Malnutrition in the Developing World: The Lack of Food Scenario

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Introduction

The current literature concurs that the prevalence of malnutrition, and stunting among children in particular, is a reasonably accurate reflection on the prevailing socioeconomic status in a given environment. In this regard, malnutrition is known to adversely impact on mental development, scholastic achievement, productivity, child and woman morbidity and mortality as well as the risk for infection. As such, it is hardly surprising that nutritional status is one of the key Millennium Development Goals [1]. Poverty and food insecurity are almost universally accepted to be very significant contributory factors. Although slow, but welcome improvements are being achieved in many developing countries, child malnutrition, poverty and household food insecurity appear to be actually increasing (fig. 1) in India and Sub-Saharan Africa [2]. In South Africa for instance and at the national level, three of four households have been reported to be either ‘hungry’ or at ‘risk of hunger’ (table 1), the extent of hunger being related to adverse growth patterns (fig. 2), lower energy intake (fig. 3), lower income as well as a lower intake of a number of nutrients among children 1–9 years of age [3]. In this regard, the World Bank and the International Monetary Fund have recently predicted [4] that although the income poverty goal is likely to be achieved at the global level, Africa will fall well short. The predicted shortfalls appear especially serious for the health and environmental goals, namely child and maternal mortality, and access to safe drinking water and basic sanitation. The likely increasing number of malnourished people in these regions assumes even greater importance against the background of the HIV/AIDS pandemic in such developing countries, since HIV/AIDS exacerbates food insecurity by decreasing the available agricultural labor force and food production [2].
Child Growth in Relation to Food Insecurity

Against this background, few will question the importance and necessity of providing or creating access to food as a means of alleviating the effects of poverty and food insecurity with a view to improving nutritional status. Nevertheless, and despite the available evidence indicating that malnutrition is being steadily reduced in much of the world, in some parts of the African continent nutritional status improvement indicators remain unfavorable or further deteriorate, despite continuing, and expensive, nutritional interventions.

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**Fig. 1.** Changes in the number of undernourished people in developing sub-regions of the world. From the FAO [2] with permission from the publishers.

**Table 1.** Household hunger risk classification in South Africa, 1999

<table>
<thead>
<tr>
<th>Hunger risk classification</th>
<th>Province classification</th>
<th>EC</th>
<th>FS</th>
<th>G/TENG</th>
<th>KZN</th>
<th>M/GA</th>
<th>NC</th>
<th>NP</th>
<th>NW</th>
<th>WC</th>
<th>RSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td></td>
<td>398</td>
<td>209</td>
<td>409</td>
<td>525</td>
<td>150</td>
<td>144</td>
<td>332</td>
<td>226</td>
<td>342</td>
<td>2,735</td>
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<tr>
<td>Food secure, %</td>
<td></td>
<td>4.3</td>
<td>45.5</td>
<td>36.7</td>
<td>26.7</td>
<td>21.3</td>
<td>13.2</td>
<td>19.3</td>
<td>13.3</td>
<td>39.8</td>
<td>25.0</td>
</tr>
<tr>
<td>At risk of hunger, %</td>
<td></td>
<td>12.6</td>
<td>16.8</td>
<td>21.5</td>
<td>25.9</td>
<td>26.0</td>
<td>23.6</td>
<td>26.2</td>
<td>25.2</td>
<td>29.0</td>
<td>22.9</td>
</tr>
<tr>
<td>Experience hunger, %</td>
<td></td>
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<td>37.8</td>
<td>41.8</td>
<td>47.4</td>
<td>52.7</td>
<td>63.2</td>
<td>54.5</td>
<td>61.5</td>
<td>31.3</td>
<td>52.2</td>
</tr>
</tbody>
</table>

EC = Eastern Cape; FS = Free State; G/TENG = Gauteng; KZN = KwaZulu-Natal; M/GA = Mpumalanga; NC = Northern Cape; NP = Northern Province (now Limpopo); NW = North West Province; WC = Western Cape; RSA = Republic of South Africa. From Labadarios [3] with permission from the publishers.

*Significant difference between provinces, p < 0.01, $\chi^2$ test.

