CHARLOTTE LOZIER INSTITUTE

Written Testimony of Sheila Page, DO
Developmental Neuroanatomy and Physiology of Pain Perception
Ohio House Community and Family Advancement Committee

SB127: The Pain-Capable Unborn Child Protection Act
October 2015

Dear Chairman Derickson and Distinguished Members of the House Community and Family Advancement Committee,

My name is Sheila Page, DO. I am an Osteopathic physician, board certified in Neuromusculoskeletal Medicine. I have practiced for 23 years treating many patients with pain and various diseases, some at advanced stages. Although I treat patients of all ages, I have a special interest in children with disabilities and serious irreversible medical conditions, especially those who have little hope for recovery or improvement in their quality of life. I have found that the skills I developed over the years have enabled me to help improve their quality of life and ease their suffering.

The question that all physicians have heard many times before performing a medical procedure or treatment is "will it hurt?" Doctors go to great lengths to minimize and prevent pain for their patients. Requiring proof that a patient has pain before treating is in opposition to the ethical training of physicians. The physician anticipates pain in certain circumstances and protects people from pain whenever possible.

The discussion of fetal pain is centered on the definition of pain, which can alter the direction of study and therapeutic protocol. There are two general definitions of pain that appear in literature**:** the subjective perception, and the objective observation.

The JAMA article (6) that has often been used as the authoritative paper proving that the unborn child does not feel pain uses a psychological definition: "Pain is a subjective sensory and emotional experience that requires the presence of consciousness to permit recognition of a stimulus as unpleasant." (Bioethics) This statement is a hypothesis that is dependent on subjective and negative data for its conclusion.

The basic science definition of pain is formed by objective observation: "Pain is a protective mechanism for the body. It occurs whenever any tissues are being damaged, and it causes the individual to react to remove the pain stimulus." (Guyton)

Embryological Concepts

One of the most accomplished scientists in the study of embryology was Eric Blechschmidt, MD, (1904-1992), a German anatomist and physiologist who worked for more than forty years studying the development of the human form in the first eight weeks of life after conception. He produced more than 120 scientific papers and numerous books on the form and function of the developing human. Blechschmidt focused on the evidence presented by the embryo itself, producing more than 200,000 serial sections of embryos of different ages and sixty-four enlarged total reconstructions that have been on display at the University of G**o**ttingen.

Dr. Blechschmidt's observations were unique in his whole-body approach to the embryo. He considered the function of all parts of the developing embryo to parallel the structure. "The development of the central nervous system implies the simultaneous development of functioning afferent and efferent central pathways (tracts) and centers. Nothing has been found to support the idea that the function of the nervous system is added *after* the development of its shape and cell structure. It is the author's opinion that the function and structure develop simultaneously. The beginning of the nervous system implies the simultaneous beginning of function." (7) P.105.

Basic Science Observations

There are three scientific classifications of pain:

1. Pricking pain is felt when a needle is stuck into the skin or when the skin is cut with a knife, or when widespread area of the skin is irritated.
2. Burning pain is felt when the skin is burned, can be excruciating, and is most likely to cause suffering.
3. Aching pain is a deep pain with varying degrees of annoyance. Aching pain of low intensity in widespread areas of the body can summate into a very disagreeable sensation.

Each of these types of pain stimuli are carried along different neurofibers in the organism:

1. Pricking pain: carried along fast Delta type A fibers
2. Burning pain: carried along slow type C fibers
3. Aching pain: carried along slow type C fibers

The pricking pain pathway produces a rapid response to pain at the spinal cord level and travels to the reticular activating system (reticular formation of brainstem and intralaminar nuclei of thalamus), where the majority of the pain fibers terminate. Type A fibers enter the spinal cord, synapse with an interneuron, cross over, and travel up in the anterolateral pathway. Very few Type A fibers travel directly to the thalamus via the spinothalamic tract, terminating in the ventrobasilar complex and posterior nuclear group. These fibers connect with neurons that synapse with the somatic sensory cortex for the purpose of localizing the pain.

