Canadian Council for Donation and Transplantation

Severe Brain Injury to Neurological Determination of Death: A Canadian Forum

April 9–11, 2003

Vancouver, British Columbia

Report and Recommendations

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CD-ROM

The CD-ROM attached to the inside back cover of this document includes electronic copies of the following documents:

1. Planning Committee, Severe Brain Injury to Neurological Determination of Death–A Canadian Forum. *Report on Severe Brain Injury to Neurological Determination of Death–A Canadian Forum*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
2. Shemie, Sam D. and Young, Kimberly. *Checklist for Neurological Determination of Death: Adults and Children Aged ≥ 1 year*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
3. Shemie, Sam D. and Young, Kimberly. *Checklist for Neurological Determination of Death: Infants Aged < 1 year and Newborns > 36 Weeks Gestation*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
4. Shemie, Sam D., Doig, Christopher and Belitsky, Philip. "Advancing toward a modern death: the path from severe brain injury to neurological determination of death" in the *Canadian Medical Association Journal*, Vol. 168(8), April 2003, pp. 993-995. Reprinted by permission of the publisher, ©2003 Canadian Medical Association.
5. Baron, Leonard, Shemie, Sam D. and Doig, Christopher. *A Review of Literature on the Neurological Determination of Death: Full Version*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
6. Baron, Leonard, Shemie, Sam D. and Doig, Christopher. *A Review of Literature on the Neurological Determination of Death: Short Version*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
7. Burke, Kathryn and Associates. *Legal Foundations for the Neurological Determination of Death*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
8. Burke, Kathryn and Associates. *Factors Affecting Referral of Severely Brain Injured Patients to Critical Care for Prognostication and Treatment*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
9. *Abstracts on the Diagnosis of Brain Death*. Edmonton: The Canadian Council for Donation and Transplantation, 2003.
10. Tomlinson, Paul. *The Dissemination-Implementation Challenge*. Ottawa: Strachan•Tomlinson and Associates, 2003.

Preface

The management of patients with severe brain injury falls within the disciplines of emergency medical services, trauma, critical care, neurology and neurosurgery. Consultation and collaboration of these disciplines with stakeholders involved in end-of-life care, donation and transplantation is required to standardize and optimize the management of severely brain injured patients who evolve to neurological death.

Despite widespread national, international and legal acceptance of the concept of death as defined by neurological criteria, substantial variability exists in the standards and their application. In all Canadian provinces and territories, brain death is legally defined as "according to accepted medical practice."[1] These practices are largely determined by individual hospitals or regions. Surveys of Canadian hospital guidelines reveal variation and inconsistency of these practices,[2] with similar observations noted internationally.[3] Surveys of Canadian critical care and neuroscience physicians strongly support the need for national standards.[4] Guidelines established by the Canadian Congress Committee on Brain Death in 1988[5] and Canadian Neurocritical Care Group in 1999[6] initiated clarification of the criteria, but have not lead to uniform practice.

Acknowledging variability in the recognition, diagnosis and documentation of neurological death, this Forum and the ensuing recommendations are the result of a national multidisciplinary effort sponsored by the Canadian Council for Donation and Transplantation. Within the Forum, expert panels provided recommendations reflecting feedback from extensive and multidisciplinary plenary discussions.

The recommendations from this Forum have significant implications for organ donation in Canada. Severe brain injury is a prerequisite for neurological determination of death (NDD), and NDD, commonly referred to as brain death, is a prerequisite for cadaveric organ donation. The right to entertain the option of organ and tissue donation is increasingly supported by society and will become legislated in some Canadian jurisdictions. Collaborative efforts are required to optimize the care of patients who may become eligible for donation.

This comprehensive national collaboration is the first of its kind in Canada in this domain. The recommendations in this report provide minimum standards and a code of practice for the care of patients whose injuries result in NDD. They are intended as a framework for the development of regional or site-specific guidelines and provide an opportunity for international leadership. Consistency and standardization will optimize care, promote community confidence in NDD and enhance the conduct of organ and tissue donation.

Sam D. Shemie, MD
Forum Chair, Severe Brain Injury to Neurological Determination of Death

Participating Organizations

- Alberta Health and Wellness
- British Columbia Transplant Society
- Canadian Association of Critical Care Nurses
- Canadian Association of Emergency Physicians
- Canadian Association of Neuroscience Nurses
- Canadian Association of Transplantation
- Canadian Bioethics Society
- Canadian Congress of Neurological Sciences
- Canadian Critical Care Society
- Canadian Hospice and Palliative Care Association
- Canadian Institute for Health Information
- Canadian Medical Association Journal
- Canadian Medical Protective Association
- Canadian Neurological Society
- Canadian Neurosurgical Society
- Canadian Nurses Association
- Canadian Organ Replacement Registry
- Canadian Society of Transplantation
- Collège des Médecins du Québec
- College of Family Physicians of Canada
- College of Physicians and Surgeons of British Columbia
- Chief Coroners and Medical Examiners of Canada
- Health Canada
- National Emergency Nurses Affiliation
- Nova Scotia Department of Health
- Quebec Society of Intensivists
- Québec Transplant
- Trauma Association of Canada
- Trauma Coordinators of Canada
- Trillium Gift of Life Network
- Urban Futures Institute

Forum Overview

The purpose of the Forum "Severe Brain Injury to Neurological Determination of Death" (SBINDD) was to initiate the development of a national agreement on the processes of care, commencing with severe brain injury and culminating with neurological determination of death (NDD). A priori, the Forum accepted brain death as a medical and legal concept of death in Canadian society and restricted the discussion to optimal practice in the field. Objectives were:

1. To review global and Canadian legislation, policies and practices related to NDD.
2. To create a made-in-Canada definition of NDD for children and adults to ensure consistency and reliability in its diagnosis, declaration, documentation and reporting.
3. To discuss and agree on policies and practices in relation to Emergency Department (ED), Neurological/Neurosurgical and Intensive Care Unit (ICU) management of critically injured patients with poor neurological prognoses.
4. To develop recommendations to the Canadian Council for Donation and Transplantation (CCDT) and other interested organizations and groups on the dissemination of these definitions, policies and practices across Canada.

