Wasting disease in African children: the challenges ahead

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The painful mouth, fever, diarrhea, and purulent foci, in addition to loss of appetite, severely impair the nutritional state of the child existing on a poor diet......At the same time, the child whose diet lacks, calories or other essential nutrients may be the child whose skin and other epithelial surfaces are affected by.........in such a way as leads to severe, and at times dangerous, form of the disease with its many “complications”..... David Morley, 1978

Malnutrition is an important contributing factor in 5.6 million children who die annually. Severe acute malnutrition (SAM) is a direct cause in 2.7 million deaths. While the clinical syndrome kwashiorkor has impressed clinician and journalist alike, it are stunting, wasting disease and micronutrient diseases like anemia, vitamin A and iodine deficiency which contribute most to the large global burden of malnutrition (-related) disease. As discussed in part I of this trilogy, 6 decades of understanding of the pathophysiology of severe malnutrition in children has enabled the world community and WHO to develop evidence-based therapeutic guidelines curing most malnourished children. We tend to have become less dogmatic and in anticipation of the many different, often adverse, environments realise why and how children become malnourished. Jackson and Golden defined the varied clinical presentations of malnutrition as determined by the severity, duration and complexity of interactions of specific macro- and micronutrient deficiencies. Both the impact of the nutrient deficits and susceptibility for infection decrease with age, the young being most vulnerable.

However, 30 years ago the HIV pandemic struck sub-Saharan Africa (s-SA) and its effects are dramatic. One disease altered the epidemiology, aetiology, clinical presentation, pathophysiology, case-management, and survival of severely malnourished children. Like measles, HIV infected children act differently, still incompletely understood and are currently not well served by the paradigm and therapeutic guidelines developed prior to HIV, as described in part 1 of this trilogy. This part II presents recent evidence hereof and describes how the Blantyre Working Group drafted an agenda for research, intervention and education, as published in the Lancet’s Viewpoint during the MDG Countdown Series.

WHO therapeutic guidelines need revision in the context of HIV-co-morbidity

Current guidelines do not deal with the needs of HIV infected malnourished children, neither are these implemented universally in the region of highest need, where health services are severely eroded. In the past Nutrition Rehabilitation Units (NRU) typically admitted sick severely malnourished children during the post-weaning period. We now admit many HIV-infected malnourished children outside this age range and these cannot be managed according to standard guidelines without adaptation. HIV-infected (exposed or affected) young infants admitted with SAM are either perinatally infected with HIV or victims of early weaning in PMTCT programmes. These infants present with multiple pathology and suffer from diseases like diarrhoea, pneumonia, PCP, extensive skin infections and oral thrush. In addition, older children (2-8 y) are admitted with persistent and profuse diarrhoea due to HIV-related bacterial and parasitic infections of the gut; their response to therapy is poor and their case fatality is high. Increasingly extremely wasted and -stunted young adolescents, previously rarely admitted outside famines, are now admitted for nutritional recovery and present with HIV related multi-system disease. These include HIV related chronic lung disease, recurrent tuberculosis, HIV related cardiomyopathy, nephropathy, and encephalopathy, and recurrent infections, severe anaemia and Kaposis Sarcoma. Consequently, case-fatality rates still range between 20 and 50% despite the use of the WHO guidelines, SAM complicated by HIV has largely been neglected as an impediment to improving Child Survival. Presently in s-SA, severely malnourished children, within a wider age range, suffer both the synergistic effects of malnutrition and acute, severe infection with the additional complication of HIV infection. Whilst the concept of reductive adaptation in severe malnutrition has assisted us to understand and treat the derangements in malnourished children, whether this is applicable in HIV-infected malnourished children remains to be resolved. Thus there is an urgent need to reconsider this paradigm in the context of HIV in order to determine the best approach to immediate care and optimal nutritional rehabilitation.

Changing paradigm of care

In high HIV prevalence communities where poverty, food insufficiency, epidemics and repeated infectious diseases are common, HIV may be the main driver of wasting or one of several co-morbidities in the individual child with SAM. Again this has changed the epidemiology of SAM as previously oedematous malnourished children were the typical sick malnourished ones facing us with therapeutic dilemmas. In addition, SAM and HIV infection often occur in a social milieu of extreme poverty and food insecurity, with the result that a high HIV infectious pressure affects even uninfected children, without infecting them, through all the socio-economic consequences of their caretakers’ chronic and lethal disease. Severely HIV infected children presenting with SAM, and acute or chronic co-morbidity present challenging therapeutic and care pathways, also including palliative care. In the Malawian NRUs readmission is common and stands at 10%. In Zambia and Malawi more than half of the admissions to NRUs are HIV infected with up to 40% in hospital mortality in this group, in contrast to HIV uninfected SAM children who have a mortality rate of less than 10%. Under conditions where no early introduction of HAART takes place the fate of these HIV infected, still partially malnourished, children is disastrous. Cumulatively two third of the original sample admitted to hospital don’t survive.

