Royal College of Paediatrics and Child Health

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Supplemental digital content for Appendix 2 of the 2025 AoMRC Code of Practice for the diagnosis and confirmation of death

Methodology report: Diagnosis and Confirmation of Death using Neurological Criteria in infants, children, and adolescents, 2025

January 2025

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This Supplemental Digital Content (SDC) document was produced by a Working Group (WG) appointed by the Royal College of Paediatrics and Child Health (RCPCH). The aim of the WG was to provide an update to the 2015 RCPCH report on the Diagnosis of Death by Neurological Criteria in Infants Less than 2 Months Old[1] as an Appendix to the 2025 Academy of Medical Royal Colleges A Code of Practice for the Diagnosis and Confirmation of Death (Academy Code)[2].

The SDC describes the methodology underlying the literature searches used to answer six clinical questions:

- What is the lower gestational age limit that can be used for the diagnosis and confirmation of death using neurological criteria?
- At what age should an infant or young child transition to undergoing the diagnosis and confirmation of death using the same neurological criteria as adults?
- What type of apnoea test is appropriate for older children, and at what age?
- What should be the interval between apnoea testing in young children?
- At what age can ancillary investigation be used in infants and young children to support the diagnosis and confirmation of death using neurological criteria?
- What ancillary investigations are feasible in the United Kingdom (UK)?

Contents

Acknowledgements

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1. Methodology

1.1. Remit

The RCPCH working group (WG) aimed to review the evidence base for age thresholds, apnoea test, use of ancillary investigations in infants, children, and adolescents that would inform the 2025 AoMRC update[2] to the 2008 Code of Practice for the diagnosis and confirmation of death[3].

1.2. Target audience

The evidence identified in the literature searches is intended for use by all UK paediatric and neonatal health care practitioners and other groups involved in the regulation or practice of the health care of critically ill neonates and young infants. It is also relevant to adult (intensive care unit) ICU professionals since occasionally older children will be managed on an adult ICU at the end of life.

1.3. Population covered

- Groups covered: Infants born at term 37 to 42 weeks' gestation (postmenstrual) to 18 years old.
- Groups not covered: Pre-term infants under 37 weeks' gestation (post menstrual)

1.4. Clinical issues covered

It is accepted that the diagnosis and confirmation of death using neurological criteria in infants older than 37 weeks' gestation (post menstrual) and children up to 18 years is a clinical diagnosis. The issues that need to be covered are:

- Age cut-off: In the 2008 Academy Code[3] and 2015 RCPCH reports[1], chronological age is considered, with two discrete groupings: 37 weeks' gestation (post menstrual) to two months (post term), and older than two months to 18 years. Since other jurisdictions use different age groupings, the WG will review the RCPCH position regarding age cut-off.
- Apnoea test criteria: The WG will review current criteria for the apnoea test in the context of discussions relating to age limits.
- Ancillary tests: The WG will seek to examine the role of ancillary tests in children of all ages and seek to advise at what age ancillary tests can be undertaken and/or are required to support the diagnosis and confirmation of death using neurological criteria.

1.5. Clinical issues not covered

- Broader issues around withdrawal or withholding medical treatment in children
- Issues surrounding organ donation and transplantation
- Philosophical concepts of death

1.6. Lay involvement

- The WG included lay representatives

2. Evidence review

2.1. Topic areas

The literature review focused on new literature about the diagnosis and confirmation of death using neurological criteria in infants older than 37 weeks' gestation (post menstrual) to 18 years of age.

2.2. Clinical questions

The objective of the literature review focused on six questions:

- What is the lower gestational age limit that can be used for the diagnosis and confirmation of death using neurological criteria?
- At what age should an infant or young child transition to undergoing the same criteria for the diagnosis and confirmation of death using neurological criteria as adults?
- What type of apnoea test is appropriate for older children, and at what age?
- What should be the interval between apnoea testing in young children?
- At what age can ancillary investigation be used in infants and young children to support the diagnosis and confirmation of death using neurological criteria?
- What ancillary investigations are feasible in the UK?

2.3. Literature search

A focused search was carried out on Medline and EMBASE databases from 1 January 1990 until to 31 December 2023. A search strategy was developed by the RCPCH project team to ensure that all publications were identified using appropriate filters to return publications that meet the pre-defined inclusion and exclusion criteria. Searches were not limited by English language, nor was hand searching of journals undertaken.

All searches were updated and completed by 31 December 2023 and no publications after this date were considered.

