SENATE
PUBLIC HEALTH, WELFARE & SAFETY

Exhibit No. 4
Date 4/1/2015
Bill No. HB 479

LC# 2187

Senate Co-sponsors

Chief Sponsor must sign front page of original bill
Co-sponsors must sign this sheet and may sign the front of the bill

Ankney
Arntzen
Barrett, Deb
Barrett, Dick
Blasdel
Brenden
Brown, D
Brown, T
Buttrey
Caferro
Cohenour
Connell
Driscoll
Facey
Fielder
Hamlett
Hansen
Hinkle
Hoven
Howard
Jones
Kary
Kaufmann
Keane
Keenan
Larsen
Malek
McNally
Moe
Moore
Phillips
Pomnichowski
Ripley
Rosendale
Sales
Sands
Sesso
Smith
Stewart-Peregoy
Swandal
Taylor
Thomas
Tutvedt
Vance
Vincent
Vuckovich
Webb
Whitford
Windy Boy
Wolken

HOUSE RULE CHANGE FOR 2015 LEGISLATIVE SESSION

H40-30. Cosponsors. (1) Prior to submitting legislation to the Chief Clerk for introduction, the chief sponsor may add representatives and senators as cosponsors. A legislator shall sign the cosponsor form attached to the legislation in order to be added as a cosponsor.

(2) After legislation is submitted for introduction but before the legislation returns from the first House committee, the chief sponsor may add or remove cosponsors by filing a cosponsor form with the Chief Clerk. This filing must be noted by the Chief Clerk for the record on Order of Business No. 11.

LC# 2187

House Co-sponsors

Chief Sponsor must sign front page of original bill
Co-sponsors must sign this sheet and may sign the front of the bill

Ballance	Nancy Ballance	Hill		Pease-Lopez	
Bennett, B		Hollandsworth		Peppers	
Bennett, J	Jerry Bennett	Holmlund		Perry	
Berglee	Seth Berglee	Hunter		Person	
Berry		Jacobson		Pierson	
Brodehl		Jones		Pinocci	[illegible]
Brown, B	[illegible]	Karjala		Pope	
Brown, Z		Kelker		Price	
Burnett	Tom Burnett	Kipp		Randall	
Clark		Knudsen	[illegible]	Redfield	
Cook		Lamm		Regier	Keith Regier
Court		Lang		Ricci	
Cuffe		Laszloffy		Richmond	[illegible]
Curdy		Lavin		Salomon	
Custer		Lieser		Schreiner	
Doane	Shirley Dover	Lynch		Schwaderer	
[illegible]dik		MacDonald		Shaw	
[illegible]nwell		Mandeville		Smith, B	
Eck		Manzella		Staffanson	
Ehli	[illegible]	McCarthy		Steenberg	
Ellis		McClafferty		Swanson	
Essmann		McConnell		Tropila	
Fiscus	Clayton Fiscus	McKamey		Tschida	[illegible]
Fitzpatrick		Mehlhoff		Wagoner	
Flynn		Meyers		Webber	
Funk		Miller		Welborn	
Garner		Monforton	[illegible]	White	
Glimm	[illegible]	Moore		Williams	
Greef		Mortensen	[illegible]	Wilson	
Hagstrom		Noland	Mark Noland	Wittich	
Harris		Noonan		Woods	
Hayman		Olsen		Zolnikov	
Hertz		Olszewski			
Hess	[illegible]	Osmundson	[illegible]		

House Rule Change for 2015 Legislative Session

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I am writing in support of HB 479, the Montana Unborn Child Pain and Suffering Prevention Act.

As both a Neonatologist who cares for vulnerable preterm infants born as early as 23 weeks gestation, and a Developmental and Behavioral Pediatrician who monitors the long term effects of medical interventions on the fetus and neonate, I have witnessed the evolution in our understanding of the extremely preterm infant's perception of pain. Early in my career I witnessed extremely preterm infants suffering through painful procedures without anesthesia, due to the perception that preterm infants did not feel pain. I then saw, in these same infants, the long term effects of this early and profound overstimulation of their developing nervous system's pain centers.

Fortunately, we have learned a great deal about the development of the human nervous system over the past 2 decades. We now understand that the somatosensory system...the part of our nervous system that senses touch, pressure, hot and cold, and most importantly pain...has already developed by 20 weeks of gestation. We have also learned that infants cared for in the NICU as early as 23 weeks are actually so sensitive to pain that they easily become OVER stimulated by painful experiences, which can result in significant long term effects.

At any viable age, whether still a fetus, or born too soon, an infant perceives pain. With this awareness, we provide even our tiniest, most vulnerable patients with anesthesia for any painful procedure. And knowing this, it seems inhumane to perform any painful procedure on a fetus or neonate at 20 weeks or more without appropriate anesthesia.

Thank you for considering HB 479.

Bonnie Stephens, MD
Neonatologist and Developmental-Behavioral Pediatrician
Community Medical Center
Missoula

Subject: Re: Fetal Anesthesia Bill

Date: Tuesday, March 10, 2015 9:01:48 PM MT

From: Shaun J. Gillis

To: Olszewski, Albert (Rep), aolszewski@flatheadortho.com

Dear Representative Olszewski,

I am writing in SUPPORT of HB 479, the bill that would require anesthesia for fetal surgery or abortions on fetuses at or beyond 20 weeks of gestation. This is a timely bill as we know there are fetal surgical procedures performed in Montana and those human babies deserve to have anesthesia as much as any person who can feel pain.

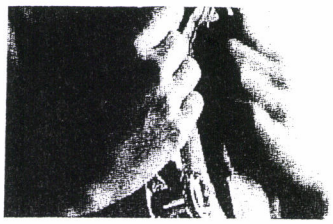
Speaking to the fact that fetal procedures are being done, within the last few years I personally witnessed a fetal bladder decompression of over 2 liters of fluid in a term baby who had severe anomalies and whose bladder was inhibiting a vaginal delivery. The baby tolerated it but it was difficult to imagine the discomfort he felt during the multiple times the needle was inserted through his abdomen into his bladder.

Regarding fetal pain, there is scientific evidence proving that fetuses beyond 20 weeks of gestation can feel pain. Personally I have witnessed it while performing amniocenteses on women beyond the 20 week gestational age. On occasion, during the procedure, the baby's hand or foot will inadvertently hit the needle and the baby quickly recoils from the pain of being poked with that needle just as you or I would.

Representative Olszewski, thank you for your work on this important issue.

Warmly,

Shaun J. Gillis, MD
Bozeman Deaconess Women's Specialists
Bozeman, MT 59715



Fetal Pain: The Evidence

The **eleven points** below summarize the substantial medical and scientific evidence that unborn children can feel pain by 20 weeks after fertilization.

www.doctorsonfetalpain.org

first posted March 14, 2011, (updated February, 2013)

1: Pain receptors (nociceptors) are present throughout the unborn child's entire body by no later than 20 weeks after fertilization and nerves link these receptors to the brain's thalamus and subcortical plate by no later than 20 weeks after fertilization.

DOCUMENTATION:

a. **Pain receptors (nociceptors) are present throughout the unborn child's entire body by no later than 20 weeks.**

1. **Myers, 2004**, p.241, para.2, "The first essential requirement for pain is the presence of sensory receptors, which first develop in the perioral area at approximately 7 weeks gestation and are diffusely located throughout the body by 14 weeks.[95]"

   Myers LB, Bulich LA, Hess, P, Miller, NM. Fetal endoscopic surgery: indications and anaesthetic management. *Best Practice & Research Clinical Anaesthesiology.* 18:2 (2004) 231-258.

   [95]Smith S. Commission of Inquiry into Fetal Sentience. London: CARE, 1996.

2. **Derbyshire, 2010**, p.7, para.2, "For the foetus, an existence of 'pain' rests upon the existence of a stimulus that poses a threat to tissue, being detected by a nervous system capable of preferentially

responding to stimuli that pose a threat to tissue. The entire experience is completely bounded by the limits of the sensory system and the relationship between that system and the stimulus. If pain is conceived of in this manner then it becomes possible to talk of foetal pain anytime between 10 and 17 weeks GA [gestational age] when nociceptors develop and mature, and there is evidence of behavioural responses to touch."

Note: Derbyshire's other published works indicate that he believes pain requires subjective human experience, not possible until after birth; nonetheless, he acknowledges this finding.

Derbyshire SW, Foetal pain? *Best Practice & Research Clinical Obstetrics and Gynaecology* 24:5 (2010) 647-655.

3. **Anand, 1987**, p.2, para.2, "Cutaneous sensory receptors appear in the perioral area of the human fetus in the 7th week of gestation; they spread to the rest of the face, the palms of the hands, and the soles of the feet by the 11th week, to the trunk and proximal parts of the arms and legs by the 15th week, and to all cutaneous and mucous surfaces by the 20th week.[25,26]"

   Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. *New England Journal of Medicine.* 317:21 (1987) 1321-1329.

   [25]Humphrey T. Some correlations between the appearance of human fetal reflexes and the development of the nervous system. *Progress in Brain Research.* 4 (1964) 93-135.

   [26]Valnaan HB, Pearson JP. What the fetus feels. *British Medical Journal.* 280 (1980) 233-234.

4. **Vanhatalo, 2000**, p.146, col.2, para.2, "First nociceptors appear around the mouth as early as the seventh gestational week; by the 20th week these are present all over the body."

   Vanhalto S, van Nieuwenhuizen O. Fetal Pain? *Brain & Development.* 22 (2000) 145-150.

