - *Fever* → pneumonia or to bacterial meningitis or viral encephalitis.
  - An excessively high body temperature (42 or 43°C) → anticholinergic activity.
  - Hypothermia is observed in patients with alcoholic or barbiturate intoxication, drowning, exposure to cold, peripheral circulatory failure, and myxedema.
- *Slow breathing* points to opiate or barbiturate intoxication and occasionally to hypothyroidism.
- Deep, rapid breathing (Kussmaul respiration) should suggest the presence of pneumonia, diabetic or uremic acidosis, pulmonary edema, or the less common occurrence of an intracranial disease.

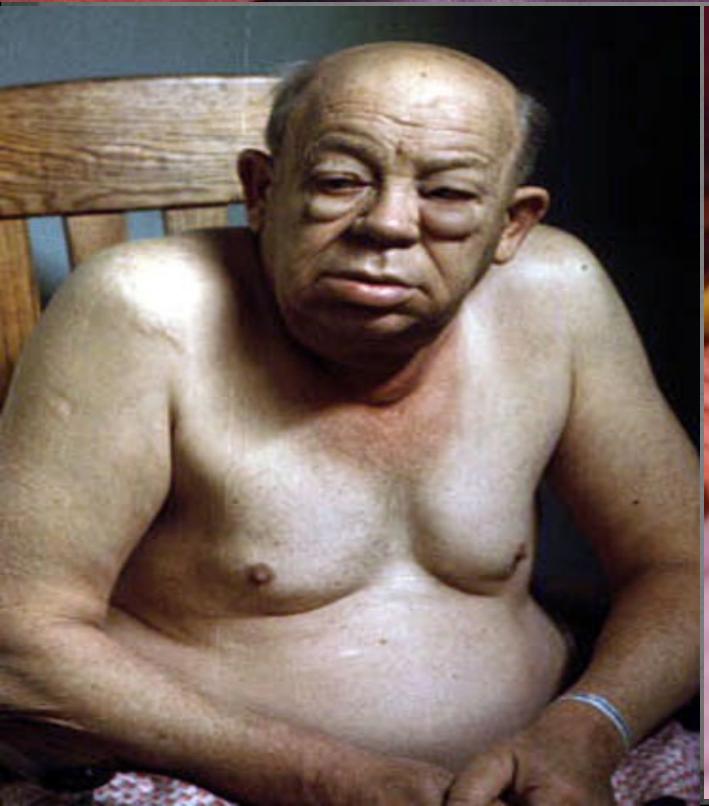
- Diseases that elevate ICP or damage the brain often cause slow, irregular, or cyclic Cheyne-Stokes respiration.
- *Vomiting* $\rightarrow$ pronounced hypertension, is highly characteristic of cerebral hemorrhage within the hemispheres, brainstem, cerebellum, or subarachnoid space.
- The *pulse rate*, if slow, should suggest heart block from medications such as tricyclic antidepressants or anticonvulsants, or if combined with periodic breathing and hypertension.an increase in intracranial pressure that reflects the presence of a mass lesion. A myocardial infarction of the inferior wall may also be the cause of bradycardia

