

## Science of Fetal Pain at 20 Weeks

### Unborn babies can feel pain by 20 weeks gestation or earlier

- The old, uninformed notions that unborn and newborn babies cannot feel pain are refuted by a growing body of scientific evidence. The published scientific literature shows that unborn babies can experience pain at 20 weeks gestational age (20 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: Probable post-fertilization age (PPF, 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>1</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 unbiased review of the scientific evidence and agreement on existence of fetal pain, as early as 12 weeks and certainly after 18 weeks, comes from two highly credentialed doctors, one pro-choice. "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 shows presence of pain sensory mechanisms and neurophysiology. The basic anatomical organization of the human nervous system is established by 6 weeks.<sup>2</sup> The earliest neurons in the cortical brain (the part responsible for thinking, memory, and other higher functions) are established starting at 6 weeks.<sup>3</sup> Nerve synapses for spinal reflex are in place by 10 weeks.<sup>4</sup> Sensory receptors for pain (nociception) develop first around the mouth at 7 weeks, and are present throughout the skin and mucosal surfaces by 20 weeks.<sup>5</sup> Connections between the spinal cord and the thalamus (which functions in pain perception in fetuses as well as in adults<sup>6</sup>) are relatively complete by 20 weeks.<sup>7</sup>
- Contradicting the claim that the brain cortex is necessary to experience pain and suffering, 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 obviously can experience pain.<sup>8</sup>
- Fetal reactions provide evidence of pain response. 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>9</sup> There is extensive evidence of a hormonal stress response by unborn babies as early as 18 weeks<sup>10</sup> including "increases in cortisol, beta-endorphin, and decreases in the pulsatility index of the fetal middle cerebral artery."<sup>11</sup> Two independent studies in 2006 used brain scans of the sensory part of unborn babies' brains, showing response to pain.<sup>12</sup> They found a "clear cortical response" and concluded there was "the potential for both higher-level pain processing and pain-induced plasticity in the human brain from a very early age."
- 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>
- Brain responses & connections. In 2013 a study used functional magnetic resonance imaging (fMRI) to study the brains of healthy human babies still within the womb, from 24-39 weeks. They found that functional neuronal connections sufficient to experience pain already exist by 24 weeks.<sup>14</sup>
- Increased sensitivity to pain. In 2010 one group noted that "the earlier infants are delivered, the stronger their response to pain."<sup>15</sup> 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.<sup>16</sup> This means that unborn, as well as newborn and preterm, infants show “hyperresponsiveness” to pain.<sup>17</sup> 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.”<sup>18</sup> 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.

### **Unborn babies are treated as patients by fetal surgeons, and receive pain medication**

- Fetal surgeons recognize unborn babies as patients. A leading children’s hospital performed nearly 1,600 fetal surgeries between 1995 and June 2017.<sup>19</sup> Perinatal medicine now treats unborn babies as young as 18 weeks for dozens of conditions. Pain medication for unborn patients is routinely administered as standard medical practice.<sup>20</sup>
- One of the premier fetal surgeons makes the obvious point: “Fetal therapy is the logical culmination of progress in fetal diagnosis. In other words, the fetus is now a patient.”<sup>21</sup>
- A European fetal surgery team states: “The administration of anesthesia directly to the fetus is critical in open fetal surgery procedures.”<sup>22</sup>
- The leading textbook on clinical anesthesia says: “It is clear that the fetus is capable of mounting a physiochemical stress response to noxious stimuli as early as 18 weeks.”<sup>23</sup>
- A recent review of the evidence concludes that from the 15<sup>th</sup> week of gestation onward, “the fetus is extremely sensitive to painful stimuli, and that this fact should be taken into account when performing invasive medical procedures on the fetus. It is necessary to apply adequate analgesia to prevent the suffering of the fetus.”<sup>24</sup>
- A prenatal surgery group that has performed many fetal surgeries informs the mother before the surgery:<sup>25</sup> “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.<sup>33</sup>

<sup>1</sup> Derbyshire SWG and Bockmann JC, Reconsidering fetal pain, *J Med Ethics* 46, 3-6, 2020

<sup>2</sup> Carlsson BM, *Patten’s Foundations of Embryology*, 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>3</sup> Bystron I *et al.*, The first neurons of the human cerebral cortex, *Nature Neuroscience* 9, 880, 2006.