2.4. Selecting the evidence

Abstracts were screened for relevance by the two Co-Chairs and project lead. Full copies were sought and screened according to pre-defined inclusion and exclusion criteria below by one member of the RCPCH project team as well by one of the Co-Chairs of the WG. The full text of studies was reassessed by the Co-Chairs to further exclude any study that did not meet the predefined criteria below.

Inclusion criteria

- Any primary study reporting on:
  - The clinical assessment of death using neurological criteria in infants and children up to 18 years old
  - The clinical assessment and use of ancillary tests in infants and children up to 18 years of age

  - Any systematic review reporting on the clinical assessment of death using neurological criteria or the clinical assessment and the use of ancillary tests in infants and children
  - Guidelines
  - Reports and expert consensus guidelines

Exclusion criteria

- Studies of children where data could not be extracted
- Publications excluded based on quality standards predefined criteria
- Publications that are of the following type:
  - Personal practice, comments, letters, and correspondence
  - Reviews (except systematic reviews)
  - Book chapters (unless based on systematic review)
  - Conference proceedings
  - Publications published in languages other than English

2.5. Data extraction and appraisal

The full text of studies meeting the above criteria were sent to both Co-Chairs of the WG. Each reviewer independently extracted the data, and their findings were compared. Extracted data were then placed in an evidence table by the RCPCH team and discussed by the WG as they developed recommendations.

Publications were critically appraised using checklists developed by the Institute of Health Economics[4] and the Joanna Briggs Institute critical appraisal for case reports[5] and key information about the study's population, methods and results were extracted.

Five principles were applied to assessing the appropriateness of any evidence in the context of clinical practice in the UK.

Principle I	Consideration of new evidence since the 2015 RCPCH Report.
Principle II	Alignment with the 2025 Academy Code, and its framework to minimise differences across the whole age span (unless overruled by other principles)[2].
Principle III	Consideration of paediatric guidelines published during 2020 to 2023 from International, Australia and New Zealand, Canada, and the United States professional groups[6-9].
Principle IV	Maximum safeguarding of the security of the diagnosis and confirmation of death using neurological criteria in very young children.
Principle V	Feasibility when considering the use of ancillary investigations in children; specifically, the extent of expertise and experience in the health system in the UK (NHS) to inform a pragmatic approach for such infrequent investigations and diagnoses.

2.6. Evidence summaries

For each clinical question, the Co-Chairs and the RCPCH WG prepared evidence tables summarising the evidence.

2.7. Consensus

For areas where there was a lack of evidence available to answer the clinical question, informal WG consensus was applied.

2.8. Funding and conflict of interests

The report update was internally funded by the RCPCH and all WG members declared all conflicts of interests, which were recorded. The views or interest of the funding body have not influenced the final recommendations ensuring editorial independence. No conflict of interests were declared.

3. Search strategies

Search #1: Death by neurological criteria

MEDLINE and EMBASE
- Embase 1974 to 2023 December 31
- Ovid MEDLINE(R)1946 to 2023
- Ovid MEDLINE(R) Daily Update 31 December 2023
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

(Dates searched: 1 January 1990 - 31 December 2023)
1. exp infant/
2. exp newborn/
3. exp baby/
4. exp child/
5. exp adolescent/
6. exp juvenile/
7. exp young adult/
8. (young adult* or young people or adolescen* or teen* or youth* or minor or juvenile).mp.
9. (infant or neonate* or newborn or baby or babies or child or children or full term).mp.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. exp brain death/di [Diagnosis]
12. (brainstem death or brain stem death or brain death or neurological death or neurologic death or irreversible coma or cerebral death or cerebral coma or brain damage or irreversible brain damage).mp.
13. (diagnosis or diagnoses or diagnostic procedures or diagnostic criteria or assessment or clinical observations).mp.
14. exp diagnosis/
15. 13 or 14
16. 12 and 15
17. 11 or 16
18. 10 and 17
19. limit 18 to (human and English language and yr="1990 - 2023")

Search #2: Conditions

MEDLINE and EMBASE
- Embase 1974 to 31 December 2023
- Ovid MEDLINE(R) 1946 to 2023

- Ovid MEDLINE(R) Daily Update 31 December 2023
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

(Dates searched: 1 January 1990 - 31 December 2023)

