

# SHORT REPORTS

## Possible treatment for cold sores

Boric acid has long been known to have feeble bacteriostatic properties and is widely used as a mild disinfectant. We were most interested when one of our patients reported that her recurring vulval herpes infection responded to locally applied boric acid. We report here an investigation of the effect of sodium borate on the replication of herpes simplex virus, and the results of a preliminary trial using boric acid to treat cold sores.

### Patients, methods, and results

Subconfluent monolayers of baby hamster kidney cells (BHK 21 cells)<sup>1</sup> prepared in 5-cm-diameter disposable plastic Petri dishes were infected with either type 1 (HF strain) or type 2 (3345 strain)<sup>2</sup> herpes simplex virus at a multiplicity of one plaque-forming unit per cell. They were then incubated for 24 hours at 37°C in 4 ml of medium containing the required concentration of sodium borate. The virus yields from infected cultures were titrated by Russel's plaque method.<sup>3</sup> Sodium borate concentrations of 20 mmol/l (762.8 mg/100 ml) or greater completely inhibited virus replication, and no virus cytopathic effects (CPE) were seen (table). A concentration of

*Replication of herpes simplex virus in medium containing varying concentrations of sodium borate*

Sodium borate concentration (mmol/l)	Virus yield (plaque-forming unit per cell)	
	Type 1 herpes virus	Type 2 herpes virus
0	5.1	1.1
0.45	3.6	0.68
0.90	2.6	0.60
1.90	1.4	0.52
3.80	0.5	0.26
7.50	0.01	0.07
15.00	<0.001	<0.001
30.00	<0.001	<0.001

Conversion: SI to traditional units—Sodium borate: 1 mmol/l  $\approx$  38.1 mg/100 ml.

10 mmol/l (381.4 mg/100 ml) permitted some replication and minimal CPE. Lower concentrations permitted more replication and corresponding CPE until at a concentration of 1 mmol/l (38.1 mg/100 ml) replication and CPE were the same as for the controls. Uninfected BHK cells survive for 72 hours in sodium borate concentrations of 25 mmol/l (1143 mg/100 ml) and replicate normally after reincubation in borate-free medium; the cells will also replicate in concentrations of 4 mmol/l (146 mg/100 ml).

In the double-blind trial we studied patients with typical herpetic cold sores who were attending a general practitioner's surgery in Cannock. Eleven patients received the placebo (four men, seven women; eight in social classes III and IV; average age 29) and 14 the boric acid ointment (eight men, six women; nine in social class III; average age 37). There was no significant difference in the frequency of previous cold sores or in the duration of the cold sores before treatment. The patients were asked to apply either paraffin ointment containing 4% boric acid or paraffin ointment alone four times daily for five days. After one week they were asked whether they thought the ointment had helped and how long the cold sore had lasted. Of the 14 who received the boric acid, 13 thought it had helped, whereas only three of the 11 in the placebo group thought the ointment had helped. The duration of the cold sore was  $4.1 \pm \text{SE}$  of mean 0.61 days in the treatment group and  $5.9 \pm 0.96$  days in the placebo group. As two patients were considered to be highly unreliable historians their answers were discarded. No adverse effects were reported.

### Comment

Borate salts clearly inhibit replication and cytopathic effects of herpes simplex virus, but the mechanism is not clear. The inhibition may be entirely a consequence of cessation of intracellular macromolecular activity, which is supported by the fact that borate concentrations of 25 mmol/l (1143 mg/100 ml) or more also inhibit both virus- and cell-protein synthesis (interestingly, this effect seems to be reversible). This effect on macromolecular function may preclude using borates as systemic antiviral agents but should not preclude topical usage.

The results of our preliminary trial may encourage further investigation of the use of borates as a local antiherpetic agent. It

may be possible to use higher concentrations of boric acid, as Cope did in treating burns without adverse effects.<sup>4</sup> Isolated reports exist, however, of boric acid intoxication, although usually after large doses.<sup>5</sup> We limited our patients' total prescription to 1 g of boric acid. We are now starting a more extensive trial of borates in treating recurrent oropharyngeal and genital herpetic infections.

We thank the patients in Cannock who kindly co-operated in this trial. The boric acid and placebo ointments were provided by the pharmacy, Queen Elizabeth Hospital, Birmingham.

<sup>1</sup> McPherson, I, and Stoker, M, *Virology*, 1962, **16**, 147.

<sup>2</sup> Geder, L, and Skinner, G R B, *Journal of General Virology*, 1971, **12**, 179.

<sup>3</sup> Russel, W C, *Nature*, 1962, **195**, 1028.

<sup>4</sup> Cope, O, *New England Journal of Medicine*, 1943, **229**, 138.

<sup>5</sup> Kingsma, H, *Canadian Medical Association Journal*, 1958, **78**, 620.

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## Sclerosant treatment for hydroceles and epididymal cysts

Chemical obliteration of scrotal cysts has been used for centuries.<sup>1-3</sup> The procedure has never been enthusiastically endorsed, but when Moloney<sup>4</sup> reported excellent results from injecting phenol its reappraisal seemed worth while.

### Materials, methods, and results

Thirty-four patients were treated, of whom 20 had hydroceles (bilateral in three) and 14 epididymal cysts (bilateral in two and unilaterally multiple in three). We used two sclerosants—namely, phenol (Moloney's preparation<sup>4</sup>) and tetradecyl sulphate (STD, Pharmaceutical Research)—and followed Moloney's technique. The volume injected depended on sac size, but not more than 15 ml was instilled at one time. The average size of hydrocele was 450 ml, and epididymal cyst 200 ml; the smallest lesion treated was 5 ml, and the largest 1500 ml. The sclerosant dosage followed Moloney's usage, being mostly in the range from one part for every five aspirated in small sacs to one part for every 60 in large ones.

The patients were seen monthly, when reaccumulated fluid was tapped; if light in colour more sclerosant was added, and if dark none was necessary. The final assessment was originally planned for three months after the end of treatment, but when recurrences were found to take longer to appear the patients were recalled a year or more later. At that review 25 patients were seen in the outpatient clinic, six had replied to a questionnaire, and three were lost to follow-up (two had died).

**Hydroceles**—Ten hydroceles (in eight patients) were apparently cured (50% of the total treated in patients available for review). Two of these patients, however, had required an operation for complications of the injection. Of the 13 other treated hydroceles, 10 were seen in the clinic to have recurred (six were later excised) and three were in patients lost to follow-up. One of these had also needed surgical attention for an injection complication.

**Epididymal cysts**—Five epididymal cysts (31% of the 16 treated) may have been cured. Proof of cure in two cases, however, depended on the patients' own evidence by letter, and two other patients were noted in the clinic to have a small mass in the epididymis. The other 11 showed moderate or complete recurrence, and four were later excised.

**Complications**—Four patients had surgical complications. In two a large, hard mass developed, in one due to thick, concentric layers of fibrin, and in the other due to old clot. Both settled completely after debridement. In the other two patients the lesions became infected. One settled with drainage, but the other eventually required orchidectomy for a persistently discharging fibrotic empyemic mass. Comparing complicated and uncomplicated cases showed no differences in the treatment regimen employed. Both cases of infection, however, occurred in patients with large hydroceles (1200 and 1050 ml).