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Acute Bacterial Sinusitis Complicating Viral Upper Respiratory Tract Infection in Young Children

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Abstract

Background—Acute bacterial sinusitis (ABS) is a common complication of viral upper respiratory tract infections (URI). Clinical characteristics of URIs complicated by ABS in young children have not been well studied.

Methods—We identified ABS episodes in a prospective, longitudinal cohort study of 294 children (6 to 35 months of age at enrollment), who were followed-up for one year to capture all URI episodes and complications. At the initial URI visit seen by the study personnel (median day=4 from symptoms onset), nasopharyngeal samples were obtained for bacterial cultures and viral studies.

Results—Of 1295 documented URI episodes, 103 (8%) episodes (in 73 children) were complicated by ABS, 32 of which were concurrent with acute otitis media. The majority (72%) of ABS episodes were diagnosed based on persistent symptoms or a biphasic course. Average age at ABS diagnosis was 18.8±7.2 months; white children were more likely to have ABS episodes than blacks (p=0.01). Hispanic/Latino ethnicity (p<0.0001) was negatively associated, and adequate PCV-7 immunization status (p=0.001) appeared to increase the risk of ABS. Girls had more ABS episodes than boys (0.5±0.8 vs 0.3±0.6 episodes/year, respectively, p=0.03). Viruses were detected in 63% during the initial URI visit; rhinovirus detection was positively correlated with ABS risk (p=0.01). Bacterial cultures were positive in 82/83 (99%) available samples obtained at the initial URI visit; polymicrobial (56%), *Moraxella catarrhalis* (20%) and *Streptococcus pneumoniae* (10%) were the most common cultures. Presence of pathogenic bacteria overall and presence of *M. catarrhalis* during URI were positively correlated with the risk for ABS (p=0.04 for both).

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Conclusion—ABS complicates 8% of URI in young children. Girls have more frequent ABS episodes than boys. Presence of rhinovirus and *M. catarrhalis* during URI are positively correlated with the risk for ABS complication.

Keywords

sinusitis; common cold; respiratory virus; rhinovirus; *Moraxella catarrhalis*

INTRODUCTION

Acute rhinosinusitis is an inflammatory process of the paranasal sinuses; the term implies an acute bacterial infection and mostly diagnosed clinically without bacteriologic documentation. Acute bacterial sinusitis (ABS) is one of the most frequent infectious diseases among the pediatric population, although only the maxillary and the ethmoidal sinuses are partially aerated at early childhood (1). Most ABS episodes occur following viral upper respiratory tract infections (URIs) (2). The clinical manifestations of ABS in children are similar to those of viral URI (3).

Common URI complications include acute otitis media (AOM) and ABS. While AOM diagnosis relies on otoscopic findings, ABS diagnosis relies on the patient's history, and particularly the persistence and severity of sinonasal symptoms, which may help differentiate uncomplicated viral URI from ABS. Surprisingly, the descriptions of clinical, epidemiological and microbiological characteristics of ABS in children are rare, and the majority of those reports were published before the introduction of 7-valent pneumococcal conjugate vaccine (PCV-7) (4–6).

In this report, we sought to characterize the relationship between the preceding viral URI episode and ABS complication in young children in the PCV-7 era. In particular, we were interested in the association between URI inducing respiratory viruses, the interactions between URI viruses and the presence of bacteria in the nasopharynx during the preceding URI, and the occurrence of ABS complicating URI.

