NEUROLOGICAL EMERGENCY

The management of medical coma

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The patient who is brought to the hospital casualty department, or seen on the Intensive Care Unit, though not having been exposed to evident trauma, may be harbouring delayed effects of trauma such as a subdural haematoma or meningitis arising from a basal skull fracture. The problems of raised intracranial pressure following a parenchymal haematoma in a hypertensive patient, the decompensation of a cerebral tumour or collection of pus, means that all possible causes of loss of consciousness must be considered by the physician when dealing with a patient in coma. Thus in the diagnosis of medical coma it is not easy to exclude the patient in coma following head injury.

If one excludes patients with a transient loss of consciousness following seizure, syncope, cardiac dysrhythmia or hypoglycaemia and those unresponsive due to impending death, and considers patients who have been unconscious for some five to six hours, then 40% of such patients seen in medical practice will have taken some form of sedative drugs with or without alcohol.¹ Of the remainder just over 40% will have suffered hypoxic ischaemic insult as the result of cardiac arrest or anaesthetic accident, a third will be unconscious as a result of cerebrovascular accidents, either haemorrhage or infarction, and about a quarter will be unconscious as a result of metabolic coma including infection, renal failure, hepatic failure and complications of diabetes mellitus. If one considers only those cases who are initially regarded as "of unknown aetiology" the proportion of drug overdoses is about 30%, mass lesions about 34% and diffuse metabolic causes account for 36%.²

Few problems are more difficult to manage than the unconscious patient because the potential causes of loss of consciousness are considerable and because the time for diagnosis and effective intervention is relatively short. All alterations in arousal should be regarded as acute and potentially life threatening emergencies until vital functions are stabilised, the underlying cause of the coma is diagnosed and reversible causes are corrected. Delay in instituting treatment for a patient with raised intracranial pressure may have obvious consequences in terms of pressure coning but similarly the unnecessary investigation of patients in metabolic coma with imaging techniques may delay the initiation

of appropriate therapy. It is therefore essential for the physician in charge to adopt a systematic approach initially to ensure resuscitation, and then to direct further tests towards producing the most rapid diagnosis and the most appropriate therapy. The development of such a systematic approach demands an understanding of the pathophysiology of consciousness and the ways in which it may be deranged.

The causes of coma

The phenomenon of consciousness depends upon an intact ascending reticular activating substance in the brainstem to act as the alerting or awakening element of consciousness together with a functioning cerebral cortex of both hemispheres which determines the content of that consciousness. The ascending reticular activating substance is a continuous isodentritic core extending from the medulla through the pons to the mid-brain which is continuous caudally with the reticular intermediate grey lamina of the spinal cord and rostrally with the subthalamus, the hypothalamus and the thalamus.³ Its functions and interconnections are considerable and its role greater than that of a simple cortical arousal system. There are named nuclei throughout the reticular formation and, although it was originally considered that cortical arousal depended upon projections from the reticular formation via the midline thalamic nuclei to the thalamic reticular nucleus and the cortex, it now seems unlikely that the thalamic reticular nucleus is the final relay and the specific role of the various links from the reticular formation to the thalamus has yet to be identified.

Similarly the neurotransmitters involved in this arousal system are not fully determined though it seems likely that, in addition to cholinergic and monoaminergic systems, gamma aminobutyric acid (GABA) may be important in controlling consciousness.⁴⁻⁶

It follows from recognition of the anatomy and pharmacology of the ascending reticular activating substance that structural damage to this pathway or chemical derangement of the neurotransmitters involved are mechanisms whereby consciousness may be impaired. Such conditions will occur with focal lesions in the brainstem, mass lesions in the posterior fossa impinging directly on the brainstem or

mass lesions involving the cerebral hemispheres causing tentorial pressure coning and consequently compromising the ascending reticular activating substance either by direct pressure or by a process of ischaemia. In addition toxins, most commonly ingested drugs, may have a significant depressant effect upon the brainstem ascending reticular activating substance and thereby result in loss of consciousness.

The content of consciousness resides in the cerebral cortex of both hemispheres. Unlike those discrete cortical functions such as language or vision which are focally located within the cortex, the content of consciousness can best be regarded as the amalgum of all cognitive function. Coma arising from disruption of this cortical activity requires a diffuse pathology such as generalised anoxia or ischaemia, commonly seen after cardiac arrest or anaesthetic accidents, or the effects of presumed cortical vasospasm seen in infective meningitis or the chemical meningitis following subarachnoid haemorrhage where generalised cortical ischaemia is believed to be the cause of disruption of function.

For the physician attempting to diagnose the cause of coma consideration must be given to:-

A) *Supra or infra tentorial mass lesions.* Typically these will provide evidence of raised intracranial pressure and commonly produce focal signs. Pathologies such as neoplasm or haematoma, infarction with cerebral oedema, abscess, focal encephalitis and venous sinus thrombosis should be considered.

B) *Subtentorial destructive lesions or the local effect of toxin.* These pathologies will directly damage the ascending reticular activating substance as in brainstem infarction, rhombencephalitis, brainstem demyelination and the much more common effects of self-poisoning with sedative drugs.