5. **Brusseau, 2008**, p.14, para.3, "The first essential requirement for nociception is the presence of sensory receptors, which develop first in the perioral area at around 7 weeks gestation. From here, they develop in the rest of the face and in the palmar surfaces of the hands and soles of the feet from 11 weeks. By 20 weeks, they are present throughout all of the skin and mucosal surfaces.[19]

   Brusseau R. Developmental Perpectives: is the Fetus Conscious? *International Anesthesiology Clinics.* 46:3 (2008) 11-23.

   [19]Simons SH, Tibboel D. Pain perception development and maturation. *Seminars on Fetal and Neonatal Medicine.* 11 (2006) 227-231.

6. **Rollins, 2012**, p.465, "Immature skin nociceptors are probably present by 10 weeks and definitely present by 17 weeks. Nociceptors develop slightly later in internal organs. Peripheral nerve fibers that control movement first grow into the spinal cord at about 8 weeks of gestation."

Mark D. Rollins, Mark A. Rosen, "Anesthesia for Fetal Intervention and Surgery", in *Gregory's Pediatric Anesthesia*, ed. George A. Gregory & Dean B. Adropoulos (West Sussex: Wiley-Blackwell, 2012), 444–474, 465.

b. nerves link these receptors to the brain's thalamus and subcortical plate by no later than 20 weeks after fertilization.

1. **Van Scheltema 2008**, p.313, para.1 — "The connection between the spinal cord and the thalamus (an obligatory station through which nearly all sensory information must pass before reaching the cortex) starts to develop from 14 weeks onwards and is finished at 20 weeks."

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review*. 19:4 (2008) 311-324.

2. **Glover, 1999**, p.882, col.1, para.1, "Most incoming pathways, including nociceptive ones, are routed through the thalamus and, as stated above, penetrates the subplate zone from about 17 weeks… These monoamine fibres start to invade the subplate zone at 13 weeks and reach the cortex at about 16 weeks. This puts an early limit on when it is likely that the fetus might be aware of anything that is going on in its body or elsewhere."

   Glover V. Fetal pain: implications for research and practice. *British Journal of Obstetrics and Gynaecology*. 106 (1999) 881-886.

3. **Lee, 2005**, p.950, col.1, "In contrast to direct thalamocortical fibers, which are not visible until almost the third trimester, thalamic afferents begin to reach the somatosensory subplate at 18 weeks' developmental age (20 weeks' gestational age)[16] and the visual subplate at 20 to 22 weeks' gestational age. These afferents appear morphologically mature enough to synapse with subplate neurons.[17]"

   Note: Lee et al. believe that pain requires conscious cortical processing, which they deem unlikely until 29 or 30 weeks; nonetheless, they acknowledges this finding.

   Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association*. 294:8 (2005) 947-954.

   [16]Kostovic I, Rakic P. Developmental history of the transient subplate zone in the visual and somatosensory cortex of the macaque monkey and human brain. *Journal of Comparative Neurology*. 297 (1990) 441-470.

   [17]Hevner RF. Development of connections in the human visual system during fetal mid-gestation: a Diltracing study. *Journal of Experiemental Neuropathology & Experimental Neurology*. 59 (2000) 385-392.

4. **Gupta, 2008**, p.74, col.2, para.1, " Peripheral nerve receptors develop between 7 and 20 weeks gestation… Spinothalamic fibres (responsible for transmission of pain) develop between 16 and 20 weeks gestation, and thalamocortical fibres between 17 and 24 weeks gestation."

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain*. 8:2 (2008) 71-75.

5. **Van de Velde, 2012**, p 206, para.3, "To experience pain an intact system of pain transmission from the peripheral receptor to the cerebral cortex must be available. Peripheral receptors develop from the seventh gestational week. From 20 weeks' gestation [= 20 weeks post-fertilization] peripheral receptors are present on the whole body. From 13 weeks' gestation the afferent system located in the substantia gelatinosa of the dorsal horn of the spinal cord starts developing. Development of afferent fibers connecting peripheral receptors with the dorsal horn starts at 8 weeks' gestation. Spinothalamic connections start to develop from 14 weeks' and are complete at 20 weeks' gestation, whilst thalamocortical connections are present from 17 weeks' and completely developed at 26–30 weeks' gestation. From 16 weeks' gestation pain transmission from a peripheral receptor to the cortex is possible and completely developed from 26 weeks' gestation."

   Marc Van de Velde & Frederik De Buck, Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures. *Fetal Diagn Ther* 31(4) (2012) 201-9.

2: By 8 weeks after fertilization, the unborn child reacts to touch. After 20 weeks, the unborn child reacts to stimuli that would be recognized as painful if applied to an adult human, for example by recoiling.

DOCUMENTATION:

a. **By 8 weeks after fertilization, the unborn child reacts to touch.**

1. **Gupta, 2008**, p.74, col.2, para.2, "Movement of the fetus in response to external stimuli occurs as early as 8 weeks gestation…"

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain.* 8:2 (2008) 71-75.

2. **Glover, 2004**, p.36, para.4, "The fetus starts to make movements in response to being touched from eight weeks, and more complex movements build up, as detected by real time ultrasound, over the next few weeks."

   Glover V. The fetus may feel pain from 20 weeks; The Fetal Pain Controversy. *Conscience.* 25:3 (2004) 35-37.

3. **Myers 2004**, p.241, para.6, "A motor response can first be seen as a whole body movement away from a stimulus and observed on ultrasound from as early as 7.5 weeks' gestational age. The perioral area is the first part of the body to respond to touch at approximately 8 weeks, but by 14 weeks most of the body is responsive to touch."

   Myers LB, Bulich LA, Hess, P, Miller, NM. Fetal endoscopic surgery: indications and anaesthetic management. *Best Practice & Research Clinical Anaesthesiology.* 18:2 (2004) 231-258.

4. **Derbyshire, 2008**, p.119, col.2, para.4, "Responses to touch begin at 7–8 weeks gestation when touching the peri-oral region results in a contralateral bending of the head. The palms of the hands become sensitive to stroking at 10-11 weeks gestation and the rest of the body becomes sensitive around 13-14 weeks gestation.[35]"

   Note: Derbyshire's other published works indicate that he believes pain requires subjective human experience, not possible until after birth; nonetheless, he acknowledges this finding.

   Derbyshire SW. Fetal Pain: Do We Know Enough to Do the Right Thing? *Reproductive Health Matters*. 16: 31Supp. (2008) 117-126.

   [35]Fitzgerald M. Neurobiology of fetal and neonatalpain. In:Wall P, Melzack R, editors. Textbook of Pain. Oxford Churchill Livingstone, 1994. p.153–63.

5. **Kadić, 2012**, page 3, "The earliest reactions to painful stimuli motor reflexes can be detected at 7.5 weeks of gestation (Table 2)."

   Salihagić Kadić, A., Predojević, M., Fetal neurophysiology according to gestational age, *Seminars in Fetal & Neonatal Medicine.* 17:5 (2012) 1–5, 3.

b. After 20 weeks following fertilization, the unborn child reacts to stimuli that would be recognized as painful if applied to an adult human, for example by recoiling.

1. **Gupta, 2008**, p. p.74, col.2, para.2, "Behavioural responses... Response to painful stimuli occurs from 22 weeks gestation [= 20 weeks post-fertilization]."

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain.* 8:2 (2008) 71-75.

2. **Giannakoulopoulos, 1994**, p.77, col.2, para.3, "We have observed that the fetus reacts to intrahepatic vein needling with vigorous body and breathing movements, which are not present during placental cord insertion needling."

   Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet.* 344 (1994) 77-81.

3. **Lowery, 2007**, p.276, col.2, para1, "Fetuses undergoing intrauterine invasive procedures, definitely illustrative of pain signaling, were reported to show coordinated responses signaling the avoidance of tissue injury.[15]"

   Lowery CL, Hardman MP, Manning N, Clancy B, Hall RW, Anand KJS. Neurodevelopmental Changes of Fetal Pain. *Seminars in Pernatology.* 31 (2007) 275-282.

   [15]Williams C. Framing the fetus in medical work: rituals and practices. *Social Science & Medicine.* 60 (2005) 2085-2095.

4. **Mellor, 2005**, p.457, col.1, para.2, "For instance, the human fetus responds to intrahepatic needling (versus umbilical cord sampling) by moving away and with an increase in the levels of circulating stress hormones. . .[71,72,74,75]"

   Note: Mellor et al. believe that the unborn child is kept 'asleep' in utero, *and therefore does not perceive pain; nonetheless, they recognize this finding.*

   Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. The importance of 'awareness' for understanding fetal pain. *Brain Research Reviews.* 49 (2005) 455-471.

   [71] Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet.* 344 (1994) 77-81.

   [72]Giannakoulopoulos X, Teixeira J, Fisk N. Human fetal and maternal noradrenaline responses to invasive procedures. *Pediatric Research.* 45 (1999) 494-499.

   [74]Gitau R, Fisk NM, Teixeira JM, Cameron A, Glover V. Fetal hypothalamic–pituitary–adrenal stress responses to invasive procedures are independent of maternal responses. *Journal of Clinical Endocrinology and Metabolism.* 86 (2001) 104-109.

   [75]Gitau R, Fisk NM, Glover V. Human fetal and maternal corticotrophin releaseing hormone responses to acute stress. *Archives of Disease in Childhood - Fetal Neonatal Edition.* 89 (2004) F29-F32.

5. **Bocci, 2007**, page 31-32, "By week 14, the repertoire of movements is complete. Fetal movements may be spontaneous, reflecting individual needs of the fetus, or may be evoked, reflecting fetal sensitivity to its environment."

   C. Bocchi et al, Ultrasound and Fetal Stress: Study of the Fetal Blink-Startle Reflex Evoked by Acoustic Stimuli. *Neonatal Pain*, ed. Giuseppe Buonocore & Carlo V. Bellieni (Milan: Springer, 2007), 31–32.

