necessary to allow the patient's transfer elsewhere —for rehabilitation, for example.

In conclusion, the cornerstone of control of methicillin resistant *S aureus* is good infection control practice, as I stated in my review. Infection control teams wish to prevent and control the spread of any multiresistant organism as the antimicrobial armamentarium against these organisms is reduced. Additionally, the few available antibiotics tend to be expensive and may be toxic. Unfortunately, epidemic strains of methicillin resistant *S aureus* still exist, and unaffected hospitals should remain vigilant to prevent their arrival and spread.

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Managing the third stage of labour

Nausea is a fair price for preventing haemorrhage

EDITOR,—Susan J McDonald and colleagues conclude that there are "few advantages but several disadvantages for the routine use of oxytocin-ergometrine when prophylactic active management of the third stage of labour is practised."[1] The disadvantages were significantly higher rates of nausea, vomiting, and high blood pressure measured in the labour ward. The results suggested, however, that if women received oxytocin alone an additional 8-11 women per 1000 would experience a severe postpartum haemorrhage. This is roughly one patient a week in an average hospital with 5000 deliveries a year. Although this increased incidence did not reach significance, it might have done had more women been recruited to the trial, as suggested by the results of meta-analysis.[2]

As the authors point out, postpartum haemorrhage is an important cause of death both in Britain and, more particularly, in the Third World. As it is far more important than the transient side effects that did reach significance, I believe that the conclusion reported was misleading. Until further studies with increased doses of oxytocin prove it to be as effective as the combined oxytocin-ergometrine preparation at reducing the incidence of postpartum haemorrhage, my preference will not change.

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Oxytocin more stable in tropical climates

EDITOR,—Susan J McDonald and colleagues conclude that parenteral oxytocin is as effective as a combination of oxytocin and ergometrine in reducing the risk of postpartum haemorrhage when used routinely in the third stage of labour but that the combination is associated with nausea, vomiting, and increased blood pressure.[1] In selecting the most appropriate injectable oxytocic drug for developing countries additional arguments should be used, such as the stability in tropical climates and cost. The stability of these lifesaving drugs is crucial as a serious lack of the active ingredient in samples of ergometrine has been reported from several developing countries.[2]

As part of a systematic research programme by the World Health Organisation to reduce maternal mortality we have studied the stability of different injectable oxytocic drugs at various temperatures and in various light conditions. Ampoules of 11 brands of injectable ergometrine, methylergometrine, and oxytocin were stored in the dark at 4·8°C, 21-25°C, 30°C, 40°C, and 50°C and in daylight (but protected from direct sunlight) at room temperature (21-25°C). The amount of active ingredient was measured at 0, 0·5, 1, 2, 3, 6, and 12 months. When stored at 4-8°C in the dark all three drugs retained acceptable amounts of active ingredient (table). All three drugs, however, showed a gradual loss of the active ingredient over time, the decline being faster at higher temperatures. In addition, ergometrine and methylergometrine were both very unstable when exposed to light, with an average loss of 21% and 27%, respectively, of the active ingredient in one month (range 14-61%) and over 90% after one year. Short exposure (2-4 weeks) to temperatures of 40-50°C in the dark—which often occurs during transport in tropical countries—had no serious effect on any of the drugs. Full results have been reported.[3]

Active ingredient of injectable oxytocic drugs after one year of controlled storage (values are mean percentage of initial amount (95% confidence interval))

	Storage condition		
	Dark, 4-8°C	Dark, 30°C	Light, 21-25°C
Ergometrine	95 (90 to 100)	69 (56 to 83)	9 (2 to 15)
Methylergometrine	96 (92 to 100)	82 (69 to 94)	9 (0 to 22)
Oxytocin	101 (99 to 102)	86 (83 to 90)	93 (91 to 95)

Under tropical conditions of temperature and light, oxytocin is more stable than either ergometrine or methylergometrine. This is especially relevant as ampoules of oxytocic drugs are often kept in open trays ready for use in pharmacies and labour wards in developing countries. The non-profit world market prices of generic 0·5 mg ergometrine and 10 IU oxytocin are similar at around $0·11 per phial. The better stability in tropical climates and equal cost are additional reasons why oxytocin is the drug of choice for routine use in active management of the third stage of labour in developing countries.

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Reduction in haemorrhage is a major advantage

EDITOR,—Susan J McDonald and colleagues make recommendations about the most effective oxytocic agent in the managment of the third stage of labour.[1] We are surprised at their conclusion that a potential 1% reduction in severe postpartum haemorrhage is of minimal advantage compared with the "serious" disadvantages of vomiting and a rise in blood pressure. As their observed rate of severe postpartum haemorrhage was 4%, a 1% reduction is in effect a 25% reduction in the overall incidence. We consider this to be a major advantage, especially in the developing world, compared with the "non-serious," albeit unpleasant, disadvantages of vomiting and changes in blood pressure of uncertain adverse clinical effect.

The interpretation of the data remains subjective. We think that it is worth detecting a true reduction of 1% in the incidence of severe postpartum haemorrhage in view of the contribution of postpartum haemorrhage to maternal mortality globally. This would have required a sample size of 8300, so we would have recommended the extension of the McDonald and colleagues' trial. The reduction of postpartum haemorrhage deemed to be clinically important remains arbitrary.

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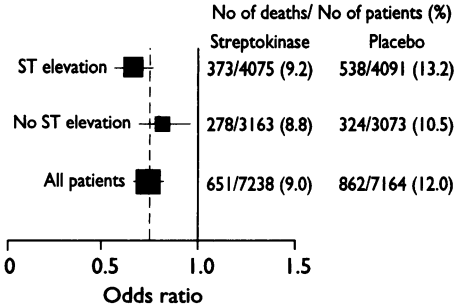
Deciding who should have thrombolysis

EDITOR,—K S Channer[1] and other correspondents[2] seem to misunderstand the results of clinical trials of thrombolytic agents. In 17 000 patients in the second international study of infarct survival (ISIS-2) the odds of dying were reduced by 25% by streptokinase compared with placebo (figure).[3] With such large numbers the confidence intervals, which indicate where the "true" result is to be found with 95% certainty, are narrow.

The reduction in odds was greater than average for those with ST elevation in the presenting electrocardiogram and less than average for those without ST elevation. The confidence intervals did not include unity for either group, so a significant



Odds ratios and 95% confidence intervals for death within 35 days after streptokinase or placebo in patients with or without ST elevation in second international study of infarct survival