

## **Letter to the Editor**

### **Aetiology of Kwashiorkor then and now – still the Deposed Child?**

**Dear Editor:**

Kwashiorkor, described by Cecily Williams in 1933 as the disease of the child “deposed” from breastfeeding, still poses an enigma to scientists today as it did then. Almost nine decades after it was described, there has been a decline in prevalence in some parts of the world, but it remains prevalent in other parts, especially in East Africa where it is reported to be more common than marasmus (1). Changes in the nomenclature and current treatment modalities make it seem as if the two conditions are the same, though distinct pathophysiological differences exist between the two conditions (2). Kwashiorkor is a multisystem disease, characterised by oedema and multiorgan dysfunction resulting from the body's inability to maintain cell membrane integrity, leading to potassium and water loss from all categories of cells. It is associated with consumption of monotonous diets, consisting mainly of maize, cassava and rice (3). Pathological changes such as deposition of fat in the liver, villous atrophy and anaemia have been observed. However, the primary aetiology is largely unknown at this time, but the search goes on.

Several factors are implicated in the aetiology of kwashiorkor, though many have been disputed. These include prolonged breast feeding, inadequate protein intake, hypoalbuminemia, intoxication from aflatoxins, excessive oxidant stress and measles infection. (3) More recent animal studies have shown that hepatic steatosis or the fatty liver changes in kwashiorkor can be prevented by feeding mice with a maize vegetable diet supplemented with choline, suggesting that choline insufficiency maybe a contributory factor (4). Others have observed DNA hypomethylation and linked this to the slow turnover of 1-carbon cycle metabolites such as methionine (5). An increased proportion of proteobacteria and more frequent cultures of fusobacterium from gut microbiota have been found in Kwashiorkor compared to marasmus, supporting hypothesis that gut microbiota produce toxins that cause the cell damage. (6) Studies have shown low levels of antioxidants such as beta carotene in diets of these children (7).

One hypothesis that remains difficult to discard is the role of inadequate protein intake and hypoalbuminemia in the aetiology. Sumba in his narrative on “The Rise and Fall of Protein Malnutrition” provides a succinct historical account of global efforts made in the past to support this theory, close the protein gap and the controversies that ensued. It is striking to note that today, stunting which is a milder form of malnutrition that affects millions of children globally, and considered by some to be a pre-morbid state of kwashiorkor has been linked to inadequate protein intake with correctional efforts aimed at improving protein intake [8]. So perhaps it is time to reconsider the role of protein or its components in the aetiology of Kwashiorkor.

Thus, although significant progress has been made since Dr Cecily William's description of

Kwashiorkor in 1933, the aetiology remains elusive, probably because there are several causal factors using different pathways or influencing a common pathway. Current advances in medicine and genetic sequencing, more than ever, provide a unique opportunity to investigate proposed hypotheses, resolve controversies and discover new concepts about undernutrition and disease conditions associated with kwashiorkor and marasmus.

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