The Blantyre Working Group’s response: a research,
intervention and policy agenda
In 2007, fifty clinical and public health child scientists and
practitioners from diverse areas within s-SA gathered in
Blantyre-Malawi and established the Blantyre Working
Group (BWG). This was the first time that this regional
capacity was drawn together. Participants, collectively caring
for more than 100,000 severely malnourished children per
year, included many who have been trainers on the WHO
therapeutic guidelines. As a consequence most NRUs and
CTC programs in the region now follow these protocols.
However it is clear that, despite all efforts, the disease
burden and case-fatality rates remain high and that present
WHO therapeutic guidelines should address today’s realities
in the region . The members of BWG presented and
discussed recent experiences, dilemmas and challenges in
the management of SAM in the context of HIV and concluded
that SAM in the HIV infected individual is genuinely a
different clinical entity, and treating them requiring a new
paradigm.

The challenges ahead
Despite the widespread availability of HIV diagnostic
testing, HAART, the implementation of WHO guidelines and
RUTF, the HIV infected child with complicated SAM in
s-SA is likely to have slower recovery rate, and case-fatality
rates more than 4 times greater than in SAM without HIV
xvii. Hence, the results in our region do not approach those
suggested by the WHO guidelines and the increased fatality
rate is not simply the result of failing to effectively implement
WHO standard management guidelines. This was recognised
during the WHO consultations 2004 and 2005 . Therapeutic
options in both SAM and HIV have increased, but many
questions have arisen and new therapeutic guidelines are
urgently needed based on evidence from the region of high
HIV prevalence. The BWG formulated four areas to guide
the development of improved treatment recommendations,
and one to improve the continuum of care of SAM children
infected with HIV. It is anticipated that presentations and
deliberations during the 10th CAPGAN conference will
strengthen and extend this agenda for improving Child
Survival in sub-Saharan Africa.

The management of systemic infections
Severe illness occurring in children with HIV and SAM is
often due to the coincidence of multiple infections and the
metabolic adaptations of malnutrition, and the case fatality
rates remain high . As early in-hospital mortality is high
appropriate initial treatment strategies should include both
antimicrobial therapies and supportive care. The former
depends on knowledge of aetiology and antimicrobial
susceptibilities, pharmacokinetics in malnourished children
and complex interactions with HAART and/or other
anti-infective drugs including TB therapy. Improving
supportive care requires rapid identification and correction
of life threatening complications, which is the standard
recommended for non-malnourished children, but not
currently advocated for this group due to fears of adverse
outcome in the malnourished child which has adapted to
its reduced body mass and -functions. There is evidence
that antimicrobial sensitivity to first line antibiotic
treatment according WHO guidelines is totally inadequate
and second line (usually a combination of ampicillin /
chloramphenicol and gentamicin) varies between centres,
and that recommended second line agents may not be ideal
. The prevalence of childhood tuberculosis has doubled in
the region due to HIV. In South Africa, among children with
community acquired lower respiratory tract infection, TB
was identified 22 times more commonly among HIV-infected
children . New and creative approaches to diagnosis are
needed in children with SAM and concurrent HIV infection
and tuberculosis as clinical scoring systems perform poorly,
tuberculin skin testing is insensitive, radiological appearances
are frequently non-specific, lymphocyte stimulation tests
yet do not distinguish active- from latent disease, sputum
samples are difficult to obtain and often have low numbers
of mycobacteria and culture facilities are expensive and rarely
available in the region.

