



AAPLOG

PRACTICE GUIDELINE

Number 2, October 2017, Updated 2021

Fetal Pain

Pain is defined by biologists as aversive behavioral and physiological reactions in response to noxious stimuli, and does not require an intact cerebral cortex. There is significant evidence that fetuses can perceive noxious stimuli and demonstrate physiological and behavioral reactions to them—fetuses are not numb to invasive or harmful interaction. The purpose of this document is to present the available evidence for fetal pain, discuss implications for procedures in pregnancy, and to provide relevant recommendations for termination of pregnancy.

Background

Definition of Pain

The definition of “pain” is intensely debated among embryologists, family planning professionals, ethicists, and politicians. Certainly, the adult person’s perception of pain is a complex physical and psychological interplay with long-term consequences for society.¹ Without a developed psychology and without behavior to analyze, discussion of this type of pain is difficult in fetuses.

In biology, pain is defined as “aversive behavioral and physiological reactions and...suspension of normal behavior in response to noxious stimuli.”² This

definition applies to non-human organisms, whose pain is increasingly and rightly recognized publicly. Typical human adult neurological function is not required for suffering. This broad definition of pain will be used in this guideline.

Pain with a Cerebral Cortex

In mature humans, painful stimuli are received by nociceptors in the skin and viscera; these communicate impulses via afferent sensory neurons through the spinal cord, are processed in the thalamus, and are received by the sensory cortex before a motor response is elicited. These motor responses are part

AAPLOG Practice Guideline. This document was developed by [number] authors on the Research Committee. Practice Guidelines are evidence-based documents informing pro-life providers with high-quality, peer-reviewed literature.

of the “aversive behavioral [reactions and] suspension of normal behavior” in the definition of pain above. Humans also have reflex arcs that operate through motor neurons in the spinal cord’s dorsal root ganglia, allowing the body to cause behavioral changes without the cortex for the sake of speed.³ Cognition, memory, and other higher functions can add to behavioral changes, but a response to pain does not require them: pain during sleep changes behavior even if consciousness adds more behavioral changes.^{4,5}

Processing pain either through the cortex or via a reflex arc is associated with hormonal responses including epinephrine (also known as adrenaline) and cortisol, which represent the “physiological reactions” included in the above definition of pain.^{6,7}

Non-Human Animals

In non-human animals, nervous systems are much simpler, with animals such as nematodes or octopi reacting to noxious stimuli with only nerves and ganglia.^{8,9} Activism surrounding animal pain (termed “pain”) is evidence-based and related to vertebrates,^{10,11} fetal vertebrates,¹² and insects,^{13,14} some of which lack functional cerebral cortices.

Embryology and Fetal Development

Nociceptive signaling differs throughout human development. Neonates use different structures than adults.¹⁵

In fetuses, mature configurations for pain processing do not exist, but this does not rule out the possibility of using other structures to perceive pain as defined in this document.^{16,17} Fetuses process pain using subcortical and peripheral centers¹⁸⁻²⁰ while they develop final structures, just as they use an immature set of functioning renal structures before mature kidneys are complete.²¹

Decades of histologic research has illustrated that sensory receptors, including nociceptors, are present throughout the fetus between 10 and 14 weeks gestational age, starting as early as 7 weeks.^{18,22-26} This begins in the perioral area at 7 weeks, followed by the palms and soles at 11 weeks, and the remainder of the integument by 20 weeks.^{27,28}

Superficial nociceptors, followed later by nociceptors in viscera, are connected by afferent fibers from the spinal column to the thalamus and from the thalamus to the subcortical plate between 16 and 20 weeks gestational age.^{16,29-32} These afferent fibers are mature enough to cause a central response to noxious stimuli as early as 16 weeks’ gestational age.^{30,33}

There is also evidence of the necessary components for a reflex arc in the fetus. Sensory fibers are present from 7-14 weeks, a spinal cord is present from 5-7 weeks, and peripheral fibers that control movement grow into the spinal cord at 8 weeks gestation.²⁸ These are the three tissue components of a mature reflex arc.

