

# A prospective evaluation of community acquired gastroenteritis in paediatric practices: impact and disease burden of rotavirus infection

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## Abstract

**Aims**—To examine the disease burden and epidemiology of community acquired rotavirus gastroenteritis in Austrian children treated in a paediatric practice.

**Methods**—A prospective, population based, multicentre study in four paediatric practices and two children's hospitals (Innsbruck and Leoben). Children  $\leq 48$  months of age presenting with gastroenteritis during a six month period of rotavirus peak between December 1997 and May 1998 were included. Prospective testing of stool samples for rotavirus was performed using ELISA.

**Results**—A total of 6969 children were enrolled; 171 (2.4%) had community acquired gastroenteritis. Of 144 children who could be included in further analysis, 49 (34%; median age 16.7 months) were rotavirus positive, and 95 (66%; median age 17.0 months) were rotavirus negative. Three of the rotavirus positive children (median age 14.6 months) were hospitalised. The severity of rotavirus positive gastroenteritis was significantly higher than that of rotavirus negative gastroenteritis. The incidence of community acquired gastroenteritis was 4.67 per 100 children per year, and of rotavirus positive gastroenteritis 1.33 per 100 children per year.

**Conclusion**—Rotavirus is a relevant cause of community acquired gastroenteritis in children aged 4 years and younger treated by a paediatrician. The data can be used as a basis for developing strategies to prevent infection.

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Keywords: rotavirus; gastroenteritis; prospective; incidence; severity

The large number of children visiting a paediatrician or hospitalised with gastroenteritis is an indication of the continuing importance of this disease. Among the many viruses causing diarrhoea, rotavirus is the most common cause of severe illness.<sup>1</sup> Studies from temperate climates show a striking seasonal pattern of rotavirus infection, with most cases occurring during the colder months of the year.<sup>2–3</sup> Based on studies of hospitalised patients, it has been shown that the highest frequency is usually observed in children younger than 5 years.<sup>4–6</sup> Despite improved treatment of diarrhoea, the disease has been not controlled; use of live oral

vaccine<sup>7–10</sup> was discontinued and the vaccine withdrawn from the US market because of its possible association with intussusception.<sup>11</sup> This raises questions regarding the need for national intervention programmes based on reliable epidemiological data. Worldwide, only limited data are available on laboratory confirmed cases of rotavirus associated gastroenteritis, because a specific diagnosis of rotavirus infection is rarely made by paediatricians on cost grounds and also because diagnosis does not alter treatment or outcome. No national reporting system is available for Austria, underlining the need for investigating rotavirus disease. Assessment of rotavirus disease burden would require testing for rotavirus infection in a representative sample of children who visit a health care facility because of community acquired diarrhoea. We therefore performed a prospective study to evaluate the frequency and disease burden of rotavirus positive gastroenteritis in children  $\leq 4$  years of age, seen by a paediatrician.

## Methods

### DESIGN

A prospective, population based, multicentre study, involving four paediatric offices in different parts of the country and two children's hospitals in Austria (Department of Paediatrics, University of Innsbruck and the Children's Hospital Leoben) was performed. The paediatricians are part of the primary health care system and not private clinicians; the hospitals offer primary to tertiary level of care. The study was performed during the winter season between December 1997 and May 1998. Innsbruck (hospital and two paediatric offices) is an urban area, whereas the area of Leoben (hospital and the two paediatric offices) is more rural. All children aged between 0 and 48 months were registered with the participating paediatricians, and all who consulted a paediatrician because of gastroenteritis were enrolled.

### DEFINITION AND IDENTIFICATION

Gastroenteritis was defined as the occurrence of vomiting and/or diarrhoea. Diarrhoea was defined as the passing of two or more liquid or semi-liquid stools or a single watery stool per day by a child. Children with chronic diarrhoea, intoxication, etc were excluded. The determination that symptoms were present for less than seven days was made by the parent. Identification of the disease as a gastroenteritic episode was made by the paediatrician.

