



Otitis Media: An Update in 2004

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Why do we need an update?



- Is the disease changing?
 - Why do we treat otitis media (OM)?
 - Do we need to treat OM?
- Is our understanding of the pathophysiology changing?
 - Viral OM or just a setup
 - Eustachian tube dysfunction from allergy, reflux disease, family history

Why do we need an update?



- Are there "new" treatments?
 - New antibiotics
 - Vaccines
 - Reflux medication
- Is there new information on old treatments?
 - Steroids
 - Resistance
 - Biofilms



Why is OM worthy of discussion?



- Except for the common cold, OM is the most common disorder for which pediatric care is sought.
- AOM leads the diagnosis list of indications for outpatient antibiotic therapy in the US.
- Almost all children in the US will have at least one ear infection by 3 years of age.

History of Otitis Media



- Before antimicrobial therapy, acute OM(AOM) was associated with complications such as mastoiditis, epidural abscess and sigmoid sinus thrombosis, etc.
- After the advent of antimicrobials, treatment of AOM with antibiotics became the standard of care.
- Incidence of complications were decreased.



History of Otitis Media



- US economy - Two parent income
 - daycare
 - missed days of work
- US - antibiotic treatment for fever and red ear
 - out of daycare until afebrile or on antibiotics for 24 hours
- Europe - wait 48 hours
 - antibiotics for non-resolving patients

History of Otitis Media

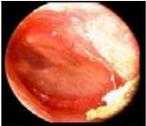


- Beginning 1993 streptococcus resistance was traced to Dallas daycare.
- No current antimicrobial is 100% effective in eradicating the pathogens of OM.
- Avoidance of antibiotics is now being taught.
- Reemergence of complications may occur with the decrease of antimicrobial therapy.

Natural History of Acute Otitis Media



- Spontaneous resolution 60-80% (>2yr old)
- Treat 7-8 children with antibiotics to get 1 child to improve beyond expected course
- Acute mastoiditis incidence <0.25% in observed group




Rosenfeld RM, Evidence Based OM, 2nd ed. 2003

Natural History of Otitis Media with Effusion




- OME secondary to AOM
 - untreated 74% clear in 3 months
 - antibiotic treatment 90% in 3 months
- OME not known to be associated with AOM
 - 28% clear at 3 months
 - 42% clear at 6 months
- OME present 3 months have poor prognosis
 - 27% clear at 6 months, 32% clear at 1 year.

Rosenfeld RM, Evidence Based Otitis Media 2003: 180-98.

Why treat Otitis Media?




- Relieve suffering of recurrent AOM
 - reduce symptoms
 - reduce frequency
- Restore hearing loss associated with OME
- Avoid middle ear sequelae
 - atelectatic drums
 - cholesteatoma
- Prevent learning disabilities



What is Otitis Media?



- Acute otitis media - “the presence of middle-ear effusion in conjunction with the rapid onset of one or more signs or symptoms of inflammation of the middle ear”
 - 3 components to make diagnosis
 - effusion
 - rapid symptom onset
 - signs or symptoms of inflammation of the middle ear
 - in review of 80 studies on AOM tx, none used all three parts of the above definition

Takata GS, Chan LS, et al. Pediatrics. 2001;108:239-254

Definition of Acute Otitis Media

Clinical Practice Guideline 2004



- Diagnosis requires 3 things:
 1. an acute onset of signs and symptoms
 2. presence of middle ear effusion (MEE)
 - Bulging of the tympanic membrane (TM)
 - Limited or absent TM mobility
 - Air fluid level or otorrhea
 3. signs or symptoms of middle ear inflammation

Diagnosis of AOM Clinical Practice Guideline 2004



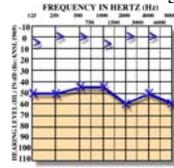
- Diagnosis has some uncertainty.
- History alone insufficient
 - 90% fever, earache, excessive crying in child with AOM
 - 72% same symptoms without AOM
- Pneumatic otoscopy requires seeing TM
 - May not have adequate training
 - May not be able to clear cerumen to see
- AOM vs. OME difficult to distinguish

Niemela, Ped Inf Ds 1994; Pichichero, Ped 2002

What is Otitis Media with Effusion?



