LETTERS TO THE EDITOR

Susceptibilities to aciclovir in viral isolates from children with varicella

EDITOR,—Varicella, caused by primary infection with varicella zoster virus (VZV), is a common and highly contagious disease of childhood, and accounts for about one million cases per year in Japan. In 1994, the Welfare Ministry of Japan approved the use of oral aciclovir to treat varicella infections in otherwise healthy children. In spite of the recommendation that the treatment should not be used routinely for varicella in otherwise healthy children, the number of children treated with oral aciclovir has been increasing gradually in Japan.

It has rarely been reported that immunocompromised children with chronic VZV infection became resistant to aciclovir. However, no evidence that oral aciclovir treatment in otherwise healthy children with varicella leads to the appearance of resistant virus has been shown. To know the potential of antiviral resistance, we measured the susceptibilities to aciclovir in the paired isolates from otherwise healthy children with varicella, before and during the oral aciclovir treatment.

This study was conducted at the paediatric outpatient clinic of Showa Hospital for one month in 1996. Six otherwise healthy children with varicella diagnosed by characteristic skin lesions of primary VZV infection were included in this study with an age range from 11 months to 5 years. All received oral aciclovir for five days, starting at the first visit to the clinic. Each patient received 20 mg/kg of aciclovir per day adjusted to the body weight of 1 kg, and recovered completely. Informed consent was obtained from the parents.

For VZV isolation, an attempt was made to take vesicular fluid serially twice from the patients, before and during the oral aciclovir treatment. The procedure for virus isolation from vesicles was described in a previous paper.1

The susceptibilities of the isolated viruses to aciclovir were determined by examining the effective concentration for 50% and 80% plaque reduction (EC50 and EC80).2 Briefly, confluent cell monolayers in 6 cm plastic dishes in duplicate were infected with 100 plaque forming units of the cell-free isolated viruses for hour hour, and incubated in maintenance medium (Eagle’s minimal essential medium supplemented with 2% bovine calf serum) containing aciclovir (0, 0.5, 1, 2, and 5 μg/ml). After five days of incubation, the number of plaques were counted with a microscope. This assay was performed three times. With the mean values, the EC50 and EC80 were determined graphically. The statistical difference in susceptibilities (EC50 and EC80 values) of VZV isolates to aciclovir was evaluated using the Student’s t test.

The age, sex, and time of VZV isolation are shown in table 1. Oral aciclovir treatment was started within 48 hours of illness in the six patients. The paired isolates were taken at intervals of one to three days. Table 2 shows the EC50 and EC80 values of the isolates to aciclovir. In both values, there was no significant difference between before and during the oral aciclovir treatment.

In our previous study,1 the rate of VZV isolation from vesicles in otherwise healthy children with varicella, who received no antiviral treatment was 100% during the first two days after the onset of the disease, and declined gradually with time to 17% on the sixth day of illness. In another study (unpublished), we showed VZV was isolated easily from vesicles of patients with varicella in the first two days after oral aciclovir treatment, as in this study, but the rate declined with time more rapidly than from those without the aciclovir treatment. This is why there was variation in the timing of the paired isolates between one and three days.

No statistical difference of susceptibility to aciclovir was demonstrated between the two groups (EC50 and EC80) in each pair and mean value. We showed no evidence of the appearance of resistant virus to aciclovir when otherwise healthy children with varicella received the oral aciclovir treatment within three days. However, the number of patients in this trial was too small to enable us to draw any firm conclusions. It remains unknown whether the oral aciclovir treatment of varicella in otherwise healthy children increases the chance of aciclovir resistant mutant strains emerging.

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Randomised trial of suprapubic puncture versus urethral catheterisation for cystography

EDITOR,—Because urethral catheterisation for micturating cystography frequently causes discomfort and embarrassment in children, and is not always successful, we wondered whether suprapubic puncture would provide a suitable alternative,1 and began a prospective randomised trial.

