Seasonal Invasive Pneumococcal Disease in Children: Role of Preceding Respiratory Viral Infection
Krow Ampofo, Jeffrey Bender, Xiaoming Sheng, Kent Korgenski, Judy Daly, Andrew T. Pavia and Carrie L. Byington

Pediatrics 2008;122;229
DOI: 10.1542/peds.2007-3192

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/122/2/229.full.html
Seasonal Invasive Pneumococcal Disease in Children: Role of Preceding Respiratory Viral Infection

Krow Ampofo, MB, BS*, Jeffrey Bender, MD*, Xiaoming Sheng, PhD*, Kent Korgenski, MS, MT(ASCP)*, Judy Daly, PhD*, Andrew T. Pavia, MD*, Carrie L. Byington, MD*

*Division of Pediatric Infectious Diseases, Department of Pediatrics, and Department of Family and Preventive Medicine, University of Utah Health Sciences Center, Salt Lake City, Utah; †Primary Children’s Medical Center, Intermountain Health Care, Salt Lake City, Utah

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVE. Our objective was to demonstrate correlations between invasive pneumococcal disease in children and circulating respiratory viruses.

METHODS. This retrospective study included 6 winter respiratory viral seasons (2001–2007) in Intermountain Healthcare, an integrated health system in the Intermountain West, including Primary Children’s Medical Center in Salt Lake City, Utah. Children <18 years of age who were hospitalized with either invasive pneumococcal disease in any Intermountain Healthcare facility or culture-confirmed invasive pneumococcal disease at Primary Children’s Medical Center were included. We analyzed the correlation between invasive pneumococcal disease and circulating respiratory viruses.

RESULTS. A total of 435 children with invasive pneumococcal disease and 203 with culture-confirmed invasive pneumococcal disease were hospitalized in an Intermountain Healthcare facility or Primary Children’s Medical Center during the study period. During the same period, 6963 children with respiratory syncytial virus, 1860 with influenza virus, 1459 with parainfluenza virus, and 818 with adenoviruses were evaluated at Primary Children’s Medical Center. A total of 253 children with human metapneumovirus were identified during the last 5 months of the study. There were correlations between invasive pneumococcal disease and seasonal respiratory syncytial virus, influenza virus, and human metapneumovirus activity. The correlation with invasive pneumococcal disease was strong up to 4 weeks after respiratory syncytial virus activity. For influenza virus and human metapneumovirus, the correlations were strong at 2 weeks after activity of these viruses. Pneumonia was the most common clinical disease associated with culture-confirmed invasive pneumococcal disease, mostly attributable to serotypes 1, 19A, 3, and 7F.

CONCLUSIONS. In the post–pneumococcal conjugate vaccine era, seasonal increases in respiratory syncytial virus, influenza virus, and human metapneumovirus infections in children were associated with increased pediatric admissions with invasive pneumococcal disease, especially pneumonia caused by nonvaccine serotypes. Pediatrics 2008;122:229–237

INVASIVE PNEUMOCOCCAL DISEASE (IPD) continues to be a major cause of morbidity and death among children throughout the world.1–5 IPD exhibits seasonal variations, with peak incidence during the winter season in temperate regions of the world. A variety of host and environmental factors have been explored as potential explanations for the seasonality of IPD, including viral respiratory tract infections, pollution, humidity, temperature, and rainfall.6–9 An association between influenza virus (IV) and pneumococcal infection has been postulated for many years, and respiratory viral infections are more common in children than adults.10,11 However, studies examining the relationship between respiratory viral infections and IPD have shown more-consistent correlations among adults than children. Respiratory viruses that have been implicated in predisposing children to IPD include IV, respiratory syncytial virus (RSV), and adenovirus; however, the findings from previous studies have not been consistent.12
In the United States, the introduction and widespread use of the heptavalent pneumococcal conjugate vaccine (PCV-7) (Prevnar; Wyeth Lederle Vaccine, Philadelphia, PA) have been associated with decreasing rates of IPD in children <5 years of age.\(^1\)\(^-\)\(^5\) Since the introduction of PCV-7, however, many regions, including Utah, have reported increasing rates of IPD caused by non–PCV-7 serotypes in children.\(^17\)\(^-\)\(^20\) Studies exploring the association of viral infection and IPD were conducted before the profound changes in the epidemiological features of IPD resulting from the introduction of PCV-7.\(^21\)

