

**Fact Sheet: Science of Fetal Pain** 

September 2022

## Unborn babies can feel pain at least by 15 weeks gestation and possibly earlier

- The idea that unborn and newborn babies cannot feel pain is obsolete, refuted by an extensive and growing body of scientific evidence. The myth that unborn babies cannot feel pain comes from a bygone era when newborns were strapped down for surgery without pain relief. The substantial published scientific literature on the topic shows that unborn babies can experience pain at least by 15 weeks gestational age (15 weeks LMP, since Last Menstrual Period, the fetal age estimate used by most obstetricians) or earlier. Two common methods are used to measure the age of an unborn baby: Post-fertilization age or post-conception weeks (PCW), used by embryologists, measures the age of the unborn baby from the actual date of conception, while gestational age measures from the first day of the mother's last menstrual period (LMP, approx. two weeks before conception). Medical practitioners have been using the latter method as standard medical practice for decades, and for the purpose of this paper, ages refer to gestational age unless otherwise indicated.
- A comprehensive review of the scientific literature<sup>2</sup> including neural development, psychology of pain sensation, and moral implications of fetal pain, concludes that unborn babies may experience pain as early as 12 weeks. The review notes that neural connections from periphery to brain are functionally complete after 18 weeks. "Nevertheless, we no longer view fetal pain (as a core, immediate, sensation) in a gestational window of 12–24 weeks as impossible based on the neuroscience." The review points out that a fetus may not experience pain in the same way as an adult, but does indeed experience pain as a real sensation, and that this pain experience has moral implications. Significant because this <u>unbiased review of the scientific evidence and agreement on existence of fetal pain</u>, as early as 12 weeks and certainly by 18 weeks, comes from <u>two highly credentialed medical professionals</u>, one <u>pro-choice</u>. "The two authors came together to write this paper through a shared sense that the neuroscientific data, especially more recent data, could not support a categorical rejection of fetal pain."
- Embryological development occurs early for pain sensory mechanisms and neurophysiology. The basic anatomical organization of the human nervous system is established by 6 weeks.<sup>3</sup> Nerve synapses for spinal reflex are in place by 10 weeks.<sup>4</sup> Pain receptors (nociceptors) begin forming at 7 weeks' gestational age.<sup>5</sup>
- Nerves linking these pain receptors to the brain's thalamus and subcortical plate form between 12- and 20-weeks' gestational age. The thalamus functions in pain perception in fetuses as well as in adults.
- Numerous lines of evidence now show the fallacy in the claim that the brain cortex is necessary to experience pain and suffering, including the fact that decordate individuals as well as animals lacking higher cortical structures obviously do feel pain. In fact, the human brain cortex does not fully mature until approximately 25 years of age, yet infants, children, and teenagers also obviously can experience pain.
- <u>Fetal reactions provide evidence of pain response</u>. The unborn baby reacts to noxious stimuli with avoidance reactions and stress responses. As early as 8 weeks, the baby exhibits reflex movement during invasive

procedures.<sup>10</sup> The application of painful stimuli to an unborn child is associated with significant increases in stress hormones in the unborn child, known as the stress response.<sup>11</sup> In fact, evidence indicates that subjection to painful stimuli as a fetus is associated with long-term harmful neurodevelopmental effects, such as altered pain sensitivity and, possibly, emotional, behavioral, and learning disabilities later in life.<sup>12</sup>

