

reduce subjective and objective aspects of pain to the common denominator? If we accept the first possibility—that there is a causal relation between physical and mental processes in the brain—then it is possible to have a perfect description of the neurophysiological mechanism of the fetus and yet not know what is it like to be a fetus.<sup>1 2</sup> If we choose the second option we can argue that ascertaining some specific neurophysiological event is identical with ascertaining pain. So we could argue that the fetus is in pain because the pain can be detected through physiological changes in its body such as increase in heart rate, release of hormones and other substances, etc.

What happens if a dog is stung by a wasp? Certainly there is a complex reaction in its body, probably similar to the physiological processes in my body, and a frantic reaction of screaming, whining, or whimpering. For many people (including some philosophers) this behaviour is conclusive proof that the dog is in pain. I also am ready to accept that conclusion. But I am still dubious about what happens between the stimulus and the behavioural reaction of the dog. Even if we admit that some animals have a conscious experience of the world around them it is still problematic whether they can be subjects of their own conscious experiences—that is, whether they can reflect on their own experiences. Though the behaviour of the dog suggests that it is in pain, I cannot say if its relation to its pain is exactly the same as mine. I do not know if the dog is conscious of its

body and can identify, reflect upon, and control its pain. I do not know if there is any self in the dog.

What happens if in the course of amniocentesis a fetus is accidentally pricked by the needle? If the fetus is in the 30th week of pregnancy it perhaps feels some pain. But what if it is in the ninth or 10th week? Even if we could decide precisely when a capacity to feel pain emerges (and it is no doubt related to the level of development of the brain and nervous system) we would still have a problem with defining the ontological status of the fetal pain. Is it more like the animal pain or is it more like the human conscious, subjective, qualitative pain? I do not think we can experience pain unless we are aware of ourselves and our own bodies. On the other hand, if we admit to a possibility of unconscious mental events or unconscious pain<sup>3</sup> we can argue that there is a moment in fetal development when the fetus begins to react to noxious stimuli signalled by its neurophysiological system even though no self is yet present. The moral and clinical consequences of that fact are different and highly controversial.<sup>4 5</sup>

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## Reflex responses do not necessarily signify pain

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Can a fetus feel pain? This question is appropriate, as medical interventions during pregnancy,<sup>1</sup> fetal surgery,<sup>2</sup> and possibly termination of pregnancy expose the fetus to noxious stimuli. To answer the question we need definitions of “feeling” and “pain.” The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” and goes on to emphasise the importance of experience related to past injury. To feel something is defined as “to have the emotions excited, to experience a sensation.” These definitions imply that the brain must achieve a certain level of neural functioning, as well as having prior experience, before pain can be understood.

Neural maturation of any brain region includes so many stages and events that it is inadequate to use the presence or absence of any one event as evidence of functioning, but a critical factor must be the arrival of thalamocortical connections. These first penetrate the frontal cortical plate at 22-34 weeks,<sup>3</sup> and their arrival correlates well with evoked potential studies, which show that the distinct component signalling the arrival of sensory impulses at a cortical level cannot be detected before 29 weeks.<sup>4</sup>

### Role of sensory processing at lower levels

But is it appropriate in fetal and neonatal medicine to concentrate on the conscious perception of pain? Instead, should we not consider the neuronal activity that noxious stimulation produces in the pathways and nuclei concerned in sensory processing at lower levels of the central nervous system?

The development of the human spinal cord is a highly orchestrated process in which neurone and glial specific genes are induced in a manner closely similar to that in experimental animals.<sup>5</sup> It becomes functional early in fetal life, and reflex movements to somatic stimuli can

be evoked between 7.5 and 14 weeks while at the same time the fetus begins to move spontaneously in the absence of any obvious external stimulation. It is important to emphasise the reflex nature of these movements even though they may involve extensive body regions and therefore intersegmental and brain stem connections. They occur (in abnormal patterns) in anencephalic fetuses at 16-35 weeks even when only parts of the spinal cord are intact.<sup>6</sup>

Early reflexes are evoked by tactile stimulation or light pressure and are not necessarily nociceptive. In fact, small diameter afferent nerve fibres known to subservise nociception have not penetrated the fetal spinal cord at 19 weeks.<sup>7</sup> However, by 26 weeks even very low birthweight infants show a clear and measurable flexion withdrawal reflex to noxious stimulation, suggesting that nociceptive afferent input to the spinal cord is present.<sup>8</sup> Though these studies were carried out after birth, it is reasonable to assume that such responses would also occur in utero.

