

**TABLE 1.** Parasite Distribution by Species and Pupil Gender Among Finger-sucking and Nonfinger-sucking Children

Parasite	Population Occurrence N (%)	Finger-sucking			Nonfinger-sucking		
		Male	Female	Total	Male	Female	Total
<i>Entamoeba histolytica</i>	44 (33)	14 (35)	16 (38)	30 (37)	6 (26)	8 (29)	14 (28)
<i>Ascaris lumbricoides</i>	30 (23)	10 (25)	9 (21)	19 (23)	4 (17)	7 (25)	11 (22)
<i>Enterobius vermicularis</i>	23 (17)	6 (15)	7 (17)	13 (16)	4 (17)	6 (21)	10 (20)
<i>Trichuris Trichiura</i>	19 (14)	4 (10)	6 (14)	10 (12)	4 (17)	5 (18)	9 (18)
<i>Giardia duodenalis</i>	17 (13)	6 (15)	4 (10)	10 (12)	5 (22)	2 (7)	7 (14)
Total	133	40	42	82 (62)	23	28	51 (38)

of the environment in the study community.<sup>13,14</sup> School age children have also been known to be more exposed to the risks of being infected with these fecal oral parasites because of their poor level of personal hygiene, coupled with the fact that they involve themselves in activities that facilitate contact with the soil where the ova and cysts of these parasites are found. The toilet facilities available to most of these school children have also been reported to be poorly used and lack regular water supply.<sup>11</sup>

There was no significant difference in sex regarding parasite infection among FS pupils, but a higher percentage of females (82%) were infected than males (46%) among NFS pupils. This is similar to the result of Ekpenyong and Eyo study,<sup>8</sup> in which prevalence of infection was significantly more common in females than males.

History of previous treatment of intestinal parasites had no effect on the prevalence of infection among FS pupils as observed in this present study. All finger suckers who had been previously treated for these parasites and those who had not been treated were positive for infection. This shows that the FS habit exposed these pupils to reinfection, despite previous treatment of the parasites. An earlier study in Abeokuta and other towns in the state using a Monrate tool predicted a 3-month reinfection period for helminth in school children,<sup>10,15</sup> FS would probably increase the reinfection period because of the continuous hand-to-mouth activities of FS children.

These results strengthen the need for education of parents and their children on the risks associated with FS, especially in areas where there is a high level of fecal contamination. The need to improve sanitary conditions is also to be emphasized.

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## THE BURDEN OF INFECTIONS BY PARAINFLUENZA VIRUS IN HOSPITALIZED CHILDREN IN SPAIN

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**Abstract:** We designed a prospective study to describe the clinical impact of the parainfluenza virus (PIV) types detected in hospitalized children with respiratory tract infections from September 2008 to August 2010 in Spain. PIV infections were a significant proportion of viral respiratory detections (11.8% of cases). PIV types 3 and 4 were most commonly detected. There were clinical differences between PIV and respiratory syncytial virus infections.

**Key Words:** parainfluenza virus, respiratory tract infections, hospitalized children

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Parainfluenza viruses (PIVs) are responsible for a significant proportion of respiratory tract infections in children. The rate of PIV detections is variable depending on the pathology (upper or lower tract infections) and whether one simulates ambulatory or

hospitalized children. A few articles have focused on this virus in the last years.<sup>1-3</sup>

Human PIVs are divided into following 2 genera: respirovirus (types 1 and 3) and rubulavirus (types 2 and 4). PIV types 1 and 2 are associated with laryngotracheobronchitis and type 3 with lower tract infections such as bronchiolitis, recurrent wheezing, and pneumonias. Type 4, although less frequent, is associated with lower respiratory infections in infants.<sup>4</sup> There are few data about this type of PIV.

We designed a prospective study with the objective of describing the clinical impact of the different PIV types detected in hospitalized children with respiratory tract infections in Spain. To clarify whether PIV infections have specific characteristics, clinical and epidemiologic features were compared with respiratory syncytial virus (RSV) infections, the most prevalent respiratory virus in the same population.

## MATERIALS AND METHODS

**Clinical Assessment.** The study population comprised of all children less than 14 years old with a respiratory tract disease admitted to the secondary public hospital Severo Ochoa (Leganés, Madrid), between September 2008 and August 2010. The study was approved by The Medical Ethics Committee. Informed consent was obtained from parents or legal guardians. All patients were evaluated by an attending physician. Clinical characteristics of patients with PIV detection were analyzed. During the hospital stay, and as part of the study, a physician filled out a study-questionnaire with the clinical data.

Upper respiratory tract infection was diagnosed in patients with rhinorrhea and/or cough, no signs of wheezing, dyspnea, crackles or bronchodilator use, with or without fever. Asthma was diagnosed on the basis of the National Asthma Education and Prevention Program guidelines.<sup>5</sup> All other episodes of acute expiratory wheezing were considered to be recurrent wheezing. Acute expiratory wheezing was considered to be bronchiolitis when it occurred for the first time in children younger than 2 years. Laryngotracheobronchitis was associated with inspiratory dyspnea and wheezing and laryngitis with inspiratory dyspnea without wheezing. Cases with both focal infiltrates and consolidation in chest radiographs were, in the absence of wheezing, classified as pneumonia.