PATIENTS AND METHODS

Study Design and Subjects

In a prospective, longitudinal study, healthy children aged 6–35 months who resided in Galveston, TX were enrolled into the study from the University of Texas Medical Branch (UTMB) pediatric clinics between January 2003 and March 2006, as previously described (7, 8). The study was approved by the UTMB Institutional Review Board; written informed consent was obtained for all subjects. The study was designed to capture all viral URI episodes that occurred during a one-year follow-up period in each child, in order to study the clinical characteristics and complications of URI. Subjects with chronic medical conditions or with anatomic/physiologic defects of the ear/nasopharynx were excluded. Demographic and AOM risk factors information were collected at enrollment. Parents were asked to report to the study personnel as soon as the child began to have URI/AOM symptoms (nasal congestion, rhinorrhea, cough, sore throat, fever, ear pain/tugging). Children were seen

shortly after the onset of URI and then examined again in a few days later (e.g. days 3–7 of URI onset). At each visit, parents were asked about current symptoms, medications, and history of viral illness exposure. Evaluation included physical examination, pneumatic otoscopy and tympanometry. Each URI episode was monitored closely for at least 3 weeks for any development of complications, such as AOM or ABS.

Nasopharyngeal (NP) swab and secretions were collected for bacterial and viral studies during the initial URI visit (median day=4 of URI onset) and when AOM was diagnosed. Parents were contacted bi-weekly for information about URI symptoms and the occurrence of any URI/AOM episodes since the last contact. In addition, we reviewed and extracted pertinent data from each child's electronic medical records after subjects had completed the study. Since the UTMB is the sole pediatric care provider on Galveston Island, it allowed the capture of all clinical diagnoses and management of URI complications in our study patients.

Acute Bacterial Sinusitis Definitions and Diagnosis

Diagnosis of ABS was made in association with 116 URI episodes. Diagnosis was made by the study physicians in 83 ABS episodes; another 33 ABS diagnoses were made by other primary care physicians. The study physicians consisted of 2 board-certified pediatric infectious disease specialists (JP, TC) and a board-certified general pediatrician (KR) who used the clinical criteria available during the study period, per the 2001 guidelines published by the American Academy of Pediatrics (AAP) (9). ABS was defined as either: 1) *acute/severe*, when symptoms had been severe or abrupt, and included concurrent temperature 102°F (39°C) and purulent rhinorrhea in an ill-looking child within 3 days of URI onset; 2) *persistent*, when URI symptoms had lasted for >10 days without clinical improvement; or 3) *biphasic*, when URI symptoms had worsened after an initial improvement. In each case, the study physician diagnosed ABS based on patient's history and clinical findings only. No imaging studies or laboratory tests were performed. We reviewed the clinical data from 116 ABS episodes to reaffirm the diagnosis. Of these, 13 ABS episodes (not diagnosed by the study physicians) were considered to be questionable/unlikely or less likely after thoroughly reviewing the medical records; hence, these episodes were excluded. Consequently, 103 ABS complicating URI episodes are included in this report. Patients were treated with antibiotics according to the standard of care. None had experienced intra- or extra-cranial complications.

Microbiologic Studies

Bacterial cultures—NP swabs were cultured for pathogenic bacteria according to the Clinical and Laboratory Standards Institute methods, as previously described(10).

Viral studies—Viral studies were performed by viral cultures, RSV-antigen detection by enzyme immunoassay and real-time PCR, as previously described (7). The original real-time PCR assay, performed at the University of Wisconsin, targeted adenovirus, coronavirus (OC43, 229E, NL63), enterovirus, influenza virus (type A and B), parainfluenza virus (type 1–3), respiratory syncytial virus (RSV), and rhinovirus. In addition, archived specimens were tested by in house quantitative PCR for RSV, human metapneumovirus, and human

bocavirus (hBoV) (11, 12). All positive results for respiratory viruses were combined in this study. Cytomegalovirus (CMV) was detected by culture alone in 11 samples, and with other viruses in another 16 samples. Because prolonged shedding of CMV may result from congenital or acquired infection, and because CMV is not considered a respiratory virus, CMV data were not included in the analyses.

