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. The dose of aciclovir was 20 mg/kg four times a day, 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.

The susceptibilities of the isolated viruses to aciclovir were determined by examining the effective concentration for 50% and 80% plaque reduction (EC50 and EC80), respectively. 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 during 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 otherwise healthy children with varicella in children who received 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 disease. 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 significantly 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 statistically 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.

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 1</td>
<td>Day 4</td>
</tr>
<tr>
<td>3</td>
<td>0.9/M</td>
<td>Day 2</td>
<td>Day 5</td>
</tr>
<tr>
<td>4</td>
<td>5/M</td>
<td>Day 0</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>EC50* (µg/ml)</th>
<th>EC80* (µg/ml)</th>
<th>EC50* (µg/ml)</th>
<th>EC80* (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.27 (0.15)</td>
<td>2.33 (0.78)</td>
<td>1.32 (0.26)</td>
<td>2.03 (0.51)</td>
</tr>
<tr>
<td>2</td>
<td>1.45 (0.15)</td>
<td>2.48 (0.81)</td>
<td>1.30 (0.09)</td>
<td>2.30 (0.64)</td>
</tr>
<tr>
<td>3</td>
<td>1.57 (0.47)</td>
<td>2.57 (1.01)</td>
<td>1.47 (0.29)</td>
<td>2.98 (0.90)</td>
</tr>
<tr>
<td>4</td>
<td>1.55 (0.22)</td>
<td>3.55 (0.22)</td>
<td>1.41 (0.32)</td>
<td>2.67 (0.69)</td>
</tr>
<tr>
<td>5</td>
<td>1.24 (0.17)</td>
<td>3.00 (0.53)</td>
<td>1.42 (0.37)</td>
<td>3.28 (0.63)</td>
</tr>
<tr>
<td>6</td>
<td>1.46 (0.26)</td>
<td>2.72 (0.79)</td>
<td>1.26 (0.16)</td>
<td>2.03 (0.59)</td>
</tr>
<tr>
<td>Mean</td>
<td>1.42 (0.14)</td>
<td>2.78 (0.44)</td>
<td>1.36 (0.08)</td>
<td>2.48 (0.47)</td>
</tr>
</tbody>
</table>

Both EC50 and EC80 before v during aciclovir were not significant.

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.

JULIE HENDERSON
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1 Bryndorf J, Christensen ER, Sandoe E. Su-
prapubic puncture because it followed a
‘natural route’ rather than making a false one.

Toma. These children are now all in good
health. In the five remaining infants the
tumour was 2.5–6 cm. In all cases, the
physician was normal.

presence of an abdominal tumour and their
these children had symptoms implying the
reasons for referral were the investigation of
ultrasonography centre in order to have an
evaluate the use of abdominal ultrasound
preclinical diagnosis of abdominal
tumours by ultrasound examination

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
evaluation 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-esophageal reflux. The study was ini-
tiated 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 two
infants the tumour was <2 cm and they were
followed up, with repeat ultrasound examina-
tions, until the mass disappeared completely.
They are now both 4 years of age and in
good health. In the five remaining infants the
tumour was 2.5–6 cm. In all cases, the
mass disappeared completely.

The incidence of neuroblastoma in chil-
dren 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

1 Woods WG, Tuchman M, Robison L, et al. A
population-based study of the usefulness of
screening for neuroblastoma. Lancet

2 Hayden CK Jr. Ultrasonography of the acute
paediatric abdomen. Radiol Clin North Am

Ultrasoundography as an adjunct in the diagnosis
of acute appendicitis: a 4-year experience. J

Minor head injury

EDITOR,—As part of his useful review on head
injuries Dr Beattie briefly discussed aetiology
and prevention.1 The role of road traffic acci-
dents (RTAs) as a major cause of serious or
fatal head injury is highlighted and ‘preventa-
tive measures’ such as cycle helmets, seat
belts, and pedestrian education are men-
tioned. This summary misses the point that it
is motor vehicles and their drivers that cause
RTAs; more specifically, too many vehicles
being driven too fast and parked
inappropriately.

Cheap investigation, it could be initially
seen as quite high and one
inappropriate.

injured. We regret that Dr David Burger’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.

Correction
Nitric oxide and severe sepsis
Arch Dis Child 1997;77:463
We regret that Dr David Burger’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: Prof. Shaul Harel/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, Depart-
ment of Child Health, Singleton Hospital,
Sketty, Swansea SA2 8QA

11–12 September, Elgin
Further details: Dr Anne Attenburrow, Paed-
iatric Department, Dr Gray’s Hospital, Elgin,
Morayshire IV30 1SN
Neonatal Society  
26 February, London  
29 October, London  
Further details: Dr M E 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 Lechartier, 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 Öztay Mukaf, 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 CxCommunications Meeting Services, Crown House, 28 Winchester Road, Romsey, Hampshire SO51 8AA (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 Communities  
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, Centro di Bio-medical Engineering, Politecnico di 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-4036 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, 31005 Toulouse, France (fax (+33) 5 61 21 28 54)

XXVth European Congress of Perinatal Medicine  
10–13 June, Zagreb, Croatia  
Further details: Globtour Zagreb, Teg 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) (131) 325 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 Piaccente, 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  
9–11 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)

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 Asian 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 Petit, 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
Further details: Ms Andrina Wlamsley, Short House Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH (fax +44 (0)171 831 0488)

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, Presernova 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, Presernova 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 Institutions, 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 Bvd 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 Congr-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)