<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>5</sup> Brusseau R, Developmental Perspectives: Is the Fetus Conscious?, *International Anesthesiology Clinics* 46, 11, 2008; Lowery CL *et al.*, Neurodevelopmental Changes of Fetal Pain, *Seminars in Perinatology* 31, 275, 2007.

<sup>6</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>7</sup> Van de Velde M and De Buck F, Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures, *Fetal Diagnosis and Therapy* 31, 201, 2012; Van Scheltema PNA *et al.*, Fetal Pain, *Fetal and Maternal Medicine Review* 19, 311, 2008.
- <sup>8</sup> Arain M *et al.*, Maturation of the adolescent brain, *Neuropsychiatr Dis Treat.* 9, 449, 2013
- <sup>9</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>10</sup> Myers LB *et al.*, Fetal endoscopic surgery: indications and anaesthetic management, *Best Pract Res Clin Anaesthesiol* 18, 231, 2004; Brusseau R and Mizrahi-Arnaud A, Fetal Anesthesia and Pain Management for Intrauterine Therapy, *Clinics in Perinatology* 40, 429, 2013.
- <sup>11</sup> Lin EE and Tran KM, Anesthesia for fetal surgery, *Seminars in Pediatric Surgery* 22, 50, 2013.
- <sup>12</sup> Slater R *et al.*, Cortical Pain Response in Human Infants, *J Neuroscience* 25, 3662, 2006; Bartocci M *et al.*, Pain Activates Cortical Areas in the Preterm Newborn Brain, *Pain* 122, 109, 2006.
- <sup>13</sup> Qiu J, Does it hurt?, *Nature* 444, 143, 2006.
- <sup>14</sup> Thomason ME *et al.*, Cross-Hemispheric Functional Connectivity in the Human Fetal Brain, *Sci Transl Med* 5, 173ra24, 2013.
- <sup>15</sup> Badr LK *et al.*, Determinants of Premature Infant Pain Responses to Heel Sticks, *Pediatric Nursing* 36, 129, 2010.
- <sup>16</sup> Brusseau R and Bulich LA, Anesthesia for fetal intervention, in *Essential Clinical Anesthesia*, Charles Vacanti, Pankaj Sikka, Richard Urman, Mark Dershwitz, B. Scott Segal, Eds., Cambridge University Press, NY; July 2011; 772-776.
- <sup>17</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>18</sup> Goksan S *et al.*, fMRI reveals neural activity overlap between adult and infant pain, *eLife* 4:e06356, 2015.
- <sup>19</sup> "Volumes and Outcomes: Fetal Anomalies," Children's Hospital of Philadelphia, 2017, <http://www.chop.edu/centers-programs/center-fetal-diagnosis-and-treatment/volumes-outcomes#.VLbMhCvF8T->. See also, "Fetal Family Reunion," Children's Hospital of Philadelphia, 2017, <http://www.chop.edu/events/fetal-family-reunion>.
- <sup>20</sup> See, e.g., Ramirez MV, Anesthesia for fetal surgery, *Colombian Journal of Anesthesiology* 40, 268, 2012; Tran KM, Anesthesia for fetal surgery, *Seminars in Fetal & Neonatal Medicine* 15, 40, 2010; Schwarz U and Galinkin JL, Anesthesia for fetal surgery, *Semin Pediatr Surg* 12, 196, 2003; Anand KJS and Hickey PR, Pain and Its Effects in the Human Neonate and Fetus, *N Engl J Med* 317, 132, 1987.
- <sup>21</sup> Adzick NS, Prospects for fetal surgery, *Early Human Development* 89, 881, 2013.
- <sup>22</sup> Mayorga-Buiza MJ *et al.*, Management of fetal pain during invasive fetal procedures. Lessons learned from a sentinel event, *European Journal of Anaesthesiology* 31, 88, 2014.
- <sup>23</sup> Brusseau R and Bulich LA, Anesthesia for fetal intervention, in *Essential Clinical Anesthesia*, Charles Vacanti, Pankaj Sikka, Richard Urman, Mark Dershwitz, B. Scott Segal, Eds., Cambridge University Press, NY; July 2011; 772-776.
- <sup>24</sup> Sekulic S *et al.*, Appearance of fetal pain could be associated with maturation of the mesodiencephalic structures. *J Pain Res.* 9, 1031, 2016
- <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: <https://www.bapm.org/posts/109-new-bapm-framework-on-extreme-preterm-birth-published>
- <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, <https://www.nih.gov/news-events/news-releases/survival-rate-may-be-improving-extremely-preterm-infants>; 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.