Reflections on pellagra, the then and the now

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Abstract. By the mid-20th century, pellagra had virtually been eradicated from the USA and Europe. In contrast, outbreaks of pellagra, as diagnosed by skin lesions, today still occur in sub-Saharan Africa. We argue that outbreaks of pellagra in sub-Saharan regions are not only maintained by food insecurity, but that it is further aggravated by the burden of communicable diseases and excessive alcohol consumption. In addition, we argue from a historical point of view, that the prevalence of pellagra is underestimated when based only on dermatological symptoms.

Key words: niacin-deficiency, nutritional disorder

Pellagra is a nutrition-deficiency disease characterised by dermatological, gastrointestinal, and neuropsychiatric manifestations. The term 'pellagra' is derived from the Italian 'pelle agra' meaning sour or rough skin, and skin lesions, typical for the disease, are major diagnostic criteria. Pellagra is caused by deficiency of niacin and/or tryptophan, the precursor for *de novo* synthesis of niacin. Niacin (vitamin B3) is the precursor of NAD, the indispensable co-enzyme required for cellular energy production, cellular repair, and defence, and for genomic stability (1). The symptoms of pellagra were first documented in 1735 in poor peasants of the Asturian region of Spain. By the second half of the 19th century, it had been reported throughout Europe. In the USA, although suspected to have already been present after the Civil War, it was officially first recorded in 1902 (1). By the mid-20th century, pellagra appeared to have been eradicated in large parts of the world. This decline in the prevalence coincided with improvements in the socio-economic conditions and nutritional status of workers, recognition of pellagra as a nutrition-deficiency disease, and later, with food enrichment programmes (1).

In sub-Saharan Africa ambiguity exists about the historical prevalence of pellagra, but it is clear that eradication of the disease lags behind that in Europe and the USA.

The first quantitative documentation of pellagra in South Africa dates back to 1906 when 150 political prisoners were diagnosed with the disease. The prevalence peaked around mid-century, when pellagra was all but eradicated in Europe and the USA, reaching near-eradication only towards the end of the 20th century. However, it is noteworthy that urine analysis, during the second half of the 20th century, showed subclinical niacin deficiency in disadvantaged sectors of the South African population, implying the presence of latent pellagra (2). In Lesotho the first cases were officially recorded in 1907, with the prevalence peaking around 1963 (3). Outbreaks of pellagra have since 1988 been recorded in Angola, Ethiopia, Malawi, Eswatini (Swaziland), Zimbabwe and the DRC, primarily in food aid-dependent populations such as refugees, internally displaced people, refugee returnee populations and in communities surrounding refugee camps (4). Outbreaks of pellagra have been reported as recently as 2015/2016 in food insecure communities of general sub-Saharan populations (5,6). Diagnosis of pellagra in sub-Saharan areas are generally based on the typical skin lesions associate with the disease.

This is in contrast with Europe, the USA and Egypt where much attention was given to the neuropsychiatric symptoms and where special hospitals existed for mentally-ill pellagrins (1).

Although pellagra is primarily a nutritional deficiency disorder associated with food insecurity, a number of conditions and drugs can negatively impact on niacin, and by implication, NAD levels (1). Two concerns are of specific relevance to pellagra in sub-Saharan Africa, i.e., alcohol and tuberculosis. Excessive alcohol consumption can cause pellagra by inducing malnutrition and by inhibiting the conversion of tryptophan to niacin (2). Alcohol has previously been implicated in the prevalence of pellagra in sub-Saharan Africa (2), and according to the WHO, the region is still faced with a growing burden of harmful alcohol consumption. The burden of tuberculosis is also increasing in Africa, partially as a result of the link between tuberculosis and HIV/AIDS (6). Isoniazid, an antibiotic used for the treatment of active, as well as latent, tuberculosis, interferes with the conversion of tryptophan to niacin and several authors have reported pellagra symptoms in patients treated with isoniazid (2). This potential of isoniazid to contribute to the development of pellagra, especially in nutritionally vulnerable populations, has recently (2022) again been confirmed by the results of a study performed during mass scale-up of isoniazid tuberculosis preventive therapy in Malawi (6).

In view of the ever-escalating food insecurity, it is feasible to surmise that outbreaks of pellagra, latent or overt, may continue to occur in sub-Saharan regions and that the situation could be compounded by the growing burden of communicable diseases such as tuberculosis, as well as by excessive alcohol consumption. In contrast to earlier, pellagra is today diagnosed primarily on its dermatological symptoms, generally disregarding a potential subclinical deficiency, as well as neuropsychiatric and gastrointestinal symptoms not accompanied by overt dermatological lesions.

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