- Dr. Ruth Grunau, a pediatric psychologist at the University of British Columbia, said, "We would seem to be holding an extraordinary standard if we didn't infer pain from all those measures." <sup>13</sup>
- <u>Increased sensitivity to pain</u>. In 2010 one group noted that "the earlier infants are delivered, the stronger their response to pain." This increased sensitivity is due to the fact that the neural mechanisms that inhibit pain sensations do not begin to develop until 34-36 weeks, and are not complete until a significant time after birth. This means that unborn, as well as newborn and preterm, infants show "hyperresponsiveness" to pain. Authors of a 2015 study used the fMRI technique to measure pain response in newborns (1-6 days old) vs. adults (23-36 years old), and found that "the infant pain experience closely resembles that seen in adults." Babies had 18 out of 20 brain regions respond like adults, yet they showed much *greater* sensitivity to pain, responding at a level four times as sensitive as adults.
- Through technological advancements, the peer-reviewed evidence has only become more compelling as ultrasonographic studies have literally given us a window into the womb for the first time. A study published earlier this year found that fetuses at approximately 31 weeks' gestation grimaced with pain when their thighs were injected with anesthetic prior to a painful intrauterine surgery. Another 2021 study observed the same result a pained grimace upon being pricked with a needle with anesthetic with a 23 weeks' gestation fetus about to undergo heart surgery in the womb.<sup>18</sup>

## Standard of medical care now calls for direct fetal analgesia and anesthesia during fetal surgery, beginning at least by 15 weeks

- Fetal anesthesia is now routine medical practice and recommended for all fetal surgeries from the second trimester onward.<sup>19</sup>
- Current medical evidence has concluded that from the 15th week gestational age onward, "the fetus is extremely sensitive to painful stimuli," making it "necessary to apply adequate analgesia to prevent [fetal] suffering."<sup>20</sup>
- Fetal surgeries are now being performed even into the first half of gestation, and routinely incorporate anesthesia and analgesia in the protocols. As one of the world's leading fetal surgeons on the development of fetal surgery points out, using spina bifida as an example of good medical practice for *in utero* surgical intervention: "Fetal therapy is the logical culmination of progress in fetal diagnosis. In other words, the fetus is now a patient." 22
- Fetal surgeons recognize unborn babies as patients. The growth in maternal-fetal medicine recognizes this acceptance. Since the first fetal surgery performed in 1981 in the United States, the number of centers devoted to fetal surgeries has grown until today (in 2022), there are **37** medical centers in the United States that perform advanced *in-utero* fetal therapeutic procedures.<sup>23</sup>
- A recent review of the evidence concludes that objections to the concept of fetal pain are "obsolete," and based on the totality of evidence, "the human fetus can feel pain when it undergoes surgical interventions and direct analgesia must be provided to it."<sup>24</sup>
- A prenatal surgery group that has performed many fetal surgeries informs the mother before the surgery: 25 "You will be given general anesthesia, and that anesthesia will put your baby to sleep as well. In addition, during the prenatal surgery, your unborn baby will be given an injection of pain medication and medication to ensure that the baby doesn't move."

## Babies are surviving and thriving at ever younger pre-term ages when given appropriate care and treatment

- Survival of extremely preterm infants has increased significantly as doctors realize advantages of active care for such young patients. Ages of survival have dropped from 28 weeks to 24 weeks and now less than 22 weeks.<sup>26</sup>
- The British Association of Perinatal Medicine (BAPM) now recommends that all babies born as early as 22 weeks' gestation be given active care and resuscitation.<sup>27</sup>
- A *Journal of Perinatology* study found that if extremely preterm babies were routinely given care, as many as 53% of those born at 22 weeks' gestation survived, compared to only 8% if active care was not given, <sup>28</sup> challenging physician attitudes on survival as well as thoughts about the age limit of viability. <sup>29</sup>
- Survival of babies born at 22 weeks' gestation in Sweden increased to 58 percent if the preterm babies were given intensive care, demonstrating what is possible if active care and caring attitudes are applied.<sup>30</sup>
- Groundbreaking *New England Journal of Medicine* study demonstrated that babies delivered as young as 22 weeks can survive, and active intervention for treatment greatly improves their survival.<sup>31</sup>
- An NIH-funded study of infants who were delivered at 22-24 weeks and who received active treatment observed increasing rates of survival without any neurological impairment. Yet, three-fourths of those delivered at 22 weeks still received no active care.<sup>32</sup>
- 60% of infants born at 22 weeks who receive active hospital treatment will survive. 33

