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before the

Subcommittee on the Constitution
Oversight Hearing

Chairman Canady, and members of the Subcommittee. My name is Jean A. Wright MD., MBA. I am an Associate Professor of Pediatrics and Anesthesia at Emory University School of Medicine in Atlanta. I am also an Associate Professor at the Emory Center for Clinical Evaluation Sciences. I am board certified in Pediatrics, Anesthesia, and in both sub-boards of Critical Care Medicine. I have been a faculty member and a practicing physician since 1983.

I appreciate the invitation to testify before the Committee on the topic of the effects of anesthesia administered to a mother during a partial birth abortion. I understand that this committee was considering legislation which would ban 'partial birth abortions', and that this is the second hearing on this topic. I will focus my testimony on the **ability of the fetus to feel and respond to pain during this procedure**, and on the effects of the anesthetic upon the fetus while administered to the mother.

My testimony will be divided into three parts. 1) The developmental aspects of pain in the fetus; 2) The increased sensitivity of preterm infants to pain compared to term or older infants; and 3) the effects of maternally administered anesthetics to blunt or alter the effect of this pain.

1. Development of the pain system in the human fetus and neonate:

Very preterm neonates have the **neuroanatomic substrate** and functional physiologic and chemical processes in the brain responsible for mediating pain or noxious stimuli (known as nociception). [Fitzgerald and Anand]. [See Chart from Anand & Hickey, NEJM, 1987]. **Anatomic studies** have shown that the density of the skin pain fibers (cutaneous nociceptive nerve endings) in the late fetus and newborn infant may **equal or exceed** that of adult skin. Early studies by Hooker showed that cutaneous sensory perception appears around the mouth of the human fetus in the **seventh week of gestation** and gradually spreads to all skin and mucous surfaces by 20 weeks.

Traditionally, lack of myelination (or the layer around the nerve fibers) has been proposed as an index of immaturity in the neonatal nervous system and used frequently to support the argument that neonates and infants are not capable of pain perception. However, pain (nociceptive) impulses in adults are conducted by unmyelinated or thinly myelinated fibers. Furthermore, Gilles has shown that nerve tracts associated with pain in the spinal cord and brain stem are completely myelinated (up to the thalamus) by 30 weeks of gestation.

Several types of observations speak for the **functional maturity** of the brain (cerebral cortex) in the fetus and neonate. First are reports of **fetal and neonatal EEG patterns**, including cortical components of visual and auditory evoked potentials, that have been recorded in preterm babies of less than 28 weeks gestation. Cortical evoked potentials to somatosensory stimuli (touch, pain, heat, cold) were also recently documented in preterm neonates from 26 weeks gestation. Well defined periods of sleep and wakefulness are present in utero from 28 weeks gestation onward.

Ultrasonographic findings report **specific fetal movements in response to needle punctures *in utero*** (Robinson & Smotherman, 1992; Sival 1993). Moreover, a controlled study of intrauterine blood sampling and blood transfusions in fetuses between 20 and 34 weeks of gestation showed that hormonal responses that were consistent with fetal perception of pain, and were correlated with the duration of the painful stimulus (Giannakoulopuolos et al, 1994). Preterm neonates born at 23 weeks gestation show **highly specific and well-coordinated physiologic and behavioral responses to pain**, similar to those seen in full-term neonates, older infants, and small children (summarized in *"Pain in Neonates"*, Anand & McGrath, 1993).

2. Increased sensitivity to pain in preterm infants.

Contrary to previous teaching, current data indicate that preterm neonates have greater pain sensitivity than term neonates or older age groups. Several lines of scientific evidence support this concept. I will review these from the most basic science, to that which reflects clinical practice.

1. **Studies of reflex responses:**

The Cutaneous Flexor Reflex - has a lower threshold in preterm neonates than in term neonates or adults [Fitzgerald; Woolf]. The study of this reflex has been used to establish when connections between the skin and the spinal cord are first made in the fetus, and they have Been used to study the maturation of ascending motor pathways. This reflex has been shown in man to **parallel pain perception exactly** in terms of threshold, peak intensity, and sensitivity to analgesics.

2. **Studies of neurotransmitting substances in the spinal cord:**

Neurotransmitter development in the dorsal horn of the spinal cord has demonstrated the early and abundant expression of the neurotransmitters mediating pain (e.g. substance P, L-glutamate, VIP, CGRP), and increased somatosensory excitability in the premature spinal cord. In contrast, the neurotransmitters contained in descending inhibitory fibers from supraspinal centers (5-HT, Norepi, Dopamine) were expressed postnatally, [Anand & Carr, 1989] implying **poorly developed gate control mechanisms for pain in preterm infants.**

3. **Receptors for pain in the fetal brain:**

Opioid receptor labeling in the brain stem of fetuses 19-21 weeks gestation demonstrated very high densities in supraspinal centers associated with sensory perception [Kinney et al, 1990]. (These inhibitory Opioid receptors may protect developing neuronal systems from constant over stimulation, given the underdeveloped gate control mechanism in the dorsal horn of the spinal cord.)