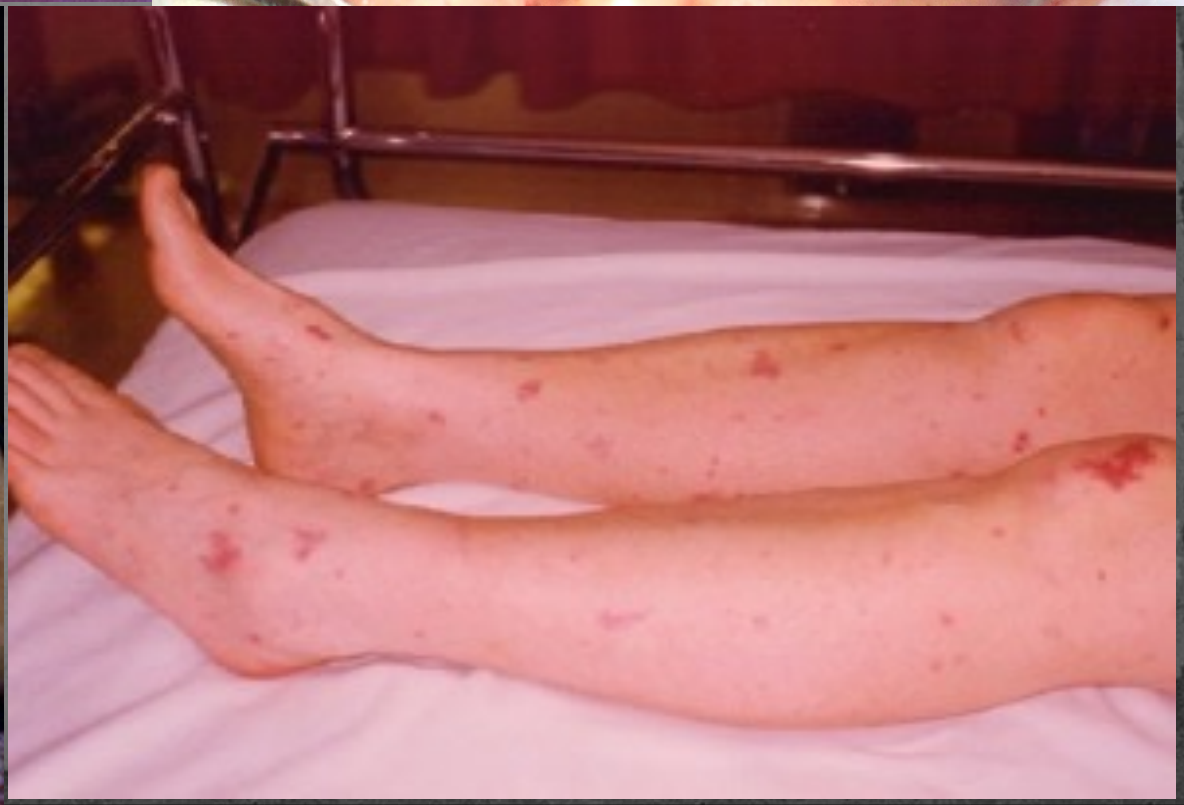
- Marked *hypertension* → cerebral hemorrhage and hypertensive encephalopathy and sometimes in those with greatly increased intracranial pressure.
- *Hypotension* → diabetes, alcohol or barbiturate intoxication, internal hemorrhage, myocardial infarction, dissecting aortic aneurysm, septicemia, Addison disease, or massive brain trauma.

Inspection of the skin

- Cyanosis of the lips and nail beds signifies inadequate oxygenation.
- Cherry-red coloration is typical of carbon monoxide poisoning.
- Multiple bruises (particularly a bruise or boggy area in the scalp), bleeding, CSF leakage from an ear or the nose, or periorbital hemorrhage greatly raises the likelihood of cranial fracture and intracranial trauma.
- Telangiectases and hyperemia of the face and conjunctivae $\rightarrow$ of alcoholism;
- Myxedema imparts a characteristic puffiness of the face, and hypopituitarism.
- Marked pallor suggests internal hemorrhage.







- A maculohemorrhagic rash indicates the possibility of meningococcal infection, staphylococcal endocarditis, typhus, or Rocky Mountain fever.
- Excessive sweating suggests hypoglycemia or shock, and excessively dry skin, diabetic acidosis or uremia.
- Skin turgor is reduced in dehydration.
- Large blisters, $\rightarrow$ acute barbiturate, alcohol, and opiate intoxication.
- TTP, DIC, and fat embolism $\rightarrow$ diffuse petechiae.

- The *odor of the breath* Alcohol, The spoiled-fruit odor of diabetic coma, the uriniferous odor of uremia, the musty fetor of hepatic coma, and the burnt almond odor of cyanide poisoning.