The Forum was held in Vancouver on April 9–11, 2003, and was attended by 89 participants who were invited as experts in their fields and agents of change. Participants included health care professionals such as emergency, trauma and critical care physicians, neurologists, neurosurgeons, nurses and advanced nurse practitioners, as well as representatives of licensing colleges, health administrators, policy makers, coroners, experts in end-of-life care, donation/transplant agencies and ethicists–a multidisciplinary group representing all regions of the country. Discussions focused on collaboration at a national level.

The following three challenge areas and related questions were addressed at the Forum.

Challenge A–Canadian Medical Standards for Neurological Determination of Death: Definition, Criteria and Minimum Testing

Questions for Challenge A explored:

Minimum Clinical Criteria for NDD

Confounding Factors

Minimum Temperature

Apnea Testing

Examination Interval

Ancillary Tests

Concept

Physicians Declaring NDD and

Age-related Criteria.

Challenge B–Representation of NDD: Incidence, Reporting and Legal Issues

Questions for Challenge B explored:

Legal Timing of Death

Reporting

Reporting Mechanism and

Legal Issues.

Challenge C–Severe Brain Injury: From Emergency Department to Intensive Care Unit

Questions for Challenge C explored:

Recognition of NDD

ED to ICU Triage–Evolving Neuroprotective Therapies and

End-of-Life Care.

Each challenge was addressed using the following process:

a. Presentations by experts were followed by plenary discussions that were supported by fact sheets, substantial background papers[1,6,7,8,9] and surveys[2,4] provided by the Planning Committee in advance of the Forum.

b. Small group discussions focused on specific questions related to the processes of care.

c. Meetings of the Forum Recommendations Group (FRG) and the Pediatric Reference Group (PRG) reviewed the results of small group discussions, developed unanimous recommendations for adults and children and returned these for plenary discussion.

Process

Discussions at the Forum were intense, rich in content and collegial. Members of the FRG and PRG panels came to unanimous agreement on recommendations that mark a significant, positive advance on existing guidelines. Group members were invited to sit on these panels both as representatives of their professional associations and as respected practitioners providing the benefit of their experience and expertise. Both panels were facilitated by an external, objective facilitator.

Forum recommendations were developed for infants, children, adolescents and adults, with Drs. Paul Byrne and Sam Shemie sitting on both the FRG and the PRG and providing consistent pediatric input during the development of guidelines in plenary and at FRG and PRG meetings.

Expert Panel Members

Dr. Natalie Anton	Division of Pediatric Critical Care, Stollery Children's Hospital, University of Alberta Canadian Critical Care Society	Pediatric Reference Group
Dr. Andrew Baker	Medical Director, Trauma and Neurosurgery ICU, St. Michael's Hospital, University of Toronto Chair, Clinical Advisory Committee, Trillium Gift of Life Network	Forum Recommendations Group
Dr. Paul Byrne	Interim Director, John Dossetor Health Ethics Centre, University of Alberta Clinical Director, Neonatal Intensive Care Unit, Stollery Children's Hospital Clinical Professor, Department of Pediatrics, University of Alberta	Forum Recommendations Group Pediatric Reference Group
Dr. Dan Cass	Chief of Emergency Medicine, St. Michael's Hospital, University of Toronto Canadian Association of Emergency Physicians	Forum Recommendations Group
Dr. Bernard Dickens	Professor, Faculty of Law, Joint Centre for Bioethics, University of Toronto	Forum Recommendations Group
Dr. Christoper Doig	Multisystem Intensive Care Unit, Foothills Hospital, University of Calgary Associate Professor, Department of Critical Care, University of Calgary Chair, Donation Committee, Canadian Council for Donation and Transplantation	Forum Recommendations Group

Dr. Catherine Farrell	Division of Pediatric Intensive Care, Hôpital Sainte-Justine Associate Clinical Professor, University of Montreal Canadian Critical Care Society	Pediatric Reference Group
Dr. Cameron Guest	Chief, Department of Critical Care Medicine, Sunnybrook and Women's College Health Sciences Centre Assistant Professor, Critical Care Medicine and Anaesthesia, University of Toronto Chief Medical Officer, Trillium Gift of Life Network	Forum Recommendations Group
Ms. Karen Hornby	Critical Care Nurse, PICU, Montreal Children's Hospital, McGill University Health Centre Research Coordinator, PICU, Montreal Children's Hospital, McGill University Health Centre Canadian Association of Critical Care Nurses	Pediatric Reference Group
Dr. James Hutchison	Director of Education, Department of Critical Care Medicine, Hospital for Sick Children, University of Toronto Associate Professor, Department of Pediatrics, University of Toronto Scientist, Hospital for Sick Children Research Institute	Pediatric Reference Group
Ms. Rosella Jefferson	Member/Past President, Canadian Association of Critical Care Nurses ICU Children's and Women's Health Centre of BC	Forum Recommendations Group
Ms. Lisa McCarthy	Coordinator, Organ Donation Program, Department of Critical Care Medicine, Hospital for Sick Children In-Hospital Organ Donation Coordinator, Trillium Gift of Life Network Canadian Association of Transplantation/Canadian Association of Critical Care Nurses	Pediatric Reference Group

