Outline the important management principles in treating a patient who has been admitted to your ICU intubated and ventilated immediately following successful resuscitation from an out of hospital cardiac arrest.

Post-resuscitation care has an impact on overall outcome and consists of ongoing resuscitation and organ support, neuroprotection, treatment of the cause of the cardiac arrest and management of underlying co-morbidities.

- Check adequacy of **airway**, ETT position, ventilation and circulatory status
- Appropriate monitoring and intravenous access
- **Ventilation:**
  - Control CO2
  - Avoid hypoxia and hyperoxia
- **Circulation:**
  - Stabilise circulation with fluid therapy and vasoactive drugs
  - Consider early echo
  - Diagnosis / treatment of acute coronary syndrome with angiography/PTCA or thrombolysis
  - Evaluation for pacemaker or ICD if primary dysrhythmia
  - Mechanical support - use of IABP for cardiogenic shock in acute MI has recently been questioned.
  - Some centres may consider use of ECMO
- **Neurological:**
  - Therapeutic hypothermia at 32-34oC for 12-24 hr appears to be neuroprotective with improved neurological outcome although the optimal method and timing of cooling is still to be determined.
  - Treatment of seizures
- **Diagnosis and management of precipitating event**

Let us deconstruct this answer. This question interrogates the candidate's ability to approach a post-arrest patient in a systematic manner. Of course, the natural tendency of any ICU trainee would be to immediately start ranting about therapeutic hypothermia (hard to blame them, of course - it is indeed an exciting topic). And then to strat ranting about family discussions. The savvy candidate will note that there is no mention of family discussions in the model answer.
The answer is organised in a familiar A-B-C-D of resuscitation. I have both a brief summary of post-resuscitation care, and a prolonged elaboration of this topic. In brief, a structured answer would resemble the following:

**Airway support:**
- The comatose patient should be intubated, and the ETT secured.

**Breathing:**
- Mechanical ventilation (mandatory mode) should be commenced
- No unique recommendation - standard ventilation
- Aim for normoxia and normocapnea.
- Avoid hyperoxia.
- Anticipate aspiration pneumonia, pneumothorax, pulmonary oedema, pulmonary contusions, and ARDS.

**Circulation**
- Anticipate distributive shock, potentially with cardiogenic shock
- Vasopressor support, inotropes and fluids as required to maintain a MAP >65
- Urgent coronary angiogram, if there is no obvious non-cardiac cause of arrest.
- Urgent TTE
- Watch for QTc prolongation

**Disability (.. or prevention thereof)**
- Therapeutic hypothermia to 32-24° if the patient remains comatose;
- Targeted temperature management is a valid alternative, and may be preferred
- Avoid hyperthermia
- Sedation and neuromuscular blockade; avoid benzodiazepines.
- EEG

**Electrolytes**
- Watch for hypokalemia
- Replace electrolytes to prevent arrhythmias

**Fluids and renal function**
- Renal function may deteriorate due to hypoxic injury
- Hypothermia may result in hyperviscosity; use crystalloid
- Anticipate a vigorous diuresis with hypothermia

**Gastrointestinal and nutritional support**
- Normoglycaemia maintained with an insulin-dextrose infusion
- No need to start feeds until after rewarming

**Haematological issues**
- Avoid invasive procedures while hypothermic
- Platelet dysfunction coagulopathy and thrombocytopenia of hypothermia are reversible.
- If the patient has ongoing uncontrolled bleeding, therapeutic hypothermia is contraindicated.

**Infectious complications**
- Most common complication is pneumonia (staphylococcal)
- Most common bacteraemia is gram negative (bacterial translocation from the gut)
- In hypothermia, leucocyte migration and phagocytosis are impaired, predisposing to infection.
First, the college wants you to acknowledge that the patient is intubated, and that you are concerned about their ETT position. This, as a matter of general principle, is never wrong.

Secondly, the college wants you to acknowledge that you would pursue normoxia and normocapnea. TTE, angiography, fluids and vasopressors are mentioned - again, this is consistent with the AHA guidelines.

Therapeutic hypothermia is mentioned, and it would be amiss to write an answer to this question without discussing this.

Overall, the model answer expects nothing surprising or inventive from the candidate. The only unusual feature is the mention of ECMO, which (unlike the rest of the answer) does not have strong evidence behind it in post-resuscitation care.

---


Critically evaluate the use of therapeutic hypothermia in intensive care practice.

Maintenance of a target temperature to provide neuroprotection. A range of different temperatures employed with 'mild hypothermia' traditionally 32-34oC; more recently 36oC post TTM trial.

