THE NORTHERN HOSPITAL

COMA AND ALTERED CONSCIOUS STATES

"Danaid", in marble, 1885, Auguste Rodin.

...We turned our backs upon that dismal valley,
First climbing up the bank that circles it,
then crossing over, while speaking not a word.

Here it was, less than night and less than day -
I could not see too far ahead.
But I heard a horn blast that would have made

the loudest thunderclap seem faint.
To find its source I turned my eyes
back to the place from which the din had come.

After the woeful rout when Charlemagne
had lost his holy band of knights,
Roland did not sound so terrible a blast.

I had not looked that way for long
when I saw what seemed a range of lofty towers,
and I said, "Master, tell me what city is this?"

(Dante and Virgil approach the Ninth Circle of Hell)
Dante Alighieri, The Inferno, XXXI, 7-27 (1306-1317)

In ancient Greek mythology the Danaïdes were the fifty daughters of King Danaus, ruler of a large North African kingdom. Aegyptus his twin brother and king of Egypt had fifty sons and so he ingeniously proposed that his sons marry the daughters of Danaus. But Danaus realized that his brother merely wanted to get control of his kingdom through his sons and so he refused. Aegyptus threatened war and so Danaus fled with his fifty daughters and lived in exile in the Greek city of Argos. Aegyptus then threatened war on Argos, and so Danaus pretended to go along with Aegyptus and allow his daughters to marry Aegyptus' sons. Danaus, however instructed his daughters to stab to death their husbands on their wedding night, which they duly did, at least all but one of them, Hypermnestra, who actually fell in love with her husband. Because of the crime the daughters of Danaus committed, in the afterlife they were condemned to the Tartarus, the ultimate Ninth Circle of Dante's Hell.

In 1885 the French state commissioned Auguste Rodin to produce a set of large bronze doors for the proposed new Museum of Decorative Arts in Paris. Taking inspiration from Lorenzo Ghiberti's, "The Gates of Paradise" from the Cathedral Baptistery in Florence, Rodin decided to produce "The Gates of Hell". He used motifs from Dante's Inferno to produce figures of the damned which included most famously "The Thinker", who seethe over and dissolve into one another in sensuous and sometimes sexually charged contortions.

One of Rodin's greatest works is without doubt the "Danaid", a vision of touching despair. In the afterlife she is condemned to the Tartarus, one of the worst places in Dante's Inferno, where she along with her sisters are compelled to lift great pitchers and fill an enormous well with water. The well, however, is bottomless and so her back breaking task will continue for all eternity. When learning of her fate she flings herself down on the ground in unimaginable despair. The beautiful figure of the Danaid, in fact never appeared on Rodin's

"Gates of Hell", but rather as a stunning stand-alone marble work. The poet Ranier Maria Rilke was entranced and described it in 1903:

"It is wonderful to walk slowly about this marble, to follow the long line that curves about the richly unfolded roundness of the back to the face, which loses itself in the stone as though in a great weeping. … There were undulations without end."

Auguste Rodin's beautiful "Danaid" of ancient Greek mythology depicts one of the fifty daughters of King Danaus, condemned to the underworld for the murder of their husbands, flinging herself to the ground in despair at the gates of Hell. The unfortunate Danaid also demonstrates the correct "coma" position of head down and to the side, for any patient suffering from a reduced conscious state.

COMA AND ALTERED CONSCIOUS STATES

Introduction

The term "**coma**" does not have a precise definition.

Generally it is taken as a GCS of **8 or less.**

In older terminology, coma was considered to be a state of unconsciousness from which a patient could not be roused, (c.f. "stupor", a state of unconsciousness from which a patient could be roused but not fully).

It is more useful to think of a patient as having a reduced conscious state, with a spectrum that varies from mild to severe, the severity of which is most commonly *scaled* according to the GCS.

All patients should have a **BSL** checked

In *general* terms a CT scan is usually sufficient for diagnosis in cases of trauma, unless a vascular injury needs to be specifically excluded.

It cases of **non-trauma**, **vascular** and **contrast scans** will be required.

Pathophysiology

Altered conscious states pathologically are due to one or both of bilateral depression of cortical function and/ or depression of the reticular activating system within the brainstem.

Causes

The causes of an altered conscious state fall broadly into 10 categories:

1. Drugs and toxins:

- Generally any CNS depressant in overdosage:

  Most commonly:

  - ♥ Alcohol
  - ♥ Opioids
  - ♥ Benzodiazepines
  - ♥ Antidepressants (tricyclics in particular).
  - ♥ Minor and major tranquilizers.
  - ♥ A large range of poisons and toxins.