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**Child Growth in Relation to Food Insecurity**

Against this background, few will question the importance and necessity of providing or creating access to food as a means of alleviating the effects of poverty and food insecurity with a view to improving nutritional status. Nevertheless, and despite the available evidence indicating that malnutrition is being steadily reduced in much of the world, in some parts of the African continent nutritional status improvement indicators remain unfavorable or further deteriorate, despite continuing, and expensive, nutritional interventions.
In this regard, the role of nutrition, on its own, as the factor predisposing to poor growth or for that matter adverse pregnancy outcomes [5, 6], has been frequently questioned [7, 8]. The better understanding of the causes of stunting and its consequences on short- and long-term health, therefore, is not only of scientific interest but it also has important implications in monetary and policy considerations. The factors thought to have been contributory to poor growth improvement outcomes include the timing of such interventions, the role of specific macro- and micronutrients, energy intake, dietary protein quality, intervention leakages as well as diarrheal disease [7]. Importantly though, available evidence indicates that improvement in living conditions

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**Fig. 2.** Hunger risk classification as related to anthropometric status nationally in children aged 1–9 years: South Africa 1999 (p < 0.001). From Labadarios [3] with permission from the publishers.

**Fig. 3.** Hunger risk classification as related to the intake of energy nationally and by area of residence in children aged 1–9 years: South Africa 1999 (p < 0.001 urban vs. rural). From Labadarios [3] with permission from the publishers.
either through migration or adoption is associated with marked improvements in growth patterns [10, 11]. Although the latter may be due to combined nutritional and environmental improvements, the importance of environmental improvements should not be underestimated [12]. In fact, it has been proposed [13] that the failure of children to grow adequately in developing countries may be due to the presence of the acute phase response, without necessarily the manifestation of any overt clinical signs, induced by adverse environmental conditions.

**Child Growth in Relation to Chronic Inflammation**

Global estimates for the year 2000 indicate that 135 and 162 million children under the age of 5 years were respectively underweight and stunted [14] of which 31 and 45 million respectively are African children. Also globally and on the basis of the analysis of 39 nationally representative surveys from developing countries, the pattern of growth faltering appears to be remarkably similar [15]. Thus weight for age starts to falter at approximately 3 months of age whereas length/height for age starts to falter immediately after birth. In Africa and more specifically in the Gambia, the available evidence indicates that the marginal adequacy of the infants’ diet could not, on its own, explain the adverse growth patterns of such children [16]. Indeed, the outcomes of a number of nutritional intervention studies aimed at improving growth have been neither consistent nor significant, with only a few such studies showing a measure of growth improvements [16, 17]. Furthermore and although diarrheal disease, as opposed to gastrointestinal disease, may be associated with acute weight loss, the impact of the former on long-term growth faltering has been questioned [18, 19]. The latter, namely gastrointestinal disease diagnosed as an enteropathy on the basis of impaired gastrointestinal mucosa permeability using the lactulose:mannitol test, has been associated with poor infant growth and is reported to explain more than 43% of the growth faltering of Gambian infants [20, 21]. The proposed mechanism of the reported association includes villar atrophy with attendant maldigestion and malabsorption as well as translocation of macromolecules with the attendant induction of local and systemic immune and inflammatory response [20]. Of further interest is that the enteropathy has recently been histologically described and includes crypt hyperplasia, villous stunting, a high number of intraepithelial lymphocytes and an increase in cytokine immunoreactive mononuclear cells with a proinflammatory response [22]. The presence of the inflammatory response in relation to contrasting environments has also been reported in stunted Nepali children [23], and impaired intestinal permeability has also been reported in stunted rural Bangladeshi and mildly stunted Nepali infants and children [24]. Moreover a longitudinal study [25] in rural Gambian infants has documented evidence of chronic
immunostimulation (raised white cell, lymphocyte and platelet counts together with frequently elevated C-reactive protein), impaired intestinal permeability associated with impaired growth, and raised endotoxin and immunoglobulin (Ig)G-endotoxin core antibody which was related both to growth and measures of mucosal enteropathy. It would thus appear that the consequences of the presence of the inflammatory response may not only be of equal importance as that of dietary inadequacies, but, additionally may, in the long-term, impact adversely on health and well being.