All children needing micturating cystography were invited to be randomised to have either suprapubic puncture or urethral catheterisation; the study had ethics committee approval and informed consent. Families received an information pack, were encouraged to contact the study nurse in advance, and met her before the cystogram to discuss their wishes, and for play preparation. Urethral catheterisation or suprapubic puncture were performed in the same manner by a consultant or trainee paediatric radiologist; suprapubic puncture was under ultrasound control2 after using local anaesthetic cream (EMLA), then lignocaine. Urine was tested for blood, and microscopied for bacteria.

Parents and older children made an assessment of the procedure immediately, and two weeks later. Power calculations indicated it would be necessary to enrol 100 children into each limb to demonstrate whether there was a significant difference between the two procedures, but we stopped the study with just 10 in each limb because families regarded urethral catheterisation as clearly preferable. For the 20 children randomised, suprapubic puncture took a little longer than urethral catheterisation, and scored a little worse for discomfort, and despite thorough preparation, many children having suprapubic puncture appeared frightened by the needle.

Eighteen families refused randomisation because of their anxieties that the suprapubic puncture needle would be painful, or would make the procedure ‘too involved’ or ‘more like surgery’. The only two patients strongly

Table 1 The time of VZV isolation from vesicles

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age(years)/sex</th>
<th>Before aciclovir*</th>
<th>During aciclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2/F</td>
<td>Day 1†</td>
<td>Day 3</td>
</tr>
<tr>
<td>2</td>
<td>2/M</td>
<td>Day 2</td>
<td>Day 4</td>
</tr>
<tr>
<td>3</td>
<td>0.9/M</td>
<td>Day 0</td>
<td>Day 2</td>
</tr>
<tr>
<td>4</td>
<td>5/M</td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>5</td>
<td>3/F</td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>6</td>
<td>5/M</td>
<td>Day 2</td>
<td>Day 4</td>
</tr>
</tbody>
</table>

* The first day of the oral aciclovir treatment. † Day 0 is the day of appearance of rash.

Table 2 Comparison of aciclovir susceptibilities in isolated VZV between before and during the oral aciclovir treatment

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Before aciclovir</th>
<th>During aciclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EC50*</td>
<td>EC80*</td>
</tr>
<tr>
<td>1</td>
<td>1.27 (0.15)</td>
<td>2.33 (0.78)</td>
</tr>
<tr>
<td>2</td>
<td>1.45 (0.15)</td>
<td>2.48 (0.81)</td>
</tr>
<tr>
<td>3</td>
<td>1.57 (0.47)</td>
<td>2.57 (1.01)</td>
</tr>
<tr>
<td>4</td>
<td>1.55 (0.22)</td>
<td>3.55 (0.22)</td>
</tr>
<tr>
<td>5</td>
<td>1.24 (0.17)</td>
<td>3.00 (0.53)</td>
</tr>
<tr>
<td>6</td>
<td>1.46 (0.26)</td>
<td>2.72 (0.79)</td>
</tr>
<tr>
<td>Mean</td>
<td>1.42 (0.14)</td>
<td>2.78 (0.44)</td>
</tr>
</tbody>
</table>

Both EC50 and EC80 before † during aciclovir were not significant. * μg/ml.
enthusiastic about suprapubic puncture were older girls who had been highly embarrassed at the thought of having urethral catheterisation performed.

Though families recognised that urethral catheterisation may be unpleasant, most felt strongly that it seemed safer and preferable to suprapubic puncture, because it followed a ‘natural route’ rather than making a false one.

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Preclinical diagnosis of abdominal tumours by ultrasound examination

EDITOR,—The purpose of this preliminary childhood population based study was to evaluate the use of abdominal ultrasound examination to determine the incidence of abdominal tumours and to investigate the possibility of early diagnosis of these tumours at a preclinical stage.

