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The Burden of Human Metapneumovirus and Respiratory Syncytial Virus Infections in Hospitalized Norwegian Children

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Background. The burden of severe human metapneumovirus (HMPV) respiratory tract infections (RTIs) in European children has not been clarified. We assessed HMPV in Norwegian children and compared hospitalization rates for HMPV and respiratory syncytial virus (RSV).

Methods. We prospectively enrolled children (<16 years old) hospitalized with RTI and asymptomatic controls (2006–2015). Nasopharyngeal aspirate samples were analyzed with polymerase chain reaction (PCR) tests for HMPV, RSV, and 17 other pathogens. We genotyped HMPV-positive samples and assessed shedding time in 32 HMPV-infected children.

Results. In children with RTI, HMPV was detected in 7.3% (267 of 3650) and RSV in 28.7% (1048 of 3650). Among controls, 2.1% (7 of 339) had low HMPV levels detected by PCR, but all were culture negative. HMPV primarily occurred from January to April and in regular epidemics. At least 2 HMPV subtypes occurred each season. The average annual hospitalization rates in children <5 years old with lower RTI were 1.9/1000 (HMPV) and 10.4/1000 (RSV). Among children with RTI, the median HMPV shedding time by PCR was 13 days (range, 6–28 days), but all were culture negative (noninfectious) after 13 days.

Conclusions. HMPV appears in epidemics in Norwegian children, with a hospitalization rate 5 times lower than RSV. Low levels of HMPV are rarely detected in healthy children.

Keywords. burden of respiratory tract infections; hospitalization rate; human metapneumovirus; respiratory syncytial virus; virus shedding time.

Human metapneumovirus (HMPV) causes upper and lower respiratory tract infections (RTIs) in children, including severe diseases, such as pneumonia and bronchiolitis, of hospitalization [1–4]. HMPV is an epidemic virus that occurs in outbreaks all over Europe [5–9] and in other continents as well [10–14]. Aberle et al [15] showed that in Austria the occurrence of HMPV had a biennial pattern, with alternating winter and spring seasons of high activity. HMPV is included in the Pneumoviridae family, with 2 main genotypes (A and B) and at least 4 subtypes (A1, A2, B1, and B2) [16–19]. Previous research has shown that HMPV genotypes A and B often circulate during the same season, whereas the dominant subtype may differ between epidemics [6, 7, 15, 19].

Although HMPV has been known for more than a decade, limited information is available concerning hospitalization rates associated with HMPV infections in European children. In 3 studies from the United States, the average annual rates of hospitalization were reported to range from 1.0 to 1.2 per 1000 children <5 years old, with higher rates in the youngest children [1, 20, 21]. Two European studies have reported somewhat higher rates [22, 23]. However, these studies had a limited duration, and there was a need for a population-based European study covering a longer period.

In recent years, sensitive polymerase chain reaction (PCR) tests have been used to detect airways viruses, and it has been shown that RTI is often associated with the detection of nucleic acids from >1 virus [4, 24]. Still, viral codetections may be common, even in asymptomatic children [25, 26]. It has been suggested that prolonged viral shedding after an infection may be one explanation of subsequent codetections in both asymptomatic and infected children [27–29]. Even so, a few studies with a limited number of patients found that HMPV may have a rather short excretion time [30, 31], which could also explain why HMPV has been detected in asymptomatic controls less often than several other respiratory viruses [1, 3].

In a population-based hospital study performed over a 9-year period, we recently reported that HMPV genotypes and viral codetections had no impact on clinical manifestations and outcomes in HMPV-infected children [4]. Moreover, we found no

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differences in age-adjusted LRTI diagnoses between HMPV and respiratory syncytial virus (RSV), whereas disease severity differed according to age: HMPV-infected children <6 months old had milder LRTIs than those with RSV, but the opposite was observed in children 12–23 months old [4].