### Proposed Consequences of Impaired Child Growth

The human and financial costs of malnutrition, apart from those well-described and related to short-term morbidity and mortality aspects, are, in the longer-term, likely to be considerably higher than currently estimated. Emerging evidence indicates that malnutrition early in life appears to be associated, among emerging populations in the nutrition transition, with an increased risk for the so-called degenerative diseases of the developed world. It has been postulated that, in countries undergoing the nutrition transition, stunting appears to be associated with overweight later in life [26]. Stunted children in South Africa, China and Russia appear to be at a two- to sevenfold increased relative risk of being overweight. In Brazil, the greatest increase in the prevalence of obesity has been reported among poor women from the most affluent region of the country, the prevalence of obesity increasing with income among men and poverty among women [27]. Furthermore, in a longitudinal study over a period of 2 years among school girls in Sao Paulo documented a higher increase in weight-for-height in stunted as compared with non-stunted girls when an increased amount of energy was derived from fat [28]. Also of interest is that increasing body fatness together with dietary changes to a more Western type of diet and decreased physical activity in Brazil appears to be associated closely with an increasing prevalence of overweight, type-2 diabetes and cardiovascular disease [29]. Stunting has also been associated with the metabolic syndrome [30], and observations from Brazil indicate that stunted individuals have higher fasting plasma glucose, triglyceride, total cholesterol and low-density lipoprotein cholesterol when compared with individuals of normal stature [31].

### Chronic Inflammation and Degenerative Diseases

The available evidence indicates that inflammation may play an important and significant role in the etiology of the so-called chronic degenerative diseases in the Western world. In the case of atherosclerosis, elevated
concentrations of such inflammatory markers as C-reactive protein have been reported to be at least as strong, if not stronger, predictors of cardiovascular events [32]. Endothelial cell activation and the inflammatory response are thought to be initiated by oxidized lipoproteins, hypertension, diabetes mellitus as well as obesity [33]. Systemic inflammation has also been reported to be associated with insulin resistance and incident cardiovascular disease and diabetes [34]. In this regard, the apparent predisposition of the undernourished child to become overweight/obese later in life, especially in countries undergoing the nutrition transition with the attendant urbanization and changes in dietary patterns, has been proposed as a possible mechanism to explain the rapidly and consistently increasing prevalence of diabetes and cardiovascular disease [29, 35]. Certainly, preliminary evidence indicates that circulating levels of the proinflammatory cytokines interleukin-6 and tumor necrosis factor-α were significantly higher in urban middle class and urban slum dwellers and were related to body mass index when compared with rural village dwellers. Moreover, in Indian Asians living in England the geometric mean C-reactive protein concentrations have been reported to be 17% higher than those in European whites affording an estimated 14% increase in population coronary heart disease risk among Indian Asians when compared with European whites [36].

Common Pathways of Under- and Over-Nutrition

The consistency of the available evidence is supportive of the role of chronic inflammation in the diseases of affluence [32–34]. In relation to food and poor food choices and their role in increasing the risk of these diseases, the concept is emerging that some foods may have greater or lesser proinflammatory properties. For instance, a diet with a high glycemic load has been documented to predict plasma C-reactive protein concentrations in apparently healthy middle-aged women [37], independent of the conventional risk factors for ischemic heart disease, especially in overweight women prone to insulin resistance. This of course contrasts the reported anti-inflammatory properties of n-3 fatty acids [38] which, in some people at least, are known to suppress tumor necrosis factor-α by peripheral blood mononuclear cells in healthy men [39]. In the developing world, chronic inflammation appears to be associated with undernutrition, within the context of food insecurity and unfavorable environmental influences. Especially in countries undergoing the nutrition transition with the attendant urbanization and very significant adverse dietary changes, the apparent tendency of the previously malnourished to the metabolic syndrome and obesity may in itself and by itself be mediated by chronic inflammation. Adipose tissue-derived cytokines [40] for instance may contribute to a proinflammatory environment which may be further accentuated by adverse environmental and low grade infectious
influences (fig. 4). These latter associations underscore the importance, and urgency, for an improved understanding of the multifactorial causes of malnutrition with a view to establishing cost-effective interventions for its prevention, be it among the over- or undernourished.

