Understanding the Apnea Test: Procedure with a Predetermined Purpose

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ABSTRACT: The concept of "brain death" is controversial but widely accepted in practice. Current practice generally attempts to make a determination of death by using neurological criteria alone as a way to show "irreversible cessation of all functions of the entire brain, including the brain stem." This determination is to be made "in accordance with accepted medical standards" according to the 1981 Uniform Determination of Death Act (UDDA). Many state statutes are modeled on the UDDA. The apnea test is the final test in many protocols for a person in unresponsive coma of known cause, presumably irreversible, and is considered by some the "sine qua non" for "brain death." But even some physicians who are in favor of the concept of brain death and vital organ procurement have called it "not defensible." In this paper we review the apnea test procedure in the context of basic respiratory physiology and ventilator use. We examine its rationale and summarize its flaws. In particular, we bring attention to the recent Nevada statute that mandates use of the American Academy of Neurology Guidelines (AANG) to declare "brain death," including the use of the apnea test without consent.

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THE CONCEPT OF "BRAIN DEATH" is controversial, even if generally accepted in practice.[1] Determination of death by using neurological criteria alone ("brain death") to show "irreversible cessation of all functions of the entire brain, including the brain stem," is supposed to be made "in accordance with accepted medical standards," according to the 1981 Uniform Determination of Death Act (UDDA), after which many state statutes are modeled.[2] The apnea test is the final test in many protocols for a person in an unresponsive coma of known cause that is presumed irreversible. It is considered by some the *sine qua non* for the determination of "brain death."[3] Other physicians have called it "not defensible."[4]

In this paper we review the apnea test procedure in the context of basic respiratory physiology and ventilator use. We examine its rationale and summarize its flaws. In addition, we bring attention to the recent Nevada statute that mandates use of the American Academy of Neurology Guidelines (AANG) to declare "brain death," including the use of the apnea test without consent.[5]

Nevada Statute

Nevada has recently enacted a statute governing the determination of "brain death" for adults and for children. It requires the use of the 2010 AANG and the 1987 Task Force Report of the Pediatric Section of the Society of Critical Care Medicine or any subsequent revisions of either document. Consent is not explicitly needed. Care is to be withdrawn after the declaration of "brain death" unless the patient is pregnant with a "probable" live birth or

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[1] R.M. Sade, "Brain Death, Cardiac Death, and the Dead Donor Rule," *Journal of the South Carolina Medical Association* 107/4 (2011): 146–49.

[2] See http://healthcare.findlaw.com/patient-rights/what-is-the-uniform-declaration-of-death-act-or-udda.html (accessed 7-29-17).

[3] C. Machado, J. Perez, C. Scherle, A. Areu, & A. Pando, "Brain Death Diagnosis and Apnea Test Safety," *Annals of Indian Academy of Neurology* 12/3 (2009): 197–200, http://doi.org/10.4103/0972-2327.56326.

[4] J. Tibballs, A.R. Joffe, "The Diagnosis of Brain Death: Apneic-Oxygenation as a Self-Fulfilling Diagnostic Test" in *Considering Consciousness Clinically*, ed. G. Leisman and J. Merrick (Hauppauge NY: Nova Biomedical Books, 2016), pp. 47-56.

[5] See https://www.leg.state.nv.us/Session/79th2017/ Bills/AB/AB424_EN.pdf (accessed July 23, 2017).

is an organ donor. A "reasonable effort" is to be made to inform the family of the "death." The patient's estate or family may be responsible for what is termed "organ-sustaining treatment" (the original wording, "life-sustaining treatment," has been stricken).[6] The new wording seems to codify the view that the "brain dead" patient is no more than a container of organs.