- OME- “presence of serous, mucoid, or mucopurulent fluid in the middle ear without acute symptoms.”
- may have associated hearing loss



Darrow, Derkay Current Opinion in Oto HNS 2003

Otitis Media Survey OS-8



			
0: Normal, or effusion only, no erythema	1: Erythema only, no effusion-myringitis	2: Erythema, air/fluid level or bubbles, clear fluid	3: Erythema, complete effusion, clear fluid
			
4: Erythema, air/fluid level, opaque fluid, no bulging	5: Erythema, complete effusion and opacification	6: Erythema, bulging, rounded doughnut appearance of TM	7: Erythema, bulging

If we can diagnose, can we understand the problem?

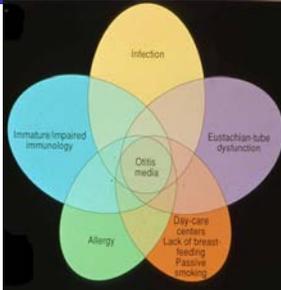




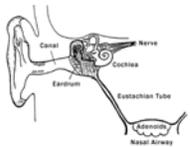

Pathophysiology



- Functional changes that accompany otitis media
- Multifactorial
- Interdependent



Pathophysiology of AOM

- Often begins with viral URI
- Eustachian tube congests and becomes dysfunctional
- Effusion develops in middle ear and is seeded by pathogens in the nasopharynx
- Immune response may eradicate infection but then contribute to further Eustachian tube dysfunction

Pathophysiology of AOM



- May have other inciting causes of Eustachian Tube Dysfunction
 - allergy
 - reflux disease
 - adenoid pad
 - pacifier use
 - anatomic abnormalities (cleft palate, Trisomy 21)
 - trauma or tumor in the nasopharynx
- Chronic negative pressure results in transudate of serous fluid

Tasker, et al Laryngoscope 2002, 112:1930-4

Update Pathophysiology of OM



- Bacterial biofilm formation may cause persistence of effusion and antibiotic therapy to be ineffective. (Fungus can form biofilms as well.)
- Bacteria organize under an exopolysaccharide matrix that prevents normal phagocytosis.
- Relative resistance to antibiotics
- Results in decreased growth in tissue culture

Ehrlich JAMA 2002, 287:1710-15; Post Laryngoscope 2001, 111:2083-94

If we understand the process, how do we treat it?






Treatment of Acute Otitis Media



- Observational therapy
- Medical therapy
 - Antibiotic therapy
 - Non-antibiotic therapies
- Surgical therapy
 - Directly ear related
 - Adjuvant therapies



Medical Treatment



- What are we treating?
- Infection
 - usually improves symptoms in 48-72 hours
- Inflammation
 - can inflammation be decreased after it starts
 - can inflammation be prevented
- Learning disabilities
 - studies plagued by methodological flaws and confounding variable

Treatment of Pain Clinical Practice Guideline 2004



- Management of pain, especially in the first 24 hours of AOM, should be addressed whether or not antibiotics used.
- Otolgia therapies are not well studied. Options include:
 - Acetaminophen, ibuprofen
 - Home remedies: distraction, oil, warm/cold packs
 - Topical agents – benefit older children >5-6 yrs
 - Homeopathic agents
 - Narcotic analgesia

The Assessment & Management of Acute Pain, Ped 2001

Treatment of Infection



- prophylaxis - was effective in reducing recurrent AOM before resistance: now felt to select for resistant organisms - 1.5 episode ↓
- vaccine - Prevnar 7 potent serotypes of 90 possible serotypes present
 - decreased all AOM by 6% in Finland
 - decreased AOM due to 7 serotypes by 57%
 - concern raised for increased % of *H. flu* need for second line therapy earlier
 - complete 3 shot course before respiratory season

Rosenfeld RM. Evidence-Based Otitis Media 1999:179-205

Treatment of Infection



- watchful waiting
 - European recommendation to wait 48 hours with symptoms before evaluation
- safety net approach
 - 667 patients in Friedman OM severity study
 - 35% had non-severe symptoms and non-severe otoscopy
 - abx prescription given - to be started if symptoms did not improve or worsened in next 2-3 days.