References

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Discussion

Dr. Haschke: Can you elaborate on anti-chymotrypsin? What does it really tell you, and is there anything in the elderly which is related to the activity?

Dr. Labadarios: Anti-chymotrypsin is one of what we call a positive acute phase protein. It arises in the presence of infection or inflammation, just like C-reactive protein (CRP). The advantage of the chymotrypsin is that it stays elevated much longer than CRP, so there is the advantage of actually picking up an infectious or an inflammatory state for longer after the process of inflammation or infection has actually stopped. As for data in the elderly, I do not know of any that have been done in normal or apparently healthy elderly. The only relation that I can give you in that regard is the data of Ridker et al [1] from the United States which includes a component of the elderly population at risk of myocardial infarction, but that is in a group sense rather than in a sort of study in which a specific relationship has been studied. I don’t know whether anybody else here can help. I don’t know of any such data. Nevertheless, one must not forget that aging is an inflammatory process.

Dr. Elia: You eluded to this syndrome, that seems to be quite common in developing countries, of stunting in overweight children. Presumably there is sufficient energy available, but the children are not growing. What do you think the mechanism might be? Why aren’t these children growing? Why are they stunted while at the same time they have excess energy? Presumably the dietary intake of energy is adequate but this does not allow normal growth to proceed. What is blocking it?

Dr. Labadarios: I think your data give us a little bit of a glimpse of what may be happening. The energy question of course is a little bit more complicated and that was my purpose in showing those slides on weight loss in relation to CRP and glycemic load. It may be the case that it is not so much how much you eat, but what you eat. There was an excellent publication recently [2] regarding the obesity of poverty because obesity is equally common if not more common among poor people. So the question that arises here is that of the energy density of food and, in relation to that, we know that the more energy dense the food the greater the risk of weight gain, and in relation to inflammation, the greater the risk of having elevated inflammatory markers, at least CRP, that we know about. I would think the energy density of food is something that is emerging as a real entity in the developing world. The reason people eat energy-dense food is not by choice; so it happens that energy dense food is the cheapest food to eat, if you compare maize for instance with fruits and vegetables: people
cannot afford fruits and vegetables. So it is a matter of choice, it is a matter of circumstances, it is a matter of education, and quite honestly very often it is a matter of what is available. In the survey that I showed, we went into households that had no food in their cupboards; none. On the basis of a food inventory questionnaire we administered, in addition to other data. So if you have nothing to eat the cheapest food available is the one that you go for and with that goes energy density. I think that it is not the whole concept that is emerging; they are stunted and if they cannot grow in height, I suppose they can only ‘grow’ weight. And if they happen to eat dense food then the process is accelerated. Now I am quite sure it is not as simple as that, but at least that is what one can say at the moment.

_{Dr. Powell-Tuck:}_ I enjoyed your talk immensely and I obviously look at this sort of problem from the outside, working in the UK. But over the years we have been talked into distinguishing between kwashiorkor and marasmus: kwashiorkor on one hand being hypoalbuminemic, and marasmic children less so and with greater stunting. Yet in your studies and those that you quoted by Panter-Brick et al. [3], we are seeing that this hypoalbuminemia, low blood albumin is associated with cytokine drive, etc. I wonder if the classification is changing now or whether the emphasis on a distinction between kwashiorkor and marasmus is still as strong as it was traditionally 20 years ago? Would you like to comment on that? Again it is about stunting versus hypoalbuminemia and perhaps inflammation.

