Understanding of the aetiology and pathophysiology of kwashiorkor, Madarounfa, Maradi, Niger

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Study summary

Kwashiorkor is a major public health problem in many parts of the world. While the primary cause of severe acute malnutrition (SAM), of which kwashiorkor is a specific expression, is the lack of sufficient food intake, the specific aetiology of kwashiorkor remains elusive despite well-designed studies over the last decades. Unfortunately, none of the hypotheses suggested so far (including insufficient protein or specific amino-acids intake, dysadaptation to a low protein high carbohydrate diet, disruption of sulphated glycosaminoglycans, kidney dysfunction, aflatoxins, or oxidative stress) appeared convincing enough to enable an improvement in kwashiorkor prevention or in its clinical management

Several recently developed biochemical technologies offer the possibility to provide a better and more coherent understanding of the aetiological and pathogenic pathways underlying kwashiorkor. This has the potential to open doors for developing effective prevention strategies, improving management and treatment, and reducing mortality. This study aims to "go back to the drawing board" with these new technologies and perspectives to shed more light into the pathogenesis of kwashiorkor.

A matched case-control study design will be implemented in Madarounfa, Maradi, Niger. Children aged 6 to 59 months with kwashiorkor (n=60, with varying levels of oedema), marasmus (n=60) and non-malnourished children (n=60) will be recruited at the Madarounfa District Hospital, the ambulatory therapeutic feeding centre (ATFC) and the health center of Madarounfa. Study participation will involve clinical and biological sample (blood, urine, faeces) collection at one to three timed intervals from admission to recovery (Table).

	Nutrition status	Inclusion			Transfer from hospital to ATFC	Discharge from ATFC or from hospital
		Blood	Faeces	Urine	Blood	Blood
Health center ATFC	Non-malnourished	2mL	1g	10mL		
	SAM (Kwashiorkor or marasmus)	2mL	1g	10mL		2mL
District hospital	Non-malnourished	2mL	1g	10mL		2mL
	SAM (Kwashiorkor or marasmus)	2mL	1g	10mL	2mL	2mL

Blood, urine and faeces samples will be shipped to Belgium where they will be subjected to metabolomics, metagenomics, and proteomics analysis in order to determine biochemical markers and microbial genetic factors that could potentially distinguish kwashiorkor from marasmus and children without malnutrition. Further, the role of the renin-angiotensin system will be re-evaluated by comparing the urinary sodium/potassium ratio and urine protein content in kwashiorkor versus marasmus and non-malnourished controls. Moreover, the role of a new metabolic target, the farnesoid X receptor, will be explored with respect to the aetiology of kwashiorkor

Lastly, results from all approaches will be examined and integrated to ensure that the results are both physiologically and clinically relevant.

Hence, it is hoped that the results of this project will increase our understanding of the pathophysiology of kwashiorkor and, in so doing, will provide further hypotheses showing the way for the development of effective solutions for high burden kwashiorkor populations.