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# **Treating Fetal Pain: Standard of Care for Some, But Not for All**

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**ABSTRACT:** Fetal pain is a hot topic of debate, but not amongst the neonatologists who daily treat premature babies. The uncontroversial medical standard of care for this population's treatment includes avoiding, minimizing, or intentionally treating pain, and this standard has evolved due to the data of multiple lines of research. While it is true that unsettled debate over how to best define "pain" continues, this debate does not change the fact that premature babies' outcomes are better when what seems to be painful stimuli is removed or treated. Thus there is an uncomfortable paradox between the current standard of care for neonatologists, and what remains legal for obstetricians to do to the same patient. While this article is not an all-inclusive literature review, it is a brief presentation of the information that informs current neonatal practice but does not equally inform national law.

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As an actively practicing neonatologist and medical director of a fifty-bed neonatal intensive care unit (NICU), avoiding, minimizing, or intentionally treating pain in premature babies is part of my job; this is today's medical standard of care.<sup>1</sup> Yet, non-neonatologists argue that babies of the same gestational are not pain-capable

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<sup>1</sup> "Prevention and Management of Procedural Pain in the Neonate: An Update." *Pediatrics*, vol. 137, no. 2, 2016, doi:10.1542/peds.2015-4271.

due to their lack of awareness.<sup>2,3</sup> This discussion sustains an uncomfortable paradox between the *medical* standard of care that neonatologists and anesthesiologists provide their patients, and the *legally* permissible painful procedures that obstetricians can intentionally do to their patients. These painful procedures may be legal, but they are not medically or ethically appropriate. Here is why.

As recently as 1992, there was a randomized trial that compared neonates who received either “deep” or “lighter” anesthesia during their cardiac surgery.<sup>4</sup> Results showed: the babies who received lighter anesthesia had increased levels of multiple stress hormones, hyperglycemia, and lactic acidemia during surgery; those who received deep anesthesia had statistically significant decreases in their incidence of sepsis, metabolic acidosis, disseminated intravascular coagulation, and fewer postoperative deaths.<sup>5</sup> Today, the medical ramifications of poor pain management are so uncontroversial that no institutional review board (IRB) could ethically allow this kind of study to be repeated.

Since 1992, the standard of care for treating neonatal pain management has changed. The changes are most succinctly described in the 2016 American Academy of Pediatrics (AAP) updated policy for preventing and managing specifically neonatal procedural pain.<sup>6</sup> The policy is the joint work of the Committee on Fetus and Newborn and the Section on Anesthesiology and Pain Medicine. They state that: prevention and alleviation of pain in neonates, particularly in preterm infants is important not only because it is ethical, but also because exposure to repeated painful stimuli early in life is known to have short and long term adverse sequelae. These sequelae include physiologic instability, altered brain development, and abnormal neurodevelopment, somatosensory and stress response systems, which can persist into childhood.<sup>7</sup>

The extensive research reviewed by the involved AAP committees led to the conclusions that not only do term infants have measurable short and long-term changes when exposed to painful procedures, but also the babies who are premature. Because of the data, the AAP committee recommended that “preventing or minimizing pain in neonates should be the goal of pediatricians and other health care professional who care for neonates.”<sup>8</sup> The joint policy also recommends: individual NICUs have written guidelines for prevention and treatment of pain, use of nonpharmacologic and phar-

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<sup>2</sup> Derbyshire, Stuart W.G. “Foetal Pain?” *Best Practice & Research Clinical Obstetrics & Gynaecology*, vol. 24, no. 5, 2010, pp. 647–655., doi:10.1016/j.bpobgyn.2010.02.013.

<sup>3</sup> Lee, Susan J., et al. “Fetal Pain.” *JAMA*, vol. 294, no. 8, 2005, p. 947., doi:10.1001/jama.294.8.947.

<sup>4</sup> Anand, KJS. “Halothane-Morphine Compared with High-Dose Sufentanil for Anesthesia and Postoperative Analgesia in Neonatal Cardiac Surgery.” *New England Journal of Medicine*, vol. 326, no. 1, 2 Jan. 1992, pp. 1–9.

