In conclusion, this case shows that there are significant negative correlations between plasma catecholamine concentrations and skin blood flow in a child with a phaeochromocytoma, demonstrating that skin blood flow may be used as a non-invasive and real-time indicator of plasma catecholamine concentration in such circumstances. This technique may assist the surgeon who is uncertain whether a phaeochromocytoma has been completely isolated from the systemic circulation.

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Difficult in brainstem death testing in the presence of high spinal cord injury

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In the UK, when the standard brain death criteria are met, further investigations are not necessary. Confirmatory tests can be useful, however, when it is not possible to carry out all of the brainstem tests. We report the case of a patient with multiple trauma and a high spinal cord injury who was apnoeic. Confirmatory tests (EEG, brainstem, auditory evoked potential) were essential in supporting the diagnosis of brainstem death to allow withdrawal of artificial ventilation, as organ donation was being considered.

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Keywords: brain, braindeath; brain, electroencephalography; brain, evoked potentials; complications, brainstem death

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A 48-yr-old lady was admitted following a road traffic accident. She was a rear seat passenger in a car that collided with the vehicle in front and was subsequently struck from the vehicle behind. She initially was reported to have a GCS of 15 at the scene of the accident, and complained of neck and left-sided chest pain. However, her GCS deteriorated rapidly to 3, whereupon the ambulance crew performed bag and mask ventilation until arrival in the accident and emergency department. A spinal board and hard collar were in place during the transfer.

She was intubated on arrival while performing manual in-line stabilization. At the same time, a left-sided chest drain
was inserted because of the clinical suspicion of rib and sternal fractures and a left-sided pneumothorax. She had bruising of her chest consistent with a seat belt injury. Her systolic arterial pressure was noted to be 60 mm Hg with cool peripheries and she was hypothermic with a rectal temperature of 34°C. Abdominal examination was unremarkable. Central nervous system examination revealed bilateral fixed and dilated pupils and generalized hypotonia with no elicitable reflexes or anal tone.

A cervical spine X-ray showed a Hangman’s fracture of C2 (fracture of the pedicle) with displacement and a likely traction injury to the spinal cord (Fig. 1). A chest X-ray confirmed the position of the chest drain in situ with left-sided shadowing, and the pelvic X-ray was unremarkable. Unfortunately, on that day the CT scanner was not available, so she underwent a chest and abdominal ultrasound scan which showed a 3 mm pericardial effusion but no obvious abdominal trauma. All blood tests were normal apart from a white cell count of 26.5 × 10⁹ litre⁻¹. Following initial fluid resuscitation, she was started on dopamine and norepinephrine and transferred to the ITU.

On day 3, a CT scan of the brain showed loss of grey-white differentiation, widespread oedema, and reduced attenuation consistent with coning. Her case was discussed between the ICU consultants who decided to proceed with a brainstem death test in the hope of offering non-heart beating donation. The EEG showed a grossly abnormal trace with no evidence of cerebral activity. The evoked potentials showed an A-line ARX Index (AAI) of not greater than 12 at any time (mostly 4–6), and frontalis activity was completely absent (Fig. 2). The AEP line did not show any improvement at any time.

Mid-latency 40 Hz AEP signals are recorded with the Alaris AEP Monitor™ (Alaris AEP™ monitor, Alaris Medical Systems, Danmeter A/S, Denmark). This monitor measures depth of anaesthesia by tracking changes in the mid-latency auditory evoked potential (MLAEP) waveform. The MLAEP are elicited with a bilateral click stimulus of 65 dB (Sound Pressure Level) intensity, 2 ms duration, and repetition rate of 9 Hz delivered through a pair of headphones. Three silver-silver chloride electrodes (A-Line®, Danmeter, Denmark) are positioned at the middle forehead (+), left forehead (reference), and the left mastoid (−). Evoked potentials are then extracted from the EEG by autoregressive with exogenous input (ARX) modelling. The changes in the MLAEP are reflected as an index (AAI). An AAI value under 30 is considered to be appropriate for surgical anaesthesia and an AAI over 60 indicates onset of consciousness. The monitor also provides a measure of the frontalis electromyographical (EMG) activity and the burst suppression ratio.

The patient’s husband and family were kept informed throughout, and when the results of the CT scan were
confirmed, they requested that cardiopulmonary resuscitation should not be performed in the event of a cardiac arrest. When all the test results were available, the family requested that treatment be withdrawn. The lead consultant discussed the case with the Coroner and was advised to obtain legal advice.

