

Important notice: Death determination by neurologic criteria (DNC), including confounders assessment, is a matter of clinical judgment and a medical act under the responsibility of the treating team.

The following guide is intended as a reference tool for clinicians. In case of doubt, contact Transplant Québec's medical director – organ donation or his/her delegate.

Delay clinical assessment or consider ancillary investigation	
Confounding factors	Considerations
Hypothermia	<p>Prior to the clinical assessment of the DNC, the core temperature of the potential donor must be at least 36°C ($\geq 36^\circ\text{C}$).</p> <p>After hypothermia $\leq 34^\circ\text{C}$, induced (targeted temperature control) or by pre-hospital environmental exposure, a waiting period of 24 hours is recommended when the core temperature of the potential donor has reached 36°C.</p> <p>Induced hypothermia for renal protection in potential donors does not require a waiting period once the core temperature has reached the target of 36°C.</p> <p>Transient hypothermia following loss of thermoregulation of the potential donor does not require a waiting period if supported by clinical judgment.</p>
Sustained hemodynamic instability	<p>Unresuscitated shock, severe hypotension and/or shock inadequately treated with volume resuscitation or vasoactive agents must be corrected.</p> <p>Prior to clinical assessment, adults should approximatively have a systolic blood pressure ≥ 100 mm Hg, or a mean arterial pressure ≥ 60 mm Hg.</p> <p>Pediatric patients should have age-appropriate targets.</p>
Decompressive Craniectomy	Should be considered a potential confounding factor requiring more observation time or ancillary investigation.
Severe metabolic/endocrine/electrolyte imbalances/abnormalities, including but not limited to : <ul style="list-style-type: none"> - Hyper/Hyponatremia - Hypophosphatemia - Hypoglycaemia - Hyper/Hypomagnesemia - Hypokalemia - Hyper/Hypothyroidism - Hepatic and/or renal impairment 	<p>Severe metabolic, acid-base and endocrine derangements, that could affect the examination, should be corrected. If these disorders cannot be corrected and are judged to potentially contribute to the loss of brain function, ancillary investigation should be considered.</p> <p>Hypernatremia may commonly occur during ICU treatment but does not contribute to the cause of devastating brain injury. If the primary etiology does not fully explain the clinical picture, and if the treating physician believes hypernatremia may play a role, it should be corrected.</p>
Pharmacological neuromuscular blockade potentially accounting for motor unresponsiveness	Pharmacological paralysis can be excluded through use of a train-of-four (TOF) stimulator if available, or assessment of the presence of deep tendon reflexes if a TOF stimulator is not available.
Pharmacological confounding including : Therapeutic or neuroprotective sedatives (e.g., benzodiazepines, propofol, barbiturates) and opioids administered to patients during resuscitative efforts Drugs taken in an overdose setting (e.g., illicit substances, alcohol, muscle relaxants, antidepressants, antiepileptics)	<p>A blood and/or urine toxicology screen can be used for diagnostic purposes to establish the presence or absence of potentially confounding drugs.</p> <p>If serum drug concentrations are quantified and found to be supratherapeutic, clinical assessment may be subject to confounding factors. Serial measurements can be used to establish trends in drug concentration over time. When they decrease below supratherapeutic levels, neurological assessment may be considered reliable. The therapeutic ranges of drug concentrations are not considered confounding.</p> <p>If alcohol intoxication is suspected or confirmed, the alcohol blood level should be ≤ 80 mg/dL at the time of death determination</p> <p>When quantitative or qualitative drug monitoring is not available, wait for at least five (5) elimination half-lives before conducting the clinical assessment. If prolonged drug elimination is expected (e.g., due to renal or hepatic impairment, obesity, hypothermia, prolonged exposure, or continuous administration of the drug by infusion), additional waiting time should be added. If there is uncertainty regarding the elimination of drugs or unknown drug exposures, additional time is required, or ancillary investigation should be considered.</p>
Various conditions	There have been several reports of reversible mimics of DNC in the setting of diffuse leptomeningeal carcinomatosis, rabies encephalitis, and botulism.

CONFOUNDING FACTORS RELATIVE



CONFOUNDING FACTORS ABSOLUTE	Ancillary investigation required	
	Confounding factors	Considerations
	Infratentorial brain Injury	If the brain injury remains isolated to the brainstem without supratentorial involvement, an ancillary investigation is required.
	Severe facial trauma or skull fractures (including basal skull fracture with hemotympanum)	May interfere with pupillary response, oculovestibular reflexes, and cranial pain response.
	Ocular trauma, anophthalmia	Interferes with pupillary, corneal, and oculovestibular reflexes.
	Spinal cord injury	May confound corporal pain response, apnea test.
Neuromuscular disorders	For pre-existing severe or acquired neuromuscular disorder, such as amyotrophic lateral sclerosis, Guillain-Barré syndrome or a pre-existing severe sensory neuropathy, or phrenic nerve injury, ancillary investigation should be performed.	

Clinical assessment in death determination by neurologic criteria (DNC)				
	Components of the Exam	How to do it	Consistent response with DNC	Clinical Considerations
Newborn only	Cardinal reflex (<i>rooting</i>)	Stroke the cheeks and corners of the mouth of the newborn with a finger.	No head movement should be observed.	Both reflexes are present in newborns at birth.
	Sucking reflex	Insert a gloved finger into the newborn's mouth.	The newborn's lips should not close around the finger. No pressure on the finger should be felt between the tongue and the roof of the mouth.	The cardinal points reflex disappears between the ages of 3 and 6 months. The transition from a primitive sucking reflex to a voluntary reflex typically occurs at around 4 months of age.

