Pediatric Pharmacotherapeutics 2019: Children Are Not Little Adults!

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Owner: Partners in Healthcare Education, LLC

1

Disclosures

- Speaker Bureau: Sanofi-Pasteur, Merck, Pfizer
- Consultant: Sanofi-Pasteur, Pfizer, Merck, GSK

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2

Objectives

- Upon completion of this program, the participant will be able to:
  - Identify ways in which children are different than adults in terms of pharmacotherapeutics
  - Discuss common pediatric prescribing errors
  - Discuss strategies to prevent pediatric prescribing errors
  - Identify medications with new pediatric approvals

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Why are we here today?

- "Research shows that the potential for adverse drug events within the pediatric inpatient population is about three times as high as among hospitalized adults."
- Why are there issues:
  - Most medications used in the care of children are formulated and packaged primarily for adults.
  - Most health care settings are primarily built around the needs of adults.
  - Children—especially young, small and sick children—are usually less able to physiologically tolerate a medication error due to still developing renal, immune and hepatic functions
  - Many children, especially very young children, cannot communicate effectively to providers regarding any adverse effects that medications may be causing

Kaushal R, et al: Medication errors and adverse drug events in pediatric inpatients. *Journal of the American Medical Association,* 2001, 285:2114-2120

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Medication development

- Until the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), most medications were not developed or even tested initially in children
  - There is no reliable formula to convert adult dosages to those which are safe or effective in children
  - When manufacturers do not test drugs in infants and children, it has led to disastrous results
    - Gray baby syndrome: chloramphenicol in children
    - Sulfonamide-induced kernicterus in newborns

Goodman, Louis S., Alfred Gilman, Joel G. Hardman, Alfred Goodman Gilman, and Lee E. Limbird. *Goodman & Gilman's the pharmacological basis of therapeutics*. 9th ed. New York: McGraw-Hill, Health Professions Division, 1996. Print.

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Pediatric studies and approvals

- The Pediatric Research Equity Act (PREA) mandates that almost all new medicines be studied in children if pediatric use of the product is likely
- In addition, the Best Pharmaceuticals for Children Act (BPCA) opens the door for an additional 6 months of market exclusivity for sponsors that submit completed pediatric studies to the FDA

http://www.medscape.com/viewarticle/820978 accessed 07-01-2014

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FDA approval of medications in children

- 25% of all of the drugs approved by the FDA have any specific indications for children
- In the past 10 years, 12% of all prescriptions written in the US were prescribed for children < 9 years of age

Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

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Pediatric Medication Errors

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Children: Are they different?

- Children differ from adults in regards to the following:
  - Drug absorption
  - Distribution
  - Biotransformation
  - Excretion/Elimination

Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

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Absorption

- Most orally administered medications are absorbed in the small intestine
  - Infants have proportionately larger small intestinal surface areas, this can lead to unpredictable absorption when compared with adults
- Infants also have increased intestinal motility, which alters the absorption of drugs with limited water solubility, such as phenytoin (Dilantin) and carbamazepine (Tegretol)

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What about topical medications?

- Newborns and infants have greater skin absorption - due to increased hydration and thinner stratum corneum than adults
- Systemic toxicity can occur with relatively small amounts of topical application of medications such as diphenhydramine (Benadryl and many other products), lidocaine, corticosteroids and hexachlorophene (PhisoHex)
- **Caution with prescribing topical medications**

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Actual example

- Pediatric studies led to relabeling of betamethasone dipropionate (Diprolene, Diprosone) and betamethasone dipropionate-clotrimazole (Lotrisone)
  - These studies documented hypothalamic-adrenal axis suppression in 23% to 73% of pediatric patients depending on formulation used

Roberts R, Rodriguez W, Murphy D, Crescenzi T. Pediatric drug labeling: improving the safety and efficacy of pediatric therapies. *JAMA*. 2003;290:905-911.