**Rationale:**

Hypothermia may lessen the brain injury through a number of mechanisms:

- Cerebral metabolic rate decreases by ~6-10% per degree Celsius drop in temperature
- Reduced release of excitatory amino acids / glutamate which mediate neuronal injury
- Reduced ischaemia reperfusion induced reactive oxygen species release
- Reduced inflammation – both cellular response and cytokine expression
- Reduced apoptosis
- Preservation of blood brain barrier (reduced NO, aquaporin 4, metallo-proteinases)

**Clinical utility and evidence:**

Post cardiac arrest:

- Standard of care
- HACA and Bernard studies in 2002 cooled VF/VT patients to 32-34 for 12-24 hrs.
- TTM trial 2013 showed no difference between target 33 and 36 in patients with out of hospital arrest of presumed cardiac cause. Fever avoided for 72 hrs in TTM.
- Current ARC/ILCOR guideline remains 32-34 but either approach reasonable.
- Avoidance of hyperthermia may be more important than hypothermia.
- ILCOR draft guidelines for 2015 recommend 32-36 for all arrests with unresponsiveness post ROSC for 24 hours (weak recommendation, very low quality evidence.)
- Prehospital cooling with crystalloid confers no benefit with increased APO
- Studies that suggest benefit of TTM in patients with cardiac arrest post hanging
- HYPERION trial underway to evaluate TTM 32.5 – 33.5 in non-shockable cardiac arrest survivors

**Traumatic brain injury:**

- Multiple studies have looked at TH to treat severe TBI i.e. prophylaxis.
- Meta-analysis of trials spanning over 20 yrs suggests a beneficial effect on mortality and favourable outcome.
- When limited to higher quality trials no significant mortality benefit.
- BTF guidelines level III recommendation for prophylactic hypothermia with no significant decrease in mortality but association with higher GOS
- Cooling associated with lower ICP and higher incidence of pneumonia
Most trials using 32-35 degrees for at least 48 hrs
- POLAR awaited – TH for severe TBI
- Eurotherm 3235 awaited – TH for Intracranial hypertension
- TH commonly used to treat intracranial hypertension rather than as prophylaxis.
- Contemporary data evaluating this practice is lacking

Other potential uses

Hepatic encephalopathy
- Intracranial hypertension common in grade III/IV encephalopathy related to ALF
- Some advocate cooling as a treatment of strategy to manage intracranial HT
- Controversial
- No RCTs

Meningitis
- Evidence of potential harm

Stroke
- Fever associated with two-fold risk of death after haemorrhagic or ischaemic stroke
- Pharmacologic methods of fever control have not shown improved outcome
- NINDS and European (EuroHYP-1) funded trials looking at induced hypothermia underway

Seizures
- Case reports with HYBERNATUS trial underway evaluating TH for refractory SE

SAH
- No good data to support the use of TH in SAH.
- Small studies have looked at TH in patients with intracranial HT
- Fever associated with worse outcomes

Neonatal encephalopathy
- Results of RCTs recommend cooling 33-34 for 72hr

Adverse effects:
- Bradycardia / Arrhythmias
- Increased SVR and venous return with cold diuresis
- Hypokalaemia during cooling and rebound hyperkalaemia during rewarming
- Immunosuppression / infectious Complications
- Coagulopathy
- Altered drug metabolism / reduced clearance sedative drugs
- Requirement for sedation +/- paralysis
- Concern regarding rebound intracranial hypertension during warming phase
- Challenge of achieving and maintaining target temperature

Practice:
- Reasonable statement of candidates practice re TH

Additional comments:
Candidates mentioned detail that was not requested, such as methods of cooling. Candidates also showed poor breadth of knowledge related to the potential use of hypothermia in conditions such as TBI / SAH / CVA.

Rationale for therapeutic hypothermia:
- Therapeutic hypothermia has been advanced as a means of improving survival and good
neurological outcome following cardiac arrest. It has also been offered as a means of controlling intracranial hypertension which is refractory to other modalities. Therapeutic hypothermia modulates the activity of body proteins and electrolytes. This modulation is thought to have some beneficial effects in scenarios where inflammatory damage is anticipated. This also involves the down-modulation of the overall metabolic rate, which decreases the metabolic demands of the organism in situations where supply of metabolic substrate may be compromised. Decrease in oxygen consumption matches decreased demand with decreased supply in “penumbra” areas, at the watersheds, where hypoxic injury has caused oedema.

Advantages of therapeutic hypothermia

- Decreased granulocyte migration into tissue
- Decreased cerebral oedema
- Intrinsic anticonvulsant effects of hypothermia

Well-accepted indications:

- Mild therapeutic hypothermia for survivors of cardiac arrest
- Therapeutic hypothermia for traumatic brain injury

Evidence for use in cardiac arrest:

- Pseudorandomised unblinded trial in 1996 - promising results
- Bernard et al demonstrated a survival benefit in out of hospital VF arrest survivors
- A recent Cochrane review supports the use of therapeutic hypothermia, finding a 1.35 risk reduction for mortality.
- The recent TTM trial has demonstrated non-inferiority of a more conservative hypothermia (36℃) with standard temperature goals, in terms of mortality.

