The Clinical Challenge of Preventing and Treating Malnutrition

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Abstract

Malnutrition remains a major problem in children in large parts of the developing world. About 150 million young children in the developing world are either wasted or stunted, and it has been estimated that over half of childhood deaths are attributable to the potentiating effects of malnutrition. Thus, tackling both mild-moderate and severe malnutrition effectively is essential if the millennium development goals are to be achieved. Intervention strategies to promote exclusive breastfeeding for about 6 months in the absence of maternal HIV infection will result in significant improvements in nutrition, and are key to prevention strategies for malnutrition. Careful evaluation and effective counseling of HIV-positive mothers regarding feeding choices is essential. Evidence from a number of randomized controlled trials shows that ready to use foods have an important role to play in the prevention and treatment of both outpatient and inpatient malnutrition. Such foods were initially produced commercially, but it has been shown, particularly in Malawi, that such foods can be locally produced at low cost. In some parts of the world, HIV is a major underlying cause of malnutrition in children and is associated with high mortality rates in those with severe malnutrition. Strategies for the prevention and treatment of children with HIV need to be escalated.

Introduction

Interventions to improve child health over the past few decades have concentrated on issues such as immunization, oral rehydration and treatment of infections. Specific nutritional interventions have been relatively neglected. Malnutrition affects a large proportion of the world’s children. While malnutrition includes both under- and overnutrition, this chapter will deal with undernutrition. It has been estimated that about 150 million young children
in the developing world are either wasted or stunted. In highly affected countries, rates of children who are wasted may exceed 10%, while up to 40% of all children less than 5 years of age may be stunted [1]. Infectious diseases have been recognized as the leading cause of death in children under the age of 5 in developing countries for many years. However, it is only more recently that the potentiating effects of malnutrition on infectious diseases have been appreciated. Pelletier et al. [2] in a study on data from 53 developing countries estimated that 56% of child deaths were attributable to the potentiating effects of malnutrition. Somewhat surprisingly, over 80% of these deaths were attributable to mild-to-moderate malnutrition as opposed to severe malnutrition, reflecting the fact that the vast majority of undernourished children are in the former category. Black et al. [3] recently presented an updated analysis of the total burden of maternal and child undernutrition on childhood deaths. The main factors that they identified were stunting, severe wasting and intrauterine growth restriction combined, vitamin and trace element deficiencies, and suboptimal breastfeeding. All of these together, accounting for coexposure of these nutrition-related factors, were estimated to be responsible for 35% of childhood deaths and 11% of the global burden of disease.

Furthermore, children who survive the effects of undernutrition may have impaired cognitive development, reduced capacity for physical work and be at higher risk for some adult-onset chronic diseases [4]. Thus, the prevention and treatment of malnutrition are important for both child and adult health in large parts of the developing world.

Prevention of malnutrition is clearly a complex subject, and many factors responsible for malnutrition have their roots in the socioeconomic circumstances of communities and families. Poverty, poor quality food sources, overcrowding, and the lack of clean water and sanitation all contribute to a high burden of disease which in turn leads to inadequate food intake and increased energy requirements to combat disease. Thus, prevention of malnutrition requires a multi-layered approach, and this is reflected to some extent in the various components that make up the Millennium Development Goals.

**Breastfeeding**

The advantages of breastfeeding have been known for centuries and relate to a number of properties of breast milk. These include the appropriate composition of breast milk with respect to the growing term human infant, its many anti-infective properties and the important immune modulating effects. Numerous reports have indicated that the mortality of infants who are not breastfed is several times higher than that of breastfed infants in low-income countries, but it is often difficult to separate out the many
social factors that are associated with non-breastfed infants such as family disruption, alcohol and drug abuse, maternal and infant illness including prematurity, etc. However, in their comprehensive analysis, Black et al. [3] estimated that suboptimal breastfeeding was responsible for 1.4 million child deaths globally.