Physiologic Responses

Fetuses have a neurohormonal response similar to adults when faced with noxious stimuli.^{20,34,35} While the role of the fetal cortex is still under discussion, it is clear that cortical tissue receives this hormonal response as early as 16-18 weeks gestational age, along with other end-organs such as the fetal heart and skeletal muscle.^{9,15}

Identical hormonal responses in neonates are associated with noxious stimuli and produce adverse long-term outcomes, much like adult human pain.^{36,37}

Fetal Surgical Experience

Experience of fetal surgeons and other physicians performing invasive procedures matches these histologic findings. As early as 7.5 to 8 weeks' gestational age, a fetus moves in response to stimuli.^{32,38-40}

Language varies in reports of fetal responses but Giannakoulopoulos *et al.* describe this response as "vigorous body and breathing movements"²⁰ and Williams reports "coordinated responses signaling the avoidance of tissue injury."⁴¹ No later than 22 weeks' gestational age, the fetus responds to what an adult would consider painful, such as a needle penetrating the skin.³² Trials have been performed to optimize opiates for fetal anesthesia,⁴² which lower the hormonal response to stimuli as in adults.⁴³

Conclusions

Although language and subjective experience of pain is hotly debated, if "pain" is taken simply as a perception and response to noxious stimuli, it is clear that fetuses are capable of pain by 22 weeks' gestational age at the latest, and likely earlier, as fetuses respond to touch as early as 7 to 8 weeks.

Clinical Questions and Answers

Q *Should the word "pain" be used when speaking of organisms which may not have consciousness?*

"Pain" is used in other fields of biology to mean the perception and response to noxious stimuli that would be considered painful by a human person. It is

irrelevant to many disciplines, such as marine biology, whether fish or crustaceans are conscious; advocates for these organisms see fit to use the word “pain” to refer to a mutually understood concept of evolutionary response to adverse external stimuli.^{2,44} It is difficult to look at the evidence of histology (fully formed structures resembling those found in adults) and the experience of physicians operating on fetuses and conclude that the fetus is not sensitive to adverse external stimuli.

Q Does the ability to experience pain depend on the cerebral cortex and afferent thalamocortical fibers?

The response to pain in mature humans can be induced simply with the imagination,⁴⁵ and it clearly utilizes the cerebral cortex. Experienced (not imagined) pain requires afferent fibers from the thalamus (thalamocortical fibers).⁴⁶

Afferent thalamocortical fibers develop closer to the third trimester, and some neuroscientists assume that the cortex as primary for pain perception.^{30,47} If this is true, and cortical activity is required for fetal pain, then fetuses do not feel pain until closer to 23-30 weeks gestation.^{30,48,49} This assumption and corollary is best articulated by authors of a systematic review and meta-analysis on fetal pain:

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 non-painful stimuli and occur without conscious cortical processing.³⁰

However, recent studies suggest that cortical activity is not necessary for the experience of pain in humans after birth. This is largely from experience with decorticate children, lacking functional cortex due to congenital anomalies, perinatal brain damage, or commissurotomy.⁵⁰⁻⁵⁹ These children respond to pain and also interact socially in simple ways, such as to faces and music.⁶⁰

Moreover, it appears that if the cortex is not strictly speaking required for basic perception of pain, the thalamus is the next level of neurological centralization. The thalamus, as noted above, is connected to peripheral nociceptors between 16 and 20 weeks' gestational age.^{26,30,33} This would match what occurs in adults: cortical input does not alter pain perception, but thalamic input does.⁶¹⁻⁶³ Even more dramatically, in the adult with loss of significant amount of cerebral cortex, consciousness can be preserved.⁶⁴

These studies challenge whether pain in simpler organisms, including human

fetuses, requires a functional cortex. The conclusion that fetuses are unable to feel pain because they lack complete cortical inputs is unproven and should not be the default hypothesis given their histology, neuroscience in other animals, and the evidence available from fetal intervention.¹⁷

Q Are fetuses awake in utero?