C) *Diffuse damage to the cerebral cortex.* Bilateral cortical injury is most commonly seen in states of hypoxia and ischaemia but may be mimicked by hypoglycaemia, ketoacidosis, electrolyte abnormalities, bacterial meningitis, viral encephalitis and diffuse post-infectious encephalomyelitis. It is also the likely pathology of coma following subarachnoid haemorrhage.

Definitions

There is a continuum from the individual in full consciousness to the patient in deep coma. The terminology which is most usually employed derives from the Brain Injuries Committee of the MRC:-

A) *Confusion*—"disturbance of consciousness characterised by impaired capacity to think clearly and with customary repetition and to perceive, respond to and remember current stimuli; there is also disorientation". Confusion involves a generalised disturbance of cortical cerebral function which is usually associated with considerable EEG abnormalities. Some authors describe an intervening state between normal consciousness and confusion, that of clouding of consciousness.²

B) *Delirium*—"a state of much disturbed consciousness with motor restlessness, transient hallucinations, disorientation and perhaps delusions".

C) *Obtundation*—"a disorder of alertness associated with psychomotor retardation".

D) *Stupor*—"a state in which the patient, though not unconscious, exhibits little or no spontaneous activity". Although the individual appears to be asleep he or she will awaken to vigorous stimulation but show limited motor activities and usually fail to speak.

E) *Coma*—"a state of unarousable psychologic unresponsiveness in which the subjects lie with eyes closed and show no psychologically understandable response to external stimulus or inner need". This may be shortened to "a state of unarousable unresponsiveness" which implies both the defect in arousal and in awareness of self or environment manifest as an inability to respond. A more useful assessment of coma is derived from the hierarchical Glasgow Coma Scale⁸ in which patients who fail to show eye opening in response to voice, perform no better than weak flexion in response to pain and make, at best, only unrecognisable grunting noises in response to pain, are regarded as being in coma. This allows the patients to have an eye opening response of two or less, a motor response of four or less and verbal response of two or less. The sum Glasgow score of eight should not be regarded as being definitive of coma since the total score can be achieved in several different ways (table 1).

F) *Vegetative state.* When the cortex of the cerebral hemispheres of the brain recover more slowly than the brain stem or when the cortex is irreversibly damaged there may arise a situation in which the patient enters a vegetative state without cognitive function. It may be a transient phase through which patients in coma pass as they recover or deteriorate but, and commonly after anoxic injuries to the brain, there develops a state in which the brain stem recovers function but the cerebral hemispheres are not capable of recovery. When this occurs the patient enters a "persistent vegetative state" described by Jennett and Plum.⁹ Such patients may survive for long periods, on occasion for decades, but never recover outward manifestations of higher mental activity and the condition,

Table 1 The Glasgow coma scale

Eyes	Open	Spontaneously	4
		To verbal command	3
		To pain	2
	No response		1
Best motor response	To verbal command	Obeys	6
	To painful stimulus	Localises pain	5
		Withdrawal	4
		Flexion	3
		Extension	2
		No response	1
Best verbal response		Orientated	5
		Disorientated	4
		Inappropriate words	3
		Incomprehensible sounds	2
		No response	1

which is comparatively newly recognised, relates to the development of modern resuscitative techniques. Other terms have been used in the past to identify similar conditions. These include coma vigil, the apallic syndrome, cerebral death, neocortical death, and total dementia.

G) *Akinetic mutism* has been defined as a similar condition of unresponsiveness but apparent alertness, as demonstrated by reactive alpha and theta electroencephalographic rhythms in response to stimuli. The major difference from the vegetative state, in which there is tone in the muscles and extensor or flexor responses, is that patients with akinetic mutism have flaccid tone and are unresponsive to peripheral pain. It is thought that this state is due to bilateral frontal lobe lesions, diffuse cortical lesions or lesions of the deep grey matter.¹⁰

H) *The locked in syndrome*. Feldman¹¹ described a de-efferented state due to bilateral ventral pontine lesion involving damage to the corticospinal, corticopontine and corticobulbar tracts. The patient has total paralysis below the level of the third nerve nuclei and although able to open, elevate and depress the eyes has no horizontal eye movements and no other voluntary eye movement. The diagnosis depends upon the physician being able to recognise that the patient can open the eyes voluntarily and can signal assent or dissent by responding numerically with eye closure. Similar states are occasionally seen in patients with severe polyneuropathy, myasthenia gravis and after the use of neuromuscular blocking agents.

I) *Pseudo coma*. Rarely, patients who appear in coma without structural, metabolic, toxic or psychiatric disorder being apparent, can be shown by tests of brainstem function, to have intact brainstem activity and corticopontine projections and not to be in coma.