<sup>&</sup>lt;sup>1</sup> McGrath PJ, Science is not enough: The modern history of pediatric pain, Pain 152, 2457-2459, 2011, doi: http://dx.doi.org/10.1016/j.pain.2011.07.018

<sup>&</sup>lt;sup>2</sup> Derbyshire SWG and Bockmann JC, Reconsidering fetal pain, *J Med Ethics* 46, 3-6, 2020

<sup>&</sup>lt;sup>3</sup> Carlson BM, <u>Patten's Foundations of Embryology</u>, Sixth Edition, McGraw-Hill, Inc., New York; 1996; Nikolopoulou E *et al.*, Neural tube closure: cellular, molecular and biomechanical mechanisms, *Development* 144, 552, 2017.

<sup>&</sup>lt;sup>4</sup> Okado N et al., Synaptogenesis in the cervical cord of the human embryo: Sequence of synapse formation in a spinal reflex pathway, J. Comparative Neurol. 184, 491, 1979; Okado N, Onset of synapse formation in the human spinal cord, J. Comparative Neurol. 201, 211, 1981.

<sup>&</sup>lt;sup>5</sup> Myers LB *et al.*, Fetal endoscopic surgery: indications and anaesthetic management, *Best Pract Res Clin Anaesthesiol* 18, 231, 2004, doi: 10.1016/j.bpa.2004.01.001; Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. *New England Journal of Medicine*. 317, 1321-1329, 1987, doi: 10.1056/NEJM198711193172105

<sup>&</sup>lt;sup>6</sup> Derbyshire SWG and Bockmann JC, Reconsidering fetal pain, *Journal of Medical Ethics* 46, 3-6, 2020, doi: 10.1136/medethics-2019-105701; Kostović I, Judaš M, The development of the subplate and thalamocortical connections in the human foetal brain, *Acta Paediatr* 99, 1119–1127, 2010, doi: 10.1111/j.1651-2227.2010.01811.x; Van de Velde M, De Buck F, Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures, *Fetal Diagnosis and Therapy* 31, 201, 2012, doi: 10.1159/000338146

<sup>&</sup>lt;sup>7</sup> Chien JH *et al.*, Human Thalamic Somatosensory Nucleus (Ventral Caudal, Vc) as a Locus for Stimulation by INPUTS from Tactile, Noxious and Thermal Sensors on an Active Prosthesis. *Sensors (Basel)*. 17, 2017

<sup>&</sup>lt;sup>8</sup> Dobbs v. Jackson. Brief of Maureen L. Condic, PhD and the Charlotte Lozier Institute as Amici Curiae supporting petitioners, 2021. <a href="https://lozierinstitute.org/wp-content/uploads/2021/07/CLI-Dobbs-Amicus-Brief.pdf">https://lozierinstitute.org/wp-content/uploads/2021/07/CLI-Dobbs-Amicus-Brief.pdf</a>

<sup>&</sup>lt;sup>9</sup> Arain M et al., Maturation of the adolescent brain, Neuropsychiatr Dis Treat. 9, 449, 2013

<sup>&</sup>lt;sup>10</sup> Ohashi Y *et al.*, Success rate and challenges of fetal anesthesia for ultrasound guided fetal intervention by maternal opioid and benzodiazepine administration, *J Maternal-Fetal Neonatal Medicine* 26, 158, 2013.

<sup>&</sup>lt;sup>11</sup> Myers LB et al., Fetal endoscopic surgery: indications and anaesthetic management, Best Pract Res Clin Anaesthesiol 18, 231, 2004, DOI:

<sup>10.1016/</sup>j.bpa.2004.01.001; Brusseau R and Mizrahi-Arnaud A, Fetal Anesthesia and Pain Management for Intrauterine Therapy, Clinics in Perinatology 40, 429, 2013, DOI: 10.1016/j.clp.2013.05.006

<sup>&</sup>lt;sup>12</sup> Fink RJ, *et al.*, Remifentanil for fetal immobilization and analgesia during the ex utero intrapartum treatment procedure under combined spinal–epidural anaesthesia, *British Journal of Anaesthesia* 106, P851–855, 2011, DOI: <a href="https://doi.org/10.1093/bja/aer097">https://doi.org/10.1093/bja/aer097</a>

<sup>&</sup>lt;sup>13</sup> Qiu J, Does it hurt?, Nature 444, 143, 2006.