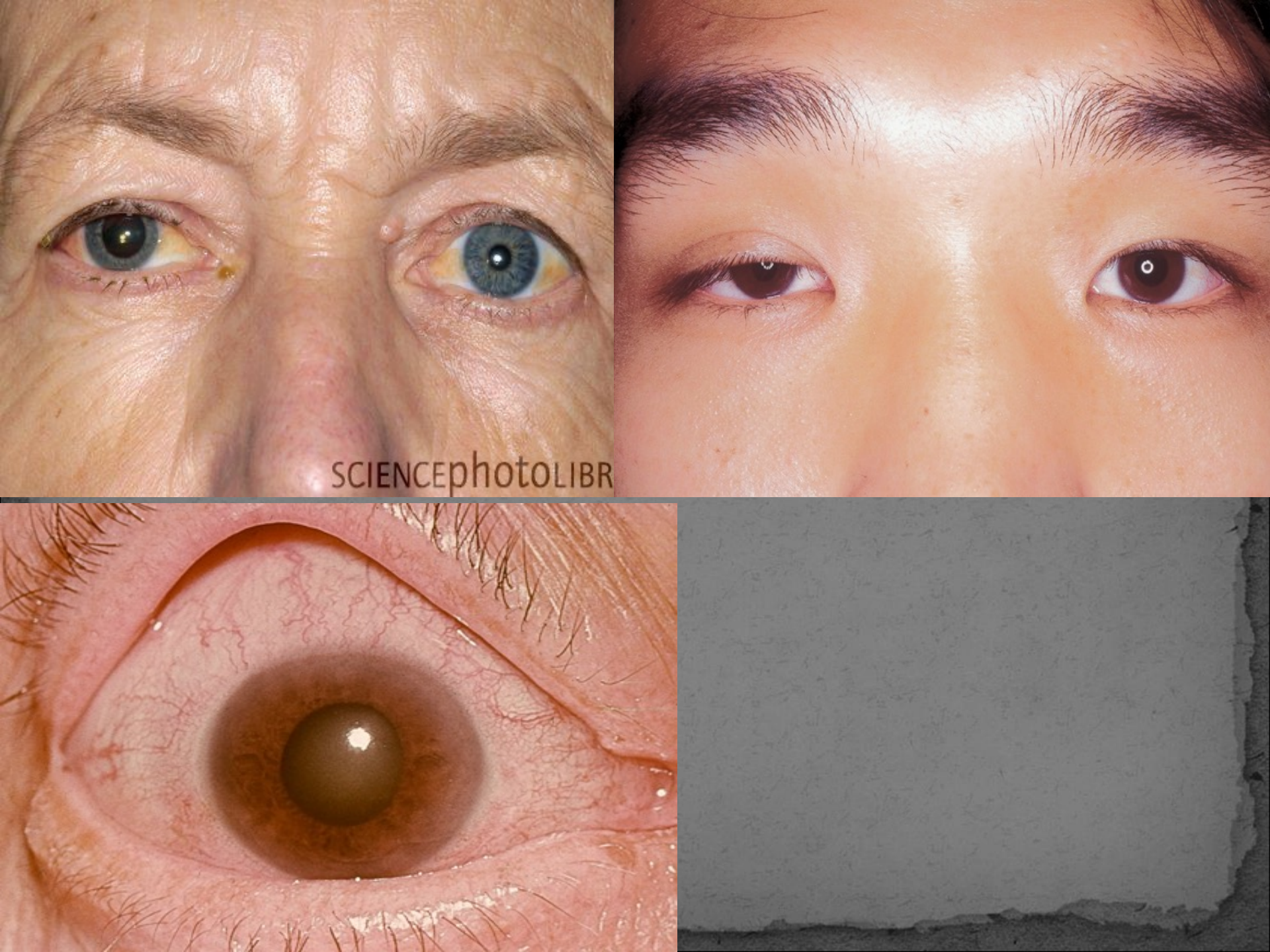
Neurologic Examination

- Grimacing and deft avoidance movements of the stimulated parts are preserved in light coma; their presence substantiates the integrity of corticobulbar and corticospinal tracts.
- Yawning and spontaneous shifting of body positions indicate a minimal degree of unresponsiveness.
- It is usually possible to determine whether coma is associated with meningeal irritation .
- It should be noted that in some patients the signs of meningeal irritation do not develop for 12 to 24 h after the onset of subarachnoid hemorrhage.