2. Infections:

   - Within the CNS:
     - ♥ Meningitis
     - ♥ Encephalitis
     - ♥ Cerebral abscess
   - Severe generalized sepsis

3. Trauma:

   - Direct brain injury (including diffuse axonal injury)
   - Cerebral edema
   - Space occupying hematomas, (intra or extra axial)

4. Environmental:

   - Hyperthermia
   - Hypothermia
   - Electrocution / Lightning strike

5. Metabolic:

   - Electrolyte disturbances, (predominantly **hyponatremia**, hypercalcemia and severe acid/base disturbances)

- Glucose disturbances, (**hypoglycemia** and hyperglycemia)
- Respiratory failure, (**hypoxia and hypercapnia**)
- Renal failure with severe uremia
- Hepatic failure (encephalopathy)
- Endocrine:
    - ♥ Adrenal insufficiency eg: Addison's disease
    - ♥ Myxedema coma
- Thiamine deficiency (Wernicke's encephalopathy)
- Other rare causes (acute porphyrias)

6. Seizure activity:
    - Post ictal
    - End stage status epilepticus (uncommon but very important cause and often overlooked). *There may not be any motor activity to suggest this.*

7. Stroke:
    - Infarcts or hemorrhage, including SAH.

      Supratentorial lesions usually need to be extensive to cause a reduction in conscious state, (to produce bilateral cortical depression).

      Lesions within the posterior fossa are more likely to cause a reduction in conscious state, due to direct compression of the reticular activating system of the brainstem.

      Lesions within the **brainstem** (such as basilar artery thrombosis) are especially likely to result in altered states of consciousness, in association with protracted vomiting.

8. CVS:
    - Hypertensive encephalopathy
    - Shock or poor perfusion states (from any cause).

9. Raised intracranial pressure in general:

- Space occupying lesions
- Hydrocephalus
- Cerebral edema, (of any cause).

10. Psychogenic conditions:
    - Hysterical conversion reactions
    - Catatonic states
    - Severe depression.

Complications

There are a number of important secondary complications of "coma" including:

1. Airway problems:
    - Obstruction.
    - Aspiration.
2. Hypothermia:
    - In prolonged cases or more acutely in very cold environments.
3. Rhabdomyolysis;
    - With prolonged immobilization, especially in relation to **hypekalemia.**
4. Pressure areas, (with prolonged immobilization)
5. Trauma, including cervical spine.

Clinical Assessment

Important points in history:

1. History from any witnesses:
    - Collapse
    - Period of unconsciousness
    - Any actual or possibility of trauma.

- Environmental conditions, in particular for:
    - ♥ Hypothermia
    - ♥ Hyperthermia
    - ♥ Patient in a confined space with fires (carbon monoxide poisoning)
- Any features of seizure activity.

2. Possibility of **overdose**, including alcohol consumption.
3. Past history, especially of:
    - Diabetes
    - Seizures
    - Drug / alcohol use.
4. Medications, especially:
    - DOACs/ warfarin
    - CNS depressants.

Important points of examination:

1. Initial assessment of ABC.
2. **Check glucose on all patients with an altered conscious state.**
3. Assess for any evidence of trauma, especially head injury, including hemotympanum.
4. Check vital sings including temperature.
5. Assess neurological status:
    - GCS
    - Pupils and responses:

      Pinpoint pupils are characteristic of:
        - ♥ Some drug toxicities, and toxins, classically:
            - ♥♥ **Opioids**

- ♥♥ **Organophosphates**
- ♥♥ **Phenothiazines**
- ♥♥ **Clonidine**

♥ Midbrain (classically **pons**) pathology.

- Lateralizing signs.

6. Skin:
   - Rashes, in particular petichial.
   - "Track marks", suggestive of drug use, (**see also heroin overdose document in Toxicology folder**)
7. Neck stiffness (unless cervical spine injury is suspected)

Many texts also describe abnormalities in patterns of respiratory effort or ocular reflex movements when discussing the assessment of the comatose patient. Whilst academically interesting they usually add little or nothing to immediate diagnosis or management, **(see appendix 1 below**).

Investigations

The extent of investigation will depend on how unwell the patient is and the degree of suspicion for any given condition or secondary complication.

