

# Nitrous Oxide on the Labour Ward: Will We Still Be Laughing in Ten Years?

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## Abstract

A recent article in this journal addressed the safety issues concerning prolonged exposure to nitrous oxide in pregnancy. What many obstetricians may be unaware of is an ongoing controversy about the effect of nitrous oxide on neonatal brain development. This letter briefly summarises the concerns about nitrous oxide and asks whether advice given to mothers should change.

Sir:

A case of severe neutropenia after intermittent use of nitrous oxide in pregnancy was recently reported in The Internet Journal of Gynaecology and Obstetrics.<sup>1</sup> Whilst rare, the potential for nitrous oxide to cause bone marrow suppression has been well recognised by the anaesthetic community for many years.

Obstetricians may however be unaware of another area of recent concern involving nitrous oxide and other anaesthetic agents. In the United States The Food and Drug Administration (FDA) and The National Institute for Health (NIH) has authorised an expert working panel to review the issue of anaesthesia induced apoptotic neurodegeneration in the fetal and neonatal brain.<sup>2</sup>

Recent experimental work on primarily rat models has highlighted the ability of anaesthetics that are NMDA antagonists or have GABA mimetic properties to trigger neuroapoptosis in the developing fetal and neonatal brain. In rats this apoptosis has been associated with permanent brain damage with impairment in memory and learning. Drugs in frequent use in Obstetric Anaesthesia including nitrous oxide, volatile anaesthetics and midazolam have been implicated. It would also appear that anaesthetic cocktails consisting of drugs from both these classes are particularly effective at triggering neuroapoptosis. An editorial in Anaesthesiology<sup>3</sup> highlighted the difficulties in extrapolating the data the data on rat neurodevelopment to humans. There is also doubt in some quarters that as to whether such changes could occur in clinical settings with

lower doses, shorter exposure times and tight physiological monitoring.

The FDA and the editorial in Anaesthesiology both concluded that a change in clinical practice is premature without further evidence. This controversy does raise important questions for Obstetrics. Paediatric anaesthetists have few alternatives to these classes of drugs. Indeed withholding anaesthesia and analgesia from term or pre-term infants is associated with increased operative complications and development of neurodevelopmental, cognitive and behavioural deficits.<sup>4</sup> Obstetric Anaesthetists have other alternatives including systemic opioids and regional anaesthetic and analgesia techniques, which give us the option to avoid nitrous oxide and volatile anaesthesia. Indeed the advent of Remifentanyl Patient Controlled Analgesia in labour may give an effective alternative to those women needing analgesia but not wanting a regional technique.

If we can avoid the use of Nitrous Oxide for labour analgesia, should we still be using it routinely knowing that there is concern about its effect on the unborn fetus? In particular should the mother with fetal distress be prevented from using Nitrous Oxide to avoid exacerbating any neuronal injury caused by hypoxia? Does Nitrous Oxide still have a role in General Anaesthesia for emergency Caesarean Section? Should we revise the advice we give expectant mothers? The information leaflet available from the Royal College of Anaesthetists in the United Kingdom states "the gas does cross the placenta but is not known to have an adverse effect on the baby".<sup>5</sup> The Obstetric Anaesthetists'

Association (also in the UK ) leaflet says of Nitrous Oxide ,  
“it does not harm your baby and it gives extra oxygen, which  
may be beneficial for you and your baby”.

We must await the results of further investigations into the  
effects of these drugs on human neuronal development but  
the findings could spell the end of Nitrous Oxide on the  
Labour Ward.

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