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Children: Drug clearance pathways

- Most drug clearance pathways develop over the first year of life
  - Although not all pathway development is fully known in children, most develop by 1 year
  - For instance:
    - CYP1A2 pathway, studies were performed in children using caffeine which showed that by year one the pathway is developed.
    - Important: if drugs such as theophylline which also used this pathway are administered before 1 year, significant toxicity occurs
    - At puberty, clearance begins to decline

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Goodman, Louis S., Alfred Gilman, Joel G. Hardman, Alfred Goodman Gilman, and Lee E. Limbird. *Goodman & Gilman's the pharmacological basis of therapeutics*. 9th ed. New York: McGraw-Hill, Health Professions Division, 1996. Print.

13

CYP450 pathways and children

Activity in Enzyme	Fetus/Neonate	Age Adult Level Achieved
CYP1A2	Nearly absent	4 months
CYP2C	Nearly absent	6 months
CYP2D6	Nearly absent	3-5 years
CYP3A4	Low	6-12 months
CYPP3A7	High	Declines in first week of life; not present in adults

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Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

14

Important take away

- 7 day neonate will be very different from a pharmacokinetic perspective than a newborn
- The dosage that is appropriate for a 10 year old may be an overdose for a 16 year old
- All dosages need to be checked for age and weight repeatedly

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What Medications Are Involved in Most Pediatric Outpatient Prescribing Errors?

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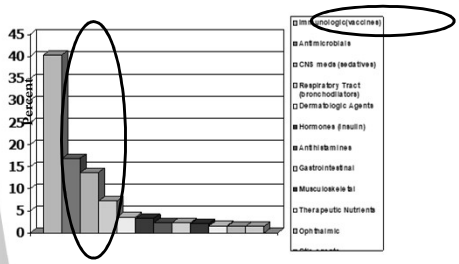
Results: Medications Involved



https://www.google.com/search?newwindow=1&site=&source=hp&q=pediatric+prescriptions&oq=pediatric+prescriptions&gs_l=hp.3..0j0i22i30l8.1146.6430.0.7963.23.17.0.6.6.0.144.1907.4j13.17.0....0...1c.1.48.hp..0.23.1993.Ph2SE2iWdpA Accessed 07-01-2014

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Important take away

- Two people should check vaccine record prior to administration of vaccines, if possible
- Two people should look at actual vaccine prior to administration, if possible

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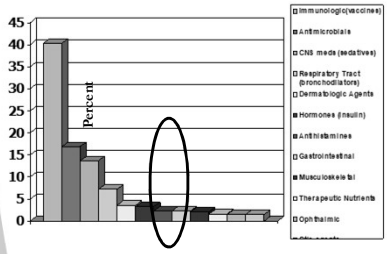
Results: Medications Involved



https://www.google.com/search?newwindow=1&site=&source=hp&q=pediatric+prescriptions&oq=pediatric+prescriptions&gs_l=hp.3..0j0i22i30l8.1146.6430.0.7963.23.17.0.6.6.0.144.1907.4j13.17.0....0...1c.1.48.hp..0.23.1993.Ph2SE2iWdpA
Accessed 07-01-2014

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19

Dosing medications in children

- Most medications are dosed by mg/kg/day
  - However, there are many drugs which are reported as total dosage vs. others which are dosed two – three times daily
  - 1 kg = 2.2 pounds
- Double check your references
  - Epocrates
  - Lexi-Comp
  - http://www.empr.com/pediatrics-edition/section/1299/

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Reasons for errors: Recommended doses can differ

Source	Recommended pediatric dose for oxycodone
Harriet Lane Handbook	0.2 to 0.9 mg/kg/day q 4-6 hours
HMO Formulary	No weight-based dose provided.
Children's Hospital Formulary	0.2 to 1.6 mg/kg/day q 3-4 hours

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Doses may be higher in children: amoxicillin

6 year-old 40kg male with otitis failed conservative therapy

↓

Amoxicillin 90 mg/kg/day divided bid

↓	↓
Appropriate pediatric dose:	Appropriate adult dose:
3600 mg/day (1800mg bid)	2000 mg/day (1000 bid)

