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ORIGINAL ARTICLE

## Are empiric antibiotics for acute exudative tonsillitis needed in children?

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### KEYWORDS

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**Background:** Empiric antibiotics are frequently given for children with acute exudative tonsillitis. A few studies have investigated the causative agent of acute “exudative” tonsillitis in children to evaluate the necessity of antibiotic therapy. This study tried to explore the common causative agent of acute exudative tonsillitis among children.

**Methods:** From April 2009 to March 2010, throat swabs were obtained and cultured for viruses and bacteria from children who visited the pediatric emergency rooms of two medical centers in central Taiwan with acute exudative tonsillitis. Demographic data and microbiological results were analyzed.

**Results:** A total of 294 children with acute exudative tonsillitis were enrolled during the 1-year prospective study, and 173 (58.8%) of them were younger than 7 years. Group A streptococci were isolated from only three (1.0%) children, and they were all older than 6 years. A total of 143 viruses were isolated from 140 (47.6%) children. Adenovirus (18.7%) and enterovirus (16.3%) were the most common viral etiologies, followed by influenza virus (5.4%), parainfluenza virus (5.1%), herpes simplex virus Type 1 (2.7%), and respiratory syncytial virus (0.3%). Group A streptococcus only contributed to a minimal portion of acute exudative tonsillitis.

**Conclusion:** Routine or immediate antibiotic therapy for acute exudative tonsillitis in children is not necessary.

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## Introduction

Acute exudative tonsillitis is one of the common diseases among children in pediatric emergency services. Exudative tonsillitis is commonly associated with adenovirus, Epstein–Barr virus (EBV), and Group A streptococcus (GAS), though influenza virus, parainfluenza virus (PIV), or enterovirus (EV) has been reported.<sup>1,2</sup> GAS pharyngitis or pharyngotonsillitis is usually the main reason to initiate antimicrobial therapy because of its potential to develop rheumatic fever and post-streptococcal glomerulonephritis if left untreated.<sup>3–7</sup> To distinguish the causative agent of acute exudative tonsillitis—virus or *Streptococcus pyogenes*—it is always a stress in clinical practice to determine whether to initiate antimicrobial therapy or not.<sup>1,2,8,9</sup> Empiric antibiotics were frequently given for children with acute exudative tonsillitis in clinical practice and led to the emergence and spread of antibiotic-resistant bacteria.<sup>10</sup> Thus, the epidemiological data of causative agent of acute exudative tonsillitis plays an important role.

Some studies already showed that GAS is the leading cause of acute pharyngitis and may account for 15–30% of cases in children.<sup>3–6</sup> Anne Putto<sup>1</sup> reported a total of 13 (12%) Group A  $\beta$ -hemolytic streptococcus among 110 children with febrile exudative tonsillitis in Turku, Finland. A hospital-based study in north Taiwan demonstrated a low percentage of GAS pharyngitis among children in the outpatient department.<sup>2</sup> However, it did not focus on “exudative” tonsillitis. To elucidate the causative agent of acute exudative tonsillitis and to evaluate the necessity of empiric antibiotic therapy, we conducted a 1-year survey strictly in the pediatric emergency room.

## Materials and methods

### Patients

A prospective 1-year study, from April 2009 to March 2010, was performed at the pediatric emergency room

of Taichung Veterans General Hospital (TCVGH) and China Medical University Hospital (CMUH), which were two medical centers in Taichung, Taiwan. There were estimated 900 and 2,200 visits, respectively, at pediatric emergency room per month. Children younger than 18 years with the clinical diagnosis of exudative tonsillitis were enrolled in our study. The diagnosis was based on the congested and enlarged tonsils with exudates. Patients were excluded if they only had red pharynx or enlarged tonsils without exudates.

All of these children with the diagnosis of acute exudative tonsillitis were enrolled and received both throat viral and bacterial cultures. The rapid antigen test for GAS was performed selectively only if the test was available.

### Virus culture

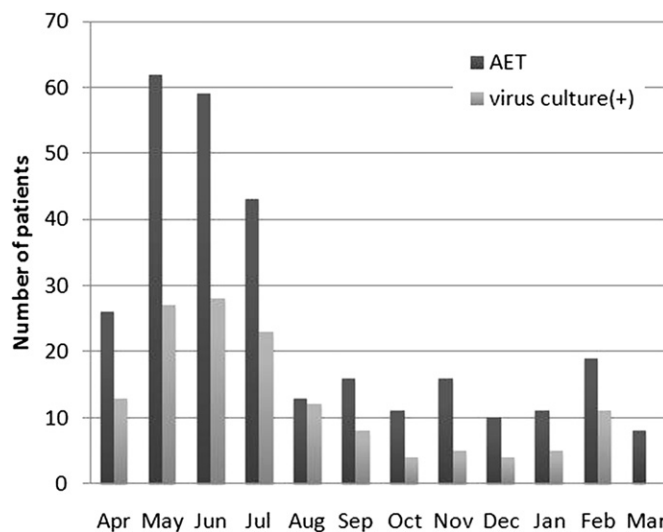
The viral laboratories of TCVGH and CMUH were both qualified contract laboratories by Centers for Disease Control of Taiwan. Throat swab specimens were stored at 4°C in the refrigerator no more than 3 days before inoculation. Four cell lines, including monkey kidney epithelial cell (Vero), human rhabdomyosarcoma cell (RD), human epidermoid carcinoma cell (A-549), and Madin–Darby canine kidney cell, were routinely used for virus isolation. The cytopathic effect of cell culture was checked daily and confirmed by direct fluorescence assays of suspect virus.