Observation as first line therapy Clinical Practice Guideline 2004



- Observation means deferring abx therapy 48-72 hours while managing pain.
 - Otherwise healthy 6mo-2yr olds with non-severe illness AND uncertain diagnosis
 - Otherwise healthy >2yr olds with non-severe symptoms OR uncertain diagnosis
- Requires
 - follow-up ensured
 - Abx started if symptoms persist or worsen

Criteria for Initial Abx vs. Observ



Age	Certain Diagnosis	Uncertain Diagnosis
<6 months	Antibacterial therapy	Antibacterial therapy
6 months – 2 years	Antibacterial therapy	Abx if severe illness, observ if nonsevere
≥ 2 years	Abx if severe Observ if non-severe illness	Observation

CPG: Dx and Mx of AOM 2004

Observation vs. Antibiotic therapy CPG 2004



- Studies looking at placebo vs. antibiotic tx flawed particularly by not using true definition of AOM – no difference seen in groups if weak definition
- Antibiotics shorten symptoms by one day in 5-14% of patients vs. antibiotic side effects in 5-10%
- If observation is chosen need adult to observe, bring back if needed, know what to look for.
- Strategies include: parent initiated phone call/visit, scheduled revisit at 48-72 hours or phone contact, safety-net abx prescription.

Treatment of Infection



- antibiotics
 - ideal would be culture directed
 - use in higher risk patients
 - less than 2 years old
 - attend daycare
 - AOM in last 3 months
 - use for those with severe symptoms
 - use appropriate dosing regimens

Pathogens



- No change in the last 20 years for AOM
 - *Strep pneumoniae* 40%
 - *H. influenzae*
 - *Moraxella catarrhalis*
- OME
 - failure to grow (?biofilms)
 - β -lactamase producing
 - resistant *S. pneumo*
- Viral infection

16.230-41

Resistance



- *Strep. Pnuemo* up to 90% drug resistant in some communities
- Nationwide, *S. pneumo* 30% pcn resistant
 - 50% highly resistant
- *H. flu* 50% β -lactam resistant
- *M. cat* 100%

Antibiotic therapy CPG 2004



- First line for most children Amoxicillin 80-90mg/kg/day
- Risk factors for resistance are child care, recent abx therapy and <2 year old.
- If severe illness or desire coverage for *H. flu* or *M. cat*, amox-clavulanate high dose
- If allergic to amox (not type 1) give:
 - Cefdinir 14mg/kg/day
 - Cefpodoxime 10mg/kg/day
 - Cefuroxime 30 mg/kg/day divided BID

Antibiotic therapy CPG 2004



- B-lactam allergic:
 - Azithromycin 10mg/kg/day – 5 mg/kg/day for 4 d
 - Clarithromycin 15 mg/kg/day divided BID
 - erythromycin-sulfisoxazole 50 mg/kg/d of erythr
 - Sulfa/trimethoprim 6-10 mg/kg/d trimethoprim
- Alternative for pcn allergic treated for known *S. pneumoniae* clindamycin 30-40 mg/kg/d divided TID
- IF vomiting or not tolerating po:
 - Ceftriaxone 50 mg/kg/day

Antibiotic therapy in treatment failure cases originally observed

Temperature $\geq 39^\circ$ C and/or severe otalgia	Recommended	Penicillin Allergy alternative
No	Amoxicillin 80-90 mg/kg/day	Non-type 1: cephalosporin; Type 1: macrolide
Yes	Amoxicillin-clavulanate (90mg/kg/day)	Ceftriaxone, 1 or 3 days



Antibiotic therapy in treatment failure cases initially treated with antibiotics

Temperature $\geq 39^\circ$ C and/or severe otalgia	Recommended	Penicillin Allergy alternative
No	Amoxicillin-clavulanate (90mg/kg/day)	Non-type 1: Ceftriaxone, 3 days; type 1: clindamycin
Yes	Ceftriaxone, 3 days	Tympanocentesis, clindamycin



CPG 2004

Acute Otitis Media with tympanostomy tubes



- Children in daycare get 3-5 episodes of AOM/year with tubes in place.
- Children not in daycare expect less than one episode of AOM/year with tubes in place.



