

Neurological determination of death (NDD)

Neurologically determined death is defined as the “irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breathe” (Canadian Neurocritical Care Group 1999). Previously, the terms “brain death”, “neurological death” and “death by neurological criteria” were used interchangeably.

Trillium Gift of Life Network (TGLN) accepts criteria developed at a consensus conference coordinated by the Canadian Council for Donation and Transplantation (CCDT) in 2003 as the standard for neurological determination of death (NDD). The CCDT states that diagnosing neurological death involves determining the irreversible loss of brain stem reflexes, such as cough or gag, as well as absence of pupillary response to light. There is no spontaneous movement or central response to pain, although spinal reflexes may persist. The person is also no longer able to breathe (apneic), requires mechanical ventilation and their capacity for consciousness has been irreversibly lost.

What conditions may lead to neurological death?

Acute brain injury: Head trauma from motor vehicle collisions, intracranial hemorrhage from any cause including stroke, intracranial tumor or acute hydrocephalus.

Hypoxic-ischemic encephalopathy: Post-cardiac or respiratory arrest, near drowning, asphyxia, hypovolemic shock.

Central nervous system (CNS) infection: Meningitis, encephalitis, generalized sepsis.

Miscellaneous: Metabolic encephalopathy from liver disease; diabetic ketoacidosis, metabolic disorders, acute hyponatremia or vasculitis.

What qualifications are needed to determine neurological death?

Physicians declaring neurological death should have full and current licensure for independent medical practice in Ontario (or relevant Canadian jurisdiction) and have skill and knowledge in the management of patients with severe brain injury and in the diagnosis of NDD. For donations to be eligible for transplantation, two physicians must declare the patient’s death. The *Trillium Gift of Life Network Act* states a physician whose judgment might be influenced owing to an association with a transplant program or a proposed recipient cannot take any part in the declaration of death.

What is the legal time of death?

The time of the ***first completed determination of neurological death*** is the legal time of death – this is the time that is written on the death certificate.

What are the minimum clinical criteria needed for NDD?

The following minimum clinical criteria are required for NDD:

1. Proof of etiology that is capable of causing neurological death (in the absence of reversible conditions capable of imitating neurological death).

2. Absence of reversible causes of coma, or confounding factors including:
 - a. Unresuscitated shock.
 - b. Low core body temperature < 34 degrees Celsius (or < 36 degrees Celcius for term newborns).
 - c. Treatable metabolic/endocrine/electrolyte disturbances (including hypernatremia, hypoglycemia, severe hypophosphatemia, liver and/or renal dysfunction).
 - d. Peripheral nerve or muscle dysfunction due to disease or neuromuscular blocking agents (pancuronium, succinylcholine, etc.).
 - e. CNS depressants/significant drug intoxications (e.g. alcohol, barbiturates, sedatives) – note that therapeutic levels of anticonvulsants, sedatives and analgesics do not preclude the diagnosis.
3. Absence of brain stem reflexes/absence of bilateral movement, both spontaneous and in response to stimulation (including seizures). **Spinal cord reflexes are exempt.** Deep pain testing must include all extremities and above the clavicles.
4. Absence of respiratory effort, as established by apnea testing.

Assistance for the determination of neurological death is available by contacting the Trillium Gift of Life Network's Provincial Resource Centre at 1-877-363-8456 or 416-363-4438 (in the Toronto area).

What are the testing criteria to determine neurological death?

The following tests are done to determine neurological death:

1. **CNS-mediated motor response to pain:** Testing must include all extremities and above the clavicles. Spinal cord reflexes are exempt.
2. **Brain stem reflexes:** All reflexes must be tested bilaterally (except cough and gag).
 - a. **Pupillary response:** In a darkened room, shine light into each eye and observe change in pupil size. Absent reflex involves fixed dilated pupils that are unreactive to light. Intravenous drugs, including conventional doses of atropine may influence pupil size, but the light response remains the same. Topical ocular instillation of drugs, however, may produce non-reactive pupils.
 - b. **Corneal reflex:** Stimulate the cornea with a tissue and observe both eyelids for any response. If no response such as blinking is observed, the reflex is absent.
 - c. **Gag reflex:** Stimulate the pharynx with a tongue blade /Yankauer. If it elicits no response, the reflex is absent.
 - d. **Cough reflex:** If bronchial suctioning fails to initiate a cough, the reflex is absent.
 - e. **Oculo-vestibular reflex (cold calorics):** With head of bed elevated 30 degrees, syringe about 50 cc of ice-cold water into each ear canal ensuring patient's eyes are open. *Any* movement of one or both eyes excludes the diagnosis of neurological death. Prior to testing, a tympanic membrane assessment is required as testing of this reflex is contraindicated if there is impaired integrity of the tympanic membrane. Initial flushing of the ear canal may be needed if wax is obstructing the membrane.
3. **Apnea testing:** Apnea testing involves driving up PaCO₂ levels to a maximum point to elicit the respiratory response (while supporting oxygenation). Cooler body temperature may impact clinical testing for neurological death and can prolong the time required for apnea tests, due to the decreased amount of CO₂ produced by the body.