**Virus Detection.** Specimens from patients consisted of nasopharyngeal aspirates (NPA) taken from each patient at admission (Monday through Friday). Each specimen (1 for each patient) was sent for virologic investigation to the Influenza and Respiratory Virus Laboratory at the National Microbiology Center (ISCIII, Madrid, Spain). Specimens were processed within 24 hours after collection. Upon receipt of NPAs, 3 aliquots were prepared and stored at  $-70^{\circ}\text{C}$ . The reception and the NPA sample aliquoting areas were separate from those defined as working areas.

**Polymerase Chain Reaction Methods for Detection of 16 Respiratory Viruses.** Three reverse transcription (RT)-nested polymerase chain reaction (PCR) assays were performed to detect the 16 respiratory viruses. In these assays, RT and first amplification round were carried out in a single tube using the Qiagen OneStep RT-PCR kit (Qiagen). Influenza A, B, and C viruses were detected by using previously described primer sets only to amplify influenza viruses in a multiplex PCR assay.<sup>6</sup> A second multiplex PCR was used to detect PIVs 1 to 4, human coronaviruses 229E and OC43, enteroviruses (EV), and rhinoviruses (RV).<sup>7</sup> Presence of RSV-A and -B types, hMPV, HBoV, and adenoviruses (AD) were investigated by a third multiplex RT-nested PCR-bronchiolitis method.<sup>8</sup>

**Statistical Analysis.** Values were expressed as percentages for discrete variables, or as mean and standard deviation for continuous variables. Clinical characteristics of patients with infections associated with PIV were compared with those associated with

infection by RSV. Clinical characteristics and laboratory variables were compared using the Student *t* test, the Mann-Whitney *U* test, the  $\chi^2$  test, and Fisher exact test. A 2-sided value of  $P < 0.05$  was considered statistically significant. Results were adjusted to age. All analyses were performed using the Statistical Package for the Social Sciences, version 13.0 (SPSS Inc., Chicago, IL).

## RESULTS

**Patient Characteristics and Screening of Viruses.** The study population consisted of 1106 hospitalized children less than 14 years old. A total of 916 patients were analyzed and 190 patients were excluded either because of lack of NPA samples or because they refused to participate. One NPA sample was included in the study from each patient and positive results were obtained in a total of 740 NPA samples (80.8% of the 916 tested). Out of positive samples, 540 were single virus infections (73%) and 200 children had dual or multiple viral infections (27%). Specific viruses detected and identified in the total population of 916 children are listed in Table 1, in descending order of frequency.

PIVs were detected in 82 patients, 11.8% of positive cases, 8.9% of the whole analyzed group. There were 47 males (57.3%), 57 had fever (69.5%), 43 had hypoxia (52.4%), and in 33 an infiltrate was present in chest radiographs (40.2%). Antibiotic therapy was prescribed for 24 patients (29.3%). Fourteen children had been born preterm (17.1%). The mean age of the group was  $522 \pm 586$  days, and the stay in the hospital was  $3.7 \pm 1.2$  days. Diagnoses in order of frequency were recurrent wheezing or asthma (45%), bronchiolitis (26%), pneumonia (14%), and laryngitis (5%). PIV type 1 was detected in 12 cases (14.6%), PIV type 2 in 8 cases (9.8%), PIV type 3 in 47 cases (57.3%), and PIV type 4 in 15 cases (18.3%). Thirty-six patients had associated coinfection with other viruses (43%), mainly rhinovirus and adenovirus. Two patients were admitted to the intensive care unit suffering pneumonia with pleural effusion.

**Clinical Findings Associated With the Presence of the 4 PIV Types.** PIV was detected in 82 patients, of whom 46 had only PIV. Table, Supplemental Digital Content 1, <http://links.lww.com/INF/A767>, shows clinical data about PIV 3 and 4 infections, because they were the most prevalent groups in our population.

We observed an increased proportion of single infections associated with PIVs in relation with other viruses. In a previously published article of our group,<sup>9</sup> during 2005 to 2007 single PIV infections were 4.8% of the total viral infections in the same population, and in the present study the proportion was 11.8%. We observed an increase of the proportion of PIV 3 and 4 infections during the period of study. Notably, 55% of the cases were detected in the last year, 2010 ( $P = 0.06$ ).

**TABLE 1.** Frequency of Viruses Detected in 916 Children Hospitalized for Respiratory Tract Infections\*

Total Virus (n = 970)	N (%)	Single Infections (n = 540)
Respiratory syncytial virus	261 (26.9%)	170 (31.6%)
Rhinovirus group	282 (29%)	160 (29.6%)
Adenovirus group	90 (9.3%)	36 (6.6%)
Parainfluenza virus	82 (8.4%)	46 (8.5%)
Human bocavirus	77 (7.9%)	17 (3.1%)
Human metapneumovirus	66 (6.8%)	45 (8.3%)
Influenza virus	66 (6.8%)	55 (10.2%)
Enterovirus	24 (2.5%)	8 (1.5%)
Coronavirus	22 (2.3%)	2 (1.5%)

\*Patients, 916; single infections, 540; multiple infections, 200; and negatives, 176.