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General techniques to avoid prescribing errors

- Clear writing and documentation
  - EHR, if available
- Double check dosages
- Avoid writing RX's when patient is talking to you or sitting in front of you
- Have a list of high risk drugs; when you see this list – bells should go off in your head
- Double check interactions

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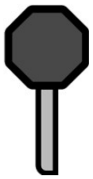
DO NOT DEVELOP EHR ALERT FATIGUE



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Additional elements of safe prescription writing

- Include diagnosis on prescription
- Many prescriptions now enable provider to write kg or weight on RX
- Never write a prescription without a 0 or number before the decimal point
  - For instance: 0.5 milligrams
- Never put a zero after a decimal point
  - For instance: 10 milligrams NOT 10.0 mg
- Always calculate out the amount of the total medication needed
  - This serves as a double check system
  - 10 mL two times daily x 10 days = 200 Ml
  - Do not write quantity sufficient

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Pediatric Medication Adherence

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Factors affecting medication adherence

- Frequency of dosing
- Palatability
- Route of administration
- Cost
- Administration instructions

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Adherence to Medication Regimens

- Adherence to a regimen decreases as the frequency of a drug increases
  - In an NIH published trial, mean dose-taking compliance was 71% +/- 17% (range, 34%-97%) and declined as the number of daily doses increased
  - For instance: 1 dose = 79% +/- 14%, 2 doses = 69% +/- 15%, 3 doses = 65% +/- 16%, 4 doses = 51% +/- 20% (P < 0.001 among dose schedules)
  - Compliance was significantly higher for once-daily versus 3-times-daily (P = 0.008), once-daily versus 4-times-daily (P < 0.001), and twice-daily versus 4-times-daily regimens (P = 0.001)

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. Clinical Therapeutics, 23(8), 1296-1310.

28

Children: Palatability

- Another issue which significantly affects medication utilization in children is taste and palatability
- This is more so in pediatrics than any other age group

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Flavoring is routinely available

- In general, the following medications have poor taste
  - Penicillins
  - Prednisone
  - Clindamycin
  - Azithromycin
  - Trimethoprim/sulfamethosazole
- Better tasting:
  - Cephalosporins

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Length of Prescriptions

- Increasing trend to decrease length of prescriptions
- Recent studies have shown that for most conditions in children, shorter courses may provide same benefits, often with fewer side effects and better adherence

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Duration of treatment for AOM

- Results
  - 10 days: Patients <2 years old or those with severe symptoms
  - 7 days: Age 2-5 years of age with mild – moderate AOM
  - 5 – 7 days: 6 years and older with mild – moderate symptoms

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 5-11-2013

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Specific Medications and Warnings in Pediatrics

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Cough and cold medications in children

Public Health Advisory: FDA Recommends that Over-the-Counter (OTC) Cough and Cold Products not be used for Infants and Children under 2 Years of Age

http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/drugsafetyinformationforheathcareprofessionals/publichealthadvisories/ucm051137.htm accessed 07-01-2014

34

Acetaminophen vs. Ibuprofen vs. Aspirin

- Acetaminophen dosage:
  - 10-15 mg/Kg/dose q 4-6 hours
  - Max 5 doses in 24 hours
- Ibuprofen dosage:
  - 5-10 mg/Kg/dose q 6-8 hours
  - Max OTC dosing 40 mg/Kg/day OR 1.2 Gm/day
- What about aspirin?
  - NONE < 19 YEARS DUE TO RISK OF REYE'S SYNDROME
  - Keep in mind that many products contain salicylates

http://www.aafp.org/afp/2009/1215/p1472.html accessed 07-01-2014

35

Stevens-Johnson Syndrome

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 1, 2013 – Acetaminophen: The U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that acetaminophen has been associated with a risk of rare but serious skin reactions. Acetaminophen is a common active ingredient to treat pain and reduce fever; it is included in many prescription and over-the-counter (OTC) products. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels.