- Resistance to movement of the neck in all directions may be part of generalized muscular rigidity (as in phenothiazine intoxication) or indicate disease of the cervical spine.
- A temporal lobe or cerebellar herniation or decerebrate rigidity may also limit passive flexion of the neck and be confused with meningeal irritation.
- A moan or grimace may be provoked by painful stimuli on one side but not on the other, reflecting the presence of a hemianesthesia; also during grimacing, facial weakness may be noted.

Pupillary Reactions

- A unilaterally enlarged pupil (5.5 mm diameter) is an early indicator of stretching or compression of the third nerve and reflects the presence of an ipsilateral hemispheral mass.
- A loss of light reaction alone usually precedes enlargement of the pupil.
- As a transitional phenomenon, the pupil may become oval or pear-shaped or appear to be off center (corectopia) due to a differential loss of innervation of a portion of the pupillary sphincter.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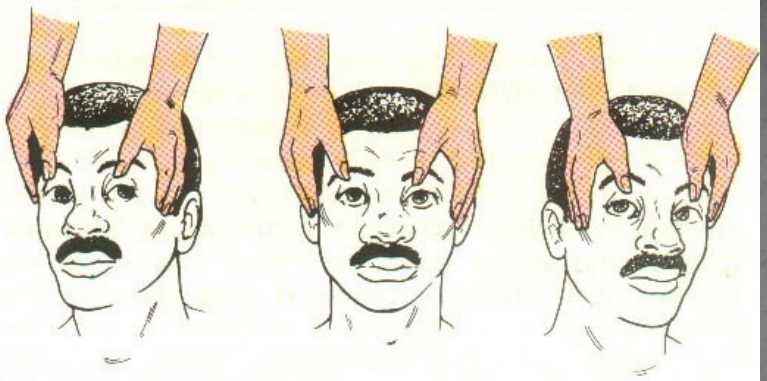
- The light-unreactive pupil continues to enlarge to a size of 6 to 9 mm diameter and is soon joined by a slight outward deviation of the eye,
- As midbrain displacement continues, both pupils dilate and become unreactive to light as a result of compression of the oculomotor nuclei in the rostral midbrain
- Pontine tegmental lesions cause extremely miotic pupils (<1 mm in diameter)
- The ipsilateral pupillary dilatation from pinching the side of the neck (the ciliospinal reflex) is also lost in brainstem lesions.

- A Horner syndrome (miosis, ptosis, and reduced facial sweating) may be observed ipsilateral to a lesion of brainstem or hypothalamus or as a sign of dissection of ICA.
- With coma due to drug intoxications and metabolic disorders, pupillary reactions are usually spared, but there are notable exceptions.
  - Opiates or barbiturates cause pinpoint pupils with a constriction to light
  - Poisoning with atropine or with drugs that have atropinic qualities, especially the tricyclic antidepressants (wide dilation and fixity of pupils)

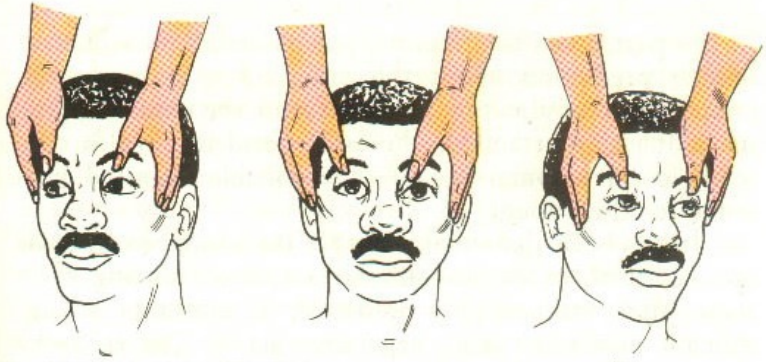
Movements of Eyes and Eyelids and Corneal Responses

- The eyes may be turned down and inward (looking at the nose) with hematomas or ischemic lesions of the thalamus and upper midbrain (a variant of Parinaud syndrome)
- Retraction and convergence nystagmus and "ocular bobbing," occur with lesions in the tegmentum of the midbrain and pons, respectively.
- Ocular dipping in which the eyes move down slowly and return rapidly to the meridian, may be observed with coma due to anoxia and drug intoxications; horizontal eye movements are preserved

