Paradoxical pain

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Relation of birth variables to death from cardiovascular disease

EDITOR—D J P Barker and colleagues’ study puts a further nail in the coffin of those who doubt that the intrauterine environment influences later health—in this instance, death from cardiovascular disease.1 A theme running through the study is that if we respond to this topic it is that maternal nutrition is primarily responsible for reduced prenatal growth. Though there can be no doubting the importance of maternal malnutrition as a cause of reduced fetal growth in poor countries and stresses on the mother resulting in complications, in the early part of this century, where Barker and colleagues’ cohorts were born and brought up, there is no strong evidence of undernutrition now being responsible for restraining intrauterine growth in developed countries.

Maternal diet is only one of the many factors that can lead to fetal growth retardation. To begin to understand mechanisms that might link the environment of fetal life and infancy with later development of disease, it is necessary to consider the question of how nutrition in early life influences adult hypertension, and how low birth weight could be mediated through dysfunction of the placental barrier to maternal cortisol.2

D P DAVIES
J MATTHEWS
Department of Child Health, University of Oxford, College of Medicine, Cardiff CF4 2XN

Paradoxical pain

EDITOR—David Bowsher defines paradoxical pain as pain in a patient with advanced cancer that does not respond to morphine.3 It is more generally understood as pain that is made worse rather than better by increasing doses of morphine. It has been reliably reported with large doses of intrathecal morphine and diamorphine and probably occurs occasionally with large daily doses of the same drugs intravenously. Bowsher and his colleagues have made a good case for paradoxical pain being the result of a genetic inability to metabolise morphine to the potent morphine 6-glucuronide,4 leaving large quantities of morphine 3-glucuronide (a putative morphine antagonist or a non-specific cerebral stimulant, or both) 5 unopposed. It is difficult, therefore, to understand why Bowsher has opted for an alternative definition.

It is also disturbing that he has used “overwhelming pain” as a synonym for paradoxical pain. Overwhelming pain is a term used to emphasise a consequence of chronic unrelied severe cancer pain.6 It almost always responds to adequate amounts of morphine, coanalgesics if appropriate, and, usually, an anxiolytic. A comparable situation is sometimes seen despite large doses of morphine when the patient variety of fears and worries has been addressed. Thus, in one case, a patient with inoperable cancer of the oesophagus was still in pain despite receiving 12 g of oral morphine a day when he was admitted to a hospice; a week later he was free of pain when taking 60 mg of morphine a day and 10 mg of diazepam at night. His seemingly morphine resistant nociceptive cancer pain responded to listening, explanation, and the setting of positive rehabilitation goals. Nociceptive pain is also relatively resistant to morphine and other opioids when there is peripheral or central neural sensitisation. Sensitisation occurs in damaged tissue and the surrounding area and in areas subserved by either an injured peripheral nerve or an intact part of the central nervous system. Pain associated with inflammation is a typical example of peripheral sensitisation,7 hence the need to use a non-steroidal anti-inflammatory drug in most patients with painful soft tissues, skin, and bone metastases. Morphine alone is often inadequate, but there is nothing paradoxical about this. Central sensitisation may also occur in such cases as part of a secondary “wind up” phenomenon in the dorsal horn. Occasionally this can be specific—for example, a patient with an N-methyl-D-aspartate receptor blocker such as ketamine.8 Central sensitisation in neurogenic pain is more complex and, as Bowsher points out, demands a range of alternative measures.9

ROBERT TWYCROSS

In 1967 Cicely Saunders described the concept of total pain, which encompasses the psychological, emotional, and spiritual turmoil of some patients with severe pain. Might this be what Bowsher refers to as overwhelming pain?10

G W C HANKS
W M O’NEILL
M T FALLOn

United Medical and Dental Schools, Division of Oncology, Department of Palliative Medicine, St Thomas’ Hospital, London SE1 7EH


12. Taxkier RR, Donw歉 D, Deafferentiation and central sensitisation.


9. The concept of paradoxical pain and its relation to morphine metabolites raises many questions. There are several conceptual errors inherent in this description. One of the most fundamental is that the pain syndromes as described should at any time actually respond to opioids. This makes the assumption that so called paradoxical pain is nociceptive pain, with the second assumption that all nociceptive pain

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