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## COLLECTION OF STOOL SAMPLES AND PATIENT ENROLMENT

Two stool specimens were obtained either by the parents or paediatricians within seven days of the onset of symptoms. The first was immediately investigated by trained physician assistants using an enzyme linked immunosorbent assay (ELISA) kit (TestPack Rotavirus; Abbott, Delkenheim, Germany). The second was stored at  $-20^{\circ}\text{C}$  until G and P serotyping by reverse transcription polymerase chain reaction was performed.<sup>12</sup> Written informed consent was obtained from the parents, allowing data collection. Children with missing stool samples or missing informed consent were excluded from further analysis. For all children with gastroenteritis a case report form was completed by the paediatrician. If a paediatrician referred a child with gastroenteritis to one of the hospitals, the case report form was completed by the designated research personnel in the hospital. Documentation included demographic (age, sex, nationality) as well as disease characteristics: occurrence of diarrhoea and/or vomiting; maximum temperature until consultation; maximum frequency of diarrhoeal stools per day until consultation; maximum frequency of vomiting per day until consultation; temperature at consultation; duration of diarrhoea and vomiting; and severity of dehydration, which was estimated by weight loss and clinical signs. Furthermore, concomitant diagnosis, for example, upper or lower respiratory tract infection, otitis media, urinary tract infection, etc, as well as recurrent rotavirus infections were documented. For description of clinical severity, a 20 point numerical score (Vesikari) was used.<sup>13</sup> Following Joensuu *et al*, cases with

complete scores were divided in two subgroups: 1–10 points in the moderately severely ill group, and 11–20 points in the severely ill gastroenteritis group.<sup>8</sup>

## LABORATORY METHODS

Presence of rotavirus in a stool sample was investigated with ELISA (TestPack, Abbott, Delkenheim, Germany). The test was performed according to the manufacturer's protocol immediately after collection of the first sample. The sensitivity of this test was 95% and the specificity 90%.<sup>14</sup>

## STATISTICAL METHODS

For data entry and analyses the statistical analysis system (Version 7, SAS Institute Inc., Cary, North Carolina, USA) was used. All data were entered twice and compared. The crude incidence is the ratio of the number of cases of gastroenteritis (rotavirus positive or negative) divided by the number of children months. Children months are the number of children multiplied by the sum of months the children were under observation. For the sake of convenience, we present the incidence ratio per 100 children per year. We applied Poisson regression models and estimated the incidence adjusted for region and month. As the incidences vary over the month, such an adjustment is necessary. We used December 1997 as a reference month in order to adjust for the effect of seasonal pattern. The models were estimated by maximum likelihood method.

## Results

## GENERAL

The study population at risk comprised 6969 children up to the age of 4 years. All were cared for by one of the four participating paediatricians. A total of 2720 were domiciled in the area of Innsbruck and 4249 in the area of Leoben. A total of 171 children presented with community acquired gastroenteritis during the course of the study, which constitutes 2.4% of the study population at risk. Five patients were excluded from further analysis because of missing informed consent. Of the remaining 166 children, a further 22 had to be excluded because a stool specimen was not available or was taken more than seven days after consultation (13.3% drop outs). In one child, questionnaire data were incomplete (table 1, 29 cases from Leoben); however, the data were included in the estimation of incidence (table 2, 30 cases in Leoben).

Table 1 Characteristics of children and prevalence of gastroenteritis in children  $\leq 4$  years seen in paediatric practices during December 1997 and May 1998

	Rotavirus positive No. (%)	Rotavirus negative No. (%)
Total	49	95
Median age (mth)	16.7	17.0
Age		
0–3 mth	0	3 (3.2)
4–6 mth	5 (10.2)	8 (8.4)
7–9 mth	4 (8.2)	15 (15.8)
10–12 mth	6 (12.2)	6 (6.3)
13–23 mth	26 (53.1)	34 (35.8)
24–36 mth	6 (12.2)	18 (18.9)
37–48 mth	2 (4.0)	11 (11.6)
Sex		
Male	34 (69.4)	29 (30.6)
Female	15 (30.6)	66 (69.4)
Nationality		
Austrian	41 (83.7)	74 (77.9)
European	8 (16.3)	21 (21.1)

Table 2 Incidence of acute gastroenteritis (per 100 children per year) in paediatric offices based on observation between December 1997 and May 1998

