Epidemiology

OUTLINE

Current Factors Likely to Alter the Epidemiology of Otitis Media
Role of PCV 7 in changing the epidemiology of otitis media
Guidelines for diagnosis and management of acute otitis media
Programs for physicians and parents to limit inappropriate use of antimicrobial agents

Historical Perspective
Incidence of Otitis Media
- National survey data
  - Regional and community studies
- Temporal trends
- Antibiotic use and surgical procedures as indicators of incidence of otitis media
- Utilization of services for otitis media based on insurance data
- Office visits
  - “Otitis-prone” child
- Persistence of middle-ear effusion after acute otitis media
- Risk features
- Middle-ear effusion in healthy children

Age
- Newborns
- Infants and toddlers
- School-age children, adolescents, and adults
- Age at first episode of recurrent otitis media
- Age and duration of middle-ear effusion

Sex

Race
- Native American and Inuit studies
- Children in developing areas
- The “safe ear”
- Chronic granulomatous otitis media
- African-American children
- Anthropologic and physiologic factors

Social and Economic Conditions
Day-Care Centers
  - Parental paid leave
Pacifier Use
Sleep Position

Season
- Smoking and Ambient Air Pollution
- Genetic Factors
- Breast-Feeding
- Altered Host Defenses and Underlying Disease
  - Cost analyses

Epidemiologic data about otitis media in infants and children provide information about risk features of children who have recurrent and severe disease, indicate temporal trends in incidence and severity of disease, and suggest a basis for methods of prevention and therapy. Longitudinal studies are a particularly rich source of information about otitis media. Among the longitudinal studies of value (in order of year of publication) are the Arctic Health Research Center study of middle-ear disease in Alaskan Inuit children1,2; studies by two pediatricians, Virgil Howie and John Ploussard of Huntsville, AL, of the natural history of otitis media in children seen in their office practice3,4; a prospective study of otitis media in 2,565 children observed from birth by pediatricians in the greater Boston area5; studies by members of the Department of Pediatrics, University of North Carolina School of Medicine, of respiratory disease in children attending the Frank Porter Graham Child Development Center6-10; a prospective study of 2,404 children born in Malmö, Sweden, in 197711; studies of Finnish children and adults12,13; a study of Nashville children observed from birth to the age of 2 years14; studies of Pittsburgh-area infants during the first two years of life15,16; a study of Australian aboriginal and non-aboriginal infants in the first year of life17; a study of otitis media with effusion in children from birth to the age of 3 years in the Oxford
area\textsuperscript{18}; a study of Greenlandic children from birth to the age of 8 years\textsuperscript{19}; and a study of Minnesota infants observed from birth to the age of 6 months\textsuperscript{20}.

Host factors that lead to increased risk include male sex and a genetic susceptibility to severe and recurrent disease. Environmental factors include day care outside the home, parental smoking, use of a pacifier, and not being breast-fed\textsuperscript{31}. Other risk features include race, altered host defenses, underlying disease, early occurrence of infection (early and often appears the rule), respiratory season, and environmental pollution. Each of these risk features is discussed in this chapter.

**CURRENT FACTORS LIKELY TO ALTER THE EPIDEMIOLOGY OF OTITIS MEDIA**

Three factors are likely to alter the epidemiology of acute otitis media (AOM) in the United States in the next few years: first, the introduction of the seven-valent pneumococcal conjugate vaccine (PCV 7) in 2000; second, the publication of management guidelines by the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) in 2004, which included an option of “watchful waiting” rather than immediate use of antimicrobial drugs\textsuperscript{22}; and third, the educational campaign to influence parents and physicians to avoid inappropriate uses of antimicrobial agents for trivial, usually viral, respiratory infections because of concern for development of multi-drug resistance. Any one or all of these factors may play a role in decreasing the number of diagnoses of AOM, as well as alter the microbiology of AOM, decrease the number of surgical procedures for severe and recurrent otitis media, and reduce the volume of antimicrobial agents used in infants and children.

**Role of PCV 7 in Changing the Epidemiology of Otitis Media**

PCV 7 was introduced in 2000 in the United States in a four-dose schedule for universal immunization of infants. By December 2005, 80 million doses had been distributed in the United States (P. Paradiso, personal communication, December 2005). Although the vaccine has been extremely effective in reducing the incidence of invasive pneumococcal disease (eg, bacteremia and meningitis), the reduction of episodes of AOM in immunized children has been limited. Three clinical trials have been performed and are discussed in Chapter 8, “Management”: a clinical trial of PCV 7 in Northern California documented vaccine efficacy of a reduction in office visits for otitis media of 7.8%, a reduction of antibiotic prescriptions by 5.7%, and a reduction in surgery for tympanostomy tube placements by 24\textsuperscript{33}; a trial in Finland identified a 6% decrease in the incidence of AOM in PCV 7 recipients, a reduction of 57% of AOM due to vaccine serotypes and a reduction of 51% of episodes due to cross-reactive serotypes, but a 33% increase in disease due to non-vaccine serotypes and an 11% increase in episodes of acute otitis media due to nontypeable *Haemophilus influenzae*\textsuperscript{24}; an 11-valent pneumococcal vaccine conjugated to a carrier protein D of nontypeable *H. influenzae* was studied in the Czech Republic and Slovakia and was found to prevent 52% of AOM episodes due to pneumococcal vaccine serotypes and 65.5% of episodes due to vaccine-related cross-reactive pneumococcal serotypes with no increase in episodes of AOM due to non-vaccine serotypes\textsuperscript{25}; the vaccine was also effective in reducing the incidence of episodes due to nontypeable *H. influenzae* by 35.3%.

In summary, regions with widespread use of a conjugate pneumococcal vaccine are likely to see fewer episodes of AOM and consequently less antibiotic use and fewer surgeries for placement of ventilating tubes. The vaccine efficacy for prevention of AOM is based, in part, on prevention of nasopharyngeal carriage of vaccine serotypes. But replacement with non-vaccine serotypes occurs over time so that the incidence of nasopharyngeal carriage of pneumococcus is not altered in immunized children. At this time (November 2006), there is uncertainty about the role of replacement of nasopharyngeal carriage
by non-vaccine serotypes in immunized children and the potential of these serotypes to cause AOM and blunt the effect of the conjugate pneumococcal vaccines. At least two studies suggest a change in the microbiology of AOM with a shift to nontypeable H. influenzae being the most frequently isolated pathogen rather than the pneumococcus.\textsuperscript{26,27}

**Guidelines for Diagnosis and Management of Acute Otitis Media**

In 2004, the American Academy of Pediatrics and the American Academy of Family Physicians, published a set of guidelines for diagnosis and management of AOM.\textsuperscript{22} The committee that prepared the guidelines included representatives of the Centers for Disease Control and Prevention (CDC) and the American Academy of Otolaryngology—Head and Neck Surgery. The guidelines focused on therapeutic measures including choice of antimicrobial agents and pain medications and guidelines for watchful waiting rather than use of an antimicrobial agent at onset of AOM. In addition, the guidelines emphasized the criteria for diagnosis and the importance of physicians maintaining skills in otoscopy and the use of adjunctive techniques such as tympanometry and acoustic reflectometry. The presentation of a uniform set of criteria for diagnosis of AOM may limit the number of ambiguous diagnoses and result in more accurate estimates of the incidence of AOM.

**Programs for Physicians and Parents to Limit Inappropriate Use of Antimicrobial Agents**

Concern for multi-drug resistance in the 1990s spurred the CDC and a number of professional organizations to limit inappropriate use of antimicrobial agents.\textsuperscript{28} Although much of drug resistance is due to the genetic composition of the various pathogens, extensive use of antimicrobial agents promotes selection of resistant strains by eliminating susceptible strains in the upper respiratory and gastrointestinal tracts, and permits resistant strains to flourish. There are data that indicate that the educational programs have been effective; a reduction of 25% in antibiotic scripts for children less than 6 years of age was identified in the records of nine health plans during the period 1996 to 2000. A decrease in prescriptions for otitis media accounted for 59% of the total reduction in antibiotic prescriptions.\textsuperscript{29} The parent has become an informed consumer and concerned about excessive usage of antibiotics; parental pressure to use antibiotics for inappropriate uses has decreased. In addition, physicians faced with uncertain diagnoses of AOM may be more likely to observe rather than prescribe an antimicrobial agent, as suggested in the AAP guidelines. The result may be a decrease in the incidence of diagnosed episodes of AOM based on physician judgment rather than a real change in incidence of the disease.