### Bacterial culture

The throat swab specimens were processed with standard techniques, as described previously.<sup>7</sup> Bacterial identification focused on Group A  $\beta$ -hemolytic streptococci only.

### GAS rapid antigen test

Clearview Step A device (Unipath limited, Bedford, UK) was used for GAS rapid test in TCVGH. It was a qualitative immunoassay to detect the GAS antigen from throat swab.



**Figure 1.** Number of children with acute exudative tonsillitis (AET) and positive virus cultures each month from April 2009 to March 2010.

**Table 1** Viruses isolated from 294 children with acute exudative tonsillitis

Virus	n (%) of children
Adenovirus	55 (18.7)
Enterovirus	48 (16.3)
Coxsackie A	36 (12.4)
Coxsackie B	6 (2.0)
Echo virus	1 (0.3)
Nontypable enterovirus	5 (1.7)
Influenza virus	16 (5.4)
Type A	15 (5.1)
Type B	1 (0.3)
Parainfluenza virus	15 (5.1)
Type 1	6 (2.0)
Type 2	5 (1.7)
Type 3	4 (1.4)
Herpes simplex virus Type 1	8 (2.7)
Respiratory syncytial virus	1 (0.3)
<b>Total</b>	<b>143 (48.6)<sup>a</sup></b>

<sup>a</sup> More than one virus was recorded in three children.

## Statistical analysis

Analysis for association between acute exudative tonsillitis case and age and between virus isolates and age was performed with Mann–Whitney *U* test. For all analysis, a *p* value less than 0.05 was considered statistically significant.

## Result

A total of 294 children with acute exudative tonsillitis were enrolled in this study, and 182 (61.9%) of them were boys. There were 164 (55.8%) cases enrolled between May 2009 and July 2009 (Fig. 1). These children were aged from 0.6

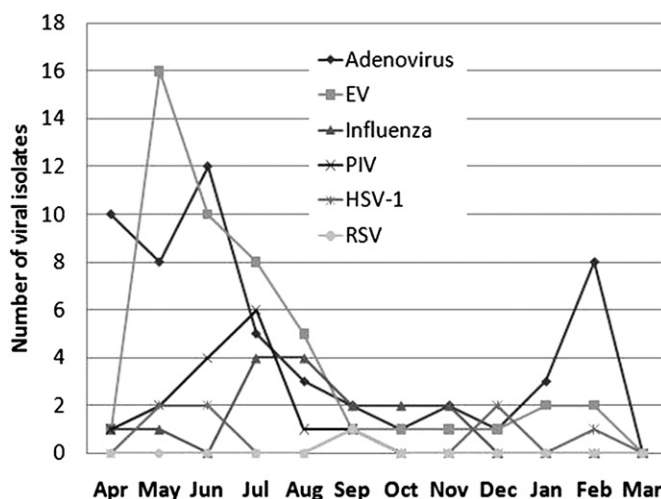
years to 17 years, and 101 (34.3%) of them were younger than 3 years; 130 (44.2%) were aged 3–6 years, 43 (14.6%) were aged 7–12 years, and 20 (6.8%) were aged 13–17 years. The median age was 3.9 years, and the mean age was  $5.1 \pm 4.0$  years. Children younger than 7 years (infancy, toddlerhood, and preschool) were more in number than those older than 7 years (school age and adolescence), and the percentages were 78.6% and 21.4%, respectively. Interestingly, most of these children (220 cases, 74.8%) had visited local outpatient clinics before the pediatric emergency services.

Throat cultures were positive for GAS in three (1.0%) children aged 6 years, 7 years, and 8 years, respectively. GAS mixed with coxsackie A virus was found in one (0.3%) patient. GAS rapid antigen test was performed among 84 (28.6%) children and was positive in two children who also had positive GAS cultures. None of those with positive GAS cultures got negative results for rapid GAS antigen test.

A total of 143 viruses were isolated from 140 (47.6%) children (Table 1). Adenovirus was the most common viral agent (18.7%), and EV (16.3%) was the second one. Three children were found to have more than one virus in their throat swabs: two of them had adenovirus and coxsackie A virus, and one of them had influenza A virus and coxsackie A virus.

Monthly distribution of these viruses from children with acute exudative tonsillitis is shown in Fig. 2. Adenovirus was isolated every month of the year except March 2010. EV had the highest activity in May 2009 and significantly decreased after fall 2009. Unusual increased number of influenza A virus was isolated since July 2009, and it dramatically decreased after December 2009, which was compatible with the novel H1N1 pandemic worldwide. PIV was only isolated from April 2009 to September 2009. Herpes simplex virus Type 1 was found yearly without any seasonal peak. There was only one respiratory syncytial virus isolated on September 2009.