It has been asserted that the fetus never experiences a state of true wakefulness in utero and is kept in a sleep-like unconscious or sedated state, due to elevated levels of neuroinhibitors like adenosine and pregnanolone.^{49,65,66}

This hypothesis is not rigorously tested. Given the lack of evidence that these hormones predominate and produce sleep, these hormones should not be subjectively viewed as more important than the cortisol and epinephrine.

Further, fetuses are unlikely to be asleep because they require paralytic drugs for fetal surgery. Sleep includes suppressed motor function especially during rapid-eye movement (REM) sleep,⁶⁷ but fetuses demonstrate “vigorous” movements and need drugs that adults also need for muscle paralysis.⁴¹

And, as has been highlighted above, even if fetuses were asleep, pain felt in sleep still impacts human organisms.^{4,5}

Q How should fetuses undergoing surgery be anesthetized?

Following the lead of fetal surgeons, analgesia should be provided for procedures that affect fetal tissue with nociceptors, such as repair of open neural tube defects. This analgesia is in addition to paralytics, since paralytics cannot modify the physiologic response to aversive stimuli.⁶⁸ Further or more specific assertions regarding fetal surgery are beyond the scope of this document.

Q Should abortion by dismemberment or cranial decompression be performed after gestational ages when fetal susceptibility to pain is documented?

There is mounting evidence that fetuses perceive noxious stimuli on a spectrum beginning at 7-10 weeks' gestational age. As a result, careful consideration should be given at increasing gestational ages regarding abortion by dismemberment.

Piercing or dividing fetal tissue with instruments constitute noxious stimuli, which is why fetal surgery requires opioid analgesia. Dismemberment should be seen as especially noxious, since there is evidence that dividing afferent tracts has similar effects to painful stimuli in adults (long-term effects demonstrated in an animal model).¹⁰

Evacuating cranial contents may lead to more rapid cessation of pain (due to direct destruction of the thalamus) but is still a noxious stimulus and does not affect reflex arcs.

Q *Can dilation and curettage (D&C), dilation and evacuation (D&E), or dilation and extraction (D&X) be performed for deceased fetuses?*

Dilation and removal of products of conception causes no pain if an embryo or fetus is deceased. There are no ethical issues with these procedures, although psychological difficulties for the maternal patient and her family may arise when piecemeal removal of a desired fetus is performed.

Q *Should termination of pregnancy by any other method be performed after gestational ages when fetal susceptibility to pain is documented?*

Saline induction leads to constriction of capillaries in skin, the gastrointestinal tract, the respiratory tract, and the placenta. Animal models suggest that the mechanism of death of these fetuses is suffocation, which is likely associated with a neurohormonal response associated with stress. Moreover, constriction of capillaries and tissue necrosis likely results in nociceptive feedback after

nociceptors are present at 10-14 weeks gestational age.

Early induction of labor does lead to the end of pregnancy but results in delivery of an intact and possibly living fetus. Induction of labor without feticide is different from the previously described methods of termination of pregnancy because it does not directly aim at the death of the fetus.

If induction is initiated before viability, particularly fragile fetuses (e.g. those with growth restriction) may not be born alive; this does not change the nature of induction of labor. If born alive, parents of periviable infants may elect not to proceed with resuscitation; this also does not change the nature of induction of labor. Induction of labor remains fundamentally different in its moral object if it does not aim to end the life of the fetus.

Q *Should abortion by any other method be performed after the lowest age of viability?*

When there is need to separate the mother from the fetus at or greater than 22 weeks, delivery of a live fetus, followed by adequate neonatal analgesia (even when neonatal resuscitation is not planned) should be preferred to abortion by any method.

Q *Would legislation to prohibit abortions after 14 weeks gestational age ban all abortions? What about after 21s weeks?*

Bans on abortions after 14 weeks gestational age will ban a small minority of abortions. In 2019, the most recent year for which the CDC has provided data as of publication, 7.3% of abortions occur after 13 weeks.⁶⁹

Bans on abortion after 21 weeks would prohibit only 1.1% of abortions.⁶⁹

Q *Would legislation to prohibit abortions starting in the second trimester be dangerous for the maternal patient?*

Most abortion bans have an exception which allows the physician to legally use any method of separation of the mother and fetus when the life of the mother is at stake. A surgical abortion at this gestational age would typically take at least ten minutes, and potassium chloride or other feticide followed by induction of labor would take several hours (up to a number of days).