AAN Guidelines for Apnea Test Procedures

According to the AANG, "brain death" is a clinical determination of the "cessation of all functions of the entire brain, including the brainstem." Physicians are to determine the cause of what they take to be an unresponsive coma, demonstrate the absence of brainstem reflexes, and exclude conditions that would mimic coma. The patient is to be observed for an unspecified "period of time" to show "irreversibility."[7]

Now, it is important to understand the physiological background. The brainstem has respiratory control centers that affect breathing. Under normal conditions even slightly elevated levels of carbon dioxide in the blood (hypercarbia) will increase respiratory drive and result in an increase in ventilation (increase in respiratory rate and/or tidal volume). Chemoreceptors that respond to carbon dioxide in the blood are located in the brainstem and the aorta.[8] The rationale for the apnea test is to provide a carbon dioxide challenge to stimulate spontaneous breathing. If the patient is not observed by the physician to take a breath or gasp in response to hypercarbia, then the brainstem is assumed to be non-functional and the person is declared "brain dead." On this basis, "brain death" or the declaration of "death" using clinical neurological criteria alone is considered legal "death" even without making any determination of an irreversible cessation of the heartbeat, circulatory, or

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[6] See https://www.leg.state.nv.us/Session/79th2017/ Bills/AB/AB424_EN.pdf (accessed July 23, 2017).

[7] See http://www.neurology.org/content/74/23/1911.full.pdf+html (accessed 7-31-17). Eelco F.M. Wijdicks, Panayiotis N. Varelas, Gary S. Gronseth, and David M. Greer, "Evidence-Based Guideline Update: Determining Brain Death in Adults," Report of the Quality Standards Subcommittee of the American Academy of Neurology in *Neurology 74* (2010): 1911-18, doi: 10.1212/WNL.0b013e3181e242a8:1526-632X.

[8] Brendan Caruana-Montaldo MD, Kevin Gleeson MD, and Clifford W. Zwillich MD, FCCP, "The Control of Breathing in Clinical Practice," *Chest* 117 (2000): 205-25. See http://202.74.245.22:8080/xmlui/bitstream/handle/ 123456789/982/Chapter%2041-45.pdf?sequence=11 (accessed 7-31-17).

respiratory systems.[9] There is a general moral consensus known as the "dead donor rule" that states (1) that the person must be dead before organ procurement and (2) that organ procurement is not to be the cause of death.[10] Because "brain death" is considered death, once a person is declared "brain dead," the patient's vital organs such as the heart, lungs, liver, kidneys, and so on can legally be taken. This practice is also known as organ procurement or harvest.

Death, however, is more than unresponsiveness and mere cessation of breathing, heartbeat, circulation and respiration. This has always been the case. Further, it is important to understand that the term "irremediable" (as in "irremediable cessation") is not the same as the term "irreversible." "Irreversible" is a term for a prognosis that is contradicted when a successful new treatment is developed.[11] The ventilator was at one time just such a new treatment. Further, destruction and absence of functioning are empirical observations, but irreversibility is not.

Procedure of the Apnea Test

An "apnea test" done according to the 2010 AANG includes checklists that may seem rigorous but that in reality are general and vague. The guidelines do not specifically require consideration of many clinical details important to ruling out underlying conditions such as hormone deficiencies and residual drug effects, which could exacerbate not only coma but the patient's ability to breathe. Residual drugs, for instance, may still be in the patient's system without being recognized as clinically contributing to coma and apnea. Much is left to physicians' clinical judgments.[12]

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[9] See http://www.uniformlaws.org/shared/docs/determination%20of%20death/udda80.pdf (accessed 7/31/17).

[10] J.A. Robertson, "Delimiting the Donor: The Dead Donor Rule," *Hastings Center Report* 29 (1999): 6–14, doi:10.2307/3527865.

[11] P.A. Byrne, S. O'Reilly, P.M. Quay, "Brain Death: An Opposing Viewpoint, *Journal of the American Medical Association* 242/18 (1979) 1985-90, doi:10.1001/jama.1979.0330018002902.