1. exp infant/
2. exp newborn/
3. exp baby/
4. exp child/
5. exp adolescent/
6. exp juvenile/
7. exp young adult/
8. (young adult* or young people or adolescen* or teen* or youth* or minor or juvenile).mp.
9. (infant or neonate* or newborn or baby or babies or child or children or full term).mp.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. exp brain death/di [Diagnosis]
12. (brainstem death or brain stem death or brain death or neurological death or neurologic death or irreversible coma or cerebral death or cerebral coma or brain damage or irreversible brain damage).mp.
13. (diagnosis or diagnoses or diagnostic procedures or diagnostic criteria or assessment or clinical observations).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
14. exp diagnosis/
15. 13 or 14
16. 12 and 15
17. 11 or 16
18. 10 and 17
19. *Guillain Barre syndrome/ or brains stem encephalitis.mp.
20. hyperosmolar coma.mp
21. (uremia coma or uremic coma).mp.
22. hypophosphatemia.mp. or *hypophosphatemia/
23. hypophosphataemia.mp. or *hypophosphatemia/
24. *hypotension/ or hypotension.mp.
25. hypothermia.mp. or *hypothermia/
26. 19 or 20 or 21 or 22 or 23 or 24 or 25
27. 18 and 26
28. limit 27 to (human and English language and yr=”1990 - 2023”)

Search #3: Ancillary testing

MEDLINE and EMBASE

- Embase 1974 to 31 December 2023
- Ovid MEDLINE(R) 1946 to 2023
- Ovid MEDLINE(R) Daily Update 31 December 2023
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

(Dates searched: 1 January 1990 - 31 December 2023)

1. exp infant/
2. exp newborn/
3. exp baby/
4. exp child/
5. exp adolescent/
6. exp juvenile/
7. exp young adult/

8. (young adult* or young people or adolescen* or teen* or youth* or minor or juvenile).mp.
9. (infant or neonate* or newborn or baby or babies or child or children or full term).mp.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. exp brain death/di [Diagnosis]
12. (brainstem death or brain stem death or brain death or neurological death or neurologic death or irreversible coma or cerebral death or cerebral coma or brain damage or irreversible brain damage).mp.
13. (diagnosis or diagnoses or diagnostic procedures or diagnostic criteria or assessment or clinical observations).mp.
14. exp diagnosis/
15. 13 or 14
16. 12 and 15
17. 11 or 16
18. 10 and 17
19. *angiography/
20. MRI angiography.mp. or *magnetic resonance angiography/
21. cerebral arteriography.mp. or *brain angiography/
22. *radionuclide ventriculography/ or radionuclides angiography.mp.
23. nuclear brain scanning.mp.
24. core temperature.mp.
25. euvolemia.mp.
26. cerebral blow flow.mp.
27. electroencephalography.mp.
28. EEG.mp. or exp electroencephalogram/
29. exp evoked brain stem auditory response/ or brainstem auditory evoked response*.mp.
30. BAER.mp
31. apnoea test.mp.
32. apnea test.mp.
33. exp pH/ or pH.mp.
34. PO2.mp.
35. PO2.mp.
36. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
37. 18 and 36
38. limit 37 to (human and English language and yr="1990 - 2023")

4. References

1. Royal College of Paediatrics and Child Health. *The diagnosis of death by neurological criteria in infants less than two months old*, 2015 (Archived).
2. Academy of Medical Royal Colleges. *A code of practice for the diagnosis and confirmation of death*, 2025.
3. Academy of Medical Royal Colleges. *A code of practice for the diagnosis and confirmation of death,* 2008 (Archived).
4. Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014. Available from: http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about.
5. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, CARE Group. The CARE Guidelines: Consensus-Based Clinical Case Reporting Guideline Development. *Headache: The Journal of Head and Face Pain*, 2013;53(10):1541-1547.
6. Greer DM, Shemie SD, Lewis A, et al. Determination of brain death/death by neurologic criteria: the world brain death project. *JAMA*. 2020; 324(11):1078–97.
7. Australia and New Zealand Intensive Care Society (ANZICS). The statement on death and organ donation, Edition 4.1, 2021. See https://www.donatelife.gov.au/sites/default/files/2022-01/anzics-statement-on-death-and-organ-donation-4.1.pdf (accessed February 2024).
8. Shemie SD, Wilson LC, Hornsby L, et al. A brain-based definition of death and criteria for its determination after cardiac arrest of circulation or neurologic function in Canada: a 2023 clinical practice guideline. *Can J Anaesth* 2023; 70:483-557. See https://link.springer.com/journal/12630/volumes-and-issues/70-4 (accessed February 2024).
9. Greer DM, Kirschen MP, Lewis A et al. Pediatric and Adult Brain Death/Death by Neurologic Criteria Consensus Guideline: Report of the AAN Guidelines Subcommittee, AAP, CNS, and SCCM. *Neurology* 2023; 101:1-21.
10. Haun SE, Tobias JD, Deshpande JK. Apnea testing in the determination of death: is it reliable? *Clin Intensive Care* 1991; 2:182-184.
11. Okamoto K, Sugimoto R. Return of spontaneous respiration in an infant who fulfilled current criteria to determine brain death. *Pediatrics* 1995; 96:518-520.
12. Brilli RJ, Bigos D. Altered apnea threshold in a child with suspected brain death. *J Child Neurol* 1995; 10:245-246.
13. Vardis R, Pollack MM. Increased apnea threshold in a pediatric patient with suspected brain death. *Crit Care Med* 1998; 26:1917-1919.
14. Joffe AR, Kolski H, Duff J, et al. A 10-month-old infant with reversible findings of brain death. *Pediatr Neurol* 2009; 41:378-382.
15. Hansen G, Joffe AR. Confounding brain stem function during pediatric brain death determination: two case reports. *J Child Neurol* 2017; 32:676-679.
16. Sosa T, Berrens Z, Conway S, et al. Apnea threshold in pediatric brain death: a case with variable results across serial examinations. *J Pediatr Intensive Care* 2019; 8:108-112.