Dr. Graeme Rocker	Critical Care Program, Queen Elizabeth II Health Sciences Centre, Halifax, NS Professor of Medicine, Dalhousie University President, Canadian Critical Care Society	Forum Recommendations Group
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Dr. Sam D. Shemie	Division of Pediatric Critical Care, Montreal Children's Hospital, McGill University Health Centre Associate Professor of Pediatrics, McGill University Honourary Staff, Department of Critical Care Medicine, Hospital for Sick Children, University of Toronto Forum Chair, Severe Brain Injury to Neurological Determination of Death	Forum Recommendations Group Pediatric Reference Group
Dr. Michael Shevell	Division of Pediatric Neurology, Montreal Children's Hospital, McGill University Health Centre Associate Professor, Departments of Neurology/Neurosurgery and Pediatrics, McGill University President, Canadian Association of Child Neurology Chair, Ethics Committee, Child Neurology Society	Pediatric Reference Group: Post-Forum Collaboration
Dr. Jeanne Teitelbaum	Associate Professor of Neurology and Critical Care, Montreal Neurological Institute and Hospital, McGill University Associate Professor of Neurology and Critical Care, Maisonneuve-Rosemount Hospital, University of Montreal President, Canadian Neurocritical Care Group, an affiliate society of the Canadian Congress of Neurological Sciences Co-author, Canadian Neurocritical Care Guidelines	Forum Recommendations Group

Dr. Brian Wheelock	Division of Neurosurgery, Dalhousie University Atlantic Health Sciences Corporation President, Canadian Neurosurgical Society	Forum Recommendations Group
Ms. Kimberly Young	Senior Program Analyst, Canadian Council for Donation and Transplantation Secretariat, Health Canada Forum Project Manager, Severe Brain Injury to Neurological Determination of Death	Forum Recommendations Group

General Considerations

During discussions, FRG and PRG members recognized that:

- recommendations must be in the best interests of patients with severe brain injury
- optimal end-of-life care is a priority for all patients who may die after severe brain injuries
- the wishes of patients and their families are of paramount importance
- there is a need to clarify and standardize terminology, e.g., ancillary and supplementary testing, brain death, neurological determination of death, neurologically determined death or death by neurological determination (see Appendices #2, #3)
- the current evidence base for the existing NDD guidelines is inadequate
- clear medical standards for NDD and defining qualifications of physicians performing NDD augment the quality and rigor of the determination.

Overarching Recommendation

In discussions related to Recommendations A4—Apnea Testing, A5—Examination Interval and A7—Concept, FRG members identified the following overarching recommendation that applies to all challenges:

We recommend that after a neurological determination of death, the patient be declared dead.

Existing provincial and territorial laws indicate that for the purposes of a post mortem transplant, the fact of death shall be determined by at least two physicians in accordance with accepted medical practice.[1] There is no clear medical basis for the law requiring a second physician to determine death prior to post mortem transplantation.

The first and second physicians' determinations, required by law, may be performed concurrently. However, if the determinations are performed at different points in time, a full clinical examination, including apnea testing, must be performed at each determination. No fixed interval of time is recommended for the second determination, except where age-related criteria apply.

Challenge A

Canadian Medical Standards for Neurological Determination of Death:

Definition, Criteria and Minimum Testing

Recommendation A1: Minimum Clinical Criteria for NDD

We recommend the use of the following minimum clinical criteria as a Canadian medical standard for neurological determination of death:

a. Established etiology capable of causing neurological death in the absence of reversible conditions capable of mimicking neurological death

b. Deep unresponsive coma

c. Absent brainstem reflexes as defined by absent gag and cough reflexes and the bilateral absence of
   - motor responses, excluding spinal reflexes
   - corneal responses
   - pupillary responses to light with pupils at mid-size or greater and
   - vestibulo-ocular responses

d. Absent respiratory effort based on the apnea test

e. Absent confounding factors.

Key Considerations

- A prerequisite for NDD is the absence of clinical neurological function with a known, proximate cause that is irreversible. There must be definite clinical and/or neuroimaging evidence of an acute central nervous system (CNS) event that is consistent with the irreversible loss of neurological function.
- Deep unresponsive coma implies a lack of spontaneous movements as well as an absence of movement originating in the CNS such as cranial nerve function, CNS-mediated motor response to pain in any distribution, seizures, decorticate and decerebrate responses. Spinal reflexes, or motor responses confined to spinal distribution, may persist.
- Minimum should not necessarily be understood as minimal. "Minimal" refers to the least possible that can be done and is an absolute value. "Minimum" refers to the lowest acceptable standard, which is a relative standard, often pitched above the minimal. The standard recommended by the Forum sets minimum clinical criteria for NDD.

Recommendation A2: Confounding Factors

We recommend that, at the time of assessment for NDD, the following confounding factors preclude the clinical diagnosis:

a. Unresuscitated shock

b. Hypothermia (core temperature <34 degrees Celsius)

c. Severe metabolic disorders capable of causing a potentially reversible coma

   Severe metabolic abnormalities including glucose, electrolytes (including phosphate, calcium and magnesium), inborn errors of metabolism, liver or renal dysfunction may play a role in the patient's clinical presentation. If the primary etiology does not fully explain the clinical picture, and if in the treating physician's judgment the metabolic abnormality may play a role, it should be corrected.

d. Peripheral nerve or muscle dysfunction or neuromuscular blockade potentially accounting for unresponsiveness

e. Clinically significant drug intoxications (e.g., alcohol, barbiturates, sedatives, hypnotics); therapeutic levels and/or therapeutic dosing of anticonvulsants, sedatives and analgesics do not preclude the diagnosis.

