

Acute Otitis Media

A Public Health Perspective

Derek Drummond, MD

March, 1999



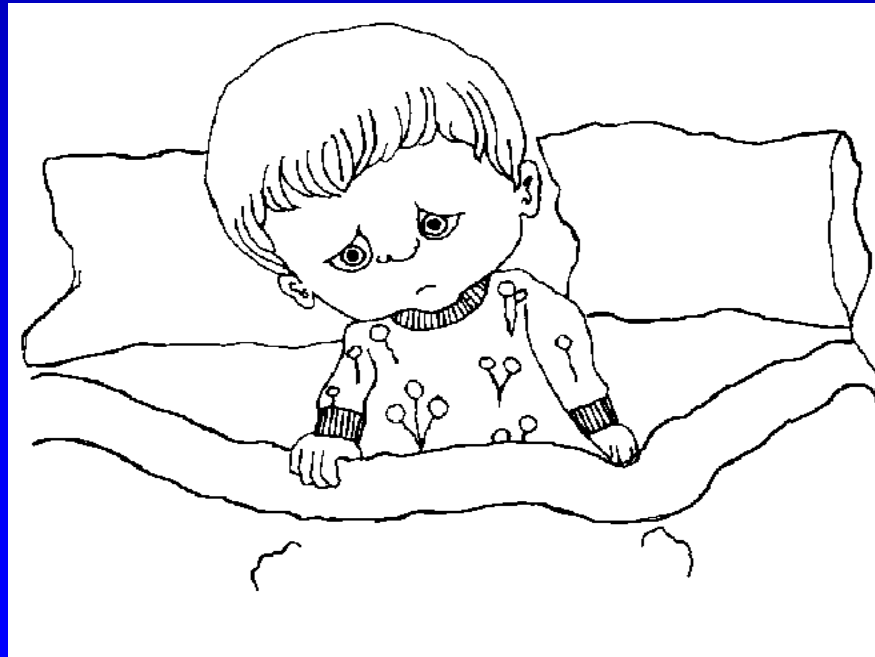


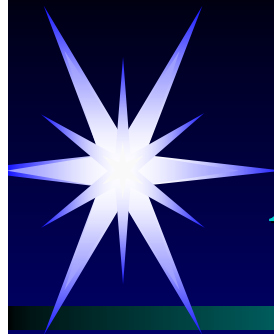
Acute Otitis Media - Definition

- **Otitis Media** - a generic term used to indicate an inflammatory process in the middle ear cavity.
- **Acute Otitis Media (AOM)** - a term used to describe the clinical entity that is heralded by the sudden onset of symptoms and signs related to acute infection of the middle ear (e.g. fever, irritability, otalgia, anorexia, vomiting, bulging tympanic membrane, middle ear effusion)

Acute Otitis Media

➤ “... this disorder is one of the most important unsolved pediatric problems in otolaryngology” (Gates)

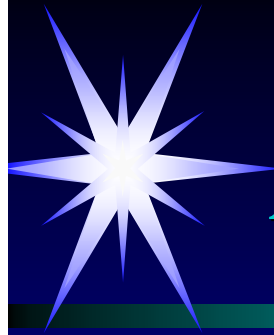




AOM - History

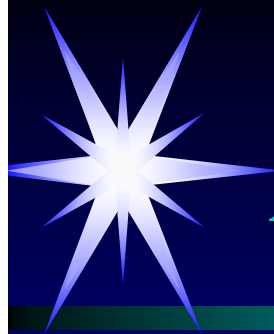


- Have humans always had acute infections of the middle ear?
- 2600 year old Egyptian mummies - perforated TMs, destruction of the mastoid (Lynn, 1974)



AOM - History

- Iranian skeletal material from 1900-800 BC - evidence of middle ear disease (Rathbun, 1977)
- 1932 - AOM accounted for 27% of pediatric admissions to Bellevue hospital (Bakwin, 1939)



AOM - Epidemiology

- Centers for Disease Control - (National Survey 1990)
 - 24.5 million visits to office practices in the US were for otitis media.
 - In children < 15 years old, otitis media was the most frequent diagnosis in office practice.
- Second only to the common cold as a cause of infectious illness during the first year of life in 246 Rochester children (Hoekelman, 1977).