This study in general population is very difficult because of organisational problems and high cost. Therefore, we studied children under 1 year of age who were referred by their paediatricians, for another reason, to an ultrasound centre in order to have an ultrasound examination. The most common reasons for referral were the investigation of the urinary tract after a urinary tract infection and the investigation of vomiting for possible gastro-oesophageal reflux. The study was initiated on January 1992, when we asked the radiologists of this centre to examine the whole abdomen of the referred children. In a five-year period (January 1992 to December 1996) 7500 infants were examined. None of these children had symptoms implying the presence of an abdominal tumour and their physical examination was normal.

The results were as follows: seven infants (0.09%) were found to have an abdominal tumour. Six of them were under 4 months of age and one was 6 months. In five infants the tumour was located in the adrenal gland and in two in the sympathetic spinal chain. In the five infants the tumour was <2 cm and they were followed up, with repeat ultrasound examinations, until the mass disappeared completely.

They are now both 4 years of age and in good health and remain in complete remission.

The incidence of neuroblastoma in children is about one in 7000.1 The incidence of seven in 7500 seems to be quite high and one could say that the examined infants comprise a ‘high risk’ group. It would be possible that the non-specific symptom of vomiting or the urinary tract infection in children might be more frequent and, somehow, associated with abdominal tumours. Abdominal ultrasound seems to be an excellent tool for the early diagnosis of abdominal tumours. As it is not a cheap investigation, it could be initially applied in children who are referred for an ultrasound examination for another reason.1 1

These preliminary results may justify its use as a screening method in the general population for the early diagnosis of abdominal tumours, especially neuroblastoma. In the meantime, we believe that physicians should be encouraged to have a low threshold in referring children for an ultrasound examination, as it is non-invasive, painless, and safe.

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Minor head injury

EDITOR,—As part of his useful review on head injuries Dr Beattie briefly discussed aetiology and prevention.2 The role of road traffic accidents (RTAs) as a major cause of serious or fatal head injury is highlighted and ‘preventative measures’ such as cycle helmets, seat belts, and pedestrian education are mentioned. This summary misses the point that it is motor vehicles and their drivers that cause RTAs; more specifically, too many vehicles on inappropriate roads, and too many drivers who are either insensitive or more commonly not responsible for their children’s driving.3

Traffic calming, 20 mph speed limits, reduction of through traffic, and parking restrictions have a major, primary, preventive role in making our streets safer for children. Countries that have acted to control traffic speed and flow have reduced their child RTA mortality to a much greater extent than countries, such as the UK, that rely on education programmes of unproven and limited benefit.4 Education and secondary preventive measures such as cycle helmets do have a role but it is important not to blame victims for failing to protect themselves from injuries caused by vehicles.

Currently RTAs kill more children than leukaemia and asthma combined. Paediatricians have a major part to play, both locally and nationally, in supporting active road safety measures.

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Dr Beattie comments:  
Thank you for giving me the opportunity to reply to Dr Ball and Dr Williams. As someone who has published extensively on injury prevention I fully endorse their views with regard to the role of primary injury prevention, secondary injury prevention, and education with regard to safety. The general thrust of the article was to discuss head injuries briefly and the lack of space meant that, by default, not every aspect of injury prevention could be discussed.

In my experience, however, a substantial number of significant head and brain injuries could be avoided were the simple measures alluded to implemented more widely. They take little more than education to achieve, together with some peer pressure to ensure that children do continue to use their helmets, and parents continue to restrain their children appropriately in rear seats.

The other measures may well be more effective in the long run but they will take a substantial change in society to achieve. Recently there has been correspondence in the general press and national news media regarding a solicitor who is objecting to sleeping policemen in his road. As long as attitudes like these prevail then other measures will have to be introduced.

Finally I did not mean to give the impression that children are responsible for their own injuries. As someone who has both children of his own and who sees 90 children a day in the accident and emergency department, I realise how little children are to blame for the injuries they sustain.


Correction

Nitric oxide and severe sepsis  
(Arch Dis Child 1977;77:463)

We regret that Dr David Burgner’s address was incorrectly given in the above letter. His correct address is Department of Paediatrics, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU.