In 2000, Primary Children’s Medical Center (PCMC) (Salt Lake City, UT) began routine respiratory viral surveillance using direct fluorescent antibody (DFA) assays and viral cultures. Despite PCV-7 vaccination rates among children in Utah similar to the US rates, IPD rates are high.\(^3\)\(^,\)\(^19\)\(^,\)\(^21\) We recognized an opportunity to examine the relationship between circulating respiratory viruses, including IV, RSV, adenoviruses, parainfluenza viruses (PIVs), and human metapneumovirus (hMPV), and IPD among children residing in Utah during the 6 years after the introduction of PCV-7.

**METHODS**

**Human Subjects Protection**

This study was approved by the institutional review boards of the University of Utah and PCMC. Informed consent was waived.

**Setting and Study Population**

PCMC is the only children’s hospital in the Intermountain West. The facility is owned and operated by Intermountain Healthcare (IH), a large, vertically integrated, health care system. PCMC is a 250-bed children’s hospital that serves both as a community pediatric hospital for Salt Lake County, Utah, and as a tertiary referral center for 5 states in the Intermountain West (Utah, Idaho, Wyoming, Nevada, and Montana). Eighty percent of pediatric hospital admissions in Salt Lake County and 73% in the state of Utah are at PCMC. The PCMC emergency department evaluates ~40 000 children per year and has ~11 000 hospital admissions per year.

Hospitalization rates for IPD, as defined below, and associations with respiratory viral activity, measured as the number of total positive tests each week, were determined for Utah-resident children <18 years of age between January 2001 and March 2007. We analyzed IPD hospitalization rates for all Utah-resident children who received care at an IH facility or at PCMC. Children evaluated at all IH facilities included those admitted to PCMC. We focused on the time period of 2001–2007 to encompass a period of changing pneumococcal epidemiological features after the introduction of PCV-7 in our region, with a predominance of respiratory IPD, particularly empyema.\(^19\) We hypothesized that there would be stronger correlations with respiratory viruses and empyema than reported previously.

**Respiratory Viral Testing**

The PCMC laboratory has offered testing for respiratory viruses (IV, RSV, PIVs, and adenoviruses) through viral cultures and DFA panels (Simulfluor respiratory screen; Light Diagnostics, Temecula, CA) since December 2000. In the autumn of 2006, hMPV (hMPV monoclonal antibody Analyte Specific Reagents conjugate; Diagnostic Hybrids, Athens, OH) was added to the respiratory viral panel. The total cost of DFA testing is approximately $36.00 per patient.

DFA testing is available throughout the year and is performed 5 times per day. Viral cultures were performed by using 4 shell vials with 72-hour and 10-day exit stains for all DFA-negative specimens from January 2001 to November 2005. In November 2005, the viral culture procedure was changed to 1 cell line (R-Mix-Too; Diagnostic Hybrids) with an exit stain at 72 hours. The sensitivity and specificity of DFA testing, compared with viral cultures, for IV, RSV, PIVs, adenoviruses, and hMPV in our institution were described previously. The sensitivity of DFA testing, compared with viral culture, was 90% for IV, 72% for IV-B, 99% for RSV, 77% for PIV, and 92% for hMPV, with specificity of ≥90% in our laboratory.\(^22\)\(^,\)\(^23\)

During the study period, direct respiratory sampling (principally nasopharyngeal aspiration) was performed for most children evaluated in the PCMC emergency department for respiratory complaints and virological testing was required for all hospitalized children with respiratory symptoms (eg, upper or lower respiratory tract infection, bronchiolitis, asthma, or bacterial or viral pneumonia). In addition, respiratory viral testing was recommended for all febrile infants 1 to 90 days of age. Test results were used to inform patient cohorting and isolation procedures and to assist with medical management.

