neuronal damage associated with ischaemia.[9] However, magnesium sulphate also affects many other organs,[10] and it would be implausibly fortuitous if these effects were exclusively beneficial.

For example, magnesium sulphate is known to relax smooth muscle and in many parts of the world is widely used as a tocolytic agent for preterm labour (despite little evidence from randomised trials to support this use[11]). However, if the tocolytic effect is significant at doses used for pre-eclampsia, magnesium sulphate administration could increase the length of labour—and the risks of caesarean section and of postpartum haemorrhage. These effects, if they exist, would be especially important in resource poor settings, where pre-eclampsia may be particularly common.[12]

The fetus is also not immune to potential effects, beneficial or harmful, because magnesium readily crosses the placenta. Hypermagnesaemia in the neonate is associated with flaccidity, hyporeflexia, and respiratory depression.[13] It has been suggested that prenatal magnesium administration may reduce the risk of cerebral palsy for very low birthweight babies.[14] This observation comes from several high quality case-control studies; but a small randomised trial evaluating magnesium sulphate as a tocolytic agent reported an increased paediatric mortality in the magnesium arm.[15] Whatever the true effects for these low birthweight preterm babies, reassurance is also required about the short and long term effects of in utero exposure to magnesium sulphate on term babies.

Determining the best care for women with pre-eclampsia is an important common problem in obstetrics. In a recent survey of obstetricians in Britain and Ireland over half the respondents expressed interest in collaborating in a trial to evaluate magnesium sulphate for women with pre-eclampsia.[3] To be clinically worthwhile, treatment with magnesium sulphate would probably need to reduce the risk of eclampsia by at least 50%, and this seems a realistic expectation based on currently available evidence.[6] To show such a halving in risk with reasonable certainty requires a trial of 14 000 women ($\alpha = 0.05$, $\beta = 0.1$). This is the challenge taken up by the Magpie Trial Collaborative Group. The magpie trial aims, for the reasons discussed above, to evaluate other possible and important effects on women and their children of magnesium sulphate for pre-eclampsia. The trial is now recruiting, and new collaborators are very welcome.*

Lelia Duley *Obstetric epidemiologist*

Magpie Trial Coordinating Centre, Institute of Health Sciences, Oxford OX3 7LF

James P Neilson *Professor of obstetrics and gynaecology*

University of Liverpool, PO Box 147, Liverpool L69 3BX

*Both authors are principal investigators for the magpie trial. For further information please contact the trial coordinating centre: tel 44 1865 226642, fax 44 1865 227173, magpie@ndm.ox.ac.uk .

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A little bit of measles does you good

Even if measles is eradicated, immunisation may still be desirable in developing countries

Measles still kills 800 000 children in developing countries every year,[1] although immunisation has substantially reduced the number of deaths. Immunisation lowers mortality primarily by reducing the incidence of measles, but it may also lower mortality by increasing the age at which children are infected and by reducing the severity of infection in immunised children and their contacts.[2] Morever, the vaccine itself may reduce mortality from conditions other than measles.

Epidemiological research has shown two important characteristics of measles: the severity of clinical illness is largely determined by the infecting dose, and, surprisingly, mild infection and standard doses of Schwarz vaccine substantially reduce mortality from conditions other than measles.[3] Children infected with a large dose of measles virus have a shorter incubation period, more severe disease, and a higher mortality. Children who are infected outside the home (primary cases) have milder disease than secondary cases (who are infected in the household with, on average, a larger dose of virus).[2] This can result in an amplification effect, where each generation of cases becomes progressively more severe; conversely, if index cases are mild or there are only a few generations of cases, perhaps because of immunisation, mortality will be low.[2 3]

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What is the evidence for the remarkable hypothesis that standard doses of Schwarz vaccine reduce mortality from conditions other than measles? Firstly, measles causes only 10% of child mortality, but the vaccine reduces mortality in developing countries by at least 30%.[4] Secondly, immunised children who have not had measles have a much lower mortality than unimmunised children who have not had measles.[3 4] This reduction in non-measles mortality is greater in girls than in boys.[5]

In developed countries measles vaccine is usually given at 12-15 months of age because seroconversion rates are higher at that age than in younger children. However, in developing countries many children die from measles before they are 12 months old, so measles vaccine is usually given at 6-9 months. In 1990 the World Health Organisation recommended that high doses of the Edmonston-Zagreb vaccine should be given at the age of 6 months,[3] because this gave much higher seroconversion rates than standard doses of Schwarz vaccine given at 6 months. However, this recommendation was rescinded when it was found that girls given the high titre Edmonston-Zagreb vaccine had a higher mortality than girls who had received the standard Schwarz vaccine.

The higher mortality was not due to vaccine failure: the girls did not have more measles, and they did not have a higher mortality than unimmunised children. The explanation seems to be that high titre Edmonston-Zagreb vaccine did not protect against mortality from conditions other than measles (an effect that is more marked in girls than boys).[3] A little bit of vaccine does you good—but a lot of vaccine is not so good.

When standard doses of Schwarz vaccine are given at 4-8 months of age seroconversion rates are lower than after vaccination at 9 months and more children get measles. However, case fatality rates are lower in the excess cases, and the protection against non-measles deaths occurs earlier, so total mortality is lower with immunisation at 6 months despite the lower seroconversion rate.[6]

Severe measles has a high fatality rate, so it is not surprising that many studies have found that children who have measles have a higher mortality than children who do not have it. However, many of the children who do not get measles have been immunised, which reduces their mortality from diseases other than measles. Compared with unimmunised children who have not had measles, unimmunised children who have measles as primary cases (with a small innoculum) have a lower mortality, but secondary cases (with a larger innoculum) have a similar or higher mortality.[7] A little bit of measles does you good—but a lot is bad.

These observations suggest two important conclusions: when measles occurs after immunisation this does not necessarily imply total vaccine failure, and the effects of a new vaccine cannot therefore be assessed solely by antibody responses and protection data. Vaccine trials will provide more useful information if they concentrate on mortality rather than laboratory evidence of seroconversion and clinical illness.

We have the ability to eradicate measles.[1] However, there is strong evidence that measles vaccine protects against death from conditions other than measles, so it might be sensible to continue to give measles vaccine to children in developing countries even if we eradicate the disease.

Frank Shann *Director of intensive care*

Royal Children's Hospital, Melbourne, Victoria 3052, Australia

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Evaluating NHS Direct

Early findings raise questions about expanding the service

The creation of NHS Direct reflects a number of different political and policy concerns. One is consumerism and the growth of the 24 hour society.[1 2] Another is the need for demand management against a background of growing demand for primary and emergency care and problems in recruiting and retaining nurses and general practitioners. Is the recently announced expansion of NHS Direct supported by its preliminary evaluation?[3] This has been reported as showing that it is a success,[4] but a closer look at the detailed results reveals a more equivocal picture.

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NHS Direct is a telephone triage system operated by nurses to advise callers on the most appropriate form of care. The evaluation has so far looked at three aspects of the service in the first three pilot sites: a descriptive account of the organisation and users of NHS Direct; caller satisfaction; and a "before and after" assessment of its effects on other services.[3] This last aspect is important because at least part of the rationale for NHS Direct is to reduce unnecessary demand on other NHS services.

The results to date show lower call rates than expected, with only one third of the predicted total