MEETINGS IN 1998

2nd International Symposium on New Horizons in Pediatric Neurosurgery/Neurology  
9–13 February, Jerusalem, Israel

Further details: Professor Shaul Haral/Dr Shlomo Constantini, c/o Secretariat, PO Box 29041, Tel Aviv 61290, Israel (fax +972 3 517 5155)

Paediatric Research Society  
20–21 February, Swansea

Further details: Dr Michael Cosgrove, Department of Child Health, Singleton Hospital, Skenby, Swansea SA2 8QA

11–12 September, Elgin

Further details: Dr Anne Attenburrow, Paediatric Department, Dr Gray’s Hospital, Elgin, Morayshire IV30 1SN

Neonatal Society
26 February, London
Further details: Mrs E M Symonds, School of Human Development, Division of Child Health, University Hospital, Queen’s Medical Centre, Nottingham NG7 2UH
19–20 June, Rennes, France
Further details: Dr P Bétrémieux, Pavillon Lecharrer, CHU Pontchaillon, 35033 Rennes Cédex, France

XXII Biennial Congress of the Urological Association of South Africa
1–5 March, Cape Town, South Africa
Further details: Mrs Sally Elliott, Postgraduate Conference Division, UCT Medical School, Observatory 7925, Cape Town, South Africa (fax +27 21 448 6263)

International Conference on Paediatric Asthma
3–4 March, Maastricht, The Netherlands
Further details: Castle House Conferences, 3 Linden Close, Tunbridge Wells, Kent TN4 8HH (fax +44 (0)1892 517773/517005)

Clinical Genetics Society
12 March, London
Further details: Dr Peter Farndon, Clinical Genetics Unit, Birmingham Maternity Hospital, Edgbaston, Birmingham B15 2TG

The Spectrum of Developmental Disabilities XX: Autism
30 March–1 April, Baltimore, USA
Further details: Johns Hopkins Medical Institutions, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

2nd Annual Meeting of the Royal College of Paediatrics and Child Health
31 March–3 April, York
Further details: Miss Amanda Ambalu, Royal College of Paediatrics and Child Health, 5 St Andrew’s Place, Regents Park, London NW1 4LB

The Paediatric Oesophagus: An Interdisciplinary Symposium
20–22 April, Kusadasi, Turkey
Further details: Professor Dr Özkay Maluf, Department of Paediatric Surgery, Ege University Faculty of Medicine, Bornova, 35100 Izmir, Turkey (fax +90 232 375 12 88)

26th Annual Pediatric Trends
20–25 April, Baltimore, USA
Further details: Johns Hopkins Medical Institutions, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

European Paediatric Congress
24–26 April, Madrid, Spain
Further details: Congress Management International, 7 rue de Caumartin, 75009 Paris, France

6th International Paediatric Haematology and Oncology Update Meeting
6–8 May, Edinburgh
Further details: Conference Secretariat, Index Communications, Meeting Services, Crown House, 28 Winchester Road, Romsey, Hampshire S05 1AA (fax +44 (0)1794 511455)

31st Annual Advances and Controversies in Clinical Pediatrics
7–9 May, San Francisco, USA
Further details: Office of Continuing Medical Education, Room MCB-630, University of California School of Medicine, San Francisco, CA 94143-0742, USA (fax +1 415 476 0318)

The Seventh International Conference on Safe Community
13–15 May, Rotterdam, The Netherlands
Further details: Dr Wim Rogmans, Consumer Safety Institute, PO Box 75169, 1070 AD Amsterdam, The Netherlands (fax +31 20 5114510)

Pediatric Allergy and Immunology for the Practitioner
14–15 May, Baltimore, USA
Further details: Johns Hopkins Medical Institutions, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

European Consensus Development Conference on Neonatal Hearing Screening
15–16 May, Milan, Italy
Further details: Dr F Grandori, Centre of Biomedical Engineering, Politecnico of Milan, Piazza Leonardo da Vinci 32, 20133 Milan, Italy (fax +39 2 239 93360)