There are comparable alternatives which do not affect fetal body integrity: if there is need for immediate separation, cesarean section can be accomplished in as little as one minute from decision to separation. If more time is available, an induction of labor can be

sought, which may take a number of days.

Q *Is preventing fetal pain proportionate to the present and future morbidity of a classical cesarean section?*

One in four women with a classical cesarean section will suffer morbidity, including uterine rupture, asymptomatic dehiscence, postpartum hemorrhage, and need for transfusion of blood products.⁷⁰ These risks should not be taken lightly, but they should be weighed against respect for the bodily integrity of the fetal patient.

It should be kept in mind, especially with cardiovascular threats such as pulmonary hypertension or peripartum cardiomyopathy, that vaginal delivery is preferable and most fluid shifts occur postpartum regardless of mode of delivery.

Q *Other professional organizations have noted that fetuses cannot feel pain. What are the sources for their conclusions?*

The Society for Maternal-Fetal Medicine (SMFM) and the Society of Family Planning (SFP) published a joint guideline on fetal pain.⁷¹ This guideline heavily relies on interpretations of physiology and behavior that overlay adult human

responses and ignore terminology from other mammalian biology. One of these pieces openly agrees with the neuroscience and embryology laid out in this document, but describes that these cannot be interpreted to mean pain:

Neurobiological features that develop at 7, 18 and 26 weeks gestation suggest an experience of pain in utero. Pain, however, cannot be inferred from these features because they are not informative about the state of consciousness of the fetus and cannot account for the content of any presumed pain experience.⁷²

The author of this piece and others like it is a coauthor in the Royal College of Obstetricians and Gynaecologists' guideline on fetal pain, which comes to similar conclusions.⁶⁶ This same author has since reconsidered his own position, citing that fetal pain can be truly experienced "without the capacity for self-reflection." While remaining pro-choice, this author wrote as of 2020 that

neuroscience cannot definitively rule out fetal pain before 24 weeks.... [F]etal pain does not have to be equivalent to a mature adult human experience to matter morally....¹⁷

Moreover, the definition of pain in the joint SMFM-SFP document is from the International Association for the Study of Pain (IASP), which describes pain as

"[a]n unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."⁷³ IASP is largely an organization for human pain, but does have a special interest group for non-human pain, and one of its members defined pain as "the aversive sensation that comes from higher processing of something that starts out as tissue damaging."⁷⁴ This broader definition, validated by the special interest group of IASP, imports less of the adult human experience and matches the definition of the present document.

Summary of Recommendations and Conclusion

The following recommendations are based on good and consistent scientific evidence (Level A):

1. Fetuses as early as 7 weeks' gestational age respond with an increasing spectrum of aversive behavioral and physiological reactions to noxious stimuli that cause pain in mature humans.
2. The zygote expresses adrenergic receptors, which have a role in response to noxious stimuli.

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1. A human fetus may feel pain as early as 12 weeks' gestation.
2. Fetal pain perception is mediated by structures that develop by 12 to 24 weeks.
3. Subjecting an un-anesthetized fetus to noxious stimuli is associated with long-term adverse neurodevelopmental effects such as hypersensitivity to pain.

The following recommendations are based primarily on consensus and expert opinion (Level C):

1. Pain in human fetuses, as in nonhuman animals, do not need to be equivalent to adult human pain in order to change practice.
2. Abortions involving noxious stimuli, such as dismemberment, should be avoided after 14 weeks' gestational age.
3. When necessary, pregnancy should be ended after 14 weeks' gestational age only by induction of labor or cesarean section, depending on the gestational age and clinical circumstances.
4. Analgesia should be considered in neonates delivered after 14 weeks, even if resuscitation is not planned.

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