3: In the unborn child, application of such painful stimuli is associated with significant increases in stress hormones known as the stress response.

DOCUMENTATION:

1. **Tran, 2010**, p.44, col.1, para.7, "Invasive fetal procedures clearly elicit a stress response…"

   Tran, KM. Anesthesia for fetal surgery. *Seminars in Fetal & Neonatal Medicine.* 15 (2010) 40-45.

2. **Myers, 2004**, p.242, para.2, "Human fetal endocrine responses to stress have been demonstrated from as early as 18 weeks' gestation. Giannakoulopoulos et al[99] first demonstrated increases in fetal plasma concentrations of cortisol and β-endorphin in response to prolonged needling of the intrahepatic vein (IHV) for intrauterine transfusion. The magnitude of these stress responses directly correlated with the duration of the procedure. Fetuses having the same procedure of transfusion, but via the non-innervated placental cord insertion, failed to show these hormonal responses. Gitau et al[100] observed a rise in β-endorphin during intrahepatic transfusion from 18 weeks' gestation, which was seen throughout pregnancy independent both of gestation and the maternal response. The fetal cortisol response, again independent of the mother's, was observed from 20 weeks' gestation.[100] Fetal intravenous administration of the opioid receptor agonist, fentanyl, ablated the β-endorphin response and partially ablated the cortisol response to the stress of IHV needling, suggesting an analgesic effect.[101] A similar, but faster, response is seen in fetal production of noradrenalin to IHV needling. This too is observed in fetuses as early as 18 weeks, is independent to the maternal response and increases to some extent with gestational age.[102] Thus, from these studies one can conclude that the human fetal hypothalamic– pituitary–adrenal axis is functionally mature enough to produce a β-endorphin response by 18 weeks and to produce cortisol and noradrenalin responses from 20 weeks' gestation."

   Myers LB, Bulich LA, Hess, P, Miller, NM. Fetal endoscopic surgery: indications and anaesthetic management. *Best Practice & Research Clinical Anaesthesiology.* 18:2 (2004) 231-258.

   [99] Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet.* 344 (1994) 77-81.

   [100] Gitau R, Fisk NM, Teixeira JM, Cameron A, Glover V. Fetal hypothalamic–pituitary–adrenal stress responses to invasive procedures are independent of maternal responses. *Journal of Clinical Endocrinology and Metabolism.* 86 (2001) 104-109.

   [101]Fisk NM, Gitau R, Teixeira MD, Giannakoulopoulos, X, Cameron, AD, Glover VA. Effect of Direct Fetal Opioid Analgesia on Fetal Hormonal and Hemodynamic Stress Response to Intrauterine Needling. *Anesthesiology.* 95 (2001) 828-835.

   [102]Giannakoulopoulos X, Teixeira J, Fisk N, Glover V. Human fetal and maternal noradrenaline responses to invasive procedures. *Pediatric Research.* 45(1999) 494-499.

3. **Derbyshire, June 2008**, p.4, col.1, para.5, "Another stage of advancing neural development takes place at 18 weeks, when it has been demonstrated that the fetus will launch a hormonal stress response to direct noxious stimulation."

Note: Derbyshire believes that pain requires subjective human experience, not possible until after birth; nonetheless, he acknowledges this finding.

Derbyshire SW. Fetal Pain: Do We Know Enough to Do the Right Thing? *Reproductive Health Matters*. 16: 31Supp. (2008) 117-126.

4. **Gupta, 2008**, p.74, col.2, para.3, "Fetal stress in response to painful stimuli is shown by increased cortisol and β-endorphin concentrations, and vigorous movements and breathing efforts.[7,9] There is no correlation between maternal and fetal norepinephrine levels, suggesting a lack of placental transfer of norepinephrine. This independent stress response in the fetus occurs from 18 weeks gestation.[10]"

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain.* 8:2 (2008) 71-75.

   [7]Boris P, Cox PBW, Gogarten W, Strumper D, Marcus MAE. Fetal surgery, anaesthesiological considerations. *Current Opinion in Anaesthesiology.* 17 (2004) 235-240.

   [9]Giannakoulopoulos X, Teixeira J, Fisk N. Human fetal and maternal noradrenaline responses to invasive procedures. *Pediatric Research.* 45 (1999) 494-499.

   [10]Marcus M, Gogarten W, Louwen F. Remifentanil for fetal intrauterine microendoscopic procedures. *Anesthesia & Analgesia.* 88 (1999) S257.

5. **Fisk, 2001**, p.828, col.2, para.3, "Our group has shown that the human fetus from 18-20 weeks elaborates pituitary-adrenal, sympatho-adrenal, and circulatory stress responses to physical insults." p.834, col.2, para.2, "This study confirms that invasive procedures produce stress responses…."

   Fisk NM, Gitau R, Teixeira MD, Giannakoulopoulos, X, Cameron, AD, Glover VA. Effect of Direct Fetal Opioid Analgesia on Fetal Hormonal and Hemodynamic Stress Response to Intrauterine Needling. *Anesthesiology.* 95 (2001) 828-835.

6. **Kadić, 2012,** page 3, "As early as 16-18 weeks, fetal cerebral blood flow increases during invasive procedures.[26,27] An elevation of noradrenaline, cortisol, and beta-endorphin plasma levels, in response to needle pricking of the innervated hepatic vein for intrauterine transfusion, was registered in a 23-week-old fetus [= 21 weeks post-fertilization]." (Table 2)."

   Salihagić Kadić, A., Predojević, M., *Fetal neurophysiology according to gestational age*, SEMINARS IN FETAL & NEONATAL MEDICINE (2012) 1–5, 3, doi:10.1016/j.siny.2012.05.007.

   [26] Teixeira JM, Glover V, Fisk NM. Acute cerebral redistribution in response to invasive procedures in the human fetus. Am J Obstet Gynecol 1999;181:1018e25.

   [27] Smith RP, Gitau R, Glover V, et al. Pain and stress in the human fetus. Eur J Obstet Gynecol Reprod Biol 2000;92:161e5.

4: Subjection to such painful stimuli is associated with long-term harmful neurodevelopmental effects, such as altered pain sensitivity and, possibly, emotional, behavioral, and learning disabilities later in life.

DOCUMENTATION:

1. **Van de Velde, 2006**, p.234, col.1, para.3, "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.[22,33] These findings should focus the attention of clinicians on the long-term impact of early painful experiences, and highlight the urgent need for developing therapeutic strategies for the management of neonatal and fetal pain."

   Van de Velde M, Jani J, De Buck F, Deprest J. Fetal pain perception and pain management. *Seminars in Fetal & Neonatal Medicine.* 11 (2006) 232-236.

   [22] Vanhalto S, van Nieuwenhuizen O. Fetal Pain? *Brain & Development.* 22 (2000) 145-150.

   [33]Anand KJS. Pain, plasticity, and premature birth: a prescription for permanent suffering? *Nature Medicine.* 6 (2000) 971-973.

2. **Vanhatalo, 2000**, p.148, col.2, para.4, "All these data suggest that a repetitive, or sometimes even strong acute pain experience is associated with long-term changes in a large number of pain-related physiological functions, and pain or its concomitant stress increase the incidence of later complications in neurological and/or psychological development."

   Note: Vanhalto & Niewenhuizen believe that pain requires cortical processing; nevertheless, they acknowledge that, "noxious stimuli may have adverse effects on the developing individual regardless of the quality or the level of processing in the brain...after the development of the spinal cord afferents around the gestational week 10, there may be no age limit at which one can be sure noxae are harmless." (p.149, col.1, para.2).

   Vanhalto S, van Nieuwenhuizen O. Fetal Pain? *Brain & Development.* 22 (2000) 145-150.

3. **Gupta, 2008**, p.74, col.2, para.3, " There may be long-term implications of not providing adequate fetal analgesia such as hyperalgesia, and possibly increased morbidity and mortality."

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain.* 8:2 (2008) 71-75.

4. **Lee, 2005,** p.951, col.1, para.3, "When long-term fetal well-being is a central consideration, evidence of fetal pain is unnecessary to justify fetal anaesthesia and analgesia because they serve other purposes unrelated to pain reduction, including ... (3) preventing hormonal stress responses associated with poor surgical outcomes in neonates[71,72]; and (4) preventing possible adverse effects on long-term neurodevelopment and behavioral responses to pain.[73-75]"

   Note: Lee et al. believe that pain requires conscious cortical processing, which they deem unlikely until 29 or 30 weeks; nonetheless, they acknowledges this finding.

Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association.* 294:8 (2005) 947-954.

[71]Anand KJ, Hickey PR.Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. New England Journal of Medicine. 326 (1992) 1-9.

[72]Anand KJ, Sippell WG, Aynsley-Green A. Randomised trial of fentanyl anaesthesia in preterm babies undergoing surgery: effects on the stress response. *Lancet.* 329 (1987) 62-66.

[73]Johnston CC, Stevens BJ. Experience in a neonatal intensive care unit affects pain response. *Pediatrics.* 98 (1996) 925-930.

[74]Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. *Lancet.* 349 (1997) 599-603.

[75]Taylor A, Fisk NM, Glover V. Mode of delivery and subsequent stress response. *Lancet.* 355 (2000) 120.

5. **Rosen, 2009,** p131-132, "Although we do not know exactly when the fetus can experience pain, noxious stimulation during fetal life causes a stress response, which could have both short- and long-term adverse effects on the developing central nervous system."

   Mark A. Rosen, "Anesthesia for Fetal Surgery and Other Intrauterine Procedures," in Chesnut's *Obstetric Anesthesia: Principles and Practice*, ed. David H. Chestnut et al (Philadelphia: Mosby, 2009), 131-132.

6. **Van de Velde, 2012,** "This nociceptive stimulation of the fetus also has the potential for longer-term effects, so there is a need for fetal analgesic treatment."

