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CHILD HEALTH

CURRENT ISSUES

CONTENT

IT TAKES A VILLAGE TO RAISE A CHILD

Most of you will have heard this African saying before. This edition of MT underlines this wisdom, something which I could not get out of my mind when reflecting on the theme of child health.

As I walk through my own city in the Netherlands, I ponder on what would be the ideal conditions in a village or city that make for a good, healthy upbringing of a child. What defines a village is a set of houses, grouped together in a more or less orderly way, inhabited by people. A house implies some kind of protection, a shelter, a home: a safe place for a child to grow up in, with parents taking care of him or her. That is one of the major differences between children and adults - their dependency on caregivers. If parents are absent or traumatized, this directly influences a child's health, both physically and emotionally. In this edition, you find the report of the congress on refugee children which was organized by the working group on Global Child Health. Reading these accounts makes one realize again how devastating the lack of a safe and stable place can be for a child.

As I walk on, I pass by another institution that has a big influence on a child's development and health, the school. It is for a good reason that universal primary education was one of the MDGs, and that 'promotion of quality education and lifelong learning opportunities' now features among the sustainable development goals to be achieved by 2030. Education is a basic requirement to acquire life skills, jobs and status, and the lack of it during childhood is difficult to correct later on in life. School is also a place to make friends and relate to peers, which is especially important in adolescence. All of you who are working in the area of sexual and reproductive health or HIV/AIDS know the dynamics of reaching out to young people.

Passing by a playground makes me think about pre-school and its importance for young children, to be able to play and laugh, without having to worry about food, security or other problems. It is incredible that even in the harshest circumstances, like war zones or refugee camps, children will be playing as soon as they get the chance to do so. However, traumatic experiences during childhood may mark their lives.

I stop by a church, the place where religious communities gather to meet, pray and celebrate. Religion can be very influential in people's lives, and the use of religious rituals can be comforting or harmful, depending on the context.

Finally, I arrive at a health centre of course, at last. Especially in paediatrics, the hospital does not have the biggest influence on a patient's health, fortunately, I would say. But it is the working place for many of us, and it can be a beautiful place, where our healing influence can change a whole person's life!

I notice one big difference between this evening's city walk and the ones I had in Africa, namely children playing on the street! In Africa, children often set the scene; you see them everywhere. With their laughter and play, they give life to a place —

SO MAYBE THE SAYING WORKS THE OTHER WAY AROUND AS WELL: IT TAKES A CHILD TO MAKE A VILLAGE.

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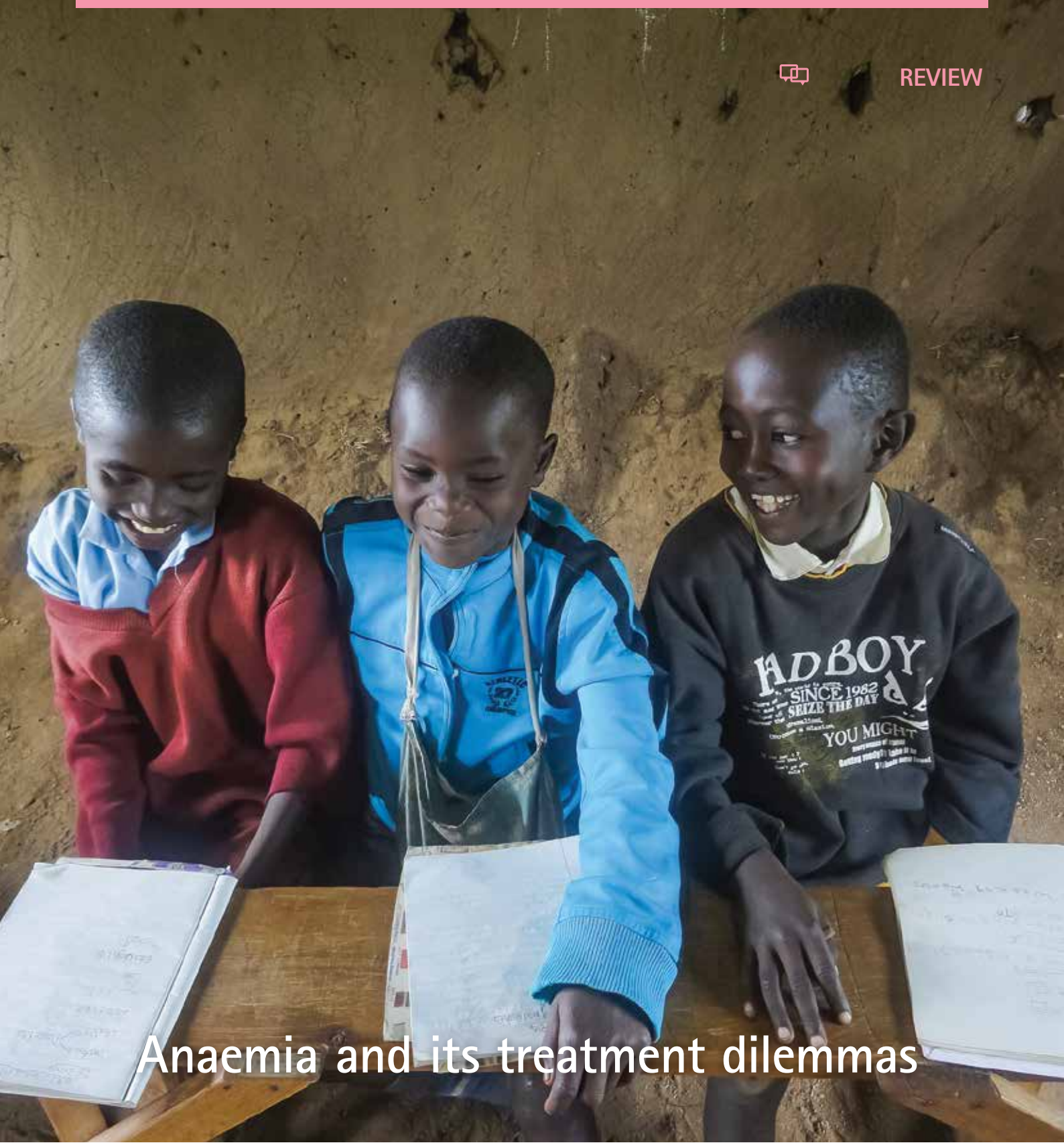

Anaemia and its treatment dilemmas

In developing countries, the prevalence of anaemia is high in children. In large parts of Africa, two out of three children are anaemic (defined by a haemoglobin [Hb] of <11 mg/dl or 6.6 mmol/L). A relatively small percentage (< 5%) of these children are severely anaemic (Hb < 5 mg/dl or 3.0 mmol/L). The mortality due to severe anaemia can be up to 18%, and severe anaemia is therefore, in many regions, a major contributor to the high Under-5-Mortality-Rate.