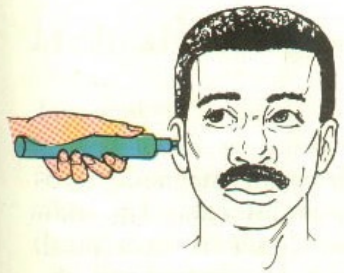
Oculocephalic reflexes (doll's-eye movements)



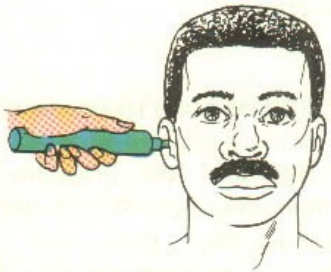
A. NORMAL REACTION:
Eyes move from side to side when head is turned



B. ABNORMAL REACTION:
Eyes remain in fixed position in skull when head is turned



C. NORMAL CALORIC:
Eyes deviate to side of ice water application



D. ABNORMAL CALORIC:
Eyes do not deviate

Oculovestibular or *caloric* test

- Irrigation of each ear with 10 mL of cold water (or room-temperature water if the patient is not comatose) normally causes slow conjugate deviation of the eyes toward the irrigated ear, followed in a few seconds by compensatory nystagmus (fast component away from the stimulated side).
- The ears are irrigated separately several minutes apart.
- In comatose patients, the fast "corrective" phase of nystagmus is lost and the eyes are tonically deflected to the side irrigated with cold water or away from the side irrigated with warm water; this position may be held for 2 to 3 min.

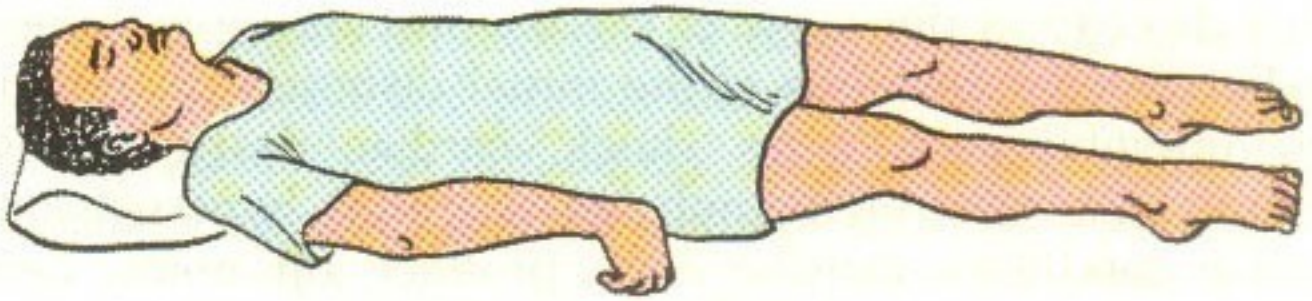
- With brainstem lesions, these vestibulo-ocular reflexes are lost or disrupted.
- If only one eye abducts and the other fails to adduct, one can conclude that the medial longitudinal fasciculus has been interrupted (on the side of adductor paralysis).
- The opposite, abducens palsy, is indicated by an esotropic resting position and a lack of outward deviation of one eye with the reflex maneuvers.
- The complete absence of ocular movement in response to oculovestibular testing indicates a severe disruption of brainstem tegmental pathways in the pons or midbrain or, as mentioned, a profound overdose of sedative or anesthetic drugs.