_{Dr. Labadarios:}_ I think the easiest point of reference would be the perfectly normal adult who encounters some kind of accident and is admitted to an intensive care unit. Now the albumin of that well-nourished person would obviously be well within the normal range, and yet if you measure the same albumin the following day a difference of 7–8 g can be found, and in my experience that depends on the severity of the injury. Granted there are a lot of fluid shifts in relation to trauma, and part of the decrease in plasma albumin is actually accounted for by that, but not all of it. At the moment, as best as we understand it, the mechanism is that the acute phase response switches off albumin synthesis in the liver in favor of the acute phase proteins synthesis which really explains what we observe. Now in analogy to what I described in the study in Nepal, I would not be surprised if the mechanism is not the same, except that the grade of inflammation is much lower. I am not saying that this is what it is, but I am saying that it is a real possibility because there are data from another field of nutrition [4] and the authors went to great pains to explain that there was no food shortage at the time of their study; so food was not plentiful but sufficient to meet nutrient requirements. As to the definition, I actually prefer to keep the definitions for marasmus and kwashiorkor until such time that we understand things a little better, because if I was to chose between the two I would rather chose to be marasmic than have kwashiorkor in terms of morbidity and mortality, particularly mortality. So having said that it is really a matter of time before these definitions actually change. I think Dr. Elia can help me here. In the study that I saw from Campbell et al. [5] late last year, they had a few marasmic children in their study, and interestingly their inflammatory response was suppressed. So it is not an easy sort of thing to come to grips with until we understand things a little bit better.

_{Dr. Elia:}_ I would just like to comment on that because of the complexity of the etiology of these overlapping syndromes. If you have a child in England who may be edematous and short as in the nephrotic syndrome, for example, what is the difference between that and kwashiorkor? There are difficulties in the definitions, and for this reason international agencies have tended to move a little away from classifying children as kwashiorkor and marasmic or marasmic kwashiorkor, and put marasmus on more descriptive terms such as edematous and non-edematous malnutrition for children. This is the position that is taken by the World Health Organization, for example, in their recent protocols about how to manage malnourished children.
Dr. Buchman: You mentioned the increasing intestinal permeability in these children and young adults in Africa. I have always had a hard time trying to resolve what this means and whether the increasing intestinal permeability seen in Crohn's disease [6, 7], for example, which is also another intestinal inflammatory disorder, is really more of a cause and effect. But we do know that lactulose and mannitol are very small and that endotoxin is thousands of times larger than either of those molecules, so that increased permeability to these micromolecules does not suggest that there is an increased permeability to endotoxin and even bacteria for that matter. We know from studies done 25 years ago in Nigerian children that chronic parasitic infections are associated with hypoplasia as well as neutrophilic inflammation in the small intestine [8–10], and rather than the intestinal inflammation, as you suggested, being an effect of dietary antigen intake, I wonder if a better and perhaps alternative explanation would be chronic parasitic inflammation?

Dr. Labadarios: The interesting part of your question regarding inflammatory bowel disease is that one of the major problems is failure to grow or failure to thrive. So at least we have one common sort of outcome. What Campbell et al.'s study does not show is a cause and effect relationship, but on the other hand there are the regressions that they reported. There is an overlap of permeability at the IgG antibody and growth and, if I remember correctly, that accounts for some 77% of the lack of growth or the slow growth. They seem to be part of one another rather than independent entities contributing to growth failure. In fact the article confirms that malnutrition affects the integrity of the gut, but now the concept is emerging that in fact it is the inflammatory process in the first instance that impairs permeability. In my opinion it is obviously an original and very interesting finding. It will have to be verified but we already have verification in terms of permeability from other countries like Bangladesh and Nepal. So the emerging concept is actually the reverse of what was previously thought to be the case, namely that the inflammatory process is started and actually induces the alterations in the structure function of the gut.