<sup>5</sup> *Ibid.*, pg 1.

<sup>6</sup> “Prevention and Management of Procedural Pain in the Neonate: An Update.” *Pediatrics*, vol. 137, no. 2, 2016, doi:10.1542/peds.2015-4271.

<sup>7</sup> *Ibid.*, p 2.

<sup>8</sup> *Ibid.*, p 8.

macologic treatment strategies, and as possible continued research into both strategies as well as better neonatal pain assessment tools.<sup>9</sup>

Given what we already know, practicing neonatologists are not asking whether or not our patients are affected by pain. Instead, current clinical studies involve trying to determine the safest way to minimize and/or directly treat it.<sup>10</sup> Performance improvement projects in many NICUs (include my own unit), have moved beyond just decreasing obviously painful procedures to also rethinking how the entire NICU environment affects the babies, particularly our youngest and most vulnerable patients.<sup>11,12</sup> Two examples of changes we have made to our practice include increased use of “kangaroo care” where the premature baby is placed skin to skin on their parent’s chest, and cue based care times, where instead of checking vital signs every three hours the nursing staff tries not to interrupt sleep and uses (within reason), the babies’ cues that they are awake or in need of being tended to. These changes have been implemented in the care of our youngest/sickest babies—those born at the edge of viability. As part of the Vermont Oxford Network, a 1200 hospital collaborative devoted to the care of neonates,<sup>13</sup> preliminary data from our unit is encouraging and echoes what others have already found.

The edge of viability is currently around 22-23 weeks gestational age.<sup>14</sup> At this gestational age, the ability to reflexively react to painful (or noxious) stimulation and move away from it, is present.<sup>15,16</sup> However, the International Association for the Study of Pain (IASP) has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”<sup>17</sup> According to this frequently quoted definition, “pain requires subjectivity, which

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<sup>9</sup> Ibid., p 9.

<sup>10</sup> Allegaert, Karel, and John N. Van Den Anker. “Neonatal Pain Management: Still in Search for the Holy Grail.” *Int. Journal of Clinical Pharmacology and Therapeutics*, vol. 54, no. 07, 2016, pp. 514–523., doi:10.5414/cp202561.

<sup>11</sup> Altimier, Leslie, and Raylene M. Phillips. “The Neonatal Integrative Developmental Care Model: Seven Neuroprotective Core Measures for Family-Centered Developmental Care.” *Newborn and Infant Nursing Reviews*, vol. 13, no. 1, 2013, pp. 9–22, doi:10.1053/j.nainr.2012.12.002.

<sup>12</sup> Morris, Mindy, et al. “Small Baby Unit Improves Quality and Outcomes in Extremely Low Birth Weight Infants.” *Pediatrics*, American Academy of Pediatrics, 1 Oct. 2015, [pediatrics.aappublications.org/content/136/4/e1007](http://pediatrics.aappublications.org/content/136/4/e1007).