No large population studies of the incidence of AOM have been presented since the introduction of the conjugate pneumococcal vaccine (2000), the publication of the AAP guidelines (2004), and the educational programs to limit inappropriate use of antibiotics in the late 1990s. The available data suggest that one or all of the programs will alter the incidence and other features of the epidemiology of otitis media, but we can only speculate about the effects until the results of populations studies are available.

**HISTORICAL PERSPECTIVE**

It is likely that humans have always suffered from acute infection of the middle ear and its suppurative complications. Ear problems were a major concern for early peoples. Studies of 2,600-year-old Egyptian mummies reveal perforations of the tympanic membrane and destruction of the mastoid.\textsuperscript{30} Evidence of middle-ear disease was also apparent in skeletal material from a prehistoric Iranian population (1900 to 800 BC).\textsuperscript{31} Studies of interest about otitis media by physical anthropologists were reviewed by Daniel and colleagues.\textsuperscript{32}
Before antimicrobial agents were introduced, otitis media either resolved spontaneously (by central perforation of the tympanic membrane or evacuation of the middle-ear contents through the eustachian tube) or came to the attention of a physician who drained the middle ear by means of myringotomy. Purulent otitis media was a frequent reason for admission to a hospital. In 1932, purulent otitis media accounted for 27% of all pediatric admissions to Bellevue Hospital. Mastoiditis and intracranial complications were common. The introduction of sulfonamides in 1935 and subsequent antibacterial drugs limited the severity of otitis media and reduced the incidence of suppurative complications. Otitis media in children from developing countries with limited access to medical care today resembles the disease seen in the United States and Western Europe before the era of chemotherapy.

INCIDENCE OF OTITIS MEDIA

National Survey Data

Otitis media is one of the most common childhood infectious diseases. A survey of diagnoses made in office practices in the United States in 1990 by epidemiologists at the Centers for Disease Control and Prevention (CDC) identified 24.5 million visits at which the principal diagnosis was otitis media. For children younger than 15 years, otitis media was the most frequent diagnosis in office practices. Diagnoses of otitis media increased from 9.91 million visits in 1975 to 24.5 million visits in 1990 (Figure 1). Using data from the Third National Health and Nutrition Examination Survey, Auinger and colleagues described trends in the prevalence of ever having otitis media and repeated otitis media (3 or more episodes) among US children for the periods 1988–1991 to 1991–1994. The prevalence of ever having otitis media increased to 69.7% from 66.7%, and the prevalence of repeated otitis media increased to 41.1% from 34.8%.

The results of a survey of ambulatory surgery in the United States in 1994 included data on myringotomy with insertion of tympanostomy tube, tonsillectomy with or without adenoidectomy, and adenoidectomy without tonsillectomy and are listed in Table 1; myringotomy with insertion of tympanostomy tube was the most frequent ambulatory surgical procedure in children younger than 15 years (circumcision is more common but was not included in the survey).

Regional and Community Studies

Otitis media was second only to the common cold as a cause of infectious illnesses in Rochester children. Boston children had an average of 1.2 and 1.1 episodes of otitis media in the first and second years of life, respectively. Using a sample size of approximately 3.9 million children born in the United States each year, one can extrapolate from the Boston data that approximately 20 million episodes of AOM occur each year in children from birth through the seventh year of life, a figure consistent with the 24.5 million office visits identified by the CDC (see Figure 1).

Temporal Trends

Because of differences in definition and techniques of diagnosis of AOM, it is difficult to compare incidence data from time to time unless the same set of observers are responsible. In addition, change may occur over time in factors that could affect the diagnosis of otitis media, including health care and reporting systems, access to and use of medical care, and parents’ and physicians’ awareness of the disease and its importance. Nevertheless, many studies suggest...
that there has been an increased number of
diagnoses of otitis media in recent years (see
Figure 1), including a 150% increase from 1975
to 1990 identified in the CDC survey described
earlier. An increased number of operative
procedures, including myringotomy and place-
ment of tympanostomy tubes, was identified in
Montreal children during only a 2-year period
from 1981 to 1983. The reasons for the
apparent increase in diagnoses and courses of
therapy are uncertain but may represent
increased awareness of the disease and perceived
need for aggressive use of antimicrobial agents
and operative procedures, an increase in expo-
sure as may occur with the large number of
children in day care, or another unknown
epidemiologic feature. As noted above, the
introduction of the pneumococcal conjugate
vaccine, publication of the AAP and AAFP
guidelines on diagnosis and management of
AOM and increased awareness by physicians
and parents about the development of multi-drug
resistance may alter these trends in the incidence
of AOM.

**Antibiotic Use and Surgical Procedures as
Indicators of Incidence of Otitis Media**

Most use of oral antibiotics for infants and
children in the United States is for otitis media,
and the number of prescriptions suggests the
incidence of the disease and temporal trends in
diagnoses. Investigators from the United States
Food and Drug Administration found that
nearly half of the courses of antibiotics pre-
scribed for children younger than 10 years in
1986 were administered for otitis media; 44.5
million courses were prescribed, and 42% of the
prescriptions were for treatment of otitis media. The number of prescriptions for anti-
fungicides represented 38% of all outpatient
prescriptions. An increase in antibiotic use
was noted during the 10-year period 1977 to
1986 of the survey for children younger than 3
years; 125 uses per 100,000 children in 1977
increased to 185 uses per 100,000 children in
1986. A study of 222 children enrolled in the
Primary Care Clinic at Johns Hopkins Hospitals
from birth to the age of 5 years identified otitis
media as the most frequent diagnosis for all
prescriptions; amoxicillin was the most fre-
cently prescribed drug (31.7% of all prescriptions). In a study of 2,253 Pittsburgh-area
infants, the mean number of days of antimicro-
bial therapy for otitis media was 41.9 and 48.6
for the first and second years of life, respectively;
infants received antimicrobial therapy for other
reasons for a mean of only 1.9 and 4.1 days in
the first and second years of life, respectively.
Because of concern for the increasing incidence
of resistant bacterial pathogens associated with
the extensive use of antimicrobial agents, author-
itative groups, including the CDC, AAP and
AAFP, have provided educational materials
directed to parents and physicians to reduce
use of antimicrobial agents for trivial, usually
viral, infections. The educational materials
appear to have been successful. A study of
health plans for the period 1996 to 2000
identified a decrease in antibiotic rates for
children 3 months to 3 years from 2.46 to 1.89
antibiotics per patient per year; a decrease of

### Table 1. **NATIONAL SURVEY OF AMBULATORY SURGERY PROCEDURES, 1994: MYRINGOTOMY WITH INSERTION OF TUBE,
TONSILLECTOMY WITH OR WITHOUT ADENOIODECTOMY, AND ADENOIODECTOMY**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number in Thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myringotomy and tube</td>
<td>579</td>
</tr>
<tr>
<td>Tonsillectomy with or without</td>
<td>378</td>
</tr>
<tr>
<td>Adenoidectomy only</td>
<td>152</td>
</tr>
</tbody>
</table>

**Republished with permission from Kozak LJ et al.**

Epidemiology
24%. Similar decreases were noted for older children. A decrease in prescriptions for otitis media was responsible for 59% of the decrease in antibiotics and was accompanied by a decrease in number of diagnoses of otitis media.\(^{29}\)

The high attack rate of otitis media in the infant and toddler years is also reflected in the number of surgical procedures performed for otitis media. The national data for ambulatory surgery provide the rate of procedures for tympanostomy tubes, adenoidealctomy, and mastoidectomy to age 13 years (Table 2). These data are similar to those described by investigators in Pittsburgh and Boston.\(^{16,42}\) The percentage of subjects undergoing tympanostomy tube operations was 1.8 and 4.2 in the first and second years of life of Pittsburgh children. A similar proportion of Boston children also had tympanostomy tube placement, 1.5% and 5.7% among children with at least one episode of AOM in the first and second years of life.\(^{42}\) Regional differences in rates of procedures for placement of ventilating tubes are to be expected because the criteria for surgery remain a matter of judgment of defining severe and recurrent AOM and/or persistence of middle-ear effusions and the impact of ear disease on the child. Coyte and colleagues found substantial variation in areas of Ontario; there was an almost tenfold difference between areas with highest and lowest rates.\(^{43}\) The results of clinical trials of the conjugate pneumococcal vaccine in Northern California and Finland indicated a 25% decrease in surgeries for children with severe and recurrent otitis media (most for placement of ventilating tubes) but there are no national data that corroborate these results.\(^{24,44}\)

**Utilization of Services for Otitis Media Based on Insurance Data**

Berman and colleagues have used Colorado Medicaid data to track utilization of services for otitis media by children younger than 13 years\(^{45}\) and otitis media–related outcomes, expenditures, and antibiotic-prescribing patterns.\(^{46}\) The utilization data for 1991 and 1992 included ambulatory visits for otitis media of 0.7 per child-year for all children enrolled in Medicaid, and 2.8 visits per child-year for children with otitis media; drug fills were 0.5 per child-year for all children and 1.8 per child-year for children with otitis media. Surgical procedures for management of children with otitis media were 16.9/1,000 child-years and 64/1,000 child-years. Surgical procedures by age from the Medicaid data are listed in Table 2.