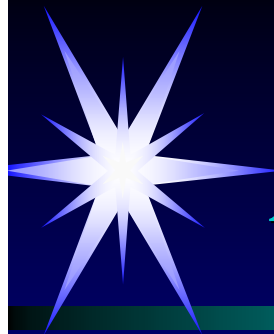




AOM - Epidemiology

➤ Antibiotic Usage

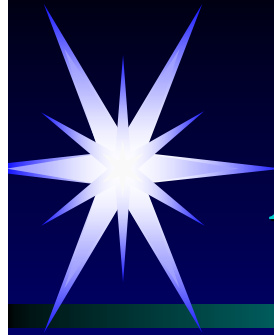
- 33% of all prescription medication was for the treatment of otitis media (Foraselli, 1987)
- USDA 1986 - in children younger than 10 years old, 42% of prescriptions (44.5 million) were issued for otitis media.
- 90% of antibiotic usage in children under 2 years old is for the treatment of OM (Paradise, 1997)



AOM - Epidemiology

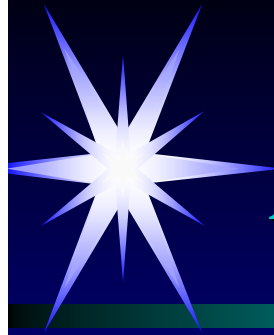
- Greater Boston Otitis Media Study (Teele 1989) - Prospective study of 2565 children from the Boston area observed from birth.
 - 93% had at least one episode of AOM
 - 46% had three or more episodes of AOM by 3 years of age
 - Incidence
 - 1.2/year - first year
 - 1.1/year - second year





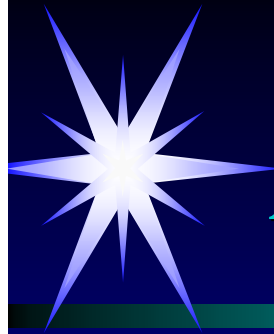
AOM - Epidemiology

- Is the incidence of AOM increasing?
 - CDC reported a 250% increase in the number of diagnosis of AOM from 1975 to 1990.
 - Increased awareness of the disease?
 - Perceived need for aggressive treatment?
 - Increased virulence of pathogens?
 - Increased exposure to pathogens?
 - Another unknown factor?



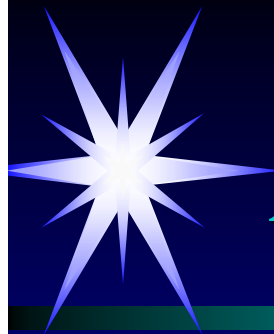
AOM - Epidemiology

- By 3 years of age children may be categorized into 3 approximately equal sized groups (Bluestone, 1996)
 - Free of ear infections
 - Occasional episodes of otitis media
 - Otitis prone



AOM - Risk Factors

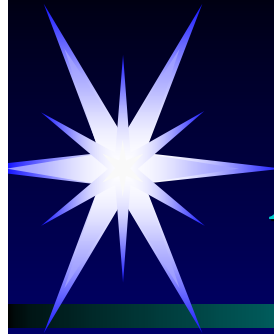
- Age - 6 to 18 months (also 5-6 years old)
- Day Care - 25% increase in frequency of AOM in Danish children (Vinther, 1982)
- Early occurrence of AOM - prior to 6 months of age
- Exposure to smoke in the household
- Social and Economic Conditions
 - crowded living conditions, poor nutrition, poor sanitation, inadequate medical care



AOM - Risk Factors

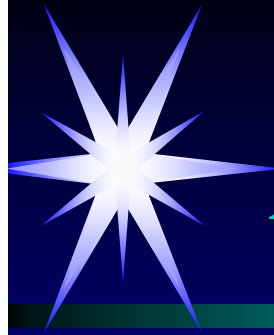
➤ Paradise (1997)

- Large prospective study looking at the epidemiology of OM in 2253 Pittsburgh-area children during the first 2 years of life
- Did not distinguish between AOM and OME
- The most important risk factors were low socioeconomic status and repeated exposure to a large number of other children



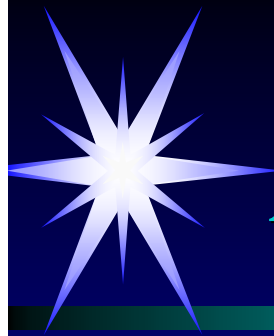
AOM - Risk Factors

- Native Americans and Inuits have a high incidence and prevalence of severe OM
 - 31% of Canadian Inuits under age 10 had a draining ear at the time of examination (Ling, 1969)
- 25% of aboriginal children in Queensland 4-12 months of age had TM perforations (Dugdale, 1982)



AOM - Risk Factors

- Early studies identified a predominance of AOM in white children when compared to black children (up to a 10 fold difference in incidence rates)
- These studies may be biased by the lower number of medical visits by black children
- 1995 - Casselbrant followed 138 black and 60 white Pittsburgh children from birth to age 2 and found no difference in incidence of AOM (cumulative incidence 43% vs. 42%)



AOM - Risk Factors



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AOM - Risk Factors

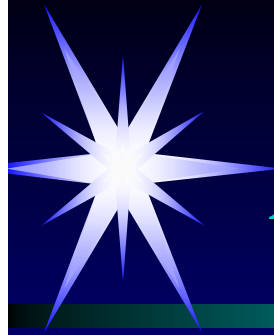
- Does breast feeding prevent otitis media?
 - Earlier studies from Canada demonstrated an inverse relationship between middle-ear disease and duration of breast feeding (Schafer 1971, Timmerman 1980)
 - prevalence of AOM or TM perforation in Inuit children controlling for breast feeding 67/160 vs. 0/21
 - These findings were independently confirmed by 2 large prospective studies (Saarinen 1982, Teele 1989)



AOM - Risk Factors

➤ Hypothesis

- Immunological components of breast milk?
- Cows milk allergy?
- Is this a functional effect?