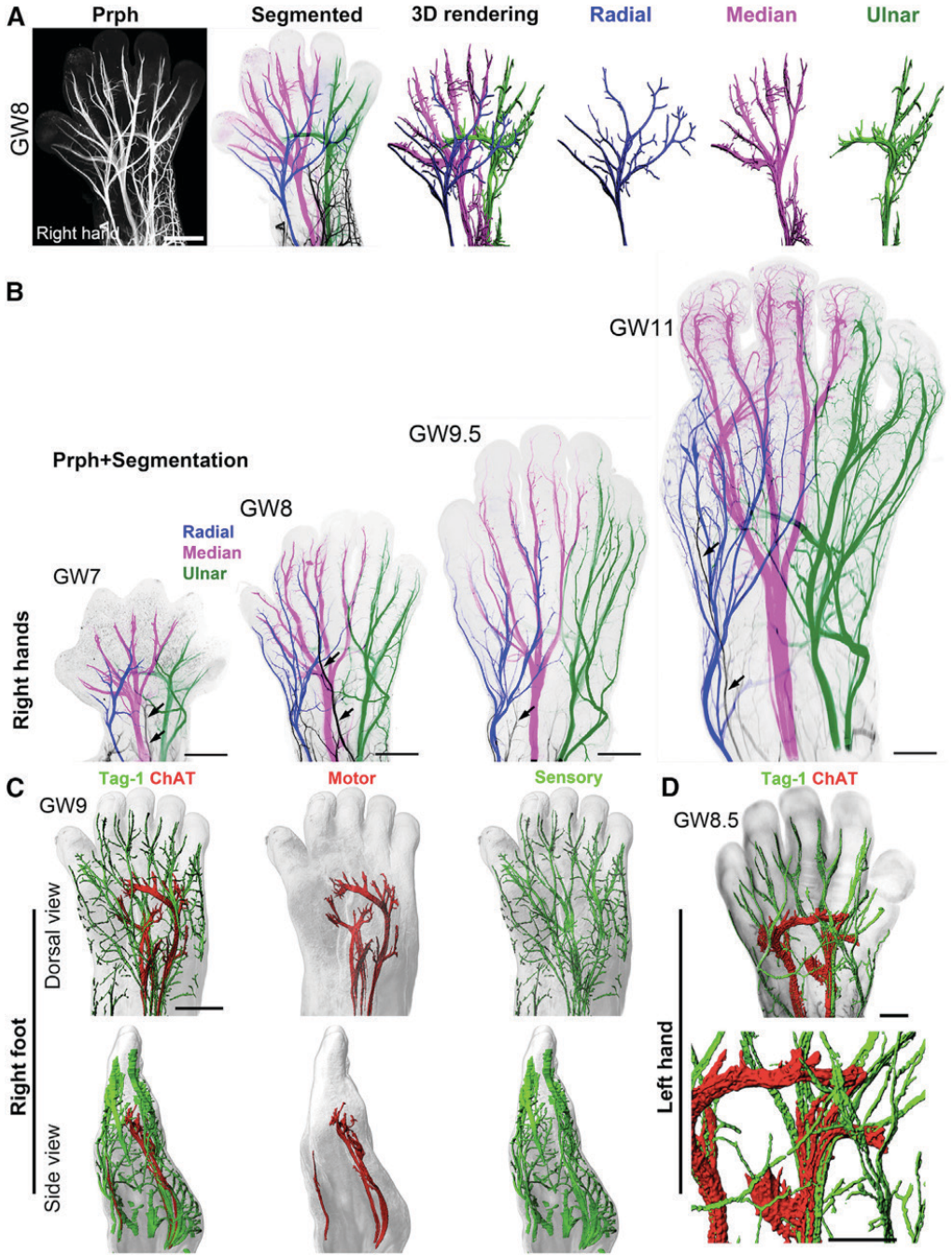
<sup>13</sup> “Home.” *Vermont Oxford Network*, [public.vtoxford.org/](http://public.vtoxford.org/).

<sup>14</sup> Raju, T N K, et al. “Periviable Birth: Executive Summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists.” *Journal of Perinatology*, vol. 34, no. 5, 2014, pp. 333–342, doi:10.1038/jp.2014.70.

<sup>15</sup> Lowery, Curtis L., et al. “Neurodevelopmental Changes of Fetal Pain.” *Seminars in Perinatology*, vol. 31, no. 5, 2007, p. 8., doi:10.1053/j.semperi.2007.07.004.

<sup>16</sup> Derbyshire, Stuart W.G. “Foetal Pain?” *Best Practice & Research Clinical Obstetrics & Gynaecology*, vol. 24, no. 5, 2010, p. 649., doi:10.1016/j.bpobgyn.2010.02.013.

<sup>17</sup> “IASP Terminology.” *IASP*, [www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698](http://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698).



in turn requires consciousness and the ability to evaluate a stimulus/situation.”<sup>18</sup> By this definition, babies (and other people who are less mentally competent), do not feel pain.