Evidence for use in traumatic brain injury

- EUROTHERM 3235 trial (2015): 387 patients; hypothermia was used as a second-line therapy to reduce ICP.
- No survival benefit was observed.
- Recruitment was suspended early owing to safety concerns.
- ICP control was in fact better in the hypothermia group (they required rescue therapies less frequently)
- The meta-analysis mentioned by the college is possibly this 2013 review by Georgiou et al; except there was no benefit in mortality when only high quality trial were included.

Extended indications:

Therapeutic hypothermia in cooling of a hyperthermic patient

- Hyperthermia is associated with substantial harm, particularly if the temperature increases beyond 41℃
- Causes of such hyperthermia may be numerous, including sepsis, malignant hyperthermia, anticholinergic drug poisoning, heat stroke, and so on and so forth.
- In brief, these causes all have specific management strategies which may take time to work.
- In the interim, the temperature must be managed, so that organ damage does not occur
- Induction of hypothermia (or maintenance of controlled normothermia) by cooling the patient can be viewed as one of the indications.

Therapeutic hypothermia for subarachnoid haemorrhage

- Theoretically, TH may be protective in SAH in the same way that it is supposed to be protective in traumatic brain injury. Areas affected by ischaemia in the context of vasospasm may benefit from having a lower metabolic rate.
- TH certainly seems to decrease the flow velocity in the MCA of subarachnoid haemorrhage patients (Seule et al, 2014), suggesting that the metabolic rate is indeed affected enough to influence cerebral blood flow.
- Animal studies have also demonstrated that hypothermia reverses vasospasm (in rats)
- In patients with “poor-grade” SAH, good functional outcome was achieved in 48% with the combination of barbiturate coma and hypothermia to 33-34℃ (Gasser et al, 2003)
A more recent case series (Seule et al, 2010) found good outcomes in 57% of severe SAH patients who developed vasospasm.

In contrast, Karnatovskaia et al (2014) found no difference in neurological outcome within their case series.

No recommendation in favour of this use of TH can be made with a straight face.

**Therapeutic hypothermia for super-refractory status epilepticus**

- Hypothemia is known to have antiepileptic effects.
- Case series (eg. Corry et al, 2008) have demonstrated its feasibility in humans (target temperature: 31–35°C)
- Neurocritical care society guidelines for status epilepticus (Brophy et al, 2012) identified only 4 articles in the literature, and were unable to make very strong recommendations.
- The HYBERNATUS trial mentioned in the college answer is apparently ongoing, but no longer recruiting participants.

**Therapeutic hypothermia for severe sepsis**

- Anti-inflammatory effects of hypothermia were studied in an animal model of severe sepsis (Kwang et al, 2012).
- The hypothermic rats (30–32 °C) did better in terms of acute lung and liver injury.
- Human applications of this are limited by concern that firstly, a fever is an antibacterial physiological response, and secondly, that the haemodynamic instability of septic shock will be exacerbated by hypothermia.

**Therapeutic hypothermia for meningitis**

- Evidence of potential harm mentioned by the college in their answer was found by a 2013 RCT (Mourvillier et al). The investigators found a higher mortality in the hypothermia group.

**Therapeutic hypothermia for neonatal asphyxia**

- Following on from the success of TH in adult cardiac arrest, this modality has been applied to neonatal hypoxic-ischaemic encephalopathy.
- Shankaran et al (2005) performed an RCT; the group of neonates who were cooled 33.5°C for 72 hours; the rate of cerebral palsy was reduced from 19% to 15%, and mortality improved from 37% to 24%. In the long term, there was no increase in disability among hypothermia-exposed survivors when compared to surviving controls (Shankaran et al, 2012)
- TOBY trial (2014) confirmed that both survival and neurological outcome is improved

**Therapeutic hypothermia for stroke**

- The college answer points out that fever is associated with two-fold risk of death after haemorrhagic or ischaemic stroke. Pharmacologic methods of fever control have not shown improved outcome in stroke.
- In animal models of stroke, mild or moderate hypothermia has been shown to decrease infarct size and lead to functional improvement when cooling was initiated within a few hours of ischemia onset (Clark et al, 2008). But... These were rats, and they were cooled to 24°C

**Therapeutic hypothermia for acute hepatic encephalopathy**

- This use of TH is an extension of the observation that TH reduces cerebral oedema in patients with traumatic brain injury.
- Some authors (Stravitz et al, 2008) have suggested that TH may be an effective bridge to liver transplant.
- Human case series support this assertion (Jalan et al, 1999); during their treatment there was no significant relapse of increased intracranial pressure.
- There are no RCTs, but a large-scale retrospective cohort (Karvellas et al, 2014) did not find any survival benefit.