<sup>&</sup>lt;sup>14</sup> Badr LK et al., Determinants of Premature Infant Pain Responses to Heel Sticks, Pediatric Nursing 36, 129, 2010.

<sup>&</sup>lt;sup>15</sup> Brusseau R and Bulich LA, Anesthesia for fetal intervention, in <u>Essential Clinical Anesthesia</u>, Charles Vacanti, Pankaj Sikka, Richard Urman, Mark Dershwitz, B. Scott Segal, Eds., Cambridge University Press, NY; July 2011; 772-776.

<sup>&</sup>lt;sup>16</sup> Greco C and Khojasteh S, Pediatric, Infant and Fetal Pain, Case Studies in Pain Management, Alan David Kaye and Rinoo V. Shah, Eds., (Cambridge: Cambridge University Press, 2014), 379.

<sup>&</sup>lt;sup>17</sup> Goksan S et al., fMRI reveals neural activity overlap between adult and infant pain, eLife 4:e06356, 2015.

<sup>&</sup>lt;sup>18</sup> Bernardes LS *et al.*, Sorting Pain Out of Salience: Assessment of Pain Facial Expressions in the Human Fetus, *Pain Reports* 6(1), e882, 2021, DOI: <a href="https://doi.org/10.1097/PR9.0000000000000882">https://doi.org/10.1097/PR9.00000000000000882</a>; Bernardes LS *et al.*, Acute Pain Facial Expressions in 23-Week Fetus, *Ultrasound in Obstetrics & Gynecology* 59, 394-395, 2021, DOI: <a href="https://doi.org/10.1002/uog.23709">10.1002/uog.23709</a>