http://www.guideline.gov/content.aspx?id=38416&search=strep+pharyngitis Accessed 07-01-2014

36

Specific Pediatric Conditions

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Allergic rhinitis

- Many OTC medications are available
- Caution:
  - First generation antihistamines
  - Anticholinergic effects
    - Sedation or agitation
    - Tachycardia
    - Dry mouth
    - Urinary retention
- Examples:
  - Diphenhydramine
  - Chlorpheniramine

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Allergic Rhinitis

- Recommendations for pediatrics
  - 2nd generation antihistamines are available OTC
  - Fewer side effects than first generation antihistamines
  - Have dosages and formulations available for children
  - Examples:
    - Loratadine (Claritin, Alavert): 2-5 years of age and > 6 years (adjust dosing with renal impairment)
    - Cetirizine (Zyrtec): 2-5 years of age and > 6 years (adjust or avoid with renal impairment)
    - Fexofenadine (Allegra): 6 months - 2 years, 2 – 5 years and > 6 years
      - DO NOT GIVE WITH FRUIT JUICE (reduces absorption of drug by > 1/3)

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Asthma

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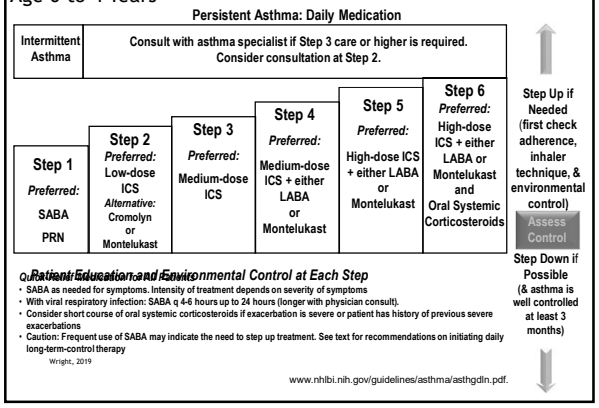
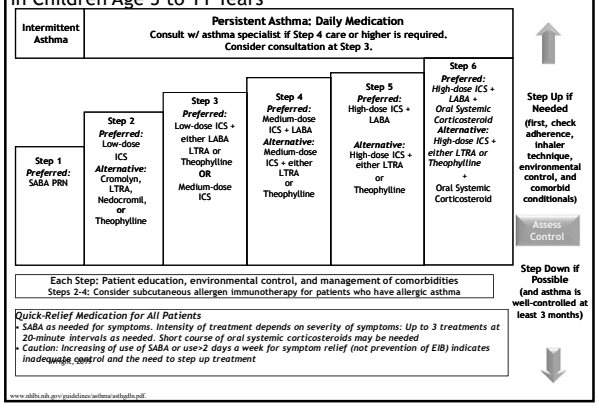
Stepwise Approach for Managing Asthma in Children Age 0 to 4 Years