At what gestational age a person’s central nervous system (particularly the thalamus and cerebral cortex) are sufficiently developed and connected to produce a conscious awareness of pain continues to be debated. Derbyshire states, if pain is defined in terms of a noxious stimulus being detected by a nervous system that can preferentially respond to stimuli, then pain can be attributed to the foetus from around 10 weeks gestational age. However, if pain is defined as an elaborate multidimensional experience that is subjective, then pain can never be attributed to the foetus.<sup>19</sup>

This sentiment is echoed by Apkarian, “there is no such thing as ‘transmission of pain information in the central nervous system’ given that ‘pain’ is not transmitted. Pain can only be subjectively experienced. . . all organisms orchestrate coordinated escape or body protection behaviors; only humans write poetry on the topic.”<sup>20</sup>

I agree that the capacity to write poetry is a uniquely human ability, but given the human brain’s ability to achieve a consciousness unlike any other creature, perhaps this is why the developing human can demonstrate immediate behavioral responses to noxious stimulation and have long term effects from it long before or even without the ability to consciously evaluate the situation. As explained by Lowery et al., “there is no scientific evidence that function in the multi-layered networks underlying pain perception wait for some cue to be ‘turned on’. The developing neural elements may be immature, but they are NOT inactive.”<sup>21</sup> Whether one is a fetus, a teenager, or a senior citizen, humans usually experience a normal progression of neurologic changes that continue throughout life. Early in our development the changes are considered growth or maturation, later in life the changes are described as aging or even deterioration. However, nowhere along this continuum does someone conceived as a human become a plant—we are always humans with different capabilities at different times. With regards to the capacity to feel pain as a premature baby: given the known short and long-term ramifications that have informed today’s medical standard of care, there is sufficient information to ameliorate and/or treat a premature baby’s discomfort while we simultaneously continue to discover more about how the immature nervous system develops.

This continuum of development is important to note because some of the research discusses fetal physiology while other areas of research involve premature babies. As

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<sup>18</sup> Apkarian, A. Vania. “Nociception, Pain, Consciousness, and Society: A Plea for Constrained Use of Pain-Related Terminologies.” *The Journal of Pain*, vol. 19, no. 11, 2018, pp. 1253–1255, doi:10.1016/j.jpain.2018.05.010.

<sup>19</sup> Derbyshire, Stuart W.G. “Foetal Pain?” *Best Practice & Research Clinical Obstetrics & Gynaecology*, vol. 24, no. 5, 2010, pp. 653, doi:10.1016/j.bpobgyn.2010.02.013.

<sup>20</sup> Apkarian, A. Vania. “Nociception, Pain, Consciousness, and Society: A Plea for Constrained Use of Pain-Related Terminologies.” *The Journal of Pain*, vol. 19, no. 11, 2018, pp. 1254., doi:10.1016/j.jpain.2018.05.010.

<sup>21</sup> Lowery, Curtis L., et al. “Neurodevelopmental Changes of Fetal Pain.” *Seminars in Perinatology*, vol. 31, no. 5, 2007, pp. 275–282., doi:10.1053/j.semperi.2007.07.004.

a neonatologist, my job predominantly involves assisting prematurely born babies transition through their fetal physiology to that of a term baby. The fetal period of development begins at 8 weeks gestation and extends all the way until term at around 38 weeks.<sup>22</sup> During the fetal developmental period there is “differentiation and growth of the tissues and organs that were formed during the [earlier] embryonic period.”<sup>23</sup> This period of differentiation and growth is distinctly different from what occurs during the earlier embryonic period where the different organ systems are being formed; by 8 weeks gestation, “all major structures are present.”<sup>24</sup> Thus from early in gestation, the programming for all of our parts and pieces is already present, extremely underdeveloped, but present. An example of how much is present that we cannot easily see and how much we have yet to discover is Belle et al’s 2017 finding of “an adult-like pattern of skin innervation [already] established before the end of the first trimester.”<sup>25</sup>

By using a combination of whole-mount immunostaining, 3 DISCO clearing, and light-sheet imaging, Belle et al revealed “previously unknown features of human development in immunostained embryos.”<sup>26</sup> How much of this previously unappreciated but genuine nerve network accounts for noxious stimuli’s long-ranging effects on an incredibly immature nervous system? We don’t have those answers yet. But whether a baby can subjectively describe it, or an adult understands how it is perceived, pain undeniably affects premature babies. Apkarian’s accusation that the case for fetal pain capacity is “based on bogus so-called science,” is simply false. The potential to eventually write poetry is present only when a human being is conceived, and that potential is more likely to continue to develop if the immature person is exposed to less pain.