4th World Conference on Injury Prevention and Control
17–20 May, Amsterdam, The Netherlands
Further details: PO Box 1558, 6501 BN Nijmegen, The Netherlands (fax +31 24 360 11 59)

6th Southeast European Congress of Paediatric Surgery: Short Bowel Syndrome
22–23 May, Graz, Austria
Further details: Dr Günther Schimpel, Department of Paediatric Surgery, Auenbruggerplatz 32, A-8036 LKH-Graz, Austria (fax +43 316 385 3775)

5th Joint Meeting of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition and the North American Society for Pediatric Gastroenterology and Nutrition
27–30 May, Toulouse, France
Further details: Europe Organisation, 5 rue Saint-Pantaléon, BP 844, 31015 Toulouse, France; Edesx, France (fax +33 5 61 21 28 54)

XXVIIth European Congress of Perinatal Medicine
10–13 June, Zagreb, Croatia
Further details: Globtour Zagreb, Trg N, Subica Zrinskog 1/1, 1000 Zagreb, Croatia

Society for Research into Hydrocephalus and Spina Bifida
10–13 June, Genoa, Italy
Further details: Miss C A Sobkowiak, Darlington Memorial Hospital, Hollyhurst Road, Darlington, Co Durham DL3 6HX (fax +44 (0)1325 743622)

International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer
19–20 June, Niagara-on-the-Lake, Canada
Further details: Diane Placent, Department of Pediatrics, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA (fax +1 716 845 8003)

Advanced Pediatric Life Support
22–24 June, Baltimore, USA
Further details: Johns Hopkins Medical Institutions, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

Advanced Course for Obstetricians and Gynaecologists
22–26 June, London
Further details: Mrs Trisha Hawkins, Royal Postgraduate Medical School, Queen Charlotte’s and Chelsea Hospital, Goldhawk Road, London W6 0XG (fax +44 (0) 181 383 8555)

International Meeting on Recent Advances in Gynaecological Surgery
29–30 June, Leeds
Further details: IMRAGS Secretariat, Congress House, 65 West Drive, Cheam, Sutton, Surrey SM2 7NB (fax +44 (0)181 661 9036)

28th British Congress of Obstetrics and Gynaecology
30 June–3 July, Harrogate
Further details: BCOG Secretariat, Congress House, 65 West Drive, Cheam, Sutton, Surrey SM2 7NB (fax +44 (0)181 661 9036)

9th Asean Paediatric Federation Conference
9–12 July, Singapore
Further details: Conference Secretariat, Academy of Medicine, Singapore, College of Medicine Building, 16 College Road #01-01, Singapore 169854 (fax +65 225 5155)

XXII International Congress of Pediatrics
9–14 August, Amsterdam, The Netherlands
Further details: Ruocongres Conference Management, Jan van Goyenkade 11, 1075 HP Amsterdam, The Netherlands (fax +31 20 673 7306)

British Association of Perinatal Medicine and the Neonatal Nurses Association
3–5 September, Cambridge
Further details: Barbara Pett, BAPM Administrator, 19 Cornwall Terrace, Regents Park, London NW1 4QP (fax +44 (0)171 487 5278)

Growth Hormone Research Society Conference
3–6 September, San Francisco, USA
Further details: Office of Continuing Medical Education, Room MCB-630, University of California School of Medicine, San Francisco, CA 94143-0742, USA (fax +1 415 476 0318)

Cerebrovascular Disease and Stroke in Children
10–11 September, London
IIIrd International Symposium on Pediatric Dermatology
10–12 September, Rome, Italy
Further details: Professor Giuseppe Fabrizi, Department of Dermatology, Catholic University of Sacred Heart, Largo A Gemelli 8, 00168 Rome, Italy (fax +39 6 3013250)

Rett Syndrome
11–12 September, Bled, Slovenia
Further details: ICNA ‘98, Cankarjev Dom, Cultural and Congress Centre, Prešernova 10, SI-1000 Ljubljana, Slovenia (fax +386 6 217 431)