The burning and aching pain pathways terminate diffusely in the reticular formation and in the thalamus, with very few connecting fibers to the cortex. It is characterized by gross localization and the ability to summate when large areas of the body are being damaged. The purpose of

these pathways is to alert the individual that damage is being inflicted. Guyton, 1986, 2010 (illustration).

Pain is directly correlated to tissue damage

A variety of approaches have been used to study pain perception. The methods for eliciting perception of pain include:

1. Pricking the skin with a pin
2. Applying pressure against a bone
3. Pinching the skin
4. Heating the skin.

One of the most reliable ways to measure a pain threshold is by gradually increasing heat applied to the skin. 'By far the greatest number of people perceive pain when the skin temperature reaches almost exactly 45C… Almost everyone perceives pain before the temperature reaches 47C." Across cultures this has been proven: there is very little difference in the threshold of pain perception, [Guyton 1986, p 592-593] but there are wide variations in response to pain. The point at which tissue begins to be damaged by heat is 45C, thus, the pain is correlated to tissue damage. "The intensity of pain has also been closely correlated to the rate of tissue damage by other effects besides heat," (contusion, chemical substances, infection, ischemia). Guyton 1986, p. 594.

The threshold at which pain is perceived in contrast with the response to pain must be discerned. As the human brain learns from various experiences and training, the response to pain may change and varies greatly with the individual. Anand p. 3, 1996., (De Buck, p. 295)

The sub-cortical neurological pathways involved in pain perception:

Type A and Type C pain fibers travel in the lateral division of the anterolateral pathway, remaining differentiated as fast or slow fibers. About three-quarters to nine-tenths of all pain fibers terminate diffusely in the reticular formation and in the thalamus (these two areas constitute the reticular activating system). The reticular formation is part of the medulla, pons, and mesencephalon. (Guyton)

Burning and aching pain fibers excite the RAS, thus activating the entire nervous system, causing arousal from sleep, creating a sense of urgency, and promoting defense and aversion reactions, alerting the individual that damage is being inflicted. The summation property of the pain fibers in the RAS, especially when large areas of the body are being damaged, causes the most intense suffering in human experience. Guyton, 1986, p. 596. Without the descending inhibitory pathways that develop after birth (Van de Velde, p 233), a pre-born baby is capable of perceiving unmitigated, intense suffering when it is crushed or torn, as is commonly experienced in an abortion procedure.

The pain perception functions remain in the lower centers and are not dependent on the cortex, although some modification of the pain threshold may occur. (Lowery p.276, Guyton p.596) Pain impulses that enter and terminate in the lower brain centers, especially the reticular

formation and the thalamus, can cause conscious perception of pain. (Guyton, 1986, p. 596) (de Buck)

Chronology of Neurological Development

The neurological development of the fetus is chronicled by various researchers, noting the appearance of structures within common timeframes. Most authors agree that nociceptors appear around the lips at around 7 weeks. At this stage, however, the free nerve endings associated with pain perception have not penetrated the epidermis (Humphrey p. 128, RCOGp4). These fibers continue to develop and mature throughout the body up to 20 weeks gestation. The cortex is developing at around 8 weeks, and the thalamus enlarges rapidly between 7 and 8 weeks along with the growth of the afferent and efferent fibers, illustrating the coordinated growth of the system of pain perception. The peripheral afferent fibers are developed by 10 weeks, and the spinothalamic connections mature at 14 weeks. These fibers continue to appear as the fetus grows. Thalamocortical tracts form at 20-22 weeks, reaching the subcortical plate, and are seen projecting to the cortex at 23 weeks. Maturation of the synapses of the thalamocortical fibers is seen at 26-34 weeks. The hypothesis that the components of the nervous system begin to be functional after the appearance of the mature anatomical form conflicts with data that suggests that the function parallels or precedes structure. (Blechschmidt, Humphrey)

Neurological Development of the Fetus

WEEKS	Anatomical Structure Developed
7-20	nociceptors
8	cortex begins to develop
10-30	peripheral afferents
7.5	spinal reflex
14-20	spinothalamic connections
20-22	Thalamocortical tracts (cortical plate)
26-34	synapses of thalamocortical fibers