The full benefits of breastfeeding are obtained if exclusive breastfeeding continues from birth for about 6 months and then breastfeeding continues together with other foods up to the age of 12 months and beyond. While the rates of initiation of breastfeeding in most developing countries are high, the numbers of infants who are exclusively breastfed for 6 months is often unacceptably low. It was estimated that in Africa, Asia, and Latin America and the Caribbean, only about 50% of infants under the age of 2 months are exclusively breastfed, and this falls significantly over the next 4 months. The results of a Cochrane review on support for breastfeeding mothers that analyzed almost 30,000 mother-infant pairs from 14 countries showed that all forms of support increased the duration of breastfeeding; the relative risk for stopping breastfeeding before 6 months was 0.91 (95% CI: 0.86–0.96), admittedly a relatively small effect [5]. However, Coovadia et al. [6] were able to achieve exclusive breastfeeding rates of 67% by 3 months of age and 40% by 6 months of age in those who initiated breastfeeding with an intensive intervention program that included frequent home visits by infant feeding counselors in a rural area of South Africa with a high HIV prevalence, showing that more intensive breastfeeding support programs can have a much greater impact. Thus, one of the priority areas for preventing malnutrition in the early months and years of life is to increase the rates of exclusive and prolonged breastfeeding by programs to support breastfeeding, and the more intensive the program, the more successful it is likely to be [7].

In many parts of the developing world, especially in sub-Saharan Africa, HIV is strongly associated with malnutrition. This in turn creates a major dilemma where breastfeeding increases the risk of HIV transmission from mother to infant which in turn may result in wasting and stunting, whereas in almost all other situations, breastfeeding results in optimal nutrition for young infants. A consensus statement by the World Health Organization (WHO) stated that where replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended; otherwise exclusive breastfeeding is recommended [8]. The challenge is to identify the infants of those families who can be fed safely with breast milk substitutes, and this requires intimate knowledge of the community on the part of the health worker. However, recent studies on providing breastfeeding mothers with antiretroviral drugs for the duration of breastfeeding show promising initial results. If these results are confirmed and provision of antiretroviral drugs is feasible on a large scale to breastfeeding HIV positive women, especially in those countries hardest hit by the HIV epidemic, this will be an enormous advance.
Weight gain has been the focus of most assessments of nutrition programs, whereas stunting and linear growth retardation are considered to be more difficult to improve. Bhutta et al. [9] estimated that only one third of stunting could be averted with available short-term interventions. This was supported by data from Guatemala, where an intergenerational study showed that women who had received nutritional supplements in utero (given to their mothers) and as children up to the age of 7 years, produced offspring who had more rapid linear growth than they had as children [10]. Those who received additional protein as part of the food supplementation had children with the largest increments in linear growth. Thus, it would seem that several generations during which good nutrition is available would be required in those parts of the world where the rates of stunting are high before the full genetic potential of linear growth is obtained – this should be the longer term goal.

### Assessing and Classifying Malnutrition

The measurements of weight and length/height have long been used in various classifications of malnutrition. However, more recently, the classification used by the WHO Manual on the Management of Severe Malnutrition has gained increasing acceptance [11]. This classification can be seen in table 1. However, in those areas where malnutrition is most common, the measurement of weight may not always be accurate, and length measurements are frequently inaccurate due to the limited availability of proper measuring equipment. In such areas, a simple method for detecting malnutrition by community health workers is needed, and the mid-upper arm circumference (MUAC) has been shown to be a good screening method for the detection of severe malnutrition. Using a cutoff for MUAC of <110 mm for children between 6 and 59 months, this method is simple and sufficiently accurate to detect severe malnutrition in children in this age range [12].

<table>
<thead>
<tr>
<th>Symmetrical edema</th>
<th>Moderate malnutrition</th>
<th>Severe malnutrition</th>
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<tbody>
<tr>
<td>no</td>
<td></td>
<td>yes (edematous malnutrition)</td>
</tr>
<tr>
<td>Weight-for-height</td>
<td>–3 ≤ SD score &lt; –2</td>
<td>SD score &lt; –3 (&lt;70% expected; severe wasting)</td>
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<tr>
<td>(70–79% expected)</td>
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<tr>
<td>Height-for-age</td>
<td>–3 ≤ SD score &lt; –2</td>
<td>SD score &lt; –3 (&lt;85%; severe stunting)</td>
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<td>(85–89% expected)</td>
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### Stunting and Intrauterine Growth Restriction

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The clinical assessment of bipedal edema together with the MUAC, both of which can be done with staff that are not highly trained health workers, is sufficient to determine whether children fit the WHO category of severe malnutrition.