Key Considerations

- Neurological assessments may be unreliable in the acute post-resuscitation phase after cardiorespiratory arrest. In cases of acute hypoxic-ischemic brain injury, clinical evaluation for NDD should be delayed for 24 hours subsequent to the cardiorespiratory arrest or an ancillary test could be performed. (Recommendation A6)
- It is recognized that there are variabilities in confounding factors that may be associated with NDD; examiners are cautioned to review these confounding issues in the context of the primary etiology and examination. If physicians are confounded by data, either absolutely or by differing perspectives, they should not proceed with clinical NDD. Clinical judgment is the deciding factor.

Recommendation A3: Minimum Temperature

The recommended minimum temperature that should be applied to the minimum clinical criteria for NDD (Recommendation A1) is 34 degrees Celsius as defined by core temperature.

Key Considerations

- Core temperature results should be obtained through central blood, rectal or esophageal/gastric measurement.
- The 32.2 degrees Celsius standard is based on precedent. The relevance of the scientific evidence and the application of the preceding standard in the context of severe brain injury is uncertain.
- Given that there is no evidence base, a decision was made to adopt 34 degrees Celsius as a rational, safe and attainable standard. This decision was based on the following rationale:
  - Ideally, temperature should be (a) as close to normal physiology as possible and (b) the minimum temperature at which the test is valid.
  - Raising a patient's temperature from 32.2 degrees Celsius to 34 degrees Celsius does not pose significant difficulty to the patient or treating physician.

Recommendation A4: Apnea Testing

We recommend that the thresholds at the completion of the apnea test should be $PaCO_2$ >=60 mmHg, and >=20mmHg rise above the pre-apnea test level, and with a pH <= 7.28. These thresholds must be documented by arterial blood gas measurement.

To correctly interpret an apnea test, the certifying physician must continuously observe the patient for respiratory effort throughout the performance of the test.

Key Considerations

- Optimal performance of the apnea test requires a period of preoxygenation followed by 100% oxygen delivered via the trachea upon disconnection from mechanical ventilation.
- The following codicil is required to address severe lung disease:

  Caution must be exercised in considering the validity of the apnea test if in the physician's judgment there is a history suggestive of chronic respiratory insufficiency and responsiveness to only supra-normal levels of carbon dioxide, or if the patient is dependent on hypoxic drive. If the physician cannot be sure of the validity of the apnea test, an ancillary test should be performed.

Recommendation A5: Examination Interval

We recommend that when a second determination is performed, there should be no fixed examination interval, regardless of the primary mechanism of the brain injury.

Recommendation A6: Ancillary Tests

We recommend that an ancillary test be performed when it is impossible to complete the minimum clinical criteria as defined in Recommendation A1. At a minimum, two particular clinical criteria must be met prior to performing any ancillary tests:

a. An established etiology capable of causing neurological death in the absence of reversible conditions capable of mimicking neurological death and

b. Deep unresponsive coma.

We recommend that demonstration of the global absence of intracranial blood flow be considered as the standard for determination of neurological death by ancillary testing.

Key Considerations

- Prior to performing an ancillary test, unresuscitated shock and hypothermia (Recommendation A2) must be corrected.
- The term "ancillary" should be understood as an alternative test to one that otherwise, for any reason, cannot be conducted. It replaces previous terminology such as "supplemental" (in addition to an already conducted test) or "confirmatory" (confirms a previously conducted test).
- Existing evidence, although not firmly established, suggests that for patients who fulfill minimum clinical criteria (Recommendation A1) under the circumstances of high dose barbiturate therapy utilized for refractory intracranial hypertension to achieve deep coma or electrocerebral silence, NDD can be confirmed by the demonstration of absent intracranial blood flow.
- A description of ancillary testing is provided in Appendix #3.

Recommendation A7: Concept

We recommend that neurologically determined death be defined as the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions (as defined in Recommendation A1), including the capacity to breathe.

Key Consideration

- Death determined by neurological criteria may occur as a consequence of intracranial hypertension and/or primary direct brainstem injury. In instances of intracranial hypertension, ancillary testing demonstrating absence of intracranial blood flow confirms death when application of minimum clinical criteria (as defined in Recommendation A1) cannot be completed, or if the interpretation of clinical criteria is confounded. There are currently no satisfactory ancillary tests for confirmation of neurologically determined death in instances of isolated primary brainstem injury.

Recommendation A8: Physicians Declaring Neurological Death

We recommend that the minimum level of physician qualification required to perform NDD is:

a. Full and current licensure for independent medical practice in the relevant Canadian jurisdiction and

b. Skill and knowledge in the management of patients with severe brain injury and in the NDD.

In cases of NDD for the purposes of post-mortem donation, we recommend that any physician who has had any association with the proposed recipient that might influence the physician's judgment shall not take any part in the declaration of death.

Key Considerations

- For the purposes of this recommendation, a physician with "full and current licensure for independent practice in the relevant Canadian jurisdiction:"
  - is any physician licensed by the College of Physicians and Surgeons in that jurisdiction
  - excludes physicians who are only on an educational register
  - does not require a particular level of specialty certification; non-specialists can declare NDD if they have the requisite skill and knowledge.
- The authority to perform NDD cannot be delegated.