Resuscitation

Although resuscitation is commonly performed by the casualty officer or the anaesthetist in the Intensive Care Unit rather than by the neurologist it is appropriate that the neurologist remembers that, in patients who are unconscious, protection of the airway, respiration, support of the circulation and provision of an adequate supply of glucose are all important in stabilising the patient. It is frequently necessary to intubate the trachea in a patient in coma, not only to ensure an adequate airway but also to prevent the aspiration of vomit. It is also important to note the respiratory rate and pattern before intubation and certainly before instituting mechanical ventilation; since depressed respiration is a frequent clue to drug overdose or metabolic disturbance, increased respiration to hypoxia, hypercapnia or acidosis and fluctuating respiration may indicate a brainstem lesion. The possibility that respiratory failure is the cause of coma should always be considered in a patient with disordered respiration.

Once adequate oxygenation and circulation

are ensured and monitored, blood should be withdrawn for the determination of blood glucose, biochemical estimations and toxicology. It is then reasonable to give a bolus of 25–50g of dextrose despite the present controversy about the use of intravenous glucose in patients with ischaemic or anoxic brain damage. It can be argued that extra glucose in this situation may augment local lactic acid production by anaerobic glycolysis and potentially worsen ischaemic or anoxic damage. In practice in the situation of ischaemic or anoxic brain damage and even in the presence of a diabetic ketoacidosis the administration of such a quantity of glucose will not be immediately harmful and in the hypoglycaemic patient it may well be life saving. A reasonable compromise would be to obtain an early assessment of the level of blood glucose by dextrostix testing but these are not sufficiently accurate to preclude the need for formal laboratory assessment. When glucose is given in this situation an argument can be made for giving a bolus of thiamine at the same time to prevent precipitation of Wernicke's encephalopathy.¹²

An essential part of resuscitation includes the establishment of baseline, blood pressure, pulse, temperature, the establishment of an intravenous line and the stabilisation of the neck together with an examination for meningitis. It may be difficult in those patients who have sustained some degree of trauma in their collapse to assess the stability of the neck but the establishment of an adequate airway certainly takes precedence and the identification of meningismus in a febrile patient probably takes precedence over the stabilisation of neck movements. In a comatose febrile patient with meningismus seen outside the hospital environment the intramuscular injection of penicillin before transfer is now recognised to carry a significant advantage.

History

Once the patient is stable it is important to obtain as much information as possible from those who accompanied the patient to hospital or who watched the onset of coma. The circumstances in which consciousness was lost are of vital importance in helping to identify the diagnosis. Generally, coma is likely to present in one of three ways; as the predictable progression of an underlying illness; as an unpredictable event in a patient with a previously known disease; as a totally unexpected event. Distinctions between these presentations are often achieved by the history of the circumstances in which consciousness was lost. In the first category are patients following focal brainstem infarction who deteriorate or those with known intracranial mass lesions who show similar deterioration. In the second category patients with recognised cardiac arrhythmia or the known risk factor of sepsis from an intravenous line. In the final category it is important to determine whether there has been a previous history of seizures, trauma, febrile illnesses, or focal neurological distur-

bances. The history of a sudden collapse in the midst of a busy street or office indicates the need for different investigations from those necessary for the patient who is discovered at home in bed surrounded by empty bottles of sedative tablets.

Examination and monitoring

The third phase of the management of the patient in coma involves a rapid but systematic examination to identify possible causes of the coma.

Temperature

Fever usually indicates infection and rarely a brainstem or diencephalic lesion affecting the temperature centres.¹³ Most commonly the combination of fever and coma indicates systemic infection such as pneumonia, septicaemia or a cerebral cause such as meningitis, encephalitis or abscess. When seizures occur together with fever the possibility of encephalitis or cerebral abscess is greatly increased. Heat stroke may present as a febrile comatose patient when the clue to the diagnosis is in the environment.

Hypothermia is most commonly seen as a complication of an accident or cerebrovascular disease when an elderly patient is discovered having lain for hours or days in an underheated room. It may also be seen following intoxication with alcohol or barbiturates, with peripheral circulatory failure and rarely with profound myxoedema.

Heart rate

A tachyarrhythmia or bradyarrhythmia may be significant in identifying the cause of cerebral hypoperfusion. Irregularity of the pulse always raises the question of atrial fibrillation and associated embolic disease.

Blood pressure

Hypotension might indicate shock, myocardial infarction, septicaemia or intoxication. It may also indicate diabetes mellitus or Addison's disease. Hypertension is of less help in the diagnosis of the patient in coma as it may be the cause, as in cerebral haemorrhage or hypertensive encephalopathy, but it can also be the result of the cerebral lesion.

Respiration

For those reasons already given, assessment of respiration may be compromised by the needs of resuscitation but generally, slow and shallow breathing raises the question of drug intoxication. Deep, rapid respiration suggests pneumonia or acidosis which may also occur in brainstem lesions causing central neurogenic hyperventilation.

Integument

The appearance of the skin and mucous membrane may identify anaemia, jaundice, cyanosis or raise the possibility of carbon monoxide poisoning. Bruising over the scalp or mastoids, the presence of blood in the external auditory meati or nostrils will raise

the possibility of a basal skull fracture and bruising elsewhere in the body raises the question of significant trauma. An exanthem may indicate the presence of a viral infection causing meningoencephalitis, meningococcal septicaemia or raise the question of haemorrhagic disease. Hyperpigmentation raises the possibility of Addison's disease, and the presence of bullous skin lesions is frequently seen in barbiturate intoxication. Evidence of Kaposi sarcoma, anogenital herpetic lesions or oral candidiasis would raise the question of an acquired immune deficiency syndrome (AIDS) with the consequent plethora of possible CNS disease.