AOM - Risk Factors

➤ Seasonal Influence

- Teele 1984 - in observations over 3 years in the Boston study
 - summer - 27% of children had an episode of AOM
 - spring and fall - 48%
 - winter - 51%

➤ Genetic Factors

- genetic susceptibility does exist, although further research is needed.



Middle Ear Anatomy

- System extends from the nasopharynx at the opening of the eustachian tube to the mastoid air cells (gas reservoir)
- Ciliated respiratory mucosa (except the mastoid air cells which are lined with cuboidal epithelium)
- The tympanic mucus blanket is continually being swept towards the nasopharynx via the eustachian tube



Normal Tympanic Membrane



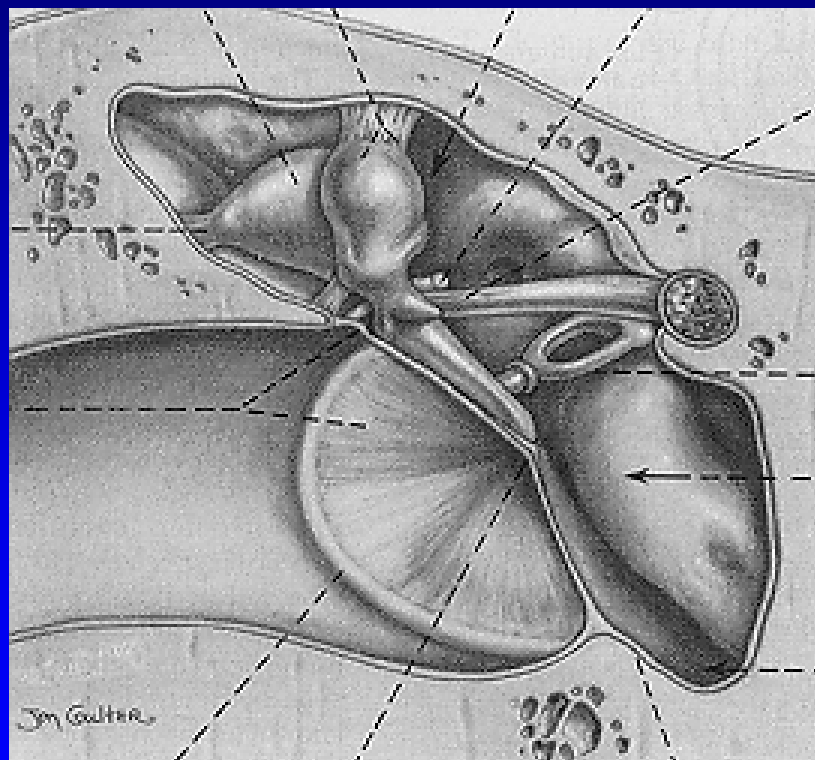
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Hawke, 1995





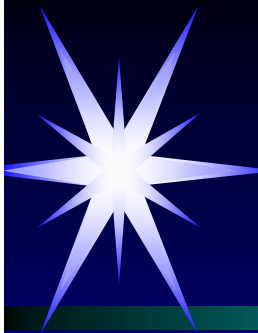
Middle Ear Anatomy



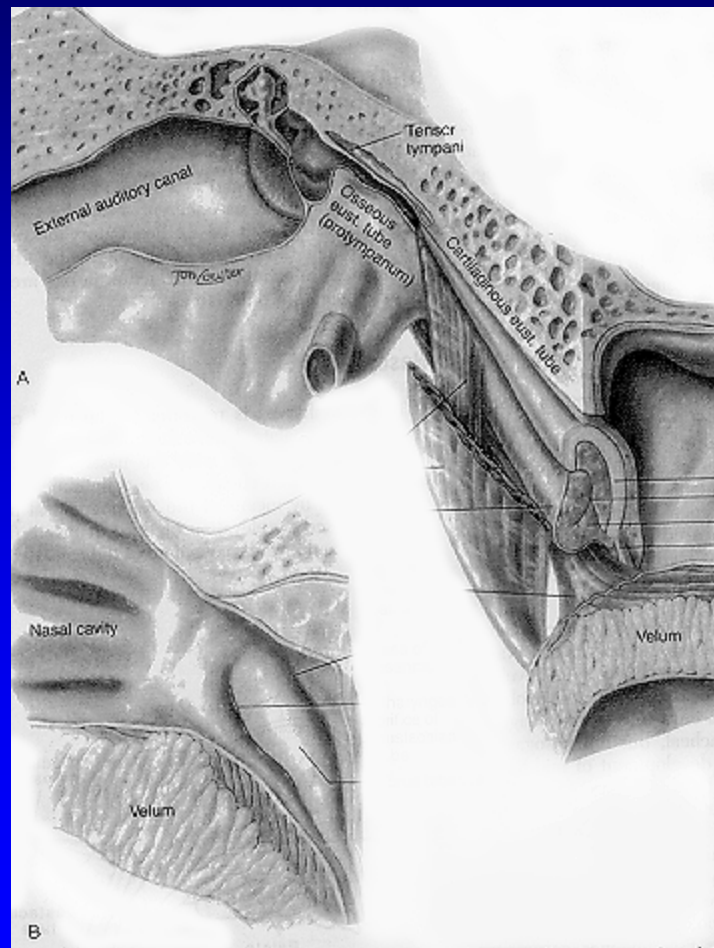
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Bluestone, 1990