Therapeutic diets composition, timing and long-term effects
The introduction of evidence based therapeutic diets,
like F75, F100, ReSoMal and Ready to Use Therapeutic
Food (RUTF) has improved the rehabilitation process and
shortened admission times of non-HIV infected severely
malnourished children and contributed to a continuum of
care within district child health systems. They have become
vehicles to adequately address micro- and macronutrient
deficiencies, despite the fact that the use of F100 and RUTF
in the transition phase is still not well established due to
frequently occurring diarrhoea resulting from their increased
osmolarity. However, with the advent of young HIV-infected
infants suffering from SAM the question of requirements and
formulations needs further consideration and investigation.
The metabolic requirements and -system in the HIV infected
child suffering from SAM is altered, but we are not yet fully
aware to which extent and how to remedy this. RUTF and
its local production has revolutionised the management of
children suffering from SAM and assisted African child
health services to use their limited (human) resources more
effectively and efficiently. However, dietary advice during
recovery from severe malnutrition in HIV infected children
is almost certainly inadequate which warrants further studies.
What are the optimal diets? We perceive that the metabolic
needs are different, but in what way? Is there a problem with
the damaged gut and traditional therapeutic foods? Is there
a need for a new food, in the acute resuscitation phase of
the management of SAM, and/or diets that can be used in
transition to RUTF? Do SAM HIV-infected children always
enter a phase of reductive adaptation and why do they more
often present with marasmus than with kwashiorkor? Are
diets with higher energy and nutrient densities tolerated
in the reductive adapted phase, and will their use result in
higher intakes? Is appetite still a useful guide to recovery
in HIV infected severely malnourished children? Which
supplementary micronutrients do in HIV infected SAM
children reduce morbidity and mortality, and at which
transition to RUTF? Do SAM HIV-infected children always
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supplementary micronutrients do in HIV infected SAM
children reduce morbidity and mortality, and at which
stage of recovery should these be given? Feeding regimes
during the occurrence of purging diarrhoeas in the different
rehabilitative stages in severe malnourished children pose a
problem, as presented from Lusaka where unmanageable
diarrhoea, mainly caused by C. parvum is often associated
with an increased case fatality irrespective of HIV status.
Suitable diets for use in children under 6 months of age are
needed as the present F 75 and F100 are inadequate for them
. However, the low resourced environments in which our
HAART in these children-despite energy intakes double normal requirements-will not recover without HAART. HAART in these children in whom nutritional therapy fails to cause weight gain and overall, recovery can occur. Similarly, those children immunological recovery will be necessary before, nutritional CMV), it is recognised that control of viral load, and initial acute malnutrition and opportunistic infections have been with TB treatment. Current practice is to start ART after addition of HAART is unknown or how to coordinate in SAM complicating HIV viii, and the optimal timing of HAART in SAM, and this will require an RCT of early (after initial stabilisation), versus later (after discharge) HAART in HIV related SAM. The outcome of interest for children recovering from SAM. However, the more important question (which cannot be resolved before pharmacokinetic data is available), will be the optimal timing of HAART in SAM, and this will require an RCT of early (after initial stabilisation), versus later (after discharge) HAART in HIV related SAM. The outcome of interest would be long term survival and nutritional status after 6-12 m. of treatment. Until this is addressed we are unable to advise on the optimal timing to start HAART.

A Wasting Diseases

A Continuum and Synergy of Care

A particular advantage of CTC is the smaller number of staff that is needed to run CTC programmes and that compliance is higher. In order to develop regionally appropriate and local child health specific programs maintaining this continuum of care for these children - who often are orphans and thus without direct caretakers - the roles and functions of the entire child health system need to be transparent and clear, the triage, admission and discharge criteria of these children at each level of care need to be unambiguous, and adequate numbers of staff need to be present and educated to understand and handle these hitherto incompletely understood clinical syndromes. Latter is an important task
of medical schools and nursing colleges which hitherto do not avail as yet over up to date learning materials, texts or textbooks. Local production of weaning foods and a variety of therapeutic foods in Malawi has offered affordable and appropriate infant feeding solutions to child health systems. Can operational projects be translated into more programmatic child health systems approaches in the region? Operational studies should explore the indications for use, the delivery chain, local manufacturing options of these commodities and the role of governments and non-governmental organisations.

The way ahead: moving the agenda and ownership to the area of high prevalence

Ideally, major curative medical advances are based on careful clinical observations framed within a pathophysiologically paradigm, followed by hypothesis generation and testing. Resulting research data should inform improved management protocols that are then introduced to the operational settings. The BWG is convinced this will be true for childhood SAM and HIV. Randomized controlled trials exploring the timing and dosing of ART in SAM, the therapeutic feeding of individuals with SAM and HIV, and the management of acute infection and diarrhea based on successful pilot projects are urgently needed. There is a critical mass of thoughtful clinician scientists engaged to address the issue with the will to succeed. Young clinical scientists from s-SA need to be recruited to this body and talented young physicians need to be supported. The synergism between HIV/AIDS, malnutrition and (opportunistic) infections, contributing to much of the child mortality in s-SA, makes it morally imperative to utilise –with the limited human resources available in s-SA- the large sums presently available for Maternal Neonatal Child Health Initiatives and for HIV/AIDS in a joint manner. Only than are we able to develop and drive effective interventions, operational research in a manner which guarantees ownership locally and support to educational institutions and health systems which are so neglected.

Funding agencies need to better understand the context in which such conditions are treated and the operational conditions in which research will be undertaken. Support is needed, not just in providing funds, but to optimise the design and implementation of studies that are patently tackling the right issues. This will not only address the research questions but will also serve to build the scientific base and competency within the region. Operational support is needed for facilities and national programs committed to treated these children in accordance with the best available evidence and systematically document lessons and insights. A call to action is in order - that the international scientific, health and donor communities join together to defeat the devastating scourge HIV and malnutrition, which was barely acknowledged in national AIDS plans and the 2003 Child Survival Series.

References


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