Breath

The odour of the breath of an unconscious patient may indicate the presence of intoxication with alcohol, raise the question of diabetes or suggest that the cause of coma is uraemic or hepatic.

Cardiovascular

Auscultation and examination of the heart may indicate valvular disease and raise the possibility of endocarditis. Bruits over the carotid vessels might indicate the presence of cerebrovascular disease and splinter haemorrhages seen in the nail bed would raise the possibility of sub-acute bacterial endocarditis or collagen vascular diseases.

Abdomen

Examination of the abdomen may reveal signs of trauma or rupture of viscera, hepatomegaly or splenomegaly may indicate the possibility of a portocaval shunt and the findings of polycystic kidneys would raise the possibility of subarachnoid haemorrhage.

Meningismus

Examination of the skull and spine is important and the physician should always look for neck stiffness. Kernig's test in which the resistance of flexion of the thigh with the leg extended is examined or Brudzinski's tests in which flexing of one thigh is noted to cause flexion of the other thigh, should be performed to help in differentiating neck stiffness, due to meningeal irritation, from that due to a developing tonsillar pressure cone. If the Kernig and Brudzinski tests are positive together with neck stiffness this implies inflammation in the lumbar theca and suggests a diffuse meningitic process. If these tests are negative, however, then the neck stiffness alone is more suggestive of a foramenal pressure cone.¹⁴

Fundal examination

The presence of papilloedema, fundal haemorrhage or evidence of emboli, together with the findings of hypertensive, vascular or diabetic retinopathy are important. The fundal appearances may be diagnostic as in the finding of subhyaloid haemorrhage but more commonly only help to confirm or refute evidence of raised intracranial pressure. The absence of papilloedema does not necessarily

mean that there is no increased intracranial pressure.

Neurological examination

The position, posture and spontaneous movements of the unconscious patient should be noted. The formal neurological examination consists of the elicitation of various reflex responses.¹³ The most important aspects of neurological examination are those which define the level of consciousness, identify the activity of the brainstem and search for evidence of lateralisation (table 2).

A) The level of consciousness

The Glasgow Coma Scale⁸ provides the most useful hierarchical assessment of the level of consciousness. The response to commands, calling the patient's name and painful stimuli are observed for eye opening, limb movement and voice. Painful stimuli such as supraorbital pressure for central stimulation and nail bed pressure for peripheral stimulation are useful and reproducible. Eye opening is relatively easy to assess though the fixed and unresponsive opening of the eyes sometimes seen in deep coma must not be confused with the volitional or reflex opening of the eyes from a closed position in response to stimuli. All four limbs are tested individually for movement and the best response is recorded in assessing the Glasgow Coma Scale but an asymmetry between responses may be of importance in the overall assessment (vide infra). Patients in lighter grades of coma still retain the ability to vocalise and may grimace and withdraw their limbs from pain. These responses are progressively lost as the coma deepens and it is important to test pain bilaterally in the periphery and cranially since patients may only vocalise or respond to painful stimuli on one side raising the possibility of hemianaesthesia and providing evidence for a focal lesion. A grimace response to painful stimulation is believed to indicate intact corticobulbar function² but there are patients in coma, particularly after hypoxic ischaemic insults, who show grimace in response to minor peripheral stimulation yet have no associated peripheral motor response. When this situation is seen it always raises the question of a ventral pontine lesion or of a cervical cord injury but more commonly evolves into a vegetative state and is, generally, a poor prognostic sign.

The level of coma should be documented

Table 2 Neurological assessment of coma

Glasgow coma scale	Eye opening Motor response Verbal response
Brainstem function	Pupillary reactions Corneal responses Spontaneous eye movements Oculocephalic responses Oculovestibular responses Respiratory pattern
Motor function	Motor response Muscle tone Tendon reflexes Seizures

serially and is one of the most important indicators of the need for further investigation. Thus when the level of consciousness can be seen to be improving there is no need to make urgent decisions but when deterioration occurs then management decisions must be made. It may of course be correct, when the prognosis is recognised to be hopeless, to make a decision not to undertake further investigation or therapy.

