acid. Lipopolysaccharide endotoxin in the cell wall is toxic to ciliated respiratory cells, and when circulating in the bloodstream produces all the features of endotoxemia. \textsuperscript{\textsc{\textcopyright} Capsules and C3b, p. 394}

### Localized Disease
Nonencapsulated \textit{H. influenzae} produce disease under circumstances in which they are entrapped at a luminal site adjacent to the normal respiratory flora such as the middle ear, sinuses, or bronchi (Figure 31–2). This is usually associated with some compromise of normal clearing mechanisms, which is caused by a viral infection or structural damage. Consistent with their relative prevalence in the respiratory tract, nontypable organisms account for more than 90% of localized \textit{H. influenzae} disease, particularly otitis media, sinusitis, and exacerbations of chronic bronchitis. Nonencapsulated \textit{H. influenzae} attach to host epithelial cell using pili and the outer membrane proteins.

### IMMUNITY
Immunity to Hib infections has long been associated with the presence of anticapsular (PRP) antibodies, which are bactericidal in the presence of complement. The infant is usually protected by passively acquired maternal antibody for the first few months of life. Thereafter, actively acquired antibody increases with age; it is present in the serum of most children by 10 years of age. The peak incidence of Hib infections in unimmunized populations occurs at 6 to 18 months of age, when serum antibody is least likely to be present. This inverse relationship between infection and serum antibody is similar to that for \textit{N. meningitidis} (see Figure 30–4). The major difference is that substantial immunity is provided by antibody directed against a single type (Hib) rather than the multiple immunotypes of other bacteria. Thus, systemic \textit{H. influenzae} infections (meningitis, epiglottitis, cellulitis) are rare in adults. When such infections develop, the immunologic deficit is the same as that with meningococci—lack of circulating antibody. \textsuperscript{\textsc{Meningococcal immunity, p. 541}}

Like other polysaccharides, Hib PRP behaves as a T-cell–independent antigen, and antibody responses from immunization are poor in a child younger than 18 months of age. Significant secondary responses from boosters are not elicited. Conjugation of PRP to protein dramatically improves the immunogenicity by eliciting the T-cell-dependent responses typical while preserving the specificity for PRP. \textsuperscript{\textsc{T-cell dependent and independent responses, p. 37}}

### MANIFESTATIONS
Of the major acute Hib infections, meningitis accounts for just over 50% of cases. The remaining cases are distributed among pneumonia, epiglottitis, septicemia, cellulitis, and septic arthritis. Localized infections can be caused by capsulated strains including Hib, but most are noncapsulated \textit{H. influenzae}.

#### Meningitis
Hib meningitis follows the same pattern as other causes of acute purulent bacterial meningitis (see Chapter 65). Meningitis is often preceded by signs and symptoms of an upper respiratory infection, such as pharyngitis, sinusitis, or otitis media. Whether these represent a predisposing viral infection or early invasion by the organism is not known. Just as often, meningitis is preceded by vague malaise, lethargy, irritability, and fever. Mortality is 3% to 6% despite appropriate therapy, and roughly one third of all survivors have significant neurologic sequelae.

#### Acute Epiglottitis
Acute epiglottitis is a dramatic infection in which the inflamed epiglottis and surrounding tissues obstruct the airway. Hib is one of a number of causes. The onset is sudden, with fever,