**Therapeutic hypothermia in ARDS :**

- Recent studies (Zhicheng et al, 2012) have confirmed that mild hypothermia improves gas exchange, lung compliance, duration of ventilation and the levels of IL-6 in local lung tissue.
Of particular interest is the use of hypothermia to reduce the whole-body oxygen demand in situations where even veno-venous ECMO is powerless to oxygenate the patient (Hayek et al, 2015)

**Intraoperative therapeutic hypothermia**

- Cardiothoracic surgery, routinely in use (including DHCA).
- Neurosurgery for aneurysm clipping: IHAST trial, 2005; no benefit (“good-grade” SAH patients)
- Vascular surgery, to protect the spinal cord during prolonged aortic cross-clamp

**Suspended animation for delayed resuscitation**

- In essence, this is a practice of stopping the circulation with deep hypothermia, so as to buy time to the definitive management of the cause of the cardiac arrest.
- Animal studies have demonstrated success with up to 90 minutes of no-flow (Safar et al, 2002)
- Wu et al (2006) subjected dogs to rapid haemorrhage, and then used a 2°C saline aortic flush to achieve a brain temperature of 10°C. The dogs remained on ice for 2 hours, and were then revived on cardiopulmonary bypass. Intact neurological outcome was achieved in 4 out of 6 dogs.


**Question 8**

Outline the advantages and limitations of the various sites for measuring body temperature in critically ill patients.

*(You may tabulate your answer)*.

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAC</td>
<td>Considered gold standard, continuous measurement</td>
<td>Invasive, needs a PA catheter</td>
</tr>
<tr>
<td>Bladder</td>
<td>Continuous measurement, minimally invasive, stable measurements regardless of urine flow rates</td>
<td>Costly, needs a monitor for display.</td>
</tr>
<tr>
<td>Rectal probe</td>
<td>Intermittent or continuous measurements</td>
<td>Few tenths of a degree higher than core temperature, intrusive, may be difficult with patient positioning in ICU, risk of spread of pathogens, rectal trauma</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>Provide continuous readings</td>
<td>Probe position difficult to confirm as they are not</td>
</tr>
</tbody>
</table>
Always radio-opaque, risk of oesophageal trauma or perforation, uncomfortable in spontaneous or alert breathing patients.

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tympanic</td>
<td>Reflects hypothalamic and core temperature.</td>
<td>Poor agreement with other methods, presence of wax or ear pathology may distort measurements.</td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>Similar to oesophageal</td>
<td>Sinusitis, can’t be used in BOS #. Accuracy depends on position</td>
</tr>
<tr>
<td>Oral</td>
<td>Safe, convenient, and familiarity</td>
<td>Needs cooperative patients, presence of ET and oro gastric tubes may limit this in ICU patients, mouth breathing, drinking hot or cold fluids may distort measurements.</td>
</tr>
<tr>
<td>Forehead</td>
<td>Dot technique, non-invasive</td>
<td>Poor agreement with PAC in ICU patients,</td>
</tr>
</tbody>
</table>
The answer table from the college is a comprehensive response, and it is difficult to improve upon it without a swamp of useless detail.

The key point is that the PA catheter is the gold standard, and everything else is measured against it. The general trend can be described thus: the closer your probe gets to the heart, the more accurate your measurement to the temperature of intracardiac blood.

It would make sense that intracardiac blood should be a good measure of body temperature, as the blood has been circulating all around the body, exchanging heat everywhere. However, not all agree that this is a valid viewpoint. Some have suggested that the better temperature to be guided by is the temperature of the hypothalamus, because it is the organ which is responsible for regulating temperature.

### Methods of Measuring Body Temperature in the ICU

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAC</td>
<td>- Considered gold standard, continuous measurement</td>
<td>- Invasive.</td>
</tr>
<tr>
<td></td>
<td>- PAC has a number of serious complications associated with its use</td>
<td>- Costly,</td>
</tr>
<tr>
<td></td>
<td>- Not as accurate as PAC, but better than rectal and surface methods</td>
<td>- needs a monitor for display</td>
</tr>
<tr>
<td></td>
<td>- Not as accurate as PAC, but better than rectal and surface methods</td>
<td>- Source of infection</td>
</tr>
<tr>
<td>Bladder</td>
<td>- Continuous measurement, minimally invasive, stable measurements regardless of urine flow rates</td>
<td>- Costly,</td>
</tr>
<tr>
<td></td>
<td>- Not as accurate as PAC, but better than rectal and surface methods</td>
<td>- needs a monitor for display</td>
</tr>
<tr>
<td></td>
<td>- Not as accurate as PAC, but better than rectal and surface methods</td>
<td>- Source of infection</td>
</tr>
<tr>
<td>Rectal probe</td>
<td>Intermittent or continuous measurements</td>
<td>Bacterial metabolism renders the rectum slightly hotter than core temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Invasive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of traumatic insertion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potential source of bacteraemia</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>Provide continuous readings</td>
<td>- Position-dependent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Risk of oesophageal trauma</td>
</tr>
<tr>
<td>Method</td>
<td>Description</td>
<td>Problems</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Tympanic     | Reflects hypothalamic and core temperature.  | • Poor agreement with other methods  
• Ear canal obstruction or ear pathology may distort measurements. |
| Nasopharyngeal | Similar to oesophageal                                                      | • Risk of sinusitis  
• Contraindicated in base of skull fractures  
• Position-dependent  
• May erroneously measure the temperature of the humidified gas in the ETT |
| Oral         | Safe, convenient, and familiar  | • Needs cooperative patients  
• Presence of ET and oro gastric tubes may limit this in ICU patients  
• Mouth breathing, drinking hot or cold fluids may distort measurements. |
| Forehead     | Dot technique, non-invasive                                                | • Poor agreement with PAC in ICU patients  
• Intermittent data |
| Axillary     | Non-invasive                                                               | • Less than core body temperature  
• Intermittent data |


Prognostication after cardiac arrest may be very difficult and involve a number of modalities.