Diagnostic Procedures and Techniques in Child Neurology
11–12 September, Venice, Italy
Further details: PTS Congress Division, 69 Via Filippo Civinini, 00197 Rome, Italy (fax +39 6 8088 088)

8th International Child Neurology Congress
13–17 September, Ljubljana, Slovenia
Further details: ICNA ‘98, Cankarjev Dom, Cultural and Congress Centre, Prešernova 10, SI-1000 Ljubljana, Slovenia (fax +386 6 217 431)

20th Congress of the European Society of Parenteral and Enteral Nutrition
16–19 September, Nice, France
Further details: Luc Cynober, c/o Hôpital Saint-Antoine Service de Biochimie A, 184 rue du Fbg Saint-Antoine, 75012 paris, France (fax +33 1 49 28 22 31)

Pediatrics for the Practitioner Update ‘98
17–18 September, Baltimore, USA
Further details: Johns Hopkins Medical Institution, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

Longitudinal Studies in Children At-Risk
18–20 September, Vienna, Austria
Further details: Dr Georg Spiel, Department of Neurology, Psychiatry and Special Education for Children and Adolescents, General Hospital Klagenfurt, St Veiter-Straße 47, A-9020 Klagenfurt, Austria

European Respiratory Society Annual Congress
19–23 September, Geneva, Switzerland
Further details: ERS Headquarters, 1 Boulevard de Grancy, CH-1006 Lausanne, Switzerland (fax +41 21 617 2865)

Habitation and Rehabilitation in Child Neurology
20–24 September, Budapest, Hungary
Further details: Ms Enikő Gaskó, Instant Congrès-Ex Ltd, H-1364 Budapest 4, PO Box 210, Hungary (fax +36 1 118 3418)

European Society for Paediatric Endocrinology
24–28 September, Florence, Italy
Further details: Dr M O Savage, Paediatric Endocrinology Section, Department of Endocrinology, St Bartholomew’s Hospital, London EC1A 7BE

British Human Genetics Conference
28–30 September, York
Further details: Dr Peter Farndon, Clinical Genetics Unit, Birmingham Maternity Hospital, Edgbaston, Birmingham B15 2TG

Consequences of Curing Childhood Cancer
30 September, Edinburgh
Further details: Eileen Strawn, Symposium Coordinator, Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh EH2 1JO

Medical Problems facing Obstetricians and Gynaecologists in Pregnancy
7–9 October, London

Further details: Mrs Trisha Hawkins, Royal Postgraduate Medical School, Queen Charlotte’s and Chelsea Hospital, Goldhawk Road, London W6 0XG (fax +44 (0) 181 383 8555)

North American Society for Pediatric Gastroenterology
22–25 October, Orlando, USA
Further details: NASPGN Manager, Slack Inc, 6900 Grove Road, Thorofare, NJ 08086-9447, USA

Bone Marrow Transplantation in Childhood
28–30 October, Manchester
Further details: Index Communications Meeting Services, Crown House, 28 Winchester Road, Romsey, Hampshire SO51 8AA (fax +44 (0)1794 511455)

Advances in Pediatric Nutrition
2–3 November, Baltimore, USA
Further details: Johns Hopkins Medical Institutions, Office of Continuing Medical Education, 720 Rutland Avenue, Turner 20, Baltimore, MD 21205–2195, USA (fax +1 410 955 0807)

2nd International Conference on Emerging Zoonoses
5–9 November, Strasbourg, France
Further details: Target Tours Ltd, PO Box 29041, Tel Aviv 61290, Israel (fax +972 3 5175155)

Diploma Course in Paediatric Gastroenterology
5–10 December, London
Further details: Professor J A Walker-Smith, University Department of Paediatric Gastroenterology, Royal Free Hospital, Pond Street, London NW3 2QG (fax +44 (0)171 830 2146)

Further details: Ms Andrina Williams, Short House Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH (fax +44 (0)171 831 0488)
Susceptibilities to aciclovir in viral isolates from children with varicella

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