   Marc Van de Velde & Frederik De Buck, Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures. *Fetal Diagn Ther* 31(4) (2012) 201-9.

5: For the purposes of surgery on unborn children, fetal anesthesia is routinely administered and is associated with a decrease in stress hormones compared to their level when painful stimuli are applied without such anesthesia.

DOCUMENTATION:

a. **For the purposes of surgery on unborn children, fetal anesthesia is routinely administered.**

1. **Giuntini, 2007,** "It has also been shown that fetuses feel pain from week 18. This has given rise to the practice of using fetal anesthesia for surgery or invasive diagnostic procedures in utero."

   L. Giuntini & G. Amato, *Analgesic Procedures in Newborns.*, in NEONATAL PAIN 73 (Giuseppe Buonocore & Carlo V. Bellieni ed., 2007).

2. **Van de Velde, 2005**, p.256, col.2, para.2, "Therefore, it has been suggested that pain relief has to be provided during *in utero* interventions on the fetus from mid-gestation (20 weeks) on.[32-34]"

   Van de Velde M, Van Schoubroeck DV, Lewi LE, Marcus MAE, Jani JC, Missant C, Teunkens A, Deprest J. Remifentanil for Fetal Immobilization and Maternal Sedation During Fetoscopic Surgery: A Randomized, Double-Blind Comparison with Diazepam. *Anesthesia & Analgesia.* 101 (2005) 251-258.

   [32]Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling *Lancet.* 344 (1994) 77-81.

   [33]Giannakoulopoulos X, Teixeira J, Fisk N. Human fetal and maternal noradrenaline responses to invasive procedures. *Pediatric Research.* 45 (1999) 494-499.

   [34]Anand KJS, Maze M. Fetuses, fentanyl, and the stress response. *Anesthesiology.* 95 (2001) 823-825.

3. **Myers, 2004**, p.236, para.3, "The anaesthesiologist is required to provide both maternal and fetal anaesthesia and analgesia while ensuring both maternal and fetal haemodynamic stability…Since substantial evidence exists demonstrating the ability of the second trimester fetus to mount a neuroendrocrine response to noxious stimuli…fetal pain management must be considered in every case."

   p.240, col.5, "A substantial amount of both animal and human research demonstrated that the fetus is able to mount a substantial neuroendocrine response to noxious stimuli as early as the second trimester of pregnancy. Fetal neuroanatomical development further substantiates this research. Evidence also exists that suggests that these responses to noxious stimuli may, in fact, alter the response to subsequent noxious stimuli long after the initial insult. This is the rationale behind providing fetal anaesthesia and analgesia whenever surgical intervention is thought to potentially provide a noxious insult to the fetus."

   Myers LB, Bulich LA, Hess, P, Miller, NM. Fetal endoscopic surgery: indications and anaesthetic management. *Best Practice & Research Clinical Anaesthesiology.* 18:2 (2004) 231-258.

4. **Gupta, 2008**, p.74, col.2, para.4, "As with any procedure, the provision of analgesia depends on the likely severity of pain associated with the intervention. However, analgesia is recommended for:
   (i) endoscopic, intrauterine surgery on placenta, cord, and membranes;
   (ii) late termination of pregnancy;
   (iii) direct surgical trauma to the fetus."

   Gupta R, Kilby M, Cooper G. Fetal surgery and anaesthetic implications. *Continuing Education in Anaesthesia, Critical Care & Pain.* 8:2 (2008) 71-75.

5. **Giannakoulopoulos, 1994**, p.80, col.2, para.4, "Just as physicians now provide neonates with adequate analgesia, our findings suggest that those dealing with the fetus should consider making similar modifications to their practice. This applies not just to diagnostic and therapeutic procedures on the fetus, but possibly also to termination of pregnancy, especially by surgical techniques involving dismemberment."

   Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet.* 344 (1994) 77-81.

6. **Van Scheltema, 2008**, p.320, para.3, "Neuroanatomical, neurophysiological, hormonal, haemodynamic and behavioural data indicate that a fetus is capable of reacting to noxious stimuli, implying that the fetus can experience stress and possibly even pain... The changes described can be long-lasting, perhaps even life-long...We therefore think that when performing invasive intrauterine procedures it is important to accomplish fetal anaesthesia to protect the fetus from possible harmful effects on the developing neural system. It is difficult to determine from what gestation onwards fetal anaesthesia should be provided; however, we feel that it should be considered from at least mid-gestation."

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review.* 19:4 (2008) 311-324.

7. **Rollins, 2012,** p.466, "Despite ongoing debate regarding fetal capacity for pain perception, fetal anesthesia and analgesia are warranted for fetal surgical procedures."

   Mark D. Rollins, Mark A. Rosen, "Anesthesia for Fetal Intervention and Surgery", in *Gregory's Pediatric Anesthesia*, ed. George A. Gregory & Dean B. Adropoulos (West Sussex: Wiley-Blackwell, 2012), 444–474, 466.

8. **Rosen, 2009,** p131-132, "Although the link between the stress response and pain is not always predictable, the threshold for pain relief is typically below that for stress response ablation, and the stress response to noxious stimulation is clear evidence that the fetal nervous system is reactive. Administration of fetal anesthesia has been the standard practice since the inception of fetal surgery more than 25 years ago, and it is practiced worldwide. The importance of fetal immobility, cardiovascular homeostasis, analgesia, and perhaps, amnesia have always been emphasized in fetal surgery practice."

   Mark A. Rosen, "Anesthesia for Fetal Surgery and Other Intrauterine Procedures," in Chesnut's *Obstetric Anesthesia: Principles and Practice*, ed. David H. Chestnut et al (Philadelphia: Mosby, 2009), 131-132.

9. **Danzer, 2011** "The objective of the trial was to determine if intrauterine surgery for MMC [one of the most common congenital malformations] between 19 and 25 weeks of gestation improves outcomes compared with standard postnatal neurosurgical repair...In addition to the anesthesia the fetus receives via the placental circulation, the fetus also receives an intramuscular injection of a narcotic and muscle relaxant just prior to the start of the fetal portion of the operation (see below).... The initial clinical efforts succeeded based on careful and cautious application in a highly selected patient cohort and were recently confirmed in a properly controlled randomized clinical trial which has provided a definitive answer regarding the efficacy of fMMC surgery."

   Danzer, E., Johnson, M. P. and Adzick, N. S., Fetal surgery for myelomeningocele: progress and perspectives. *Developmental Medicine & Child Neurology*, 54 (2012) 8–14.

10. **Sudhakaran, 2012**, page 17, "Early fetal surgical repair helps avoid or minimise the secondary damage. Adzick, a doyen in this field, suggested that the timing for fetal surgical procedure is ideally between 19 and 25 weeks of gestation to minimise the length of time secondary damage can occur."

    N. Sudhakaran et al., "Best practice guidelines: Fetal surgery," 88 *Early Hum Dev* (2012), 17.

b. Fetal anesthesia ... is associated with a decrease in stress hormones compared to their level when painful stimuli is applied without such anesthesia.

1. **Fisk, 2001**, p.834, col.2, para.3, "This study provides the first evidence that direct fetal analgesia reduces stress responses to intervention *in utero*."

   Abstract, "The authors investigated whether fentanyl ablates the fetal stress response to needling using the model of delayed interval sampling during intrahepatic vein blood sampling and transfusion in alloimmunized fetuses undergoing intravascular transfusion between 20 and 35 weeks.

   "Fentanyl reduced the β endorphin (mean difference in changes, -70.3 pg/ml; 95% confidence interval, -121 to -19.2;$P = 0.02$) and middle cerebral artery pulsatility index response (mean difference, 0.65; 95% confidence interval, 0.26-1.04;$P = 0.03$), but not the cortisol response (mean difference, -10.9 ng/ml, 95% confidence interval, -24.7 to 2.9;$P = 0.11$) in fetuses who had paired intrahepatic vein transfusions with and without fentanyl. Comparison with control fetuses transfused without fentanyl indicated that the β endorphin and cerebral Doppler response to intrahepatic vein transfusion with fentanyl approached that of nonstressful placental cord transfusions.

   "Conclusions: The authors conclude that intravenous fentanyl attenuates the fetal stress response to intrahepatic vein needling."

   Fisk NM, Gitau R, Teixeira MD, Giannakoulopoulos, X, Cameron, AD, Glover VA. Effect of Direct Fetal Opioid Analgesia on Fetal Hormonal and Hemodynamic Stress Response to Intrauterine Needling. *Anesthesiology*. 95 (2001) 828-835.

2. **De Buck, 2008**, p.294, col.2, para.4, "The autonomic and endocrine responses to noxious stimuli, the stress response, consist of the activation of the hypothalamic, pituitary, and adrenal axis.[15]

Rises in blood levels of noradrenaline, cortisol and b-endorphin during invasive procedures in the human fetus are seen. Alterations in the brain blood flow have been seen as early as in the 18th week of pregnancy.[15] These autonomic effects of noxious stimulation can be suppressed by the administration of analgesics.[16]"

De Buck F, Deprest J, Van de Velde M. Anesthesia for fetal surgery. *Current Opinion in Anaesthesiology.* 21 (2008) 293-297.

[15]Rychik J, Tian Z, Cohen MS, Ewing SG, Cohen D, Howell LJ, Wilson RD, Johnson MP, Hedrick HL, Flake AW, Crombleholme TM, Adzick NS. Acute cardiovascular effects of fetal surgery in the human. *Circulation.* 110 (2004) 1549-1556.

[16]Smith RP, Gitau R, Glover V, Fisk NM. Pain and stress in the human fetus. *European Journal of Obstetrics and Gynecology and Reproductive Biology.* 92 (2000) 161-165.

