The question remains as to whether a higher dose of acyclovir more effectively prevents or modifies the clinical course of the disease in the first group than that observed in the present study.

1 Gershon AA, LaRussa P. Varicella-zoster virus infections. In: Krugman S, Katz SL, Gershon AA, Wilfert CM, eds. *Infectious diseases of children.* 9th Ed. St Louis, Missouri: CV Mosby, 1992: 587–614.
2 Ross AH. Modification of chicken pox in family contacts by administration of gamma globulin. *N Engl J Med* 1962; **267:** 369–76.
3 Asano Y, Albrecht P, Behr DE, Neff BJ, Vickers JH, Rastogi SC. Immunogenicity of wild and attenuated varicella-zoster virus strains in rhesus monkeys. *J Med Virol* 1984; **14:** 305–12.
4 Asano Y, Takahashi M. Studies of neutralization of varicella-zoster virus and serological follow-up of cases of varicella and zoster. *Biken Journal* 1978; **21:** 15–23.
5 Grose C. Variation on a theme by Fenner: the pathogenesis of chickenpox. *Pediatrics* 1981; **68:** 735–7.
6 Ozaki T, Ichikawa T, Matsui Y, *et al.* Viremic phase in non-immunocompromised children with varicella. *J Pediatr* 1984; **104:** 85–7.
7 Asano Y, Itakura N, Hiroishi Y, *et al.* Viremia is present in incubation period in nonimmunocompromised children with varicella. *J Pediatr* 1985; **106:** 69–71.
8 Asano Y, Itakura N, Hiroishi Y, *et al.* Viral replication and immunologic responses in children naturally infected with varicella-zoster virus and in varicella vaccine recipients. *J Infect Dis* 1985; **152:** 863–8.
9 Balfour HH, Kelly JM, Suarez CS, *et al.* Acyclovir treatment of varicella in otherwise healthy children. *J Pediatr* 1990; **116:** 633–9.
10 Dunkle LM, Arvin AM, Whitley RJ, *et al.* A controlled trial of acyclovir for chickenpox in normal children. *N Engl J Med* 1991; **325:** 1539–44.
11 Asano Y, Toshikawa T, Suga S, *et al.* Post-exposure prophylaxis of varicella in family contact by oral acyclovir. *Pediatrics* 1993; **92:** 219–22.
12 Asano Y, Albrecht P, Vujcic LK, Quinnan GV Jr, Kawakami K, Takahashi M. Five-year follow-up study of recipients of live varicella vaccine using enhanced neutralization and fluorescent antibody membrane antigen assays. *Pediatrics* 1983; **72:** 291–4.
13 Myers MG, Connelly BL. Animal models of varicella. *J Infect Dis* 1992; **166** (suppl 1): S48–50.
14 Kallander CFR, Gronowitz JS, Olding-Stenkvist E. Varicella zoster virus deoxythymidine kinase is present in serum before the onset of varicella. *Scand J Infect Dis* 1989; **21:** 255–7.

Commentary

Varicella is common, with a 1992 general practitioner consultation rate >600 per 100 000 population. Almost all infected children suffer at least a moderate constitutional illness, but the otherwise normal child will usually have no new lesions after four days and complications are rare. We must ask whether we want to interfere with varicella, an essentially benign illness in normal children. There is a growing pressure to intervene by administration of acyclovir within the first 24 hours of the rash. Balfour *et al* and Dunkle *et al* have shown in three recent publications that 2–18 year olds so treated have less severe disease.[1–3] Their results were statistically impressive but clinically unconvincing, for example 0·5 days less of new lesion formation. Certain patient groups might benefit more, for example the immunosuppressed, adolescents, children with chronic chest disease, and pregnant women. Children exposed to intrafamilial spread of varicella are also susceptible to more severe infection which may respond well to early acyclovir treatment. Varicella is most infectious in its prodrome and secondary cases in the family are not prevented when acyclovir is given to the index case.

The paper by Suga *et al* tries to answer the question whether oral acyclovir can minimise or even prevent secondary infection if given to susceptible family members during the incubation period? (But remember to keep asking, do we want to *prevent* infection in otherwise normal children?)