Important considerations will include:

Bloods tests

1. FBE
2. CRP
3. U&Es/**glucose**
4. LFTs
5. Clotting profile
6. CK and troponin levels
7. ABGs/ VBGs/ lactate

8. Blood cultures

9. Toxicological screen, according to clinical suspicion.

    - **In particular blood alcohol, paracetomol levels.**

10. TFTs, if thyroid pathology is suspected.

Urine via IDC

Test for:

1. M&C

2. Drug screen:

    - Not helpful acutely, but may be very helpful as documentation for future reference.

3. Myoglobin, (rhabdomyolysis in cases of prolonged coma)

ECG

Look for:

1. Hyperkalemia secondary to rhabdomyolysis.

2. Evidence of hypothermia.

Plain Radiography:

CXR for signs of aspiration, if there is clinical suspicion for this.

CT scan/ CT angiogram/ CT venogram:

The threshold must always be **low** to do a cerebral CT scan.

It is mandatory when the diagnosis is unclear.

Remember that more than one pathology may exist; the "drunk" patient may also have a head injury.

In general terms a **plain CT** scan is usually all that is necessary in cases of **trauma**

CT with contrast may be needed for **cerebral tumours**

In cases of **non-trauma** a **CT angiogram** should be done if a **vascular** pathology is suspected or needs to be excluded including:

- **Stroke syndromes (where a CT perfusion scan will also be required)**
- **Subarachnoid hemorrhage**
- **Carotid or vertebral artery trauma/ dissections**

CT venograms are required for:

- **Cerebral venous thrombosis**
- **Cavernous sinus thrombosis**

MRI

If the cause of coma remains unclear following CT scan/ CT angiography, an **MRI** scan may be considered according to the clinical picture.

Cerebral infarcts, unusual infections or space occupying lesions, toxic encephalopathies, ischemic encephalopathies, cerebral vein thrombosis may not show up well / at all on initial CT scans.

MRI can be problematic in unwell/ intubated patients. It may be done later when a patient is more stable. Importantly MRI scan should not delay empirical treatments of potentially serious pathologies (e.g., encephalitis, meningitis).

Lumbar Puncture

The role of LP in this setting is controversial because of the concern regarding raised intra-cranial pressure, which cannot be reliably ruled out on CT scan alone.

Altered conscious state itself can be a sign of raised ICP.

It is safest in the first instance to simply treat for meningitis/encephalitis if these conditions cannot be ruled out

EEG

This is useful when end-stage status epilepticus or ongoing seizure activity is suspected, however this is not widely available outside of specialist tertiary centers.

Management

Empirical management will depend on:

- How unwell a patient is.
- The degree of airway compromise.

- The degree of clinical suspicion for any given condition.
- The degree of clinical suspicion for any given secondary complication of coma.

In general empirical terms|:

1. ABC:

    - **Attention to any ABC issues will be the immediate priority in all cases.**

      Once initially stable the patient may be managed in the coma position in cases of non-trauma or immobilized with additional spinal precautions as necessary in cases of trauma or suspected trauma.

      Establish IV access, take blood tests and establish monitoring, (blood pressure, ECG and pulse oximetry). Intubated patients must also have end tidal CO_2 monitoring.

2. **Check the glucose level by finger prick testing.**

3. **Empirical coma treatments:**

    Careful thought should be given to each of these rather than their indiscriminate use in all cases, as each has potential hazards in particular settings. [1]

    - Glucose:

      Glucose for any hypoglycemia is mandatory and potentially life saving.

      Note however that 50% glucose can worsen neurological outcomes in patients with ischemic cerebral injury; [2] hence a finger prick glucose level to confirm hypoglycemia is best done, if possible prior to its administration.

    - Naloxone:

      Naloxone is safe and effective if opioid intoxication is suspected.

      It may potentially result in severe withdrawal symptoms and aggression in chronic opioid abusers.

      Its effect is relatively short lived and uncooperative patients may not be willing to undergo further observation upon wakening.

      The aim should be to avoid dangerously depressed levels in conscious state or respiration that may require intubation, rather than achieving full alertness.

In the hospital setting where there are staff with advanced airway skills careful observation may be the best management.

Where these skills do not exist full reversal is preferred.

In all cases initial BLS measures must still take priority over naloxone administration.

- Flumazenil:

  Flumazenil is generally *avoided* as a *routine* empirical drug in cases of altered conscious state of uncertain etiology because of concerns about the precipitation of seizures in patients with epilepsy, chronic benzodiazepine use and in unrecognized TCA co-ingestion.[3]

  It may be used to avoid intubation in cases where these concerns can be specifically and reliably ruled out.