**Advances in the Development of Ready to Use Foods**

Based on formulae that had been developed in emergency and refugee settings [13], the WHO recommended the use of a high-energy formula, so-called F100 containing 100 kcal/100 ml, during the rehabilitation phase of children recovering from severe malnutrition [11]. This is a liquid formula prepared from dried skimmed milk, oil, sugar and a vitamin and mineral mix. However, these liquid formulae were susceptible to bacterial contamination and could thus be safely prepared only in settings where there could be close supervision and where there was access to clean water.

Subsequently Briend et al. [14] reported the successful results of a small study in Chad using a ready-to-use therapeutic food (RTUF) for treatment of marasmus. The nutritional composition was similar to F100 but was manufactured in the form of a paste with groundnuts as one of the main ingredients. It contained 543 kcal/100 g, tasted like peanut butter, was considered to be palatable by children and appeared to be resistant to bacterial contamination, thus giving it excellent storage properties. They speculated that it might be useful in centers where there was potential for bacterial contamination of liquid feeds and that it might also be useful for home treatment.

Several studies were performed on both moderately and severely malnourished children utilizing the WHO classification, which can be seen in table 1. Maleta et al. [15] supplemented moderately malnourished children in Malawi with either an RTUF or a locally produced supplement consisting of maize and soy flour. While both groups showed modest weight gain, the group receiving RTUF had better weight gain even after cessation of the supplement. Two studies, one in Senegal and the other in Malawi, evaluated the effects of RTUF supplements on severely malnourished children in non-hospital settings [16, 17]. In the Senegalese study, RTUF was compared with F100 and resulted in improved weight gain when compared with F100. The comparator in the Malawian study was again blended maize and soy flour. The RTUF group gained weight and height more quickly than those on maize/soy flour and was considered to warrant further work in operational settings.

In all of these studies, a commercially prepared RTUF produced in France was used. Concerns regarding these studies were expressed with regard to the cost of the product and the fact that this focused on technological interventions as a solution to what is fundamentally a geopolitical and socioeconomic problem. However, Manary [18] has demonstrated that
local production of RTUF similar to the commercially available product is possible using locally available milk powder, vegetable oil and peanuts. This locally produced RTUF could be produced in both small and large quantities in underresourced settings in Malawi, and this should be feasible in most settings in the world. However, further work needs to be done on alternative ingredients in areas where locally available foods may differ and modifications to the RTUF may be necessary. Further published studies have demonstrated the effectiveness of this locally produced RTUF in Malawi. Six-month-old infants were supplemented with RTUF for 1 year and compared with a second group randomly assigned to receive a micronutrient-fortified maize-soy flour supplement. The group receiving RTUF had similar weight gain to the maize-soy flour group, but showed significantly better linear growth which was maintained for a further 2 years after the supplement was stopped [19, 20].

Severe Acute Malnutrition

In addition to the definition of severe acute malnutrition (SAM) seen in table 1, it has been proposed that an MUAC <110 in children 1–5 years of age should be added as an alternative criterion when accurate measurements of weight and length/height are not feasible. The mortality rates for children admitted to hospital with SAM have remained at 20–30% for decades in spite of management protocols which, if properly implemented, should reduce these rates to <5% [21]. The WHO-published protocols for the management of SAM consisted of 10 steps that were divided into two phases: stabilization and rehabilitation [11]. However, these protocols required trained staff and admission to hospital in the initial stages to implement them fully and have not led to widespread decreases in case-fatality rates in developing countries. In a South African study in two poorly resourced rural hospitals with high HIV prevalence rates, following the introduction of the WHO protocols together with training of staff, case fatality rates of SAM fell from 46 to 21% in one hospital and 25 to 18% in the other. However, when new untrained staff took over in one of the hospitals, the improvement in case fatality rates was reversed [22].