3. **Derbyshire, 2008**, p.119, col.2, para.1-2, "Anand's seminal work with neonates undergoing surgery demonstrated that fentanyl added to the anaesthetic regimen significantly reduces the stress response to invasive practice.[4] Specifically, plasma adrenalin, noradrenaline, glucagon, aldosterone, corticosterone, 11-deoxycorticosterone and 11-deoxycortisol levels were significantly increased in the nonfentanyl group up to 24 hours after surgery. Reducing the normal stress response was considered to be responsible for the improved clinical outcome of the fentanyl group who required less post-surgical ventilator support and had reduced circulatory and metabolic complications.

"More recently, the stress response to invasive practice has been examined in the fetus to demonstrate increased cortisol and h-endorphin circulation following intrauterine needling of the fetus beyond 18 weeks gestation.[25] Further studies have demonstrated that the fetal stress response includes haemodynamic changes in blood flow to protect essential organs, such as the brain, and blunting the stress response when providing opioid analgesia to the fetus.[26,27]"

Note: Derbyshire believes pain requires subjective human experience, not possible until after birth; nonetheless, he acknowledges this finding.

Derbyshire SW. Fetal Pain: Do We Know Enough to Do the Right Thing? *Reproductive Health Matters.* 16: 31Supp. (2008) 117-126.

[4] Anand KJ, Sippell WG, Aynsley-Green A. Randomised trial of fentanyl anaesthesia in preterm babies undergoing surgery: effects on the stress response. *Lancet.* 329 (1987) 62-66.

[25] Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet.* 344 (1994) 77-81

[26] Fisk NM, Gitau R, Teixeira MD, Giannakoulopoulos, X, Cameron, AD, Glover VA. Effect of Direct Fetal Opioid Analgesia on Fetal Hormonal and Hemodynamic Stress Response to Intrauterine Needling. *Anesthesiology.* 95 (2001) 828-835.

[27]Teixeira J, Fogliani R, Giannakoulopoulos X, Glover V, Fisk NM. Fetal haemodynamic stress response to invasive procedures. *Lancet.* 347 (1996) 624.

4. Bellieni, 2012, pages 1-6, "Mellor et al[92], discussed the importance of stress hormones increase as an affordable marker of fetal pain, and argued that the presence of hormonal responses to pain does not mean pain perception. But, anaesthetized patients do not show increases in stress hormones during surgery. According with Desborough et al[106], "regional anaesthesia with local anaesthetic agents inhibits the stress response to surgery and can also influence postoperative outcome by beneficial effects on organ function" and the same is shown for general analgesia."

Carlo V. Bellieni & Giuseppe Buonocore, "Is fetal pain a real evidence?," *The Journal of Maternal-Fetal and Neonatal Medicine* (2012), 1–6.

[92]Leader LR, Fifer WP. The potential value of habituation in the prenate. In: Lecanuet JP, editor. *Fetal development: a psychobiological perspective*. Hillsdale, NJ: Lawrence Erlbaum Associates Publishers; 1995. pp 83–404.

[106] Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2000;85:109–117.

6: The position, asserted by some medical experts, that the unborn child is incapable of experiencing pain until a point later in pregnancy than 20 weeks after fertilization predominately rests on the assumption that the ability to experience pain depends on the cerebral cortex and requires nerve connections between the thalamus and the cortex. However, recent medical research and analysis, especially since 2007, provides strong evidence for the conclusion that a functioning cortex is not necessary to experience pain.

DOCUMENTATION:

a. **The position, asserted by some medical experts, that the unborn child is incapable of experiencing pain until a point later in pregnancy than 20 weeks after fertilization predominately rests on the assumption that the ability to experience pain depends on the cerebral cortex and requires nerve connections between the thalamus and the cortex.**

1. **Anand, 2006**, p.3, col.1, para.4 – col.2, para.2, "[R]ecent reviews purporting to rule out the occurrence of fetal pain.[3,4,22]... presuppose that cortical activation is necessary for fetal pain perception.[3,4,22] Based upon this assumption, the lack of evidence for pain-specific thalamocortical connections support their contention against fetal pain."

   Anand KJS. Fetal Pain? *Pain: Clinical Updates.* 14:2 (2006) 1-4.

   [3] Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association.* 294:8 (2005) 947-954.

   [4] Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. The importance of 'awareness' for understanding fetal pain. *Brain Research Reviews.* 49 (2005) 455-471.

   [22]Derbyshire SWG. Can fetuses feel pain? *British Medical Journal.* 332 (2006) 909-912.

2. **Royal College of Obstetricians & Gynecologists, 2010**, Summary, para.2, "In reviewing the neuroanatomical and physiological evidence in the fetus, it was apparent that connections from the periphery to the cortex are not intact before 24 weeks of gestation and, as most neuroscientists believe that the cortex is necessary for pain perception, it can be concluded that the fetus cannot experience pain in any sense prior to this gestation."

   Fetal Awareness: Review of Research and Recommendations for Practice. Report of a Working Party. *Royal College of Obstetricians and Gynecologists.* March 2010.

3. **Lee, 2005**, Abstract, para.3, "Pain perception requires conscious recognition or awareness of a noxious stimulus. Neither withdrawal reflexes nor hormonal stress response to invasive procedures prove the existence of fetal pain, because they can be elicited by nonpainful stimuli and occur without conscious cortical processing. Fetal awareness of noxious stimuli requires functional thalamocortical connections. Thalamocortical fibers begin appearing between 23 to 30 weeks' gestational age, while eletroencephalography suggests the capacity for functional pain perception in preterm neonates probably does not exist before 29 or 30 weeks."

   Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association.* 294:8 (2005) 947-954.

4. **Brusseau, 2006**, p.190, col.2, para.4, "... such reflex responses to noxious stimuli have not been shown to involve the cortex and, thus, traditionally have not been thought to be available to conscious perception."

   Brusseau R, Myers L. Developing consciousness: fetal anesthesia and analgesia. *Seminars in Anesthesia, Perioperative Medicine and Pain.* 25 (2006) 189-195.

5. **Mellor, 2005**, p.464, col.2, para.4, "[D]espite the presence of intact nociceptive pathways from around mid-gestation, the critical aspect of cortical awareness in the process of pain perception is missing."

   Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. The importance of 'awareness' for understanding fetal pain. *Brain Research Reviews.* 49 (2005) 455-471.

6. **Derbyshire, 2006**, p.910, col.1, para.2, "Current theories of pain consider an intact cortical system to be both necessary and sufficient for pain experience.[9,10]"

   Derbyshire SWG. Can fetuses feel pain? *British Medical Journal.* 332 (2006) 909-912.

   [9]Coghill RC, McHaffie JC, Yen YF. Neural correlates of interindividual difference in the subjective experience of pain. *Procedings of the National Academy of Science of the United States of America.* 100 (2003) 8538-8542.

   [10]Derbyshire SWG, Whalley MG, Stenger VA, Oakley DA. Cerebral activation during hypnotically induced and imagined pain. *Neuroimage.* 23 (2004) 392-401.

7. **Derbyshire, 2010**, "Although there is a general consensus that certain cortical structures are necessary for pain, legitimate arguments that cortical structures are not necessary continue to be raised.9,11,12"

   [9]Lowery CL, Hardman MP, Manning N et al. Neurodevelopmental changes of fetal pain. *Sem Perinatol*, 2007; 31: 275–282.

   [11]Anand KJS. Consciousness, cortical function, and pain perception in non-verbal humans. *Behav Brain Sci.* 2007; 30: 82–83.

   [12]Merker B. Consciousness without a cerebral cortex: a challenge for neuroscience and medicine. *Behav Brain Sci.* 2007; 30:63–81.

b. However, recent medical research and analysis, especially since 2007, provides strong evidence for the conclusion that a functioning cortex is not necessary to experience pain.

1. **Merker, 2007**, p.80, col.2, para.3, "The evidence and functional arguments reviewed in this article are not easily reconciled with an exclusive identification of the cerebral cortex as the medium of conscious function... The tacit consensus concerning the cerebral cortex as the 'organ

of consciousness' would thus have been reached prematurely, and may in fact be seriously in error."

Merker B. Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. *Behavioral and Brain Sciences.* 30 (2007) 63-81.

1. **Anand, 2007**, p.82, col.2, para.1, "A reappraisal of the mechanisms of huan consciousness, differentiating it from its attributes, functions, or contents, is long overdue. Widely held concepts about the key mechanisms of consciousness, or its fullest expression via the human brain, have not been reexamined in the light of accumulating evidence since the 1970's. Merker presents the organization of a subcortical system...with multiple lines of anatomical, neurophysiological, behavioral, clinical, andneuropathological evidence, and a teleological rationale – all of which support a persuasive argument for the subcortical control and temporal sequencing of behavior.... One distressing impact of associating consciousness with cortical function, briefly mentioned by Merker in section 6 of the target article, pertains to the mistaken notions regarding pain perception in patient populations with impaired cortical function or cortical immaturity."

   Anand KJS. Consciousness, cortical function, and pain perception in nonverbal humans. *Behavioral and Brain Sciences.* 30:1 (2007) 82-83.

2. **Anand, 2006**, p.2, col.2, para.5, "Multiple lines of evidence thus corroborate that the key mechanisms of consciousness or conscious sensory perception are not dependent on cortical activity:"

   col.1, para.4, "Penfield and Jasper proposed that 'the highest integrative functions of the brain are not completed at the cortical level, but in a system of highly convergent subcortical structures supplying the key mechanism of consciousness.'"

   col.2, para.3, "Further clinical evidence for conscious perception mediated by subcortical centers comes from infants and children with hydranencephaly.[12,13]"

   col.2, para.4, "Thus, a subcortical system... mediates the organization of consciousness.[15]... That intact forebrain commissures are not required for high levels of cognitive function[16] provides further evidence for the subcortical integration..."