Tympanostomy Tube Otorrhea



- Drainage in an ear known to recently have had a functioning PE tube
- Pulsatile draining through a tube seen to be in the ear drum
- Can occur in 21-50% of children with tubes



Why can't we use what we always have used?



- Resistance to systemic antibiotics.
 - No resistance to topical drops
- New information on ototoxicity
 - aminoglycosides
 - used for ablating vestibular apparatus topically
 - preservatives can be ototoxic
- Oral antibiotics don't cover common organisms
 - Pseudomonas, S. aureus, S. pneumoniae, H. influenzae, P. mirabilis

Academy of Otolaryngology Recommendations for Treatment of Otitis Media 2000

- Acute Otitis Media with PE tube or perforation
 - Floxin Otic solution 5-10 drops BID
 - treats middle ear disease - viscosity
 - topical - does not induce resistance
 - no potential ototoxicity
 - No systemic antibiotics unless additional symptoms



Preservatives in Otopical drops



- 1980 propylene glycol caused hearing loss and concluded that drops containing this preservative were not to be used in ears with perforations.
- Benzalkonium in concentrations >1.0% has produced cochlear and middle ear toxicity. (Floxin Otic contains 0.0025%)

Aminoglycoside Toxicity



- FDA letter Nov. 21, 1996
 - "Neomycin can induce permanent Sensorineural Hearing Loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti."
- Committee on Safety of Medicines (FDA of Canada) 1981 and 1998
 - "Doctors are reminded that topical treatment with aminoglycosides is contraindicated with tympanic membrane perforation."
- Successful lawsuits in multiple states.

Consensus Panel Report on the Use of Otopical Antibiotics in Acute Otitis Externa, Tympanostomy Tube Otorrhea, and Chronic Suppurative Otitis Media

- June 2000 publication Oto-HNS pp934-940.
- pediatric infectious disease, pharmacology, microbiology and pediatric otolaryngology, otology, head and neck surgery specialists



Consensus Panel Report to treat draining ears with tubes



- Conclusions:
 - In the absence of underlying systemic infection or serious underlying disease, topical antibiotics alone constitute first-line treatment.
 - Systemic antibiotics alone or in combination with topical preparations do not improve treatment outcomes compared with topical antibiotics alone.

Consensus Panel Report



- Conclusions (cont.)
 - Topical preparations should be chosen based on expected bacteriology or culture results.
 - Nonototoxic preparations should be considered when there is or may be a perforation in the tympanic membrane.

Consensus Panel Update 2004 Efficacy and Safety of Topical Antibiotics in Treatment of Ear Disease

- When possible use topical antibiotics free of potential ototoxicity. Particularly avoid aminoglycoside-containing drops.
- If potentially ototoxic drops are used, use only in infected ears. (Thickened mucosa may be protective.)
- If potentially ototoxic drops are prescribed warn the patient/parent and give specific instructions for return evaluation.



Consensus Panel Update 2004 Efficacy and Safety of Topical Antibiotics in Treatment of Ear Disease

- Fluoroquinolone topical drops are not inferior in efficacy to aminoglycosides and may be more effective than aminoglycosides.
- Drop toxicity must also take into account preservatives, particularly propylene glycol (Vosol)
- Topical drops rarely (if ever) induce resistance either locally in the ear or remotely in other parts of the aerodigestive tract



Treatment of Inflammation



- steroids- may speed effusion resolution
 - decrease inflammation of the Eustachian tube
 - decrease inflammatory mediators concentrations
 - decreased glycoprotein production by goblet cells
 - Mandel, etal (2002) Amox and prednisilone had ↑ resolution over placebo, but 70% of those that resolved recurred by 4 month visit
- intranasal steroids- evidence for short term treatment of OME, not shown to hold out long-term.

Lin J, etal: Acta Otolaryngol 1997; 117:406-13.

Treatment of Inflammation

- non-steroidals - Use of ibuprofen which is a prostaglandin inhibitor showed effect in chinchilla study in decreasing AOM occurrence
 - personal communication P Nicklaus 1996
- reflux disease - Multiple reports on GERD contributing to OM
 - helpful in patients with red drums and discomfort post PE tubes but no drainage

Treatment of Inflammation

- smoking cessation - reports conflict. Passive smoking and gestational tobacco exposure were found to increase OM in one prospective study.
 - Analysis of national health survey data did not demonstrate same increased risk
- allergy treatment - likely contributes, but since OM peaks between 6-18 months often older children with persistent ear problems treated for allergy.