Recommendation A9: Age-Related Criteria

We recommend that the Forum Recommendations (A1 to A8) for NDD should be applied to infants, children and adolescents with the following qualifications:

NDD Recommendations Specific to Children and Adolescents:

a. All children age>=1 year (corrected for gestational age) should have NDD as per standards established at the Forum. A second physician performing the NDD is required by law for the purposes of post-mortem transplantation, with no fixed interval of time required, regardless of the primary mechanism of the brain injury. (Recommendation A5)

b. The minimum level of physician qualifications should be understood as specialists with skill and knowledge in the management of children and/or adolescents with severe brain injury and NDD. (Recommendation A8)

NDD Recommendations Specific to Infants:

Infants >= 30 days and <1 year (corrected for gestational age)

a. The minimum clinical criteria include the oculo-cephalic reflex, as this test may be more reliable than the vestibulo-ocular reflex in infants due to the unique anatomy of the external auditory canal. (Recommendation A1)

b. Given less widespread experience with NDD for this age range, a repeat examination at a different point in time is recommended to ensure independent confirmation by another qualified physician, regardless of the primary mechanism of the brain injury. It is prudent to have an independent examination because of the lack of collective experience and research on brain death in this age group. There is no recommended minimum time interval between determinations. Should uncertainty or confounding issues arise that cannot be resolved, the time interval may be extended according to physician judgment, or an ancillary test demonstrating absence of intracranial blood flow may be used.

c. The minimum level of physician qualifications should be understood as specialists with skill and knowledge in the management of infants with severe brain injury and NDD. (Recommendation A8)

Key Considerations

- Studies should be undertaken to evaluate the necessity of this second examination relative to the risks (e.g., risk of repeating the apnea test, time delays with impact on family stress and donor stability).
- The recommendations for NDD for newborns < 30 days of age have been addressed in a separate forum and appendixed to this document (Appendix #1).

Challenge B

Representation of NDD:

Incidence, Reporting and Legal Issues

Recommendation B1: Legal Timing of Death

We recommend that the legal time of death should be marked by the first determination of death.

Recommendation B2: Reporting

We recommend that NDD should be reported when determined.

Key Consideration

- Given that NDD is a prerequisite for cadaveric organ donation, there is a need to capture this information for comparative analysis of statistics on organ donation.

Recommendation B3: Reporting Mechanisms

We recommend that the mechanism for reporting the incidence of NDD should be through the medical certificate of death and that hospitals be responsible for directing completed information to the appropriate agencies, e.g., the Canadian Institute for Health Information.

Key Considerations

- Physicians should be required to report NDD through a single mechanism.
- Specific provisions to report on NDD should be included on the medical certificate of death. If the NDD portion of the certificate is not completed, it should be returned to the physician for completion.

Recommendation B4: Legal Issues

We recommend that Canadian medical requirements for the NDD (determined at this Forum) be embodied in medical standards and clinical practice guidelines.

Key Consideration

- Hospital practices related to NDD vary across the country. There is a need to align hospital practices (e.g., accreditation) with medical standards and clinical practice guidelines related to NDD.

Challenge C

Severe Brain Injury:

From Emergency Department to Intensive Care Unit

Recommendation C1: Recognition of NDD

We recommend that all patients who are suspected of being brain dead have an assessment for NDD unless this has no implication for prognostication or management, including end-of-life care (see Recommendation C3).

Recommendation C2: ED to ICU Triage– Evolving Neuroprotective Therapies

We recommend that all patients with severe brain injury who may benefit from treatment and/or prognostication and/or optimal end-of-life care within an ICU should have access to these services.

Key Considerations

- Patient and family wishes must be considered, e.g., clinician consultations, advance directives, organ donor cards, organ donor registry.
- ICU is defined as care provided in an ICU, not critical care offered in an ED.
- Access to ICU services for patients with severe brain injury should be in addition to preserving access to ICU for other critically ill patients.
- Resource and societal issues require consideration.
- Clinicians need to have some flexibility in decision making.

Recommendation C3: End-of-Life Care

We recommend that for patients who die as a result of severe brain injury, standard post-mortem care should include the option of organ and tissue donation for eligible patients.

Key Consideration

- Other issues related to care for the dying (e.g., non-therapeutic ventilation) will be addressed through subsequent initiatives.

Dissemination

Dissemination of Forum recommendations is planned in two phases. The first phase involves reporting to the CCDT, which in turn will report to the Conference of Deputy Ministers of Health (CDM). The second phase involves:

a. Dissemination of knowledge and Forum agreements through publication of the Forum proceedings in the Canadian Medical Association Journal and

b. Dissemination and implementation of agreements via Forum participants, FRG and PRG panel members and stakeholder organizations and groups represented at the Forum, e.g., relevant professional associations (see page ii.)

Appendix #1: Neonatal Recommendations

Following the SBINDD Forum, a Neonatal Reference Group was formed (based on a pre-existing Clarica Neonatal Brain Death Study Group) to consider neonatal guidelines in the context of the SBINDD recommendations. Members of this group included:

Dr. Natalie Anton	Division of Pediatric Critical Care, Stollery Children's Hospital, University of Alberta Canadian Critical Care Society
Dr. Keith Barrington	Director, NICU, Royal Victoria Hospital, McGill University Health Centre Chair, Newborn and Fetus Committee, Canadian Pediatric Society
Dr. Paul Byrne	Interim Director, John Dossetor Health Ethics Centre, University of Alberta Clinical Director, Neonatal Intensive Care Unit, Stollery Children's Hospital Clinical Professor, Department of Pediatrics, University of Alberta
Dr. Catherine Farrell	Division of Pediatric Intensive Care, Hôpital Sainte-Justine Associate Clinical Professor, University of Montreal Canadian Critical Care Society
Dr. Cecil Hahn	Chief Resident, Neurology, Hospital for Sick Children, University of Toronto Research Fellow, Neonatal Brain Death Study
Dr. Jonathan Hellmann	Clinical Director, NICU, Hospital for Sick Children Associate Professor of Pediatrics, University of Toronto
Ms. Karen Hornby	Critical Care Nurse, PICU, Montreal Children's Hospital, McGill University Health Centre Research Coordinator, PICU, Montreal Children's Hospital, McGill University Health Centre Canadian Association of Critical Care Nurses
Ms. Lisa McCarthy	Coordinator, Organ Donation Program, Department of Critical Care Medicine, Hospital for Sick Children In-Hospital Organ Donation Coordinator, Trillium Gift of Life Network Canadian Association of Transplantation Canadian Association of Critical Care Nurses

