Editorial

Focusing on Malnutrition Management to Improve Child Survival in India

Over 10 million children under five years of age die each year and 22% of these deaths occur in India (1). This proportion is substantially higher than for other countries, the next highest being Nigeria which accounts for 8%. Since India carries the main burden of child deaths globally, India's performance in improving child survival will define whether the Millennium Development Goal 4 will be achieved by 2015 (*i.e.*, global child deaths reduced by two-thirds).

Diarrhea and pneumonia account for approximately half the child deaths in India, and malnutrition is thought to contribute to 61% of diarrheal deaths and 53% of pneumonia deaths(1). In fact, some of the first studies to demonstrate the importance of this synergism between malnutrition and infection emanated from India(2). Part of the explanation for the important underlying role of malnutrition in child deaths is that most nutritional deficiencies, including vitamin A and zinc, impair immune function and other host defences leading to a cycle of longer lasting and more severe infections and ever-worsening nutritional status. Thus inadequate intake, infection and poor nutritional status are intimately linked. Well-nourished children rarely die from diarrhea, pneumonia and other common childhood infections, and maintaining a good nutritional status is an integral part of improving child survival. Interventions to prevent malnutrition in all its forms should therefore receive the highest priority. It is against this background that the International Union of Nutritional Sciences in August 2005 at the XII International Congress of Nutrition in South Africa launched the International Malnutrition Task Force (IMTF) to raise the profile of malnutrition among policy makers and donor agencies and to advocate for increased recognition of its importance in child survival. A key objective is to develop capacity building partnerships to prevent and treat malnutrition, and to advocate for inclusion of malnutrition in curricula to train medical, nursing and other health professionals(3).

In hospitals in developing countries, severely malnourished children comprise a significant proportion of pediatric deaths. This is not because there are more admissions for severe malnutrition than for other conditions but because a much higher proportion of them die. This disproportionate contribution of severe malnutrition to inpatient deaths is rarely recognized by doctors or administrators: children may not be routinely weighed on admission and malnutrition is likely to be entered as a diagnosis only if there are no other presenting clinical conditions. Most severely malnourished children are reported as cases of gastroenteritis or pneumonia, so malnutrition often does not even appear in hospital statistics. The reason why severely malnourished children have a disproportionately higher mortality in hospital than other children is that treatment practices for severe malnutrition are often poor and outdated, so many children die unnecessarily. Case fatality rates of 20-40% are not unusual. The decision by the Indian Academy of Paediatrics (IAP) to disseminate treatment guidelines for severe malnutrition(4) is therefore timely and commendable and will surely contribute to India's progress in achieving MDG4.

The basis for the guidelines is that there are physiological and metabolic changes which occur in severe malnutrition and which need to be taken into account when prescribing treatment. For example there are reductions in the functional capacity of organs and slowing of cellular activities, a process known as 'reductive adaptation'. If these changes are ignored, severely malnourished children are put at increased risk of death from hypoglycemia, hypothermia, electrolyte imbalance, heart failure and untreated infection. The guidelines for standardized treatment reduce the risk of death from these conditions.

The IAP guidelines are based primarily on the

international guidelines developed by WHO(5) which set out 10 steps for routine case-management, and a select group of health professionals forming the IAP Task Force adapted these to the situation of India. The initial stabilization phase focuses on the following:

- feed every 2-3 hours, day and night to prevent hypoglycaemia and hypothermia;
- keep warm;
- rehydrate with low-sodium fluids: monitor closely for signs of fluid overload: avoid intravenous fluids, except in shock;
- give 100 kcal/kg body weight/day and 1 g protein/kg/day;
- give potassium and magnesium to correct electrolyte imbalance: restrict sodium;
- give micronutrient supplements: do not give iron; and
- give broad-spectrum antibiotics even when clinical signs are absent as infections can be silent.

The rehabilitation phase includes:

- rebuilding wasted tissues with high energy, high protein diets and micronutrients;
- psychosocial stimulation to improve mental development; and
- preparation for continuing care and follow-up after discharge.

Experience over the past decade, indicates that survival of malnourished infants improves substantially if the WHO guidelines are followed systematically. A halving of deaths, from 40% to 20%, has been regularly reported when the guidelines are substantially followed (*e.g.*, special feeds day and night, antibiotics, electrolytes, avoiding IV fluids except in shock, and not giving diuretics for edema). Mortality can be reduced to <10% when the guidelines are followed assiduously. This involves training all incoming staff, careful supervision of junior staff, careful monitoring of intake to guide selection of oral or nasogastric feeding, careful monitoring during rehydration to prevent fluid overload, daily ward rounds to identify children with new episodes of diarrhea or illness, good hygiene to prevent nosocomial infections, attentiveness to danger signs, and diligence in performing all tasks. To reduce mortality to <5% requires the specialized skills of experienced pediatricians as these residual deaths are usually among very seriously ill children.