[12] See http://www.neurology.org/content/74/23/1911.full.pdf+html (accessed 7-31-17). Eelco F.M. Wijdicks, Panayiotis N. Varelas, Gary S. Gronseth, and David M. Greer, "Evidence-Based Guideline Update: Determining Brain Death in Adults," Report of the Quality Standards Subcommittee of the American Academy of Neurology in *Neurology 74* (2010): 1911-18, doi: 10.1212/WNL.0b013e3181e242a8:1526-632X. See http://www.neurology.org/content/45/5/1003. F.M. Eelco and M.D. Wijdicks,

The apnea test is more correctly termed a procedure. It is not simply making an observation of a patient but includes the procedure of taking away the life-supporting ventilator. Even though the guidelines list various prerequisites and cautionary measures such as administering oxygen before and during the procedure, it can be dangerous, for it could leave a patient not breathing for as long as ten minutes or more. During this time the patient cannot exhale the carbon dioxide, which is an acid waste product that can be harmful, especially to a critically ill patient with an injured brain. An arterial blood sample (arterial blood gas) is drawn at 8-10 minutes of apnea; while this sample is being analyzed, the patient is reconnected to the ventilator. If no breath is observed to have been taken during the procedure and the arterial blood carbon dioxide (PaCO2) is ≥ 60 mm Hg or if there is a 20 mm Hg rise from a normal baseline value, then the patient may be declared "brain dead."[13]

Ruben Restrepo and Zaza Cohen state: "It must be remembered that although designed to measure spontaneous respiratory drive, the apnea test truly measures the respiratory effort. For example, the patient may have preserved drive but weak effort due to concomitant illness, leading to shallow and ineffective respirations that do not make the chest rise or affect paCO2 levels."[14] Marked atrophy of the muscle fibers of the diaphragm, a major respiratory muscle has been shown in "brain dead" patients on a ventilator for 18 to 69 hours, which the authors note could be clinically significant.[15]

Positive Test

The apnea test is considered "positive" if the patient is observed by the physician not to have taken a breath or gasp. The test is then repeated at a later time. The presence or absence of any respiratory effort is a clinical assessment made by the clinicians. As with any clinical endeavor, it is not unreasonable to

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"Determining Brain Death in Adults," *Neurology* 45 (1995): 1003-11 (accessed 8-1-17).

[13] See http://www.neurology.org/content/74/23/1911.full.pdf+html (accessed 7-31-17).

[14] Ruben D. Restrepo and Zaza Cohen, Neurologic Assessment in *Wilkins' Clinical Assessment in Respiratory Care*, 7th ed., ed. Albert J. Heuer, Craig L. Scanlan, and Robert L. Wilkins (St. Louis MO: Elsevier Mosby, 2014), p. 124.

[15] S. Levine, T. Nguyen, N. Taylor et al., "Rapid Disuse Atrophy of Diaphragm Fibers in Mechanically Ventilated Humans," *New England Journal of Medicine* 358/13 (2008): 1327-35.

assume that clinicians can err in their knowledge, assessments, clinical skills, and observations. A review article by Van Norman notes a study by Youngner et al. that "found that two-thirds of physicians involved in declaring brain death were unable to correctly identify or apply the whole brain criteria for determination of brain death."[16]

Negative Test

One might assume that if the patient breathes during the apnea test procedure (a negative finding for "brain death"), the patient would be considered alive and treated as such. The AANG update does not explicitly state what to do but calls attention to an "inconclusive" result and recommends repeating the test for a possibly longer period of apnea. It is expected that additional apnea tests may be done by consulting neurologists during any subsequent examinations for "brain death."[17] The apnea test procedure will do nothing to benefit a patient with an injured brain; it only risks doing harm each time that it is done. If full and complete information were provided, it is doubtful that consent would be given.[18]

The goal of an apnea test is to declare death by "neurological criteria" alone without damage or destruction to transplantable vital organs or killing the patient. If organs are not to be taken or if there is no fetus to be gestated by a "brain dead" mother, then the determination of "brain death" effectively makes the doctors and hospital, not the patient's surrogate, the final decision-makers as to whether or not to discontinue ventilator support, treatments, and care.