Statistical Analysis

A total of 1295 URI and 103 eligible ABS episodes were included in the analysis. Differences in age were evaluated using a two-tailed Student's t-test, while simple differences in incidence rates were evaluated using two-tailed Fisher's exact test. Numbers of ABS episodes and risk factors were tested using a Poisson regression model, while concurrence with AOM was tested using a Poisson mixed model. Finally, the influence of bacterial and viral presence was modeled with a binomial mixed model, using subject as a random intercept terms a standard modeling procedure for data with multiple observations per subject(13). All calculations were done in the R software (The R Foundation for Statistical Computing, Vienna, Austria). $P < 0.05$ was considered significant.

RESULTS

A total of 294 children (144 girls, 49%) who were followed for 256 child-years contributed 1295 URI episodes(7). Demographic and risk factor data for the study population have been previously reported(7). Of the URI episodes, 671 (52%) were documented in girls. A total of 103 URI episodes were complicated by ABS met our inclusion criteria. Thus, the rate of ABS complicating URI was 8% (103/1295). During the study years, the annual ABS rate was stable (~ 0.4 ABS episode/child-year). One child with ABS required hospitalization due to complicating periorbital cellulitis, and was treated conservatively. The remaining of the patients were treated on an outpatient basis. There was no surgical intervention required for the ABS episodes reported here.

Demographic Characteristics

Table I compares the demographic data and risk factors at enrollment for patients who were diagnosed with ABS and for those without. White children were more likely to have ABS episodes than black children ($p=0.01$). Hispanic/Latino ethnicity ($p<0.0001$) was negatively associated with ABS occurrence. ABS was more common in children who had been fully immunized with PCV-7 vaccine ($p=0.001$). Other well-known AOM risk factors, i.e. breast-feeding, number of siblings, day-care attendance and smoking exposure, were not associated with ABS.

ABS episodes ($n=103$) occurred in 73 children (41 girls, 56%). Among children who completed the entire year-long study ($n=201$), girls had more ABS episodes than boys (0.5 ± 0.8 vs. 0.3 ± 0.6 episodes/year, respectively, $p=0.03$), after accounting for age at enrollment. Fifty-one (70%) children (24 boys, 27 girls) had one ABS episode during their one year follow-up period; 14 (19%) patients (7 girls, 7 boys) had 2 episodes, and 8 (9%) patients (7 girls, 1 boy) had 3 episodes. Of the 103 ABS episodes, 41 (40%) were documented in boys and 62 (60%) episodes were in girls, representing a 7% (41/624) and

9% (62/676) incidence rate of ABS complicated URI episodes in each gender, respectively ($P=0.1$). This trend of female predominance was also observed after stratification of ABS episodes according to age at diagnosis.

The average age at URI diagnosis without ABS was 19.3 ± 8.4 months, while the average age at diagnosis of ABS was 18.8 ± 7.2 months ($p=0.56$). ABS complicated 6% (16/258), 10% (69/701), 5% (15/278) and 5% (3/58) episodes in children aged 6–11, 12–23, 24–35, and 36–48 months, respectively ($p=0.23$).

The diagnosis of ABS was made, on average, on the 11th day of URI symptoms. The majority of ABS episodes were diagnosed due to *persistent* symptoms (61/103, 59%), followed by an *acute/severe* presentation (28/103, 29%) and a *biphasic* course (13/103, 13%). This distribution was equal in all age groups in both genders ($p=1.00$, OR =0.25–4). Nearly 60% of ABS episodes were detected in the winter season (November–April), in parallel with the increased incidence of URI episodes in our population.