4. **Pain and stress are reflected in the hormones produced by the fetus.**

Pain in the fetus and neonate can be measured in two dimensions. Pain and surgical stress are demonstrated by a coordinated outpouring of pituitary, adrenal, and pancreatic hormones. Secondly, cardiovascular responses, such as increases in blood pressure, heart rate, dysrhythmias, or poor cardiac output may signal pain. The magnitude of hormonal (endocrine-metabolic) and other stress responses to invasive procedures or surgical operations was **much greater in neonates** as compared to adults; with neonatal catacholamine and metabolic responses up 3 - 5 times those of adult patients undergoing similar types of surgery [Anand].

5. **Pain felt as a fetus or neonate has a long term effect on the child's well-being:**

The effects of anesthesia on the neonatal stress responses are important and may contribute to the effects of stress suppression on postoperative clinical outcome. In a randomized controlled trial, preterm babies undergoing ligation of the patient ductus arteriosus were given nitrous oxide and curare, with or without the addition of intravenous fentanyl. The hormonal responses of neonates receiving nitrous oxide alone were associated with significant increases in blood glucose, lactate, and pyruvate; these were prevented in neonates given therapeutic doses of fentanyl. This study went on to show that **aggressive anesthesia not only decreased the stress responses of neonates undergoing surgery but also improved their postoperative clinical outcome**. Similarly, neonatal intensive care patients who are exposed to a single (circumcision) or repeated painful events (heelsticks) have been shown to have procedural memory for the event, and may have long term effects, even into adulthood.

6. **The amount of medicine needed to achieve a desired effect:**

   Pharmacokinetic studies of anesthetic drugs have shown **higher plasma concentrations were required to maintain effective surgical anesthesia in preterm neonates** as compared to old age groups [Yaster; Greeley & de Bruijn].

Developmental changes occur in the expression of pain which differentiate preterm from term or older infants; however, these findings illustrate a **communicational specificity** and **not changes in pain threshold during development** [Johnston]. The studies cited above indicate a lower pain threshold in preterm neonates, and the occurrence of further decreases in pain threshold following exposure to a painful stimulus or experience [Fitzgerald].

3. Effects of Anesthesia on the fetus

Obstetrical anesthesia has become a very safe practice, with many women a year receiving an anesthetic during the time of their pregnancy. These women are in addition to those who receive an anesthetic at the time of delivery. It is from this patient population that the effects of anesthesia on the fetus can be derived.

Local anesthetics rarely have any affect on the fetus. By their nature, their affect is to numb the nerves and tissues around the injection site, and only minuscule amounts of drug enter the mother's circulation, and even less reach the fetus.

The administration of intravenous sedation/anesthesia has minimal effects on the unborn due to two mechanisms: 1) The mother's liver clears much of the drug, and 2) the drug must cross from the mother's blood stream into the placenta before reaching the fetus.

Since the fetus has a much higher density of Opioid (pain) receptors, **scientific reasoning postulates that higher doses of Opioids will be required to saturate the increased number of receptors, and achieve a therapeutic response.**

Preliminary evidence for this therapeutic response is obtained from the decreased levels of steroid stress hormones in the amniotic fluid of fetuses whose mothers had received anesthesia as compared to the those that did not receive anesthesia in response to fetoscopy performed at 16-21 weeks gestation (Partsch et al, 1991). The mothers who had received anesthesia had a infant that was less stressed by the procedure.

CONCLUSIONS

The scientific literature reviewed above and my clinical experience in the delivery of general anesthesia, systemic analgesia, conscious sedation, local and regional anesthesia to a wide variety of patients lead me to believe that:

1 The anatomical and functional processes responsible for the perception of pain have developed in human fetuses that may be considered for 'partial birth abortions'. (At this stage of neurologic development, human fetuses respond to the pain caused by needle puncture *in utero* in a similar manner as older children or adults, within the limits of their behavioral repertoire).

2. It is likely that the **threshold for such pain perception is lower** than that of older preterm newborns, full-term newborns, and older age groups. Thus, the pain experienced during 'partial birth abortions' by the human fetus would have **a much greater intensity than any similar procedures performed in older age groups.**

3. Current methods for providing maternal anesthesia during 'partial birth abortions' are unlikely to prevent the experience of pain and stress in the human fetuses before their death occurs after partial delivery.