In the present study, we aimed to assess the burden of HMPV infections in Norwegian children admitted to the hospital, compared with RSV. For this purpose, we described the occurrences of HMPV, HMPV genotypes and subtypes, and RSV using the same data set [4], and we compared population-based hospitalization rates of children with LRTI due to HMPV or RSV. In addition, we wanted to evaluate HMPV in healthy children. For that reason, we assessed the occurrence of HMPV in a group of asymptomatic hospital controls and studied the shedding time for HMPV in children with RTI.

METHODS

Study Design and Population

Children (<16 years old) admitted for acute RTI with a nasopharyngeal aspirate (NPA) sample obtained for clinical indications were prospectively enrolled at the Pediatric Emergency Department and Pediatric Department at St Olavs Hospital, University Hospital of Trondheim, Norway, from November 2006 to July 2015 (Supplementary Figure S1*A*). Children receiving cytostatic or immunosuppressive treatment were excluded. During the period from June 2007 to April 2015, similarly aged children hospitalized for elective surgery were prospectively enrolled as healthy controls (Supplementary Figure S1*B*). No controls were admitted for ear, nose, and throat surgery, and controls with caregiver-reported symptoms of RTI during the past 2 weeks or at inclusion were excluded.

The hospital is the only hospital for children in Sør-Trøndelag County in mid-Norway, with a population of 58 443 children <16 years and 18 768 children <5 years of age [32]. Informed written consents to participate were collected during the hospital stay from caregivers for most of the children and from children aged ≥12 years. Some children with RTI were enrolled after hospital discharge after passive consent; caregivers received written information, and children were included if the caregivers did not resist enrollment by contacting the hospital within 2 weeks. In addition, we enrolled some children with acute HMPV infection, who were available for analyses of HMPV shedding time. These children were sampled during the hospitalization period and regularly after discharge during home or outpatient visits, and until the HMPV test results turned negative. We systematically collected baseline characteristics from a questionnaire filled out by caregivers. Clinical information was abstracted from medical records, and Regional Committees for Medical and Health Research Ethics, Central Norway, approved the study.

Clinical Classifications and Laboratory Investigations

Children admitted for acute RTI were examined and treated routinely at the discretion of physicians; upper RTI and lower RTI (LRTI) were diagnosed as described elsewhere [4]. The NPA samples were collected from children with RTI at admission and during general anesthesia in the controls, and they were placed in a standard virus transport medium without antibiotics. Flocked swabs (Copan Italy) were used to collect follow-up nasopharyngeal samples and placed immediately into a transport medium (UTM-RT; Copan Italy).

All samples were analyzed at the Department of Medical Microbiology, St Olavs Hospital, University Hospital of Trondheim, using in-house TaqMan real-time PCR assays and conventional viral cultures for 19 respiratory pathogens, as described elsewhere [4, 33]. Semiquantitative results from the PCR tests were based on the cycle threshold value (Ct value), with values >42 regarded as negative. In all, 222 HMPV-positive specimens (83%) were genotyped using real-time PCR and DNA sequencing by primers targeting the F gene of HMPV [18], as described elsewhere [4]. Some NPA samples were not typeable owing to low viral loads, and others were not available. Phylogenetic comparisons were performed of F gene sequences of 169 isolates from patients and 36 GenBank sequences representing each of the 5 described HMPV subtypes (A1, A2a, A2b, B1, and B2). Multiple sequences were aligned using MUSCLE (version 1) and Clustal W (version 1.2.2) software (available for free from http://www.ebi.ac.uk/). Phylogenetic analysis was inferred using the neighbor-joining method, with evolutionary distances calculated with the Tamura-Nei method and Geneious software (version 9.0.2).

Definitions and Statistical Analyses

A season was defined as the beginning of August to the end of July of the following year. An epidemic was the time between onset month and offset month during 1 season. The onset month was the first of 2 consecutive months when the monthly proportion of all NPA samples was ≥10% positive for a virus. The offset month was the last month when the monthly positive proportion for a virus was ≥10%, preceding 2 consecutive months with <10% positive samples. The peak activity month during an epidemic was the month with the most children with the respective virus. Sixteen children had both HMPV and RSV in their NPA samples and were included in the HMPV group.