While the programs for the treatment of SAM in the 1980s and 1990s met with limited success, more recent experience with RTUF have met with more success in non-hospital settings as discussed above. This has resulted in fewer children requiring initial hospital admission as only those with complications require hospital admission [21]. These complications include pitting edema, MUAC <110 mm, anorexia, lower respiratory tract infection, severe dehydration, etc. For those that do require hospital admission, a shorter hospital stay is possible, thus maximizing the use of hospital care for the sickest children.
HIV and Malnutrition

Attempts to achieve improvements in the prevention and treatment of malnutrition have been complicated in some countries, particularly those in Southern and East Africa, by the HIV pandemic. In South Africa, the prevalence of HIV-positive women attending antenatal clinics in South Africa rose from <1% in 1990 to close to 30% over the following 10–15 years depending on the region of the country. This has been largely responsible for the increase in under 5 mortality from 60 to 69 per thousand live births between 1990 and 2005, with over half of the deaths in 2005 being attributable to HIV as the underlying cause [23]. A similar trend has been seen in other Southern African countries, and the rates of severe malnutrition have also risen substantially over this period.

In a study of hospitalized children with severe malnutrition in a rural part of South Africa with a high prevalence rate of HIV, the traditional risk factors such as poor household food security, unhealthy feeding practices including low rates of exclusive breastfeeding and lack of adequate food diversity after the age of 6 months were still found to be important risk factors. However, of equal importance was the role of HIV either directly with respect to an infected child or indirectly where the child’s parents were infected and ill or had died. The mortality rate in this study for those with severe malnutrition was 25% despite reasonable standards of hospital care, and it was felt that HIV infection played an important role in this high mortality rate [24].

In another study performed at three teaching hospitals in Johannesburg, South Africa, 51% of children admitted for severe malnutrition were infected with HIV [de Maayer, pers. commun.]. In those infected with HIV the mortality was 19%, whereas in the uninfected group the mortality rate was 3.6%. Thus, attaining a <5% mortality rate in children with severe malnutrition requiring hospital admission as proposed by the WHO would seem to be unrealistic in areas with high HIV prevalence.

The Future

Promotion of exclusive breastfeeding for about 6 months should be a priority, but careful consideration needs to be given to the circumstances of HIV-positive mothers when making feeding choices. RTUF has been shown to be extremely effective in the prevention and treatment of malnutrition, but is only available in a few countries. Development of RTUF made locally at low cost from locally available foods should be a priority so that widespread use of these products can be introduced in areas with high rates of malnutrition. In some parts of the world, HIV infection is a major contributor to childhood malnutrition, and interventions to prevent mother to child transmission of HIV and to treat those children infected with HIV should be rapidly escalated.
**References**


Preventing and Treating Malnutrition


Discussion

Dr. Hussain: Are the majority of malnourished children under or over 6 months old?

Dr. Cooper: In terms of the age we see both. Under 6 months of age is usually related to the lack of breastfeeding or HIV infection itself, and particularly those that are infected during pregnancy rather than at the time of delivery where they develop the illness very early on and become symptomatic within 6–8 weeks after birth and present with poor growth. But I would think that the majority of the children we see are over 6 months of age, as I am sure is the case in your country. That relates to either stopping breastfeeding or inadequate infant foods. In our country and in most parts of Southern Africa, maize is the staple food. Some children in many parts of the rural areas get very little else, and it has been calculated that in order to just get enough calories, let alone protein, micronutrients, etc., the amount that needs to be eaten by a young infant or child is huge, and so it’s a lack of a varied and substantial diet.

Dr. Solomons: I would like to talk about pure microbiologically safe water. Much of the diseases which lead to severe malnutrition are caused by water-borne infections, and as the use of ready to use food is becoming more and more widespread, provision of safe water is a must.

Dr. Cooper: I agree with your comment. I think it sounds easy to say we should be providing safe water for everybody, but our country which is one of the better resourced ones in Africa is still battling with that, particularly in the rural areas. I think safe water is almost a sort of fundamental building block that will then determine so many other things.