All of the children with GAS infection were older than 6 years, whereas most of the viruses (48.3% of all virus isolates) were isolated from children between 3 years and 6



**Figure 2.** Number of different viral isolates each month from April 2009 to March 2010. EV = enterovirus; HSV-1 = herpes simplex virus Type 1; PIV = parainfluenza virus; RSV = respiratory syncytial virus.

**Table 2** Group A streptococci and viruses isolated from throat swabs of children with acute exudative tonsillitis

Age (yr)	GAS	Adenovirus	Enterovirus	Influenza	PIV	HSV-1	RSV
<3	0	20	14	3	5	4	1
3–6	0	29	24	4	10	2	0
>6	3	6	10	9	0	2	0

GAS = Group A streptococcus; HSV-1 = herpes simplex virus Type 1; PIV = parainfluenza virus; RSV = respiratory syncytial virus.

years old, 32.9% from children younger than 3 years, and 18.8% from children older than 6 years (Table 2). In Taiwan, most children went to the kindergarten during 3–6 years of age and to elementary school after 6 years of age. Adenovirus and EV significantly infected children younger than 7 years ( $p < 0.001$  and  $p = 0.011$ ). None of the children older than 6 years got PIV infection. Influenza virus and herpes simplex virus Type 1 were not significantly related to age groups.

## Discussion

Many studies have reported the causative agent of acute pharyngitis or tonsillitis in children, but only a few studies have focused on “exudative” tonsillitis. Acute exudative tonsillitis is a common disease in the pediatric emergency department. However, it may be difficult for clinicians to distinguish between GAS and viruses by clinical characteristics and basic laboratory tests.<sup>1,2,8,9,11</sup> This 1-year prospective study enrolled children with acute exudative tonsillitis at pediatric emergency rooms in two medical centers—TCVGH and CMUH—and is the largest-scale epidemiologic survey about causative agent of acute exudative tonsillitis up to date.

GAS is the most important cause of bacterial pharyngitis among children because of its potential to develop rheumatic fever and post-streptococcal glomerulonephritis if left untreated.<sup>3–7</sup> The diagnosis of streptococcal pharyngitis was not easily made on clinical grounds alone,<sup>8,11</sup> though it most frequently colonized and attacked the school children.<sup>9</sup> GAS rapid antigen tests have been used worldwide. However, its sensitivity varied.<sup>12–14</sup> Since the era of wide antibiotic usage in clinical practice, GAS was not the common cause of acute exudative tonsillitis, and there were only 12% of the cases attributed to GAS by Anne Putto’s<sup>1</sup> study. This study reported an even lower percentage (1%) of GAS acute exudative tonsillitis. All of these children were older than 6 years, and the age distribution was similar to those of previous reports.<sup>1,9,15</sup> There were 74.8% of children who had visited local outpatient clinics before they were brought to pediatric emergency services. According to a research by the institution of nation health insurance, among patients with diagnosis of common cold in Taiwan, 31.3% received antibiotic treatment, especially among pediatric patients.<sup>16</sup> Most parents did not make sure whether their children had received antibiotic therapy. Antibiotic usage before entering the study might have led to underdiagnosis of GAS infection.

Anne Putto’s<sup>1</sup> study in Finland showed that 42% of 110 children with febrile exudative tonsillitis were associated with viruses, and adenovirus (19%) and EBV (9%) were the two most common viral agents. In this study, children did not routinely receive EBV serologic tests unless infectious

mononucleosis was suspected, and 10 children were proven to have EBV infection. Viruses played a prominent role in acute exudative tonsillitis and were identified in 47.6% of these children. GAS was isolated more from older children with acute exudative tonsillitis, whereas viruses (81.1%) were isolated mainly from younger children. The most common viral agent was adenovirus (18.7%), followed by EV (16.3%). Most of the species of EV were coxsackie A viruses (12.4%), and there was no EV71 isolated during this study period. No significant seasonal variation was observed for adenovirus, but EV peaked between May and July 2009. Previous studies on respiratory viral infections among children in Taiwan showed a similar result from surveillance.<sup>17,18</sup> Influenza season started in autumn, usually in December; however, there were many influenza A virus isolates in summer–autumn during this study period. This was because of the pandemic of novel swine-origin influenza A (H1N1) virus in 2009.<sup>19</sup> Some respiratory tract viruses, such as rhinovirus, EBV, human metapneumovirus, human bocavirus, and others, are identified with difficulty by cell cultures and viral rapid antigen tests, and special cell lines, culture conditions, or polymerase chain reaction may provide a better chance to identify them.<sup>20–22</sup> In this study, polymerase chain reaction and serologic tests were not used to recognize potential pathogens, and a proportion of virus agents may be missed.

In conclusion, the overwhelming majority of causative agent of acute exudative tonsillitis in children in this study was a viral agent. The most common viral isolates were adenovirus and EV. GAS were rare in this disease and were isolated only in children older than 6 years. Routine or immediate antibiotic therapy for acute exudative tonsillitis in children is not necessary.

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