To calculate annual hospitalization (incidence) rates we used study data, *International Classification of Diseases, 10th Revision* (ICD-10) diagnosis statistics from the patient administrative system and population data from Statistics Norway [32]. These data were categorized by age group and season. From our study, we calculated the number of HMPV- and RSV-positive children with LRTI diagnosis hospitalized for ≥24 hours. Twelve children with LRTI had both HMPV and RSV and were included in the HMPV group. These ICD-10 codes included pneumonia (J10.0,

J11.0, J12.0–J12.9, and J13–J15), bronchitis (J20), bronchiolitis (J21), unspecified LRTI (J22), and asthma exacerbation (J45–46).

The duration of HMPV shedding was estimated by Kaplan-Meier analysis in 32 available children. In total, 93 respiratory specimens, 3 per child on average, were collected at median intervals of 4.0, 8.5, and 13.0 days after symptom onset. Four HMPV-positive specimens in the last sampling were censored. Samples with Ct values >42 were encoded with a Ct value ≥42.1 for the HMPV shedding analysis.

We used χ^2, Fisher exact, Student *t,* Mann-Whitney *U,* or Kruskal-Wallis tests to compare categorical, parametric, and nonparametric variables, as appropriate. Repeated measures were analyzed by means of Friedman test for ordinal and Cochran *Q* test for dichotomous variables. Differences were considered statistically significant at $P < .05$ (2 sided), and data were analyzed using IBM SPSS Statistics 22 and SigmaPlot 13.0 software.

RESULTS

HMPV and RSV Among Children with RTI and Asymptomatic Controls

Among 3650 children admitted with RTI, HMPV was detected in 7.3% (267 of 3650), RSV in 28.7% (1048 of 3650); 64.0% had other viruses or were virus negative (Supplementary Figure S1*A*). Infected children with HMPV and RSV had median ages of 17.7 (interquartile range [IQR], 9.1–29.7) and 7.4 (2.5–17.7) months ($P < .001$), respectively. Baseline and clinical characteristics are presented in Table 1. Three children were hospitalized twice with HMPV infection within a 5-year period, elicited by unknown or different subtypes. Among the asymptomatic controls, with a median age of 39.4 (IQR, 21.0–63.3) months, HMPV was detected in 2.1% (7 of 339) and RSV in 3.2% (11 of 339) (Supplementary Figure S1*B*). HMPV and RSV more frequently were detected among children with RTI than among controls (both $P < .001$). The median Ct value of HMPV among children with RTI (28.0; IQR, 24.2–32.1) was lower than among controls (38.9; 37.6–39.2) ($P < .001$). In all 43.8% of infected children (117 of 267) were HMPV culture positive at admission, compared with none of the controls (0 of 7). Similarly, the median Ct value of RSV among children with RTI (23.5; IQR, 20.9–26.8) was lower than among controls (30.9; 30.3–33.2) ($P < .001$), and 91.4% (958 of 1048) and 54.5% (6 of 11), respectively, were RSV culture positive in the same 2 groups.

Seasonal Trends and Epidemics

The detection of HMPV varied from 2.6% to 12.4% of the samples in each of 9 seasons, an average of 7.3% per season (Supplementary Figure S2). RSV was more frequent than HMPV, with rates that varied from 21.3% to 39.0%, an average of 28.7% per season. Analyses of the monthly HMPV distribution during all 9 years showed that HMPV appeared mostly from January to April (74.2%; 198 of 267 samples). Going more into detail, HMPV appeared from January to March in 62.5%, from April to June in 23.2%, from October to December in 13.1%, and from July to September in 1.1%. Furthermore, the occurrence of HMPV in the period from January to March was equal in odd and even years (even year: eg, 2006–2007) ($P = .73$) (Supplementary Figure S3). RSV was particularly frequent from January to March (71.2%; 746 of 1048). Considering epidemics, HMPV appeared from October to July in 2–6 consecutive months, with a median outbreak duration of 3.5 months (Supplementary Figure S2). Four seasons had peak activity in January and February, and the other 4 seasons had peak activity in March or later. The winter HMPV epidemics had higher peaks (winter vs spring-summer, 11–20 vs 3–8 HMPV positive per month) and a longer duration (median for winter vs spring-summer, 5 vs 2.5 months) than the spring-summer HMPV epidemics ($P = .004$ and $P = .057$, respectively). RSV epidemics occurred in all 9 seasons and had a median duration of 5 months, varying from 5 to 8 months, from October to July. RSV epidemics had a longer median duration than HMPV epidemics ($P = .01$), and HMPV epidemics appeared before, during, or after RSV epidemics.