CHILDHOOD ANAEMIA IN RESOURCE POOR SETTINGS

With an estimated prevalence of 57%, pregnant women are another important high-risk group for anaemia in these regions. Anaemia during pregnancy negatively influences growth and development of the foetus and increases the risk of complications during labour. Despite the multifactorial aetiology of anaemia in resource poor settings, treatment programs are still mainly focused on iron supplementation, despite its possible harmful effects. A shift of focus in the treatment of (childhood) anaemia in these settings is needed.

AETIOLOGY AND PATHOPHYSIOLOGY OF ANAEMIA

Since iron is essential for synthesis of haemoglobin, iron deficiency is often considered the primary cause of anaemia. The terms anaemia, iron deficiency and iron deficiency anaemia are often interchanged, although they mean different things. Besides being confusing in terms of definitions, this ignores the fact that anaemia can occur even with sufficient iron stores. And iron deficiency does not necessarily lead to anaemia, as in the initial stages of iron deficiency, erythropoiesis is not restricted.

Recent studies have shown that the aetiology of anaemia is complex and that multiple factors, through different pathophysiological pathways, may lead to anaemia. Blood loss, haemolysis and decreased erythropoiesis are the three mechanisms leading to (severe) anaemia, each of them having its own set of aetiological factors (Table 1). It is important to note that the contribution of the various aetiological factors varies by region and population. For example, infections such as hookworm and schistosomiasis are frequently found in children living in rural areas (prevalence may be above 20%), but are rarely found in children living in urban settings (prevalence often below 2%).[1] It is noteworthy that hookworm may cause serious infection already at a very young age (< 1 year).[2] Another example of a cause of anaemia that varies by region is vitamin B12 deficiency. In Cameroon, prevalence varied between 11% and 30%, whereas in Malawian children, the prevalence of vitamin B12 deficiency did not vary by region but was correlated with the severity of anaemia (15% in moderate anaemic and 30% in severely anaemic children.[1] Iron deficiency was found to play a role in the development of mild and moderate anaemia, but no association was identified between iron deficiency and severe anaemia in a Malawian study.[1]

Besides the geographic diversity of factors causing anaemia, the individual factors may interact or correlate. For example, it has recently been shown that the association between vitamin A and severe anaemia could in part be explained by the effect of vitamin A deficiency on susceptibility to malaria and bacterial infection.[1] In addition, HIV can be a direct cause of anaemia by infecting bone marrow stem cells, which causes apoptosis of these cells and thereby affects the red cell production capacity. Yet HIV may, due to its immune-suppressive effect, also increase the susceptibility to infections and thereby the risk of anaemia via suppression of the bone marrow through a non-specific inflammatory response.[3]

TREATMENT AND PREVENTION OF ANAEMIA

With respect to the role of iron in the treatment of anaemia, it is important to note that over the past decades there has been an on-going debate on the complex interaction between iron deficiency, iron supplementation, and susceptibility to infections. Iron deficiency may increase risks of infection, as iron is required for normal immune function, including bactericidal activity of macrophages and T-cell function.[4]

However, on the other hand, since iron is also an essential nutrient for many pathogens, iron deficiency may protect the host against infections. This was demonstrated by studies indicating that iron deficiency is associated with a reduced risk of malaria infection.[5,6] This so-called protective functional iron deficiency is largely mediated by hepcidin.[7,8]

In 2006, a large trial in Zanzibar found that iron was associated with an increase in morbidity and mortality in iron supplemented children.[9] More recent studies have found a strong positive relationship between iron supplementation and susceptibility to malaria.[10] As a result, the World Health Organization has decided to restrict its recommendations for iron supplementation to children with severe anaemia or proven iron deficiency. The problem is, however, that iron status is difficult to assess due to lack of available iron markers which are not influenced by the acute phase response occurring during an infection.[11] Furthermore, in severely anaemic children, hepcidin levels were found to be low, despite concurrent severe infections, thereby possibly missing the protective effect of inhibited iron absorption in the gut (which would be the response to a high hepcidin level) and increased infection risk.[12] Besides the above mechanism, the harmful effects of iron supplementation are likely to be context-specific, because exposure to pathogens and thereby the risk of infection differs by area.[5,6,7]

Folic acid deficiency is also generally regarded as a potential cause of anaemia in children. However, few studies have measured folic acid levels in children living in developing countries. Studies in Gambia and Malawi detected very few children who were folic acid deficient and found no beneficial effect of folic acid supplementation on haemoglobin recovery.[13] In addition, one has to take into account that folic acid supplementation, if not indicated, may not be a harmless treatment. Folic acid may stimulate the growth of Plasmodium falciparum and inhibit the effectiveness of the antimalarial drug sulphadoxine-pyrimethamine (SP).

Although vitamin A deficiency is an important cause of anaemia, supplementation had surprisingly little effect on the incidence of severe anaemia in children, which might indicate that other concurrent conditions had caused the anaemia.

CONCLUSIONS

Management of (severe) anaemia must be underpinned by a detailed knowledge of the multifactorial aetiology which varies geographically, seasonally and between sub-populations. Therefore, anaemia is unlikely to be amenable

Mechanism		Etiological factors
Blood loss	Through urine, stool or trauma	Hookworm Schistosomiasis Shigellosis Traffic accident, crocodile or hippo bite
Haemolysis	Intra- or extra- vascular	Malaria Sepsis Haemoglobinopathies (SCD, Thalassemia, G6PD)
Decreased erythropoiesis	Bone marrow failure through infections	*Parasitic:* Malaria *Bacterial:* Tuberculosis, 'Non-typhoid Salmonella' *Viral:* HIV, Parvovirus, EBV, CMV
	Micronutrient deficiencies	Deficiency of Iron, folic acid, vitamin B12, vitamin A

Table 1: Mechanisms and possible etiological factors of (severe) anaemia in children in southern Africa

to a single intervention, and global strategies are usually not applicable. It is increasingly clear that restoring the function of the bone marrow is essential in the treatment of anaemia. However, multiple bone marrow suppressive factors are often at play simultaneously. All these factors need to be addressed, as otherwise the bone marrow will remain blocked. More research and strong partnerships between programmes are needed to determine appropriate intervention packages that are tailored to the local causes of anaemia.

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Mortality reduction in preterm births in low resource settings

What is the place of antenatal corticosteroid therapy?