A different argument advanced by those who deny any fetal ability to experience pain is that the fetus is never sufficiently awake in-utero due to the presence of neuroinhibitory substances.<sup>27</sup> Interestingly, these same neuroinhibitory substances can have varying blood levels in both the fetuses and their mothers without clear correlation to analgesia in either of one of them.<sup>28</sup> Regardless, “neuroinhibitors are not anesthetics, but sedatives and no sedation can eliminate or prevent pain.”<sup>29</sup> Because of this fact as well as improvements in outcome when pain is treated, intentionally providing fetal

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<sup>22</sup> Moore, Keith L., et al. *Before We Are Born: Essentials of Embryology and Birth Defects*. Saunders, 1993, pp 1-6.

<sup>23</sup> *Ibid.*, p 6.

<sup>24</sup> *Ibid.*, p 6.

<sup>25</sup> Tridimensional Visualization and Analysis of Early Human ...[www.cell.com/cell/fulltext/S0092-8674\(17\)30287-8](http://www.cell.com/cell/fulltext/S0092-8674(17)30287-8).

<sup>26</sup> *Ibid.*

<sup>27</sup> Mellor, David J., et al. “The Importance of ‘Awareness’ for Understanding Fetal Pain.” *Brain Research Reviews*, vol. 49, no. 3, 2005, pp. 455–471, doi:10.1016/j.brainresrev.2005.01.006.

<sup>28</sup> Sekulic, Slobodan, et al. “Appearance of Fetal Pain Could Be Associated with Maturation of the Mesodiencephalic Structures.” *Journal of Pain Research*, Volume 9, 2016, pp. 1032, doi:10.2147/jpr.s117959.

<sup>29</sup> Bellieni, Carlo V. “New Insights into Fetal Pain.” *Seminars in Fetal and Neonatal Medicine*, 2019, p 3. doi:10.1016/j.siny.2019.04.001.

anesthesia during surgery has become an important asset to the operation's success. According to Dr. Bellieni, given the lack of pain control present with or without these neuroinhibitors, anesthesia during fetal surgery is "important for three main reasons: medical ethics, the risk of long-term consequences of pain on the development of the brain, and the possibility of sudden [fetal] movements induced by pain that can jeopardize the surgeon's work."<sup>30</sup> Anesthesiologists Van De Veld and De Buck state "it is becoming increasingly clear that experiences of pain will be 'remembered' by the developing nervous system, perhaps for the entire life of the individual."<sup>31</sup>

### Conclusion

"Nowadays no physician is permitted to expose babies to a potentially painful treatment without providing analgesia," and yet there are doctors who legally do so. That said, I agree that "the rights and wrongs of terminating fetal life are not resolved by deciding if and when the fetus becomes pain-capable." But since the days when abortion law was created, not only has the edge of viability changed, so has the frequency of survival and how well extremely premature babies are surviving. Current law has failed to adequately reflect these medical advances and has remained subservient to interests other than the babies. Given where the science and technology have moved today's medical standard of care, this is an invitation for the law to also be equally moved by the same medical and ethical truths.

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<sup>30</sup> *Ibid.*, p3.

<sup>31</sup> Velde, Marc Van De, and Frederik De Buck. "Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures." *Fetal Diagnosis and Therapy*, vol. 31, no. 4, 2012, pp. 206., doi:10.1159/000338146.

<sup>32</sup> Bellieni, Carlo V. "New Insights into Fetal Pain." *Seminars in Fetal and Neonatal Medicine*, 2019, p 3. doi:10.1016/j.siny.2019.04.001.

<sup>33</sup> Apkarian, A. Vania. "Nociception, Pain, Consciousness, and Society: A Plea for Constrained Use of Pain-Related Terminologies." *The Journal of Pain*, vol. 19, no. 11, 2018, p 1255, doi:10.1016/j.jpain.2018.05.010.

