Testimony of
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Chairman Franks, Congressman Nadler, distinguished members of the subcommittee, I am Dr. Maureen Condic, Associate Professor of Neurobiology and Adjunct Professor of Pediatrics at the University of Utah School of Medicine. I am Director of Human Embryology instruction for the Medical School and of Human Neuroanatomy for the Dental School at my institution. Thank you for this opportunity to testify regarding certain aspects of the District of Columbia Pain-Capable Unborn Child Protection Act (H.R. 1797).

What is Pain?

The experience of pain is complex, with physical, psychological and mental elements. In the simplest sense, pain is an aversive response to a noxious (physically harmful or destructive) stimulus. The medical dictionary administered by the National Institutes of Health (NIH)[1] supports this view, defining pain as, "a basic bodily sensation that is induced by a noxious stimulus, is received by naked nerve endings, is characterized by physical discomfort (as pricking, throbbing, or aching), and typically leads to evasive action." As humans, we share this basic experience of pain with many other animals, from very simple creatures like reptiles and birds, up to mammals and primates.

Yet pain has more complex dimensions. The NIH dictionary also offers the following, more nuanced definition of pain: "a state of physical, emotional, or mental lack of well-being or physical, emotional, or mental uneasiness that ranges from mild discomfort or dull distress to acute often unbearable agony, may be generalized or localized, and is the consequence of being injured or hurt." This definition also defines pain as a response to a noxious stimulus or injury, but acknowledges that the response can have emotional or mental dimensions as well. And, like all mental experiences, it is difficult for any one of us to fully appreciate another person's psychological experience of pain. Every individual's reaction to pain is unique. Experiences one person might find extremely painful may seem insignificant to someone else. Moreover, even for a single individual, the perception of what is and what is not painful can change over time. Experiences a young woman might find painful (e.g. being snubbed at a social event) may seem trivial to a more experienced woman in middle age. And experiences a middle-aged woman might find painfully difficult (e.g. death of a colleague) may be far less painful to a young woman who has a less acute sense of her own mortality.

[1] See definition "b" at: http://www.merriam-webster.com/medlineplus/pain.

How do we know if others are experiencing pain?

While the psychological and mental aspects of pain are important to us, they are also fundamentally *personal*, and therefore not something that can be fully understood by anyone else. We can listen to someone's explanation of their painful experience. We can empathize. We can measure certain physical, neurological and endocrine responses to painful stimuli. But we cannot directly share another individual's experience of pain.

Importantly, our inability to fully understand someone else's experience of pain does not prevent us from making rational and prudent judgments about painful situations and how they obligate us to behave. We do not justify inflicting pain on another person by saying, "I can't possibly know how anyone else experiences me punching them in the face, therefore I am not obligated to restrain from this behavior." When considering the pain-experience of other humans, we are guided by three simple principles: what we know about pain, what we observe about another individual's reaction to a painful stimulus and what we can reasonably conclude from our own experience of pain.

What we know. When scientific data provides evidence that an experience causes harm or imposes significant risk of harm to another individual (i.e. it involves a "noxious" stimulus), this experience is reasonably viewed as "painful." Even if the individual's perception of this harmful stimulus is compromised in some manner (perhaps by a genetic condition that limits their ability to receive painful neural information or by drugs that have temporarily limited this ability), we are nonetheless obligated to avoid causing pain to another human individual, both out of compassion and out of justice.

What we observe. When observation, either casual or scientific, provides reasonable evidence that an individual perceives an experience as "painful," (the individual withdraws, cries out, grimaces, or shows elevated respiration, heart rate or stress hormones), we are obligated to avoid causing pain to that individual.

What we experience ourselves. When our own reaction to the experience another individual is having would be one of pain, we can reasonably conclude it is painful to them as well. Perhaps not in precisely the same manner or to the same degree, but things that hurt us tend to be hurtful to others as well.

Scientific data regarding fetal brain development and pain perception

The ability to perceive noxious stimuli and react to them develops over a very long period of time in humans, continuing well after birth and (as noted above) changing significantly across any individual's lifespan.

The earliest “rudiment” of the human nervous system forms by 28 days (four weeks) after sperm-egg fusion. At this stage, the primitive brain is already "patterned"; i.e. cells in different regions are specified to produce structures appropriate to their location in the

nervous system as a whole.[2] Over the next several weeks, the brain will grow enormously and generate many complex connections, but the overall organization of the nervous system is established by four weeks. This is significant because it shows that even at this early stage, the brain is not anything like a mere collection of cells or a "blank slate" to be written upon by later developmental processes. Like all embryonic organs, the structure of the early brain "anticipates" the function of the mature system.