INTRODUCTION

Worldwide, almost 10% of births are preterm, causing more than a third of all neonatal deaths per year, in total almost one million.[1] Prevention of preterm birth is difficult, and emphasis is put on premature baby care and management of premature labour. Antenatal corticosteroid therapy for foetal pulmonary maturation could have a significant impact on neonatal survival by reducing complications of prematurity. Labour is postponed for two days while maternally administered corticosteroids trigger foetal lung maturation. In the most recent systematic review, there was a 34% reduction of respiratory distress syndrome, a 46% reduction of intraventricular haemorrhage and a 31% reduction in neonatal mortality.[2] The use of corticosteroids is incorporated in many guidelines worldwide, but most studies have been done in a high-resource setting.

A review of the use of antenatal corticosteroids in several middle-income countries showed a neonatal mortality reduction of 53%, and the effect in low-income countries might be even greater.[3] However, some doubts have been voiced regarding the effectiveness of corticosteroid therapy in a low-resource setting, and these doubts were strengthened when in 2015 the results of an antenatal corticosteroid trial was published in The Lancet by Althabe et al.[4] This population-based, multi-country study did not show a positive effect in the preterm infants group, even though nearly half of them received therapy. The results prompted the World Health Organization (WHO) to recommend that the following four conditions be met before antenatal corticosteroid administration is considered for women at risk of preterm delivery between 24-34 weeks of gestation: (a) gestational age is accurately assessed, (b) preterm birth is imminent, (c) there is no evidence of infection, and (d) adequate childbirth care and care for the preterm neonate are available.[5]

In this review, we will discus what factors can explain the above findings and what place there might be for corticosteroid therapy in a low-resource setting.

POSSIBLE REASONS FOR DIFFERENCES IN EFFECT BETWEEN HIGH- AND LOW-INCOME COUNTRIES

The clinical trial reported by Althabe et al. does not identify the reason for the adverse effects of antenatal corticosteroids. However, three different reasons for increased risk and lower effectiveness of antenatal corticosteroids in low-income countries can be assumed.[6,7,8]

(1) *Suboptimal administration of antenatal corticosteroids.* Uncertainty about gestational age is the main challenge in selecting patients for therapy. In a setting of late booking, unreliable history of last menstrual period and absence of ultrasound facilities, it is difficult to identify women who are at risk for preterm delivery and eligible for corticosteroid administration. In the trial, only 16% of pregnant women who received corticosteroids delivered a preterm infant (using birth weight as a proxy for gestational age). Not only will this dilute any positive effects of therapy, but women and babies are also exposed to the risk of corticosteroids without the benefits.

In low-resource settings, it can also be more difficult to identify women with imminent preterm birth, as few women present with preterm labour. Without symptoms of preterm labour, women might deliver at home or arrive in the hospital too late to start tocolytics. In the large trial, the most common indication (77%) for corticosteroid therapy was preterm labour, and 70% of women completed the therapy.[4] Ultimately, more than half of the women who received treatment delivered at term. Since few women present at hospitals with premature labour, antenatal corticosteroids are mostly given to women with severe maternal disease requiring preterm termination of pregnancy, almost always severe hypertensive disorder. Although in Western countries the evidence and benefits for this type of treatment are clear, the considerations may be different in a low resource setting, since the risks are different. Antenatal corticosteroid therapy requires postponing delivery, but women with severe diseases who are at risk cannot always be monitored and treated adequately.

(2) *Increased risk of corticosteroids use.* As an unintended side-effect, corticosteroids increase the susceptibility to infection and decrease the immune function.[9] This can explain the higher rate of suspected infection in the trial by Althabe et al. In low-income countries, the infectious disease burden is higher and the level of antisepsis lower. Sepsis is one of the main causes of foetal and maternal mortality, and therefore administering corticosteroids is potentially dangerous.

(3) *Limited possibility for adequate preterm birth care and postnatal care.* In settings with overburdened and understaffed labour wards and limited possibilities for maternal and foetal monitoring, infection and foetal distress can go undetected. Keeping the foetus in this situation without the ability to check its condition can lead to undetected foetal distress and eventually death. Causes of neonatal mortality of preterm infants in resource-limited settings include hypothermia, hypoglycaemia, birth asphyxia, infection and respiratory issues. Addressing only the latter cause when the others can not be managed adequately has been called 'useless'.[10]

The trial by Althabe et al. is not necessarily applicable to all hospitals. The WHO has issued general precautions that would need to be considered before starting antenatal corticosteroid treatment. These seem logical in view of the considerations above, but the preconditions are not very specific and the relative importance of each precondition is not known. Corticosteroids have the potential of reducing neonatal morbidity and mortality when used properly. Further studies can hopefully make it clear under which circumstances antenatal corticosteroid therapy can be used in low-income countries.

CONCLUSION

Adverse effects of antenatel corticosteroid therapy are more prominent in low-income countries. Reliability of gestational age estimation, epidemiology of preterm birth, exposure to infections, foetal monitoring and quality of neonatal care are likely to influence the effect of corticosteroids, but it is unclear what the exact preconditions are for corticosteroid therapy to be effective and safe. Further studies and audits are needed to determine in which settings and under which circumstances corticosteroids are safe for both mothers and their unborn babies. Until then, the WHO precautions seem reasonable.

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Normative global growth charts or descriptive national charts?

Since the end of the 19th century, studies on human growth in representative samples of healthy children have been performed in European countries and the USA, and in the last 70 years growth studies have been carried out in almost all countries of the world. Measurements of height, weight and various other anthropometric parameters have been used to study patterns of infant, child and adolescent growth and to generate growth charts. Growth charts visualize growth and enable the comparison of individual growth with that of a reference population; they are used for clinical purposes and to monitor trends in child nutritional status in entire communities. A growth chart is considered a 'road to health'. However, growth charts differ quite a bit between countries, so the question arises: which growth chart should be used to determine if a child grows normally?

This dilemma is evident in many low- and middle-income countries, and particularly in Asian and Latin-American populations. As it is a priori not decidable whether differences in child growth are due to differences in ethnicity, in health and nutrition, or due to socio-cultural and economic factors, the dilemma has led to two alternative concepts of describing child growth: **1)** by *descriptive growth charts* and **2)** by *prescriptive* or *normative growth charts*. Descriptive growth charts, also called *growth references*, describe how children **do** grow; normative charts, also called *growth standards*, describe how children **should** grow.[1]

The rationale for normative growth charts reaches back to recommendations of a Working Group on infant growth, established in the early 1990s by the World Health Organization (WHO), which emphasised the similarity in early childhood growth among diverse ethnic groups.[1] The recommendations are based on six longitudinal child growth studies from birth to the age of five from Brazil, Ghana, India, Norway, Oman and the United States. These children had been exclusively or predominantly breastfed, grew up under affluent conditions, and showed similar growth patterns.[2] The observations fuelled the assumption that growth is driven by the environment.[1] This idea implies that the same growth standard can be used for all countries in the world and can detect unfavourable living conditions (WHO Child Growth Standards, WHO-CGS). As it was not considered feasible to perform similar longitudinal growth studies in older children, the corresponding international 'normative' charts for 5 to 19 years of age were developed based on 1977 USA growth references.[3]