Threshold levels once the apnea test is completed should be as follows:

- PaCO₂ ≥ 60 mmHg, and
- PaCO₂ ≥ 20 mmHg rise above baseline, and
- pH ≤ 7.28

These thresholds must be documented by arterial blood gas measurement. If the apnea test is started with a normal PaCO₂ of 35 – 45 mmHg, the rise of the PaCO₂ to the level of 60 mmHg usually will occur within 10 minutes. The physician **must** be present to observe and ensure the absence of respiratory effort while the patient is off the ventilator during the apnea test. A single apnea test may be performed in children over one year and in adults if both physicians are present at the time of the test.

Instructions:

- a. Attempt to achieve normal baseline arterial blood gases: pH 7.35-7.45, PaCO₂ 35-45 mmHg, PaO₂ >100 mmHg.
- b. Preoxygenate with 100% O₂.
- c. Disconnect ETT from ventilator and insert catheter into ETT to deliver O₂ @ 1-4 L/min.
- d. Verify apnea; observe chest and abdomen **continuously** for respiratory effort while patient is off ventilator. Ensure cardiovascular status and oxygen saturations remain stable.
- e. Test arterial blood gases in 10-15 minutes, then reconnect ventilator.
- f. Absence of capacity to breathe is confirmed if: PaCO₂ ≥ 60 mmHg **and** PaCO₂ ≥ 20 mmHg rise above baseline **and** a pH ≤ 7.28.

Note: If the test fails to meet the three criteria listed above **or** an apnea test is unable to be performed due to donor instability, an ancillary test should be performed.

4. **Ancillary testing for neurological death:** Ancillary testing to determine absence of intracranial flow is indicated when any of the specific components of the clinical testing cannot be conducted or completed. Ancillary testing does not negate the need for carrying out the clinical exams by two physicians to the extent possible. Acceptable imaging techniques for ancillary testing as per CCDT guidelines include radionuclide imaging (nuclear medicine testing), 4-vessel cerebral angiogram, Xenon and computed tomography (CT), or magnetic resonance (MR) angiography. The electroencephalogram (EEG) is no longer recommended.

Are there paediatric considerations for NDD?

For the purpose of donation all children should be pronounced as per the age specific criteria outlined below. A TGLN *Paediatric Donation Resource Manual* is available for patients ≤ 18 years and can be obtained from TGLN. As with the adult population, the CCDT recommends that declaring physicians have skill and knowledge in the management of patients with severe brain injury and in the diagnosis of NDD.

	Neonates (>36 weeks gestation & <30 days) Requires specialist in Neonatology	Infants (≥ 30 days & < 1 year)	Children older than one year and adults
Assessment			
Deep Pain Stimuli	✓	✓	✓
Pupillary Response	✓	✓	✓
Corneal Reflex	✓	✓	✓
Gag Reflex	✓	✓	✓
Cough Reflex	✓	✓	✓
Oculovestibular Reflex (Cold Calorics)	✓	✓	✓
Oculocephalic Reflex (Doll's Eyes)	✓	✓	
Suck	✓		
Apnea Test	✓	✓	✓*
Ancillary Test	If unable to complete any of the above	If unable to complete any of the above	If unable to complete any of the above
Time of 1 st test	48 hours post birth	No fixed time	No fixed time
Interval between two exams	24 hours	Not specified, but at separate times	Can be done concurrently

*A single apnea test may be performed in children over one year and in adults if both physicians are present at the time of the test.