B) Brainstem function

The brainstem reflexes are particularly important in helping to identify those lesions which may affect the reticular activating substance, explain the reason for coma and potentially help in identifying the viability of the patient. The reflexes used are predominantly related to the eyes and the pattern of respiration:-

(1) PUPILLARY REACTIONS

The size, equality and reaction of the pupils to light is recorded. Unilateral dilatation of the pupil with loss of the light response suggests uncal herniation or a posterior communicating artery aneurysm. Midbrain lesions typically cause loss of the light reflex with midposition pupils, pontine lesions cause miosis but a retained light response. Fixed dilatation of the pupils is an indication of central diencephalic herniation and may be differentiated from the fixed dilatation due to atropine like agents by the use of pilocarpine eye drops which will cause miosis if the dilatation is due to loss of parasympathetic innervation but be ineffective if it is pharmacological. A Horner's syndrome may be seen ipsilateral to a lesion in the hypothalamus, thalamus or brainstem when it will be associated with anhydrosis of the ipsilateral side of the body, but can also be due to disease affecting the wall of the carotid artery when anhydrosis will only affect the face.¹⁵ Hepatic or renal failure and other forms of metabolic coma may make the light reflexes appear unduly brisk and the pupils therefore relatively small. Most drug intoxications tend to cause small and sluggishly reactive pupils and a pontine haemorrhage will cause pin point pupils due to parasympathetic stimulation.¹⁶

(2) CORNEAL RESPONSES

The corneal reflex is usually retained until coma is very deep. If it is absent in a patient who is in otherwise light coma then the possibility of drug induced coma or of local causes of anaesthesia to the cornea should be considered. The loss of the corneal response when drug overdose is excluded is a poor prognostic sign.

(3) SPONTANEOUS EYE MOVEMENT

The resting position of the eyes and the presence of spontaneous eye movements should be noted. Conjugate deviation of the eyes raises the question of an ipsilateral hemisphere or contralateral brainstem lesion. Abnormalities of vertical gaze are less common with a patient in coma but depression of the eyes below the meridian may be seen with damage at the level of the mid brain tectum

and in states of metabolic coma. The resting position of the eyes is normally conjugate and central but it may be dysconjugate when there is damage to the oculo-motor or abducens nerves within the brainstem or along their paths.

Roving eye movements seen in light coma are similar to those of sleep. They cannot be mimicked and their presence excludes psychogenic unresponsiveness.¹³ Periodic alternating gaze or "ping pong" gaze is a repetitive conjugate horizontal ocular deviation which is of uncertain aetiology.¹⁷ Spontaneous nystagmus is rare in coma since it reflects interaction between the oculovestibular system and the cerebral cortex. Retractory nystagmus in which the eyes jerk irregularly back into the orbit and convergence nystagmus may be seen with mid brain lesions.¹⁸ Ocular bobbing, an intermittent jerking downward eye movement, is seen with destructive lesions in the low pons and with cerebellar haematoma or hydrocephalus.¹⁹

(4) REFLEX EYE MOVEMENTS

These are tested by the oculocephalic and oculovestibular responses. The oculocephalic or doll's head response is tested by rotating the patient's head from side to side and observing the eyes. In coma with an intact brainstem the eyes will move conjugately and in a direction opposite to the head movement. In a conscious patient such a response can be imitated by deliberate fixation of the eyes but is not common. In patients with pontine depression the oculocephalic response is lost and the eyes remain in the mid position of the head when turned.

The oculovestibular response is more accurate and useful. It is elicited by instilling between 50–200ml of ice cold water into one external auditory meatus. The normal response in the conscious patient is the development of nystagmus with the quick phase away from the side of stimulation. A tonic response with conjugate movement of the eye towards the stimulated side indicates an intact pons and suggests a supratentorial cause for the coma. A dysconjugate response or no response at all indicates brainstem damage or depression. Both ears should be stimulated separately and if unilateral irrigation causes vertical eye movement the possibility of drug overdose arises because many drugs affect lateral eye movement.

The value of oculovestibular testing in patients without lateralising eye signs is considerable because they identify the intactness of the brainstem and corticopontine connections but may also reveal the presence of an intrinsic brainstem lesion by causing dysconjugate eye posturing. In addition they are the definitive way of identifying patients in psychogenic coma who will show normal nystagmus and frequently be distressed by the manoeuvre.

(5) RESPIRATION

Modern techniques of assisted respiration and the need to examine patients in intensive

care units where their respiration is controlled complicates the assessment of normal respiratory functions. If, however, the patient is seen before respiration is controlled then the presence of long cycle periodic respiration suggests a relatively high brainstem lesion, central neurogenic hyperventilation implies a lesion at the level of the upper pons and short cycle periodic respiration, which carries a poor prognosis, is seen with lesions lower in the brainstem. In general the presence of regular rapid breathing correlates with pulmonary complications and a poor prognosis rather than with the site of neurological disease in patients with coma.²⁰

C) Motor function

As part of the assessment of the Glasgow Coma Scale it may have been appreciated that there is lateralisation in the individual patient which implies a focal cause for the coma. The observation of involuntary movement affecting the face or limbs and asymmetry of reflexes will help to support this possibility. Focal seizures are an important indicator of a focal cause for the coma and the observation of more generalised seizures or of multifocal myoclonus would raise the possibility of a metabolic or ischaemic-anoxic cause for the coma with diffuse cortical irritation. The testing of tone as part of the assessment of muscle function can be useful in the comatose patient where it is possible to detect asymmetry of tone not only in the limbs but also in the face.

By this stage of the management of the patient in coma it should be possible to identify those patients who are unconscious with focal signs, those who are unconscious without focal signs but with the presence of meningismus and those who have loss of consciousness without either focal signs or meningismus (table 3).