Table 1. Baseline and Clinical Characteristics of Children with RTIs Due to HMPV and RSV

	Children, No. (%)[a]	
Characteristic	HMPV[a] (n = 267)	RSV (n = 1048)
Age, median (IQR), mo	17.7 (9.1–29.7)	7.4 (2.5–17.7)
Age group		
<6 mo	41 (15.4)	462 (44.1)
6–11 mo	46 (17.2)	187 (17.8)
12–23 mo	89 (33.3)	256 (24.4)
24–59 mo	75 (28.1)	126 (12.0)
≥60 mo	16 (6.0)	17 (1.6)
Male sex	154 (57.7)	603 (57.5)
Premature birth (gestational age <36 wk)	51 (19.1)	147 (14.0)
≥1 chronic disease	89 (33.3)	187 (17.8)
URTI	33 (12.4)	42 (4.0)
LRTI	234 (87.6)	1006 (96.0)
Bronchiolitis	89 (33.3)	657 (62.7)
Pneumonia	84 (31.5)	201 (19.2)
Asthma exacerbation	35 (13.1)	107 (10.2)
Obstructive bronchitis	11 (4.1)	31 (3.0)
Unspecified	15 (5.6)	9 (0.9)
Outpatient (hospital stay, <24 h)	64 (24.0)	69 (6.6)
Inpatient (hospital stay, ≥24 h)	203 (76.0)	979 (93.4)
URTI	17 (8.4)	35 (3.6)
LRTI	186 (91.6)	944 (96.4)
Length of stay of inpatients, median (IQR), d	4.0 (2.0–6.0)	4.0 (2.0–6.0)

Abbreviations: HMPV, human metapneumovirus; IQR, interquartile range; LRTI, lower respiratory tract infection (RTI); RSV, respiratory syncytial virus; URTI, upper RTI.

[a]Data represent No. (%) of children unless otherwise specified.

[b]Sixteen children had both HMPV and RSV and were included in the HMPV group only.

HMPV Genotypes and Subtypes

Genotype B was detected in 56.8% (126 of 222 samples) and genotype A in 43.2% (96 of 222). HMPV A and B cocirculated each season, although the distributions of each genotype changed during the seasons ($P < .001$) (Figure 1 and Supplementary Table S1). Among the samples positive for HMPV genotype B, 37 were subtype B1 and 89 were subtype B2. In genotype A, 12 samples were subtype A2a, 80 were subtype A2b, and 4 were subtype A2 (unassigned), and no samples were positive for subtype A1. Two or more subtypes were detected every season, and 1 or 2 subtypes dominated in each season. Phylogenetic analyses of the F gene region showed that several strains circulated each year. No clusters or new strains were detected during the 9-year study period (Supplementary Figure S4).

LRTI Hospitalization Rates During 9 Seasons

Altogether, 1130 children were hospitalized with LRTI due to either HMPV (n = 186) or RSV (n = 944). The mean annual hospitalization rate for HMPV-associated LRTI in children <5 years old was 1.9/1000 children (Table 2). The youngest children (0–11 months old) had hospitalization a rate of 3.1/1000 children, and those 12–23 months old had a rate of 3.4/1000 children. Children with RSV had higher hospitalization rates than those with HMPV: 10.4/1000 children <5 years old, 27.5/1000 children 0–11 months old, and 14.7/1000 children 12–23 months old. In children ≥24 months old, the rates gradually decreased in both HMPV- and RSV-infected children with increasing age.