These cutaneous reflexes are exaggerated compared with those in adults, with lower thresholds and more synchronised and longer lasting reflex muscle contractions. Though providing important information on how the immature nervous system reacts to noxious stimulation, they cannot be equated with true pain experience, which must involve the cortex and develop postnatally along with memory, anxiety, and other cognitive brain functions. In other words, stronger reflexes are likely to reflect the absence of the normal inhibitory control or “dampening” influences that higher brain structures normally exert at more mature stages.<sup>9</sup> Exaggerated reflex response to noxious stimulation may be protective to an organism which (by virtue of cortical immaturity or malfunction) is unable to perceive and organise a more directed response to the pain.

In addition to spinal reflexes, infants delivered at 26-31 weeks show coordinated facial actions in

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response to heel prick.<sup>10</sup> In contrast with spinal cord reflex responses, younger gestational age is associated with less reactivity in facial expression to heel prick, suggesting that the youngest infants are less able to display more complex affective reactions to pain.<sup>11</sup> In addition, from 23 weeks of gestation fetuses can mount a hormonal "stress" response when needles are inserted into the innervated intrahepatic vein.<sup>1</sup> Though noxious stimuli frequently produce a biochemical stress response, such a response does not necessarily indicate pain. The link between reported levels of pain and the hormonal stress response in adults is unpredictable and increasingly questioned.<sup>12</sup> What the fetal stress response shows is exactly the same as the behavioural studies—that noxious sensory stimulation can produce a clear reaction from the fetal nervous system.

There are great differences in neural structure and function between developing and adult pain pathways.<sup>13-14</sup> One example is that fetal spinal cord sensory neurones which respond to noxious stimuli have larger receptive fields than in adults. Diffuse central connections and large dorsal horn receptive fields are likely to lead to poorer discrimination between noxious and non-noxious events and poorer spatial localisation by the fetus. Particularly important with respect to future analgesic therapy is the fact that neurotransmitter expression, receptor function, and distribution are all quite different from those in adults. Many immature receptor systems, including opiate receptors, are diffusely localised and have unusual patterns of expression,<sup>15</sup> suggesting that opiate analgesic action in adults cannot be simply extrapolated to the fetus.

#### No "pain" but possibly altered neural development

So can a fetus feel pain? Given the definitions of feeling and pain the answer must be no. But we cannot deny that the fetal nervous system mounts protective responses to tissue injury, starting just before the last trimester. The evidence for early exposure to noxious stimuli resulting in adverse effects on future neural development is increasing.<sup>16-20</sup> In other words, noxious stimulation may not need to penetrate consciousness in order to substantially alter the course of sensory development.

If a fetus or preterm infant is to survive and mature into an adult it is essential to consider this issue. As with the clear change that has occurred in the past seven years in pain management in neonates,<sup>21</sup> it may now be

pertinent to consider pain control in medical procedures for fetuses in the last trimester. The effects of trauma of any kind on the developing nervous system should be minimised as far as possible to avoid changing the course of normal development. More research is urgently needed on the developmental pharmacology of pain and analgesia.

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#### 250th anniversary of source document verification

When the London Infirmary (later The London Hospital and now the Royal London Hospital) was founded in 1740, a physician, a surgeon, and an apothecary were appointed. Dr John Andree (1698-1785), MD Rheims, LRCP, of Huguenot descent, was the first and, for some years, the only physician on the staff. He developed a special interest in epilepsy and what were then considered to be related disorders; in 1746 his case studies and observations formed the basis of his monograph *Cases of Epilepsy, Hysteria Fits and St Vitus Dance*. At a time when quackery and medical fraud were rife Andree not only thought it necessary to affirm the accuracy of his own case descriptions but offered opportunities to his readers to verify their validity. "I am sensible that some have taken upon them to publish cases, either entirely fictitious, or embellished with a variety of symptoms and course of medicines, hatched in their own brains, to raise their reputations, which has brought this most useful way of writing into some disregard, and made me hesitate at first when I undertook this task. But facts are stubborn things, and not to be baffled; and as the present cases are

genuine and literally true in every particular (which by the by may apologise for the plainness of style they appear in), as anyone may be convinced of by inspecting our books at the Infirmary, that contain the names of the patients, places of abode, occupation and distemper."

Andree thus invited his readers to apply what is currently termed source document verification. It was taken for granted at the time that details of patients who were admitted to hospital would be widely available. For instance, every governor of the London Hospital, of whom there were at least 300 in 1760, had a right to inspect the registers of admissions at any time. There were no codes of confidentiality to limit access to the records of patients who, in the newly established voluntary hospitals of the 18th century, were the objects of charity.—DENIS GIBBS is a retired physician in London

We welcome filler articles of up to 600 on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.