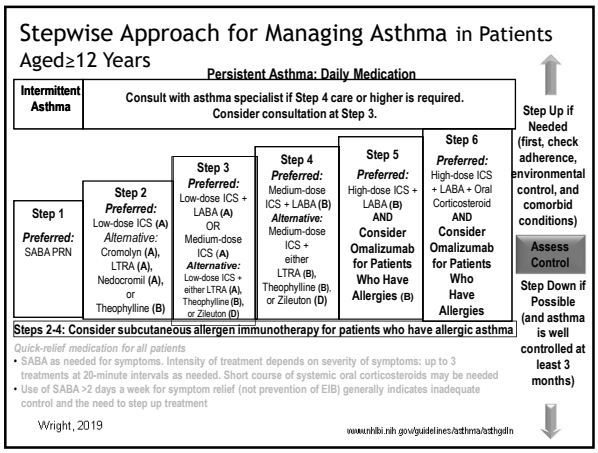


41

Stepwise Approach for Managing Asthma in Children Age 5 to 11 Years



42


Stepwise Approach for Managing Asthma in Patients Aged≥12 Years
Persistent Asthma: Daily Medication
Intermittent Asthma
Consult with asthma specialist if Step 4 care or higher is required.
Consider consultation at Step 3.
Step 1
Preferred:
SABA PRN
Step 2
Preferred:
Low-dose ICS (A)
Alternative:
Cromolyn (A), LTRA (A), Nedocromil (A), or Theophylline (B)
Step 3
Preferred:
Low-dose ICS + LABA (A)
OR
Medium-dose ICS (A)
Alternative:
Low-dose ICS + either LTRA (A), Theophylline (B), or Zileuton (D)
Step 4
Preferred:
Medium-dose ICS + LABA (B)
Alternative:
Medium-dose ICS + either LTRA (B), Theophylline (B), or Zileuton (D)
Step 5
Preferred:
High-dose ICS + LABA (B)
AND
Consider Omalizumab for Patients Who Have Allergies (B)
Step 6
Preferred:
High-dose ICS + LABA + Oral Corticosteroid
AND
Consider Omalizumab for Patients Who Have Allergies
Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma
Quick-relief medication for all patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed
• Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment
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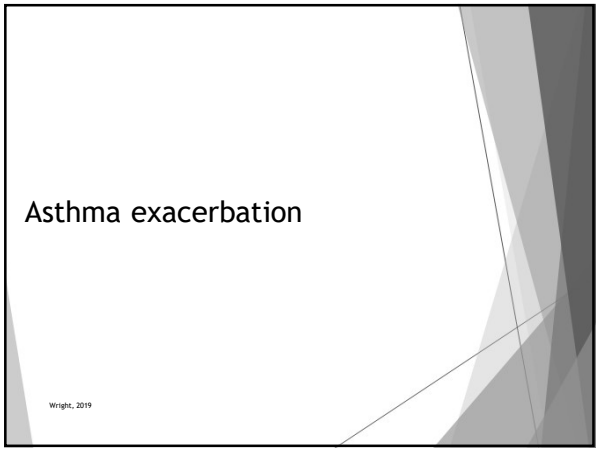
www.nhlbi.nih.gov/guidelines/asthma/asthgdln
Step Up if Needed (first, check adherence, environmental control, and comorbid conditions)
Assess Control
Step Down if Possible (and asthma is well controlled at least 3 months)

43


Asthma exacerbation
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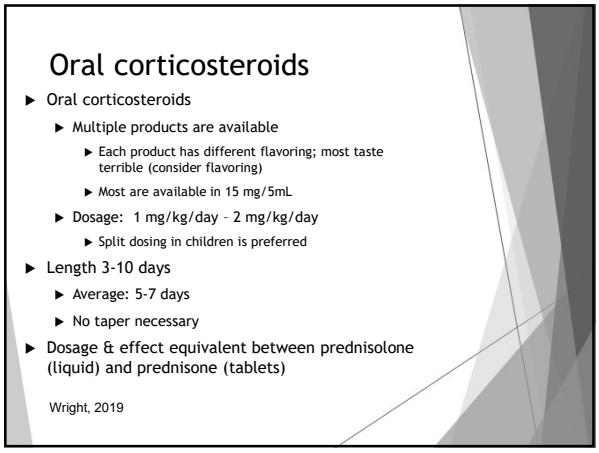
44


Oral corticosteroids
Oral corticosteroids
Multiple products are available
Each product has different flavoring; most taste terrible (consider flavoring)
Most are available in 15 mg/5mL
Dosage: 1 mg/kg/day – 2 mg/kg/day
Split dosing in children is preferred
Length 3-10 days
Average: 5-7 days
No taper necessary
Dosage & effect equivalent between prednisolone (liquid) and prednisone (tablets)
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45

Antibiotics

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46

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Diagnosis and Management of Acute Otitis Media