Basic Respiratory Physiology

There are four components to respiratory physiology: (1) movement of gases into the lung; (2) external respiration – the transport of gases from air to

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[16] Gail A. Van Norman MD, "A Matter of Life and Death: What Every Anesthesiologist Should Know about the Medical, Legal, and Ethical Aspects of Declaring Brain Death," *Anesthesiology* 91/1 (1999): 275-87. See also S.J. Youngner, C.S. Landefeld, C.J. Coulton, B.W. Juknialis, and M. Leary, "Brain Death and Organ Retrieval: A Cross-Sectional Survey of Knowledge and Concepts among Health Professionals," *Journal of the American Medical Association* 261 (1989): 2205-10.

[17] See http://www.neurology.org/content/74/23/1911.full.pdf+html (accessed 7/31/17).

[18] See https://www.youtube.com/watch?v=OS122QbiMwk (Accessed 7-30-17).

the blood; (3) transport of gases via circulation to tissues; (4) internal respiration – exchange of gases from blood to cells.[19]

Ventilators

A ventilator can be used to accomplish the first of these four components, namely, to move gases into the lungs. It does not and cannot do the other three: transport of gases from the air into the blood, which is external respiration; transport of gases via circulation to the tissues; exchange of gases from blood to cells, which is internal respiration. While the ventilator pushes gases with oxygen into the patient, that is all that it does. It does not and cannot make the cells, tissues, or organs do the tasks of gas exchange, i.e., respiration at the level of the blood and tissues, nor does it make the heart beat or provide circulation.[20]

Neither does the ventilator exhale for a patient. A patient must first have the ventilator push the gases in, so that a living patient's lungs and respiratory muscles can function in a way that will allow movement of the air with carbon dioxide to passively go out. The ventilator does not mask death. It is simply a machine that mechanically moves gases into a patient when the patient cannot do so effectively.

Problems with the Apnea Test Procedure

J. Tibballs and A.R. Joffe, who do not oppose "brain death" or organ procurement, state: "Current medical practice does not satisfy the legal, ethical, and moral requirement for certifying death of the whole brain as required before organ procurement."[21] Even with other testing and abandonment of the dead donor rule they write: "continuing with doing the apnea test is not defensible." They summarize its flaws:

(1) Hypercarbia may theoretically cause fatal harm and destruction of the brain. According to physiological principles, hypercarbia may increase cerebral

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[19] See https://docslide.us/documents/chapter-37-pulmonary-ventilation-guyton-and-hall-textbook-of-medical-physiology.html (accessed 7/31/17).

[20] Restrepo and Cohen, cited above.

[21] J. Tibballs and A.R. Joffe, "The Diagnosis of Brain Death: Apneic-Oxygenation as a Self-Fulfilling Diagnostic Test" in *Considering Consciousness Clinically*, ed. G. Leisman and J. Merrick (Hauppauge NY: Nova Biomedical Books, 2016), pp. 47-56.

blood volume, which may increase intracranial pressure, resulting in decreased blood flow and further ischemia to potentially recoverable penumbral brain tissues, thereby causing permanent damage. Hence, the test may cause "brain death" even though that is what it purports to test.

(2) Hypercarbia itself may be a confounder since it can depress the functioning of the brain including the brainstem.

(3) The apnea test has been empirically refuted by cases when the patient took a breath at levels of carbon dioxide above the levels at which the patient would have been declared dead.

(4) Potential harm from complications of the apnea test include hypoxemia, cardiac arrhythmias, adverse alterations in blood pressure, and barotrauma.

(5) The apnea test does not test for medullary (brainstem) respiratory center function, which responds to a decrease in oxygen since harmfully low levels of oxygen would be needed as a stimulus.

(6) Confounders to performing an apnea test can be present, such as cervical spinal cord injury, which causes quadriplegia and apnea. Adrenal and thyroid deficiencies, which theoretically occur as the result of dysfunction of the hypothalamus and pituitary, can also cause coma and apnea. Tibballs and Joffe comment: "Curiously, endocrine dysfunction is mentioned as a confounder in most guidelines on testing for brain death, but the fact that it should be present in suspected brain death is ignored."[22]

Ana Maria Coimbra, a neurologist and researcher, has written that "the lack of clinically detectable brain functions does not provide a safe diagnosis of brain or brain stem death," that "apnea testing may induce irreversible brain damage and should be abandoned," and that "confirmatory tests for brain death should not replace or delay the administration of potentially effective therapeutic measures."[23] Death as a result of barotrauma (pneumothorax and pneumoperitoneum) that occurred with performance of an apnea test according to AANG has also been reported.[24]

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[22] Tibballs and Joffe, cited above.