Eustachian Tube



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Bluestone, 1996

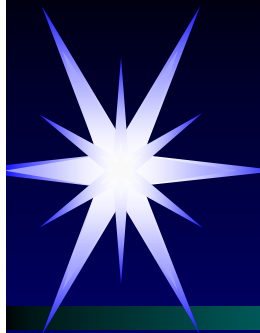




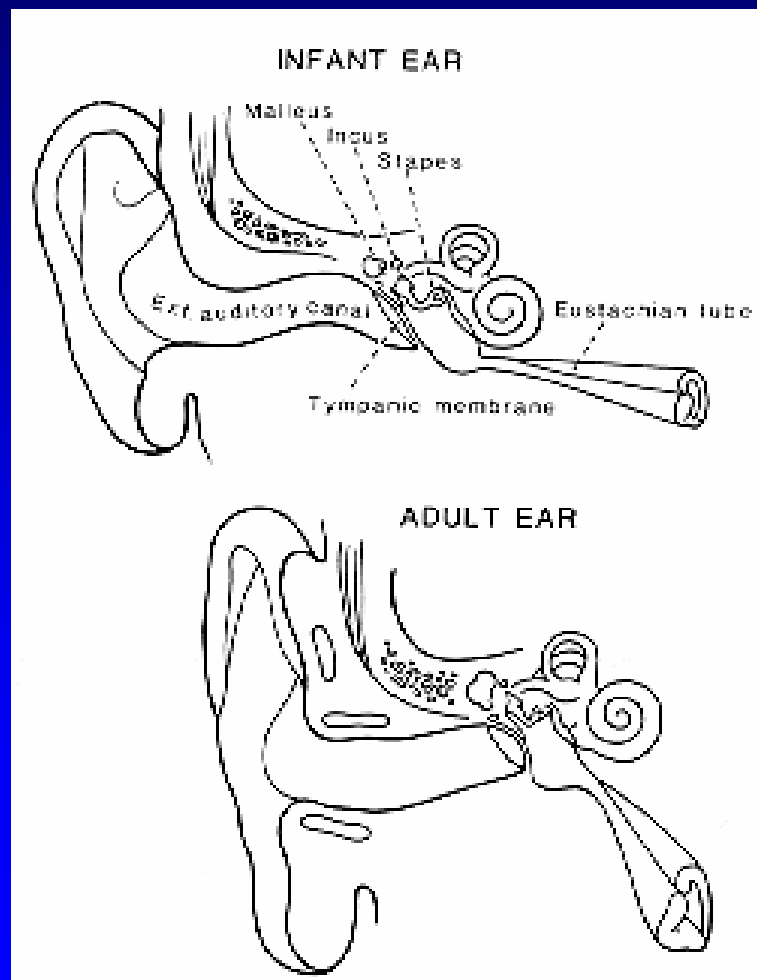
Middle Ear Anatomy

➤ Eustachian Tube

- 3 functions - ventilation, protection, drainage
- Function is not as good in children as in adults
 - Reflux is more likely to occur into the middle ear through the shortened tube of the infant
 - The tube lacks support and is more compliant in the infant
 - The tube sits at 10° in infants as compared to 40° in adults - less efficient opening



Eustachian Tube



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Bluestone, 1995





Pathophysiology of AOM

- Multifactorial
 - Eustachian tube dysfunction
 - Infection
 - Immunologic status
 - Social and environmental factors



Pathophysiology of AOM

- Functional eustachian tube dysfunction is felt to be associated with AOM, although this may be the result of AOM and not the cause of it (Gates).