Concurrent Acute Sinusitis and AOM vs. Acute Sinusitis Only

A total of 32/103 (31%) ABS episodes occurred concurrently with AOM in subjects 6–36 months of age. There were no such episodes in children 36–48 months of age. Among those presenting with concurrent ABS and AOM, there were more boys than girls ($p=0.02$). Following categorization of these ABS episodes according to gender and age at disease, boys 6–23 months of age tended to present with concurrent ABS and AOM more often than girls: there were 5 (63%) vs. 2 (25%) episodes (6–11 months) ($p=0.14$), and 11 (39%) vs. 8 (20%) episodes (12–23 months) ($p=0.08$), respectively. However, in children 24–35 months of age, boys had 2 (50%) vs. 4 (36%) concurrent ABS and AOM episodes in girls ($p=0.98$). Episodes with concurrent ABS and AOM ($n=32$), tended to occur at an earlier age, 17.5 ± 6.9 months (median, 16.8), when compared with episodes with ABS only ($n=71$), 19.5 ± 7.4 months (median, 18.4) ($p=0.17$).

Overall, there were 71 episodes of ABS complicating URI that did not occur concurrently with AOM. Figure 1 demonstrates the distribution of those episodes, analyzed by age and gender at presentation. Based on these ABS only episodes, girls were significantly more likely to develop ABS complicating URI episodes ($P=0.0006$).

Microbiologic Data

Viral Studies—Of the 103 ABS complicated URI episodes, 83 were diagnosed by our study physician and NP specimens were collected during the first URI visits. Of these, viruses were detected by culture and/or PCR in 52 (63%) URI episodes: 32 of 52 (62%) with single virus and 20 of 52 (38%) with multiple viruses. In 31 of 83 (37%) URI episodes, no viruses were detected.

Figure 2 shows the rates of ABS complicated URI by virus type. Specific respiratory viruses detected as a single agent during URI episodes overall included adenovirus ($n=91$), rhinovirus (84) and enterovirus (41), parainfluenza viruses (36), RSV (28), influenza virus (21), and coronavirus (18). Not shown in the Figure are data on hBoV, because of its prolonged shedding after an infection, and data on herpes simplex virus, because of the low

numbers (n=2). The highest rates of ABS episodes were those associated with rhinovirus and influenza viruses. Although not statistically significant, ABS associated with rhinovirus tended to be associated with an earlier clinical presentation, when compared with ABS episodes associated with other viruses (6th vs. 11th, median day in the URI course, p=0.22). After adjusting for other viruses detected, only rhinovirus (not influenza) was positively associated with ABS complicating URI (p=0.01). Enteroviruses tended to be detected more frequently in concurrent ABS and AOM episodes, when compared with ABS only episodes, but the difference was not statistically significant (p=0.06).

Bacterial Cultures—NP bacterial culture results at the first URI visit were available from 82/83 ABS episodes seen by our study group. Table 2 compares available bacterial data from URI episodes complicated by ABS episodes vs. those without ABS. Of the available NP cultures from ABS complicated URI episodes, 93% were positive for bacteria; in URI without ABS, 82% were positive for bacteria. The presence of bacteria overall during URI was positively correlated with ABS complication (p=0.04). In the ABS group, multiple bacteria species were cultured in 56% of specimens; in 36% of specimens, only one single bacterial species grew. *Moraxella catarrhalis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* were cultured as single organisms in 20, 10, and 6 of 82 cases, respectively, and as part of multiple bacteria in 43, 35 and 24 cases, respectively. Presence of *M. catarrhalis* (single or in combination) was positively correlated with ABS (p=0.04).

Viral-bacterial interactions—Bacterial and viral data were available together in 82 ABS complicating URI episodes. Table 3 shows the viral and bacterial species that were simultaneously identified. The most common finding was mixed bacterial pathogens, without an identified virus. Of 12 rhinovirus-URI episodes complicated by sinusitis only, 3 (25%) were associated with a negative bacterial culture.

DISCUSSION

In this prospective study of children aged 6–48 months, we report 8% incidence rate of ABS complicating URI, diagnosed clinically; 31% of cases occurred concurrently with AOM. Girls had more ABS episodes than boys, and were more prone to experience multiple ABS episodes. A positive association was found between the presence of rhinovirus or *M. catarrhalis* during URI and ABS complication. In addition, age appropriate PCV-7 immunization status appeared to increase the likelihood of ABS.