Salihajic, Anand, Van de Velde, Vanhatalo, Derbyshire, Lowery

Arguments and conclusions in support of the hypothesis that pre-born children are incapable of feeling pain rely on the definition that pain is a psychological perception that is dependent on intact thalamocortical fibers. Therefore, using this limitation and the research showing the appearance of thalamocortical fibers at 23 weeks in fetal development, the conclusion is that the child cannot feel pain until 23 weeks at earliest. Merskey (12), Lee, et al (6), Derbyshire (11) p119, S. Derbyshire. (13) The various articles conclude that a fetus is capable of pain at different ages, from 11-26 weeks, depending on the definition used and the limitation placed on pain perception. Many authors rely on maturation of synapses as a turning point after which a pain signal may be transmitted.

In view of the consistent observations of aversion behavior at 7-7.5 weeks, it can be concluded that at this age the embryo is responding to sensory input. The thalamus is already formed, and during the seventh week the thalamus rapidly expands (Moore. P.395) in conjunction with the

developing nociceptive system of the spinal cord, (Moore, p.395) demonstrating that the components of pain perception develop as a unit. Projections from the spinal cord can reach the thalamus from seven weeks gestation.

It is significant that the reflex exhibited by the embryo at 7-8 weeks is a coordinated response, not a localized reflex. The pattern-type behaviors appear earlier than more specific local responses, indicating more generalized communication by the nervous system. (Humphrey) Fitzgerald M. (17), Andrews KA, (18). The more specific local reflexes have been noted to appear at 9.5 weeks. This is timed with the free nerve ending contact with the basement membrane of the epithelium of the lips. (Humphrey p 127) The trigeminal nerve ganglion is one of the first to develop, and carries a rich supply of sensory and motor nerve fibers. (Moore p. 407). Sensory nerves of the trigeminal are present in embryos as small as 2.57mm (Blechschmidt Ontogenetic p. 105). The components of the reflex arc are formed and capable of function in embryos between 6-7 weeks gestation. (Blechschmidt Ontogenetic Basis…p. 103).

It is important to consider that the function develops along with the structure. (Brusseau p.20). As Blechschmidt described, the brain and spinal cord are developing functionally as a whole unit simultaneously. (Biokinetics, Blechschmidt, p.105). The principal unit of pain perception is in place and rapidly expanding at 7-8 weeks. The necessary components for pain perception are present and becoming more complex and sophisticated during the second trimester.

Consciousness

As the anatomical and physiological evidence demonstrates, the role of the cortex in consciousness and pain perception is minimal. "Although the cortex may elaborate the contents of consciousness, it's not the seat of consciousness." Merker 2007. Merker, Brusseau, and Bellieni agree that consciousness is not dependent on the presence of a cerebral cortex. These conclusions are reached by independent clinical observations of conscious behavior in individuals without a cortex. (Beshkar). Infants with hydraencephaly, in which little or no cortical fibers are present, demonstrate conscious recognition, pain perception, musical preferences, and alert, wakeful behavior. These represent counter-examples to the hypothesis that consciousness requires a cerebral cortex. The data suggest rather that consciousness is a function of the lower brain centers. Further, ablation of the somatosensory cortex does not alter pain perception in adults, underscoring the anatomical implication that pain perception occurs in the lower brain centers. (Brusseau, p.16), (Morsella).

Hormonal Responses

The hormonal stress response has been recently studied as a marker for adequate pain control and outcome of surgical procedures. (Goldman, Gupta, Kilby, and Cooper) (de Buck, p294) Derbyshire states that "the presence of an intact HPA axis at 18 weeks gestation is a suitable conclusion, but the HPA axis is a subcortical system and so its activity is not evidence for cortical awareness or conscious pain perception. Derbyshire (11). The stress response to invasive procedures has been examined in the fetus and is characterized by increased cortisol and B-endorphin circulation following intrauterine needling of the fetus beyond 18 weeks gestation. Giannakoulopoulos X. The hormonal and metabolic changes that follow physical injury or

psychologic trauma do not include any conscious components that may accompany the stress response. (Goldman RD), Gupta, p74. This is evidence that indicates that the pre-born baby is capable of perceiving pain, but it is dismissed by those who insist that the cortical connections must first be matured. (ACOG, Lee).

