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Antibodies to *Herpesvirus hominis* types 1 and 2 in malnourished Nigerian children

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SUMMARY Antibodies to *Herpesvirus hominis* (HVH) types 1 and 2 were determined by a micro-neutralisation method in 37 children with kwashiorkor, 16 with marasmus, and in 64 well-nourished control children. All the children were aged between 1 and 4 years. The prevalence of antibodies was similar in the two sexes and at different ages. HVH-1 antibodies were present in 51% of children with kwashiorkor, in 44% with marasmus, and in 26% of well-nourished children, reflecting the very poor socioeconomic conditions of malnourished children. HVH-2 antibodies too were present in about 19% of children with kwashiorkor, and in 2% of well-nourished controls; they were absent in marasmic children. It is suggested that HVH-2 infection in malnourished children is facilitated by the communal use of fomites—such as bedclothes and underwear.

Primary herpetic gingivostomatitis is apparently one of the common infectious diseases of childhood, and young children are often carriers of the virus, saliva and faeces being the main vehicles of transmission.[1] *Herpesvirus hominis* (HVH) infection is generally acquired as a result of close body contact,[2] and serological surveys for presence of neutralising antibody have shown that the infection is widespread particularly among the poor.[3–5] Two antigenic types of HVH have been recognised.[6] Type 2 *Herpesvirus hominis* (HVH-2) most commonly infects the genital tract and is therefore believed to be usually acquired by sexual contact and to be rare in children below the age of puberty.[3,7] Infection with *Herpesvirus hominis* type 1 (HVH-1) is generally nonsexual and lesions are situated in extragenital areas.[7–8] However, herpetic genital lesions do occur occasionally in children[9–10] and both HVH-1 and -2 have been isolated from such lesions in children.[11]

Protein–energy malnutrition predisposes to a variety of infections. Whereas the types and patterns of bacterial infections in malnourished children are well defined,[12–13] nonbacterial infections—such as gingivostomatitis, vulvovaginitis, and vesicular skin eruptions—commonly occur in malnourished children, who almost invariably come from the lower socioeconomic groups. The exact nature of these lesions has mainly been speculative, but such lesions are generally believed to be associated with the avitaminosis and the invasion of the buccal and ano-genital epithelium by normally dormant commensals of these sites, because of the reduced resistance to infection which occurs in malnourished states.

We recently studied the immune status of such children, and report the incidence of antibodies to HVH-1 and -2 in malnourished children compared with control children.

Materials and methods

Patients. 53 malnourished children (aged 1-4 years) attending a children's clinic at University College Hospital, Ibadan, Nigeria were studied. Using the classification of Mukherjee[14] 37 (19 boys and 18 girls) of them had kwashiorkor and 16 (9 girls and 7 boys) had marasmus. 64 (33 boys and 31 girls) well-nourished children, also aged between 1 and 4 years and of similar sex distribution, but who were in hospital for minor surgical procedures—such as release of burns contractures, herniorrhaphies, excision of keloids—served as controls.

Methods

About 5 ml venous blood was drawn from each child and the serum separated and stored at −20°C until it could be tested. The 0·5 ml blood required for the virus studies in the control children was part of blood drawn for preoperative investigations.

The sera were tested for antibody against HVH-1 and -2 by the microneutralisation method described by Sogbetun *et al.*[15]

Table *Incidence of antibodies to Herpesvirus hominis types 1 and 2 in sera from malnourished and control children*

Group	*Positive sera*		*No HVH antibody*
	HVH-1 *No (%)*	*HVH-2* *No (%)*	*No (%)*
Control (n=64)	17 (26)	1 (2)	46 (72)
Marasmus (n=16)	7 (44)		9 (56)
Kwashiorkor (n=37)	19 (51)	7 (19)	11 (30)

Results

The findings did not differ for the two sexes, nor did they differ within each age group (1–4 years), so the results for both sexes have been combined. As shown in the Table, 17 (26%) control children, 7 (44%) marasmic children, and 19 (51%) children with kwashiorkor had neutralising antibodies to HVH-1 while only one (2%) control, no marasmic child, and 7 (19%) children with kwashiorkor had antibodies to HVH-2. Thus the difference in the prevalence of antibodies to both HVH-1 and -2 in control and kwashiorkor groups was significant ($\chi^2_c = 7{\cdot}41$, $P<0{\cdot}01$ and $\chi^2_c = 12{\cdot}2$, $P<0{\cdot}001$). Although more marasmic than control children had HVH-1 antibodies, the difference is not significant ($P>0{\cdot}05$) because there were so few marasmic children.