Shedding of HMPV

Among all HMPV-positive inpatients, 32 were available for the shedding analyses. They had a median age of 16.0 months (IQR, 7.5–26.8), 30 of 32 had LRTI and 2 of 32 had upper RTI (Supplementary Table S2). A Kaplan-Meier analysis estimated that 50% (median) and 100% of 32 children were PCR negative for virus after 13.0 (95% confidence interval, 11.5–14.5) and 28.0 days, respectively, from the onset of symptoms (Figure 2), with the shedding time varying from 6.0 to 28.0 days. The NPA samples obtained at admission had a median Ct value of 23.8, and 84.4% (27 of 32) were culture positive (Supplementary Table S2). The first follow-up samples had a median Ct value of 34.7, and only 15.6% (5 of 32) were still culture positive. The second follow-up samples had a median Ct value ≥42.1, the value encoded for virus-negative samples, and none of 20 samples was culture positive. The median Ct values gradually increased, and the rate of culture-positive samples gradually decreased from admission to the first and second follow-up samples (both $P < .001$), and all children showed gradual improvement.

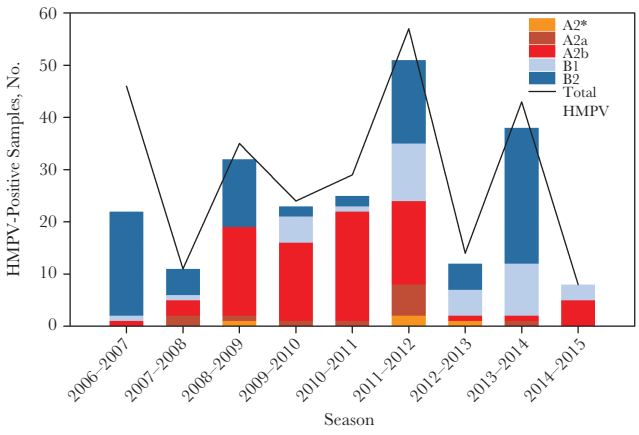

Figure 1. Distribution of human metapneumovirus (HMPV) and HMPV subtypes during 9 seasons. The number of HMPV-positive samples is shown by season. Total HMPV (*black line*) represents the total number of HMPV-positive samples, including samples with known and unknown subtypes. A2* represents unassigned A2.

DISCUSSION

The present data from our population-based study performed over nearly 9 years show that HMPV is associated with a substantial disease burden and causes an annual average of 1.9 hospitalizations per 1000 Norwegian children <5 years old, although HMPV is still associated with a 5 times lower hospitalization rate than RSV. Several findings have confirmed that HMPV is an epidemic virus. First, HMPV occurred in regular winter and spring-summer outbreaks during the entire study period. Second, the infected children initially had high viral levels but a short viral shedding time. Finally, no asymptomatic controls had an HMPV-positive culture, although a few had low levels of HMPV as detected by PCR.

On average, HMPV was detected in 7.3% of all children admitted with RTI during the whole period, but it varied considerably from only 2.6% to 12.4% per season. Most previous studies from countries in the Northern hemisphere measured the occurrence over shorter periods but found relative similar figures and seasonal variations [1, 3, 8, 13–15]. HMPV appeared mostly from January to April and regularly caused outbreaks lasting a median of 5 months, peaking in the winter months. Smaller outbreaks with a median duration of 2.5 months occurred during the spring and early summer months and coincided with a reduction in the total number of children admitted with RTIs. In addition, the occurrence of HMPV from January to March was quite similar in both odd and even years, in contrast to observations from southern Europe, with alternating epidemics in winter and spring-summer every other year [15, 34]. We speculate as to whether this difference may reflect the colder climate in our country compared with southern Europe [35]. RSV outbreaks occurred in every season, lasted an average of 5 months, and most often peaked in January to March. As reported elsewhere, HMPV outbreaks appeared before, overlapping with, or after RSV outbreaks [5].