Centre*	Number of cases	Children months under observation	Crude yearly incidence	Adjusted yearly incidence	95% confidence interval†
Acute gastroenteritis (including all cases)					
Leoben	67	25 494	3.15	3.00	2.36 to 3.82
Innsbruck	104	16 320	7.65	7.29	6.01 to 8.83
Acute gastroenteritis cases tested positive for rotavirus					
Leoben	29	25 494	1.36	1.31	0.91 to 1.87
Innsbruck	20	16 320	1.47	1.36	0.88 to 2.11

\*Each centre includes two paediatric offices with different numbers of children enrolled: Leoben:  $n = 1170$ ,  $n = 3079$ ; Innsbruck:  $n = 1231$ ,  $n = 1489$ .

†Incidence are adjusted for month under observation and expressed as yearly incidence.

Table 3 Disease characteristics of children  $\leq 4$  years with community acquired gastroenteritis seen by a paediatrician between December 1997 and May 1998

Symptoms	Rotavirus positive	Rotavirus negative
Total	49	95
Diarrhoea (%)	10 (20.4)	41 (43.2)
Diarrhoea and vomiting (%)	38 (77.6)	50 (52.6)
Vomiting (%)	1 (2.0)	4 (4.2)
Concomitant diagnoses (%)	16 (32.7)	47 (49.5)
Median duration of diarrhoea in days	4.0	3.0
Median duration of vomiting in days	2.0	1.0
Maximum frequency of diarrhoea/day	4.0	4.0
Maximum frequency of vomiting/day	3.0	1.0

Data on 144 children were therefore included (table 1). Forty nine (34%) were rotavirus positive (median age 16.7 months) and 95 (66%) rotavirus negative (median age 17.0 months). Of the rotavirus positive children, 29 (59.2%) were detected in the area of Leoben and 20 (40.8%) in the area of Innsbruck. In children younger than 1 year of age, rotavirus was detected in 30.6% (15/49). A majority of rotavirus infections (53%; 26/49) were observed between 13 and 24 months of age. More boys than girls presented with rotavirus positive diarrhoea (69.4% *v* 30.6%). The majority of children investigated (79.9%; 115/144) were Austrians; the rest belonged to other European countries. Twenty five per cent of the parents living in the rural region and none in the urban region consulted their paediatricians more than twice.

#### INCIDENCE OF ACUTE GASTROENTERITIS IN PAEDIATRIC OFFICES

Table 2 shows the number of children, the children months under observation, and the number of cases of gastroenteritis. The yearly incidence of contraction of acute gastroenteritis adjusted for month of observation was higher in the urban region of Innsbruck (7.29 per 100 children per year, confidence interval 6.01 to 8.38) than in the rural region of Leoben (3.00 per 100 children per year, confidence interval 2.36 to 3.82;  $p \leq 0.001$ ). The weighted average of the incidence of acute gastroenteritis was 4.67 per 100 children per year. The adjusted incidence for rotavirus positive gastroenteritis was 1.33 per 100 children per year. No regional difference in the incidence of rotavirus positive gastroenteritis was observed (table 2).

#### MONTHLY DISTRIBUTION

In the six month study period the peak of acute gastroenteritis in Austria occurred in March (62 of 170 cases); there were only 18 cases in

December, 23 in January, 22 in February, 19 in April, and 27 in May. At the beginning of the rotavirus season in December, only one child tested positive for rotavirus; there were eight children in January, six in February, 22 in March, five in April, and seven in May. The distribution was similar in the two study sites and the four paediatric offices.

#### DISEASE CHARACTERISTICS

Table 3 shows occurrence, duration, frequency of symptoms, and concomitant diagnosis. Of the 16 children positive for rotavirus with additional diagnosis, upper respiratory tract infection was seen in eight (50%), lower respiratory tract infection in five (31.2%), and otitis media in two (18.8%) children. No meningitis was observed. Of the 47 rotavirus negative children with concomitant diagnoses, 33 (70.2%) had an upper respiratory tract infection and 14 (29.8%) a lower respiratory tract infection. No other diagnoses were made. No case of recurrent rotavirus infection was documented.

