

## Special Report

# Nutrition as a preventive strategy against adverse maternal pregnancy outcomes – a USAID/Wellcome Trust Workshop at Merton College, Oxford, UK, 18–19 July 2002

Under the sponsorship of the US Agency for International Development (USAID) and the Wellcome Trust, an expert meeting was convened at Merton College, Oxford, UK on 18–19 July 2002 to review our understanding of the role of nutrition in reproductive health and favourable pregnancy outcomes for mother and infant. The background to the meeting was an increasing scientific awareness of the importance of these issues, combined with a lack of clarity on how they could be translated into practical recommendations. The purpose of the meeting was to review the current status of knowledge – particularly the role of micronutrients – and how they, macronutrients and energy intakes could be best applied to advance human health.

To take up this task and respond to this challenge, a multidisciplinary group of some 20 leading nutritionists, obstetricians, epidemiologists, paediatricians and physiologists from both developed and developing countries were brought together. Representatives of the World Health Organization, the US National Institutes of Health, USAID and the Wellcome Trust also attended. The workshop was the culmination of several months of activity during which study groups prepared background review papers<sup>1</sup>.

High rates of pregnancy-related mortality and morbidity persist in the poorer countries of the world, with maternal mortality rates reaching over 1000 per 100 000 live births in some countries, and millions of infants are born too early, too small or with serious infections. For these reasons, the discussions concentrated on maternal morbidity and mortality and how these contribute to pregnancy loss, prematurity, intrauterine growth restriction and perinatal morbidity – especially infection. The evidence showing direct associations between micronutrient deficiencies and poor pregnancy outcome, be it at periconception or in different stages of pregnancy, is not well documented. Nevertheless, the biological plausibility that such interactions occur through many pathways is reasonably strong and the limited data available suggest that nutrition interventions can be cost-effective.

Infections continue to account for a substantial proportion of pregnancy-associated morbidity in developing countries, some of which involve interactions with nutritional pathways. For example, parasitic diseases including malaria and certain intestinal parasites have

profound effects on pregnancy outcome; the impact being partly on changes in placental function and partly by changes in micronutrient levels. The importance of intrauterine and placental infection, including chorioamnionitis, was highlighted, although a role for undernutrition in the development of pelvic inflammation is not yet defined. A clear association between plasma micronutrient concentrations and infection has been identified, but interpreting these associations is complicated by the effect of the acute-phase response on plasma micronutrient levels. Work on this conundrum is ongoing and assays for micronutrient status that are less influenced by inflammation are being developed.

Metabolic complications that can result in adverse pregnancy outcomes are common in both developed and developing countries. They include gestational diabetes, insulin resistance, pre-eclampsia and bone mineral density of mothers and their neonates. The role of nutritional deficiencies or excesses causing – and nutrition interventions ameliorating – consequential adverse pregnancy outcomes is still uncertain. The documented beneficial effect of the most widely used nutrition intervention, namely oral iron tablets, on preventing severe anaemia was noted. However, questions were raised about possible antioxidant damage from routine use of prenatal iron supplements, although the effect of iron-induced oxidative stress on pregnancy outcomes has not yet been defined.

Additional stressors may also work through nutritional routes. These include psychosocial stress, strenuous physical work, cigarette smoking and alcohol. The negative effect of these on micronutrient status is increasingly being recognised. The association between short pregnancy intervals, particularly in women with a low body mass index, and poor pregnancy outcome was also highlighted.

Many of the studies reviewed and discussed were cross-sectional or observational; only a few were well-designed, randomised controlled trials. There are considerable knowledge gaps about the stage of pregnancy at which particular nutrition interventions would have the maximum benefit. A review of the basic elements of foetal growth and its regulation emphasised the vulnerability of the foetus to nutritional status at different stages of

development, and hence the need to consider nutritional interventions well in advance of pregnancy.

The following represented the strong consensus reached by the participants.

- Pre-maternal and/or maternal nutritional status has major effects on maternal, foetal, neonatal, infant, childhood and life-long health, creating enormous medical, economic and social burdens.
- While there is a desire to intervene, there are significant knowledge gaps that will require both basic and applied research before efficacious and effective interventions can be planned, evaluated, accepted, and then diffused into practice.
- There needs to be a far greater interactive and planned approach to resolving the outstanding scientific, clinical and public health issues. This must involve basic, clinical, epidemiological and health policy researchers.
- A formal and integrated approach between these groups is likely to make more rapid progress than isolated and individual investigator-initiated research efforts. The multinational and large research funders/charities and health policy agencies should

convene together with science leaders to develop such an approach.

These conclusions are significant in that they identify the likely health gains from focusing on this issue, the enormous knowledge gaps, and the need to undertake further biomedical, clinical, epidemiological and health policy research to advance matters. It was clear that the magnitude of the task, the complexity and cost of the research were such that a much more co-ordinated, multidisciplinary approach than has been traditional in much academic research would be most likely to make progress. This should preferably draw together scientists and funding agencies internationally.

Andrew Tomkins, Catherine Davies, Robert Goldenberg, Alan Jackson, Carl Keen, Janet King and Penelope Nestel

Correspondence to Alan Jackson (a.a.jackson@soton.ac.uk)

### Reference

- 1 Bhutta ZA, Jackson A, Lumbiganov P, eds. Nutrition as a preventive strategy against adverse pregnancy outcomes. *Journal of Nutrition* 2003; **133**: 1589S–767S.