The small placebo controlled study targeted acyclovir treatment at either the first or second viraemic period. All of the control group developed moderate to severe varicella. The clinical severity and the attack rate (91% in the first group, 27% in the second group) were reduced in both treatment groups. The data raise some important issues which are not discussed. The results are interpreted as showing seroconversion in 11 of 13 in the first group, and in 11 of 14 in the second group. Many would not accept an antibody rise from <4 to 8 (cases 7–10 in the second group) as seroconversion, reducing the number with an antibody response in the second group to seven, only 50%. Without acyclovir at least 85%–90% of susceptible household contacts will contract varicella from the index case. It may be desirable for these children to have a less severe illness (achieved in both treatment groups), but do we want 50% of them to remain susceptible to the virus later in childhood, perhaps even through to adolescence and adulthood when we know they can expect more severe disease? And how will we distinguish those who have had subclinical illness after acyclovir treatment from those who have had no illness at all? Only by serological tests on all children given acyclovir in the presumed incubation period who subsequently failed to show any clinical features of varicella. Realistically such follow up tests are unlikely to be achieved in busy general practice, resulting in potentially dangerous ignorance about the child's varicella status.

I am concerned about the efficacy of the antibody response, significantly greater in the first than the second group. Is it sufficient to prevent (a) reinfection and (b) early zoster? Information so far from children receiving acyclovir for varicella shows an adequate humoral and cellular response. However, the immune response to primary herpes simplex infection may be decreased after treatment with acyclovir, and some may suffer a more intense first herpetic recurrence. Might acyclovir given in the incubation period for varicella increase the problems of zoster? Suga *et al* seem to suggest in their discussion that we should find a higher dose to prevent more effectively clinical illness. Perhaps we should rather try to realise a dose that would allow mild clinical illness (we would know that the child had had varicella), and produce an effective and lasting antibody response, or simply treat the secondary family case promptly as recommended by Balfour *et al* and Dunkle *et al.*

Importantly, trials to date have shown acyclovir to be safe. The paper by Suga *et al* is another step in the study of the proper role of acyclovir in the treatment and prevention of varicella, but raises more questions than it answers. Further studies are awaited with interest. But if we want to prevent and/or minimise clinical varicella in high risk children (and normal children?), should we not concen-

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trate on protecting all children by active immunisation, that is by vaccination?

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1 Balfour HH, Kelly JM, Suarez CS, *et al.* Acyclovir treatment of varicella in otherwise healthy children. *J Pediatr* 1990; **116:** 633–9.
2 Balfour HH, Rotbart HA, Feldman S, *et al.* Acyclovir treatment of varicella in otherwise healthy adolescents. *J Pediatr* 1992; **120:** 627–33.
3 Dunkle LM, Arvin AM, Whitley RJ, *et al.* A controlled trial of acyclovir for chickenpox in normal children. *N Engl J Med* 1991; **325:** 1539–44.

Maternal diet and medulloblastoma

It has been suggested that the occurrence of some brain tumours in children might be related to the mother's exposure to certain substances especially nitrosamines and other N-nitroso compounds in the diet. A recent paper from America (Greta R Bunin and colleagues, *New England Journal of Medicine* 1993; **329:** 536–41) does not support the nitrosamine hypothesis but points to several possible dietary factors.

This case-control study concerns children under 6 years of age with primitive neuroectodermal brain tumours 90% of which were medulloblastomas. Both case and control parents were subjected to lengthy telephone interviews. Maternal dietary factors that appeared to be associated with a reduced risk were: fruits and fruit juices (odds ratio 0·28, p=0·003), vitamin A (0·59, 0·03), vitamin C (0·42, 0·009), nitrate (0·44, 0·002), and folate (0·38, 0·005). Certain supplements taken during pregnancy were also associated with decreased risk: iron (odds ratio 0·43, p=0·004), calcium (0·42, 0·05), vitamin C (0·35, 0·04), and multivitamins during first six weeks of pregnancy (0·56, 0·02).

The protective effects of folate and of early pregnancy multivitamins did not apply to the mothers of children who had astrocytomas whereas most of the other food factors appeared to protect against each tumour type. The authors suggest that this means that recall bias is an unlikely explanation in the case of folate and multivitamins but could have affected the results as regards the other food factors. They also point to the obvious and interesting fact that folate and multivitamins are the very factors that have been shown to be protective against neural tube defects and are not slow to suggest that primitive neuroectodermal tumours and neural tube defects may not be, biologically speaking, a thousand miles apart. It would not be too difficult to question the telephone methodology but the results are certainly interesting. Will anybody be able to organise a big enough prospective interventional study along the lines of the neural tube defect studies?

I've got mixed feelings about telephone surveys. Everybody could get onto the bandwagon. If this sort of thing catches on we'll never again be safe in the bath. I never thought anything would induce me to buy an answering machine, but now I don't know.

ARCHIVIST

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