In the region of the brain responsible for thinking, memory and other "higher" functions (the neocortex), the earliest neurons are generated during the fourth week after sperm-egg fusion.[3] This tells us that at this early date, the brain is organizing the structures that will be required for distinctively human experiences, although these structures will not be fully mature for at least two decades.[4]

There is strong scientific evidence that communication between neurons of the brain is established in the seventh week. Synapses, which are the molecular structures required for brain cells to communicate with each other, are detected in the cortex at this time.[5] In animals, synapses are functional immediately and this is likely also true of humans. Thus, the earliest function of the neocortex as a network appears to commence in the seventh week.

The neural circuitry responsible for the most primitive response to pain, the spinal reflex, is in place by 8 weeks of development. This is the earliest point at which the fetus experiences pain in any capacity.[6] And a fetus responds just as humans at later stages of

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[2] Langman's Medical Embryology, 11th Edition T.W. Sadler. (2009). Lippincott Williams and Wilkins. (ISBN-10: 0781790697) Chapters 5 and 6.

[3] Tangential networks of precocious neurons and early axonal outgrowth in the embryonic human forebrain. Bystron I, Molnár Z, Otellin V, Blakemore C. J Neurosci. 2005;25:2781-92.; ApoER2 and VLDLR in the developing human telencephalon. Cheng L, Tian Z, Sun R, Wang Z, Shen J, Shan Z, Jin L, Lei L. Eur J Paediatr Neurol. 2011;15:361-7.; The first neurons of the human cerebral cortex. Bystron I, Rakic P, Molnár Z, Blakemore C. Nat Neurosci. 2006;9:880-6. Epub 2006 Jun 18.; Development of the human cerebral cortex: Boulder Committee revisited. Bystron I, Blakemore C, Rakic P. Nat Rev Neurosci. 2008;9:110-22.

[4] Gogtay N et al (2004) Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci USA 101:8174; Sowell ER et al (2003) Mapping cortical change across the human life span. Nat Neurosci 6:309

[5] Synaptogenesis in layer I of the human cerebral cortex in the first half of gestation. Zecevic N. Cereb Cortex. 1998;8:245-52.

[6] Synaptogenesis in the cervical cord of the human embryo: sequence of synapse formation in a spinal reflex pathway. Okado N, Kakimi S, Kojima T. J Comp Neurol. 1979;184:491-518.; Onset of synapse formation in the human spinal cord. Okado N. J Comp Neurol. 1981;201:211-9.; The fine structure of the spinal cord in human embryos and early fetuses. Wozniak W, O'Rahilly R, Olszewska B. J Hirnforsch. 1980;21:101-24.; Early synaptogenesis in the spinal cord of human embryos. Milokhin AA. Acta Biol

development respond; by with withdrawing from the painful stimulus. This simple response is tremendously important for humans at all ages because it rapidly protects the body from harmful events (heat, cold, chemical injury, crushing, cutting, etc.) without requiring the time it takes to reflect on the experience.

The earliest connections between neurons in the subcortico-frontal pathways (regions of the brain involved in motor control and a wide range of psychological phenomena, including pain perception) are detected by 37 days post sperm-egg fusion and are well established by 8-10 weeks.[7] This indicates that the brain is "wiring" itself in the first trimester, well before reaching the fetal stage of life. Early establishment of connections between neurons further indicates that brain formation is an active process of progressively building the structures and relationships required for mature brain function.

Connections between the spinal cord and the thalamus, the region of the brain that is largely responsible for pain perception in both the fetus and the adult, begin to form around 12 weeks and are completed by 18 weeks.[8]

The long-range connections within the cortex that some believe to be required for consciousness do not arise until much later, around 22-24 weeks.[9] And these connections continue to develop for an exceptionally long time. Indeed, recent studies indicate that the anatomy of the human brain, and therefore the pattern of brain activity underlying all higher functions (reason, memory, emotion, language, etc.) is not fully mature until approximately 25 years after birth.[10]

What brain structures are necessary for a fetus to feel pain?