Dr. Morley: I enjoyed your talk. I have two comments. The first is if we want to try and make an integrated approach to looking at malnutrition, the easier definitions in kwashiorkor and marasmus are fundamentally to talk about lack of food intake plus minus cytokine excess because I think it is the cytokine excess that creates the real differences. But listening to your talk reminds me a little bit of the work of Westerdope [11] in Holland who has been trying to prove why women who have very few babies live longer than those who have many babies, provided this happened before the 20th century. So you have got to understand that the problems of the so-called disposable theory only work up until modern times. He went to West Africa and looked at people who have a proinflammatory cytokine excess and used TNF-α, and in those who have an anti-inflammatory, he used IL-10 as an anti-inflammatory. It turns out that if you are lucky enough to have a gene that allows you to produce a lot of cytokines you will in fact overcome a meningococcal infection and other infections. So if you start to look at it that way, it suggests that if you live in an angry environment, a place where there are lots of infections and very poor medicine, you would likely produce a lot of cytokines which would actually cause you to have many abortions as you got older because high cytokines produce spontaneous abortions, and you would live longer under those circumstances. If you make the mistake of then moving from this angry environment to a happy environment where you have good physicians with antibiotics and very few infections in the community because of good vaccinations, good housing and so on, you would fundamentally almost be the opposite, you now want an anti-inflammatory environment. I think this is what we are seeing in the developed world; we now see this with the aging process which, I agree with you, is predominantly a cytokine-based process or the acceleration of it. Many people are now talking about
a cytokine-related aging process, but what is being seen is that as you get older, if you have this proinflammatory approach, you now do worse in a good environment. So I think we have got to start looking at two totally separate environments and understand that the so-called kwashiorkor child did worse than the marasmic child; the kwashiorkor child was almost always someone who had been exposed to an infection. Within that group of exposed subjects, we almost have to look for who does better and who does worse, and it may well be that those who actually look worse do slightly better. My memory from when I practiced medicine in South Africa a long time ago is that some of the children who I thought had no hope and had very low albumin actually did better in overcoming their infections than some of the others, using albumin as a marker for cytokine. So I think we can start to put it together. I know I haven't done a good job of explaining Westerdope's data, but every time I listen to him I get confused so I am not doing any worse most probably than he is, but I do think this pro-anti-inflammatory cytokine theory is very important for understanding how we interact with our environment.

Dr. Labadarios: I think we are going to hear a lot about inflammation, we are going to hear a lot more about environment, and we are going to hear a lot more about genetics or nutrigenomics. But within the context of what we now know, your comments are extremely pertinent and I thank you for that. There are data available from India actually showing that if you are large and you stay in that percentile of large-ness, or if you are small and you stay in that percentile of smallness, then you are OK, which implies a same environment. The minute you walk out of those percentiles then diabetes is 3 or 4 times higher. Of course regarding your comment of the adverse nutritional influences on top of an inflammatory background, I think that is a very pertinent and it made me include those two slides, one from the States and the other one from South America, I think it was Guatemala. We are going to hear a lot more about the role of chronic inflammation in relation to chronic disease. I never understood what hypertension has to do with smoking or with cholesterol. I never understood why we should ask people to exercise, and I don't understand why red wine is good for you, which I incidentally like. Data are coming showing that alcohol reduces CRP levels. But don't take that as a rule. There was a publication in the Archives of Internal Medicine last year showing that exercise reduces CRP levels [12]. So we are definitely going to hear a lot more about inflammation.

Dr. Lochs: You first showed this nice correlation between permeability and inflammation, and now you mention a very interesting fact, alcohol and exercise increase permeability, and they still reduce the general inflammatory response, they reduce the CRP levels. How do you get that together?

Dr. Labadarios: I don't know. I did say they are emerging facts. The type of exercise in the study I referred to is not the "madness" that one sees in marathon running and all that, it is ordinary walking and so forth. I am not defending the study; I am just trying to put some background to your question. It is not severe exercise that will be associated with the type of permeability changes that you refer to. If there is any permeability change then of course we will wait to have a verification of the study and see what the exact mechanism is. At the moment all we know is that if one exercises regularly the chances are that CRP levels may be lower than those in individuals who do not exercise. We don't understand it, but at least in relation to the point I made for the first time we appear to have a unifying sort of entity, including aging, that actually tries to put things together and I hope we will not be in too much of a hurry to put things together quickly and be wrong as we have been in the past in relation to food. Food on its own is extremely important, nobody doubts that; starvation kills, we know that.

Dr. Oltersdorf: Thank you very much for this good discussion and I enjoyed it because I think nutrition is, as you said, at the end very easy. Food is important, no
food is death. But in between, things are quite complicated and of course I know red wine is good but too much red wine is not; permeability is important for nutrient, but too much permeability is worse; too much discussion is worse and therefore we stop here.

References