**Identification of IPD**

For this study, IPD was defined either by using International Classification of Diseases, Ninth Revision (ICD-9), codes or by culturing. All IH facilities share a computerized data record system, the Enterprise Data Warehouse. For all IH facilities, we queried for IPD cases among Utah children <18 years of age between January 2001 and March 2007 by using ICD-9 discharge diagnosis codes specific for diseases caused by *Streptococcus pneumoniae*, including codes 038.2 and 790.7 (sepsis and/or bacteremia), 320.1 and 320.2 (meningitis), 481 (pneumonia), 510 (parapneumonic empyema), 567.1 (pneumonitis), and 711.00 (abcess), all of which had a modifier indicating infection with *S pneumoniae*.

For cases of culture-confirmed IPD, we limited our query to children admitted to PCMC. The PCMC microbiology laboratory has archived and serotyped all invasive isolates of *S pneumoniae* recovered from children cared for at PCMC since 1996 (Carrie L Byington). Culture-confirmed IPD cases were defined as cases involving children <18 years of age with *S pneumoniae* isolated from a normally sterile site (eg, blood, cerebrospinal fluid, joint, pleural, or peritoneal fluid, or abscess). The PCMC microbiology laboratory information system is linked to the IH Enterprise Data Warehouse. Data abstracted from medical records included age at the time of...
S pneumoniae isolation, diagnosis, and demographic and clinical information.

Statistical Analyses
The absolute numbers of individual respiratory viruses detected with DFA assays and viral cultures at PCMC, culture-confirmed IPD at PCMC, and ICD-9–coded IPD in any IH facility were tabulated for 2-week periods for statistical analyses and for 4-week periods for construction of graphs. Rates were derived by dividing the 2-week aggregates of IPD by the yearly total number of children <18 years of age who used an IH facility or PCMC. In the calendar period January 2001 to December 2006, 179 534 to 194 722 individual children each year used an IH health facility and 9982 to 11 995 children were admitted to PCMC. The respective burden of each respiratory virus was also derived by dividing the 2-week aggregates by the total number of individual patient samples submitted for testing during the same time period. The relationships of ICD-9–coded IPD and culture-confirmed IPD with laboratory-detected respiratory viruses were examined over the study period by using the Pearson correlation coefficient. Correlations were examined by comparing the lag time for detection of respiratory viruses and culture-confirmed IPD (date culture was obtained) and the date of admission for ICD-9–coded IPD at 0, 2, and 4 weeks.

RESULTS
Identification of Viral Respiratory Tract Infections
During the study period, 33 633 unique patient samples were submitted for respiratory viral testing at PCMC. Thirty-four percent (11 352 samples) were positive for a respiratory virus in DFA assays or viral cultures, including 6963 RSV (61.3%), 1860 IV (16.4%), 1459 PIVs (12.8%), and 818 adenoviruses (7.2%). Viral testing for hMPV with DFA assays and viral cultures was initiated in November 2006. In the last 5 months of the study, 253 cases of hMPV were identified, representing 13% of all positive tests during the 5-month period. The seasonality of respiratory viral testing and positive test results is shown in Fig 1.

Seasonality of Viral Respiratory Tract Infections
The seasonal patterns of respiratory viral testing and circulating respiratory viruses are shown in Figs 1 and 2. RSV and IV showed typical winter seasonality, with 91% of positive RSV tests between December and March and 84% of positive IV tests between November and February. Except for the 2003–2004 winter virus season, there was a complete overlap of RSV and IV peaks.

The seasonality of adenoviruses and PIVs was less pronounced. Fifty-six percent of positive adenovirus tests occurred between November and March. PIVs showed biphasic peak activity; 45% of positive tests occurred between April and June and 39% between October and January. Testing for hMPV was available for <1 year; however, all positive tests occurred between December and March (Fig 2).

ICD-9–Coded IPD in All IH Facilities
With the use of ICD-9 discharge diagnosis codes, 435 children resident in Utah were diagnosed as having IPD and were admitted to IH facilities. There was an average of 67 IPD admissions per year, with the largest number of admissions (87 admissions) occurring during the 2005 calendar year. Seasonality was observed among children with ICD-9–coded IPD, with 64% of admissions for IPD being identified between December and May each year.
Culture-Confirmed IPD in Children Treated at PCMC

During the study period, 203 Utah children had *S. pneumoniae* isolates available for evaluation at PCMC. There was an average of 33 *S. pneumoniae* isolates per year from Utah residents at PCMC, with the largest number of isolates (42 isolates) being isolated during the 2005 calendar year. Sixty-seven percent of culture-confirmed *S. pneumoniae* infections occurred between December and May each year (*P* < .001, compared with IPD diagnosed between June and November) (Fig 3).