Massachusetts children younger than 10 years enrolled in a large health insurer in New England who had one or more episodes of AOM were surveyed for characteristics of otitis media management.\(^{42}\) Study subjects averaged 2.9 office visits for otitis media; among children younger than 2 years, one-quarter had six or more visits for otitis media. Amoxicillin was prescribed as initial therapy in 56.6% of all episodes of AOM, followed by cephalosporins (18.3%), trimethoprim-sulfamethoxazole (12.3%), macrolides (6.4%), and amoxicillin-clavulanate (6.0%). Surgical procedures related to otitis media (the majority of which were myringotomy and insertion of tympanostomy tube) were performed on 3.8% of all study subjects, including 4.6% of children younger than 2 years.

### Table 2. SURGICAL PROCEDURES FOR CHILDREN WITH OTITIS MEDIA

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Tympanostomy Tubes</th>
<th>Adenoidectomy</th>
<th>Mastoidectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>15</td>
<td>0.35</td>
<td>0</td>
</tr>
<tr>
<td>1–2</td>
<td>62</td>
<td>4.3</td>
<td>0.3</td>
</tr>
<tr>
<td>2–3</td>
<td>61</td>
<td>12.9</td>
<td>0.9</td>
</tr>
<tr>
<td>3–6</td>
<td>44</td>
<td>29</td>
<td>0.6</td>
</tr>
<tr>
<td>6–13</td>
<td>29</td>
<td>26.4</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Reproduced with permission from Byrns PJ et al.\(^{45}\)

*Enrolled in Colorado Medicaid program.

For children with otitis media surveyed during a 2-year period.

**Office Visits**

Of the reasons for illness for which children visit the physician, otitis media is the most frequent. In addition to the national database discussed earlier and represented in Figure 1, data from prospective studies of children in Boston and Pittsburgh
identify the prevalence of otitis media during the first years of life. The proportion of office visits of young children for otitis media was elucidated by Teele and colleagues (Table 3).\textsuperscript{47} Middle-ear disease accounted for a large proportion of visits during the first 5 years, rising from 22.7% in the first year to approximately 40% in years 4 and 5; about one visit in three made for illness of any kind resulted in the diagnosis of middle-ear disease; approximately three-quarters of all visits to follow up any illness were made for disease of the middle ear; and either AOM or asymptomatic middle-ear effusion was diagnosed at 5 to 10% of all well-child visits. In the longitudinal study of Pittsburgh children, otitis media was responsible for a mean of 2.9 and 3.1 office visits during the first and second years, respectively.\textsuperscript{16} The Northern California conjugate pneumococcal vaccine trial identified a decrease in office visits for AOM of 7.8% in immunized, contrasted with control, children.\textsuperscript{23} Since the vaccine study was blinded, the decreased number of visits will likely be replicated in other populations of immunized children. How long the protective effect for episodes of AOM will last for infants immunized in the four-dose schedule to 12 months of age is yet to be determined.

**“Otitis-Prone” Child**

The longitudinal studies suggest that by age 3, children may be categorized into three groups of approximately equal size relative to acute

<table>
<thead>
<tr>
<th>Table 3. PROPORTION OF VISITS ATTRIBUTABLE TO DISEASE OF THE MIDDLE EAR IN CHILDREN IN GREATER BOSTON (1975–1982)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose of Visits</strong></td>
</tr>
<tr>
<td>First Year of Life (2,176 Child-Years of Observation)</td>
</tr>
<tr>
<td>Illness</td>
</tr>
<tr>
<td>Follow-up illness</td>
</tr>
<tr>
<td>Well-baby visit</td>
</tr>
<tr>
<td>Totals</td>
</tr>
<tr>
<td>Second Year of Life (1,720 Child-Years of Observation)</td>
</tr>
<tr>
<td>Illness</td>
</tr>
<tr>
<td>Follow-up illness</td>
</tr>
<tr>
<td>Well-baby visit</td>
</tr>
<tr>
<td>Totals</td>
</tr>
<tr>
<td>Third Year of Life (1,317 Child-Years of Observation)</td>
</tr>
<tr>
<td>Illness</td>
</tr>
<tr>
<td>Follow-up illness</td>
</tr>
<tr>
<td>Well-baby visit</td>
</tr>
<tr>
<td>Totals</td>
</tr>
<tr>
<td>Fourth Year of Life (660 Child-Years of Observation)</td>
</tr>
<tr>
<td>Illness</td>
</tr>
<tr>
<td>Follow-up illness</td>
</tr>
<tr>
<td>Well-baby visit</td>
</tr>
<tr>
<td>Totals</td>
</tr>
<tr>
<td>Fifth Year of Life (529 Child-Years of Observation)</td>
</tr>
<tr>
<td>Illness</td>
</tr>
<tr>
<td>Follow-up illness</td>
</tr>
<tr>
<td>Well-baby visit</td>
</tr>
<tr>
<td>Totals</td>
</tr>
</tbody>
</table>

*According to patients.
Reproduced with permission from Teele DW et al.\textsuperscript{47}
middle-ear infections. One group is free of ear infections, a second group may have occasional episodes of otitis media, and a third group is “otitis-prone,” subject to repeated episodes of acute middle-ear infections. The definition of number of episodes to be identified as otitis-prone has varied among investigators, including three, four, or six episodes in various time periods. In their office practice, Howie and colleagues identified 1 in 7 children who had more than 6 episodes of otitis media by their second birthday. The Boston study showed that 46% of children had 3 episodes or more and 16% had 6 episodes or more of AOM by age 3 (Table 4). The risk features noted later should be assessed so that children who are otitis-prone may be identified as early as possible and managed aggressively with prophylactic methods.

Persistence of Middle-Ear Effusion After Acute Otitis Media

The incidence or prevalence of otitis media with effusion that is apparently asymptomatic and unrecognized by parents (and therefore not brought to medical attention) has been the subject of many studies in the United States and in Scandinavia. Persistence of middle-ear effusion for weeks to months after the onset of AOM was frequent in Boston children: 70% of children still had effusion at 2 weeks, 40% had effusion at 1 month, 20% had effusion at 2 months, and 10% had effusion at 3 months (Figure 2). The means for periods of time spent with middle-ear effusion after the first, second, and third episodes of AOM were almost identical, ranging from 39 to 44 days. Age at time of diagnosis was inversely associated with duration of middle-ear effusion after first episodes of AOM. Similar results of persistent middle-ear effusion after an episode of AOM have been noted in studies from other centers (Table 5). The type of antibiotic used to treat AOM had no effect on the duration of middle ear effusion. The prospective study of 2,253 Pittsburgh children indicated that children had a mean of 20.4 and 16.6 days with middle-ear effusion in the first and second years of life, respectively. Because of the frequency of episodes of AOM during the first years of life, the child may spend a significant proportion of these years of dynamic language development with effusion and associated hearing impairment.

Risk Features

Prolonged duration of middle-ear effusion in children has been associated with age, male gender, sibling history of ear infection, and not being breast-fed; with smoking in the household; and with attendance in day care. To determine risk for individual episodes of prolonged middle-ear effusion of 8 weeks or more, Daly and colleagues identified the following predictors: bilateral otitis media with effusion, duration of effusion for longer than 2 weeks at enrollment, and day-care attendance.