To experience pain, a noxious stimulus must be detected. The neural structures necessary to detect noxious stimuli are in place by 8-10 weeks of human development.[11]

Hung. 1983;34:231-45.; Development of pain mechanisms. Fitzgerald M. Br Med Bull. 1991;47:667-75.

[7] Development of axonal pathways in the human fetal fronto-limbic brain: histochemical characterization and diffusion tensor imaging. Vasung L, Huang H, Jovanov-Milošević N, Pletikos M, Mori S, Kostović I. J Anat. 2010;217:400-17.; Insights from in vitro fetal magnetic resonance imaging of cerebral development. Kostovic I, Vasung L. Semin Perinatol. 2009;33:220-33.

[8] Kostovic I, Goldman-Rakic PS: Transient cholinesterase staining in the mediodorsal nucleus of the thalamus and its connections in the developing human and monkey brain. J Comp Neurol 219:431-447, 1983.

[9] Functional maturation of neocortex: a base of viability. Gatti MG, Becucci E, Fargnoli F, Fagioli M, Ådén U, Buonocore G. J Matern Fetal Neonatal Med. 2012;25 Suppl 1:101-3; 3D global and regional patterns of human fetal subplate growth determined in utero. Corbett-Detig J, Habas PA, Scott JA, Kim K, Rajagopalan V, McQuillen PS, Barkovich AJ, Glenn OA, Studholme C. Brain Struct Funct. 2011;215:255-63.

[10] Ibid at 4.

[11] Ibid at 6.

There is universal agreement that pain is detected by the fetus in the first trimester. The debate concerns how pain is *experienced*; i.e., whether a fetus has the same pain experience a newborn or an adult would have. While every individual's experience of pain is personal, a number of scientific observations address what brain structures are necessary for a mental or psychological experience of pain.

First, it is clear that children born without higher brain structures ('decorticate' patients) are capable of experiencing pain and also other conscious behaviors, including smiling, recognizing and distinguishing between familiar/unfamiliar people and situations, having preferences for particular kinds of music and having averse reactions to pain.[12] This indicates that the long-range connections that develop in the cortex only after 22 weeks (and are absent in these patients) are not obligatory for a psychological perception of pain. Similarly, experimental animals that have had the cortex removed also show a vigorous response to painful stimuli,[13] again indicating that late-developing cortical pathways are not required for pain perception and response.

The observations of human decorticate patients and experimentally decorticated animals noted above are consistent with what is known about the representation of consciousness and emotion in the brain. A recent review from the prestigious "Nature" series states, "Feelings constitute a crucial component of the mechanisms of life regulation, from simple to complex. Their neural substrates can be found at *all levels of the nervous system, from individual neurons to subcortical nuclei and cortical regions*." (emphasis added).[14] Importantly, development of brainstem and thalamic nuclei (among the "subcortical nuclei" mentioned above) occurs quite early in humans, with the earliest spino-thalamic connections forming by 12-18 weeks post sperm-egg fusion.[15] Similarly, a second recent review concludes that consciousness persists in the absence of "vast

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[12] The presence of consciousness in the absence of the cerebral cortex. Beshkar M. Synapse. 2008;62:553-6.; Consciousness in congenitally decorticate children: developmental vegetative state as self-fulfilling prophecy. Shewmon DA, Holmes GL, Byrne PA. Dev Med Child Neurol. 1999;41:364-74.; The role of primordial emotions in the evolutionary origin of consciousness. Denton DA, McKinley MJ, Farrell M, Egan GF. Conscious Cogn. 2009;18:500-14.; Consciousness without a cerebral cortex: a challenge for neuroscience and medicine. Merker B. Behav Brain Sci. 2007;30(1):63-81.

[13] Effects of partial decortication on opioid analgesia in the formalin test. Matthies BK, Franklin KB. Behav Brain Res. 1995;67:59-66.; Formalin pain is expressed in decerebrate rats but not attenuated by morphine. Matthies BK, Franklin KB. Pain. 1992; 51:199-206.

[14]The nature of feelings: evolutionary and neurobiological origins. Damasio A, Carvalho GB. Nat Rev Neurosci. 2013;14:143-52.