Investigations of the patient in coma

The relevant investigations to be undertaken in the individual patient will be identified by the differential diagnosis. In general the role of investigation in the patient in coma is to help establish the aetiology of that coma and

Table 3 Classification of differential diagnosis of coma

Coma without focal or lateralising signs and without meningismus
1 Anoxic-ischaemic conditions
2 Metabolic disturbances
3 Intoxications
4 Systemic infections
5 Hyperthermia/Hypothermia
6 Epilepsy
Coma without focal or lateralising signs but with meningeal irritation
1 Subarachnoid haemorrhage
2 Meningitis
3 Encephalitis
Coma with focal brainstem or lateralising cerebral signs
1 Cerebral tumour
2 Cerebral haemorrhage
3 Cerebral infarction
4 Cerebral abscess

will vary from simple blood tests through more complex blood tests, examination of the CSF, electrophysiological tests and imaging investigation. Although the electroencephalogram has some hierarchical value in the assessment of the depth of coma and has been used to an extent to identify a prognosis of coma,^{21 22} its major role is in identifying patients who are in subclinical status epilepticus or have complex partial seizures because this will significantly alter their management.²³ It may also be useful in distinguishing between feigned or psychiatric coma, in which it will be normal, and genuine cerebral disease when it may show diffuse abnormalities or help to identify a focal lesion. The prognostic value of the EEG is probably not as great as that obtained from careful observation of clinical signs.²¹

Evoked potentials, predominantly brainstem evoked potentials and somatosensory evoked potentials, may give information relating to the intactness of brainstem pathways and to the existence of a cortical component. Theoretically the use of brainstem evoked responses could provide evidence for the presence and site of brainstem disease and, as they are relatively unaffected by drug coma, they may provide evidence on the aetiology.^{24 25} Regrettably there is as yet little correlation between evoked response studies in coma and prognosis but it seems likely that the use of somatosensory evoked potentials and brainstem auditory evoked potentials will become of value in identifying the prognosis of patients in coma. One technical problem is the need to undertake these recordings in the busy premises of an intensive care unit where considerable other electrical interference is occurring.

Brain imaging techniques including CT and MRI are important in coma in providing evidence of the diagnosis.²⁶ The former has a very significant role to play in identifying those patients who have a structural cause for coma though the latter has not yet been formally evaluated in this respect and there are problems in inserting the patient in coma together with necessary life support systems into the field of the MRI scan.

Other more complex techniques such as intracranial pressure monitoring and cerebral blood flow studies are rarely of help in the diagnosis of medical coma and their role in prognosis is not fully evaluated though they are likely to be limited by their invasiveness.²⁷ Measures of biochemical parameters in coma are predominantly diagnostic but some measures such as brain type creatinine kinase and neuron specific enolase in the cerebrospinal fluid may help in determining prognosis.²⁸

On clinical grounds patients can be allocated to one of three varieties of coma²⁹:-

1) *Coma with focal signs*

Except in those patients in whom an underlying and irreversible terminal disease is recognised, it is obligatory that CT scan or MRI scan be undertaken to identify the cause of the coma. This will define whether or not a structural abnormality is present and in many

instances give a clue to the underlying nature. If the CT scan is normal then the possibility of a nonstructural focal abnormality antedating the onset of coma or being part of the coma, as occasionally happens with hypoglycaemia or hepatic encephalopathy, must be considered. If there is no focal structural abnormality on a CT scan then other investigations including metabolic and CSF examination should be carried out.

Once the image has been obtained the question of more definitive therapy, be it neurosurgical, the reduction of intracranial pressure by the use of steroids and mannitol, the application of a specific antibacterial or antiviral agent, or the use of chemotherapy may be considered.

2) *Coma with meningeal irritation but without physical signs*

Patients in this group will usually be suffering from subarachnoid haemorrhage, acute bacterial meningitis, or viral meningo-encephalitis. The distinction between infective and noninfective can usually be made on the basis of fever and a lumbar puncture will be expected to reveal the cause. It is a counsel of perfection that, because of the theoretical potential of a collection of pus or of identifying the site of the subarachnoid haemorrhage, a CT scan should be undertaken before lumbar puncture. In practice in many hospitals throughout the United Kingdom, CT head scanning is not easily available and the presence of meningismus, particularly if associated with fever, raises the possibility of meningitis and indicates the need for an assessment of the CSF.

When CSF examination is undertaken by lumbar puncture it is important to remember that an inadequate lumbar puncture does not preclude the possibility of a pressure cone but may prevent proper assessment of the CSF. Although some authorities still recommend that only a few ml of fluid need be obtained for bacterial culture and cell count,¹² in practice once the dura and arachnoid are breached by a lumbar puncture needle the possibility of herniation does not depend solely upon the fluid which is collected but rather upon that which may leak out during subsequent hours. It is therefore important that when a decision to undertake a lumbar puncture is made sufficient CSF is obtained to enable an adequate assessment of the cell count, a gram stain and provide fluid for culture and antibody analyses together with a measure of the total protein and sugar.