### Table 4. INCIDENCE OF ACUTE OTITIS MEDIA IN BOSTON CHILDREN

<table>
<thead>
<tr>
<th>Cumulative Percentage of Children Observed with Indicated Number of Episodes of Otitis Media*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo)</td>
</tr>
<tr>
<td>≤3</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>24</td>
</tr>
<tr>
<td>36</td>
</tr>
</tbody>
</table>

*2,565 children enrolled at birth. Reproduced with permission from Teele DW et al.
Middle-Ear Effusion in Healthy Children

Surveys of healthy children for presence of middle-ear fluid have identified a high incidence of apparently asymptomatic middle-ear effusion. All surveys used tympanometry to assess middle-ear status. The prevalence of effusion varied with age and the time of year. Incidence of effusion peaked during the second year of life, and it was more prevalent in the winter than in the summer months. Repeated examinations revealed that the middle-ear fluid cleared spontaneously in most children within a few months. A survey of 2- to 5-year-old African American children in day care revealed that time with middle-ear effusion decreased progressively with increasing age; the mean proportion of examinations demonstrating bilateral effusion ranged from 12% between the ages of 24 and 30 months to 4% between the ages of 54 and 60 months.

In children from Pittsburgh aged 2 to 6 years observed monthly for a 2-year period, approximately two-thirds of the episodes of otitis media with effusion cleared within 1 month. In many children, the duration of effusion may be as short as 1 day or several days; a novel investigation of daily impedance screening of children 3 to 6 years old in a day-care center revealed that many children had tympanometric evidence of effusion (B curves) for 1 day only. Some children, however, had fluid for 6 months or longer, and it was often seen first in one ear and then in the other on subsequent examinations. Thus, asymptomatic middle-ear effusion is relatively frequent in healthy children but usually resolves without medical or surgical intervention.

### AGE

Otitis media is a disease of infancy and early childhood. The peak age-specific attack rate occurs between 6 and 18 months. Children who have had little or no experience with otitis media by the age of 3 are unlikely to have subsequent severe or recurrent disease. The occurrence of disease early in life is likely to be a result of maturing anatomic, physiologic, and immunologic factors, some of which are identifiable (eg, the change in skull configuration and vectors of the eustachian tube, a development of protective antibodies to bacterial pathogens) but many of which are still to be defined.

### Newborns

In the newborn, otitis media may be an isolated infection or it may be associated with sepsis, pneumonia, or meningitis. There is a paucity of data about the incidence of otitis media in newborns.
newborns. A partial explanation may be that otoscopy is not always a part of the examination of the neonate. Apart from the very-low-birth-weight premature infants, otoscopy in the newborn is not a formidable challenge for the experienced physician. Otitis media with effusion was identified in 24 of 70 Cleveland infants (34%) observed at or before the age of 2 months who were recruited from normal newborn nurseries. Approximately half of the children at age 2 months with otitis media with effusion were asymptomatic. Warren and Stool consecutively examined 127 infants whose birth weights were below 2,300 g and found three with middle-ear infections (at 2, 7, and 26 days). Jaffe and colleagues examined 101 Navajo infants within 48 hours of birth and identified 18 with impaired mobility of the tympanic membrane. Balkany and coworkers identified effusion in the middle ears of 30% of 125 consecutively examined infants who were admitted to a neonatal intensive care unit. The clinical diagnosis was corroborated by aspiration of middle-ear fluid. Nasotracheal intubation for more than 7 days was correlated with presence of effusion. Pestalozza observed 970 Italian newborn infants aged 2 to 25 days who were in the neonatal pathology ward; 205 infants (21.1%) were found to have otitis media by otoscopy, corroborated in two consecutive visits within 48 hours.

Low birth weight and prematurity are of uncertain importance as risk features for subsequent experience with otitis media. Neither the study of Boston children nor that of Finnish children identified low birth weight or prematurity as a factor of importance in children with serious and recurrent ear infections. An Australian study of very-low-birth-weight infants (< 1,500 g), however, did identify significant differences in the incidence of otitis media and in conductive hearing loss during the first 5 years of life contrasted with normal birth weight infants. On the basis of longitudinal data acquired by the National Maternal and Infant Health Survey, Nalluswami and colleagues reported that very-low-birth-weight infants were at increased risk for frequent otitis media in the first 3 years of life.

Although otitis media in the neonate and young infant may be accompanied by invasive bacterial infection, including bacteremia and meningitis, serious bacterial infections are uncommon. Nozicka and colleagues reported that none of 25 afebrile and 2 of 15 febrile infants less than 2 months of age with AOM developed serious bacterial infection. In another series of 137 Israeli infants with AOM who were less than 2 months of age, 70% were febrile (38°C or more). None of the febrile or afebrile infants had concurrent serious bacterial infections.

Early onset of pneumococcal otitis media has been associated with low levels of cord blood pneumococcal immunoglobulin G antibodies. Among a group of infants who had siblings with middle-ear disease, low concentrations of cord blood antibody to pneumococcal serotype 14 or 19F was predictive for recurrent episodes of otitis media in the first year of life. These results have prompted studies of maternal immunization to prevent pneumococcal disease in neonates and young infants.

**Infants and Toddlers**

Otitis media is common in infants beyond the neonatal period (after 28 days of age). In the study of children in Boston, 9% had at least one episode of otitis media by the age of 3 months, 25% had one or more episodes by the age of 6 months, and 62.4% experienced otitis media by the age of 12 months. A prospective study of infants to 6 months of age in a health maintenance organization identified one or more episodes in 39%, whereas 20% had two or more episodes. The highest age-specific incidence for all episodes of AOM (first and subsequent episodes) occurred between the ages of 6 and 13 months. Similar results were identified in Nashville children observed from birth; by age 3 months, 7% had an episode of AOM, and the peak incidence of middle-ear infection occurred at the age of 7 to 9 months. Of 3,189 Finnish
infants, 34.5% had one or more episodes of AOM during the first year of life, 24.8% had one or two episodes, and 9.7% had three or more attacks.\(^7^4\)

**School-Age Children, Adolescents, and Adults**

The incidence of otitis media declines with age after the first year of life, except for a limited reversal of the downward trend between the ages of 5 and 6 years (the time of entrance into school). Otitis media is less common in children 7 years and older. Although the incidence of AOM is limited in adults, a survey by the National Disease and Therapeutic Index published in 1970 found that there are almost 4 million visits by adults each year to private physicians for this infection.\(^7^5\) Approximately 20% of young Swedish adult men (aged 20 to 30 years) and 30% of older men (aged 50 to 60 years) had pathologic changes of the tympanic membrane; most with serious pathologic findings had histories of otitis media and otorrhea of long duration.\(^7^6\)

**Age at First Episode of Recurrent Otitis Media**

Age at first episode of AOM is significantly associated with recurrent episodes. In the Boston study, the peak incidence for first episodes of AOM occurred at the age of 6 months.\(^5^\) Age at first episode of AOM was significantly and inversely associated with risk for one or more (or two or more) episodes of AOM in the 12 months after initial diagnosis. Cleveland infants with onset of otitis media with effusion before the age of 2 months had a mean of 3.5 total months of bilateral effusion, compared with 1.2 months for those with later onset. Bilateral middle-ear effusion in these infants at 2 months of age was highly predictive of subsequent bilateral persistent otitis media with effusion (effusion for a continuous period of 3 months or longer).\(^6^3\) Navajo infants with otitis media during the first months of life had more recurrences than did those infants free of disease early in life.\(^6^5\) Alaskan Inuit children who had onset of disease during the first 2 years of life had many more middle-ear infections in later life than did children who did not have middle-ear infections early in life.\(^1^\) Howie and colleagues noted that children with two or more episodes in the first year of life had twice as many subsequent episodes of otitis media than did children who had no or only one episode in the first year.\(^4^\)

Why children with episodes of AOM early in life are at risk for recurrent disease is uncertain. These children may have an anatomic defect, such as cleft palate or submucous cleft, or a less apparent physiologic disability, as occurs with eustachian tube dysfunction or an overt (agammaglobulinemia or chronic granulomatous disease) or subtle (immunoglobulin subclass deficiency) immunologic defect that predisposes them to middle-ear infection. The early onset of infection highlights the underlying predisposing anatomic, physiologic, or immunologic deficit, analogous to an infection of the urinary tract leading to identification of the underlying anatomic or physiologic defect of the urinary tract.

**Age and Duration of Middle-Ear Effusion**

The age-specific incidence of otitis media with effusion parallels that of acute infection; the peak was at the age of 6 to 13 months in Boston children\(^5\) and 10 to 12 months in Nashville children.\(^1^4\) Persistent effusions of the middle ear were more likely in young children. Pelton and coworkers found that approximately 50% of children 2 years old or younger had effusions that lasted for 4 weeks or more after an episode of AOM, whereas only 20% of children older than 2 years had effusions of this duration.\(^7^7\)

**SEX**

As is true of most infections of infancy and childhood, males have a higher incidence of AOM than do females. In the Boston study, males had significantly more single and recurrent (three or more) episodes.\(^5\) Finnish males had significantly more episodes than did females in
eight communities studied in a 1-year period beginning June 1978. Males have more myringotomies and tympanoplasties than females, a fact suggesting that chronic or severe middle-ear infections are more common among males.