It involves consideration of:

**History**
- Underlying cause of the arrest
- Co-morbidities
- Use of therapeutic hypothermia
- Features of the arrest – down time, CPR, ROSC

**Clinical assessment**

**Timing:**
Neurological assessment timing will be determined by the use of therapeutic hypothermia and the duration and type of medication for sedation but is most reliably performed day 3 without therapeutic hypothermia – probably day 5 with TH. Suggestion is to wait 72 hours after return of normothermia. With new TTM trial suggesting 36C then 72 hours post arrest may again be appropriate.

**Examination:**
Clinical – off sedation and neuromuscular blocking agents
Cranial nerve abnormalities – absence of pupillary response and corneal reflexes are bad prognostic indicators.
Best Motor response at 72 hours with absent or extensor response associated with poor outcome.
Status / Generalised and repetitive myoclonus (as opposed to sporadic myoclonus)

**Biochemical parameters**
- Neurone specific enolase >33mcg/L at days 1-3 indicates poor outcome
- S100, CSF CKBB not accurate enough for prognostication

**Electrophysiological features**
EEG: generalised suppression, burst suppression or generalised periodic complexes strongly associated with poor outcome.
SSEPs: Bilateral absence of N20 component of SSEP with median nerve stimulation within 1-3 days is strongly associated with poor outcome.

**Imaging**

CT appearance – catastrophic changes with obvious pathology. Diffuse oedema has not been formally assessed as an indicator. MRI may be more sensitive

Predictors of better outcome are:

- Recovery of brainstem reflexes within 48 hours
- Return of purposeful response within 24 hours
- Hypothermia at the time of arrest
- Young age

The tabulated summary below is based on the most recent ERC/ESICM statement (Sandroni et al, 2014). A vast and ridiculous discussion of *prognostication after cardiac arrest* is also carried out in the Cardiac Arrest and Resuscitation section of this site.

**Predictors of Poor Outcome in Comatose Survivors of Cardiac Arrest**

<table>
<thead>
<tr>
<th>Predictive sign or investigation</th>
<th>Predictive utility</th>
<th>Confounding factors</th>
</tr>
</thead>
</table>
| Absent pupillary reflex          | 0% false positive rate at 72 hours, irrespective of cooling | • Sedation  
• Hypothermia  
• Paralysis  
• Presence of shock  
• Metabolic derangements, eg. acidosis |
| Absent corneal reflex            | 0-15% false positive rate at 72 hours | |
| Extensor motor response, or worse| May be associated with poor outcomes | • High false positive rate (~50%) |
| Myoclonic status epilepticus     | Persisting myoclonic status epilepticus has a 0% false positive rate within the first 24 hours | • Interpreter-dependent  
• Findings may be subtle  
• Paralysis interferes with interpretation |
| Somatosensory evoked potentials: absence of the N20 component | Absence of N20 predicts poor outcome with an 0% false positive rate.  
Presence of N20 does not rule out a poor outcome. | N20 responses may disappear on repeat testing.  
N20 responses |
<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burst suppression on EEG</td>
<td>May be associated with poor outcome</td>
<td>Poor predictive value; cannot be used for prognostication.</td>
</tr>
<tr>
<td>Absence of EEG reactivity</td>
<td>Low false positive rate (0-5%)</td>
<td>Confounded by sedation</td>
</tr>
<tr>
<td>Neuron-specific enolase</td>
<td>NSE over 33μg/L at 1-3 days post CPR predicts poor outcome with a false positive rate</td>
<td>NSE may be elevated for reasons other than brain injury; for instance, it may be secreted by neuroendocrine tumours</td>
</tr>
<tr>
<td>CT brain</td>
<td>On CT, an inversed gray/white matter ratio in Hounsfield units was found in patients who failed to awaken after cardiac resuscitation. However, the predictive value of CT findings is not known</td>
<td>If performed too early, the CT may not demonstrate any findings.</td>
</tr>
</tbody>
</table>


a) What are short-latency (N20) somatosensory evoked potentials (SSEPs)?

b) Describe how SSEPs can be used for prognostication in patients with hypoxic-ischaemic brain injury.

c) Explain whether, and if so how, induced hypothermia impacts on the validity of SSEP results.