A 20 point numerical Vesikari score could be completed in 117 of the 144 children included in this study; in 27 cases data on temperature were missing. Table 4 shows the median values for the severity score in the different regions and their confidence intervals. Rotavirus positive gastroenteritis was significantly more severe than rotavirus negative gastroenteritis (median score 11 *v* 7;  $p < 0.001$ ). There were 73.3% severe cases (11/15; score  $> 10$ ) in the urban region observed, compared to 44% (12/27) in the rural region. No differences were observed comparing the median scores of rotavirus positive cases between the two areas.

Three children who contracted rotavirus gastroenteritis in March were referred to the hospitals by the participating paediatricians and hospitalised. No child with rotavirus negative gastroenteritis was hospitalised during the study period. The results of evaluation are not presented, because the number of patients was too small for statistical analysis.

#### Discussion

Our prospective study provides data on community acquired rotavirus gastroenteritis in children treated in a paediatric practice and adds to the determination of worldwide pattern of rotavirus disease in children. Overall, rotavirus was detected in 34% (49/144) of the children  $\leq 48$  months of age who consulted a paediatrician because of gastroenteritis (table

Table 4 Severity of community acquired gastroenteritis using the 20 point Vesikari severity score in children seen by a paediatrician in different areas of Austria

Rotavirus test result	Region					
	Total		Urban		Rural	
	Positive	Negative	Positive	Negative	Positive	Negative
Total number with complete score*	42	75	15	41	27	34
Illness moderate (%)	19 (45.2)	58 (77.3)	4 (26.7)	28 (68.3)	15 (55.6)	30 (88.2)
Illness severe (%)	23 (54.8)	17 (22.7)	11 (73.3)	13 (31.7)	12 (44.4)	4 (11.8)
Median severity score†	11	7	11	8	10	7
5% value	6	3	3	4	6	3
95% value	17	14	18	15	13	12

\*Reduced numbers because of 27 cases with incomplete score.

†p values based on Wilcoxon two sample test.

1). The proportion is higher than the percentages observed in Spain (24%),<sup>15</sup> Finland (26%),<sup>16</sup> or England and Wales (29%).<sup>17</sup> In various other studies outside Europe, rotavirus infection accounted for an average of 8% of the cases of diarrhoea in the community and of 28% of outpatient visits.<sup>18</sup> In a recent study performed in Toronto, investigating rotavirus in outpatient settings, 20% of the stool samples obtained were rotavirus positive,<sup>19</sup> indicating the widespread character and continuing importance of this infection.

The incidence of community acquired rotavirus gastroenteritis in Austria during the study period of six months was 1.33 per 100 children per year. The incidences were obtained during the winter season; we would expect lower incidences had we observed a whole year. Taking this into account, the Austrian incidence of rotavirus gastroenteritis is much lower than that observed in Finland, where an annual incidence of 9.1 in 100 children years (714 children years and 65 episodes) up to the mean age of 2.6 years was reported.<sup>16</sup> The cumulative incidence under 5 years of age was 2.8 cases per 100 children per year.<sup>13</sup> Ford-Jones *et al* reported age dependent rates of rotavirus gastroenteritis in child care centres: 1.1 cases per 100 children months in children 0–23 months of age; 0.23 cases per 100 children months in children 24–35 months of age; and no episodes per 100 children months in children 3 years and older.<sup>19</sup> Expressed in children years, the incidence in Toronto in all ages is 4.4 cases in 100 children years (33 cases over 738 children years).

In addition to age dependence, variations observed between different countries probably reflect differences in survey methods, for example, enhanced recruitment through telephone liaison, as performed in Spain and Finland,<sup>15 16</sup> rather than the true incidence of the disease. In Switzerland, where a study with a similar design to the present one was performed, the estimated incidence of rotavirus gastroenteritis was 1.6 per 100 children years.<sup>20</sup> The regional differences in the occurrence of gastroenteritis in Austria, shown by a significantly higher incidence in the urban than in the rural area (7.29 *v* 3.00; *p* < 0.001) might be caused by the nature of living conditions, for example, more social contact, and day care users, which might promote spreading of viral and bacterial agents. Organisms such as *Campylobacter jejunii* or *Salmonella* could be potential causes, but the Austrian laboratory reporting system does not provide data differentiating between urban and rural areas.