The most common complication associated with viral URI in children is AOM; the disease occurs in >1/3 of cases, and generally occurs early in the course of URI, i.e. days 2–7(7). ABS complicating URI occurs less commonly and generally not diagnosed until later, i.e. after 10 days of persistent symptoms, partly because of the clinical definition. While we have shown in the same cohort that young age was the most important predictor of AOM during URI, ABS was not correlated with age.

Interestingly, we found that ABS occurred more often in girls than in boys. It is known that boys are more likely to develop AOM than girls (7). The gender effect on ABS may be partially explained by the fact that more boys may have received antibiotic treatment for

AOM earlier in the course of URI, and this may have prevented ABS from developing later in the URI course. Other explanations for gender difference derive from gender-based anatomical variations and/or mucociliary function. In young children, only the maxillary sinus and part of the ethmoidal cells are aerated sufficiently enough to make room for a clinically recognizable infectious process. By using a 3-dimensional reconstruction of computed tomography images, it has been demonstrated that the maxillary sinus volume in females <10 years is smaller when compared to age-matched males(14). Therefore, the smaller maxillary sinus and its opening (the osteomeatal complex, which also drains the anterior ethmoidal cells) tends to be blocked more often in girls, thus allowing the development of viral sinusitis and subsequently ABS due to ineffective mucociliary clearance(15). In any event, our gender finding is consistent with the national data in adults, showing that ABS rates in women are almost two-fold higher than in men(16).

ABS in young children may present with non-specific symptoms, such as irritability, night cough, poor appetite, throat clearing, and malodorous breath(17), whereas older children and adolescents generally complain of more specific symptoms, such as headaches, facial pain/pressure, dental pain, anosmia, and pharyngitis(17). The recent 2013 AAP guideline also emphasizes the establishment of ABS diagnosis according to symptoms before initiation of antibiotic therapy(18). In retrospect, all of our patients also meet the current guideline criteria for ABS diagnosis, since there were essentially no changes in the three ABS clinical diagnostic criteria between the two guidelines. In our cohort, symptoms were usually persistent purulent nasal discharge and cough, plus non-specific symptoms, such as irritability and decreased appetite. Based on history of present illness, ~60% of the episodes presented with *persistent* symptoms, and they were usually diagnosed on day 11 (median) in the URI course, followed by the *acute/severe* form (29%). Only 13% of the ABS episodes in this cohort had a *biphasic* presentation.

The pathogenesis of ABS complicating URI is similar to that of AOM due to the anatomic proximity of the nasopharynx to the paranasal sinuses and the middle ear, with the continuity of mucosa(19, 20). Viral URI causes local inflammation, increases bacterial attachment to the epithelial cells and disrupts local immune defense, leading to mucositis of the membranes lining the nasopharynx and paranasal sinuses, obstruction of the sinus ostia, negative sinus pressure, and aspiration of mucus, virus and/or bacteria from the nasopharynx causing contamination of paranasal sinuses(21–23). Winther(22) suggested that viral URI should be more accurately termed ‘acute viral rhinosinusitis’. It is unclear whether bacteria contaminate paranasal sinuses during the early stage of viral URI, but the term ABS is generally reserved for presentations wherein an initial viral URI is followed by a persistent illness, worsening course or by a severe onset with a high concurrent fever (18).

The offending bacteria in ABS are similar to those responsible for AOM, which reside in the nasopharynx: *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. Because invasive procedures are not generally practiced in the management of ABS, there is a lack of current data on the bacteriology of ABS. An attempt has been made to use NP bacterial culture as a surrogate of bacteria in the sinuses. A recent study reported a 78% correlation between endoscopically-assisted middle meatal cultures and maxillary sinus aspirations in children with ABS(24). Bacteriologic study of ABS in children by maxillary sinus aspirations was

last reported several decades ago(25), prior to the use of PCV-7. Older data showed that the most common pathogens isolated in pediatric ABS patients were *S. pneumoniae* (44%), *H. influenzae* (30%) and *M. catarrhalis* (30%)(25, 26). In our study, specimens were collected early in the URI course (median day=4), and not at the time of ABS diagnosis. Therefore, our data only imply to risk of ABS complicating URI by bacteria or virus detected at early URI course.