[15] Kostovic I, Goldman-Rakic PS: Transient cholinesterase staining in the mediodorsal nucleus of the thalamus and its connections in the developing human and monkey brain. J Comp Neurol 219:431-447, 1983.

regions of the cortex."[16]

Finally, direct experimental evidence from adult humans contradicts the assertion of ACOG,[17] JAMA[18] and Royal College of Obstetricians and Gynaecologists [19] that mature pain perception requires cortical circuitry. Ablation[20] or stimulation[21] of the cortex in humans does not affect pain perception, whereas ablation of lower centers, including the thalamus, does.[22] These neurological findings indicate that "mature" pain perception is largely localized to the thalamus. The spino-thalamic circuits required for pain perception are established between 12-18 weeks post sperm-egg fusion.

What we observe about fetal pain

The preceding sections of this statement have dealt with only the first principle outlined above for how we can determine whether another individual experiences pain; i.e., what we know about the neuroanatomical structures underlying pain perception. In addition, what we directly *observe* about fetal pain is very clear and unambiguous. Fetuses at 20 weeks post sperm-egg fusion have an increase in stress hormones in response to painful

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[16] Minimal neuroanatomy for a conscious brain: homing in on the networks constituting consciousness. Morsella E, Krieger SC, Bargh JA. Neural Netw. 2010;23:14-5.
[17] *Amicus Curiae Brief,* American College of Obstetricians and Gynecologists And American Congress of Obstetricians and Gynecologists. Paul A. Isaacson et al., v. Tom Horne No. 12-16670. United States Court of Appeals for the Ninth Circuit.
[18] Fetal pain: a systematic multidisciplinary review of the evidence. Lee SJ, Ralston HJ, Drey EA, Partridge JC, Rosen MA. JAMA. 2005;294:947-54.
[19] Royal College of Obstetricians and Gynaecologists, Fetal Awareness: Review of Research and Recommendations for Practice (Mar. 2010)
[20] Ibid at 12 and 13.
[21] Motor cortex stimulation in patients with post-stroke pain: conscious somatosensory response and pain control. Fukaya C, Katayama Y, Yamamoto T, Kobayashi K, Kasai M, Oshima H. Neurol Res. 2003;25:153-6.; Stimulation of the human cortex and the experience of pain: Wilder Penfield's observations revisited. Mazzola L, Isnard J, Peyron R, Mauguière F. Brain. 2012;135:631-40.
[22] Brooks JC, Zambreanu L, Godinez A, et al: Somatotopic organisation of the human insula to painful heat studied with high resolution functional imaging. Neuroimage 27:201-209, 2005; Nandi D, Aziz T, Carter H, et al: Thalamic field potentials in chronic central pain treated by periventricular gray stimulation: a series of eight cases. Pain 101:97-107, 2003; Nandi D, Liu X, Joint C, et al: Thalamic field potentials during deep brain stimulation of periventricular gray in chronic pain. Pain 97:47- 51, 2002.; Long-term outcomes of deep brain stimulation for neuropathic pain. Boccard SG, Pereira EA, Moir L, Aziz TZ, Green AL. Neurosurgery. 2013;72:221-30.; Regional cerebral perfusion differences between periventricular grey, thalamic and dual target deep brain stimulation for chronic neuropathic pain. Pereira EA, Green AL, Bradley KM, Soper N, Moir L, Stein JF, Aziz TZ. Stereotact Funct Neurosurg. 2007;85:175-83.; Penfield W, Jasper HH. Epilepsy and the Functional Anatomy of the Human Brain. Boston: Little, Brown & Co; 1954.

experiences that can be eliminated by appropriate anesthesia.[23] Multiple studies clearly indicate "the human fetus from 18–20 weeks elaborates pituitary-adrenal, sympatho-adrenal, and circulatory stress responses to physical insults."[24] All of these responses reflect a mature, body-wide response to pain.

Fetuses delivered prematurely, as early as 23 weeks, show clear pain-related behaviors[25] We know less about infants delivered prior to 23 weeks only because so few are available for study. Strikingly, the earlier infants are delivered, the stronger their response to pain.[26] These and many other direct observations of fetal behavior and physiology have resulted in a clear consensus among professional anesthesiologists (highly specialized physicians who are experts in pain management) that the use of medications to relieve pain is warranted in cases of fetal surgery.[27] Many of the advocates of fetal anesthesia make no claims regarding the *qualitative* nature of fetal pain, but based on both the scientific literature and on their own observations, they clearly conclude that pain *exists* for these fetuses and that as physicians they are obligated to address fetal pain medically, despite the many serious challenges and medical risks this procedure entails.[28]

Our own experience; Why fetal pain matters

As individuals and as a society we must choose the attitude we will embrace regarding fetal pain. Those who insist, "It is impossible to know what a fetus experiences," are denying the obvious fact that it is equally impossible to know what any other human individual experiences at any stage of life. This is not a legitimate argument for ignoring

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[23] Effect of direct fetal opioid analgesia on fetal hormonal and hemodynamic stress response to intrauterine needling. Fisk NM, Gitau R, Teixeira JM, Giannakoulopoulos X, Cameron AD, Glover VA. Anesthesiology. 2001;95:828-35.

