

## ILLUSTRATIVE CASE

# *Haemophilus influenzae* Serotype f Epiglottitis: A Case Report and Review

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## CASE

An otherwise healthy, full-term, fully immunized 5-year-old boy presented to the emergency department after he developed decreased energy, decreased appetite, sore throat, drooling, refusal to speak, and a fever to 102°F over a period of 6 hours in the setting of 5 days of rhinorrhea and a “croupy” cough.

On presentation, his weight was 22 kg and blood pressure was 102/56 mm Hg, with a respiratory rate of 32 breaths per minute, a heart rate of 132 beats per minute, a pulse oxygen saturation (SpO<sub>2</sub>) of 99% in ambient air, and a temperature of 38°C (100.4°F). He was ill-appearing and was noted to be in moderate respiratory distress, with refusal to speak and sitting with his neck extended in his mother’s lap.

Physical examination revealed an erythematous posterior oropharynx with diffuse anterior and posterior cervical lymphadenopathy. His lungs were clear to auscultation bilaterally, without stridor or stertor. The rest of the physical examination was unremarkable. Laboratory analysis including a complete blood count was notable for a white blood cell count of 27.2 with 83.8% neutrophils. A rapid mononucleosis test was negative, and blood cultures were drawn. Radiographs of his neck were obtained, which revealed inflammation of the supraglottic area, epiglottis, and subglottic areas (Fig 1). A dose of nebulized racemic epinephrine was given without clinical improvement. A pediatric otolaryngologist was consulted, who performed a bedside flexible laryngoscopy, which revealed significant edema and erythema of the epiglottis extending down the bilateral aryepiglottic folds and involving the arytenoid towers. The supraglottis was significantly edematous, and the false vocal cords were edematous and erythematous. Intubation of the patient’s trachea was deferred and he was placed on intravenous dexamethasone every 6 hours and admitted to the PICU for further monitoring.

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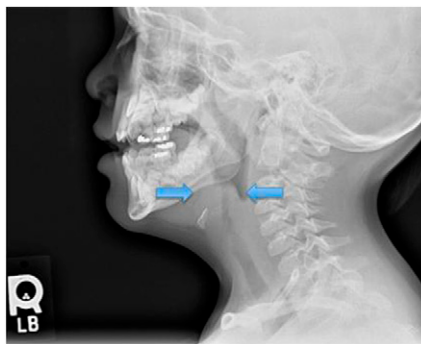
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**Question:** What upper airway emergencies should be considered in the acutely ill, febrile child?

Upper airway emergencies in young children have a wide differential, which include infectious and noninfectious etiologies, including structural abnormalities, tissue edema, foreign body, external compression, and trauma.<sup>1</sup> In the febrile child, infectious etiologies are more likely. The most common cause of upper airway compromise in the febrile child continues to be laryngotracheobronchitis (“croup”); other etiologies to consider would include epiglottitis, retropharyngeal abscess, and bacterial tracheitis.<sup>2</sup> The rapid assessment of the airway’s integrity is paramount; however, direct visualization can be difficult because agitation caused by investigation with a tongue depressor can result in life-threatening airway compromise. Importantly, imaging studies and investigation should not interfere with establishing a safe airway in patients with upper airway compromise. Typical modalities of investigation, should the child tolerate these, include lateral and anterolateral and posterolateral radiographs of the neck, which can be helpful in differentiating between various etiologies. Classically, radiographs in croup will reveal soft tissue swelling in the subglottic area, leading to a “steep sign.” Retropharyngeal abscesses will increase the amount of potential space between the vertebral bodies and the more anterior structures of the neck, including the esophagus and trachea; the typical amount of space in a healthy child is <50% of the size of the associated vertebral body. Bacterial tracheitis can appear as a ragged edge of the airway on plain films throughout the upper airway, representing swelling and sloughing of the soft tissues lining the trachea. Epiglottitis classically will appear as a “thumbprint sign” on lateral neck radiographs, which represents the enlarged and inflamed epiglottis; this finding was clearly shown in our patient (Fig 1). A common presentation of epiglottitis includes respiratory difficulty, drooling, fever, dysphagia, muffled voice, and fever,



**FIGURE 1** Lateral neck radiograph showing thickened epiglottic folds and poorly defined epiglottis, representing the classic “thumbprint sign.”

with younger children presenting with more acute symptoms due to smaller upper airway anatomy (Table 1).<sup>3</sup> Intubation of the airway has been shown to significantly reduce mortality compared with observation and is ideally done in a controlled setting, such as an operating room, with skilled practitioners.<sup>2</sup>

**CASE CONTINUATION**

In the PICU, the patient was empirically started on intravenous ampicillin-sulbactam. He progressed well overnight, and within 12 hours was able to tolerate food by mouth and speak without difficulty. The following day, he was transferred to a general pediatric inpatient service. Upon transfer, he was transitioned to oral steroids and appeared clinically well. The blood culture obtained on presentation was positive for Gram-negative rods on hospital day 2, with resultant speciation of  $\beta$ -lactamase–negative *Haemophilus influenzae* serotype f (Hif) by state laboratory serotype analysis, which was confirmed by internal laboratory genotype analysis. The patient remained afebrile and normotensive, and his oral intake improved with subsequent cultures showing no growth. He tolerated the transition to oral amoxicillin with clavulanic acid without difficulty and was discharged from the hospital on hospital day 5 to complete a total of 14 days of antibiotic therapy.