Dr. Spieldenner: Do you have information on the financial sustainability of such programs and on the acceptance in the cultural environment?

Dr. Cooper: We haven’t had experience except in one particular very small scale of study. But the group in Malawi, if one looks at their publications over the last 5 years, have taken this a long way. It’s really developed from within a country rather than coming in from outside, although there obviously has been outside help. They seem to be highly successful in utilizing local products and being able to produce them relatively cheaply. But Malawi is a small country, and I think it’s a relatively homogenous one in terms of the population, so it’s really at the infancy of this particular type of ready to use food. I think we are going to have to look much more widely as to how widely applicable it is both financially as well as culturally from an acceptability point of view.

Dr. B. Koletzko: You referred to the enormous success of the ready to use foods. Perhaps this concept could be exploited to an even greater extent. The first foods used were rich in fats and based on peanuts; they were produced in France. Now, more and more locally made ready to use foods are made available. While there is already a lot of experience in using some lipid-rich foods for feeding undernourished children, there are questions that we might wish to have answered. For example, does it matter what the composition of the fats is in these ready to use foods, and which outcomes could be enhanced by modified compositions?

Dr. Cooper: I think most of the studies that have been done thus far have really been looking at a very limited composition or mix of foods. As I mentioned earlier, and it has pretty much been replicated in the local Malawi situation, I think there aren’t any answers at this stage for what might be the optimal lipid source to use, what might
be a better mix of nutrients. So it’s really, as I would see it, at the beginning of what might be a very long road ahead, but perhaps might be a very productive one in terms of managing and treating malnutrition. I think one can virtually ask any question at this stage because they are all unanswered as far as I am aware. The important thing to me would be to look at different parts of the world and see what food stuffs are available and if one could get the same results utilizing different sources.

Dr. Dhansay: A few comments, the first one is on information and data and the fact that we look at publications, for example the *Lancet* series, and then it becomes gospel. I just want to comment on South Africa, I don't think those stunting rates are great, similarly with clinical vitamin A deficiency. It was published that we have got clinical vitamin A deficiency but we do not have clinical vitamin A deficiency. I want to tell the audience that when one looks at publications, one should also look at the background. The second point is on the fact of social determinants. Context is all. In South Africa, although we are one physical country, we are not one nation as yet. There are large differences between population groups. The majority of our population is not privileged and most of them are HIV positive, so context, I just wanted to emphasize again, is extremely important. Somebody asked about malnutrition before/after 6 months of age. I can just say, and I think Dr. Solomons will back me up, we did a full country intervention study with multiple micronutrients and the study group was specifically selected. The infants were not malnourished; they did not have low birthweight, but at 6 months of age a good percentage of them were already stunted.

Dr. Thakre: I would like to ask how do we define ideal growth? Nutrition is influenced by numerous factors which operate before and after birth. Is there a gold standard for optimal growth?

Dr. Cooper: Very good question. I think the WHO growth charts which have come out very recently at least give us an idea of early growth and what the optimal pattern should be. But even there, they were based on healthy women who were breastfeeding successfully and excluded perhaps the outliers who would have problems. But I don't think there is any easy answer to that, and perhaps this is something that we will grappling with for the next 50 or 100 years as to what is optimal growth.

Dr. Ludan: Developing countries like the Philippines have high stunting rates. Stunting is associated with zinc deficiency. Among pregnant mothers, zinc deficiency has also been related to low birthweight and premature delivery. Some studies recommend zinc supplementation to pregnant mothers during the last 5 months of pregnancy to increase the duration of gestation and also while breastfeeding because we know that the level of zinc in breast milk is low [1]. So, in developing countries with high stunting rates, low birthweight and premature deliveries, would you recommend zinc supplementation to pregnant and lactating mothers?

Dr. Cooper: That's not really an area of expertise that I have, but I am sure it must depend on regional differences. This might be recommended in the areas of high zinc deficiency, but not necessarily everywhere.

Reference