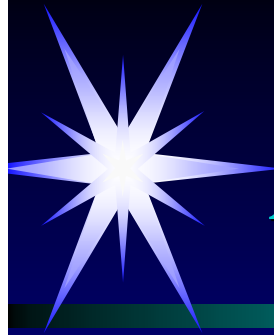
Pathophysiology of AOM

- One proposed sequence of events
 - Viral URI - edema, ciliary dysmotility, stasis
 - Reflux of pathogenic bacteria from the nasopharynx (adenoid) - swallowing, sniffing, nose blowing, patulous eustachian tube, negative pressure
 - 69% correspondence between cultures obtained from the nasopharynx and those from the middle ear (Howie, 1972)
 - Eustachian tube obstruction



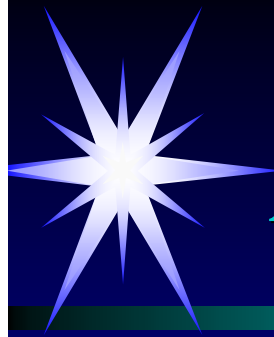
Pathophysiology of AOM

- Bacterial proliferation
- Production of bacterial toxins - bacterial LPS endotoxins were found in 80% of MEE samples taken at the time of tube placement (DeMaria, 1984)
- Mucosal damage
- Inflammation - Macrophages, Lymphocytes
TNF, IL-1, Lysozyme, Proteases, Interferon



AOM - Signs

- Fever
- Bulging tympanic membrane
- Decreased tympanic membrane mobility
- Erythema - an inconsistent finding
- Otorrhea
- WBC counts are too variable to be helpful



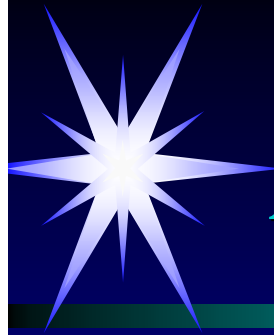
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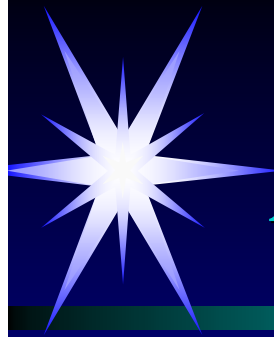
Benjamin, 1995





AOM - Natural History

- Infection progresses - pain increases
- Bulging eardrum
- +/- TM perforation
 - Purulent otorrhea
 - Pain decreases
- Cellular (WBC) + Humoral (IgA, IgG, complement) immune system clears the residual infection



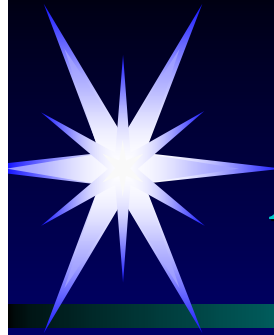
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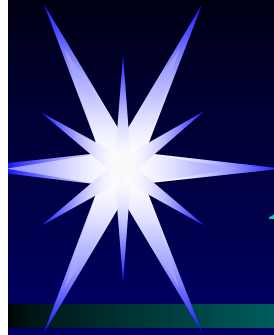
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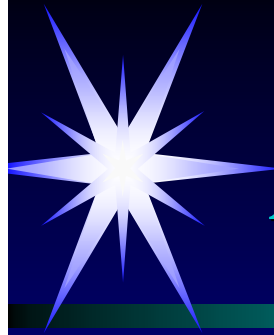
AOM - Natural History

- Difficult to determine - most placebo studies have included a drainage procedure (tympanocentesis or myringotomy)
- Historical Information
 - Before the introduction of antibiotics (prior to 1936) - watchful waiting or myringotomy
 - Most children would recover without Abx
 - There was a significantly higher incidence of intratemporal and intracranial complications



AOM - Natural History

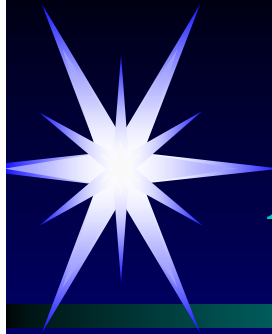
- Rosenfeld (1994) - meta-analysis of 5400 children pooled from 33 randomized trials
 - 81% (95CI 69-94%) rate of spontaneous primary control
 - “Comparative studies suggest that natural history - not antimicrobial therapy - is responsible for improvement..”



AOM - Natural History

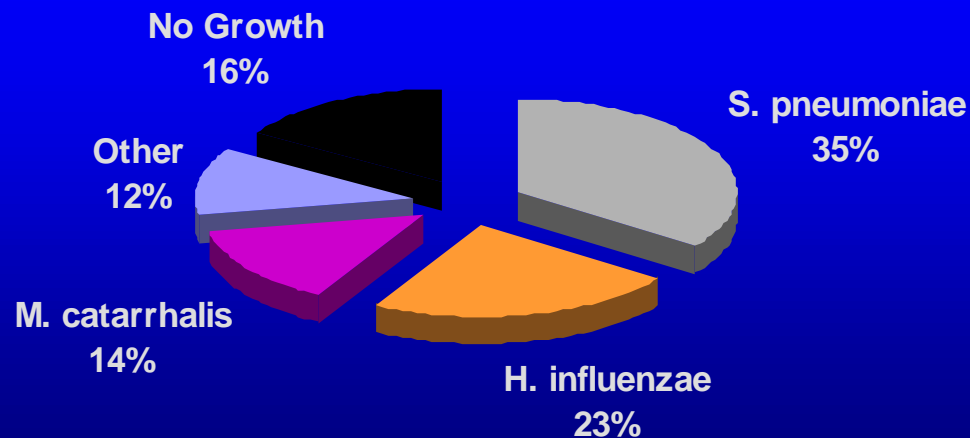
- In a well designed prospective study of over 2500 children in Boston, Teele et al. (1989) found that after an episode of AOM 70% of the children had a middle ear effusion (MEE) at 2 weeks. When followed longitudinally, 40% of these children continued to have a MEE at 1 month, 20% had an effusion at 2 months, and 10% had an effusion at 3 months.