Lieu et al. Effect of gestational and ... Arch Ped Adol Med 2002;156:147-54.

Risk Factor Reduction CPG 2004

- Unchangeable risk factors
 - Genetics, male gender, premature birth, siblings, low socioeconomic status.
- Changeable risk factors
 - Breastfeeding at least 6 months
 - Decreasing daycare exposure
 - Decreasing or eliminating pacifier use
 - Decreasing smoke exposure
 - Avoiding bottle propping
 - Intranasal influenza and pneumococcal vaccine

Treatment of Potential Speech/language difficulties

- Rosenfeld and Bluestone in Evidence Based Otitis Media 1999 reviewed data to 1999 and suggested
 - Speech reception and production are not adequately studied in preschool-aged children . Some results imply prolonged OME associated with more speech errors in school age children.
 - Persistent early OME -adverse effect on preschool language development, decreases with age . School age children not well studied.

Treatment of Potential Speech/language difficulties

- Rosenfeld/Bluestone review
 - Available trials of OME on cognition are sparse and conflicting.
 - Behavioral studies suggest children with prolonged OME are more easily distracted and less attentive extending to early school age/teen
- Paradise et al, 2003 report no difference in speech, language, cognitive or psychosocial development at 3-4 years of age when intervention for OME was delayed 6-9 months.

Conclusions Clinical Practice Guideline 2004

1. Make the diagnosis
2. Address pain
3. Observation vs. high dose amoxicillin first line
4. Reassess 48-72 hours if no response to first line therapy.
 - If observed, begin abx: If abx, change abx.
5. Reduce risk factors to prevent AOM
6. No recommendations made regarding complementary and alternative medicine (CAM)

Updates - It gets worse before it gets better

- The diagnosis of otitis media is difficult. Primary care providers may not be getting adequate training in OM diagnosis.
- Bacterial biofilm formation may change goal of antimicrobial therapy. Sensitivity is not enough.
- New risk factors: reflux, heredity



Updates -



- Medical and surgical therapy don't improve much on a 70-90% spontaneous resolution rate of AOM.
- First line therapy needs cover resistant *s. pneumo* Amoxicillin 80-90 mg/kg/day. Adult 2000mg BID
- Second line β -lactam stability Cephalosporin or Amox/clavulanic acid

Updates -



- Vaccination with Prevnar® may just alter serotypes causing OM
- Delayed management of effusion may or may not adversely affect speech/language
- Otological drops that have a proven safety record and well thought out treatment paradigms are effective in the treatment of otitis media with a patent PE tube without additional oral antibiotics.

Updates Conclusion



- This will not be your last update...
- as Dory in Finding Nemo would say, "Keep Swimming,
- Swimming,
- Swimming"...

Peggy Kelley Biography

Peggy Kelley, MD, is an assistant professor in the Department of Otolaryngology- Head and Neck Surgery at the University of Colorado Health Sciences Center, and an attending physician in the Department of Pediatric Otolaryngology at The Children's Hospital since 1998. She earned her medical degree at the University of Pittsburgh School of Medicine in Pittsburgh, Pennsylvania and completed her residencies at the University of Rochester in Rochester, NY. Dr. Kelley completed her fellowship in Pediatric Otolaryngology at Children's Hospital Medical Center in Cincinnati, Ohio. She is board certified by the American Board of Otolaryngology and serves as a member of the American Society of Pediatric Otolaryngology as well as the American Academy of Facial Plastic & Reconstructive Surgery. Dr. Kelley is the co-director of the Vascular Malformation clinic, as well as the Voice clinic director. Dr. Kelley serves as the Third Year Clerkship Director for medical students in the School of Medicine. She has lectured on otitis media and external otitis from California to New York. Dr. Kelley's specific clinical areas of interest are external ear malformations, microtia reconstruction, airway reconstruction, and voice restoration in children. Her area of research interest is in foreign bodies of the aerodigestive tract.