**Culture-Confirmed IPD in Children Treated at PCMC**

During the study period, 203 Utah children had *S. pneumoniae* isolates available for evaluation at PCMC. There was an average of 33 *S. pneumoniae* isolates per year from Utah residents at PCMC, with the largest number of isolates (42 isolates) being isolated during the 2005 calendar year. Sixty-seven percent of culture-confirmed *S. pneumoniae* infections occurred between December and May each year (*P* < .001, compared with IPD diagnosed between June and November) (Fig 3).

Clinical diseases associated with *S. pneumoniae* infection are shown in Table 1. Pneumonia complicated by empyema (29%), bacteremia alone (24%), and pneumonia with bactere-
mia (22%) were the most common clinical manifestations (Table 1). Of the 203 *S. pneumoniae* isolates, 169 (83%) were nonvaccine serotypes. The most common serotypes were 1 (12% of isolates), 19A (10%), 3 (9%), and 7F (8%).

**Correlations Between ICD-9–Coded and Culture-Confirmed IPD and Circulating Respiratory Viruses**

There were correlations of the rate of ICD-9–coded IPD admissions at IH facilities and the rate of culture-confirmed IPD admissions at PCMC with the detection of respiratory viruses. As shown in Table 2, ICD-9–coded IPD admissions were correlated with the isolation of IV ($r = 0.23$; $P = .003$), RSV ($r = 0.31$; $P < .001$), and hMPV ($r = 0.31$; $P < .001$) at time 0. When time lags of 2 and 4 weeks were applied, the correlations with RSV and hMPV increased slightly. In contrast, the correlation with IV was similar at 2 weeks but slightly weaker at 4 weeks (Table 2).

Similarly, there were correlations between admissions for culture-confirmed IPD at PCMC and IV ($r = 0.19$; $P = .01$), RSV ($r = 0.34$; $P < .001$), and hMPV ($r = 0.18$; $P = .020$) at time 0. The correlation with RSV remained unchanged at 2 and 4 weeks, whereas the correlations with IV and hMPV were similar at 2 weeks but slightly weaker at 4 weeks (Table 3). There were no correlations between adenovirus and PIV activity and ICD-9–coded IPD and culture-confirmed IPD at 0, 2, or 4 weeks.

**DISCUSSION**

Respiratory viral infections have been implicated in the pathogenesis of infections with *S. pneumoniae*. In this study, we demonstrated associations in time between peaks in RSV and IV activity and IPD, whether measured as ICD-9 coding of discharges in a large population or culture-confirmed IPD at a children’s hospital. We also found a correlation between hMPV activity and IPD. To our knowledge, this is a novel observation.

Several studies found temporal associations of different respiratory viruses and IPD. Kim et al reviewed 480

---

**TABLE 1** Clinical Syndrome Associated With Culture-Confirmed IPD in Children <18 Years of Age ($n = 203$)

<table>
<thead>
<tr>
<th>Clinical Syndrome</th>
<th>$n$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal empyema with or without bacteremia</td>
<td>59 (29)</td>
</tr>
<tr>
<td>Bacteremia alone</td>
<td>49 (24)</td>
</tr>
<tr>
<td>Pneumonia with bacteremia</td>
<td>44 (22)</td>
</tr>
<tr>
<td>Meningitis with or without bacteremia</td>
<td>27 (13)</td>
</tr>
<tr>
<td>Soft-tissue abscess with or without bacteremia</td>
<td>12 (6)</td>
</tr>
<tr>
<td>Arthritis/osteomyelitis with or without bacteremia</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Peritonitis with or without bacteremia</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Other (mastoiditis)</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>

The total number of clinical syndromes is greater than the total number of patients because *Streptococcus pneumoniae* was isolated from multiple sterile sites in some children.