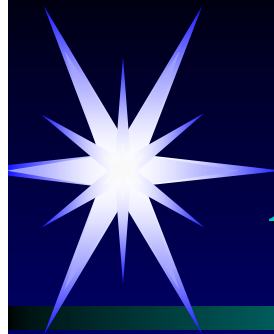




AOM - Microbiology

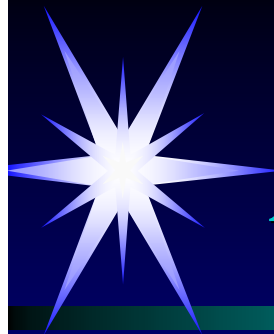
- Pittsburgh OM Study Group (Bluestone, 1992)
- 2807 middle-ear fluid cultures (1982-1989)





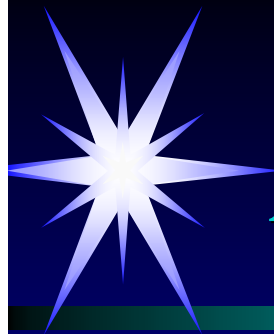
AOM - Microbiology

- *S. pneumoniae* is the most important cause of AOM
 - most common subtypes 19, 23, 6, 14, 3 and 18
- Increasing resistance to penicillin was first noted in Spain and South Africa in the 1970s - decreased binding of beta-lactam antibiotics to the cell wall
- Bluestone (1994) found that 30% of *S. pneumoniae* cultured from middle ears was either relatively or completely resistant to penicillin (no resistant strains 10 years earlier)



AOM - Microbiology

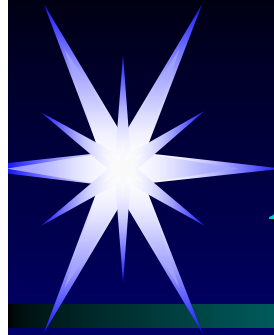
- Most strains of *H. influenzae* are nontypable
 - 10% due to type b
 - Less important in AOM occurring in preschool children
- Few beta-lactamase strains were detected prior to 1972
- Today in the US, about 30% of nontypable strains are beta-lactamase +ve (Bluestone)



AOM - Microbiology

- Prior to 1983 *M. catarrhalis* was infrequently isolated from purulent MEE
- Subsequently, reports from Pittsburgh and Cleveland noted a marked increase in incidence
- Average proportion of about 10% of AOM
- Prior to 1970 all were susceptible to penicillin, now 80%+ are resistant (beta-lactamase)

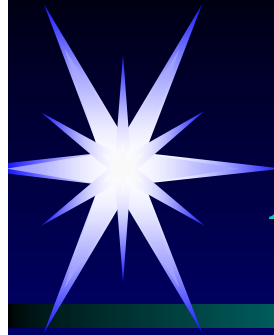




AOM - Treatment

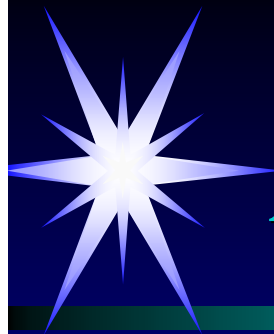
- To treat or not to treat, that is the question!
- The controversy revolves around the enormous expense that is required to treat an often self-limited condition
- The increase in antibiotic-resistant bacteria is a public health concern





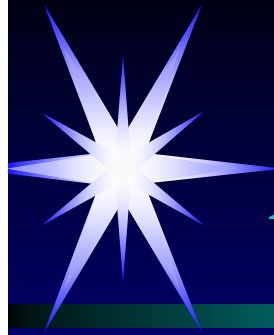
AOM - Treatment

- The primary reasons antibiotics are used to treat AOM are that they shorten the duration of unpleasant symptoms and may decrease the incidence of rare but potentially fatal complications (e.g. meningitis, brain abscess, mastoiditis)



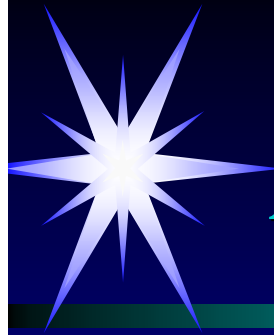
AOM - Treatment

- Those children with an accurate diagnosis of AOM who are given appropriate antibiotic treatment can expect about a 90%-95% clinical cure rate within 72 hours (Rosenfeld, 1994)
- This means that about 14% of children given antibiotics for AOM will benefit



