ARE THE SKIN LESIONS OF KWASHIORKOR PELLAGROUS?*

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During the 1940s kwashiorkor was known in most of Africa as infantile pellagra,[1] though Cicely Williams, who first described the disease,[2] thought the skin lesions were not pellagrous because they did not affect areas exposed to light. Subsequently it was found that skin lesions are not an essential feature of kwashiorkor,[3] but that they could be cured, with the other manifestations of the disease, by vitamin-free casein[4] or a mixture of pure amino acids.[5] Since then the pendulum of interest has swung away from the dermatosis of kwashiorkor. It is still uncertain whether this skin lesion is pellagrous or not.[6]

Two further facts prompted us to re-examine this question. First, in experimental pellagra in adults who stayed indoors, the face and hands were often not affected.[7] Secondly, both casein and a mixture of essential acids contain tryptophan, which is partly converted to nicotinamide in the body.[8]

The biochemical index of nicotinamide nutrition is the amount of N'-methylnicotinamide (NMN) and of its 2-pyridone excreted in the urine. The only published figures of urinary NMN in kwashiorkor[9] ranged down to levels that appear low. But no definite conclusions can be drawn because there were no controls.

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We have studied 25 children with kwashiorkor. Their skin lesions were graded severe, intermediate, or minimal by 2 observers independently. Urine was collected during the first 3 days after admission, while the children were given milk diets with a methionine supplement. All received penicillin and sulphadiazine as antibacterial treatment. Vitamin preparations were withheld, and children known to have had them shortly before admission were excluded. The 15 controls were children of the same age. Some were normal, but most had recently recovered from kwashiorkor. Any that had been treated with vitamin preparations were taken off this treatment 3 - 7 days before the 3-day urine collection. Some controls were given the standard hospital mixed diet, others were given milk and cereal only. NMN[10] and pyridone[11] were measured in the urines.

The kwashiorkor patients had a mean NMN excretion of 0·66 mg. per day (range 0·24 - 1·43 mg. per day). This was significantly less than the control range of 1·14 - 3·31 mg. per day. Pyridone excretion is more sensitive to acute changes in intake[12] and only in one case was there any overlap between kwashiorkor excretions of 0·10 - 1·84 mg. per day and control levels of 1·72 - 11·20 mg. per day.

The subgroup of kwashiorkor patients with severe skin lesions excreted (mean) 0·56 mg. NMN per day. Patients with intermediate skin lesions excreted 0·697, and those with minimal skin involvement 0·694 mg. per day. Mean serum albumins on admission in the 3 groups were 1·78, 1·56 and 2·04 G. per 100 ml. respectively.

An alternative division of the kwashiorkor patients was into those with considerable angular stomatitis and those in whom it was slight or absent. Mean urinary NMN in the former was 0·57 and in the latter 0·76 mg. per day. Although the difference was not significant ($t=1·62$), NMN excretions related more closely to angular stomatitis than did serum albumins which were 1·78 and 1·76 G. per 100 ml. respectively.

There was no correlation between urinary NMN in kwashiorkor and stool weights during the 3-day collection period.

It should be noted that: (*a*) The difference in urinary nicotinamide metabolites between kwashiorkor patients and controls is unlikely to result from the antibacterial therapy given for kwashiorkor. When sulphadiazine and penicillin were given to a control child his NMN excretion did not change. (*b*) The difference between kwashiorkor and controls remains when NMN is expressed per kg. body weight. (*c*) In case the kwashiorkor patients were short of methyl donors for methylation of nicotinamide, they were given a supplement of methionine. (*d*) Pyridoxine and probably riboflavine are co-enzymes for 2 different steps in the pathway from tryptophan to nicotinamide. The possibility that deficiency of these other B vitamins was responsible for the low urinary nicotinamide metabolites in kwashiorkor is being investigated at present by giving pyridoxine plus riboflavine to a further series of patients. The first patient studied on this regime excreted 1·12 mg. of NMN per day. Meanwhile, the fact that pure protein has cured kwashiorkor skin lesions[4,5] suggests that they are not caused by a deficiency of pyridoxine or riboflavine, for, unlike nicotinamide, these vitamins cannot be synthesized from any of the amino acids.

In the kwashiorkor patients, the lower excretions of NMN associated with severe skin lesions and with angular stomatitis suggest that these excretions were pathologically low and not just the result of poor nicotinamide intake for a few days before admission.

Our results appear to be compatible with a pellagrous aetiology of the skin lesions of kwashiorkor. Further, the finding that NMN was lowest in patients with severe dermatosis, while serum albumin was lowest in the subgroup with intermediate skin lesions, would seem to favour slightly nicotinamide deficiency over protein deficiency as a cause of the dermatosis. While agreement between the 2 observers on grading was close, it was difficult to allow for the apparent age of the lesions. Some of them, though extensive, may have been healing at the time they were examined. A second source of scatter in the 3 subgroups is the possibility that one or two patients had been given vitamins shortly before admission. It was not possible to obtain reliable histories from all the mothers.

The present results may explain why the frequency of skin lesions in kwashiorkor varies in different parts of the world and appears to be higher where maize is the staple diet.[13,14]

It must, however, be stressed that the fundamental abnormality in kwashiorkor is protein deficiency. Although skin lesions have cleared on nicotinic acid treatment in mild cases of kwashiorkor,[15] this treatment alone would be very dangerous in most cases[1] because it does nothing to correct the fundamental abnormality. Conversely, the tryptophan contained in a protein-repleting diet is an adequate source of nicotinamide for treating the dermatosis of most patients with kwashiorkor.

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