Dr. Sam D. Shemie	Division of Pediatric Critical Care, Montreal Children's Hospital, McGill University Health Centre
	Associate Professor of Pediatrics, McGill University
	Honourary Staff, Department of Critical Care Medicine, Hospital for Sick Children, University of Toronto
	Forum Chair, Severe Brain Injury to Neurological Determination of Death
Dr. Michael Shevell	Division of Pediatric Neurology, Montreal Children's Hospital, McGill University Health Centre
	Associate Professor, Departments of Neurology/Neurosurgery and Pediatrics, McGill University
	President, Canadian Association of Child Neurology
	Chair, Ethics Committee, Child Neurology Society.

Neonatal Recommendations

The Neonatal Reference Group recommends that all NDD standards established at the Forum should be adopted with the following adjustments and emphases:

NDD Recommendations for term newborns age < 30 days:

- Standards apply to newborns age >36 weeks gestation at the time of death
- NDD is a clinical diagnosis, i.e., clinical criteria have primacy
- Minimum clinical criteria include absent oculo-cephalic reflex and suck reflex
- Minimum temperature must be a core temperature of >=36 degrees Celsius
- The minimum time from birth to first determination is 48 hours
- Two determinations are required, with a minimum interval of 24 hours between exams
- Ancillary testing, as defined by demonstration of the absence of intracranial blood flow, should be performed when any of the minimum clinical criteria cannot be completed or confounding factors remain unresolved
- "Minimum level of physician qualifications" should be understood as specialists with skill and knowledge in the management of newborns with brain injury and the determination of death based on neurological criteria.

Key Considerations

- Accuracy of gestational age should be supported by clinical history (e.g., dates and prenatal ultrasound) and physical examination. Inability to confirm a gestational age > 36 weeks should preclude NDD.
- The higher recommended temperature thresholds reflect uncertainty regarding hypothermia effects on neurological function in the newborn and normothermia being an easily attainable standard.
- The 48 hour recommendation from injury to first determination reflects a reduced certainty of neurological prognostication prior to the first 48 hours of life.
- Prospective research should be done to confirm the necessity of the recommended 24 hour interval between determinations.

Appendix #2: Key Terms

The following definitions of key terms were developed as a result of discussions at the Forum.

Brain Death

Is the most ubiquitous term used in medical, nursing and lay literature; is based on the concept of complete and irreversible loss of brain function. The Canadian Neurocritical Care Guidelines[6] define brain death as "the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions including the capacity to breathe. Brain death is equivalent to death of the individual, even though the heart continues to beat and spinal cord functions may persist."

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (USA)[10] defines brain death as "irreversible cessation of all functions of the entire brain, including the brainstem. The clinical diagnosis of brain death is equivalent to irreversible loss of all brainstem function."

While brain death is an accepted concept, the definition lacks clarity in the Canadian context. Distinctions between brainstem death (UK definition) and whole brain death (US definition) are unclear in Canada.

The actual process for determining brain death is legally stated as "according to accepted medical practice." A purpose of this Forum is to clearly define and standardize "accepted medical practice."

Neurologic Death

A term that is similar to brain death, but not commonly used.

Neurological Determination of Death

Is the process and procedure for determining death of the individual. It is not a new definition of death. It is intended to be a clear and standardized process for the determination of death based on neurologic or brain-based criteria. For the purposes of this Forum, the term "brain death" has been replaced by NDD.

Non-therapeutic Ventilation

(Discussion of this issue was beyond the scope and objectives of this Forum.)

Also known as Elective Ventilation, Ventilation for the Purposes of Organ Donation, Extended Ventilation. Refers to extending the duration of mechanical ventilation in patients who have suffered acute and severe brain injury and whose prognosis is hopeless. Rather than withdraw and/or withhold life support in this situation, ventilation is continued with the short term aim of allowing the potential progression to brain death and thus eligibility for organ donation.

Appendix #3: Ancillary Testing

The demonstration of the absence of intracranial blood flow is considered the standard as an ancillary test for NDD. Currently validated imaging techniques are cerebral angiography and radionuclide angiography. It is recognized that additional cerebral blood flow imaging technologies may further develop or evolve, but, at this time, cannot be recommended. Electroencephalograms are no longer recommended as an ancillary test, in view of limitations as discussed below.

Recommended Ancillary Tests

Cerebral Angiography

A selective radiocontrast 4-vessel angiogram visualizing both the anterior and posterior cerebral circulation. Cerebral-circulatory arrest occurs when intracranial pressure exceeds arterial inflow pressure. External carotid circulation should be evident, and filling of the superior sinus may be present. Angiography requires technical expertise and is performed in the radiology department, necessitating transport of a potentially unstable patient. Arterial puncture and catheter-related complications have been described. Radiocontrast can produce idiosyncratic reactions and end-organ damage, such as renal dysfunction.

Radionuclide Imaging Techniques

Radionuclide angiography for brain death confirmation has been widely accepted for a number of years. Newer radiopharmaceuticals, especially Tc-99m hexamethylpropylene-amine oxime (Tc-99m HMPAO), have been studied extensively in the last decade with enhanced detection of intracerebral, posterior fossa and brainstem blood flow. Tc-99m HMPAO is lipid soluble, crossing the blood-brain barrier, providing information on arterial cerebral blood flow and uptake of tracer within perfused brain tissue. Traditional gamma cameras used for this technique are immobile, necessitating patient transfer for study, but newer technologies are portable, allowing for studies to be performed at the bedside where available.