We found positive correlation between the presence of *M. catarrhalis* at the time of acute URI and later development of ABS. As *M. catarrhalis* is less pathogenic than *S. pneumoniae* and *H. influenzae*, it is possible that children colonized with more pathogenic bacteria may have developed AOM early on and treated with antibiotic. We have reported high incidence of AOM (37%) in this cohort (7). Further studies are required to determine whether *M. catarrhalis* has a predilection towards sinus cavities. We also found positive correlation between age-appropriate PCV-7 immunization status and development of ABS. The reason for this is unclear. PCV-7 targeted the most pathogenic serotypes of *S. pneumoniae*; immunized children may have increased carriage rate of less pathogenic bacteria, including other *S. pneumoniae* serotypes, *H. influenzae*, and *M. catarrhalis*. This, in turn, may have spared them from having AOM and receiving antibiotic treatment earlier in the course of viral URI. In any event, it is still controversial whether reduction of *S. pneumoniae* colonization by PCV-7 immunization increased NP colonization of other pathogens. While NP isolation rates of *H. influenzae* in children with acute maxillary sinusitis has increased by 8% in the post-PCV-7 years in one study (27), other reports did not find significant shifts in other non-*S. pneumoniae* NP pathogens (28, 29). Further studies are required to monitor the effect of new vaccines on incidence of common bacterial disease such as AOM and ABS.

When analyzing bacterial-viral interactions in our ABS episodes, no significant specific interactions were detected. While each one of the nasopharyngeal bacterial pathogens could have caused ABS without a concurrent virus, we found 3 URI episodes associated with rhinovirus complicated by ABS when there were no NP colonizing bacteria at the time of URI. Our findings suggest that rhinovirus alone may cause severe symptoms in young children, thus leading to ABS diagnosis. Yet, rhinovirus RNA shedding can persist up to 5–6 weeks after the onset of symptomatic URI(30). Therefore, the correlation between the presence of rhinovirus and subsequent ABS development needs to be interpreted with caution.

In summary, viral URI in children (6–48 months) is complicated by ABS in 8% of cases. About one-third of cases occurred concurrently with AOM. Girls seemed to be more susceptible to ABS complicating URI. In young children with URI, infection with rhinovirus and colonization with *M. catarrhalis* were associated with an increased risk for ABS.

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Figure 1.

Percentage of ABS Episodes Complicating URI, By Gender and Age*

ABS, acute bacterial sinusitis; URI, upper respiratory tract infection

*ABS only episodes (n=71), excluding concurrent ABS and AOM episodes.

†Girls significantly contributed more ABS complicated URI episodes (P= 0.0006).

Figure 2.

Rate of ABS Complicating URI, By Specific Virus[†]

ABS, acute bacterial sinusitis; URI, upper respiratory tract infection

[†]Detected as single virus, using all virus detection methods combined.

*Combined = 2 or more respiratory viruses detected.

Data on human bocavirus and herpes simplex virus are not included.