   "Whether consciousness is required for sensory perception has also been questioned by recent studies of adult patients in a persistent vegetative state.[17,18]"

p.3, col.1, para.4 – col.2, para.2, "[R]ecent reviews purporting to rule out the occurrence of fetal pain.[3,4,22]... presuppose that cortical activation is necessary for fetal pain perception.[3,4,22] Based upon this assumption, the lack of evidence for pain-specific thalamocortical connections support their contention against fetal pain. This line of reasoning, however, ignores clinical data cited above that ablation or stimulation of the primary somatosensory cortex does not alter pain perception in adults, whereas thalamic ablation or stimulation does. The thalamus plays a pivotal role in regulating the spinal-brainstem-spinal loops that mediate context-dependent descending facilitation or inhibition, coordinated via the key mechanisms underlying consciousness."

Anand KJS. Fetal Pain? *Pain: Clinical Updates.* 14 (2006) 1-4.

Penfield W, Jasper HH. *Epilepsy and the Functional Anatomy of the Human Brain.* Boston: Little, Brown & Co; 1954.

[3]Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association.* 294:8 (2005) 947-954.

[4] Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. The importance of 'awareness' for understanding fetal pain. *Brain Research Reviews*. 49 (2005) 455-471.

[12]Marin-Padilla M. Developmental neuropathology and impact of perinatal brain damage. *Journal of Neuropathology & Experimental Neurology.* 56 (1997) 219-235.

[13]Takada K, Shiota M, Ando M, et al. Porencephaly and hydranencephaly: a neuropathological study of four autopsy cases. *Brain Development.* 11 (1989) 51-56.

[14]Shewmon DA, Holmes GL, Byrne PA. Consciousness in congenitally decorticate children: Developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine & Child Neurology.* 41 (1999) 364-374.

[15] Merker B. Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. *Behavioral and Brain Sciences.* 30 (2007) 63-81. [in press at time of citation by Anand]

[16]LeDoux JE, Risse GL, Springer SP, Wilson DH, Gazzaniga. Cognition and Commissurotomy. *Brain.* 100 (1997) 87-104.

[17]Shewmon DA. A critical analysis of conceptual domains of the vegetative state: sorting fact from fancy. *Neurorehabilitation.* 19 (2004) 364-374.

[18]Schiff NDM. *Neurology.* 64 (2005) 514-523.

[22]Derbyshire SWG. Can fetuses feel pain? *British Medical Journal.* 332 (2006) 909-912.

3. **Brusseau, 2008**, p.16, para.1, "However, if one were to argue that a minimal form of consciousness might be possible without cortical involvement, then certainly one would have to consider thalamic development as a benchmark for the possible generation of such a state. As described above, thalamic structures seem to be in place somewhere between 20 and 30 weeks… Other evidence, however, points to a much earlier maturation of thalamic processing function. Thalamic connections are intimately involved in the generation of the physiochemical and endocrine responses to nociception that are seen as early as 18 weeks.[20,27]"

   p.20, para.3, "Perhaps the subcortex is necessary and sufficient for at least a minimal, Hameroffian consciousness, one that (if the data regarding anencephalic children are to be believed) may render an integrated experience of nociception that we might call pain."

   Brusseau R. Developmental Perpectives: is the Fetus Conscious? *International Anesthesiology Clinics.* 46:3 (2008) 11-23.

   [20]Teixeira Jm, Glover V, Fisk NM. Acute cerebral redistribution in response to invasive procedure in the human fetus. *American Journal of Obstetrics & Gynecology.* 181 (1999) 1018-1025.

[27]Gitau R, Fisk NM, Teixeira JM, Cameron A, Glover V. Fetal hypothalamic–pituitary–adrenal stress responses to invasive procedures are independent of maternal responses. *Journal of Clinical Endocrinology and Metabolism.* 86 (2001) 104-109.

7: Substantial evidence indicates that children born missing the bulk of the cerebral cortex, those with hydranencephaly, nevertheless experience pain.

DOCUMENTATION:

1. **Brusseau, 2008**, p.17, para.2-3, "Clinical evidence for conscious perception mediated by such a subcortical system comes from infants and children with hydranencephaly…[31-33]. Despite the total or near-total absence of cerebral cortex, these children clearly demonstrate elements of consciousness.[34]… It is important to note that these are not hydrocephalic children who possess a thin rim of intact, functional cortex, but rather children with little or no cortex at all…what little cortex may remain is generally nonfunctional and without normal white matter connectivity.[35]

   "As such, it would seem these children demonstrate that anatomic development or functional activity of the cortex may not be required for conscious sensory perception. They may, and do in fact, respond to painful or pleasurable stimuli in what may easily be argued to be a conscious, coordinated manner, similar to intact children.[36]"

   Brusseau R. Developmental Perpectives: is the Fetus Conscious? *International Anesthesiology Clinics.* 46:3 (2008) 11-23.

   [31]Counter SA. Preservation of brainstem neurophysiological function in hydranencephaly. *Journal of Neuroscience.* 263 (2007) 198-207.

   [32]Marin-Padilla M. Developmental neuropathology and impact of perinatal brain damage. *Journal of Neuropathology & Experimental Neurology.* 56 (1997) 219-235.

   [33]Takada K, Shiota M, Ando M, et al. Porencephaly and hydranencephaly: a neuropathological study of four autopsy cases. *Brain Development.* 11 (1989) 51-56.

   [34]Shewmon DA, Holmes GL, Byrne PA. Consciousness in congenitally decorticate children: Developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine & Child Neurology.* 41 (1999) 364-374.

   [35]Merker B. Life expectancy in hydranencephaly. *Clinical Neurology & Neurosurgery.* 110 (2008) 213-214.

   [36]McAbee GN, Chan A, Erde EL. Prolonged survival with hydranencephaly: report of two patients and literature review. *Pediatric Neurology.* 23 (2000) 80-84.

2. **Merker, 2007**, p.79, col.1, para.4, "My impression from this first-hand exposure to children with hydranencephaly confirms the account given by Shewmon and colleagues. These children are not only awake and often alert, but show responsiveness to their surroundings in the form of emotions or orienting reactions to environmental events… They express pleasure by smiling and laughter, and aversion by "fussing," arching of the back and crying (in many gradations), their faces being animated by these emotional states."

   Merker B. Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. *Behavioral and Brain Sciences.* 30 (2007) 63-81.

   Shewmon DA, Holmes GL, Byrne PA. Consciousness in congenitally decorticate children: Developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine & Child Neurology.* 41 (1999) 364-374.

3. **Brusseau, 2006**, p.191, col.1, para.1, "Indeed, there is evidence that hydranencephanic children responds to painful and pleasurable stimuli in a coordinated manner similar to other children.[11]"

   Brusseau R, Myers L. Developing consciousness: fetal anesthesia and analgesia. *Seminars in Anesthesia, Perioperative Medicine and Pain.* 25 (2006) 189-195.

   [11]Anand KJS. U.S. Congress. House of Representatives. Committee on the Judiciary. *Pain of the Unborn: Hearing Before the Subcommittee on the Constitution.* 109th Cong., 1st Sess., 2005.

4. **Beshkar, 2008**, p.554, col.1, para.1, "Shewmon et al. (1999) reported the cases of four children aged 5-17, with hydranencephaly involving complete or nearly complete absence of cerebral cortex. The authors observed that these children possessed a variety of cognitive capacities that were indicative of ordinary consciousness, including...appropriate affective responses."

   p.555, col.2, para.3, "Whether or not children born with hydranencephaly have consciousness is still controversial. However, the body of evidence in favor of the presence of consciousness in these patients seems to be more convincing than evidence and arguments against consciousness in such children."

   Beshker M. The Presence of Consciousness in the Absence of the Cerebral Cortex. *Synapse.* 62 (2008) 553-556.

   Shewmon DA, Holmes GL, Byrne PA. Consciousness in congenitally decorticate children: Developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine & Child Neurology.* 41 (1999) 364-374.

5. **Bellieni, 2012**, page 1-6, "If the presence of a mature cortex is the prerequisite of the experience of pain, fetal pain is improbable, as several authors argue; on the other hand, several studies[50–59] highlight the possibility of perception due to subcortical centers. Infants and children with hydranencephaly, despite total or near-total absence of the cortex, clearly possess discriminative awareness[58,59]: they discriminate familiar from unfamiliar people and environments and are capable of social interaction, visual orienting, musical preferences, appropriate affective responses, and associative learning [56]. Several stimuli are processed without the need of the cortex [51,52,57] and give useful visual information [58,59], or trigger complex experiences such as fear [53, 60]. Some authors hypothesize a similar scenario for subcortical fetal processing of pain [61,62]."

   Carlo V. Bellieni & Giuseppe Buonocore, "Is fetal pain a real evidence?," *The Journal of Maternal-Fetal and Neonatal Medicine* (2012), 1–6.

   [50]Denton DA, McKinley MJ, Farrell M, Egan GF. The role of primordial emotions in the evolutionary origin of consciousness. *Conscious Cogn* 2009;18:500–514.

   [51] Merker B. Consciousness without a cerebral cortex: a challenge for neuroscience and medicine. *Behav Brain Sci* 2007;30:63–81; discussion 81.

   [52] Johnson MH. Subcortical face processing. *Nat Rev Neurosci* 2005;6:766–774.

   [53] Ohman A, Carlsson K, Lundqvist D, Ingvar M. On the unconscious subcortical origin of human fear. *Physiol Behav* 2007;92:180–185.

[54] Marín-Padilla M. Developmental neuropathology and impact of perinatal brain damage. II: white matter lesions of the neocortex. *J Neuropathol Exp Neurol* 1997;56:219–235.

