ATTEMPTED CHICKENPOX PROPHYLAXIS WITH VIRUGON IN CONTACTS

ROBERT BRUCE, M.D., B.S.
Chester le Street

ATTEMPTS TO FIND A CHEMOTHERAPEUTIC agent with activity against viral infections resulted in the development of virugon (N', N'-anhydrobis-(β-hydroxyethyl) biguanide HCl). Initial experiments revealed low toxicity and some evidence of antiviral activity. In mice the drug displayed a protective effect against PR8 influenza virus infections (Rhodes and Herlocher 1960). Similarly a protective effect was obtained against measles virus infections in hamsters (Drake, Burnstein, Sawchuck and Farquar 1960) and against experimental herpetic keratitis in rabbits (Renard and Dhermy 1960). A trial carried out in Sweden (Zetterberg, Heller, Gustafson and Ringertz 1960) using virugon in the mass prophylaxis of soldiers revealed an approximately 39 per cent protection rate against an outbreak of influenza A2. A small trial in this country by general practitioners revealed that cases of chickenpox seemed to pursue a shortened course with second crops of vesicles being either aborted or attenuated (Wheatley 1960). On the other hand, a trial using virugon in cases of herpes zoster failed to show any beneficial effect due to the drug (GP Clinical Trials 1965). It was felt, in the case of this last trial, that the efficacy of virugon may be dependent upon early administration.

In view of the above favourable experimental and clinical evidence a small trial was planned in an attempt to assess any prophylactic effect virugon might have when given to *contacts* of cases of chickenpox. Administration to contacts it was felt, would to some extent eliminate the criticism of administration of the drug being too late to be of value. The use of the drug throughout the incubation period of chickenpox in contacts of known cases would ensure reasonably early administration..

Method of trial

The drug was given to family contacts on a double-blind basis.

The drug was made up in two strengths—one of 200 mg. and the other of 400 mg. labelled A and B respectively.

The 200 mg. (A) dose was used for children under the age of 5 years.

The 400 mg. (B) dose was used for those aged 5 years and over.

One tablet was given twice daily. Thus children under 5 years received 400 mg. daily, children over 5 years received 800 mg. daily.

Placebo tablets and the virugon tablets were randomized 1–50 in both A and

B groups, the bottles being labelled A1, A2, A3—B1, B2, B3, etc. Each bottle contained 42 tablets so that a three-week course was obtained from each bottle. The code of bottle numbers was unseen by the author and unopened until the end of the trial.

Clinical notes were kept as to patient's age, number of contacts, ages of contacts and whether chickenpox was contracted within the three-week period.

Visits were made during the three-week period to ensure that the tablets were being taken as instructed and a final visit was made at the end of the period to confirm the result of the treatment in each contact, i.e. whether chickenpox had developed or not.

Results

Total number of cases of chickenpox	19
Total number of contacts	31

Of these 31 contacts 24 developed chickenpox within the time of the trial, three did not and four contacts defaulted as to taking the tablets as instructed.

Of the 24 contacts who developed chickenpox, on breaking the code it was found that 12 contacts had received virugon and 12 had received the placebo.

It had taken nearly two years to collect these 31 cases as the incidence of chickenpox had been unusually low. The numbers of contacts finally contracting chickenpox were so high that it became obvious even without breaking the code that the therapy was either of very limited effect or had no effect at all. Breaking the code at this point did in fact reveal that there was no resultant difference between administration of the placebo or virugon.

Discussion

These findings therefore fail to reveal any protective effect as a result of virugon administration. Although no objective criteria were made, the subjective impression was that the attacks of chickenpox in the contacts were similar in severity in both those treated with virugon and those treated with the placebo.

It could be argued that earlier administration of virugon *before* the onset of incubation might reveal some protective benefit but it is difficult to see how this could be carried out as a practical measure in a disease such as chickenpox. A disease with a shorter incubation period and of epidemic proportions (e.g. influenza) would seem a more feasible problem to tackle along these prophylactic lines. The results obtained in the general practice trial (1965) of virugon in cases of herpes zoster also failed to show any protective effect due to virugon and here again the time of administration could have been too late to allow of any possible drug effect.

Summary

Prophylactic administration of virugon to family contacts of cases of chickenpox failed to reveal any protective effect due to the therapy.

Acknowledgement

I wish to thank The Bayer Products Co. for the generous supply of randomized

tablets of virugon and the placebo.

REFERENCES

Bohmansson, G. (1960). Influenza Prophylaxis with Flumidin during the Spring 1960 Epidemic. Conference on ABOB and Flumidin. Stockholm. 71.

Drake, M., Burnstein, Th., Sawchuck, S., and Farquar, J. (1960). Results with ABOB against Measles in Hamsters and in Man. Conference on ABOB and Flumidin. Stockholm. 23.

G.P. Clinical Trials (1965). *Practitioner*, **195**, 235.

Haglind, J. (1960). Influenza Prophylaxis with Vaccine, ABOB, Flumidin and Placebo among Industry Employees. Conference on ABOB and Flumidin. Stockholm. 76.

Melander, B. (1960). N', N'-anhydrobis-(β-hydroxyethyl) biguanide HCl(ABOB) in Prophylaxis and Suppression of Experimental Influenza. *Antibiot. and Chemother.*, **10**, 34.

Renard, G., and Dhermy, P. (1960). Preliminary Note on the Action of ABOB on Experimental Herpetic Keratitis in Rabbits. Conference on ABOB and Flumidin. Stockholm. 29.

Rhodes, R. E., and Herlocher, M. L. (1960). Effect of ABOB in Mouse Experimental PR8 Influenza. Conference on ABOB and Flumidin. Stockholm. 11.

Sandahl, C., and Sjoberg, M. (1960). Flumidin in Influenza Prophylaxis Winter 1960. Conference on ABOB and Flumidin. Stockholm. 58.

Sandring, L. (1960). Prophylactic and Therapeutic Medication with Flumidin in Upper Respiratory Tract Infections. Conference on ABOB and Flumidin. Stockholm. 53.

Wheatley, D. (1960). A Trial of Flumidin in Common Virus Infections seen in General Practice. Conference on ABOB and Flumidin. Stockholm. 84.

Zetterberg, B., Heller, L., Gustafson, S., and Ringertz, O. (1960). A Clinical Field Trial with Tablet Mass-Prophylaxis during the Winter-Spring 1960 Influenza Epidemic—A Serological and Epidemiological Study. Conference on ABOB and Flumidin. Stockholm. 42.

PARAZOLIDIN: A NEW COMPOUND ANALGESIC PREPARATION

M. LLOYD-JONES, L.R.C.P., L.R.C.S., L.R.F.P. & S.

AGNES U. CAMPBELL, M.B., Ch.B., F.R.C.S.E., M.R.C.O.G.

Bridgnorth, Shropshire

IN ACADEMIC CIRCLES THE USE of polypharmaceuticals is frowned upon. Whilst we do not deny the virtues of this purist approach and its validity under circumstances where patients are under constant supervision, we find that these conditions rarely apply in domiciliary medicine. This is particularly so when an elderly patient needs several different drugs