Normative growth charts are widely used. By April 2011, 125 countries had already adopted WHO growth standards. Weight-for-age has been adopted almost universally as a standard parameter, along with height-for-age (104 countries) and weight-for-height (88 countries) to fully realize 'the child's right to achieve its full genetic growth potential'.[4]

But the consequence of using normative growth charts is the so-called 'stunting syndrome'.[5] According to UNICEF's definition of stunting as a height below minus two standard deviations from the median height-for-age of the WHO standard population, the stunting syndrome is prevalent in many developing countries, particularly in Asia; growth failure is found in an estimated 165 million children below five years of age. For example, in Indonesia, based on a multistage cluster sample of 497 districts (urban and rural) of 33 provinces, including 294,959 households with 1,027,763 household members, the average prevalence of stunting below the age of five was 36.8% in 2007 and 37.2% in 2013. The average height of Indonesian 18 year old males and females is 12.5 cm and

9.8 cm below the WHO reference, respectively (Indonesian national report on basic health research as communicated by Prof. Madarina Julia, Yogyakarta, Indonesia, personal communication 2016).

Stunting is not limited to the poor and the undernourished. If we define stunting in line with the WHO and UNICEF, it is a common phenomenon also among the wealthy and healthy. 'Stunting' was common in 18th and 19th century upper-class Europeans. In Germany, up to 50% of the 7 to 18 year old students at an 18th century elite school and of sons of the wealthy upper-class societies of the second half of the 19th century were stunted according to modern criteria.[6] Figure 1 illustrates that their growth pattern was almost parallel to that of modern Indonesians.

Meanwhile, the average height of adults has increased in Europe and many non-European countries. This phenomenon is referred to as the secular trend in height. For example, in Swedish conscripts, average height increased from 168 to 180 cm between 1850 and 2000, and in the Netherlands an even greater secular trend of 19 cm was observed (from 165 to 184 cm in adult males between 1860 and 1997, without any further increase).[7,8] Secular trends are country specific. The trends started and stopped earlier among Northern than among Southern Europeans.[9] In Sweden, the trend stopped 20 years earlier than in the Netherlands, while its magnitude was 7 cm less. Trends in height usually coincide with trends in maturation tempo. Modern societies show a marked shift towards earlier pubertal development. In Japan, the secular increase of average adult height of 5.5 cm between 1960 and 2000 was accompanied by a 1 year faster maturation tempo.[10] Trends in tempo are also country specific; the onset of puberty occurs later in Northern European than in Eastern Asian and Mediterranean populations.[9,11]

Secular trends can differ between ethnicities even within the same country. In the 1997 Dutch growth study, children of Moroccan and Turkish immigrants were on average 5 cm shorter in childhood, and the differences increased to 10 cm in adulthood. Between 8% and 14 of prepubertal immigrant children (3-10 years) would be considered stunted (height SDS <-2) if compared with the 1997 Dutch reference charts. Whereas the secular trend in height has stopped in the children of Dutch origin, it seems to be continuing in migrants. In 2009, 18-year olds of Moroccan and Turkish descent were 2-3 cm taller than 12 years earlier.[12] The trend in children of South Asian origin living in the Netherlands was less marked: only a 1.3 cm and 2.3 cm increase between 1976 and 2010 in girls and boys, respectively.[13] Similar heterogeneous observations have been reported from various European and non-European countries. Figure 2 illustrates that a secular trend in height is also found in Indonesia.

The association between height, nutrition and population health has been studied intensively, with no consistent across- and within-country relationship found between height on the one hand and childhood mortality or living conditions on the other.[14] In particular, African women are taller than one would expect on the basis of their low incomes and high childhood mortality, and South Asian women are shorter. In other words, the general assumption that stunting can be considered a health indicator is at variance with the discrepancy between people's average height and their average socio-economic condition.

In view of the encouraging European experiences with multiple national growth reference charts, it appears justified to prioritize the concept of national growth reference charts over international charts, particularly for countries where children who were raised under affluent conditions differ substantially from the international norms. It is now possible to generate national growth reference charts by amalgamating information from very large international sets of growth data (based on a recent meta-analysis of 196 female and 197 male growth studies published since 1831) with regional data characterizing growth of the population of interest. Such charts have been termed 'synthetic growth references'. They are cost-effective and could be introduced for all populations that lack autochthonous national growth references.[15]

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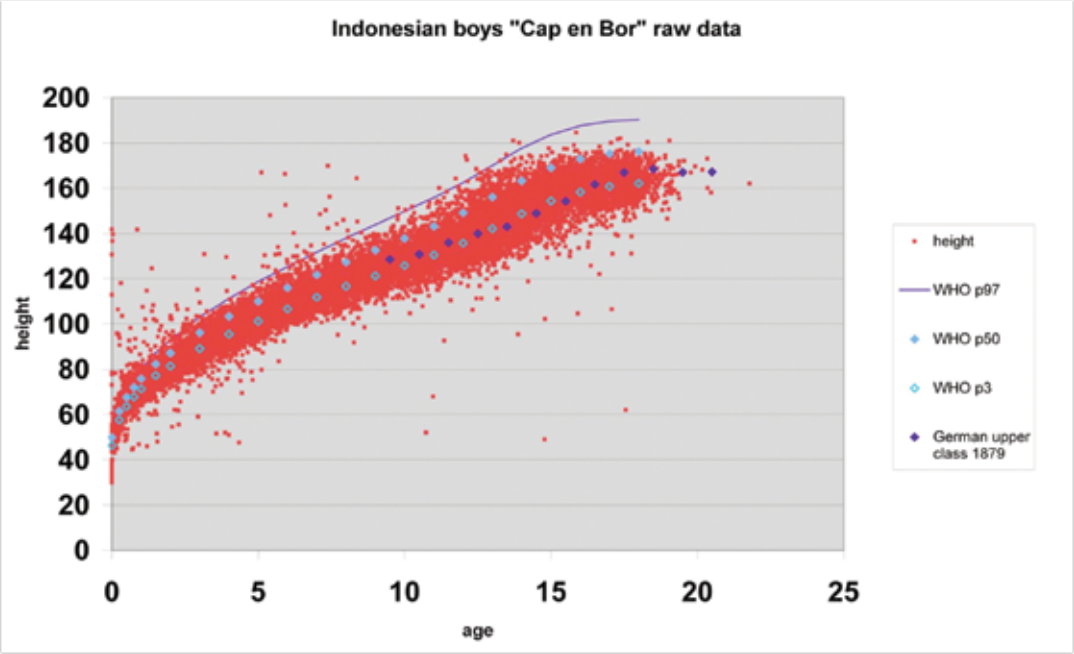

Figure 1

Height measurements of 18,640 healthy, middle-class Indonesian males aged 0 to 21 years (Cap and Bor study), mean heights of 509 healthy and very wealthy German boys measured in 1879 (blue), and the 3rd, 50th and 97th centile of normative WHO Child Growth Standards (WHO-CGS) and WHO references. Data derived from M. Julia, personal communication, and from L. Kotelmann, Die Körperverhältnisse der Gelehrtenschüler des Johanneums in Hamburg: Ein statistischer Beitrag zur Schulhygiene. Zeitschrift des Königlich Preussischen statistischen Bureau's. Berlin. 1879.