AOM - Antibiotics

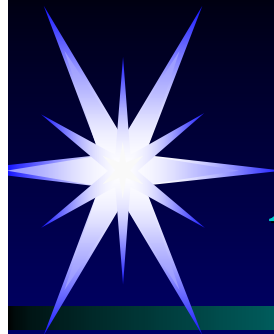
- Selection of antibiotic
 - efficacy - whether a health intervention achieves a better outcome than placebo
 - acceptable taste
 - absence of side effects and toxicity
 - convenient dosing schedule
 - low cost




AOM - Antibiotics

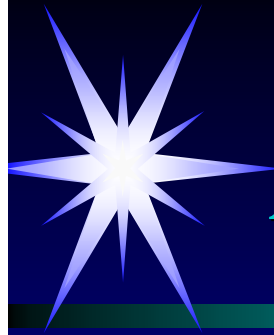
- By 1998, 16 antibiotics had been approved by the FDA for the treatment of AOM (Klein, 1998)
- The present antibiotic of first choice for the treatment of AOM is the amino-penicillin called amoxicillin that has been shown in many studies to be safe and effective (Bluestone)





AOM - Treatment

- The use of newer, more expensive antibiotics contributes to the inflation of health care costs but adds little to the efficacy of antibiotic treatment (Rosenfeld) 
- Many experts feel that we should be saving the more powerful broad spectrum antibiotics for more severe or resistant infections, and not using them indiscriminately to treat AOM as a first line of therapy.



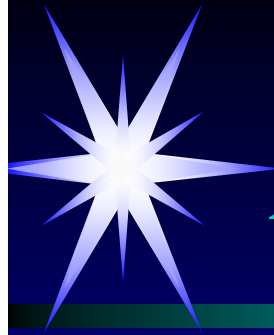
Antimicrobial Resistance



➤ Iceland

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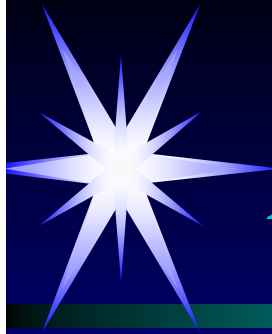




AOM - Antibiotics

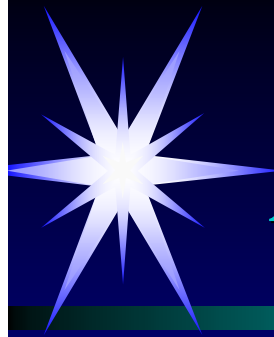
- There is also evidence showing that amoxicillin is effective in eliminating certain penicillin resistant strains of pneumococci
- Penicillin-resistant *S. pneumoniae* isolates are frequently responsible for therapeutic failure in about 40% of cases of acute otitis media (Gehanno, 1998)
- Only 2 are reliably effective against penicillin-resistant pneumococcus: high dose amoxicillin (80 to 100 mg/kg/day) and im ceftriaxone. (Blumer, 1998)





AOM - Treatment

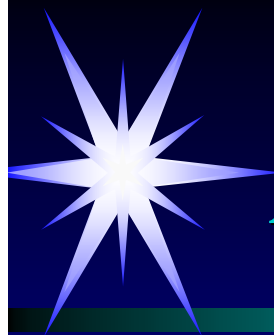
- Clinical cure - resolution of signs and symptoms (exclusive of MEE)
- Clinical failure
 - inappropriate dose
 - noncompliance
 - ineffective drug
 - drug resistant organism
 - severe disease
 - immunosuppression



AOM - Treatment

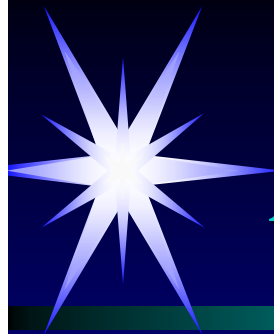
➤ Lister (1997) - In vitro analysis demonstrated that peak concentrations of amoxicillin of 6 to 9 microg/ml may be sufficient for the elimination of penicillin-nonsusceptible pneumococcal strains causing otitis media, especially those with intermediate resistance to amoxicillin.