**TABLE 2** Correlations Between ICD-9–Coded IPD ($n = 435$) and Circulating Respiratory Viruses in Utah Over 6 Years (January 2001 to March 2007)

<table>
<thead>
<tr>
<th>Respiratory Virus</th>
<th>0-wk Lag</th>
<th>2-wk Lag</th>
<th>4-wk Lag</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>0.23 ($0.03$)</td>
<td>0.24 ($0.02$)</td>
<td>0.18 ($0.04$)</td>
</tr>
<tr>
<td>RSV</td>
<td>0.31 ($&lt;.001$)</td>
<td>0.35 ($&lt;.001$)</td>
<td>0.34 ($&lt;.001$)</td>
</tr>
<tr>
<td>PIV</td>
<td>0.03 ($0.71$)</td>
<td>−0.01 ($0.83$)</td>
<td>−0.03 ($0.66$)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>0.01 ($0.90$)</td>
<td>−0.05 ($0.51$)</td>
<td>−0.08 ($0.32$)</td>
</tr>
<tr>
<td>hMPV*</td>
<td>0.31 ($&lt;.001$)</td>
<td>0.39 ($&lt;.001$)</td>
<td>0.37 ($&lt;.001$)</td>
</tr>
</tbody>
</table>

* hMPV testing started in November 2006.
cases of IPD in children and adults over a 3-year period. They identified strong temporal associations between IPD and RSV and IV among adults. In contrast, IPD was moderately correlated with isolation of adenoviruses and all respiratory viruses (RSV and IV) among children. Interestingly, there was no association with isolation of IV alone. Watson et al., in a 1-year study in New South Wales, Australia, observed that IPD in children was correlated with isolation of RSV but not with isolation of IV. Talbot et al., reported the largest study of IPD seasonality over 7 seasons, with 4147 cases of IPD in Tennessee; 28.5% of cases involved children. The authors found strong prolonged correlations between IPD and isolation of RSV among children and adults. There was a strong correlation between IPD and isolation of IV among adults, but the correlation was much less pronounced among children.

Our results are similar in several ways to those of Talbot et al. We observed strong temporal correlations between culture-confirmed IPD and isolation of RSV and IV. The correlation was stronger and more prolonged for RSV. In contrast, we found that the correlation between IPD and IV among children was statistically significant with lag periods of 2 and 4 weeks, despite a smaller number of cases. Unique to our study is the first demonstration of a strong prolonged positive correlation between ICD-9-coded IPD and isolation of hMPV, comparable to that of RSV. Similarly, there were strong positive correlations between isolation of RSV, IV, and hMPV and culture-confirmed IPD. A major difference, however, is that the present study is the first to examine the association of viral infections and IPD in children after the widespread use of PCV-7.

The introduction of PCV-7 has led to substantial reductions in disease burden but has led to complex changes in the epidemiological features of IPD. The reduction in IPD has been most apparent for bacteremia, meningitis, pneumonia, and infections with antibiotic-resistant strains. In contrast, many studies have reported stable or increased rates of pneumonia and empyema in the United States, the United Kingdom, Canada, Spain, and France. Therefore, the relative importance of lower respiratory tract infections is increasing. In our study, encompassing 6 years after PCV-7 introduction, complicated or uncomplicated pneumonia (51%) was the most common clinical disease. Similarly, Singleton et al reported an increase in the proportion of IPD attributable to empyema and pneumonia with bacteremia among Alaskan Native children after the introduction of PCV-7. Although the overall rates of IPD remain well below baseline, many centers, including some in Utah, have reported increases in IPD attributable to non–PCV-7 serotypes. In the current study, 83% of the S pneumoniae isolates were non–PCV-7 serotypes. Without further study, it is not possible to determine how the changing epidemiological features of IPD influence the relationship between S pneumoniae and viral infection of the respiratory tract.

We must emphasize that the temporal association does not prove a causal relationship. However, many lines of evidence suggest a direct role of respiratory viruses in the pathogenesis of IPD. In vitro and animal studies have provided some clues to the potentially lethal synergism between respiratory viral infections and subsequent bacterial infections. Increased adherence of S pneumoniae, Staphylococcus aureus, and group B Streptococcus to cultured cells has been reported after preinfection of culture cells with IV, RSV, adenoviruses, and rhinovirus. Studies demonstrated the formation of RSV-pneumococcal complexes that have enhanced adherence to mouse epithelial cells and increased rates of bacteremia. In humans, recent studies demonstrated that 40% of children with severe RSV infection had concomitant lower respiratory tract bacterial infection.