Corneal Reflex:

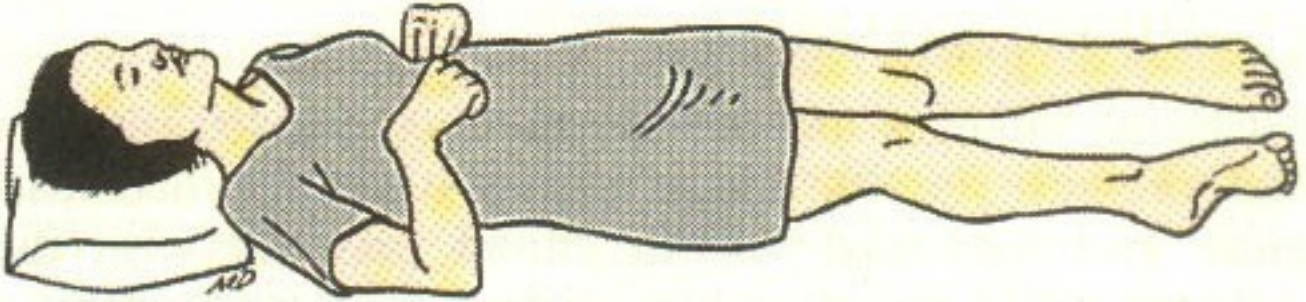
Spontaneous Limb Movements

Posturing in the Comatose Patient

- D*ecerebrate rigidity*, which in its fully developed form consists of opisthotonos, clenching of the jaws, and stiff extension of the limbs, with internal rotation of the arms and plantar flexion of the feet (brainstem at the intercollicular level).
- *Decorticate rigidity*, with arm or arms in flexion and adduction and leg(s) extended, signifies lesions at a higher level, in cerebral white matter or IC and thalamus.



A. Extension posturing (decerebrate rigidity)



B. Abnormal flexion (decorticate rigidity)

Patterns of Breathing

- *Cheyne-Stokes respiration*:
  - Period of waxing and waning hyperpnea regularly alternates with a shorter period of apnea due to massive supratentorial lesions, bilateral deep-seated cerebral lesions, or metabolic disturbances of the brain
  - This phenomenon has been attributed to isolation of the brainstem respiratory centers from the cerebrum, rendering them more sensitive than usual to carbon dioxide (hyperventilation drive).

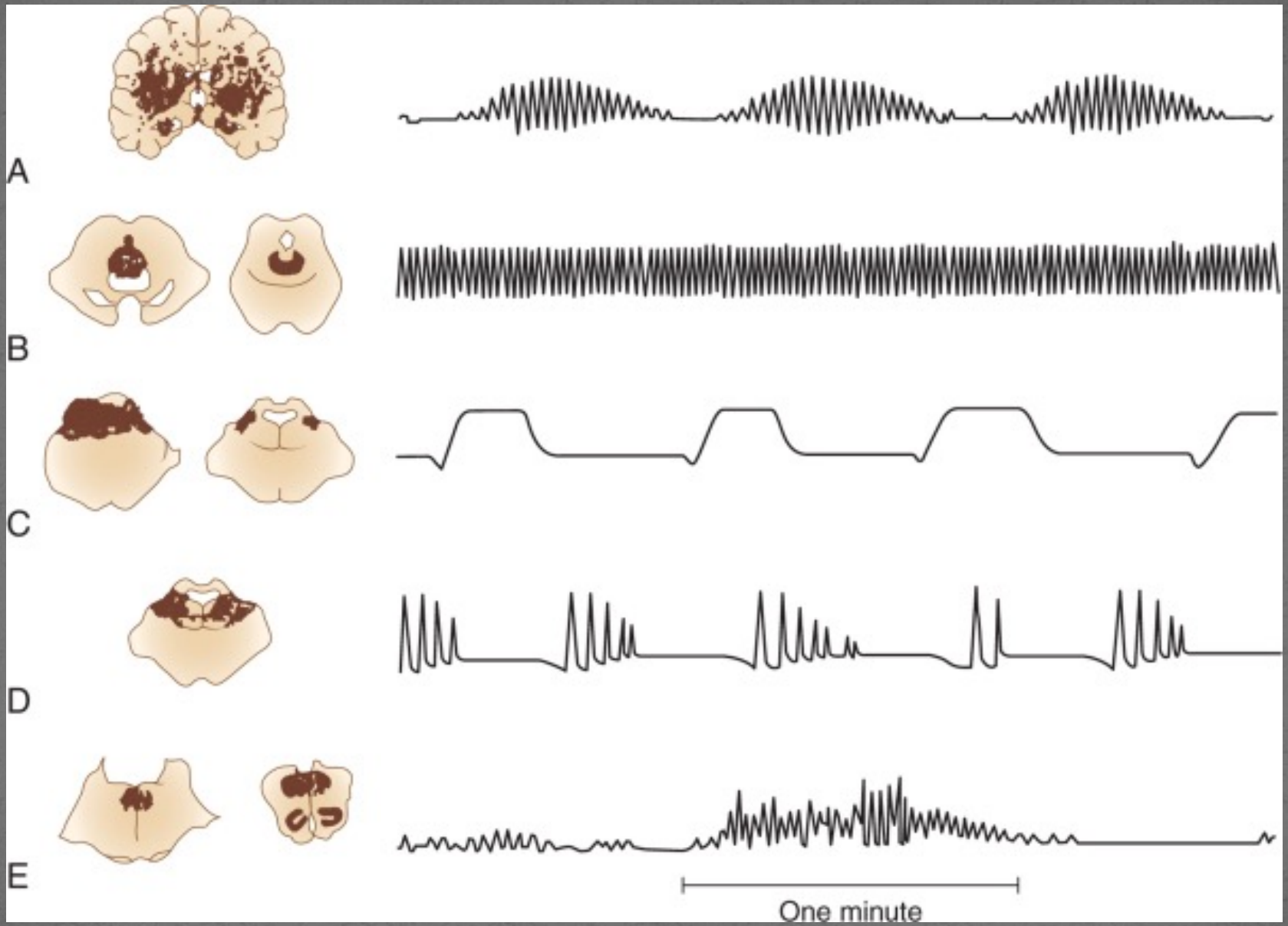
- It is postulated that as a result of overbreathing, the blood carbon dioxide drops below the concentration required to stimulate the centers, and breathing gradually stops. Carbon dioxide then reaccumulates until it exceeds the respiratory threshold, and the cycle then repeats itself.
- CSR signifies bilateral dysfunction of cerebral structures, usually deep in the hemispheres or diencephalon,
- Coma with CSR is usually due to intoxication or to a severe metabolic derangement and occasionally to bilateral lesions, such as subdural hematomas.
- It may occur during sleep in elderly individuals and can be a manifestation of cardiopulmonary disorders in awake patients.