[55]Takada K, Shiota M, Ando M, Kimura M, Inoue K. Porencephaly and hydranencephaly: a neuropathological study of four autopsy cases. *Brain Dev* 1989;11:51–56.

[56] Shewmon DA, Holmes GL, Byrne PA. Consciousness in congenitally decorticate children: developmental vegetative state as self-fulfilling prophecy. *Dev Med Child Neurol* 1999;41:364–374.

[57]Mulckhuyse M, Theeuwes J. Unconscious attentional orienting to exogenous cues: A review of the literature. *Acta Psychol (Amst)* 2010;134:299–309.

[58]Sewards TV, Sewards MA. Visual awareness due to neuronal activities in subcortical structures: a proposal. *Conscious Cogn* 2000;9:86–116.

[59]Pasley BN, Mayes LC, Schultz RT. Subcortical discrimination of unperceived objects during binocular rivalry. *Neuron* 2004;42:163–172.

[60]Morris JS, Ohman A, Dolan RJ. A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc Natl Acad Sci USA* 1999;96:1680–1685.

[61]Mahieu-Caputo D, Dommergues M, Muller F, Dumez Y. [Fetal pain]. *Presse Med* 2000;29:663–669.

[62]Anand KJ. Fetal pain? *Pain Clinical Updates*. 2006;14:1–8.

8: In adults, stimulation or ablation of the cerebral cortex does not alter pain perception, while stimulation or ablation of the thalamus does.

DOCUMENTATION:

1. **Brusseau, 2008,** p.16, para.3, "In keeping with the critical insights of Penfield and Jasper, clinical evidence suggests that either ablation or stimulation of the primary somatosensory cortex does not alter pain perception in adults (demonstrated by Penfield and Jasper themselves), whereas both thalamic ablation and stimulation have been shown to interrupt pain perception."

   p.17, para.1 "In keeping with this evidence, we should consider that if cortical activity is not a prerequisite for pain perception in adults, then by analogy neither would it be a necessary criterion for fetuses."

   Note: Brusseau is ultimately agnostic regarding the ability of unborn children to feel pain before 28 weeks.

   Brusseau R. Developmental Perpectives: is the Fetus Conscious? *International Anesthesiology Clinics.* 46:3 (2008) 11-23.

   Penfield W, Jasper HH. *Epilepsy and the Functional Anatomy of the Human Brain.* Boston: Little, Brown & Co; 1954.

2. **Van Scheltema, 2008**, p.313, para.1, "Others however, argue that thalamocortical connections are not a necessary criterion for (fetal) pain perception as clinical data show that ablation or stimulation of the thalamus alone is sufficient to alter pain perception in adults.[11-14]"

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review.* 19:4 (2008) 311-324.

   [11]Brooks JK, Zambreanu L, Godinez A, Craig AD, Tracey I. Somatotopic organization of the human insula to painful heat studied with high resolution functional imaging. *Neuroimage.* 27 (2005) 201-209.

   [12]Craig AD. Interoception: the sense of the physiological condition of the body. *Current Opinion in Neurobiology.* 13 (2003) 500-505.

   [13]Nandi D, Aziz T, Carter H, Stein J. Thalamic field potentials in chronic central pain treated by periventricular gray stimulation – a series of eight cases. *Pain.* 101 (2003) 97-107.

   [14]Nandi D, Liu X, Joint C, Stein J, Aziz T. Thalamic field potentiasls during deep brain stimulation of periventricular gray in chronic pain. *Pain.* 97 (2002) 47-51.

3. **Merker, 2007**, p.65, col.1, para.3, "Penfield and Jasper note that cortical removal even as radical as hemispherectomy does not deprive a patient of consciousness, but rather of certain forms of information, discrimination capacities, or abilities, but not of consciousness itself... What impressed Penfield and Jasper was the extent to which the cerebral cortex could be subjected to acute insult without producing so much as an interruption in the continuity of consciousness. Their opinion in this regard bears some weight, in that their magnum opus of 1954 – *Epilepsy and*

the Functional Anatomy of the Human Brain – summarizes and evaluates experience with 750 such operations."

Merker B. Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. *Behavioral and Brain Sciences*. 30 (2007) 63-81.

Penfield W, Jasper HH. *Epilepsy and the Functional Anatomy of the Human Brain*. Boston: Little, Brown & Co; 1954.

4. **Morsella, 2010**, p.15, col.1, para.3, "It seems that consciousness can persist even when great quantities of the cortex are absent."

Morsella E, Krieger SC, Bargh JA. Minimal neuroanatomy for a conscious brain: Homing in on the networks constituting consciousness. *Neural Networks*. 23 (2010) 14-15.

9: Substantial evidence indicates that structures used for pain processing in early development differ from those of adults, using different neural elements available at specific times during development, such as the subcortical plate, to fulfill the role of pain processing.

DOCUMENTATION:

1. **Anand, 2006**, p.3, col.1, para.5, "Clinical and animal research shows that the fetus or neonate is not a 'little adult,' that the structures used for pain processing in early development are unique and different from those of adults, and that many of these fetal structures and mechanisms are not maintained beyond specific periods of early development. The immature pain system thus uses the neural elements available during each stage of development to carry out its signaling role."

   Anand KJS. Fetal Pain? *Pain: Clinical Updates.* 14:2 (2006) 1-4.

2. **Van Sheltema, 2008**, p.313, para.1; "[P]ain perception during fetal and neonatal development does not necessarily involve the same structures involved in pain processing as those in adults, meaning that the lack of development of certain connections is not sufficient to support the argument that fetuses can not feel pain until late gestation.[10] Some say even that the structures used for pain processing in the fetus are completely different from those used by adults and that many of these structures are not maintained beyond specific periods of early development.[8,15]"

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review.* 19:4 (2008) 311-324.

   [10] Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association.* 294:8 (2005) 947-954.

   [8]Fitzgerald M. The Development of Nociceptive Circuits. *Nature Reviews: Neuroscience.* 6 (2005) 507-520.

   [15]White, MC, Wolf, AR. Pain and Stress in the Human Fetus. *Best Practice & Research Clinical Anaesthesiology.* 18 (2004) 205-220.

3. **White, 2004**, p.208, para.4, "The anatomical evidence shows that the nociceptive connections of the fetus are not merely immature versions of the adult but are structurally different and these differences confer differences in function. Furthermore, interference with the natural progression to adult-like status can have extensive effects. Nerve section of afferent pathways, from the forelimb in the rat during early development, results in major changes in the subsequent central connections and sensory perception from other sites.[40] Clearly this has implications for any form of fetal surgery."

   White, MC, Wolf, AR. Pain and Stress in the Human Fetus. *Best Practice & Research Clinical Anaesthesiology.* 18 (2004) 205-220.

   [40]Killackey HP & Dawson DR. Expansion of the central hindpaw representation following fetal forelimb removal in the rat. *European Journal of Neuroscience* 1 (1989) 210-221.

4. **Fitzgerald, 2005**, p.507, col.1, para.2, "Newborn infants show strong pain behaviour, but the study of the development of nociceptive pathways shows that their pain involves functional signaling pathways that are not found in the mature nervous system in healthy individuals."

   Fitzgerald M. "The Development of Nociceptive Circuits."*Nature Reviews: Neuroscience.* 6 (2005) 507-520.

5. **O'Donnell, 2008,** page 60, "Lee et al.[15] have stated that the capacity "for conscious perception of pain can arise only after thalamocortical pathways begin to function, which may occur in the third trimester around 29-30 weeks' gestational age." As discussed above, given the limitations of our current knowledge, this is unduly definite. Pain perception in the fetus may not use the same pathways as in the human adult, just as it may not in other species, such as the octopus[10]. Many fetal structures are different from those in the adult, and may function in a different way. We do not know that in the fetus thalamocortical pathways are essential for any perception of pain. Connections from the thalamus to the subplate zone may be sufficient, for example. If Lee et al.'s reasoning were correct, it would imply that the majority of premature babies in intensive care do not feel pain either."

   K O'Donnell & V. Glover, "New Insights into Prenatal Stress: Immediate and Long-term Effects on the Fetus and Their Timing," in *Neonatal Pain*, ed. Giuseppe Buonocore & Carlo V. Bellieni (Milan: Springer, 2008), 60.

   [15] Lee SJ, Ralston HJ, Drey EA et al, Fetal pain: a systematic multidisciplinary review of the evidence. *Journal Amer. Med Assoc.* 294 (2005) 947–54.

   [10] Edelman DB, Baars BJ, Seth AK, Identifying hallmarks of consciousness in non-mammalian species. *Conscious Cogn.* 14 (2005) 169–87.

10: The position, asserted by some medical experts, that the unborn child remains in a coma-like sleep state that precludes the unborn child experiencing pain is inconsistent with the documented reaction of unborn children to painful stimuli and with the experience of fetal surgeons who have found it necessary to sedate the unborn child with anesthesia to prevent the unborn child from thrashing about in reaction to invasive surgery.

DOCUMENTATION:

a. **The position, asserted by some medical experts, that the unborn child remains in a coma-like sleep state that precludes the unborn child experiencing pain...**

1. **Royal College of Obstetricians & Gynecologists, 2010**, Summary, para.2, "Furthermore, there is increasing evidence that the fetus never experiences a state of true wakefulness *in utero* and is kept, by the presence of its chemical environment, in a continuous sleep-like unconsciousness or sedation."

   Fetal Awareness: Review of Research and Recommendations for Practice. Report of a Working Party. *Royal College of Obstetricians and Gynecologists.* March 2010.