AOM - Treatment

- MEF amoxicillin penetration in 34 children with AOM (Canafax, 1998)
- The currently recommended amoxicillin dosing of 40 mg/kg/day in three divided dose is inadequate to effectively eradicate resistant *Streptococcus pneumoniae*, particularly during viral coinfection. A dosing regimen of 75 to 90 mg/kg/day is recommended for AOM



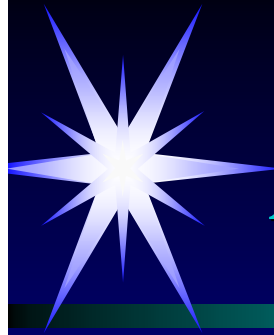
AOM - Treatment Duration

- The optimal length of time of antibiotic administration for treatment of AOM is not known
- Standard textbooks recommend a 10 to 14 day course of treatment - more traditional than scientific
- In a study of 267 children in Pittsburgh, 20 days of amoxicillin offered no advantage over 10 days in the treatment of AOM (Mandel, 1994)



AOM - Treatment Duration

- Kozyrskyj, 1998 - meta-analysis of 30 randomized controlled trials - 5 days of short-acting antibiotic use is as effective as 10 days in the treatment of uncomplicated AOM in children.
- After reviewing 9 randomized studies - short course antibiotic treatment will give less favorable results in children under 2 years old (Paradise, 1994)



AOM - Withholding Treatment?

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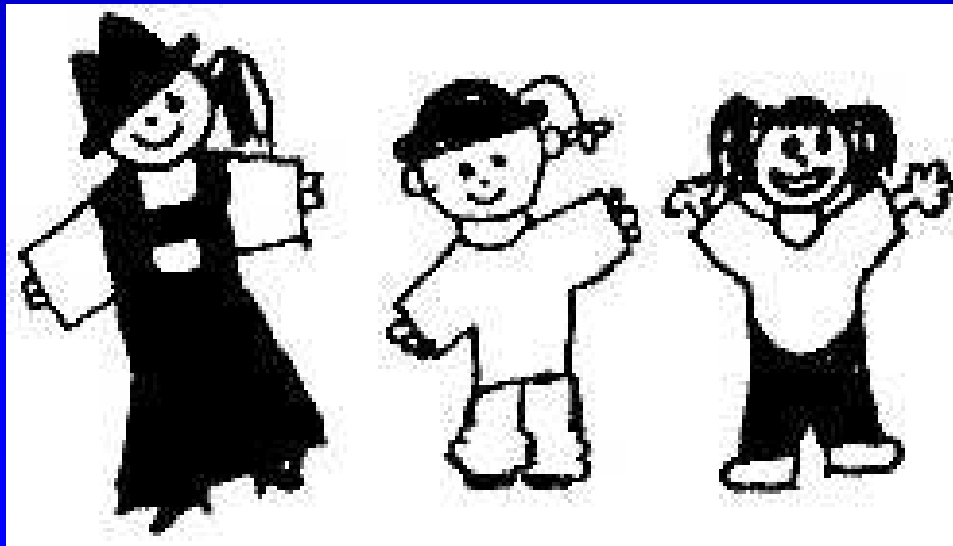


AOM - Costs To Society

- The economic impact of AOM in the United States is enormous considering that over 5 billion dollars are spent annually for the medical and surgical treatment of AOM and its sequelae
- Kaiser Permanente data (1997) - the average cost of treatment for AOM per patient (including the costs of the clinic visits and the antimicrobial drugs) was \$155

Prevention Strategies

- “At present, the vaccine approach seems to hold the greatest promise for ultimate prevention of otitis media.” (Heikkinen, 1996)





Prevention Strategies

➤ Vaccination

➤ Influenza-A vaccination of 6- to 30-month-old children in day care was associated with a decreased incidence of AOM during the influenza season - OR of 0.69 (Clements, 1995)

➤ Pneumococcal vaccination

➤ Vaccination against pneumococcal infections has become more urgent

➤ Field Studies have demonstrated low protective effects - 10-15% reduction in AOM (Makela, 1983)



Prevention Strategies

- Any of the pneumococcal polysaccharides-including those four types that are most common in OM-are not highly immunogenic in infants younger than 2 years
- The vaccine is useful in children 2 years of age and older who still have recurrent AOM (Klein, 1998)
- Pneumococcal conjugate vaccines are being developed to circumvent T-independence of these antigens and provide durable immunity at a very young age (Giebink GS, 1997)



Prevention Strategies

- Polysaccharide antigens are processed as T-lymphocyte independent antigens
- Protein antigens are processed by the T-lymphocytes
- Covalent coupling of pneumococcal capsular polysaccharides to protein carriers improves the immunogenicity of the polysaccharides - clinical trials are in progress
- Presently, researchers are trying to identify an antigen common to nontypable strains of *H. influenzae* that will elicit protective antibodies



The Management of AOM in Harris County

- To determine how primary care physicians (pediatricians and family practitioners) in Harris County manage and follow-up episodes of acute otitis media (AOM) in children less than 16 years old?
- Study design - cross-sectional survey of a random sample of all primary care physicians currently practicing medicine in Harris County



The Follow-up Examination

- Two Reasons (Gates)
 - To ensure that the infection is responding to antimicrobials
 - To determine if the MEE has resolved
- Timing of follow-up
 - infants - 3-day check
 - children - 2-week check



The Management of AOM in Harris County

Follow-up Exam After AOM