Ancillary Tests Not Currently Recommended

Transcranial Doppler Ultrasonography

Using a pulse doppler instrument, the intracranial arteries are insonated bilaterally, including the vertebral or basilar arteries. Brain-dead patients display either absent or reversed diastolic flow or small systolic spikes. The non-invasiveness and portability of this technique are advantageous, but the technology requires substantial clinical expertise for proper application and is not widely available. It has not been sufficiently validated at this time.

Magnetic Resonance Imaging

MRI based angiography and imaging hold future promise but are not easily available and have not been sufficiently validated at this time.

Electroencephalography

Electroencephalography (EEG) is readily available in most tertiary medical centres worldwide and has long been used as a supplementary test for brain death. It can be performed at the bedside, with significant limitations. The EEG detects cortical electrical activity but is unable to detect deep cerebral or brainstem function. The high sensitivity requirement for EEG recording may result in detection of electric interference from many of the devices that are commonplace in the ICU setting. The EEG is also significantly affected by hypothermia, drug administration and metabolic disturbances, thus diminishing its clinical utility. It is no longer recommended as an ancillary test.

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Appendix #5: Checklist for Neurological Determination of Death–Adults and Children ≥ 1 year

Section One: Minimum Clinical Criteria

a. Deep unresponsive coma with the following established etiology: _____

b. Confounding factors precluding the diagnosis? Yes ❑ No ❑

c. Temperature (core) _____

d. Brainstem Reflexes:

Bilateral absence of motor responses: (excluding spinal reflexes) Yes ❑ No ❑

Absent cough: Yes ❑ No ❑

Absent gag: Yes ❑ No ❑

Bilateral absence of corneal responses: Yes ❑ No ❑

Bilateral absence of vestibulo-ocular responses: Yes ❑ No ❑

Bilateral absence of pupillary response to light: (pupils ≥ mid size) Yes ❑ No ❑

Apnea: Yes ❑ No ❑

At completion of apnea test: pH_____ $PaCO_2$ _____mmHg

$PaCO_2$ ≥ 20 mmHg above the pre-apnea test level: Yes ❑ No ❑

Section Two: Ancillary Tests

Ancillary tests, as defined by the absence of intracranial blood flow, should be performed when **any** of the minimum clinical criteria cannot be completed, **or** unresolved confounding factors exist.

Ancillary testing has been performed: Yes ❑ No ❑

Date: _____ Time: _____

Absence of intracranial blood flow has been demonstrated by:

Cerebral Radiocontrast Angiography ❑

Radionuclide Angiography ❑

Other _____

Section Three: Declaration and Documentation

The first and second physician's determinations may be performed concurrently. If performed at different points in time, a full clinical examination including the apnea test must be performed, without any fixed examination interval, regardless of the primary etiology.

This patient fulfills the neurological determination of death:

Physician: Print name: _____ Signature: _____

Date: _____ Time: _____

Section Four: Standard End-of-Life Care

Is this patient medically eligible for organ and/or tissue donation? Yes ❑ No ❑

Has the option for organ and/or tissue donation been offered? Yes ❑ No ❑

Has consent been obtained for donation? Yes ❑ No ❑

Checklist for NDD–Adults and Children ≥ 1 Year

Age Definitions

Children 1–18 years of age. (Infants < 1 year and Term Newborns–refer to separate checklist.)

Overarching Principles

The legal time of death is marked by the first determination of death.

Existing law states that for the purposes of post-mortem donation, the fact of death shall be determined by two physicians. The first and second physician's determinations may be performed concurrently. If performed at different points in time, a full clinical examination including the apnea test must be performed, without any fixed examination interval, regardless of the primary etiology.

Physicians Declaring Neurological Death

Minimum level of physician qualifications to perform NDD is full and current licensure for independent medical practice in the relevant Canadian jurisdiction. This excludes physicians who are only on an educational register. The authority to perform NDD cannot be delegated. Physicians should have skill and knowledge in both the management of patients with severe brain injury and in determination of neurological death in the relevant age groups. For the purposes of post-mortem donation, a physician who has had any association with the proposed transplant recipient that might influence the physician's judgment shall not take part in the declaration of death.

Minimum Clinical Criteria

Established Etiology: Absence of clinical neurological function with a known, proximate cause that is irreversible. There must be definite clinical and/or neuroimaging evidence of an acute central nervous system (CNS) event that is consistent with the irreversible loss of neurological function. NDD may occur as a consequence of intracranial hypertension and/or primary direct brainstem injury.

Deep Unresponsive Coma: A lack of spontaneous movements and absence of movement originating in the CNS such as: cranial nerve function, CNS mediated motor response to pain in any distribution, seizures, decorticate and decerebrate responses. **Spinal reflexes**, or motor responses confined to spinal distribution, may persist.

Confounding Factors:

1. Unresuscitated shock
2. Hypothermia (core temperature <34 degrees Celsius, by central blood, rectal or esophageal/gastric measurements)
3. Severe metabolic disorders capable of causing a potentially reversible coma, If the primary etiology does not fully explain the clinical picture, and if in the treating physician's judgment the metabolic abnormality may play a role, it should be corrected or an ancillary test should be performed.
4. Peripheral nerve or muscle dysfunction or neuromuscular blockade potentially accounting for unresponsiveness, or
5. Clinically significant drug intoxications (e.g. alcohol, barbiturates, sedatives); therapeutic levels and/or therapeutic dosing of anticonvulsants, sedatives and analgesics do not preclude the diagnosis.