- *Central neurogenic hyperventilation* (CNH)
  - Lesions of the lower midbrain-upper pontine tegmentum, either primary or secondary to a tentorial herniation, may give rise to.
  - Characterized by an increase in the rate and depth of respiration to the extent that respiratory alkalosis results.

- CNH is thought to represent a release of the reflex mechanisms for respiratory control in the lower brainstem.
- It must be distinguished from hyperventilation caused by medical illnesses, particularly pneumonia and acidosis.
- It has been observed with tumors of the medulla, lower pons, and midbrain

- *Apneustic breathing*
  - Low pontine lesions, usually due to basilar artery occlusion, sometimes cause
  - A pause of 2 to 3 s in full inspiration or so-called short-cycle CSR, in which a few rapid deep breaths alternate with apneic cycles.

- Ataxic:
  - With lesions of the dorsomedial part of the medulla
  - Is chaotic, being irregularly interrupted and each breath varying in rate and depth
  - This pattern progresses to one of intermittent prolonged inspiratory gasps that are recognized by all physicians as agonal in nature and finally to apnea;


A
B
C
D
E
One minute

Clinical Signs of Increased Intracranial Pressure

- A history of headache before the onset of coma, vomiting, severe hypertension beyond the patient's static level, unexplained bradycardia, and subhyaloid retinal hemorrhages are immediate clues to the presence of increased iICP
- Papilledema develops within 12-24 h in cases of brain trauma and hemorrhage, but if it is pronounced, it usually signifies brain tumor or abscess (lesion of longer duration)
- Increased ICP produces coma by impeding global cerebral blood flow. High pressure within one compartment produces shifts of central structures and a series of "false localizing" signs due to lateral displacements and herniations

I. Diseases that cause no focal or lateralizing neurologic signs, usually with normal brainstem functions. CT scan and cellular content of the CSF are normal.