5. Appendix

Summary of seven case reports about the apnoea test in Paediatrics and level of arterial partial pressure of carbon dioxide.

Case reports questioning the validity of the PaCO2 ≥60 mmHg (8 kPa) as being an adequate test of the apnoea threshold		
Reference	**Country**	**Summary**
Haun, 1991[1]	USA	3-month-old (2 examinations and ECS) **Test 1** • No breathing PaCO2 42 → 67 mmHg (5.6 → 8.9 kPa) • 8 minutes after removal from ventilator developed regular and persistent respiration (Case discounted by American Academy of Pediatrics [AAP] expert review because only one and not two apnoea tests was performed)
Okamoto, 1995[11]	Japan	3-month-old hypoglycaemia by nesidioblastosis **Test 1 (day 3)** • No breathing PaCO2 69.3 mmHg (9.2 kPa) **Test 2 (day 5)** • No breathing PaCO2 62.1 mmHg (8.3 kPa) • Patient diagnosed as brain dead but maintained on MV **Day 43** • Infant regained spontaneous respiration 2-3 breaths per minute (Case with missing data in the report but also endocrine issues which should fall into the category of failed preconditions)
Brilli, 1995[12]	USA	3-year-old – breathed at >8 minutes when PaCO2 112 mmHg (14.9 kPa) (Case discounted by AAP experts because breathing occurring during the one and only test)
Vardis, 1998[13]	USA	4-year-old; breathed at >9 minutes when PaCO2 91 mmHg (12.1 kPa) (Case discounted by AAP experts because breathing occurring during the one and only test)
Joffe, 2009[14]	Canada	10-month-old – Drowning and 42 hours later **Test 1** • 4 minutes of apnoea PaCO2 38 mmHg (5.1 kPa) with pH 7.28 → 74 mmHg (9.9 kPa) with pH 7.04 **Test 2 (15 hours later)** • Hiccups noted and DNC not confirmed on ancillary testing **Test 3 (86 hours after event)** • Breathing during the apnoea test (Case with only one apnoea test)
Hansen, 2017[15]	Canada	15-year-old – strangulation **Test 1** • Apnoea with PaCO2 41 → 62 mmHg (5.5 → 8.3 kPa) **Test 2** • Baseline PaCO2 39 mmHg (5.2 kPa) and after 5 minutes of apnoea PaCO2 61 mmHg (8.1 kPa), but breathed while ABG being analyzed (Case with only one apnoea test)

Case reports questioning the validity of the PaCO2 ≥60 mmHg (8 kPa) as being an adequate test of the apnoea threshold		
Reference	**Country**	**Summary**
Sosa, 2019[16]	USA	3-month-old; 72-hrs post-arrest **Test 1** - Start: pH 7.32, PaCO2 44 mmHg (5.9 kPa) - 5 min: pH 7.12, PaCO2 77 mmHg (10.3 kPa) - Breathed at 6 minutes **Test 2** - Start: pH7.41, PaCO2 37 mmHg (4.9 kPa) - Remained apnoeic for 19 min: pH 7.0 and PaCO2 108 mmHg (14.4 kPa) **Test 3** - Breathed during apnoea testing (Case with only one apnoea test)