**Clinical Differences Between PIV and RSV Infections.** Clinical characteristics of PIV single virus infections were compared with RSV single infections in the same period ( $n = 170$ ). Data are shown in Table, Supplemental Digital Content 1, <http://links.lww.com/INF/A767>. Patients with RSV infection had hypoxia more frequently (73% vs. 50%,  $P = 0.01$ ) and during more days (2.9 vs. 1.95,  $P = 0.003$ ). Bronchiolitis was more frequent in RSV group (58% vs. 28%,  $P = 0.001$ ). Children with RSV infection were younger than those in the PIV groups ( $348 \pm 447$  vs.  $626 \pm 725$  days,  $P = 0.05$ ). Five patients diagnosed as bronchiolitis associated with RSV infection (4 of them with single infection), needed intensive care admission. All of them were less than 2 months of age. When results were adjusted to age (we stratified at 12 months), fever ( $P = 0.05$ ) and hypoxia ( $P = 0.02$ ) were more frequent in RSV group. Pneumonia was more frequent in PIV group ( $P = 0.02$ ), and children up to 12 months received antibiotherapy more frequent in this group ( $P = 0.08$ ). In the group of infants (<12 months), prematurity was more frequent in PIV group.

Circulation of RSV was maximal in December and the peak of PIVs circulation depended of the specific type but was statistically significant in March ( $P = 0.001$ ).

## DISCUSSION

PIV types 1 to 4 infections have a significant prevalence in hospitalized children in Spain, accounting for 11.8% of the viral infections. PIV 3 and 4 were the most important types in our population, and the main associated diagnoses were asthma or bronchiolitis.

A major strength of this study is the use of 3 multiplex RT-PCR assays, with a very high sensitivity and specificity for a complete range of respiratory viruses over 2 full calendar years. Influenza A/H1N1pdm was included in the second year. Except for CoV-NL63 and HKU1 and the recently identified polyomavirus KU, and WU, the rest of the respiratory viruses were successfully detected and identified. These technologies allow us to attribute the presence/absence for each of the 17 different viruses or group of viruses (RV, ADV, and EV). This fact, also explains the high percentage of viral agents identified (80.8%), and allows us to know the real burden of PIV infections in hospitalized children. In this context, including the influenza A/H1N1pdm pandemic peak, PIV infections were 11.8% of the positive cases (8.6% of the total group). Influenza infections were only 6.8% of the total group. There are few data about the relative burden of PIV infections. Other studies analyzed only some types of PIV,<sup>10</sup> and included outpatient<sup>1</sup> and hospitalized children.<sup>3</sup> Between 2006 and 2008, Farichock et al<sup>1</sup> while studying daycare toddlers found that PIV infections were 12% of the total respiratory viral infections, but these authors did not study human bocavirus, and did not specify how many children needed hospitalization. In our experience, between 2005 and 2007<sup>9</sup> in a similar population, we found that PIV infections were only 4.8% of total viral compared with 8.5% in the present study. This difference could be explained by annual variations.

Although, virus detection is common in NPA of children without respiratory diseases, our group published a study in 116 healthy children, and PIV was detected only in 1 patient.<sup>11</sup>

Clinical characteristics of PIV infections differed among types. PIV 1 and 2 were less frequent in hospitalized children than PIV 3 and 4. PIV 3 was the most frequent type identified in hospitalized children in previous studies<sup>1,3</sup> and mainly associated with lower respiratory tract infections (recurrent wheezing and asthma) in agreement with our data. PIV 4 is probably underestimated in the literature because few studies included the specific detection of this PIV type. Nevertheless, when PIV 4 was looked

for, it was identified in an important proportion of cases and it was associated with lower respiratory tract infections mainly in infants.<sup>1,4</sup> Comparing PIV infections with those due to RSV several significant differences were observed. RSV patients were younger than PIV children, and the most frequent clinical diagnosis was bronchiolitis. Hypoxia was more frequent and prolonged in RSV children. These data support the idea than RSV infections are more severe than those where a PIV is detected. The younger age of the patients could be an important risk factor. Nevertheless, the proportion of cases needing intensive care unit was similar in both infections.

PIV 1 and 2 were mainly detected in autumn (October) and PIV 3 and 4 in spring with an incidence peak in March. These data are in agreement with previous studies.<sup>3</sup> RSV infections occurred mainly in December and January.

We conclude that PIV infections are a significant proportion of viral respiratory detections in hospitalized children.

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## A TWICE DAILY POSACONAZOLE DOSING ALGORITHM FOR CHILDREN WITH CHRONIC GRANULOMATOUS DISEASE

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**Abstract:** Posaconazole (PSZ) may be an attractive alternative for antifungal prophylaxis in children with chronic granulomatous disease. Expe-