- Intoxications: alcohol, barbiturates and other sedative drugs, opiates
- Metabolic disturbances: anoxia, diabetic acidosis, uremia, hepatic failure, nonketotic hyperosmolar hyperglycemia, hypo- and hypernatremia, hypoglycemia, addisonian crisis, profound nutritional deficiency, carbon monoxide, thyroid states including Hashimoto encephalopathy
- Severe systemic infections: pneumonia, peritonitis, typhoid fever, malaria, septicemia, Waterhouse-Friderichsen syndrome.

- Circulatory collapse (shock) from any cause.
- Postseizure states and convulsive and nonconvulsive status epilepticu
- Hypertensive encephalopathy and eclampsia
- Hyperthermia and hypothermia.
- Concussion
- Acute hydrocephalus
- Late stages of certain degenerative diseases and Creutzfeldt-Jakob disease.

II. Diseases that cause meningeal irritation, with or without fever, and with an excess of WBCs or RBCs in the CSF, usually without focal or lateralizing cerebral or brainstem signs. CT scanning or MRI (which preferably should precede lumbar puncture) may be normal or abnormal.

- Subarachnoid hemorrhage from ruptured aneurysm, arteriovenous malformation, occasionally trauma
- Acute bacterial meningitis
- Some forms of viral encephalitis
- Neoplastic and parasitic meningitides

III. Diseases that cause focal brainstem or lateralizing cerebral signs, with or without changes in the CSF. CT scanning and MRI are usually abnormal.

- Hemispheral hemorrhage or massive infarction
- Brainstem infarction due to basilar artery thrombosis or embolism
- Brain abscess, subdural empyema, Herpes encephalitis
- Epidural and subdural hemorrhage and brain contusion
- Brain tumor
- Cerebellar and pontine hemorrhage.
- Miscellaneous: CVT, focal embolic infarction due to IE, acute hemorrhagic leukoencephalitis, ADEM, intravascular lymphoma, TTP, diffuse fat embolism
- Babinski signs and extensor rigidity, conventionally considered to be indicators of structural disease, do sometimes occur in profound intoxications with a number of agents.

- Often a convulsive seizure is marked by a bitten tongue, urinary incontinence, and an elevated CK-skeletal muscle fraction; it may be followed by another seizure or burst of seizures.
- The presence of small clonic or myoclonic convulsive movements of a hand or foot or fluttering of the eyelids requires that an EEG be performed to determine whether status epilepticus is the cause of coma. This state, called nonconvulsive status or spike-wave stupor must always be considered in the diagnosis of unexplained coma, especially in known epileptics

Laboratory Procedures

- CT scan or MRI should be obtained as the primary procedure.
- LP
- Blood and urine ("toxic screen").
- Accurate means are available for measuring the blood concentrations of phenytoin and other anticonvulsants, opiates, diazepines, barbiturates, alcohol, and a wide range of other toxic substances.
- Proteinuria for 2 or 3 days after a subarachnoid hemorrhage or with high fever.
- Urine of high specific gravity, glycosuria, and acetonuria occur almost invariably in diabetic coma; but transient glycosuria and hyperglycemia may result from a massive cerebral lesion.

- Blood counts should be obtained, a blood smear should be examined for parasites.
- It should be kept in mind that disorders of water and sodium balance, reflected in hyper- or hyponatremia, may be the result of cerebral disease (excess ADH secretion, diabetes insipidus, atrial natriuretic factor release), as well as being the proximate cause of coma.
- An EEG may be highly informative if no adequate explanation for coma is forthcoming from the initial examinations. This is the only way to reveal nonconvulsive status epilepticus as the cause of a stupor.

Management of the Acutely Comatose Patient

1. Breathing
2. Management of shock.
3. Labs: glucose, intoxicating drugs, and electrolytes and for tests of liver and kidney
4. ICP treatment
5. A lumbar puncture + ABx.
6. Convulsions should be controlled
7. As indicated above, gastric aspiration and lavage for drugs and toxins
8. Fever control
9. The bladder should not be permitted to become distended
10. Management of lytes (Na, K, etc)
11. Avoid aspiration pneumonia
12. DVT prophylaxis
13. Regular conjunctival lubrication and oral cleansing should be instituted.