We detected all known HMPV subtypes, except for subtype A1, with subtype B2 being the most frequent over the entire period. In line with other studies [6, 7, 15, 19], the distribution of subtypes showed great seasonal variation. In every season,

Table 2. Hospitalization Incidence Rates in Children with LRTI, by Virus (HMPV or RSV), Season, and Age

	Hospitalizations per 1000 Children with LRTI									
	Age 0–11 mo		Age 12–23 mo		Age 24–59 mo		Age 5–16 y		Age 0–59 mo	
Season	HMPV	RSV	HMPV	RSV	HMPV	RSV	HMPV	RSV	HMPV	RSV
2006–2007	5.9	24.9	4.3	17.9	1.8	2.2	0.2	0.2	3.2	10.4
2007–2008	0.5	35.2	2.4	8.9	0.0	3.3	0.0	0.0	0.5	11.6
2008–2009	4.0	19.7	5.0	13.4	1.2	1.5	0.1	0.1	2.5	8.3
2009–2010	3.4	25.2	1.0	13.6	1.2	2.5	0.0	0.0	1.6	9.5
2010–2011	2.4	31.8	2.5	12.9	0.6	3.7	0.0	0.1	1.3	12.1
2011–2012	5.2	18.2	6.9	12.6	2.1	1.3	0.1	0.0	3.7	7.3
2012–2013	1.5	40.7	1.3	19.4	0.5	2.9	0.0	0.1	0.8	14.1
2013–2014	2.7	18.2	6.4	10.1	1.2	1.5	0.1	0.0	2.4	6.6
2014–2015	2.5	33.3	1.0	23.1	1.0	2.1	0.0	0.4	1.3	13.4
Mean (95% CI)	3.1 (2.0–4.2)	27.5 (22.1–32.9)	3.4 (1.9–4.9)	14.7 (11.7–17.7)	1.1 (.7–1.5)	2.3 (1.8–2.8)	0.06 (.01–.11)	0.1 (.03–.17)	1.9 (1.2–2.6)	10.4 (8.6–12.2)

Abbreviations: CI, confidence interval; HMPV, human metapneumovirus; LRTI, lower respiratory trace infection; RSV, respiratory syncytial virus.

1 or 2 subtypes dominated and at least 2 subtypes circulated, but no new strains or clusters were detected. We have reported elsewhere that HMPV genotypes and subtypes were associated with very similar clinical manifestations [4].

In the present study, the average annual hospitalization rate for HMPV-related LRTI over 9 seasons was 1.9/1000 children <5 years old. Children in the youngest age groups had higher rates. We used a strict definition of severe HMPV infection, including only children with a hospital stay ≥24 hours and LRTI, which might explain why our estimates differ from those 3 US studies including a broader spectrum of respiratory infections, which reported estimated hospitalization rates of 1.0–1.2 per 1000 children <5 years old [1, 20, 21]. Two European studies reported HMPV-related hospitalization rates comparable to ours. A study from Spain [23], based on 3 seasons, reported that 2.6/1000 children <3 years old were hospitalized, and in a single-season study from the United Kingdom [22] the reported hospitalization rate was 1.3/1000 children <6 years old. Our finding of a higher hospitalization rate in children 12–23 months old differ with the findings in all previous studies [1, 20–23] and may also relate to our strict inclusion criteria. The hospitalization rates of children with RSV-related LRTI in our study were in line with findings from previous Norwegian [36], European [37, 38] and American studies [39, 40], thereby confirming that HMPV causes hospitalization less often than RSV in Europe and the United States.