We have shown that geographical differences influence the frequency of consultations, as parents in the rural area of Austria, where access to hospitals is more difficult, visit their paediatricians more often than in the urban region. However, the percentage of children with a severity score above 10 was higher in the urban region (table 3), pointing to parental confidence in the availability of health care. The delay in contacting a doctor can result in missed cases of mild disease. Severity of illness or age differences could be excluded as a cause

of frequent consultation, as median severity score or median age between children in the rural and urban region did not differ significantly (table 3).

In contrast to developing countries, rotavirus diarrhoea occurs at a higher age in industrialised countries like the USA, where the peak occurs during the second year of life.<sup>6 21</sup> Ford-Jones and colleagues<sup>19</sup> reported a mean age of 18.2 months of children who visited a paediatric practice because of rotavirus positive diarrhoea; this value is similar to the median age of 16.7 months of rotavirus positive children in our study. We observed that the average age in children with rotavirus infection (*n* = 49) was 11 months, and 13 months in all other cases of gastroenteritis. Thus, there is no difference between industrial and developing countries.

As reported by others,<sup>8 16</sup> we found rotavirus gastroenteritis to be significantly more severe than rotavirus negative gastroenteritis. Of 144 children with community acquired gastroenteritis seen by a paediatrician, three (2%) were hospitalised. All were all rotavirus positive and account for 6.1% (3/49) of all rotavirus positive children. In the Swiss study 5.5% (16/294) of children with gastroenteritis were hospitalised; 12 of them (75%) were rotavirus positive.<sup>20</sup> In comparison, 1/33 children with rotavirus gastroenteritis had to be hospitalised in Finland<sup>22</sup> and 1/40 in England and Wales.<sup>23</sup> In Canada, 24% (7/29) of rotavirus positive children seen by a paediatrician sought further care, five (17%) in an emergency department, one (3%) received intravenous infusion therapy, and one (3%) was hospitalised briefly.<sup>19</sup> Whether these differences are a result of disease severity or prompt oral rehydration therapy is not known. Age differences might be an explanation, but the age of rotavirus positive children reported by Ford-Jones and colleagues<sup>19</sup> was similar to that of the children of the present study. Stratification of disease severity by age revealed no differences, thus excluding younger children being the ones with more severe disease.

The monthly distribution confirmed the peak activity of rotavirus gastroenteritis in Austria occurring in March and is in agreement with the spread of rotavirus infection over Europe, which starts in February in Spain and ends in March/April in Norway.<sup>24</sup>

In conclusion, rotavirus infection is a relevant cause of gastroenteritis in children 48 months and younger. The present data can serve as a basis for discussion on the impact of prevention programmes to control infection. Introduction of vaccination must be based on further cost of illness and cost effectiveness studies.

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### Airline websites and health information

If you take people to exotic places do you have a duty to provide them with the information necessary for their health? Recent publicity about deep vein thrombosis has brought the risks of air travel to the front of the public mind. What about the risks of visiting tropical and subtropical countries? Should airlines be providing more information? A recent paper (Andreas Sing and colleagues. *Communicable Disease and Public Health* 2000;3:195–7) suggests that, by and large, airlines tend to avoid the issue on their websites.

The websites of 73 airlines which flew to tropical or subtropical countries were identified and 55 were found to have a functioning email address. These 55 were sent an email purporting to be from a traveller and asking for advice about malaria prophylaxis. The traveller was said to be taking an anticonvulsant drug, presumably for epilepsy, and planning to spend four weeks in a rural area of either the airline's home country (if tropical) or Thailand or Kenya. The desired answer was that mefloquine (which would usually have been recommended to non-epileptic travellers to these areas) is contraindicated in people with epilepsy and either doxycycline (in Thailand) or chloroquine and proguanil (in Kenya) should be taken instead.

They got 25 replies, 12 of which mentioned malaria. Four of the 12 said that the destination country was free of malaria when it wasn't. Only two airlines gave the wanted answer. Sixty six of the 73 airline home pages gave no medical information.

Airlines are not reliable sources of medical information. Whether they should be is perhaps debatable, as might be the use of investigative journalism techniques by doctors.

ARCHIVIST