Discussion

The anatomical and physiological mechanisms of pain perception are observable in scientific studies and the accumulation of data over time reinforces the concept that pre-born children are capable of feeling pain. (De Buck p. 294). Examining the arguments from the perspective that it is unlikely that pre-born children feel pain provides better understanding of the objections to consideration of protecting the pre-born. The most frequently quoted articles are reviews of previous studies. (Lee, Derbyshire, RCOG) The reasoning is typically vague, or suggesting that lack of data is cause for skepticism.

The following reasons are some of those offered to oppose efforts to provide pain prevention for the pre-born:

1. Pain perception requires at a minimum mature synapses between the thalamus and cortex. (RCOG, Derbyshire)
2. Limited evidence indicates that pain perception is unlikely. (Derbyshire)
3. Lack of evidence of effectiveness of direct fetal anesthetic or analgesia precludes its use. (Derbyshire)
4. Limited data is available on safety of the woman in the context of abortion. (Lee)(Derbyshire)
5. Efforts to provide pain control in the context of abortion increases the cost of care unnecessarily. (Lee)(Derbyshire)
6. Techniques used in fetal surgery don't apply in the case of abortion. (Lee)

Discussion

In spite of the many supporting studies on fetal anatomy, physiology, and behavior, the reasoning for skepticism about fetal pain is rooted in a desire to protect the abortion industry. "Evidence regarding the capacity for fetal pain is limited but indicates that fetal perception of pain is unlikely before the third trimester. Little or no evidence addresses the effectiveness of direct fetal anesthetic or analgesic techniques. Similarly, limited or no data exist on the safety of such techniques for pregnant women in the context of abortion. Anesthetic techniques currently used during fetal surgery are not directly applicable to abortion procedures." (Lee et al.) This statement reflects a disregard for the cumulative data from research that provide substantial evidence of fetal pain perception. The supposition is that the absence of data in the context of abortion is sufficient to cast doubt on the concept of fetal pain.

According to Lee, objectives of pain control during fetal surgery are not applicable to abortion because the intention is not to help the pre-born. (Lee, p951.) "In the context of abortion, fetal analgesia would be used solely for beneficence toward the fetus, assuming fetal pain exists." (P. 952.) This statement reveals the heart of the opposition—that the pre-born baby is not given

consideration as a human being. The supposed benefit to the mother or society precludes any consideration of the baby's health or experience of pain.

Rather than encouraging studies that would support or refute current data, the directive by opposition is "instead, further research should focus on when pain-related thalamocortical pathways become functional in humans." (Lee et al.). This is based on a hypothesis that has no data to support it. The anatomical evidence shows that the thalamo-cortical fibers relay information on the location of cell damage, and are not related to pain perception.

The conclusion of RCOG is that "evidence that analgesia confers any benefit on the fetus at any gestation is lacking but should be a focus of future research" (ACOG p.19). In spite of the experience and observation of surgeons who treat these pre-born children, the opposition dismiss the vast knowledge and experience that has accumulated and instead keep us focused on concepts that are confusing and based on negative data. They point repeatedly to a lack of data, without presenting valid data to prove the proposed hypothesis that a developing human is incapable of pain perception.

Conclusion

The fetus is structurally and physiologically equipped to perceive pain at a very early age, and demonstrates physiological responses consistent with pain perception. These responses are observable at 7.5 weeks and continue to develop until birth. Many of the arguments submitted against recognizing pain perception of the pre-born child are centered on a hypothesis that is already confronted with counter-examples. The rationale for opposing efforts to study pain prevention for the pre-born appears to be founded on a need to justify practices that completely disregard the life of the baby and dismiss any possibility of suffering, regardless of the preponderance of evidence to the contrary.

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