# The neglect of kwashiorkor

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Kwashiorkor is a syndrome of severe acute malnutrition in children. Its distribution was once global, but most cases are now found in sub-Saharan Africa. Globally, kwashiorkor is estimated to affect hundreds of thousands of children each year.[1] Whereas marasmus is defined by severe wasting (ie, weight-for-height Z score <–3), kwashiorkor is a syndrome of oedematous malnutrition, with an array of accompanying symptoms, including skin breakdown, gut barrier dysfunction, and increased risk for sepsis. Survivors face long-term complications, including impaired neurocognitive develoment, which is associated with lower academic performance[2] and reduced economic achievement in adulthood. Kwashiorkor perpetuates cycles of poverty and has a broad impact on human health and development. Yet kwashiorkor is often overlooked.

The burden of kwashiorkor is often downplayed or ignored completely in global nutritional health policy statements. For instance, the most recent Global Nutrition Report refers to wasting 36 times without any mention of nutritional oedema or kwashiorkor.[3] Kwashiorkor was also omitted from an influential Series on maternal and child nutrition and is similarly neglected by research institutions. Organisations known for sponsoring innovative nutritional research do not fund studies focused on kwashiorkor. This neglect has several root causes.

First, the epidemiology is uncertain. Detecting cases can be challenging. Kwashiorkor is diagnosed by the presence of bilateral pitting pedal oedema, and although severe oedema is easy to detect, mild oedema is often missed. A focused examination of the feet is necessary for reliable detection of kwashiorkor, yet the importance of screening for pedal oedema is often de-emphasised in screening guidelines and clinical practice. One of the reasons is the notion that kwashiorkor rarely occurs without wasting. Screening for wasting alone is often assumed to be adequate. This is not a safe bet. A 2015 study[4] of records from 668 975 children showed that only 34% of children with kwashiorkor had clinical wasting at diagnosis (ie, weight-for-height Z score <–2), and only 14% had severe wasting. Inadequate screening for oedema limits the detection of kwashiorkor.

Kwashiorkor's short duration poses added challenges. Children tend to die or recover within weeks, so cases occurring between surveys go uncounted. Another challenge is the syndrome's spotty distribution. In Ethiopia, for instance, marasmus predominates in the north and east, whereas in the southwest, more than 60% of children hospitalised with malnutrition have kwashiorkor. Kwashiorkor's spatial heterogeneity is also affected by conflict and weather disasters. In Niger, the burden is higher in the Zinder and Maradi regions, which are affected by drought and an influx of refugees fleeing regional conflicts. The factors that make kwashiorkor more common also tend to make surveillance more difficult. Most cases go unreported. Consequently, incidence can only be estimated from a limited number of cross-sectional surveys.

The often-shifting vernacular of malnutrition also hinders epidemiological precision. In 2007, the term severe acute malnutrition (SAM) came into wide use. This disease category includes both kwashiorkor and marasmus—oedematous malnutrition and severe wasting. Use of SAM is helpful because it streamlines the management of kwashiorkor and marasmus, which still share the same treatments. Yet epidemiological precision is lost when lumping together separate conditions of SAM without disambiguation. The recent proliferation of wasting as a catch-all substitute for SAM in certain policy statements runs similar risks.[5] The notion that wasting should now include kwashiorkor ignores current WHO definitions,[6] and the fact that most clinicians who treat malnutrition understand wasting to mean weight loss, and not the characteristic oedema of kwashiorkor. Changes to the vocabulary of malnutrition that are not consultative, coordinated, and necessary will cause confusion.

Although knowledge of kwashiorkor's epidemiology is imprecise, its effects are substantial. In 2016, an analysis of 2277 nutritional surveys from 55 countries (mostly in sub-Saharan Africa) identified 6 996 cases of kwashiorkor among 1·7 million children—roughly one in every 250 children surveyed.[1] Improved treatments and community-based management programmes have improved survival in many settings. However, reported mortality still varies widely, sometimes exceeding 40%, due to variable access to and use of effective treatments, complications such as diarrhoea, and the need for hospitalisation.[7] The total number of children who die

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from kwashiorkor is uncertain. Conservative estimates suggest kwashiorkor kills at least tens of thousands of children each year (Myatt M, Brixton Health, personal communication).

Two priorities for innovation stand out. Current treatments for kwashiorkor are not tailored to correct the syndrome's unique underlying metabolic disturbances. This deficiency is especially relevant for children who require inpatient care. In a recent multicentre trial,[8] the presence of kwashiorkor was associated with a two-fold increase in mortality among children hospitalised with malnutrition. Better stabilising treatments that target kwashiorkor's underlying disturbances may save lives. There is also a need for nutrient fortification regimens for the prevention of kwashiorkor. Filling in these gaps will require a better understanding of the nutritional deficiencies that cause kwashiorkor.

Kwashiorkor is not just oedema but a syndrome of malnutrition that is marked by fatty liver of undernutrition, increased gut permeability, and systemic one-carbon metabolism dysfunction.[9] This pattern of injury closely resembles the effects of one-carbon nutrient deficient diets in pre-clinical models. Such pathology overlap suggests that kwashiorkor is a syndrome of one-carbon dysfunction caused by specific one-carbon nutrient deficiencies. Whether kwashiorkor can be prevented and treated more effectively using interventions fortified with one-carbon nutrients, such as methionine and choline, remains to be seen.

In many aspects, kwashiorkor has been orphaned. It is now often forgotten by policy makers and institutions. In this regard, it resembles conditions recognised by WHO as neglected tropical diseases.[10] The shape of kwashiorkor's neglect is circular. It is ignored by policy makers because its epidemiology is uncertain. Scientists and institutions neglect the problem as there is no demand from policy makers. This cycle of neglect hinders the development of better treatments and prevention strategies. Change is possible, however. Including kwashiorkor in policy statements will help. More importantly, there is a pressing need for clinical trials to test new strategies for the prevention and treatment this often deadly syndrome. This work has the potential to save the lives of hundreds of thousands of children during the coming years.

We declare no competing interests.

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