itself. Surely doctors would also have to inform the woman that this perinatal mortality rate would, by their own data, still mean a risk increased 28-fold over that in delivery by caesarean section, and I doubt whether many women would find a risk presented in this way very reassuring.

But it is doubtful whether the authors are justified to use their figures for antenatal counselling purposes at all. It has to be recognised, for medicolegal as well as counselling purposes, that women for a "trial of vaginal delivery" and those who actually had a vaginal delivery represent overlapping but essentially different populations. Some women who deliver vaginally were not intended for a trial, and often were not even known to have a breech presentation, and many women who were planned to have a "trial" do not end up being delivered vaginally.

Antenatal counselling must emphasise the increased risk for intrapartum intervention, but the onus of proof for advising a routine intervention such as elective caesarean section must lie with the advocates of such a policy. Unless solid data to the contrary emerge, I will continue to counsel women with a mature fetus presenting by the breech that, given proper antenatal assessment and selection, and with modern methods of obstetric management, there is no evidence of any increase in perinatal mortality associated with a trial of vaginal delivery.

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Serotonin, gastric emptying, and dyspepsia

EDITOR,—In their paper on the role of central serotonin receptors in non-ulcer dyspepsia A Chua and colleagues claim that the prolactin response to buspirone provides an index of the function of central serotonin-1A receptors. Unfortunately for the authors, there is compelling evidence that this is not true and that antagonism of dopamine-D2 receptors is the main mechanism by which buspirone stimulates secretion of prolactin.

Firstly, buspirone binds with only slightly less affinity to dopamine-D2 receptors than to serotonin-1 receptors.¹ Secondly, in an isolated rat pituitary model buspirone was shown to antagonise the inhibitory effects of dopamine on release of prolactin.² Thirdly, in human studies comparison of buspirone with two related serotonin-1A agonists, gepirone and ipsapirone, shows that only buspirone potently stimulates secretion of prolactin whereas they all share similar effects on growth hormone, cortisol, and body temperature.³ This difference is probably due to gepirone and ipsapirone lacking significant affinity for dopamine-D2 receptors.

Fourthly, in an antagonist study using pindolol, a β blocker with serotonin-1A antagonist properties, we found that the growth hormone and hypothalamic responses to buspirone were abolished whereas there was only a small, non-significant reduction in the size of the prolactin response.⁴ Our negative finding has subsequently been replicated by another group.⁵ The study that Chua and colleagues cite in their support of their contention was of only two subjects⁶ and can be dismissed. Blockade of this response by metergoline and methysergide does occur but is probably due to their dopamine-D2 agonist properties,⁸ and, consistent with this, metergoline antagonises the prolactin response to haloperidol in normal

volunteers.⁹ Taken together, these lines of evidence mean that the authors' confident statement that secretion of prolactin stimulated by buspirone is a "good measure of the sensitivity of central serotonin-1A receptors" is not supported by the facts, which indicate dopamine-D2 mediation.

In conclusion, I remain sceptical about this and similar studies using the prolactin response to buspirone as an index of the function of serotonin-1A receptors, particularly when evidence indicates that the growth hormone or adrenocorticotrophic hormone response would be a more valid index.

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AUTHORS' REPLY,—Ian Anderson suggests that the prolactin response to stimulation with buspirone is mediated via dopamine-D2 receptors. Serum prolactin concentration can be increased by 5-hydroxytryptophan, direct acting serotonin agonists, and serotonin releasers, while serotonin receptor blockers lower prolactin concentrations.^{1,2} Investigators have also shown that the serotonergic stimulation of prolactin release is not by inhibition of dopaminergic activity.³

Buspirone is an agonist at presynaptic and postsynaptic 5-hydroxytryptamine type-1A (serotonin-1A) receptors. Its activity at presynaptic dopamine receptors, however, is not considered characteristic of the azapirones.^{4,5} When taken orally buspirone and gepirone, another azapirone with a highly selective ligand for brain serotonin-1A receptors, increase plasma prolactin concentrations.⁶⁻⁸ The fact that plasma prolactin concentrations were not affected by ipsapirone could be explained by its associated serotonin-1 receptor antagonist property.⁹ The prolactin response to buspirone seems to be at serotonin receptors, as suggested by the buspirone-metergoline study, and more specifically at the serotonin-1-like receptors (buspirone-pindolol study).⁷ The different results observed in prolactin suppression with pindolol (mixed agonist-antagonist properties at the serotonin-1A receptor) in Coccaro *et al*'s and Meltzer *et al*'s studies¹⁰ are due to the administration of different doses of D1-pindolol (higher doses tend to display serotonin-1A receptor agonist effects). Effects of buspirone on central dopaminergic receptors remain unresolved with conflicting agonist¹¹ and antagonist properties.

Studies in our unit with bromocriptine (a dopamine agonist) in patients with non-ulcer dyspepsia did not show any difference from findings in healthy controls (unpublished). Furthermore patients with non-ulcer dyspepsia treated with sertraline and fluoxetine (selective

serotonin reuptake inhibitors) show a precipitation of their symptoms initially, further supporting the theory of hypersensitive serotonergic receptors (this study is continuing).

In reply to Malcolm H Duncan's letter,¹² all the patients investigated in our study had dyspeptic symptoms of more than three months' duration with no concomitant symptoms or illness. They were all within 10% of their ideal body weight. As mentioned in our paper, they constitute up to 35% of our patients with functional dyspepsia. All the above patients underwent a full psychiatric assessment by a consultant psychiatrist, including completion of the comprehensive psychopathological rating scale.¹³ None of the patients studied had any evidence of psychiatric disorders.

Only one patient with non-ulcer dyspepsia had a prolactin response that overlapped that in the controls, though it was in the upper range of normal. One patient did have a particularly high response, but assessment of the prolactin response with geometric means showed a similar significant difference between patients and controls. Furthermore, later studies with other patients have shown similarly high responders.

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Hepatitis B vaccination

EDITOR,—There is a developing paradox in relation to hepatitis B vaccination of health care workers.

Firstly, we have the advice that, at least in adults, the immune status in relation to hepatitis B does not depend on the level of circulating antibodies—that the long term protection resides in the memory cells in the immune system.¹ We are told that no health care worker who has initially responded to the vaccine has developed hepatitis B infection or carrier status regardless of the reduc-