[24] Ibid at 22. See also; Human fetal and maternal noradrenaline responses to invasive procedures. Giannakoulopoulos X, Teixeira J, Fisk N, Glover V. Pediatr Res. 1999;45:494-9.; Fetal plasma cortisol and beta-endorphin response to intrauterine needling. Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Lancet. 1994;344:77-81.; Acute cerebral redistribution in response to invasive procedures in the human fetus. Teixeira JM, Glover V, Fisk NM. Am J Obstet Gynecol. 1999;181:1018-25.

[25] Pain behaviours in Extremely Low Gestational Age infants. Gibbins S, Stevens B, Beyene J, Chan PC, Bagg M, Asztalos E. Early Hum Dev. 2008;84:451-8.

[26] Determinants of premature infant pain responses to heel sticks. Badr LK, Abdallah B, Hawari M, Sidani S, Kassar M, Nakad P, Breidi J. Pediatr Nurs. 2010;36:129-36.

[27] Use of fetal analgesia during prenatal surgery. Bellieni CV, Tei M, Stazzoni G, Bertrando S, Cornacchione S, Buonocore G.J Matern Fetal Neonatal Med. 2013;26:90-5.; Towards state-of-the-art anesthesia for fetal surgery: obstacles and opportunities. Kuczkowski KM. Rev Esp Anestesiol Reanim. 2013 Jan;60(1):3-6.; Fetal and maternal analgesia/anesthesia for fetal procedures. Van de Velde M, De Buck F. Fetal Diagn Ther. 2012;31:201-9.

[28] Anesthesia for fetal surgery. Lin EE, Tran KM. Semin Pediatr Surg. 2013;22:50-5.; Anesthesia for in utero repair of myelomeningocele. Ferschl M, Ball R, Lee H, Rollins MD. Anesthesiology. 2013;118:1211-23.

what we know from science and from our own observations. Similarly, those who insist, "Neuroscientists agree the cortex is required for pain perception," are denying the ample modern scientific evidence from credible, professional neuroscientists that contradicts this conclusion. The absence of a universal consensus regarding what anatomical structures are required for the complex (and personal) psychological experience of "conscious" pain perception does not excuse us from making a decision based on the best evidence available.

In the end, when considering pain in any other human individual we must choose, based on what we know and what we observe, whether we will give that individual the benefit of the doubt, out of compassion, empathy and justice, or whether we will ignore the pain they experience simply because the precise psychological quality of their pain cannot be known with certainty. And this choice is as much about the kind of society we want to be as it is about the experience of the fetus.

Imposing pain on any pain-capable living creature is *cruelty*. And ignoring the pain experienced by another human individual for any reason is *barbaric*. We don't need to know if a human fetus is self-reflective or even self-aware to afford it the same consideration we currently afford other pain-capable species. We simply have to decide whether we will choose to ignore the pain of the fetus or not.

From the perspective of neuroscience, it is unclear precisely what "psychological" aspects of a mature pain experience are in place at precisely what point in either human prenatal or *postnatal* development. It is impossible for me to know with certainty whether another adult, a teenager or a fetus experiences pain in precisely the same manner I do. Yet it is *entirely* uncontested that a fetus experiences pain in some capacity, from as early as 8 weeks of development. Moreover, most modern neuroscientists have concluded that the thalamic circuitry developed by 18 weeks post sperm-egg fusion is primarily responsible for human experience of pain at all stages of life.

Given that fetuses are members of the human species—*human beings like us*—they deserve the benefit of the doubt regarding their experience of pain and protection from cruelty under the law.

In light of the scientific facts, the observations of medical professionals, our own experience of pain, and our indirect experience of others' pain, we must conclude that there is indeed a "compelling governmental interest in protecting the lives of unborn children from the stage at which substantial medical evidence indicates that they are capable of feeling pain." And this unambiguously requires a 20 week fetus to be protected from pain, as propopsed under H.R. 1797.