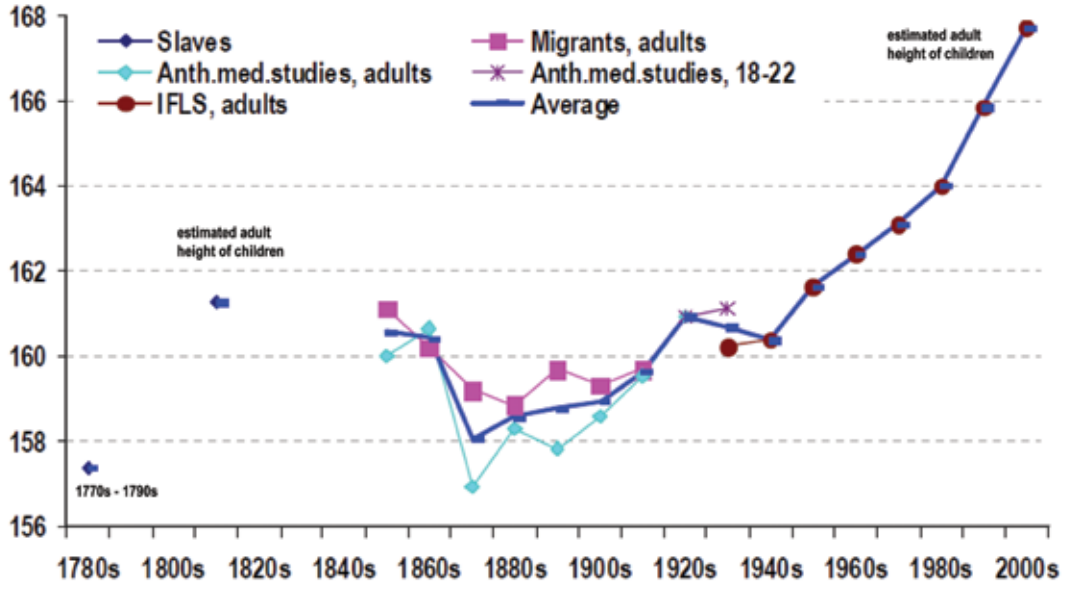

Figure 2

Average male height in Indonesia by birth decade, 1770s-2000s (cm). Reproduced from J.Baten, M.Stegl and P.van der Eng, Long-Term Economic Growth and the Standard of Living in Indonesia. Working paper No: 514, The Australian National University, 2010, ISBN: 0 86831 514 1. JEL codes: N35, O15, I31.

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Care for refugee children: A congress report

International Child Health Working Group Ouwehands Dierenpark, Rhenen – 11 March, 2016 Care for the refugee-child

In March this year, over 150 professionals with various backgrounds gathered at the annual congress of the International Child Health Working Group. Not only paediatricians, but also doctors in international health and tropical medicine (AIGTs), nurses, general practitioners, psychologists, policy makers, legal experts and volunteers found their way to 'Ouwehands Dierenpark' for this congress on refugee children.

Besides medical topics like haemoglobinopathies and tuberculosis screening, attention was given to the boat journeys that many refugees from Syria make to Europe. The Syrian paediatrician Dr Mohammed Ahmad shared his own experiences from living in the Dutch refugee camp Heumensoord as a medical professional.

Darren Cornish, general practitioner at the medical centre in Ter Apel refugee camp, gave an impassioned talk about his work with the refugees. He pointed out the need for more information about the whole process of logistics when arriving in the Netherlands. On this topic, regulations concerning health insurance appeared to be confusing and were further clarified by Christaan Rademaker, contract manager at the insurance company Menzis.[1]

One of the main problems in caring for refugee children appears to be the lack of continuity. More than 90% of the children are treated in primary care, but diagnosis may be missed because of the many different health care workers involved. For example, during weekends in the refugee camp, triage is done by Red Cross staff, who are supervised by a doctor or nurse. Only after consultation by phone, can the patient be referred to a health centre nearby. In practice, this process appears to be time-consuming and inefficient. In hospital care as well, there are gaps in continuity due to the many relocations of refugees, leading to problems with transfer of medical information.

After the lunch break in the zoo, the congress program continued with a focus on care for mother and child. Jamilah Sherally (AIGT in training) discussed the option of adding a short internship in asylum centres to the education of the AIGT and using their dedication and skills in providing care for children and pregnant women in primary care. On the same topic, Peggy van der Lans, gynaecologist, pointed out the many issues around the vulnerable group of pregnant refugees, who deliver around 600 babies annually in the Netherlands. At present, maternal mortality has a risk ratio of 10, and it is likely that problems for mother and child continue after the delivery. Stakeholders like GGD-Ghor, Menzis MCA, GCA, COA, the Dutch Society of Midwives (KNOV) and the Dutch society of gynaecologists and obstetricians (NVOG) have developed a multidisciplinary guideline for the provision of care for these women.[2] This guideline is a good example of collaboration on care for asylum seekers, but its implementation must be improved.

Irma Hein, child psychiatrist at De Bascule in Amsterdam, then gave a presentation on psychotrauma. The incidence of psychopathology in refugee children is more than 25%, and 30%-70% have some symptoms. Moreover, 13%-25% of refugee parents suffer from post-traumatic stress disorder (PTSD) or depression with all its consequences for their children, including child abuse. The many underage refugees travelling alone (AMVs) with psychopathology have only the general practitioner to turn to after they turn 18. These refugees are particularly at risk of disappearing into the illegal circuit if they are denied legal status. There is an abundant although fragmented availability of preventive psychosocial aid programs, but they are mainly aimed at refugees in AZCs. The use of a good evidence based screening method like CRIES-13 is considered necessary. However, not many treatment methods are evidence based and it is still not clear when it is best to start treatment.