Discussion

Primary infection by HVH can occur in early childhood and is often subclinical, although it may produce localised vesicular lesions with constitutional disturbance in some children.[16] The infection is acquired by close personal contact[2] such as obtains commonly in children from poor socioeconomic groups in most underdeveloped countries, and among the underpriviledged in developed countries. Thus Becker[4] found the incidence of antibody to HVH to be greater among the Bantus than the coloured population, and least among the white community in Cape Town.

Apart from the socioeconomic status, the distribution of HVH antibodies in any particular community is also related to age. Previous studies on HVH antibodies in lower socioeconomic populations[5 37] showed that at between 0 and 6 months of life, about half the number of infants had HVH antibodies which had been acquired transplacentally. Only a few children aged between 7 and 12 months had detectable antibodies to HVH, but thereafter there was a steady rise so that by age 14 years 50–70% of children had acquired antibodies after an infection which had generally been subclinical. As most genital infections in adults are due to HVH-2,[6–7] infection with HVH-2 is believed to be largely venereal[17] while HVH-1 is not. This is supported by observations that antibodies to HVH-2 only begin to appear after the age of 15 years[18] and are particularly common in the sexually promiscuous.[19] However genital herpetic infections do occur in children[9–10] and both strains of HVH have been implicated in their causation.[11] In poor socioeconomic populations HVH-1 antibodies are soon acquired after the first year of life.[15] The HVH-2 infections in children are believed to be largely nonvenereal and are similarly most likely to occur in conditions of overcrowding and poor personal hygiene.[11 15] A similar sort of setting has been adduced to be responsible for the nonsexual spread of gonococcal vulvovaginitis in young girls in Ibadan, Nigeria.[20] Recent studies by Montefiore *et al.*[21] showed that HVH-2, under humid tropical conditions, can survive sufficiently long on cloth to facilitate transmission of infection by fomites such as shared bed-clothes, towels, or underwear. Communal use of such articles is common in many poor families in tropical Africa, and it is in such households that protein–energy malnutrition is prevalent.

In the present study in the 1–4 year age group, neutralising antibody to HVH-1 was found in 51% of children with kwashiorkor, in 44% of those with marasmus, and in only 26% of fairly well-nourished control children. The equivalent figures for antibody to HVH-2 are 19% in children with kwashiorkor, 2% in control children, and none in those with marasmus. Sogbetun *et al.*[15] in a recent study of children aged between 1 and 5 years obtained similar results, allowing for the slight difference in the age group.

Although it is well known that malnourished children are susceptible to most forms of infection,[22–24] the precise aetiology of many of the epithelial lesions—such as gingivostomatitis, anovulvo vaginitis, and vesicular skin eruptions—which occur commonly in malnourished states has not been conclusively demonstrated. Herpesvirus (simplex) is normally dormant in sensory nerve ganglia and the precise mechanism of reactivation of the virus is unknown. However it is possible that due to depressed immune responses in protein–energy malnutrition,[25] malnourished children become more susceptible to herpesvirus infection. This is likely to give rise to a more severe disease in these children rather than increasing the chances of infection. On the other hand, malnourished children usually come from poor and large families living in overcrowded and unhygienic conditions, and this greatly facilitates the transmission of herpesvirus infections. The findings of this study confirm the increased frequency

of both HVH-1 and -2 infections in kwashiorkor, probably due to living conditions in both instances.

Herpesviruses are known to be associated with neoplasia in animals[38] and there is evidence that they may also be associated with human malignancies. HVH-2 has been found in association with cervical carcinoma in adults[18 26 38] and a member of the herpesvirus group has also been found in association with childhood (Burkitt's) lymphoma. The herpesvirus particles in Burkitt's lymphoma are referred to as Epstein-Barr (EB) virus.[27] This lymphoma is the most common malignant tumour in Nigerian children[28–30] and perhaps also in other parts of humid tropical Africa. The tumour is also known to occur in America, Europe, Asia,[31–33] and in the Middle East.[34] High levels of antibodies to EB virus have been reported in Burkitt's lymphoma.[35] In a recent review of 133 cases of Burkitt's lymphoma in Nigerian children at Ibadan, Aderele and Antia[36] showed that this tumour occurred almost exclusively in children from families of low socioeconomic groups. Such children are generally malnourished. Thus it would appear that the circumstances which promote the development of malnutrition predispose to infection by herpesviruses, and that infection by certain of these viruses may predispose to neoplastic changes in malnourished children although other factors have also been considered in the pathogenesis of childhood lymphomas. The epidemiological significance of these findings should continue to generate much interest for further work in these areas.

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