Similarly, IV has been shown to increase adherence and invasion by S pneumoniae. In a mouse model, the level of neuraminidase correlated directly with the development of bacterial pneumonia. However, IV, which also produces neuraminidase, did not lead to increased bacterial pneumonia. Other lines of evidence support a causal link. During an outbreak of severe pneumococcal disease, a case-control study demonstrated that children with IPD were more likely to have an influenza-like illness and evidence of seroconversion to IV. In a study of an experimental 9-valent pneumococcal conjugate vaccine, a 45% decrease in the rate of hospitalization attributable to IV-associated pneumonia was observed. In this study, the strongest correlation between IPD and IV was at 2 weeks. It is of interest that this seems to corroborate historical data on the 1918 influenza pandemic, in which many deaths resulted from pneumonia associated with S pneumoniae, with a peak mortality rate 14 days after the onset of symptoms.

We observed a strong correlation between hMPV and IPD, similar to that of RSV. Because we had <1 season of hMPV data, this observation should be interpreted with caution. However, clinical data support a link, because children who received 9-valent pneumococcal conjugate vaccine had a 45% reduced rate of hMPV lower respiratory tract infection and a 55% reduction in clinical pneumonia.

The epidemiological features of IPD in children in Utah seem to be unique in the continental United States and perhaps more similar to those of US non–Active Bacterial Core (ABC) surveillance sites, Canada, and Europe. In the pre–PCV-7 era, the seroepidemiological features of IPD in Utah were different from

<table>
<thead>
<tr>
<th>Respiratory Virus</th>
<th>0-wk Lag</th>
<th>2-wk Lag</th>
<th>4-wk Lag</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>0.19 (.013)</td>
<td>0.20 (.009)</td>
<td>0.17 (.027)</td>
</tr>
<tr>
<td>RSV</td>
<td>0.34 (&lt;.001)</td>
<td>0.35 (&lt;.001)</td>
<td>0.34 (&lt;.001)</td>
</tr>
<tr>
<td>hMPV</td>
<td>-0.02 (.831)</td>
<td>-0.11 (.165)</td>
<td>-0.01 (.943)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>-0.01 (.941)</td>
<td>-0.16 (.034)</td>
<td>-0.08 (.294)</td>
</tr>
<tr>
<td>PIV</td>
<td>0.01 (.020)</td>
<td>0.19 (.016)</td>
<td>0.13 (.096)</td>
</tr>
</tbody>
</table>

* HMPV testing started in November 2006.
those seen in the ABC sites, with serotype 1 being the most common. There were high rates of pneumonia and empyema, mainly caused by non–PCV-7 serotypes. In the post–PCV-7 era, whereas ABC sentinel sites report overall dramatic decreases in all pediatric IPD rates, Utah has seen only a modest decrease in the total IPD rate. This is likely attributable to significant increases in empyema caused by nonvaccine serotypes, especially serotypes 1, 3, and 19A. Mathematical models predicted that the determinants of serotype replacement would include the prevalence of nonvaccine serotypes before vaccine introduction and the tendency of nonvaccine strains to cause colonization and invasive disease.

In a recent case-control study of IPD in Utah, the factors associated with IPD were similar to those reported from other geographic regions, although children 2 years of age were 2.2 times (95% confidence interval: 1.3–3.7 times) more likely than younger children to have IPD caused by non–PCV-7 serotypes. Utah has the highest rates of household crowding and the greatest number of households with children in the United States. The temporal trends in IPD in Utah occur against a background of a PCV-7 immunization rate of 80% for 3 doses, compared with national rates of 87%. The combination of high rates of nonvaccine pneumococcal serotypes in Utah before the introduction of PCV-7, household crowding facilitating transmission of pneumococci, and slightly below-average immunization uptake might have allowed for more-rapid emergence of serotype-replacement disease. This may help explain why the epidemiological features of IPD in Utah are different from those reported by the ABC surveillance sites, and it highlights the importance of regional surveillance.