Coronavirus, includes coronaviruses 229E, OC-43 and NL-63; Parainfluenza, includes parainfluenza viruses type 1–3; Influenza, includes influenza viruses A and B; RSV, respiratory syncytial virus; hMPV, human metapneumovirus

Table I

Demographic data and risk factors at enrollment of the study population (n=294)

	Patients with ABS ¹ (n=73)	Patients without ABS (n=221)	P-value
Gender (girls, %)	41 (56%)	103 (47%)	0.18
Race			0.06
White	48 (63%)	125 (57%)	
Black	6 (8%)	85 (38%)	
Other ²	19 (29%)	11 (5%)	
Ethnicity			
Hispanic or Latino	18 (25%)	113 (51%)	<0.0001
Child care arrangement			0.2
Home	48 (63%)	153 (69%)	
Home day care	6 (8%)	17 (8%)	
Day care	19 (29%)	48 (22%)	
History of breast-feeding ³	37 (46%)	103 (47%)	0.60
Cigarette smoke exposure	24 (33%)	63 (29%)	0.55
Age-appropriate PCV-7 status ⁴	57 (78%)	125 (57%)	0.001 ⁴

ABS, acute bacterial sinusitis. P-values were calculated by Fisher's exact test. All P values are univariate.

¹ Includes 26 patients with concurrent AOM and acute sinusitis

² Others: Biracial or Asians. Post-hoc analysis showed a significant increase in incidence for white children over black children (p=0.01).

³ The median duration of breast-feeding was 16 weeks (range: 2–60 weeks)

⁴ Defined as 3 doses of PCV-7 at 6 months and 4 doses of PCV-7 at 15 months. PCV-7= 7-valent pneumococcal conjugate vaccine.

Table 2

NP bacterial culture results during URI episodes with and without ABS complication

Bacteria	URI with ABS (%)	URI without ABS (%)
<i>Streptococcus pneumoniae</i>	8 (10)	83 (8)
<i>Haemophilus influenzae</i>	5 (6)	91 (9)
<i>Moraxella catarrhalis</i>	16 (20)	187 (18)
Others¹	1 (1)	27 (3)
Combined	46 (56)	440 (43)
Negative	6 (7)	206 (21)
Total	82	1034

URI, upper respiratory tract infection; ABS, acute bacterial sinusitis.

Bacterial culture samples were collected during the initial URI visit (median day = day 4 of URI). Of 1295 URI episodes, bacterial culture were obtained in 80% (82/103) of URI episodes complicated by ABS and 87% (1034 of 1192) of episodes not complicated by ABS.

¹ Other bacteria include *Staphylococcus aureus*, β -hemolytic *Streptococcus* group A, *Streptococcus* group B.

Table 3

Presence of bacteria and viruses during URI episodes complicated by ABS¹

	<i>Streptococcus pneumoniae</i>	<i>Haemophilus influenzae</i>	<i>Moraxella catarrhalis</i>	Other	Negative	Total
Rhinovirus	12 (22)	6 (16)	16 (22)	0	3 (50)	37
Adenovirus	10 (18)	4 (11)	14 (19)	0	1 (17)	29
RSV	2 (4)	0 (0)	2 (3)	0	1 (17)	5
Parainfluenza ³	3 (5)	2 (5)	4 (5)	0	0	9
Enteroviruses	4 (7)	4 (11)	9 (12)	0	0	17
hMPV	1 (2)	4 (11)	4 (5)	0	0	9
Influenza ⁴	0 (0)	2 (5)	1 (1)	0	0	3
Coronavirus ⁵	4 (7)	1 (3)	5 (7)	1 (33)	0	11
Negative	19 (35)	14 (38)	19 (26)	2 (67)	1 (17)	55
Total	55	37	74	3	6	175

URI, upper respiratory tract infection; ABS, acute bacterial sinusitis; RSV, respiratory syncytial virus; hMPV, human metapneumovirus

¹ Data available for both bacteria and viruses for 81 URI episodes complicated by acute sinusitis; each specimen may contain multiple viruses and/or bacteria. Data are not shown for human bocavirus and herpes simplex virus.

² Other bacteria include *Staphylococcus aureus*, β -hemolytic *Streptococcus* group A, *Streptococcus* group B

³ Includes parainfluenza viruses type 1–3

⁴ Includes influenza viruses A and B

⁵ Includes coronaviruses 229E, OC-43 and NL-63