[ Hide Answer ]
Rationale for the use of somatosensory evoked potentials in the comatose survivor of cardiac arrest

- Peripheral nerve stimulation should evoke a central response even in the presence of sedation or hypothermia
- The absence of such a response suggests severe damage to the cortex
- Bilateral absence of response suggests global rather than focal damage
- Ergo, SSEP should act as a sensitive diagnostic tool to detect severe brain injury after cardiac arrest

Practice of somatosensory stimulation and evoked potential measurement

- Both median nerves are stimulated at the wrist with a bipolar surface electrode
- Alternative site is the tibial nerve
- Stimulus repeats at 2-5 Hz, with a duration of 0.2msec
- Surface electrodes read cortical activity at the scalp
- Evoked potentials are peaks of electrical activity which follow the peripheral stimulus with a predictable latency.
- The responses are named after their polarity (N for negative, P for positive) and their latency.
- N20 indicates a negative response over primary somatosensory cortex at ~20 ms post stimulation.

Advantages of somatosensory evoked potentials

- Non-invasive
- Portable
- Less confounded by sedation or hypothermia than EEG (in fact, not influenced by sedatives, analgesics, paralysing agents or metabolic insults)
- Bilaterally absent N20 SSEP during hypothermia is a good predictor for absent N20 SSEP after rewarming, which means you can do SSEPs during the period of hypothermia (Bouwes et al, 2010)
- Reproducible
- Interpretation is guided by specific criteria, rather than subjective expertise.

Evidence supporting the prognostic value of SSEPs

- Bilaterally absent short latency peaks (N20 peaks) have 100% predictive value for poor outcome (death or severe disability), with false positive rate nearly 0% and narrow confidence intervals.
- Recent (2014) consensus statement on prognostication following cardiac arrest suggested that SSEPs are prognostic at > 72 hours in cooled patients and at >24 hours in non-cooled patients.
- Among a total 287 patients with bilaterally absent N20 SSEPs, only one was a false positive result (Young et al, 2005).
- Post hoc analysis by independent interpreters has suggested that the false positive was simply interpreted inaccurately in the first instance.


Question 17

With regards to the determination of brain death:

a) Apart from identifying evidence of sufficient intracranial pathology, list the preconditions that must be met prior to the determination of brain death by clinical criteria:

b) What is the recommended minimum time for observation in cases of hypoxic-ischaemic brain injury, prior to performing clinical testing of brain-stem function?

c) For each of the following brainstem reflexes, list the cranial nerves that are tested:

<table>
<thead>
<tr>
<th></th>
<th>Cough reflex</th>
</tr>
</thead>
<tbody>
<tr>
<td>b</td>
<td>Vestibulo-ocular reflex</td>
</tr>
<tr>
<td>c</td>
<td>Pupilary light reflex</td>
</tr>
<tr>
<td>d</td>
<td>Corneal reflex</td>
</tr>
<tr>
<td>e</td>
<td>Gag reflex</td>
</tr>
</tbody>
</table>

d) List three contraindications to performing apnoea testing:

e) List the acceptable imaging techniques that may be used to demonstrate brain death as an alternative to clinical testing as recommended by the ANZICS Statement on Death and Organ Donation.

[Hide Answer]

a)

- Minimum period of 4 hours in which the patient is observed to have unresponsive coma, unreactive pupils, absent cough/tracheal reflex and no spontaneous respiratory effort
- Normothermia (temp >35°C)
- Normotension (SBP >90 mmHg, MAP >60 mmHg in adult)
- Exclusion of sedative drugs
- Absence of severe electrolyte, metabolic or endocrine disturbance
- Intact neuromuscular function
- Ability to examine the brainstem reflexes including at least one ear and one eye
- Ability to perform apnoea testing
b) 24 hours

c)  

<table>
<thead>
<tr>
<th>a.</th>
<th>Cough reflex</th>
<th>cranial nerve X</th>
</tr>
</thead>
<tbody>
<tr>
<td>b.</td>
<td>Vestibulo-ocular reflex</td>
<td>cranial nerve III, IV, VI, VIII</td>
</tr>
<tr>
<td>c.</td>
<td>Pupilary light reflex</td>
<td>cranial nerve II &amp; III</td>
</tr>
<tr>
<td>d.</td>
<td>Corneal reflex</td>
<td>cranial nerve V &amp; VII</td>
</tr>
<tr>
<td>e.</td>
<td>Gag reflex</td>
<td>cranial nerve IX &amp; X</td>
</tr>
</tbody>
</table>

(for each part of this question ALL cranial nerves are required in order to receive the 5 marks, no marks should be given for an incomplete response)

d)  

1.  1. Concomitant high cervical cord injury  
   Severe hypoxaemia  
   Haemodynamic instability

e)  

- Four vessel intra-arterial catheter angiography with digital subtraction (preferred)
- Radionuclide imaging with Tc-99m HMPAO and single photon emission computerised tomography (SPECT) (preferred)
- CT angiography (limited experience to date) (acceptable)

This question tests the candidate’s detailed knowledge of the ANZICS Statement on Death and Organ Donation (I have linked to Version 3.2, from 2013).

a) Apart from identifying evidence of sufficient intracranial pathology, list the preconditions that must be met prior to the determination of brain death by clinical criteria:

The below answer is taken directly from the Statement.