- <sup>19</sup> Gupta, R., Wimalasundera, R., Moore, P. (2021). Anaesthesic Considerations in Fetal Therapy. In: Goudra, B.G., Singh, P.M., Green, M.S. (eds) Anaesthesia for Uncommon and Emerging Procedures . Springer, Cham. <a href="https://doi.org/10.1007/978-3-030-64739-1">https://doi.org/10.1007/978-3-030-64739-1</a> 28
- <sup>20</sup> Sekulic S *et al.* Appearance of fetal pain could be associated with maturation of the mesodiencephalic structures. *Journal of Pain Research* 9, 1031-1038, 2016, DOI: 10.2147/JPR.S117959; Bellieni CV, Analgesia for Fetal Pain During Prenatal Surgery: 10 Years of Progress, *Pediatric Research* 89, 1612, 2020, DOI: 10.1038/s41390-020-01170-2
- <sup>21</sup> Lecointre L *et al.*, Fetoscopic Laser Coagulation for Twin–Twin Transfusion Syndrome before 17 Weeks' Gestation: Laser Data, Complications and Neonatal Outcome, *Ultrasound in Obstetrics & Gynecology* 44, 299–303, 2014, <a href="https://doi.org/10.1002/uog.13375">https://doi.org/10.1002/uog.13375</a>; Baud D *et al.*, Fetoscopic Laser Therapy for Twin–Twin Transfusion Syndrome before 17 and after 26 Weeks' Gestation, *Am J Obstet Gynecol*, 208, 197.e1-7, 2013, DOI: 10.1016/j.ajog.2012.11.027; Ramirez MV, Anesthesia for fetal surgery, *Colombian Journal of Anesthesiology* 40, 268, 2012, <a href="https://doi.org/10.1016/j.rcae.2012.07.006">https://doi.org/10.1016/j.rcae.2012.07.006</a>
- <sup>22</sup> Adzick NS, Prospects for fetal surgery, Early Human Development 89, 881-886, 2013, DOI: 10.1016/j.earlhumdev.2013.09.010
- <sup>23</sup> Tara Sander Lee, Ph.D., Mia Steupert, M.A., Fact Sheet: The Growth of Maternal-Fetal Medicine and Fetal Care Centers in the United States, July 21, 2022, accessed at: <a href="https://lozierinstitute.org/fact-sheet-the-growth-of-maternal-fetal-medicine-and-fetal-care-centers-in-the-united-states/">https://lozierinstitute.org/fact-sheet-the-growth-of-maternal-fetal-medicine-and-fetal-care-centers-in-the-united-states/</a>
- <sup>24</sup> Bellieni, Carlo V. Analgesia for Fetal Pain during Prenatal Surgery: 10 Years of Progress, Pediatric Research, 89, 1612–1618 (2021). <a href="https://doi.org/10.1038/s41390-020-01170-2">https://doi.org/10.1038/s41390-020-01170-2</a>
- <sup>25</sup> Adzick NS et al., A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele, N Engl J Med 364, 993, 2011 (from the Informed Consent section of the supplementary Protocol to the paper).
- <sup>26</sup> A. Pawlowski, 'Miracle baby': Born at 21 weeks, she may be the most premature surviving infant, *Today*, updated Nov 21, 2018, accessed at: https://www.today.com/health/born-21-weeks-she-may-be-most-premature-surviving-baby-t118610; Ahmad KA *et al.*, Two-Year Neurodevelopmental Outcome of an Infant Born at 21 Weeks' 4 Days' Gestation, *Pediatrics* 2017;140(6):e20170103
- <sup>27</sup> The BMJ, Consider active management for premature babies born at 22 weeks, says new guidance, *BMJ* 367, l6151, 2019; British Association of Perinatal Medicine, "Perinatal Management of Extreme Preterm Birth before 27 weeks of gestation A Framework for Practice," October 2019; accessed via announcement: <a href="https://www.bapm.org/posts/109-new-bapm-framework-on-extreme-preterm-birth-published">https://www.bapm.org/posts/109-new-bapm-framework-on-extreme-preterm-birth-published</a>
- <sup>28</sup> Backes CH *et al.*, Outcomes following a comprehensive versus a selective approach for infants born at 22 weeks of gestation, *Journal of Perinatology* 39, 39–47, 2019.
- <sup>29</sup> Welty S, Challenging the gestational age for the limit of viability: proactive care, *Journal of Perinatology* 39, 1–3, 2019.
- <sup>30</sup> Norman M *et al.*, Association Between Year of Birth and 1-Year Survival Among Extremely Preterm Infants in Sweden During 2004-2007 and 2014-2016, *JAMA* 321, 1188-1199, 2019; Rysavy MA and Ehret DEY, Extremely Preterm Birth Outcomes in Sweden, *JAMA* 321, 1163-1164, 2019.
- <sup>31</sup> Rysavy MA et al., Between-Hospital Variation in Treatment and Outcomes in Extremely Preterm Infants, N Engl J Med 372, 1801, May 7, 2015.
- <sup>32</sup> "Survival Rate May Be Improving for Extremely Preterm Infants," National Institutes of Health, last modified February 15, 2017, <a href="https://www.nih.gov/news-events/news-releases/survival-rate-may-be-improving-extremely-preterm-infants">https://www.nih.gov/news-events/news-releases/survival-rate-may-be-improving-extremely-preterm-infants</a>; Younge N et al., Survival and Neurodevelopmental Outcomes among Periviable Infants. N Engl J Med 376, 617, 2017; Shah PS, Neonatal Intensive Care—The Only Constant is Change, N Engl J Med 376, 694, 2017.
- <sup>33</sup> Mehler K et al., Survival Among Infants Born at 22 or 23 Weeks' Gestation Following Active Prenatal and Postnatal Care. JAMA Pediatr. 170, 671, 2016.