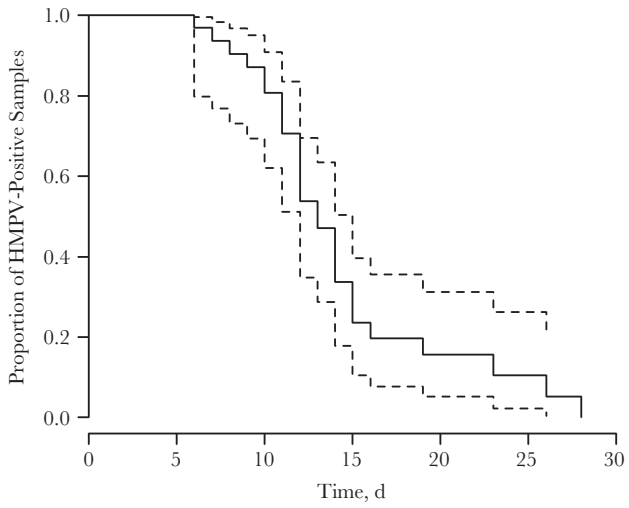

Figure 2. Kaplan-Meier analysis of human metapneumovirus (HMPV) shedding time in children with respiratory tract infection, showing the estimated proportion of HMPV-positive nasopharyngeal samples by the time from onset of symptoms until an HMPV-negative sample. Estimated proportions (*solid line*) are presented along with 95% confidence intervals (*dashed lines*).

To test the hypothesis that low detection rates and low levels of HMPV in healthy children may be a result of virus shedding after previous RTI, we first measured the rate of HMPV-positive samples among a group of asymptomatic children. A few percent had a positive PCR test with high Ct levels, thus corresponding to low viral loads, but all were virus negative by culture. We also studied a group of children with HMPV infection with repeated specimens sampled, who had low Ct values (high viral loads) and a high rate of positive cultures initially. During the progress of the disease, these children improved clinically, viral loads gradually decreased and all became virus negative by culture after 13 days. Despite these changes, half of the children were still virus positive by PCR test after 13 days and all were virus negative only after 28 days. Taken together, our observations and those of others [1, 30, 31, 41, 42], suggest that a positive PCR test for HMPV in healthy children is unlikely to indicate an asymptomatic infection, and we speculate whether it instead indicates the presence of small amounts of viral nucleic acids after a previous HMPV infection. Others [41, 43] have demonstrated a 2–3-week-long shedding time in children with RSV infection, which, in a similar way may explain the low detection rate of RSV at low viral levels in the present study's controls.

As indicated by the hospitalization rates, the incidence of severe HMPV infection, decreased by age. In addition, only 1% of previously healthy children were admitted with recurrent HMPV infections elicited by unknown or different HMPV subtypes. Previous research has shown that most children become seropositive during the first 5 years of life [44], and data from experimental studies suggest that certain HMPV subtypes may not stimulate an adequate immune response in all cell types [45]. However, our clinical data indicate that healthy children usually develop a robust immunity against most HMPV subtypes during childhood. On the other hand, outside a hospital setting, others have shown that HMPV may still cause recurrent mild RTI in children [46] and adults [47]. Moreover, children [48] and adults [49] with impaired immunity may be prone to severe HMPV infections, even with a high seroprevalence at all ages [50].

It is a strength of the present population-based study that we prospectively enrolled children at all ages from the same county in mid-Norway, and to the only existing pediatric hospital in this region during a long period. It is also an advantage that we used the same PCR tests and viral cultivation methods during the entire period. However, the controls were sampled during anesthesia, and we have not adjusted for the fact that controls were generally older than children with RTI. Moreover, controls were not contacted after sampling to determine whether subsequent RTI symptoms had occurred. All factors might have contributed to higher viral detection rates among controls. Some HMPV-positive samples were not genotyped, and a few were unassigned A2. Hence, the A1 subtype might have been present, and the pattern of circulating HMPV subtypes might have been even more heterogenic than described.

In conclusion, HMPV occurs in winter and spring-summer epidemics in Norwegian children, but the hospitalization rate is 5 times lower than for RSV. All known HMPV subtypes circulate in Norway, except A1. Children are rarely hospitalized twice with HMPV infection. Children have a short HMPV shedding time and may not be infectious after 13 days, and the short shedding time may also explain the low HMPV detection rate among asymptomatic children.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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