- Normothermia
- Normotension
- Exclusion of the effects of sedating drugs
- Absence of severe electrolyte, metabolic or endocrine disturbance
- Intact neuromuscular function
- Ability to adequately examine brainstem reflexes
- Ability to perform apnoea testing

b) What is the recommended minimum time for observation in cases of hypoxic-ischaemic brain injury, prior to performing clinical testing of brain-stem function?
Again, quoting ANZICS:

“There must be a minimum of **four hours** observation and mechanical ventilation during which the patient has unresponsive coma.”

c) For each of the following brainstem reflexes, list the cranial nerves that are tested:

<table>
<thead>
<tr>
<th>Reflex</th>
<th>Cranial Nerves</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Cough reflex</td>
<td>Vagus (CN X)</td>
</tr>
<tr>
<td>b. Vestibulo-ocular reflex</td>
<td>CN III, IV, VI, and VIII</td>
</tr>
<tr>
<td>c. Pupilary light reflex</td>
<td>CN II, CN III</td>
</tr>
<tr>
<td>d. Corneal reflex</td>
<td>CN V, CN VII</td>
</tr>
<tr>
<td>e. Gag reflex</td>
<td>CN IX, CN X</td>
</tr>
</tbody>
</table>

In this list the college have omitted the test for pain in the trigeminal nerve distribution (CN V and VII).

d) **List three contraindications to performing apnoea testing:**

- Hemodynamic instability
- Severe hypoxic respiratory failure
- High cervical cord injury

The presence of any brainstem reflexes is also a contraindication. Apnoea testing must be carried out only after the brainstem reflexes have been tested, and if any of them were found to be positive any further braindeath testing cannot continue.

e) **List the acceptable imaging techniques that may be used to demonstrate brain death as an alternative to clinical testing as recommended by the ANZICS Statement on Death and Organ Donation.**

- Four-vessel digital subtraction arterial angiography
- Tc-99m HMPAO (technetium 99m radiolabelled hexamethyl propylene amine oxime) SPECT
- CT angiography

ANZICS Death and Organ Donation Committee, THE ANZICS STATEMENT ON DEATH AND ORGAN DONATION Edition 3.2 2013
Prior to the determination of brain death by clinical examination,

a) list the preconditions that must be met before formal testing can begin

b) What are the indications for ancillary tests for brain death (ie tests that demonstrate the absence of intracranial blood flow)?

c) What are the 2 imaging techniques currently recommended by ANZICS for determining the absence of intracranial blood flow:

[Hide Answer]

**Preconditions**

a) A known cause of coma (check terminology in new ANZICS guidelines)

b) Minimum of 4 hour period observation

c) neuro-imaging consistent with acute brain pathology which could result in brain death;

d) temperature > 35C;

e) normotension (as a guide, systolic blood pressure > 90 mmHg, mean arterial pressure (MAP) > 60 mmHg in an adult);

f) exclusion of effects of sedative drugs: the time taken for plasma concentrations of sedative drugs to fall below levels with clinically significant effects depends on the dose and pharmacokinetics of drugs used, and on hepatic and renal function. If there is any doubt about the persisting effects of opioids or benzodiazepines, an appropriate drug antagonist should be administered;

g) absence of severe electrolyte, metabolic or endocrine disturbances. These include marked derangements in plasma concentrations of glucose, sodium, phosphate or magnesium, liver and renal dysfunction and severe endocrine dysfunction;

h) intact neuromuscular function. If neuromuscular-blocking drugs have been administered, a peripheral nerve stimulator or other recognised method (e.g. electromyography) should always be used to confirm that neuromuscular conduction is normal;

**What are the indications for ancillary tests for brain death?**

* Inability to adequately examine the brain-stem reflexes. It must be possible to examine at least one ear and one eye;

* Inability to perform apnoea testing. This may be precluded by severe hypoxic respiratory failure or
What are the 2 imaging techniques currently recommended by ANZICS for determining the absence of intracranial blood flow:

Four vessel intra-arterial catheter angiography, with digital subtraction; Tc-99 HMPAO SPECT radionuclide imaging

CT angio with certain caveats may be acceptable. Do not recommend MR angio

This question resembles several other questions in the past papers:

- Question 17 from the second paper of 2012 and Question 12.1 from the second paper of 2010 ask about pre-conditions for brain death testing.
- Question 12.2 from the second paper of 2010 discusses imaging modalities to assess the intracranial blood flow.

The pre-conditions for clinical brain death testing are:

- Normothermia (over 35 degrees)
- Normotension (MAP >60)
- Not sedated
- Not paralyzed
- Not in a state of electrolyte or metabolic derangement (e.g. hypoglycaemia)
- Possessing at least one intact eye and one ear (to examine brainstem reflexes)
- Able to breathe (to test for apnoea; i.e. high C-spine injury may disqualify you)
- Unresponsive coma
- A suitable explanation for why the patient is comatose, which would be consistent with the diagnosis of brain death

Otherwise, this current paper asks one original question: when must one resort to imaging?