Clinical assessment in death determination by neurologic criteria (DNC)			
Components of the Exam	How to do it	Consistent response with DNC	Clinical Considerations
<p>Motor response to central and peripheral pain</p> <p>Pain response in the cranial nerve area</p>	<p>Apply deep pressure to the following areas :</p> <ul style="list-style-type: none"> - Condyles at the temporomandibular joints - Supraorbital cavities - Sternum - All four (4) extremities (proximal and distal) 	<p>No spontaneous movement should be observed in the head or limbs.</p> <p>No central nerve system (CNS) controlled movement should be observed.</p>	<p>Any spontaneous movement excludes DNC.</p> <p>Convulsions, decerebration and decortication movements exclude DNC.</p> <p>Spinal movements may persist, but DNC may not be excluded.</p>
Pupillary reflexes	<p>Perform the assessment in a dimly lit room using a penlight.</p> <p>If not possible, create shading at eye level.</p> <p>Move the pen's light beam from the outer corner of the eye to the pupil.</p> <p>Repeat the gesture for each eye, but avoid passing the beam of light from one eye to the other over the nose.</p>	<p>Pupils (2) are non-reactive to light.</p> <p>Pupils (2) should be dilated to 4mm or more.</p>	<p>Any pupillary reaction to light rules out DNC.</p> <p>Previous ophthalmic surgery may affect the pupillary response. Ancillary investigation is recommended.</p> <p>Instillation of certain eye drops, such as anticholinergics, may cause temporary pupil unresponsiveness to light.</p> <p>Constricted pupils (<2 mm) are not consistent with DNC and may suggest intoxication or other neurological impairment.</p>
Corneal reflex	<p>Apply light pressure to the outer corner of the iris of each eye using a cotton swab or compress to touch the cornea.</p>	<p>No movement of the eyelids or jaw should be observed.</p>	<p>Care should be taken during the examination to avoid damaging the cornea.</p>
Oculovestibular reflex (OVR)	<p>Elevate the head of bed to a 30° angle.</p> <p>Check the integrity of the eardrums and ear canals before proceeding with the examination.</p> <p>Insert a syringe with a soft catheter into the ear canal and irrigate it with at least 50 ml of ice water for 60 seconds.</p> <p>Test each side separately, waiting five (5) minutes before examining the opposite side to allow the temperature to rebalance.</p>	<p>No eye movement should be observed.</p>	<p>A ruptured tympanic membrane does not negate the clinical assessment. However, a haemotympanum requires an ancillary investigation.</p>
Cough and nausea/pharyngeal (Gag) reflexes	<p>Use a suction catheter to stimulate the tracheobronchial wall at the level of the keel (cough reflex).</p> <p>Use a tongue depressor or rigid suction catheter to stimulate the posterior wall of the pharynx (nausea/pharyngeal reflex).</p>	<p>No coughing should be observed.</p> <p>No vomiting should be observed.</p>	<p>The efferent branch responsible for the cough reflex includes the phrenic nerve, which may be damaged in individuals with high cervical trauma. In such cases, an ancillary investigation is required.</p>

Assessment of the respiratory reflex (apnea test)			
Components of the Exam	How to do it	Consistent response with DNC	Clinical Considerations
Respiratory reflex (apnea test)	<ol style="list-style-type: none"> 1. Pre-oxygenate with 100% FiO₂ for 15-20 minutes. 2. Perform an arterial blood gas (pre-test gas) to determine the initial pH and PaCO₂ values. As needed, adjust ventilatory parameters to obtain the following recommended values : <ul style="list-style-type: none"> - pH between 7.35 and 7.45 - PaCO₂ between 35 and 45 mm Hg 3. Disconnect the potential donor from the mechanical ventilator and administer continuous oxygenation. If needed, use a 10 cm/H₂O PEEP valve. 4. Observe the potential donor for the duration of the test, to exclude the presence of respiratory effort. 5. Proceed with an arterial blood gas approximately 10 minutes after the start of the test, without reconnecting the potential donor to the mechanical ventilator. If the criteria are met, reconnect the potential donor to the ventilator. If the criteria are not met, wait and repeat arterial gas until target values are reached. 6. Once the test is complete, resume initial ventilatory parameters. 	<p>For the apnea test to be conclusive, all the following criteria must be met:</p> <ul style="list-style-type: none"> ○ Lack of respiratory effort ○ <u>Final Target Values</u> <ul style="list-style-type: none"> - pH ≤ 7.28 - PaCO₂ ≥ 60 mm Hg - PaCO₂ ≥ 20 mm Hg compared to the initial value 	<p>Ancillary investigation should be performed in cases of desaturation, hemodynamic instability, or when it is not possible to assess the respiratory reflex.</p> <p>Pay close attention to the gas values of potential donors with a history of lung disease. The clinical judgment of the reporting physician must confirm the validity of the test, otherwise ancillary investigation is required.</p> <p>Consult Transplant Québec's medical director – organ donation or his/her delegate for any problem related to the apnea test.</p>

Ref.: A Brain Definition of Death and Criteria for its Determination After Cessation of Circulation or Neurological Function in Canada: Clinical Practice Guidelines 2023 *Canadian Journal of Anesthesia / Canadian Journal of Anesthesia* May 2, 2023 (70, 483-557 (2023)) <https://link.springer.com/article/10.1007/s12630-023-02431-4#Abs1>

Greer DM, Shemie SD, Lewis A, et al. *Determination of brain death/death by neurologic criteria: The World Brain Death Project*. JAMA. doi:10.1001/jama.2020.11586