The Medical Defence Union were consulted in conjunction with the hospital legal team. They advised that in the absence of the ability to complete the brainstem death tests, and that providing we were confident that brainstem death had taken place, it would be advisable to obtain an expert opinion from a neurologist or neurosurgeon. If they were in agreement, it would then be appropriate to withdraw all support. They added that even if we could not reach a confident diagnosis of brainstem death, but concluded that there was no prospect of recovery in any form, then it might still be appropriate to withdraw all support, but only after further legal advice, and with the active and documented agreement of all the patient’s family. A second opinion was therefore requested from a consultant neurologist who agreed that the patient was brainstem dead. The possibility of organ donation was raised with the family but it was explained that this would require further legal advice and would therefore incur further delays. They agreed that this was undesirable. On day 4 following admission, the family visited to bid farewell before all support was withdrawn. The patient died later that evening and subsequently underwent a Coroner’s post mortem.

### Discussion

The diagnosis of brain death in most European countries and in the US, is defined as the total and irreversible loss of all brain functions (the ‘whole’ brain concept). Only in the UK is brain death defined as a non-functional state of the brainstem in which all the signs of brainstem activity are absent (the ‘lower’ brain concept). In this context, examination of cortical and subcortical bioelectrical activity is not necessary in the UK and therefore an EEG and other technical tests need not be performed.

All international brain codes follow the same step-by-step procedure of establishing aetiology, exclusion of potentially reversible syndromes, and demonstrating the clinical signs of brain death—coma, brainstem areflexia, and apnoea. However, there are important differences between countries (Table 1).

Confirmatory tests are mandatory in addition to clinical testing in France, Italy, Luxembourg, the Netherlands, and the US. The individual tests vary between these countries. In Austria, Belgium, Denmark, Finland, Germany, and Switzerland, either repetition of testing or a technical confirmatory (facultative) test is required. Confirmatory tests are not required at all in the UK or Poland, provided the clinical criteria are met unambiguously. In the US, the choice of tests is left to the discretion of the physician, but bedside tests are preferred. European apnoea test procedures are outlined in Table 2.
Neurophysiological methods for the confirmation of brain death can be divided into two groups: methods to confirm the loss of bioelectrical activity of the brain (EEG, evoked potentials); and methods to demonstrate cerebral circulatory arrest (angiography, transcranial Doppler, scintigraphy).

**EEG**

The EEG records the spontaneous bioelectrical activity of the cerebral cortex to a depth of about 5 mm but does not register the electrical activity of the lower brain stem. Following more than 8 min of complete anoxia as a result of circulatory arrest, the EEG becomes irreversibly isoelectric and is a reliable test of brain death. A number of problems with the technique are recognized. Electromagnetic fields in the ICU can pose difficulties in obtaining artifact-free traces, and the EEG is very sensitive to drug effects. It is uniform practice throughout the world only to consider the diagnosis of brain death after the exclusion of confounding factors, including the presence of sedative drugs. Blood levels of sedative drugs must therefore be tested before the EEG examination, which can only be interpreted with certainty in the absence of any sedatives. In this case, the patient was not sedated from admission with the intention of performing brainstem testing when it was appropriate to do so. The EEG should be recorded continuously for 30 min to demonstrate irreversible bioelectrical silence. All international brain codes that allow the use of confirmatory tests allow the use of the EEG, with the exception of Denmark, where angiography is required (refer to Table 1). In one series of patients fulfilling the clinical diagnosis of brain death, 20% of patients had residual EEG activity that lasted up to 168 h.

**Evoked potentials**

Evoked potentials are elicited by adequate stimulation of peripheral receptors and are recorded from the scalp. The diagnosis of brain death often uses median nerve evoked somatosensory potentials (SEP) or brainstem auditory evoked potentials (BAEP). Numerous reports have shown both the SEP and BAEP to be abolished in the presence of the clinical signs of brain death. Both tests are unsuitable for patients with primary infratentorial lesions, such as space-occupying lesions of the posterior fossa and vertebrobasilar thrombosis. The successive loss of all intracranial BAEP responses (waves II–V) in repeated tests confirms the loss of function of the acoustic pathways of the brainstem and also the clinical signs of brain death. Evoked potential testing is non-invasive and can be performed at the bedside. It is also virtually independent of the effects of sedative medication. In primary infratentorial lesions, an EEG is also mandatory, as the activity of the cerebral cortex can survive the loss of brainstem function by a number of hours or days. Evoked potentials are allowed as a technical test in half of all European countries (Table 1).