IAP vs. WHO Guidelines

The IAP Guidelines differ on some important points from the WHO Guidelines and we highlight two examples where the clinical management approach for malnourished children differs critically from that usually used for well nourished children. First, addressing the need for rehydration, the IAP Task Force considered that a low-sodium fluid is not necessarily the best treatment for dehydration and instead advocates a 75 mmol Na/L rehydration fluid. There are good physiological reasons why WHO advocates for a low-sodium IV fluid. Severely malnourished children in the early stages of treatment are unable to excrete a large sodium load as a result of impaired renal function(6), and there is a limited capacity to concentrate urine due to a loss of the urea gradient in the extracellular space of the renal medulla. In addition, increased leakiness of cell membranes and decreased activity of the Na^+/K^+ ATPase exchange pump leads to an increase in intracellular sodium and a corresponding excess in total body sodium. This is associated with a deficiency of cellular and whole body potassium, thus if sodium is not restricted, the resulting water retention may overload the intravascular space and lead to congestive heart failure (often misdiagnosed as pneumonia). Edematous children seem to be more sensitive to excess sodium than wasted children. Unless there is a very high purging rate with significant stool sodium loss as in cholera, or until specific research proves otherwise, there is limited justification to depart from the WHO guidelines(7).

Second, we will consider the suggested treatment of shock. The WHO Guidelines prescribe immediate oxygen, intravenous glucose and antibiotics, and intravenous fluid 15 mL/kg over one hour. If pulse and respirations do not improve with this intravenous fluid load, the child is assumed to have septic shock and a blood transfusion (10 mL/kg slowly over 3 h) is

recommended. Maintenance IV fluid (4 mL/kg/h) is given whilst waiting for blood. In contrast, the IAP Guidelines advocate for 30 mL/kg of normal saline over one hour as well as a blood transfusion, followed by dopamine and dobutamine. If there is no improvement, epinephrine/nor-epinephrine is given and IV steroids are to be considered. Although this corresponds to contemporary critical care practice for hemodynamic support for well-nourished children with septic shock, there is a serious risk in severe malnutrition that the high volume and high sodium infusion, in the face of potassium deficiency, may trigger heart failure. Steroids also should be used with extreme caution since they may suppress immune responses in an already compromised host. Cumulative experience of workers around the world has shown that if severely malnourished children are treated as if they were normal children, mortality rates are higher.

It is unclear to us whether there is new evidence from investigation in severely malnourished children which justifies these substantial divergences of the IAP Guidelines from WHO Guidelines in these important areas. The WHO Guidelines were developed by a group of international experts with experience in the care of malnourished infants, and the most recent version of the guidelines was examined by 83 peer reviewers from around the world. There was general consensus in each and every recommendation after much discussion and constructive dialogue. A guiding principle in their development was that the recommendations could be implemented with basic resources and limited staff. It is possible that for some issues there may be genuine differences in the nature and the interpretation of the evidence used by the WHO experts and the IAP experts. If this is the case then it is important to compare the critical evidence and its interpretation. It may be that the evidence is not sufficient to resolve these questions and there may be a need for critical additional research to clarify specific points. If so this work should be commissioned and carried out to the necessary high standard. It may be that the target audiences for whom the guidelines are intended are different. If so this should be made explicit so that there is no confusion. The WHO Guidelines are intended to address the needs of care in the context where most malnourished children are found: in resource poor environments with limited access to highly skilled staff. Nevertheless, the same principles apply to the care of malnourished individuals in locations with access to the most modern intensive support facilities.

In any case, IAP and WHO Guidelines have a common objective and the fact that there are differences in opinion offers an opportunity to identify from carefully conducted studies any potential risks or additional benefits from the proposed changes in IAP Guidelines. The aim we share is to do the most good and the least harm, so there is a need to evaluate the comparative effectiveness of the proposed IAP Guidelines: to determine the extent to which they lead to differences in outcomes relative to the existing WHO Guidelines. There is no simple answer to these important but complex issues. Given the implicit difficulties in conducting individual randomization to control for confounding factors, evaluating the effectiveness of the IAP guidelines using clusters randomized based on geography or health districts may best serve the need to prevent selection bias and provide robust evidence for a real effect(8). We are all challenged to learn from better practice and to use the experience to refine our advice on the preferred approaches to care. There may be the need to define more carefully whether what is best for most children does differ with circumstance; this can only be established by contrasting options for different approaches to care against a common reference, currently the WHO Guidelines. Guidelines should change as evidence of better practice becomes available, however we have to be confident that the evidence is secure and that the changes are for the better. This requires robust evidence that defines improved outcome. At the International Malnutrition Task Force we look forward to working with pediatricians in India and elsewhere to advance this cause and to be ready to modify what needs to be changed based on what we learn from experience. We hope that India will face this challenge and provide the world with the lessons learned in the process of combating malnutrition and enhancing child survival. The IAP is uniquely placed to take a lead role in providing the evidence which will underpin better practice.

Ann Ashworth*,
Alan Jackson,**
Ricardo Uauy*,
**Nutrition and Public Health Interventions Research Unit, London School of Hygiene and Tropical Medicine, U.K.*
***Department of Nutrition, Southampton Medical School, U.K.*

Corresponding Author:
Ricardo Uauy
E-mail: Ricardo.Uauy@lshtm.ac.uk

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