Well. The ANZICS Statement on Death and Organ Donation suggests several distinct scenarios when one cannot perform clinical brain death testing:

- Inability to adequately examine the brain-stem reflexes:
  - One ear and one eye are not intact
  - Sedation, hypothermia, paralysis
- Inability to perform apnoea testing:
  - Severe hypoxic respiratory failure
  - High cervical spinal cord injury

ANZICS Death and Organ Donation Committee, THE ANZICS STATEMENT ON DEATH AND ORGAN DONATION Edition 3.2 2013
QUESTION 1

Outline the Intensive Care management of a 25-year-old male who has fulfilled brain death criteria and is awaiting surgery for organ donation.

[ Hide Answer ]

College Answer

Temperature Maintenance:

- Hypothermia is common due to: cold fluids, heat loss through exposure, inability to vasoconstrict or shiver, reduced metabolic rate.
- Maintain normal core temperature
  - Cover patient
  - Warm room
  - Warming blanket
  - Warm fluids especially high volume
  - Humidification

Respiratory support:

- Aim to avoid fluid overload
- Aim for adequate Sp02 and normocarbia with lowest Fi02 and limit tidal volumes
- Bronchoscopy for persisting collapse
- Chest physiotherapy may be helpful

Circulatory Support:

Immediately prior to brain death there is often a period of sympathetic hyperactivity with associated tachycardia and hypertension. This is lost following brain death commonly resulting in vasodilation and hypotension

- Maintain adequate mean arterial pressure. Use judicious volume expansion and low dose inotropes (usually noradrenaline)
- Monitor peripheral perfusion and urine output regularly
- Continue maintenance fluids

Metabolic haematology and biochemistry:

Diabetes insipidus is common and if not recognized and treated can quickly lead to hypernatraemia and hyperosmolality

- Measure electrolytes and creatinine regularly and treat as appropriate to maintain normal ranges
- Treat Diabetes insipidus with desmopressin (DDAVP) 4-8µgrams intravenously and repeat if necessary, or low dose vasopressin
• Start low dose insulin infusion if blood glucose persistently above 12mmol/L
• Stop bleeding, correct coaguloapthy, thrombocytopenia and anaemia
• Avoid hypernatraemia
• Other electrolyte abnormalities – K, PO4, Ca, Mg
• Consider thyroxine replacement

Communication:
• Family - counsel, explain, keep updated
• Liaison with donor coordinator and surgical retrieval teams

Discussion

This is a straightforward question about the care of the brain-dead organ donor. A summary exists on this site, which was derived directly from the recent ANZICS guidelines. If one were to rearrange the answer to fit some sort of primitive alphabetical template, it could resemble this:

Non-clinical issues: (presumably, these have been dealt with now that the patient is "awaiting surgery for organ donation")

• Early involvement of the transplant coordinator
• Non-coercive sensitive family discussion re opportunity for donation
• Tissue typing, viral screen, further organ function tests
• Facilitate family time at bedside
• Ensure aftercare of donor family

A. The circuit should be humidified.
B. Normoxia and normocapnea must be maintained.
   There will be periodic requests for ABGs on 100% FiO2 from the donor coordinator, but afterwards the FiO2 must be minimised to prevent oxidative stress damage to the lungs.
C. Haemodynamic instability is to be expected:
   - The initial autonomic storm should be managed with nitroprusside and esmolol
   - The subsequent collapse should be treated with noradrenaline and/or vasopressin
   - Bradycardia will be resistant to atropine (no vagus to block); catecholamines or pacing will be required
   - Though they do not make a direct statement to this effect, ANZICS tacitly support CPR in the brain-dead organ donor; "cardiopulmonary resuscitation may result in recovery of cardiac function and successful transplantation".
D. Normoglycaemia must be maintained.
E. Normothermia must be maintained by warming externally, and by using warmed fluids. Electrolytes need to be maintained within normal laboratory ranges; particular attention needs to be paid to the sodium.
   DDAVP may be required as a hormone replacement.
   Other "endocrine support" (T3, hydrocortisone) should be considered in the following circumstances:
   - haemodynamic instability
   - an ejection fraction of less than 45%
   - heart donation is being considered
F. Fluid resuscitation should be conservative if you plan to donate lungs, aggressive if you plan to donate kidneys, and an intelligent compromise if both organs are being considered.
G. Nutrition must continue.
   Good nutrition (or rather, the absence of malnutrition) has been associated with improvedraft function (Singer et al, 2005)
H. Coagulopathy must be observed and corrected; if worsening coagulopathy or DIC develop, organ retrieval should be expedited.
References:

Summarized from the ANZIC statement on Brain Death and Organ Donation, Version 3.2