Maria van de Muijsenberg, general practitioner at Pharos, focused on the access to care and health insurance arrangements for the undocumented, illegal refugee child without a permit to stay. They often live with friends and family or on the street and lead an invisible life without much perspective. In this group reproductive health and behavioural or somatization issues often become problematic.[3]

Going on to discuss legal matters, Karin Kloosterboer (UNICEF Netherlands), explained that the situation with regard to children's rights for the refugee child does not correspond in practice with the rules agreed upon. The many relocations with all the attendant consequences concerning social, emotional, educational, and medical issues as well as the group denied status after litigation deserve more attention.

The congress ended with a lively debate about this last topic, in which all the earlier speakers participated. The day was summarized by Albertine Baauw (paediatrician), who highlighted three main issues:

1. The frequent relocations of refugees are harmful as they impede continuous delivery of healthcare and increase the risks of mental distress and developmental problems in children.

2. Children of traumatized parents and those travelling alone are at high risk of psychosocial problems, which often only become clear after settling in the community or in illegality.

3. There is an urgent need for early detection, valid screening, and evidence-based psycho-social interventions for this group.

All participants firmly agreed on the need to improve care for refugee children and pleaded for better collaboration between all parties involved, in order to optimize the care for this highly vulnerable group of children.

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WORKING ON THE EDGE

INTERVIEW WITH HARRIET ROGGEVEEN

At the office of Médecins Sans Frontières (MSF) in Amsterdam, we meet up with Mrs Harriet Roggeveen, 54 years old and working for MSF as a paediatric advisor since five years. Even though she always had the drive to work in tropical medicine and started her career with a yellow fever-project with MSF, she chose to specialize in paediatrics first. But after having worked happily as a paediatrician in different settings in the Netherlands, she didn't hesitate to apply for the position of paediatric advisor in 2011 to follow her lifelong dream. In this personal interview, Harriet introduces us to her work with MSF.

THE PUBLIC HEALTH POINT OF VIEW

From the beginning of our conversation, it is clear what motivates Harriet most in her work: the full picture, the broad view on paediatrics. Her role as advisor varies from providing medical advice on specific patient cases to indicating areas for improvement of paediatric care in a setting of limited resources.

As an example, she explains the situation in Haiti, where MSF started a project to reduce the high maternal mortality. As a result of many high-risk pregnancies, many premature and small-for-gestational-age babies were born, which had resulted in the development of very advanced neonatal care. 'The first time I was there, I noticed they provided Continuous Positive Airway Pressure (CPAP) and had incubators, but basic care and hygiene were inadequate. Babies of 33 weeks old were discharged even though it was uncertain whether breastfeeding would succeed, while at the same time little ones of 1000 grams were put on CPAP in an incubator.

That did not make sense! Children with good chances of surviving should be given adequate care before organizing expensive specialist care for the ones who are less fortunate, not the other way around, even though from an ethical perspective you would want to care for each individual as they come to you.'

Harriet then explains how they tried to take a step back from advanced care so as to ensure that a more basic form of care could be provided, for example by implementing kangaroo care. But she also knows how difficult that can be, especially when local staff is more interested in advanced care. 'We ran into major problems with hygiene, resulting in nosocomial infections with resistant pathogens. In order to try to control that, we appointed an infection control manager and introduced the technology to do cultures. But then again you move towards advanced care and ask yourself

'COULDN'T WE BETTER PUT THIS MONEY INTO CHILD VACCINATION?' THESE ARE DIFFICULT QUESTIONS, BUT THESE KINDS OF PUBLIC HEALTH QUESTIONS ARE ALSO WHAT MAKES OUR WORK SO INTERESTING.

EMERGENCY AID OR BUILDING SUSTAINABLE HEALTHCARE SYSTEMS?

As we continue to discuss the work of MSF, we soon come to the next challenge. Is it better to focus on providing emergency aid or on building a sustainable system of healthcare? 'Because MSF often works in so-called 'failed states' with poorly functioning healthcare systems, cooperation with the local government is often not possible. In an emergency setting that is acceptable, but from a development perspective that might not be the right way to work. And even though the core business of our organization is emergency care, in reality many projects continue for over 10 years, so should we then play a role in development. How sustainable should the work of MSF really be? Should we put more effort into training local staff and working with local ministries of health? Or should we focus on delivering emergency care and leave development work to other organizations? Of course, that influences the type of care we give and determines whether or not, for example, we engage in vaccination programs. Such questions keep my work interesting!'

An illustration of how MSF sometimes does focus on long-term care comes up when we discuss malaria, one of the biggest problems in paediatrics in tropical areas. 'In many countries, for example Congo (DRC) or South-Sudan, the burden of malaria is increasing, and then it's simply not sufficient to provide secondary, hospital-based care. In our long-term projects, we try to shift towards community-based primary health care. That is not always possible in areas where it is unsafe for our medical staff to go into the community, but sometimes it works very well, for example in one of our projects in Congo. In the community, you can provide more integrated care, treating diseases like malaria, pneumonia and gastro-enteritis at an earlier stage. It's not very sophisticated, not rocket-science, and not very new, but it works!'

MEDICAL SPECIALISTS OR GENERALISTS IN THE FIELD?

Emphasizing that it's her personal opinion, Harriet explains the importance of having both specialist and general health expertise: 'I think basic care should be the first priority, and generalists like the Dutch tropical doctors are generally very competent to do that. If there were many specialists, the care would probably become too technical. But general doctors need the input of specialists, like paediatricians, especially because the under-five population is often huge. Perhaps paediatrics should be given more attention in the training program for tropical doctors, even though western paediatrics is very different from the tropical version.

'Doctors who are not trained in paediatrics are often a bit afraid of it, especially of neonatology. But knowing that 44% of the mortality in under-fives happens in the neonatal period, you realize it's a very important area. And a lot can be achieved with relatively simple interventions, without CPAP or incubators. The best practical advice I can give to tropical doctors with no paediatric training is to make sure they know how to resuscitate new-borns by providing Neonatal Life Support (NSL) and know how to recognize and treat neonatal sepsis, hypothermia and hypoglycaemia. They should also use the training materials available from WHO (www.who.int), which describe various evidence-based, uncomplicated interventions. They will then be better prepared and better able to train local staff.'

AND A FINAL REQUEST

At the end of the interview we thank Harriet for her passionate and inspiring story, at which point she asks us to use this opportunity to send a message to our readers. 'At MSF, we are looking for medical doctors, especially people who would like to work with us in long-term assignments. Having experienced staff is very important for us, and MSF is a great organization to work with!'

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Proactive support of labour: the challenge of normal childbirth

INTRODUCTION

Medical staff involved in obstetric care across the globe are confronted with several challenges. Important issues are the rising rate of caesarean deliveries and their sequelae, high instrumental delivery rates in some centres, medical litigation issues, and psychological harm to patients who do not experience spontaneous vaginal delivery within a reasonable time. At the Livive birth centre in Tilburg, the Netherlands, the authors have introduced the concept of 'proactive support of labour' in order to systematically tackle these issues. It is in fact an adaptation of an approach advocated by O'Driscoll in Dublin during the 1970-80s. The proactive support of labour concept was developed to enhance patient satisfaction concerning obstetric care and safely reduce caesarean section rates. It only deals with singleton, cephalic, term pregnancies.