**RACE**

Selected racial groups, most in developing countries or hostile environments, have an extraordinary incidence of severe episodes of AOM with frequent perforation of the tympanic membrane and persistent suppurative drainage and necrotizing process in the middle ear, including destruction of the ossicles. However, differences among races are not necessarily explained by socioeconomic factors. As an example, in Hong Kong, rates of otitis media with effusion in white 5- to 6-year-olds were seven times higher than in same-aged Chinese children.

**Native American and Inuit Studies**

Native Americans and Alaskan and Canadian Inuit have a high incidence of severe otitis media. The following examples illustrate the extent and severity of ear disease in these populations.

In a prevalence study of an Apache community of 500 people of all ages, evidence of present or past ear infection was found in 23% (draining ear, 5.6%; perforation, 2.8%; healed perforation or tympanosclerosis or both, 13.1%). Arctic Health Research investigators found a high rate of otorrhea in Alaskan Inuit children: by the age of 1 year, 38% had at least one episode, and 20% of all children had two or more episodes; by the age of 4 years, 62% of children had had one or more episodes of otorrhea, and 40% of the children had had two or more episodes. Ling and colleagues found that 31% of Canadian Inuit children aged 10 years or younger living on Baffin Island had draining ears at the time of examination. None of the children was febrile or had evidence of AOM. Chronic suppurative otitis media was present in 6% of 142 of the 3- to 8-year-old Inuit children living in Greenland.

**Children in Developing Areas**

Children in developing areas are also afflicted by severe and disabling suppurative episodes of otitis media. Chronic suppurative otitis media and sensorineural hearing loss (probably as a sequela of the chronic infection) are frequent. Perforation and mastoiditis are relatively frequent in children presenting to ear, nose, and throat clinics, and severe complications are seen, including subperiosteal abscess, labyrinthitis, facial palsy, meningitis, and brain abscess.

Lack of access to medical care and local environmental factors are some of the causes of these severe sequelae of acute middle-ear infection. Use of herbal remedies and poultices placed in the ear canal may alter the course of infection and influence the microbiologic flora (L. Haller, personal communication, October 2000). An increase in rates of otitis media with effusion in 8- to 10-year-old Vietnamese children was thought to be due to beginning work in the rice fields. Chronic suppurative otitis media was more frequent among rural school children (9.4%) than among urban school children (1.3%) in Tanzania. In addition, the rural children had higher rates of sensorineural hearing impairment (14.1%) than did urban children (7.7%). The prevalence of perforated eardrums in an aboriginal settlement in Queensland was 25% of children aged 4 to 12 months and approximately 10% of children aged 6 to 12 years. Wet or dry perforation was observed in 4.2% of 170 children younger than 15 years living in a Nigerian village. In a prevalence study of children and adults in Micronesia, approximately half of Micronesian infants younger than 1 year had otitis media with effusion, and 4% of ears examined of persons 2 months to 25 years of age had a perforation.

**The “Safe Ear”**

A form of middle-ear infection, necrotizing otitis media, is seen in children living in developing countries but is rarely seen in children living in developed areas. An episode of acute middle-ear
infection progresses to perforation of the tympanic membrane with profuse discharge. Necrosis of the tympanic membrane follows, leaving a large central perforation that may persist for many years. This ear is called a safe ear because the perforation allows drainage of the middle-ear infection, and intracranial complications rarely occur, even without use of antimicrobial agents. However, there may be destruction of the ossicular chain, and deafness may result.\textsuperscript{89–91} Parents in these areas accept otorrhea as a way of life.

**Chronic Granulomatous Otitis Media**

Timmermans and Gerson described a more indolent form of otitis media in Canadian Inuit children that they termed *chronic granulomatous otitis media*.\textsuperscript{92} After one or more episodes of acute otitis media (usually treated with antimicrobial agents), there is a sudden onset of otorrhea without pain or fever. The discharge may persist for years, interspersed with periods of variable length in which the ear is dry. A large central perforation of the tympanic membrane is present, and granulomatous tissue fills the middle-ear cavity. Resolution occurs with a scarred tympanic membrane and a mild to moderate hearing deficit.

**African-American Children**

Early surveys of African-American children indicated that they had less otitis media than white children. The incidence of pathologic ear disorders and hearing impairment was higher in white children than in black children 6 months to 11 years of age who lived in Washington, DC.\textsuperscript{93} Ear disease was noted in 35% of 112 white children and 18% of 2,031 black children. Hearing was tested in children 4 to 11 years old; 20% of 82 white children and 6% of 1,545 black children had significant hearing impairment. The predominance of ear disease in white children was not readily explained. The results may be related to the relatively small size of the sample of white children or to socioeconomic factors unique to the white children living in a predominantly African-American community. In a second study in the Washington, DC area, investigators observed a tenfold difference in the incidence of AOM in white and black children. The disease rate in children younger than 15 years with at least one encounter for AOM was 155 per 1,000 children attending a clinic in an affluent, predominantly white suburb; it was 15 per 1,000 children attending a clinic in a blue-collar area of northeast Washington, DC, in which nearly all the patients were African-American.

The results of the interracial Washington studies are corroborated by studies from Cleveland and Boston and the CDC survey. AOM during the first year of life occurred in significantly more white Cleveland children (38 of 44) than black children (16 of 26).\textsuperscript{63} In Boston children, Pelton and coworkers noted a higher incidence of persistent effusions in white children (51% of 51 children) than in black children (21% of 42 black children).\textsuperscript{77} The CDC surveillance of office practices in the United States noted that visits for otitis media were significantly more frequent for whites younger than 15 years than for blacks in the same age group for 1980, 1985, and 1990. Whites younger than 15 years made about 25.5 visits per 100 in 1980, compared with 7.2 visits per 100 blacks in the same age group. The comparable figures in 1990 were 38.8 and 16.1, respectively, with both groups showing an increase in the time period.\textsuperscript{34} The higher incidence of ear disease in white children compared with black children is not readily explained, although the number of all visits for medical attention may be lower in the African-American community and may explain, in part, the smaller number of diagnoses of otitis media in black children as contrasted with diagnoses in white children. In contrast, Casselbrant and colleagues examined black and white Pittsburgh children, from birth at monthly intervals and whenever an upper respiratory infection or ear signs occurred and found no racial differences.\textsuperscript{15} The cumulative incidence of AOM was 60% for black children and 56% for white children.
Anthropologic and Physiologic Factors

Doyle demonstrated differences in the position of the bony eustachian tube in skulls of African-Americans, Americans of white ancestry, and Native Americans.\textsuperscript{94} Significant differences among the racial groups were present in the length, width, and angle of the tube in the groups, implicating an anatomic basis for racial predisposition to, or protection from, otitis media.

Further information about possible mechanisms was provided by Beery and associates, who studied eustachian tube function in Apache Indians living in Arizona.\textsuperscript{95} The results of inflation-deflation tests indicated that Native Americans had lower forced opening pressures than had been measured previously in a group of white subjects (with perforations secondary to chronic otitis media). The eustachian tube of the American Indian was functionally different from that of the white subjects previously studied and was characterized by comparatively abnormal, low passive tubal resistance, which may be considered to facilitate ventilatory activity but impair the protective function of the tube. The authors speculated that the difference may account for the high prevalence of otitis media with perforation (and the low incidence of cholesteatoma) in this population. Todd and Bowman studied Apache Indians in Arizona at two periods, 16 years apart, and arrived at similar conclusions.\textsuperscript{96}

Few interracial studies have been done, and we cannot therefore fully evaluate the significance of the extent and severity of ear disease in different racial groups. Poverty is a common factor among many of the nonwhite populations that have been studied. Other variables include extremes of climate (temperature, humidity, altitude), crowding in the homes, inadequate hygiene, poor sanitation, and lack of medical care. Although the difference in disease incidence for different racial groups may be real, other explanations must be considered, including differences in the perception of signs of ear infection by parents, the basis for visits to the physician, the basis of payment for medical services, and the diagnostic acumen or style of the clinic physicians.\textsuperscript{97}

SOCIAL AND ECONOMIC CONDITIONS

Poverty has been considered an important risk factor for the rate and severity of otitis media. A study of Pittsburgh children found an inverse relationship during the first 2 years of life between the total number of days with middle-ear effusion and a socioeconomic index based on type of health insurance and level of maternal education.\textsuperscript{16} Children in suburban practices (likely to be affluent) had a mean percentage of days with middle-ear effusion of 15.4 and 13.9 in the first and second years of life, respectively, compared with 27.7 and 20.8 days, respectively, in the first and second years of life of children from urban practices (more likely to include parents with low incomes).