In those centres in which a CT scan is available the detection of blood in the subarachnoid space at CT scan precludes the need for lumbar puncture but whether or not lumbar puncture has been carried out to identify the presence of subarachnoid haemorrhage the patient should then be transferred to a neurosurgical unit, probably be given intravenous nimodipine, and be subjected to angiography and surgery. In general those patients who are in coma from subarachnoid haemorrhage are less of a surgical emergency than those who have higher states of consciousness.

3) *The presence of coma without focal signs or meningismus*

These patients are likely to have a metabolic or anoxic cause for their coma. One of the commonest causes remains that of drug overdose and it is appropriate to withdraw blood to send to the toxicology laboratories in patients presenting in this way. In general there will be a clue from the circumstances in which the patient was discovered and from the previous history. Reliance is placed upon the assessment of metabolic and toxic metabolites in the blood and evidence should be sought for hepatic failure, renal failure, hyperglycaemia, hypoglycaemia, and disturbances of electrolytes or acidosis. The majority of commonly available drugs can now be assayed within blood and serum enzymes should also be estimated. Problems inevitably arise when patients who are unconscious have been consuming alcohol and an assessment of the relevant importance of this in causing the unconsciousness may be difficult. Again the problem may be helped by the expedient of measuring blood alcohol levels.

Perhaps the most important single cause of unresponsiveness, which is directly treatable and correctable, is that of hypoglycaemia and this should have already been covered during the initial resuscitation of the patient. By this time in management the formal level of blood sugar will have been estimated and appropriate treatment for hypo and hyperglycaemia may be instituted. The treatment of acid base abnormalities will require not only the routine biochemistry but arterial blood gas analysis to monitor progress. Usually a patient who has suffered from hypoxia or ischaemia will have been identified by the mode of presentation and by the normality of investigations thus far. The possibility of poisoning with carbon monoxide should be considered and excluded by the measurement of carboxyhaemoglobin. In general, patients who have suffered anoxic or ischaemic insult should be given 100% oxygen and the monitoring of PAO₂ will be important together with the maintenance of adequate circulation and oxygenation.

Patients who are in shock or hypertensive encephalopathy will be diagnosed by the level of blood pressure and those with disturbed temperature regulation by use of the thermometer, though a rectal thermometer may be required. These causes can then be corrected.

In patients with drug overdose the possibility of using specific antidotes should be considered. The use of Naloxone in patients in whom there is a high index of suspicion of opioid poisoning and Benzodiazepine antagonists in self-poisoning with Benzodiazepine. The use of analeptic agents in barbiturate poisoning cannot now be supported.³⁰ Consideration should also be given to clearing the ingested toxin from the stomach, the passage of a nasogastric tube should usually be considered and this is one indication for intubation of the trachea to prevent the risk of aspiration. The importance of the diagnosis of drug overdose coma is that such patients

have a good prognosis provided they are given adequate respiratory and circulatory support during their unconsciousness. They are, however, particularly liable to show depression of brainstem responses and if the possibility of drug overdose is not considered their level of coma may be misinterpreted and their prognosis might be thought unduly pessimistic.

The prediction of outcome in coma

Having made an assessment of the cause of coma, established its severity and introduced appropriate treatment, the physician should be able to identify the likely outcome to colleagues and to friends and relatives of the patient. Sedative drugs or alcohol overdose are not usually lethal and carry a good prognosis provided that circulation and respiration is protected. The physician can reasonably give a good prognosis in patients suffering from self-poisoning with sedative drugs provided that those complications of cardiac arrhythmia, aspiration pneumonia and respiratory arrest are avoided or corrected. In non-traumatic coma other than that which is drug induced those factors which determine the outcome have been defined³¹ and include the cause of the coma, the depth of the coma, the duration of coma and certain clinical signs, among the most important of which are brainstem reflexes. Overall only 15% of patients in non-traumatic coma for more than six hours will make a good or moderate recovery; the other 85% will die, remain vegetative, or reach a state of severe disability in which they remain dependent. Patients whose coma is due to metabolic reasons, including infection, organ failure and biochemical disturbances, have a better prognosis. Thirty five per cent of patients will achieve moderate or good recovery; of those whose coma follows hypoxic ischaemic insult only 11% make such a recovery; of those in coma due to cerebrovascular disease only 7% can be expected to make such a recovery. Twenty per cent of patients in coma following hypoxic ischaemic injury will enter the vegetative state due to the likelihood of hypoxic ischaemia resulting in bihemispheric damage with relative sparing of the brainstem.