WAKE-UP CALL

Much can go wrong in modern obstetrics and midwifery, as the authors recognize 'a progressive lack of understanding of the labour process and, consequently, declining delivery skills of today's birth professionals'. Extensive support for this provocative statement is provided. Rising caesarean section rates are seen as indicative of the problem of failing childbirth methods, in particular during the first stage of labour. What are the causes? Among others, the lack of a systematic approach to the first stage of labour, insufficient professional interest and poor counselling are mentioned. The book provides a critical evaluation of recent clinical research, including a meta-analysis that shows lower caesarean section rates among patients undergoing induction of labour.

In the second section, the book goes back to basics and provides an overview of the physiology of labour. It emphasizes the parasympathetic nature of labour, and the potentially harmful effect of stress. The importance of the physiological process of electromechanical coupling in the uterine muscle prior to delivery is described, and the possible negative consequences of induction on this process. Attention is placed on the importance of precise and consequent terminology during staff handovers.

WHAT CAN BE DONE?

The third section describes the proactive approach in detail. Essential is the correct diagnosis of labour, for which clear definitions are provided. Timely augmentation of labour, with rupture of membranes or use of oxytocin, is essential to ensure progression. A distinction between mechanic dystocia (in case of cephalo-pelvic disproportion) and dynamic dystocia is made and several causes of dynamic dystocia are unravelled, emphasizing the differences in case management between nulli- and multiparous women. The authors provide management guidelines for each type of obstructed labour. Emphasis is put on adequate pre-labour preparation and counselling, including the option of conducting a caesarean section if delivery is not imminent after 12 hours of labour. One-on-one nursing care is considered an essential component of the approach, which will require some organizational reform in most hospitals.

DISCUSSION

This book is worthwhile reading for everybody involved in birth care, especially for junior staff with limited obstetric training. The provocative style may not appeal to everyone, but it makes for an interesting read. If offers an overarching philosophy of labour and delivery, based on a solid understanding of physiology, which would increase the quality of care on labour and delivery wards both in high and low income settings. Unlike many other medical textbooks, this book does not deal only with purely medical problems and solutions but also with the organization of care, the importance of patient satisfaction and proper counselling, thereby offering a holistic approach.

The authors may encounter some resistance in denouncing the concept of latent phase of labour. Early interventions during the first stage might not appeal to all practitioners either but are worth discussing. Practitioners who read this book will be triggered to evaluate their own practice. It is a good teaching resource in developing countries and provides a good starting point for cooperation between primary and secondary care providers.

DETAILS

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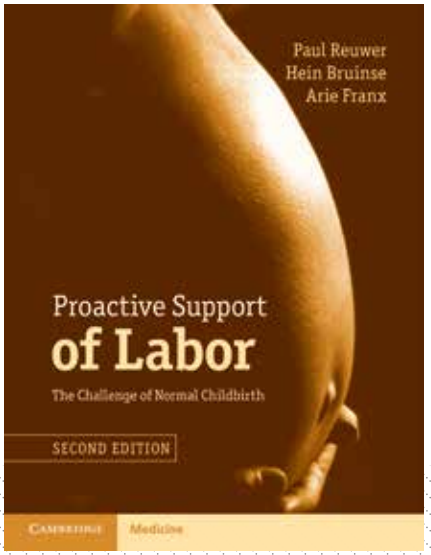

TO TREAT AS TB OR TO TREAT DIFFERENTLY: THAT'S THE QUESTION

SETTING

This case is set in Kikori District Hospital on the southwest peninsula of Papua New Guinea (PNG). The hospital is located in the Gulf province on the banks of the Purari River amidst tropical forest. The district hospital has 80 beds and very limited diagnostic tools. There is no access to laboratory tests, other than those used to diagnose HIV, syphilis, tuberculosis and malaria. Ultrasound is available, and an X-ray is about to be installed.

PNG has one of the highest tuberculosis rates in the world, with an estimated incidence of 400 per 100,000 inhabitants.[1] In the Gulf province, the incidence is about three times higher: 1290 per 100,000 patients in 2012.[2] Furthermore, there is an increasing incidence of drug-resistant strains. MDR-TB is found in 2.7% of all newly diagnosed TB patients and in 19% of patients requiring retreatment.[1]

Apart from TB, PNG has a high incidence of malaria and other tropical infectious illnesses. Significant health issues occur due to malnutrition and poor hygiene. Furthermore, physical violence is rampant partly associated with alcohol and drug use (marihuana and chewed betel nut).

CASE

A 25-year old male patient presented at the out-patient clinic with a lesion to the left foot. The wound had started five weeks earlier and was progressive, with the development of two satellite lesions. The patient was unsure how the lesion had commenced. The history mentioned water contact but no recent trauma. Apart from the lesion, the patient was healthy and did not suffer any other symptoms. He had never been diagnosed with diabetes and his vascular status was unknown. He did not use any medication but consumed large quantities of tobacco, alcohol, marihuana and betel nut. He was unemployed. Family history included an aunt with pulmonary tuberculosis.

On physical examination, a large ulcer and two smaller lesions with undermined edges and oedema were seen on the dorsolateral side of the left foot (Figure 1). There was no pain, odour or purulent exudate. There was no fever. On auscultation of the lungs, normal sounds were heard. Several small lymph nodes were palpable bilaterally in the supraclavicular region.

SPECIALIST ADVICE

A diagnosis of Buruli ulcer was made and the attending physician suggested starting rifampicin and streptomycin. However, he was concerned his suggested therapy would lead to drug resistance in this patient, whose a priori chance of having tuberculosis was high (taking into account the high incidence of TB in the region as well as the family history). Our specialists were consulted regarding two specific questions. Was a Buruli ulcer the most probable diagnosis? And would they suggest treating this patient with a regular tuberculosis regimen instead of the suggested specific antimicrobial therapy for Buruli ulcer?

Within 24 hours, three specialists (an infectiologist and two dermatologists) had responded to the enquiry. The dermatologists were unanimous in confirming the diagnosis of a Buruli ulcer. For further validation of the diagnosis, they suggested taking a smear to detect for acid-fast bacilli (AFB) to demonstrate the presence of mycobacteria. Regarding the treatment of this patient, they were less unanimous. One dermatologist recognized the concern of inducing drug resistance and advised starting the patient on a regular tuberculosis regimen (including streptomycin). The other dermatologist was not convinced of the indication for a full course of antituberculous therapy, based on the symptoms of the patient. He advised starting the patient on rifampicin/streptomycin or rifampicin/clarithromycin to treat the Buruli ulcer accordingly and to disregard a possible concurrent tuberculosis infection.