Cambon and associates noted a strong relationship between middle-ear disease and poor social conditions among First Nations people of British Columbia.\textsuperscript{98} The specific reasons for the high incidence and severity of disease were not identified. Suggested factors include crowded living conditions, poor sanitation, and inadequate medical care. "The running ear is the heritage of the poor"\textsuperscript{98} may be as true today as in the past, but we still do not understand the reasons for the high incidence and marked severity of disease among the underprivileged.

Children living in households with many members are more likely to have otitis media than are children living in smaller households. Canadian Inuit children living in camps have less disease than do children living in villages and towns.\textsuperscript{99} Finnish children living in rural areas have fewer episodes of AOM than do children living in towns,\textsuperscript{13} and Finnish children in the lowest socioeconomic classes have more AOM during the first year of life than do young infants in the highest socioeconomic class.\textsuperscript{74}
Paradoxically, data from the 1988 National Health Interview Survey on Child Health indicated an increased incidence of recurrent ear infections in children in higher socioeconomic groups\(^{100}\), the diagnosis of “repeated ear infection” occurred in 28.8% of children whose parents had family income in excess of $35,000 in 1988, whereas 21.5% of children whose parents had family income less than $10,000 had this diagnosis. These data may reflect access to medical facilities with increased number of office visits among the children in more affluent households.

**DAY-CARE CENTERS**

The setting for child day care in the preschool years (child’s home, other home or family-based care, or large center facility) is an important factor in the incidence of otitis media. The more children in the day-care group, the more exposure to respiratory pathogens and the higher the rate of respiratory tract infections, including otitis media. Early placement of the child in out-of-home group day care may discourage breast-feeding, with a decrease in the benefit of breast-feeding in reducing the incidence of otitis media in the first year of life. Use of group day care in various countries is associated with maternal leave policies. In the United States, children may be placed in day care in the first months of life, whereas children in Norway typically enter day care at about 1 year of age, and placement of infants in day care in Western Germany is less frequent than in the United States (Franz E. Babl, February 2000, personal communication).

The number of American children who receive some form of day care is large and growing (Table 6). Current estimates are that more than 11 million children receive full-time or part-time day care. More than 50% of mothers who have children younger than 6 years work outside the home. Family child care facilities may be categorized as small family child care which provide care for up to 6 children at a time; large family child care facilities provide care for 7 to 12 children; and child care centers provide care to 13 or more children. Some facilities have adequate room and ventilation, whereas others are crowded and poorly ventilated. In the day-care setting, coughing and sneezing at close range are common. Rhinovirus and respiratory syncytial virus can remain infective for hours to days in moist or dried secretions on nonporous materials such as toys, and the organisms can survive for more than 30 minutes on cloth or paper tissues saturated with secretions. Epidemics of disease due to respiratory viruses are common. Thus, there is more opportunity for spread of respiratory infections among children in day care and for higher incidence of infection in children attending day care than in children who receive care at home. Day-care attendance has increased substantially in the last 25 years (see Table 6).

In urban areas of Finland, community day-care centers are common, and children have a higher incidence of otitis media than do children living in the Finnish countryside, who are more likely to be cared for in their homes.\(^{101}\) Alho and colleagues in Oulu, Finland, identified day care in a local authority nursery as the major risk factor for acute otitis media.\(^4\) Danish children cared for outside the home have shown a history of otitis media that is 25% higher than that of children cared for in the home; in addition, effusion, identified by tympanometry, occurred more frequently in children cared for outside the home than at home.\(^{102}\) Approximately three or more episodes of otitis media occurred in 10% of 150 Swedish children aged 6 to 24 months in family day care (42) or in day-care centers (108) and in none of 57 children who received care at home.\(^{103}\)

| Table 6. CHANGING PATTERNS OF CARE OF PRESCHOOL CHILDREN IN THE UNITED STATES* |
|----------------------------------|---------|---------|
| **1965 (%)** | **1990 (%)** |
| Day-care center | 6 | 28 |
| Parent | 29 | 28 |
| Relative | 33 | 19 |
| In-home care | 15 | 3 |
| Family day care | 16 | 20 |


*Based on surveys of employed mothers.
Pittsburgh children observed from birth who were in group day care (7 children or more) had many more episodes of otitis media than did children in home care. Myringotomy and tympanostomy tube placements were performed by the second year of life in 21% of children in group day care and in only 3% of children in home care. Over time, the frequency and severity of infections diminished, with fewer days of respiratory illness in year 3 compared with years 1 and 2. Other studies that have identified the increased incidence of otitis media in children attending day-care centers include studies from Norway, Minnesota, and the metropolitan Boston area.

Parental Paid Leave

Placing infants in day care is usually necessitated by the professional needs of one or both parents. The inevitability of multiple respiratory infections, including otitis media, in the first years of life for infants placed in large group day care suggests that any measures to delay placement in day care would be a worthy step in preventing otitis media. Paid parental leave is available in many countries but is only now reaching a stage of discussion and experimental programs in the United States. The Federal Family and Medical Leave Act now guarantees only 6 weeks of unpaid leave. On December 1, 1999, the Clinton administration presented an experimental program that would allow states to expand unemployment insurance benefits to include new parents on leave. Working parents would be offered time off with pay during the first year of birth of a baby or after an adoption. Such a program of paid leave for a maximum of 26 weeks is already in place in Massachusetts, Vermont, Maryland, and Washington states. In 2004, California became the first state to offer paid family leave to both mothers and fathers, including adoptive parents, funded by an increase in employees’ payroll deductions for state disability insurance. No data are yet available about the impact of paid leave programs in these states on infectious diseases in the infant.

PACIFIER USE

Niemela and colleagues suggested that pacifier use is a significant risk factor for recurrent AOM in children attending day-care centers. Of children younger than 2 years who used a pacifier, 29.5% had more than three episodes of AOM, contrasted with 20.6% of children who did not use a pacifier. In children aged 2 to 3 years, the rates of recurrent AOM were 30.6% and 13.2% for children who did and did not use pacifiers, respectively. A meta-analysis of risk factors for AOM by Uhari and colleagues revealed that pacifier use increased the risk (relative risk, 1.66). A study of bacterial cultures of pacifiers of children with AOM indicated that pacifiers did not carry large numbers of organisms, and therefore, were unlikely to be an important cause of transmission of microbial pathogens.

SLEEP POSITION

A longitudinal study of 13,000 infants from the Medical Research Council Institute of Hearing Research in Nottingham indicated that sleep position is a determinant of middle-ear history. Children who slept in the prone position were at increased risk for otitis media, contrasted with children who slept in the supine position. The authors suggested that front-lying infants had higher airway temperature favoring bacterial colonization.