There are a number of limitations to this study. First, environmental factors such as pollution, light/dark exposure, humidity, temperature, and rainfall, which have been implicated in the seasonality of IPD, were not studied. Second, viral surveillance during the study period was performed at PCMC, which is located in Salt Lake City (north central Utah), and results may not be reflective of respiratory viral activity in the other regions of Utah. Third, there was substantial overlap between the seasonal distributions of RSV and IV for 5 of the 6 seasons, and it is difficult to determine the individual roles of the viruses. Fourth, the denominators we chose for determination of rates are not population based but are reasonable estimates of children at risk of being seen at an IH facility or admitted to PCMC, on the basis of usage and insurance data. The main purpose of deriving a rate was to adjust for the number of children at risk each year and was not to present an absolute rate. Finally, 66% of viral tests performed were negative in DFA assays and cultures. Potentially important viruses, including rhinovirus, enterovirus, and the newly described coronavirus and bocavirus, all of which cause respiratory tract infections, were not evaluated. Strengths of the study include the inclusion of 6 seasons, the use of 2 complementary methods to ascertain IPD, and the routine testing for adenoviruses and PIVs in addition to RSV, IV, and hMPV.

CONCLUSIONS

Our study provides evidence of strong temporal correlations between RSV and IV activity and IPD among children. The associations were observed in the setting of widespread use of PCV-7, with significant changes in the clinical spectrum and serotype distribution of IPD. This is the first study to demonstrate a positive correlation between hMPV activity and IPD. The potential role of hMPV in the pathogenesis of IPD requires additional study. Despite the important impact of PCV-7, Streptococcus pneumoniae is proving to be an adaptable foe and may continue to evolve in the presence of newer conjugate vaccines. We speculate that prevention of IV, RSV, and hMPV infections may ultimately prove to be an important strategy to control pneumococcal disease in the post–PCV-7 era.

REFERENCES


DAY CARE IS GOING TO THE DOGS

“These days, people are getting increasingly picky about choosing day care—for their dog. As demand for pet-care services grows, formerly bare-bones kennels have added posher day-care services. The facilities now offer everything from Webcams that allow owners to keep tabs on their pets to doggie massage. Americans will spend an estimated $43.4 billion on their pets this year, up slightly from $41.2 billion last year, according to the American Pet Products Manufacturers Association. ‘The marketplace has moved away from just having what would be referred to as a boarding facility or kennel,’ says Joseph Lyman, chief executive of the Pet Care Services Association, an industry trade group. We sent our pets to five day-care facilities across the country to find out whether the cost was worth the extra pampering and attention. At all five locations, dogs are split up into rooms by size and spend the day interacting with other pooches. Rates were about $20 to $35 a day, with discounts for buying several stays at a time. Dogs had to be picked up by closing time, or owners were charged for overnight boarding fees. All facilities required proof that our dogs were up-to-date on vaccines. Pets also had to be spayed or neutered to be placed in a room with other dogs. And all but one day-care center first evaluated our pets to ensure they weren’t too aggressive and could get along well with other pooches. We felt a little guilty about leaving our pets for the day, but veterinarians say day care can be good for dogs. Interaction with other dogs can get rid of the separation anxiety that some dogs feel when away from their owners, says Bernadine Cruz, a veterinarian at the Laguna Hills Animal Hospital in Laguna Hills, Calif. And the exercise dogs get at day care can help curb obesity.”


Noted by JFL, MD
Seasonal Invasive Pneumococcal Disease in Children: Role of Preceding Respiratory Viral Infection
Krow Ampofo, Jeffrey Bender, Xiaoming Sheng, Kent Korgenski, Judy Daly, Andrew T. Pavia and Carrie L. Byington
*Pediatrics* 2008;122;229
DOI: 10.1542/peds.2007-3192

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/122/2/229.full.html

References
This article cites 51 articles, 26 of which can be accessed free at:
http://pediatrics.aappublications.org/content/122/2/229.full.html#ref-list-1

Citations
This article has been cited by 13 HighWire-hosted articles:
http://pediatrics.aappublications.org/content/122/2/229.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
*Pulmonology*
http://pediatrics.aappublications.org/cgi/collection/pulmonology_sub
*Respiratory Tract*
http://pediatrics.aappublications.org/cgi/collection/respiratory_tract_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://pediatrics.aappublications.org/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
http://pediatrics.aappublications.org/site/misc/reprints.xhtml