   Specific to Cardiac Arrest: Neurological assessments may be unreliable in the acute post-resuscitation phase after cardiorespiratory arrest. In cases of acute hypoxic-ischemic brain injury, clinical evaluation for NDD should be delayed for 24 hours or an ancillary test could be performed.

   Examiners are cautioned to review confounding issues in the context of the primary etiology and examination. **Clinical judgment is the deciding factor.**

Apnea Test: Optimal performance requires a period of preoxygenation followed by 100% O_2 delivered via the trachea upon disconnection from mechanical ventilation. The certifying physician must continuously observe the patient for respiratory effort. **Thresholds at completion of the apnea test: $PaCO_2$ ≥ 60 mmHg and ≥ 20 mmHg above the pre-apnea test level and pH ≤ 7.28 as determined by arterial blood gases.** Caution must be exercised in considering the validity of the test in cases of chronic respiratory insufficiency or dependence on hypoxic respiratory drive.

Ancillary Tests

Demonstration of the global absence of intracranial blood flow is considered the standard for determination of death by ancillary testing. The following prerequisite conditions must be met prior to ancillary testing: i) established etiology, ii) deep unresponsive coma, iii) absence of unresuscitated shock and hypothermia. Currently validated techniques are 4-vessel cerebral angiogram or radionuclide cerebral blood flow imaging. EEG is no longer recommended. NDD can be confirmed by ancillary testing when minimum clinical criteria cannot be completed or confounding factors cannot be corrected.

Appendix #6: Checklist for Neurological Determination of Death–Infants < 1 year, Term Newborns > 36 Weeks Gestation

Section One: Minimum Clinical Criteria

a. Deep unresponsive coma with the following established etiology: _____

b. Confounding factors precluding the diagnosis? Yes ❑ No ❑

c. Temperature (core) _____

d. Brainstem Reflexes:

Bilateral absence of motor responses: (excluding spinal reflexes)	Yes ❑	No ❑	
Absent cough:	Yes ❑	No ❑	
Absent gag:	Yes ❑	No ❑	
Absent suck (newborns only):	Yes ❑	No ❑	Not Applicable ❑
Bilateral absence of corneal responses:	Yes ❑	No ❑	
Bilateral absence of vestibulo-ocular responses:	Yes ❑	No ❑	
Bilateral absence of oculo-cephalic responses:	Yes ❑	No ❑	
Bilateral absence of pupillary response to light: (pupils ≥ mid size)	Yes ❑	No ❑	
Apnea:	Yes ❑	No ❑	
At completion of apnea test: pH_____ $PaCO_2$ _____mmHg			
$PaCO_2$ ≥ 20 mmHg above the pre-apnea test level:	Yes ❑	No ❑	

Section Two: Ancillary Tests

Ancillary tests, as defined by the absence of intracranial blood flow, should be performed when **any** of the minimum clinical criteria cannot be completed, **or** unresolved confounding factors exist.

Ancillary testing has been performed: Yes ❑ No ❑

Date: _____Time: _____

Absence of intracranial blood flow has been demonstrated by:

Cerebral Radiocontrast Angiography ❑

Radionuclide Angiography ❑

Other _____

Section Three: Examination Interval, Declaration and Documentation

The first and second physician's determinations (a full clinical examination including the apnea test) should be performed at different points in time. For infants, there is no fixed examination interval. For newborns, the first exam should be delayed until 48 hours after birth and the interval between examinations should be ≥ 24 hours.

This patient fulfills the criteria for neurological determination of death:

Physician Print name: _____Signature: _____

Date: _____Time: _____

Section Four: Standard End-of-Life Care

Is this patient medically eligible for organ and/or tissue donation? Yes ❑ No ❑

Has the option for organ and/or tissue donation been offered? Yes ❑ No ❑

Has consent been obtained for donation? Yes ❑ No ❑

Checklist for NDD–Infants < 1 Year and Term Newborns > 36 Weeks Gestation

Age Definitions

Infants: ≥ 30 days, < 1 year (corrected for gestational age);

Term Newborns: >36 weeks gestation, age < 30 days (corrected for gestational age).

Overarching Principles

The legal time of death is marked by the first determination of death.

Existing law states that for the purposes of post-mortem donation, the fact of death shall be determined by two physicians. For these age groups, the first and second physician's determinations, as defined by a full clinical examination including the apnea test, must be performed at 2 different points in time. For infants, there is no fixed interval regardless of the primary etiology. For term newborns, the first examination should be delayed 48 hours after birth and the interval should be ≥ 24 hours, regardless of primary etiology.

Physicians Declaring Neurological Death

Minimum level of physician qualifications to perform NDD is full and current licensure for independent medical practice in the relevant Canadian jurisdiction. This excludes physicians who are only on an educational register. The authority to perform NDD cannot be delegated. Physicians should have skill and knowledge in both the management of patients with severe brain injury and in determination of neurological death in the relevant age groups. For the purposes of post-mortem donation, a physician who has had any association with the proposed transplant recipient that might influence the physician's judgment shall not take part in the declaration of death.

Minimum Clinical Criteria

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Confounding Factors:

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4. Peripheral nerve or muscle dysfunction or neuromuscular blockade potentially accounting for unresponsiveness, or
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   Specific to Cardiac Arrest: Neurological assessments may be unreliable in the acute post-resuscitation phase after cardiorespiratory arrest. In cases of acute hypoxic-ischemic brain injury, clinical evaluation for NDD should be delayed for 24 hours or an ancillary test could be performed.

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Project Management: Peter Ashley

Endnotes

Documents marked with an asterisk (*) are available on request from the CCDT.

1. Burke, Kathryn. *Legal Foundations for the Neurological Determination of Death.* Edmonton: The Canadian Council for Donation and Transplantation, 2003.
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