SEASON

The seasonal incidence of middle-ear infections parallels the seasonal variations of upper respiratory tract infections. Acute episodes peak during the winter but are also frequent in the fall and spring; they are least frequent in the summer. In observations during 3 years in the Boston study, 27% of children had an episode of otitis media in the summer, compared with 48% in the spring and fall, and 51% in the winter. The incidence of episodes of otitis media also increases during outbreaks of viral infections of the respiratory tract.
tract in children; these are most likely to occur in the winter and spring seasons.6

Children 4 to 5 years old in New Orleans had different prevalence rates of middle-ear effusion in winter and fall; 29% of children tested in February and 6% of those tested in September had effusion.57 Examination of Pittsburgh preschool-aged children attending a day-care center identified a prevalence of 0% for otitis media with effusion in August, 7% in September, and 25% in January and February.115 A 1-year study of 389 7-year-old Danish school children used tympanometry on 8 to 10 occasions during the year to test for the presence of middle-ear effusions. On one or more tests during the year, 26% of the children had evidence of middle-ear effusion. The prevalence varied from 5.7% in August 1978 to 9% in November through April and returned to 2.4% in August 1979. Middle-ear effusion occurring in the winter months persisted longer than effusion occurring in the summer months.55

SMOKING AND AMBIENT AIR POLLUTION

Passive smoking and environmental pollutants have come under increased scrutiny as agents responsible for structural and physiologic changes in the respiratory tree. Smoke exposure can result in goblet cell hyperplasia and mucus hypersecretion in the respiratory tract,116 ciliary stasis, and decreased mucociliary transport,117 and may play a role in altering immune defenses of the respiratory tract. The availability of a biochemical marker—salivary, serum, or urine cotinine—has made documentation of passive exposure to tobacco smoke more reliable than that provided by history alone. Cotinine concentrations were related to the number of smokers in the household.118 Concentrations of cotinine in urine were directly associated with exacerbations of asthma in children.119

Results of early studies of the effect of household cigarette smoke exposure on the incidence of otitis media were inconclusive because investigators depended on history provided by the parents and had difficulty quantifying the amount, intensity, and proximity of the exposure.5,102,120 Etzel and colleagues demonstrated that high concentrations of serum cotinine were associated with increased incidence of AOM and increased duration of middle-ear effusion after an acute episode.51 Heavy maternal smoking (more than 20 cigarettes per day) was a significant risk factor for three or more episodes of AOM (but not for any nonrecurrent AOM) in the first year of life; the rate of recurrent infections (32%) was higher in those infants whose mothers were heavy smokers during pregnancy and after delivery than among infants whose mothers were heavy smokers after delivery only (19%). The smoking effect was stronger among infants of lower birth weight.121

Exposure to tobacco smoke was associated with higher rates of carriage of Streptococcus pneumoniae in children 1 to 59 months of age. In addition, smoking mothers had a higher carriage rate of S. pneumoniae than did nonsmoking mothers. In contrast to the risk of carriage of pneumococci associated with smoking was the absence of such an effect on carriage of Haemophilus influenzae.122

Intense investigation of the effects of environmental pollutants such as ozone, carbon monoxide, airborne particulate matter, and acidic aerosols on various human diseases are under way. Kim and colleagues in Houston documented the association of invasive pneumococcal infections in children and adults with levels of sulfur dioxide (a marker for air pollution) and higher ragweed pollen counts.123 Epidemiologic studies identify increased ozone concentrations with exacerbations of asthmatic symptoms and changes in pulmonary function in children. Although there are no data relevant to eustachian tube function or middle-ear disease, it appears likely that structural or physiologic changes due to a toxin that is identified in one area of the lower respiratory tract will have a reflection in the upper respiratory tract. A statement of the American Academy of Pediatrics discusses the current status of the respiratory hazards of ambient air pollution to children.124
GENETIC FACTORS

Genetic predisposition to middle-ear infection is suggested by the aggregation of cases in families; by the association of severe and recurrent disease with genetically determined features, such as skull configuration and subtle immunologic defects; and by results of studies in twins. A genetic influence may be based on anatomic differences of the skull, nasopharynx, and eustachian tube; physiologic differences in eustachian tube function; or impairment of the immune response predisposition.

Familial predisposition to recurrent and severe disease has been identified in multiple studies. A meta-analysis by Uhari and colleagues identified an increase in risk (relative risk, 2.63) if any other member of the family had had AOM. Children enrolled in the Boston study who had single or recurrent episodes of otitis media were more likely to have siblings with histories of significant middle-ear infections than were children who had no episodes of otitis media. Adopted Apache children had more episodes of AOM than did their non-Apache siblings, and they had an illness rate similar to that of Apache children who remained on the reservation.

Studies of the incidence of otitis media in twins indicate that there is a strong genetic component to the amount of time with middle-ear effusion and the episodes of AOM in children. Casselbrant and colleagues prospectively studied 168 same-sex twin and 7 triplet sets in Pittsburgh; the estimate of heritability of middle-ear effusion was 0.73, and there was a strong correlation between members of monozygotic twins or triplet sets compared with dizygotic sets. Kvaerner and colleagues obtained retrospective histories of recurrent ear infections among 2,750 pairs of Norwegian twins; heritability of ear infections was higher in females than in males (74% vs. 45%).

Low responses to pneumococcal polysaccharides were associated in some adults with lack of certain genetic markers of immunoglobulins. Black children had fewer episodes of otitis media after immunization with pneumococcal polysaccharide vaccine than did white children. Immunoglobulin allotypes were investigated in children with recurrent episodes of AOM and in their parents by Prellner and associates; the results did not identify differences among children with recurrent otitis media and control subjects for markers of genetic loci involved in antibody responses to pneumococcal polysaccharide antigens. The epidemiologic data suggest that genetic susceptibility to middle-ear disease does exist and that further investigation of genetic markers is likely to yield useful information.

Several studies suggest the genetic basis for anatomic differences that predispose individuals to severe and recurrent otitis media. As noted in the earlier section on race, Doyle demonstrated differences in the morphology of the eustachian tube, tensor veli palatini, and cranial base relations of Inuit and Native Americans as contrasted with African-Americans and whites; the shorter, straighter tube found in American Indians is associated with a higher incidence of chronic middle-ear disease. Lateral cephalometric analysis of children with secretory otitis media revealed a significant reduction in certain skeletal and soft tissue dimensions in the nasopharynx. The degree of pneumatization of the mastoid process (possibly associated with predisposition to otitis media) was more similar in monozygotic than in dizygotic twins. Down syndrome and cleft palate that predispose to persistent middle-ear disease may occur on a genetic basis. Todd and Todd described an association of recurrent otitis media and children with congenital cardiac outflow tract anomalies. The investigators hypothesized that a neural-crest-determined branchial field defect influences development of the cardiac outflow tract and the eustachian tubes, and that children with this congenital conotruncal cardiac anomaly are otitis-prone.

BREAST-FEEDING

Breast-feeding is an important mode of prevention of respiratory and gastrointestinal infections
in infancy. Breast-feeding has been shown to diminish nasopharyngeal colonization. Does breast-feeding prevent otitis media? Various investigators have attempted to answer the question in different geographic areas and different cultural populations.

Canadian Inuit children were surveyed in five areas, including an urban center (Frobisher Bay), village settlements, and hunting camps. There was an increase in the incidence of middle-ear disease in children who lived in urban centers compared with those living in villages or camps, but in each area, there was an inverse relationship of incidence of middle-ear disease and duration of breast-feeding. Children who were breast-fed for 12 or more months had significantly less ear disease related to otitis media than did infants who were bottle-fed at birth or within the first month of life.

A prevalence study of ear disease in a small Inuit community in Labrador revealed that the number of children with evidence of otitis media (defined as AOM or wet or dry perforation) was inversely related to the age at onset of bottle-feeding. Children who were bottle-fed at or soon after birth had significantly more disease (67 of 160 children, or 42%) than children who had been bottle-fed after only 6 months of breast-feeding (0 of 21 children).

A significant decrease in episodes of otorrhea (observed or recorded by a nurse midwife) among 35 infants who lived in a rural community in India and who were breast-fed for at least 2 months was identified when they were compared with 35 bottle-fed infants matched for socioeconomic status and family size.

Children living in upstate New York were surveyed by Cunningham. A significant difference in acute lower respiratory tract infections in the first year of life occurred in infants who were breast-fed for at least 4½ months compared with infants who were bottle-fed. The incidence of otitis media was lower in the breast-fed infants, but the difference was not statistically significant.

Saarinen observed 256 healthy term infants from birth through the first 3 years of life. Breast-feeding was categorized as long (only source of milk until 6 months or more), intermediate (2 to 6 months), and little or none (2 months). The incidence of otitis media was inversely associated with the duration of breast-feeding. The differences persisted up to the age of 3 years. No differences were associated with other respiratory infections.

Boston children were observed from birth with frequent examinations and assessments of the mode of feeding by Teel and colleagues. A large number of children were studied (692), and multivariable analysis was performed; 31.2% of children were breast-fed at some time. Breast-feeding was strongly associated with decreased risk for AOM during the first year of life. Analysis of duration of feeding indicated that breast-feeding for 3 months or more was associated with decreased risk of AOM or recurrent episodes of AOM in the first year of life.

Infants in two suburban Buffalo pediatric practices were observed to assess the relationship of exclusive breast-feeding and episodes of AOM and otitis media with effusion. The cumulative incidence of first episodes of AOM increased from 25% at 6 months to 51% at 12 months in infants exclusively breast-fed; in contrast the cumulative incidence of first episodes of acute otitis increased from 54% at 6 months to 76% at 12 months in infants formula-fed from birth. A twofold elevated risk of first episodes of AOM or otitis media with effusion was observed in exclusively formula-fed infants compared with infants exclusively breast-fed for 6 months. In the logistic regression analysis, formula-feeding was the most significant predictor of AOM and otitis media with effusion episodes.