[23] Cicero G. Coimbra, "Implications of Ischemic Penumbra for the Diagnosis of Brain Death," *Brazilian Journal of Medical and Biological Research* (1999). See https://www.youtube.com/watch?v=OS122QbiMwk (accessed 7-30-17).

[24] G. Saposnik, G. Rizzo, and Jorge L. DeLuca, "Pneumothorax and Pneumoperitoneum during the Apnea Test: How Safe Is This Procedure?" in *Arquivos de Neuro-Psiquiatria* 58/3B (2000): 905-08, https://dx.doi.org/10.1590/S0004-282X2000000

In an observational study of intracranial pressure during the apnea test and "brain death" exam, which included sixteen apnea tests on thirteen patients, the authors noted that nine of the thirteen had increased intracranial pressure and that cerebral perfusion pressure was not zero.[25]

The AANG, updated in 2010 and re-affirmed in 2014, raised several questions, including whether there are patients who fulfill the criteria and yet recover brain function, the length of the observation period to ensure permanent cessation of neurologic function and the comparative safety of apnea tests. They report that "insufficient evidence" exists for all three but that "the 1995 AAN practice parameters have not been invalidated by published reports of neurologic recovery in patients who fulfill these criteria."[26]

There are, however, at least two cases in the medical literature that report "brain dead" patients breathing after fulfilling apnea test criteria. One was a 2009 report of a ten-month-old boy who started breathing fifteen hours after having fulfilled pediatric "brain death" criteria, including an apnea test. The authors concluded: "The case indicated that brain death as currently diagnosed may not always be irreversible."[27]

Another case (reported in 2011) was that of a fifty-five-year-old man who had a respiratory and cardiac arrest. He was treated at an academic medical center with therapeutic hypothermia and later fulfilled the AANG criteria for "brain death," including two positive apnea tests six hours apart. He was taken to the operating room for organ procurement, but there he was noted to be spontaneously breathing and to have brainstem, corneal, and cough reflexes. The authors stated that this case "casts doubt on irreversibility of AAN criteria after therapeutic hypothermia."[28]

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[25] C. Roth, W. Deinsberger, J. Kleffmann, and A. Ferbert, "Intracranial Pressure and Cerebral Perfusion Pressure during Apnoea Testing for the Diagnosis of Brain Death, an Observational Study," *European Journal of Neurobiology* 22 (2015): 1208–14; oi:10.1111/ene.12727.

[26] See http://www.neurology.org/content/74/23/1911.full.pdf+html (accessed 8-1-17). See also https://www.aan.com/Guidelines/home/GetGuidelineContent/432 (accessed 8-1-17).

[27] A.R. Joffe, H. Kolski, J. Duff, and A.R. deCaen, "A 10-Month-Old Infant with Reversible Findings of Brain Death," *Pediatric Neurology* 41/5 (2009):378-82.

[28] A.C. Webb and O.B. Samuels, "Reversible Brain Death after Cardiopulmonary Arrest and Induced Hypothermia," *Critical Care Medicine 39/6* (2011): 1538-42.

The AANG summary statement admits: "severe limitations in the current evidence base," a "paucity of evidence," "deficiencies in the evidence base," and cautions that "clinicians must exercise considerable judgment when applying the criteria."[29]

Even though caution is advised, there are problems. An example of a specific weakness in the guidelines is in regard to drugs that would prevent movement in a patient, thereby confounding the neurological exam and the apnea test. The AANG state: "There should be no recent administration or continued presence of neuromuscular blocking agents (this can be defined by the presence of a train of 4 twitches with maximal ulnar nerve stimulation)."[30] S.R. Thilen and S.M. Bhananker point out that four twitches is not proof of the absence of residual paralysis from neuromuscular blockers and that there are outliers and great inter-patient variability in response to these medications.[31]