Apart from the diagnosis the depth of coma affects the individual prognosis. Those patients not showing eye opening after six hours of coma have only a 10% chance of making a good or moderate recovery whereas those whose eyes opened in response to painful stimuli have a 20% chance of making a good recovery. The longer the coma persists the less likely there is to be recovery; 15% of patients in coma for six hours make a good or moderate recovery compared with only 3% who remain unconscious at one week.³¹

The study of 500 patients reported by Levey *et al*³¹ using prospective data from patients with clearly defined levels of coma, diagnoses and outcomes, showed that some clinical signs are significantly associated with a poor prognosis: in the total cohort of 500

Table 4 Clinical signs and prognosis

Time	Sign	Cohort	Patients with the sign	False positive survivors	95% confidence interval
24 hours	Absent corneal response	500	90	0	0-5%
24 hours	Absent pupillary response	210	52	0	0-5%
3 days	Motor poorer than withdrawal	210	70	0	0-5%
7 days	Absent roving eye movements	210	16	0	0-5%

Summarised from Levy *et al.*³¹

patients corneal reflexes were absent 24 hours after the onset of coma in 90 patients and this sign was incompatible with survival. In a more uniform group who suffered anoxic injury there were 210 patients: 52 of these had no pupillary reflex at 24 hours, all of whom died. By the third day 70 were left with a motor response poorer than withdrawal and all died. By the seventh day the absence of roving eye movements was seen in 16 patients all of whom died. The confidence intervals for all of these criteria were 0-95 (table 4).

At the opposite end of the scale more than 25% of patients who show roving conjugate eye movements within six hours of the onset of coma or who show withdrawal responses to pain or eye opening to pain, will recover independence and make a moderate or good recovery. The use of combinations of clinical signs help to improve the accuracy of prognosis: at 24 hours the absence of a corneal response, pupillary light reaction or caloric or doll's eye response is not compatible with recovery to independence. Patients who are able to speak words within 24 hours or who show nystagmus on caloric testing are likely to make a good recovery (table 5).³²

The most accurate prediction of outcome in a patient in medical coma is still that which

is obtained from the use of clinical signs and there is little to be added by more sophisticated testing other than in identifying the cause of the coma. It is possible to predict those patients who will not make a recovery and who will die in coma or who will enter a vegetative state within the first week of coma. It is rare for patients in medical coma who are in a vegetative state at one month to show any form of recovery.³³

Continuation of care

The long term care of patients in coma maybe undertaken in an intensive care unit, on a specialist ward or later in a long stay hospital. It is important that those patients in whom prognosis is hopeless should not be permanently exposed to the rigors of intensive care medicine, but should continue to receive basic care within routine hospital wards. So long as patients are considered to have a potential for recovery they should be looked after in intensive care units or on specialist wards. Their respiration, skin, circulation and bladder and bowel function need attention, seizures controlled and the level of consciousness regularly assessed and monitored. It is important that the mobility of joints and circulation to pressure areas are maintained during the long term care of the patient and the possibility of aspiration pneumonia, peptic ulceration and other complications of long term intensive care be considered and avoided. Techniques such as mechanical ventilation and the use of steroid therapy are not to be used routinely in the management of the comatose patient as they do not improve prognosis and may specifically compromise recovery.³⁴

The persistent vegetative state

The relative resilience of the brainstem allows it to survive injuries which may create irreversible damage to the cerebral hemispheres and then the patient will enter that state defined as vegetative. Retrospectively, after postmortem examination, it may be possible to identify massive neocortical damage which will indicate that the patient was permanently in the vegetative state,³⁵ but there are no clinical or laboratory means of confirming this before postmortem, and therefore the term persistent vegetative state rather than permanent vegetative state is used clinically. Specialists in rehabilitation are concerned that physicians may take the attitude that there is no point in treating such patients therefore creating a self fulfilling prophecy of poor prognosis, no treatment and poor outcome.³⁶

There is continuing debate as to the potential for recovery for patients who are vegetative. In patients who have suffered non traumatic injury such as anoxia and ischaemia, the prognosis for recovery from the vegetative state is poor after the first few weeks. There are some reports of patients who have suffered coma as a result of head trauma in whom an improvement from the

Table 5 Prediction of outcome of coma at 24 hours by a combination of clinical signs

		Percentage of patients with different outcomes		
		D/PVS	SD	MD/GR
500 patients				
Any two reacting: Pupils Corneals Oculovestib	No (120)	97	2	1
Yes				
Motor better than flaccid	No (183)	80	8	12
Yes				
Motor withdrawal	No (135)	69	14	17
Yes				
Verbal moans	No (106)	58	19	23
Yes (56)	46	13	41	

Summarised from Levy *et al.*³¹

vegetative state has been recognised after months, but these anecdotal cases of recovery from vegetative state are difficult to validate and it seems possible that such patients were not truly vegetative, rather in a state of profound disability but with cognition, at the beginning of the observation.³⁷⁻³⁹

Investigations do not help to identify vegetative state because many types of EEG pattern have been recorded from near normality to a flat record and CT scans usually show considerable cortical atrophy with ventricular dilatation. Somato-sensory evoked responses are said to show loss of the cortical component and PET scans to show cortical metabolic under activity. None is diagnostic in their results.⁴⁰

Patients in a persisting vegetative state will often have received artificial ventilation at sometime during their initial coma or resuscitation, but they are not truly respirator dependent and, since they are able to breathe, are only dependant upon carers for the supply of liquid and nutrients and the prevention of complications. The management of individual patients will depend upon circumstances and other aspects of the diagnosis and considered prognosis.⁴¹

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