Other studies that show a lower rate of otitis media in breast-fed versus bottle-fed infants include those of Daly and colleagues, Duncan and colleagues, and Wright and colleagues. A meta-analysis of 22 studies of risk factors for AOM identified the protective effect of breast-feeding for at least 3 months.
These studies do not provide reasons for the protective effect of breast-feeding for otitis media. Is breast-feeding beneficial, or is bottle-feeding harmful? A number of hypotheses have been suggested:

1. Immunologic factors of value are provided in breast milk, and these prevent various bacterial and viral infections. Breast milk contains important anti-infective agents, including immunoglobulins (secretory immunoglobulin A and immunoglobulin G), various leukocytes (B cells, T cells, macrophages, and neutrophils), and components of complement. Colostrum and, to a lesser extent, breast milk have neutralizing activity to respiratory syncytial virus. However, Rosen and colleagues found that antipneumococcal antibodies in breast milk did not prevent nasopharyngeal carriage of pneumococci or subsequent AOM.

2. Nonimmune protective factors include interferon, glycoproteins, lactadherin, glycolipids, glycosaminoglycans, oligosaccharides, monoglycerides, and unsaturated fatty acids. Human milk contained both specific antibodies and free oligosaccharides that corresponded to the pneumococcal carbohydrate receptor, suggesting that milk may protect against otitis media by blocking attachment of bacterial pathogens to respiratory mucosa. However, studies by Faden and coworkers indicated that adherence of nontypeable H. influenzae to respiratory epithelium was not influenced by breast-feeding.

3. Anti-inflammatory factors in breast milk that may limit the infection include antioxidants (ascorbic acid, cysteine, and \( \alpha \)-tocopherol), lactoferrin, tumor necrosis factor-\( \alpha \), soluble receptors, and interleukins 1 and 10.

4. Allergy to one or more components in cow or formula milk may alter the mucosa of the eustachian tube and middle ear.

5. The facial musculature of breast-fed infants develops differently from that of bottle-fed infants. The muscles may affect eustachian tube function and assist in promoting the drainage of middle-ear fluids.

6. Aspiration of fluids into the middle ear occurs during bottle-feeding because the bottle-fed infant is required to produce high negative, intraoral pressure, whereas breast-feeding involves nipple massage and reflex “let-down” of milk.

7. The breast-fed infant is maintained in a vertical or semi-vertical reclining position, whereas the bottle-fed infant is placed in a reclining or horizontal position. The horizontal position may result in reflux of milk through the wide and horizontal eustachian tube. The practice of propping a bottle in bed has been criticized because fluids are forced under pressure into the oral cavity, with possible reflux into the middle ear. Tully and coworkers demonstrated that a higher proportion of infants fed in the supine position had abnormal tympanographic results after feeding compared with infants fed in the semi-upright position.

The results of a study of children with cleft palate appear to diminish the importance of the positional advantage of breast-feeding. None of the 222 infants fed formula only was free of ear effusion at any examination during the first 18 months of life, whereas in 11 of 30 infants fed breast milk, one or both ears were free of effusion at one or more examinations. The results suggest that breast milk protected infants in spite of the severe anatomic disability. Because all feedings (breast milk or formula) were given through an artificial feeder, the protection afforded the infants was more likely to be in quality of the milk rather than the mode of feeding.

Although of uncertain importance for development of otitis media, breast milk may play a role in transmission of bacterial and viral pathogens. Bacterial pathogens include Staphylococcus aureus, Listeria monocytogenes, and Salmonella species. Viruses transmitted by breast milk include cytomegalovirus, human immunodeficiency virus, herpes simplex virus, and human T-lymphotropic virus 1.
ALTERED HOST DEFENSES AND UNDERLYING DISEASE

Although most children have no obvious defect responsible for chronic otitis media with effusion, a small number may have altered host defenses, including anatomic changes (cleft palate, cleft uvula, submucous cleft; alteration of normal physiologic defenses (patulous eustachian tube or barotrauma); congenital or acquired immunologic deficiencies (immunoglobulin deficiencies or chronic granulomatous disease); presence of malignant neoplasms; or use of drugs that suppress immune processes. Active middle-ear disease is an almost constant event in children with cleft palate (see Chapter 8, “Management”). Some patients may have disease states, such as nasopharyngeal tumors or connective tissue disorders that lead to otitis media. An increased incidence of otitis media occurs in children with Down syndrome.152 These conditions are too infrequent to affect epidemiologic studies but should be considered in managing individual patients.

Local and systemic bacterial infections, including otitis media, are early manifestations of acquired immunodeficiency syndrome (AIDS) in infants. Children with AIDS had a higher age-specific incidence of otitis media, beginning at the age of 6 months, compared with uninfected children or children who initially were positive for human immunodeficiency virus antibody but who seroreverted (Figure 3).153 Various procedures in the nose, throat, or airway may increase susceptibility to middle-ear infection. Nasotracheal intubation was identified as a factor in development of middle-ear effusion in neonates.66 A similar observation was made in children aged 2 days to 5 years in an intensive care unit; nasotracheal, but not nasogastric, intubation was associated with development of middle-ear effusion. Effusion was identified within 4 days of intubation and appeared earlier in the ear on the side of intubation than in the contralateral ear.154 Derkay and colleagues noted that otitis media was common in the pediatric intensive care unit and was probably caused by prolonged dysfunction of the eustachian tube associated with oral and nasally placed tubes.155 The bacteriology of the otitis media reflected nosocomial infection (including Pseudomonas aeruginosa and Staphylococcus epidermidis) rather than the usual pathogens of community-acquired disease.

Cost Analyses

Various analyses of cost of management of otitis media for the health care payer, as well as from the societal perspective, have provided additional insights into the epidemiology of otitis media.156–159 Direct costs of an episode of otitis media include health care visits and consultations, cost of drugs (antibiotics, decongestants), surgical procedures, audiometry and remedial speech and language visits, and hospitalizations related to otitis media or its complications. Indirect costs include transportation, babysitters, and lost time from work. Usually not calculated are the loss of intellectual potential and contributions to the family and community. The average total cost of treating an episode of otitis media has been estimated to be between $116 (US)160 and $131 (US).157 Antibiotics account for a relatively small proportion of these costs of acute care. In 1996, the combined cost of AOM with its sequelae was estimated to be more than $5 billion every year.161
Capra and colleagues presented data about costs of otitis media in a managed care population in Northern California for the year 1997. Mean costs of surgical procedures were as follows: myringotomy and placement of tympanostomy tube, $1,396 (US); mastoidectomy, $5,062 (US); adenoidectomy, $1,485 (US). Work-loss costs per family were an average of $120 (US); extra baby-sitting costs averaged $31 (US).

Gates estimated that the annual costs in the US varied between $3 billion (US) and $5 billion (US). Colorado Medical claims data for otitis media treatment yielded figures of approximately $4 billion (US) in 1992 dollars. The AAP and AAFP used data from 1995 to estimate total costs of $2.98 billion (US) including direct costs of $1.96 billion (US) and indirect costs of $1.02 billion (US). Schwartz and Gates discuss the various aspects of economic costs of AOM in the comprehensive reference Evidence-Based Otitis Media.

REFERENCES

94. Doyle WJ. A functiono-anatomic description of eustachian tube vector relations in four ethnic popula-
112. Brook I, Gober AE. Bacterial colonization of pacifiers of
111. Niemela M, Uhari M, Mottonen M. Otitis media in day
110. Cherney E. Family-leave advocates look to Canada for
108. Lewis DE. Clinton starts program for parental paid leave.
105. Wald ER, Guerra N, Byers C, et al. Frequency and severity of
104. Wald ER, Dashefsky B, Byers C, et al. Frequency and
103. Strangert K. Otitis media in young children in different
102. Vinther B, Elbroad O, Pedersen CB. Otitis media in childhood, socio-medical aspects with special refer-
98. Cambon K, Galbraith JD, Kong G. Middle-ear disease in
94. Strachan DP, Jarvis MJ, Feyerabend C. Passive smoking, salivary cotinine concentrations, and middle-ear effu-
98 OTITIS MEDIA IN INFANTS AND CHILDREN