### Table 2 European apnoea test procedures for adults (reproduced with permission from Springer-Verlag)

<table>
<thead>
<tr>
<th>Country</th>
<th>Preoxygenation period</th>
<th>$P_{aCO_2}$ before testing</th>
<th>$O_2$ insufflation</th>
<th>Observation period</th>
<th>Target $P_{aCO_2}$</th>
<th>Clinical objective</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Not defined</td>
<td>&gt;60 torr</td>
<td>‘Sufficient oxygen’</td>
<td>6 litre min$^{-1}$</td>
<td>14 min</td>
<td>Not defined</td>
<td>Respiratory movements</td>
</tr>
<tr>
<td>Belgium</td>
<td>100% $O_2$ 10 min</td>
<td>&gt;38 torr</td>
<td>‘Appropriate’</td>
<td>Not defined</td>
<td>Not defined</td>
<td>Not defined</td>
<td>Respiratory movements</td>
</tr>
<tr>
<td>Denmark</td>
<td>No technical details provided</td>
<td>&gt;60 torr</td>
<td>6 litre min$^{-1}$</td>
<td>‘Appropriate’</td>
<td>Not defined</td>
<td>Not defined</td>
<td>Respiratory movements</td>
</tr>
<tr>
<td>Germany</td>
<td>100% $O_2$ until</td>
<td>&gt;40 torr</td>
<td>&gt;50 torr</td>
<td>&gt;50 torr</td>
<td>Respiratory movements</td>
<td>Not defined</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>No technical details provided</td>
<td>Demonstration of hypercapnia and pH &lt;7.4</td>
<td>Not defined</td>
<td>Respiratory movements</td>
<td>Not defined</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>100% $O_2$ 10 min</td>
<td>&gt;45 torr</td>
<td>2–4 litre min$^{-1}$</td>
<td>&gt;50 torr</td>
<td>Respiratory movements</td>
<td>Not defined</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>100% $O_2$ 10 min</td>
<td>Not defined</td>
<td>2–4 litre min$^{-1}$</td>
<td>Not defined</td>
<td>$P_{aCO_2}$ &gt;60 torr, pH &lt;7.35</td>
<td>Respiratory movements</td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>100% $O_2$ 10 min</td>
<td>&gt;45 torr</td>
<td>6 litre min$^{-1}$</td>
<td>10 min</td>
<td>$P_{aCO_2}$ &gt;60 torr, pH &lt;7.35</td>
<td>Respiratory movements</td>
<td></td>
</tr>
</tbody>
</table>
**Arteriography**

Digital subtraction angiography is widely regarded as the gold standard test. It is performed with the catheter tip in the aortic arch and injection of contrast into each of the four arteries supplying the brain. At least two injections, 20 min apart, must show no filling of the intracranial arteries. While this method has the advantage of directly confirming the cessation of cranial blood flow, there are several reservations about the method. These include the hazards of transporting and positioning the patient outside the intensive care unit, the possibility of allergic reactions to the contrast media, the increased risk of nephrotoxicity from contrast media and increased rejection rate in organ recipients following such studies. The incidence of anaphylaxis with the newer anionic contrast media is unknown but is thought to be very small however, and the risk of nephrotoxicity does not affect acceptability for organ donation. Digital subtraction angiography is accepted by all countries that allow technical tests for confirmation of the clinical signs of brainstem death (Table 1).

**Transcranial Doppler**

This is a useful bedside technique. A reduction in the middle cerebral artery flow velocity to under 10 cm s⁻¹ and the observation of a counterbalancing short forward flow during early systole with a short retrograde flow in early diastole should indicate brain death. As a technique, it has been found to have a sensitivity of 91.3% and a specificity of 100%. Transcranial Doppler (TCD) occasionally demonstrates brain death patterns in patients who are clinically brain dead and who have EEG activity. The signals may also be normal in patients with primary infratentorial lesions and in patients with anoxic brain damage after cardiac arrest. The velocities may be affected by marked changes in $P_{aCO_2}$, haematocrit, and cardiac output. The technique requires considerable practice and skill. Only in Germany is TCD accepted as a confirmatory test; in Austria, angiography must be used in addition (Table 1).

**Scintigraphy**

Cerebral perfusion can be examined by sequential cerebral scintigraphy using 99mTc-labelled DPTA or more reliably, with 99mTc-labelled hexamethylpropyleneamine oxime. Following an i.v. bolus of the tracer, the absent uptake of the tracer into the intracranial cavity confirms the loss of cerebral perfusion. This method can be performed at the bedside, taking approximately 15 min, and is accepted in both Germany and Switzerland.

In our patient, an EEG and evoked potentials were chosen as these were the most readily available tests within our district general hospital. Had the EEG not been isoelectric at the time of testing, we would probably have proceeded to digital subtraction angiography or repeated the EEG. Neither scintigraphy nor transcranial Doppler were available. More recently, the assessment of brain death using instant spectral analysis of heart rate variability has been described. However, the technique has yet to be validated on a large number of patients and any patients on treatment known to interfere with the heart rate, such as inotropes, are unsuitable for testing. To our knowledge, this is the first case report of brainstem death testing in the presence of high spinal cord injury.

**References**