2. **Fitzgerald, 2005**, p.513, col.1, para.2, "Despite the existence of sensory reflexes from the first trimester of human fetal life, it is unlikely that the fetus is ever awake or aware and, therefore, able to truly experience pain, due to high levels of endogenous neuroinhibitors, such as adenosine and pregnanolone, which are produced in the feto-placental unit and contribute to fetal sleep states[144]. In preterm infants below 32 weeks most pain responses, including facial expressions, seem to be largely subcortical[145]."

   Fitzgerald M. The Development of Nociceptive Circuits. *Nature Reviews: Neuroscience.* 6 (2005) 507-520.

3. **Mellor, 2005**, p.464, col.2, para.4, "We conclude that there is currently no strong evidence to suggest that the fetus is ever awake, even transiently; rather, it is actively kept asleep (and unconscious) by a variety of endogenous inhibitory factors. Thus, despite the presence of intact nociceptive pathways from around mid-gestation, the critical aspect of cortical awareness in the process of pain perception is missing."

   Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. The importance of 'awareness' for understanding fetal pain. *Brain Research Reviews.* 49 (2005) 455-471.

b. **... is inconsistent with the documented reaction of unborn children to painful stimuli and with the experience of fetal surgeons who have found it necessary to sedate the unborn child with anesthesia to prevent the unborn child from thrashing about in reaction to invasive surgery.**

1. **Van de Velde, 2005**, p.256, col.2, para.2, "In our trial inadvertent touching of an immobilized fetus resulted in fetal 'awakening.'"

Van de Velde M, Van Schoubroeck DV, Lewi LE, Marcus MAE, Jani JC, Missant C, Teunkens A, Deprest J. Remifentanil for Fetal Immobilization and Maternal Sedation During Fetoscopic Surgery: A Randomized, Double-Blind Comparison with Diazepam. *Anesthesia & Analgesia*. 101 (2005) 251-258.

2. **Giannakoulopoulos, 1994**, p.77, col.2, para.3, "We have observed that the fetus reacts to intrahepatic vein needling with vigorous body and breathing movements, which are not present during placental cord insertion needling."

   Giannakoulopoulos X, Sepulveda W, Kourtis P, Glover V, Fisk NM. Fetal plasma cortisol and β-endorphin response to intrauterine needling. *Lancet*. 344 (1994) 77-81.

3. **Lee, 2005**, p.951, col.1, para.3, "...they [fetal anesthesia and analgesia] serve other purposes unrelated to pain reduction, including (1) inhibiting fetal movement during a procedure.[63-65]"

   Note: Lee et al. believe that pain is an emotional and psychological experience, possible only after 29-30 weeks gestation. Nonetheless, they recognize the necessity of immobilizing the unborn child during surgery before this point due to coordinated movements in response to invasive procedures.

   Lee SJ, Ralston HJP, Drey EA, Partridge, JC, Rosen, MA. A Systematic Multidisciplinary Review of the Evidence. *Journal of the American Medical Association*. 294:8 (2005) 947-954.

   [63]Seeds JW, Corke BC, Spielman FJ. "Prevention of fetal movement during invasive procedures with pancuronium bromide." *American Journal of Obstetetrics & Gynecology*. 155 (1986) 818-819.

   [64]Rosen MA. Anesthesia for fetal procedures and surgery. *Yonsei Medical Journal*. 42 (2001) 669-680.

   [65]Cauldwell CB. Anesthesia for fetal surgery. *Anesthesiology Clinics of North America*. 20 (2002) 211-226.

4. **Van Scheltema, 2008**, p.319, para.2, "Besides the argument of achieving adequate fetal anaesthesia, there are other purposes that justify the administration of drugs: the inhibiting fetal movement during a procedure...[15,67-72]"

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review*. 19:4 (2008) 311-324.

   [15] White, MC, Wolf, AR. Pain and Stress in the Human Fetus. *Best Practice & Research Clinical Anaesthesiology*. 18 (2004) 205-220.

   [67] Seeds JW, Corke BC, Spielman FJ. Prevention of fetal movement during invasive procedures with pancuronium bromide. *American Journal of Obstetetrics & Gynecology*. 155 (1986) 818-819.

   [68]Rosen MA. Anesthesia for procedures involving the fetus. *Seminars in Perinatology*. 12 (1991) 410-417.

[69] Rosen MA. Anesthesia for fetal procedures and surgery. *Yonsei Medical Journal*. 42 (2001) 669-680.

[70]Cauldwell CB. Anesthesia for fetal surgery. *Anesthesiology Clinics of North America*. 20 (2000) 211-226.

[71]Smith RP, Gitau R, Glover V, Fisk NM. Pain and stress in the human fetus. *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 92 (2000) 161-165.

[72]Schwarz U, Galinkin JL. Anesthesia for fetal surgery. *Seminars on Pediatric Surgery*. 12 (2003) 196-201.

11: Consequently, there is substantial medical evidence that an unborn child is capable of experiencing pain by 20 weeks after fertilization.

DOCUMENTATION:

1. **Wright, 2005**, p.26, para.8 – p.27, para.3, "After 20 weeks of gestation, an unborn child has all the prerequisite anatomy, physiology, hormones, neurotransmitters, and electrical current to "close the loop" and create the conditions needed to perceive pain…The development of the perception of pain beings at the 6th week of life. By 20 weeks, and perhaps even earlier, all the essential components of anatomy, physiology, and neurobiology exist to transmit painful sensations from the skin to the spinal cord and to the brain.*"

   **From the testimony of Dr. Jean A. Wright, Professor And Chair of Pediatrics, Mercer School of Medicine*

   U.S. Congress. House of Representatives. Committee on the Judiciary. *Pain of the Unborn: Hearing Before the Subcommittee on the Constitution.* 109th Cong., 1st Sess., 2005.

2. **Anand, 2005**, p.38, "My opinion is, based on evidence suggesting that the types of stimulation that will occur during abortion procedures, very likely most fetuses at 20 weeks after conception will be able to perceive that as painful, unpleasant, noxious stimulation.*"

   **From the testimony of Dr. Sunny Anand, Director, Pain Neurobiology Laboratory, Arkansas Children's Hospital Research Institute, and Professor of Pediatrics, Anesthesiology, Pharmacology, and Neurobiology, University of Arkansas College of Medicine*

   U.S. Congress. House of Representatives. Committee on the Judiciary. *Pain of the Unborn: Hearing Before the Subcommittee on the Constitution.* 109th Cong., 1st Sess., 2005.

3. **Anand, 2006**, p.3, col.2, "Our current understanding of development provides the anatomical structures, the physiological mechanisms, and the functional evidence for pain perception developing in the second trimester, certainly not in the first trimester, but well before the third trimester of human gestation."

   Anand KJS. Fetal Pain? *Pain: Clinical Updates.* 14:2 (2006) 1-4.

4. **Glover, 1999**, p.885, col.1, para.3, "Given the anatomical evidence, it is possible that the fetus can feel pain from 20 weeks and is caused distress by interventions from as early as 15 or 16 weeks."

   Glover V. Fetal pain: implications for research and practice. *British Journal of Obstetrics and Gynaecology.* 106 (1999) 881-886.

5. **Gibbins, 2007**, p.224, col.2, para.1, "Current data suggest that by 26 and even as early as 20 weeks gestation, a rudimentary pain pathway may be present."

Gibbins S, Golec L. "It Will Not Hurt a Bit," "What You Do Not Know Cannot Hurt You," and Other Myths About Fetal Surgical Pain. *Newborn & Infant Nursing Reviews.* 7:4 (2007) 224-226.

6. **Brusseau, 2006**, p.191, col.2, para.1, "In fact there are thought to be transient cholinergic neurons with functioning synapses connecting the thalamus and cortical plate from approximately 20 weeks. This time point could be taken as the absolute earliest time in gestation when a fetus could be aware of nociceptive stimuli, or to 'feel pain.'"

   Brusseau R, Myers L. Developing consciousness: fetal anesthesia and analgesia. *Seminars in Anesthesia, Perioperative Medicine and Pain.* 25 (2006) 189-195.

7. **Van Scheltema, 2008**, p.320, para.3, "Neuroanatomical, neurophysiological, hormonal, haemodynamic and behavioural data indicate that a fetus is capable of reacting to noxious stimuli, implying that the fetus can experience stress and possibly even pain...It is difficult to determine from what gestation onwards fetal anaesthesia should be provided; however, we feel that it should be considered from at least mid-gestation."

   Van Scheltema PNA, Bakker S, Vandenbussche FPHA, Oepkes, D. Fetal Pain. *Fetal and Maternal Medicine Review.* 19:4 (2008) 311-324.

8. **Giuntini, 2007**, "It has also been shown that fetuses feel pain from week 18. This has given rise to the practice of using fetal anesthesia for surgery or invasive diagnostic procedures in utero."

   L. Giuntini & G. Amato, *Analgesic Procedures in Newborns.*, in NEONATAL PAIN 73 (Giuseppe Buonocore & Carlo V. Bellieni ed., 2007).

9. **Van de Velde, 2012**, pages 201-209, "To experience pain an intact system of pain transmission from the peripheral receptor to the cerebral cortex must be available. Peripheral receptors develop from the seventh gestational week. From 20 weeks' gestation peripheral receptors are present on the whole body. From 13 weeks' gestation the afferent system located in the substantia gelatinosa of the dorsal horn of the spinal cord starts developing. Development of afferent fibers connecting peripheral receptors with the dorsal horn starts at 8 weeks' gestation. Spinothalamic connections start to develop from 14 weeks' and are complete at 20 weeks' gestation, whilst thalamocortical connections are present from 17 weeks' and completely developed at 26–30 weeks' gestation. From 16 weeks' gestation pain transmission from a peripheral receptor to the cortex is possible and completely developed from 26 weeks' gestation.

   Marc Van de Velde & Frederik De Buck, "Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures," *Fetal Diagn Ther* 31 (2012): 201–209.