**Question:** How has the epidemiology of epiglottitis changed in the postvaccination era?

Invasive disease secondary to *H influenzae*, including epiglottitis, was once a prevalent disease in the United States. Before routine vaccination, there were an estimated 20 000 cases of invasive disease secondary to *H influenzae* annually in the United States, with ~17% of these representing epiglottitis.<sup>4,5</sup> The Food and Drug Administration initially licensed the *H influenzae* type b (Hib) vaccine in the United States in 1985, which became a part of the routine immunization schedule in the United States in 1991.<sup>6</sup> Since routine vaccination against Hib, the overall incidence of hospitalization due to acute epiglottitis decreased by 91% from 1995 to 2003.<sup>7</sup> Due to the success of the vaccine, which utilizes the polysaccharide capsule conjugated to a carrier protein as the antigen, the incidence of invasive Hib disease in the United States has declined from 129 per 100 000 persons<sup>8</sup> to 1.62 per 100 000 persons from 1989 to 2008.<sup>9</sup> Before

**TABLE 1** Characteristics of Patients With Epiglottitis Due To *H influenzae*

	Value
Symptoms, %	
Respiratory difficulty <sup>a</sup>	78 <sup>b</sup>
Drooling <sup>a</sup>	42 <sup>b</sup>
History of fever <sup>a</sup>	57 <sup>b</sup>
Cough	19
Change in voice <sup>a</sup>	33
Sore throat <sup>a</sup>	65 <sup>b</sup>
Difficulty swallowing <sup>a</sup>	49 <sup>b</sup>
Physical examination findings, %	
Stridor	81 <sup>b</sup>
Change in voice <sup>a</sup>	90
Tenderness of neck	65
Pharyngitis <sup>a</sup>	61
Adenopathy <sup>a</sup>	39 <sup>b</sup>
Laboratory evaluation	
Average WBC count <sup>a</sup>	19 721 <sup>b</sup>
Abnormal radiograph, <sup>a</sup> %	96 <sup>b</sup>

Data adapted from Mayo-Smith et al.<sup>3</sup> Percentages are based on 72 patients with acute epiglottitis. WBC, white blood cell.

<sup>a</sup> Case feature.

<sup>b</sup> Significantly different from those without positive blood cultures.

routine vaccination in the United States, Hib was responsible for 95% of invasive *H influenzae* infections in children. Although invasive infection secondary to Hib has decreased, it is still the primary causative agent of acute epiglottitis. In addition, the relative incidence of invasive disease by other forms of *H influenzae*, including Hif, has increased.<sup>6,10</sup> *H influenzae* can produce  $\beta$ -lactamase, which can result in resistance to penicillins and aminopenicillins; fortunately, strains are typically susceptible to  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations,<sup>11</sup> such as ampicillin-sulbactam or amoxicillin-clavulanic acid, which the case patient received. Although  $\beta$ -lactamase-negative, ampicillin-resistant *H influenzae* strains are emerging, particularly in Japan and Europe, worldwide isolates remain 99.6% susceptible to amoxicillin-clavulanic acid.<sup>12</sup> Other infectious causes of epiglottitis, although infrequent, include *Streptococcus pneumoniae*,  $\beta$ -hemolytic streptococci, and *Staphylococcus aureus*.<sup>2,13</sup>

The unique aspect to this case surrounds the fact that the child was generally healthy, fully immunized, and without other comorbidities that predispose to invasive Hif infection (malignancy, immunosuppression, or chronic lung disease of prematurity); these comorbidities account for 75% of patients with invasive Hif infection.<sup>14</sup> The above case presentation has many features that are consistent with a common presentation of typical epiglottitis, including respiratory difficulty, drooling, fever, dysphagia, muffled voice, and fever. Of those, respiratory difficulty, drooling, fever, and dysphagia are more likely to occur in those who have a positive blood culture with *H influenzae*.<sup>3,15</sup> The case features are listed in Table 1, which are consistent with a presentation of *H influenzae* bacteremia.

## CONCLUSIONS

Upper airway emergencies in a febrile child tend to have infectious origins, with croup, bacterial tracheitis, epiglottitis, and retropharyngeal abscess as the leading etiologies. Epiglottitis is a sporadic illness

among children in the post-Hib vaccination era, with Hib as the leading etiologic agent, primarily in unvaccinated, immune-compromised, and adult patients. Although rare, invasive diseases secondary to Hif are increasing, particularly in those with comorbidities such as immunosuppression.<sup>16</sup> Despite the marked decrease in invasive Hib disease, caregivers should continue to consider the pathogen *H influenzae* as a possible etiology in the clinical setting of acute epiglottitis, with a  $\beta$ -lactam/ $\beta$ -lactamase inhibitors or third-generation cephalosporins being reasonable first-line treatment options in these patients.

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