- Thiamine:

  Thiamine should be given to chronic alcoholics in whom Wernicke's encephalopathy is suspected.

  In these cases it should initially be given intravenously, (see separate document on Thiamine in Drugs Folder and Wernicke's encephalopathy in Neurology folder).

  Wernicke's encephalopathy is a very uncommon cause of coma, far more commonly it presents with confusion, ataxia and ophthalmoplegia.

  Fears of allergic reaction to IV thiamine and the fact that coma is an uncommon presentation of Wernicke's encephalopathy have limited its use in this setting. However these fears have been overstated and in the vast majority of cases IV thiamine is safe.[4,5]

  Although coma is a rare presentation of Wernicke's the consequences of missing the diagnosis are severe and so if doubt exists IV thiamine should still be given.

  Note that large glucose doses may precipitate Wernicke's encephalopathy in **thiamine deficient** patients and so alcoholic patients who receive IV glucose should also receive thiamine.

- IV Phenytoin:

  Or other antiseizure medication if seizure activity is suspected.

4. Charcoal

- This may be considered in *intubated* patients in whom overdose is suspected or possible.

  Because of the risk of aspiration it should never be given to unintubated patients who have an altered conscious state, or in alert patients who are likely to develop a rapid deterioration in conscious state.

5. Sedation

   - Paradoxically some sedation (or even intubation) may be necessary for patient agitation, in order to assist in potentially life saving investigation and management of the patient.

6. Empiric anti - infective agents:

   If there is any concern about an infective cause:

   - **IV antibiotics should be given early**.

   - **IV acyclovir should be given early.**

   IV anti-malarials if cerebral malaria is suspected

   - **Anti-influenza treatment may also be considered when suspicion is high for influenza infection.**

Disposition

Any patient who requires ongoing observation for an altered conscious state must be admitted to a HDU or ICU where appropriate **monitoring** can occur and **appropriately trained staff** are available.

Appendix 1

Assessment of respiratory pattern

The respiratory pattern may give a clue to the level of a neurological lesion and its severity, though in pratical management terms this adds little.

Diencephalic (or Cheyne-Stokes) respiration:

Here there is loss of forebrain (ie cerebrum) control of voluntary respiration.

There are alternating periods of increasing breaths followed by periods of apnea.

This pattern may be seen in normal infants, sedated elderly or occasionally young people at altitude)

Pneumotaxic breathing:

This indicates upper brainstem or midbrain involvement.

There is rhythmic hyperventilation without pause between respirations. The I:E ratio is 1:1

Differential diagnosis is a normal hyperventilation response.

Apneustic breathing:

This indicates a pontine lesion.

There is "periodic" breathing, i.e. regular inspiratory gasps with a prolonged pause at the end of inspiration.

Ataxic breathing:

Here there is very irregular respiration indicating medullary involvement.

It is often a forerunner to "agonal" respiration and death.

Cord Transections:

Note that with a transection between the pons and medulla respiration will continue as the respiratory center is in the medulla. (The pons acts to fine tune only)

A transection below the medulla but above the phrenic nerve (C345) will result in apnea.

A transection below C5 will result in paradoxical breathing, i.e. the chest wall is drawn in on inspiration, (the diaphragm is able to act but not the intercostal muscles).

An important differential diagnosis of this pattern of breathing is upper airway obstruction.

Assessment of eye signs

Pupillary signs

- In a patient that is awake and alert a dilated pupil is not due to raised intracranial pressure.
- Papilloedema is more a feature of chronically raised intracranial pressure, not acutely raised pressure.
- With lesions above the midbrain (i.e. into the cerebrum) but without significant mass effect pupil size will be normal and react normally, however the gaze may be dysconjugate.
- Midbrain lesions result in midpoint pupils, which react sluggishly to light.
- Pontine lesions result in fixed, pinpoint pupils.
- Brain death results in fixed and dilated pupils.

Assessment of ocular movements

- Without cortical control most comatose patients will have roving eye movements providing the brainstem is intact.
- Note that eye movements may be conjugate or dysconjugate, but as long as both eyes are able to cross the midline the brainstem is intact.
- With cortical injuries eye gaze will deviate away from an irritative lesion and towards an inactive or ablative lesion e.g. during a seizure the eyes are deviated away from the seizure focus.
- To help distinguish a cortical from a brainstem lesion the “doll’s eye” response can be examined. If present the brainstem will be largely intact.

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Dr J.Hayes
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