The infectiologist offered different advice altogether. Although the ulcer could be caused by M. ulcerans, this diagnosis would not explain the lymphadenopathy. He proposed regarding the ulcers and lymphadenopathy as manifestations of the same illness and treating the patient for tuberculosis. He recognized the risk of inducing drug resistance by treating for Buruli ulcer while the patient could actually have tuberculosis.

He suggested further examination including chest X-ray and FNA of the lymph nodes. As this was not possible in Kikori district hospital, the advice was to start quadruple therapy for tuberculosis[3], adding streptomycin for 4 weeks. Also, the infectiologist suggested testing the patient for concurrent HIV infection, as disseminated TB occurs more often in HIV positive patients. Naturally, in the case of a positive test result, this would warrant treating the patient for HIV.

FOLLOW-UP

To confirm the diagnosis, a smear was taken that showed AFBs. Regarding the different treatment recommendations, the physician decided to start the patient on a full-course tuberculosis regimen. There was satisfactory healing tendency. After a week of therapy, including regular wound debridement, the oedema had disappeared and the ulcers no longer featured undermined edges. Thereafter, gradual granulation was seen. The smaller ulcers disappeared and the large ulcer decreased to about 2 cm.

Unfortunately, the patient was not compliant with his therapy and did not report for follow-up. He eventually returned after 22 days of non-compliance. His regimen was resumed, adding the 22 days he missed due to his absence in the initial phase. Thereafter, he will receive 4 months of treatment during the continuation phase.

EVALUATION

This case demonstrates that there is no simple answer to the question in the title of this article. Several different treatment strategies were proposed in line with the experience and opinion of the specialists concerned. After weighing all the options, the physician chose to treat with a full course of antituberculous therapy. It is possible, however, that the other proposed therapeutic strategies might also have led to satisfactory results. Similar cases should be evaluated individually, taking into account the incidence of Buruli ulcer, TB and MDR-TB in the region as well as the clinical evidence for either Buruli ulcer or cutaneous TB.

BACKGROUND: BURULI ULCER

A Buruli ulcer is a skin infection caused by Mycobacterium ulcerans.[4] Following tuberculosis and leprosy, it is the third most common mycobacterial infection worldwide.[5] It occurs mainly in humid, rural and tropical areas where access to health care is limited. Transmission is thought to occur through contaminated water, involving skin trauma or transmission via aquatic insects.[4]

CLINICAL MANIFESTATIONS AND DIAGNOSIS

The classic initial manifestation of a Buruli ulcer is a painless nodule, papule or plaque of less than 5 cm in diameter. After several days to weeks, this primary lesion forms an ulcer. Typically, the ulcer is painless, with undermined edges and slow progression.[5] A Buruli ulcer is most frequently located on the limbs. Systemic symptoms can be found in the occurrence of secondary bacterial infections. Infection can progress to deeper tissues (tendons, bones) and can spread contiguously or haematogenously.

TREATMENT

In up to 33% of patients, spontaneous healing occurs, although this can take months and may lead to scarring, retraction and contractions, thereby giving rise to functional disability. Treatment consists of systemic antibiotic therapy, most commonly consisting of rifampicin (10 mg/kg orally 1dd) and streptomycin (15 mg/kg IM 1dd), during 4 to 8 weeks (depending on the size of the ulcer).[4,6] Drug therapy can be complemented by surgical debridement. Prevention consists of limiting exposure to contaminated water sources.

BACKGROUND: CUTANEOUS TUBERCULOSIS

Cutaneous tuberculosis is rare and accounts for less than 1-2% of all tuberculosis cases.[7] There are three different classifications based on pathogenesis: direct inoculation from an exogenous source (e.g. tuberculous chancre), from an endogenous source (e.g. scrofuloderma) and haematogenous tuberculosis (e.g. lupus vulgaris).[8]

CLINICAL FEATURES

The diagnosis of cutaneous TB is difficult, as the clinical features vary greatly. It can present with small warty lesions, papules or plaques, but can also feature

ulcers.[8,9] Compared to Buruli ulcer, the lesion is more likely to be painful and systemic symptoms are found more often. Microbiological confirmation includes PCR and the gold standard of isolating Mycobacterium tuberculosis in culture.[7] However, this can be difficult due to a low bacillary load.[10,11]

TREATMENT

Similar to MOTT (Mycobacterium other than Tuberculosis) infections, cutaneous tuberculosis can resolve spontaneously, leaving a scar. Treatment relies on quadruple therapy as used in pulmonary TB (initial phase of isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin during 2 months, followed by a continuation phase of 4 months with isoniazid and rifampicin).[3,7]

BACKGROUND: DRUG RESISTANT TB

There are two different types of drug resistant TB. Multi-drug resistant (MDR) TB is resistant to both of the first line drugs, isoniazid and rifampicin. Extensively drug-resistant (XDR) TB-strains have an additional resistance to fluoroquinolones and second-line injectable agents (amikacin, capreomycin, kanamycin).[12,13] Of all new cases of TB worldwide, 3.3% are MDR-TB. In patients who have previously received tuberculostatic drugs, this proportion is even higher (20%).[12]

Causes of multidrug resistance include higher bacillary load, drug shortages, inappropriate drug levels, poor compliance (due to behavioural pattern or side effects) and malabsorption of medication due to associated diarrhoea.

Diagnosis of MDR-TB is difficult, and the majority of cases is not correctly identified.[12,13] Laboratory facilities for TB culture and drug susceptibility testing are limited. Extrapulmonary (including cutaneous) TB is paucibacillary and therefore difficult to recover on culture.[10,11] The pitfall is that a lack of therapeutic response in MDR-TB can be regarded as suggestive of an alternative diagnosis.[11] Better diagnostics for rapid, reliable diagnosis of MDR-TB are necessary, as earlier diagnosis will lead to more effective treatment. Currently, both GeneXpert MTB/RIF (Xpert) and Genotype MTBDRplus (DRplus) have been endorsed by WHO for rapid diagnosis of MDR-TB using molecular techniques.[14,15] The former has high sensitivity and specificity and can be carried out in 2 hours.

Treatment consists of at least five drugs during an 8-month intensive phase, followed by a continuation phase of four oral drugs for a total minimal duration of 20 months.[13] Challenges include prolonged hospitalization, nephro- and ototoxicity and poor treatment adherence. Furthermore, treatment for MDR-TB and XDR-TB is 25 times more expensive and takes three times longer than for drug susceptible TB.[12] New advances in treatment strategies include the development of vaccines.

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NVTG

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