In these procedures the patient is disconnected from the ventilator breathing circuit because of the concern that autotriggering of the ventilator would interfere with the procedure and give the false impression that the patient is taking a spontaneous breath. Capnography, monitoring of exhaled carbon dioxide, is routinely used in operating rooms while the patient is connected to the breathing circuit, not only to detect apnea but also to show shallow spontaneous breaths, difficult to detect by mere observation of the patient's chest and abdomen. It has been evaluated for possible use during the apnea test procedure and can be a more sensitive method to detect respiratory effort.[32]

Informed Consent

The apnea test procedure is considered part of the clinical neurological exam for "brain death" and so specific consent is often not sought. It might be

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[29] See https://www.aan.com/Guidelines/Home/GetGuidelineContent/432 (accessed 7/31/17).

[30] See http://www.neurology.org/content/74/23/1911.full.pdf+html.

[31] S.R. Thilen and S.M. Bhananker, "Qualitative Neuromuscular Monitoring: How to Optimize the Use of a Peripheral Nerve Stimulator to Reduce the Risk of Residual Neuromuscular Blockade," *Current Anesthesiology Reports* 6 (2016): 164–69.

[32] B. Vivien, J. Amour, A. Nicolas-Robin, M. Vesque, O. Langeron, P. Coriat, & B. Riou, "An Evaluation of Capnography Monitoring during the Apnoea Test in Brain-Dead Patients, *European Journal of Anaesthesiology* 24/10 (2007): 868-75, doi:10.1017/S0265021507000725.

done without knowledge or consent of the surrogate. For instance, in the case of Aiden Hailu, the hospital physician did an apnea test contrary to the expressed wishes of Aiden Hailu's father/legal guardian. Once declared legally "dead," i.e., "brain dead," the hospital claimed no responsibility to treat her and wanted to disconnect Aiden Hailu from the ventilator. They refused to do or allow a tracheostomy, feeding tube placement, thyroid medications, or other care that would have facilitated safe and effective transfer to a long-term care facility or even to home.[33]

The father/legal guardian took the case to the Nevada Supreme Court, which unanimously ruled in favor of the father and remanded the case back to the District Court with concerns that the AANG criteria used by the hospital to declare "brain death" did not meet the statutory requirements of complete cessation of all function of the entire brain including the brainstem.[34] Aiden Hailu had also had at least two EEGs that showed activity prior to the apnea test. These findings of brain activity were dismissed because they were not part of the AANG, which are "clinical" assessments to determine death by neurological criteria.[35] Tibballs and Joffe state: "Labeling a body as dead under bedside clinical tests alone is a pretentious fiction."[36]

Summary

The apnea test is a procedure that may be required by some sets of criteria, including the AANG, to declare a person dead by neurological criteria alone. It subjects the brain-injured patient to serious harm, even death, and is without benefit for the patient. It may be done without consent. In the state of Nevada, this one set of guidelines issued by the American Academy of Neurology is, by their own admission, plagued by "deficiencies" and "severe limitations in the evidence base," but it is now codified in law to be used to declare "brain death," explicitly without consent. Once declared "brain dead," any life-supportive care of the patient is considered only "organ-sustaining" and may

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[33] Personal communication with Paul Byrne, M.D. (7-30-17).

[34] G. Yanke, M. Rady, and J. Verheijde, "In re Guardianship of Hailu: NV Supreme Court Casts Doubt on the Standard for Brain Death Diagnosis," *Medicine, Science and Law* 57/2 (2017): 100-02.

[35] See http://nvcourts.gov/Supreme/Arguments/Recordings/In re Guardianship of Hailu/ (accessed 7-30-17).

[36] Tibballs and Joffe, cited above.

be continued at the estate or family's expense. Even physicians seemingly in favor of organ procurements have called for the apnea test to be abandoned. If at all possible, its performance should be prevented pro-actively in unconscious patients in need of a ventilator, hopefully to prevent the determination of "brain death." This would allow the patient's surrogates to be the final decision-makers and would protect the patient from further injury and allow time for healing.