Allan S. Lieberthal, Aaron E. Carroll, Tasnee Chonmaitree, Theodore G. Ganiats, Alejandro Hoberman, Mary Anne Jackson, Mark D. Joffe, Donald T. Miller, Richard M. Rosenfeld, Xavier D. Sevilla, Richard H. Schwartz, Pauline A. Thomas and David E. Tunkel

Pediatrics; originally published online February 25, 2013; DOI: 10.1542/peds.2012-3488

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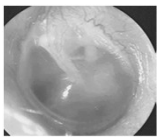
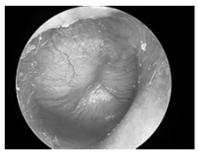
47

Variations of Tympanic Membrane

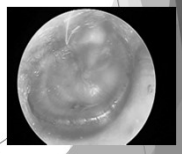
Normal TM



Acute OM



Otitis Media with Effusion



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AAP Updated Guidelines

- Diagnosis of AOM:
  - Evidence: 1A
    - Moderate - severe bulging of TM with otalgia
    - OR…new otorrhea NOT due to otitis externa with otalgia
  - Evidence: 1B
    - Mild bulging of TM and….
      - Recent (< 48 hours) onset of ear pain or….
    - Intense erythema of TM with otalgia

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640yy70jU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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49

Who Needs Antimicrobials

- Any child < 6 months of age
- Any child with severe AOM
- Any child < 24 months of age with bilateral AOM
- Any child in whom follow-up can not be ensured

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50

AAP Updated Guidelines (cont.)

- Severe AOM:
  - Prescribe antimicrobial for AOM in children 6 months or older with severe signs and symptoms
    - Moderate or severe otalgia for at least 48 hours OR…
    - Temperature: 102.2 (39 degrees Celsius)

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640yy70jU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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AAP Updated Guidelines (cont.)

- Treatment options:
  - Amoxicillin: first line
    - Provided that: no antibiotics in previous 30 days and
    - No purulent conjunctivitis and
    - Not allergic to PCN

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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52

AAP Updated Guidelines (cont.)

- Treatment options:
  - Amoxicillin/clavulanate
    - Child who has received antibiotics in previous 30 days OR….
    - Has concurrent purulent conjunctivitis OR….
    - History of AOM which is unresponsive to amoxicillin

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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53

Initial Immediate or Delayed Antibiotic Treatment

Recommended First line Treatment	Alternative Treatment (if Penicillin Allergy)
Amoxicillin (80-90 mg/kg/day) in two divided doses OR	Cefdinir (14 mg/kg/day) in one - two divided doses Cefuroxime (30 mg/kg/day) in two divided doses
Amoxicillin/clavulanate (90 mg/kg/day or amoxicillin) with 6.4 mg/kg/day of clavulanate) in two divided doses	Cefpodoxime (10mg/kg/day) in two divided doses Ceftriaxone (50 mg/kg/day IM or IV) daily for 1 or 3 days

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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54

Antibiotic Treatment After 48-72 hours of Failure of Initial Antibiotic

Recommended First line Treatment	Alternative Treatment (if Penicillin Allergy)
Amoxicillin/clavulanate (90 mg/kg/day or amoxicillin) with 6.4 mg/kg/day of clavulanate) in two divided doses	Ceftriaxone 3 day Clindamycin (30 – 40 mg/kg/day) in three divided doses with or without concomitant third generation cephalosporin
Ceftriaxone (50 mg/kg/day IM or IV) for 3 days	Clindamycin (30 – 40 mg/kg/day) in three divided doses with concomitant third generation cephalosporin Tympanocentesis Consult specialist

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

55

Remember…

- For children with OM and tympanostomy tubes:
  - You may also utilize topical medications
  - Ofloxacin (Floxin Otic) 0.3% solution
    - Age 1 - 12 years: 5 drops into affected ear bid x 10 days
  - Ciprofloxacin (Ciprodex):
    - 6 months and up: 4 drops into the affected ear bid x 7 days

56

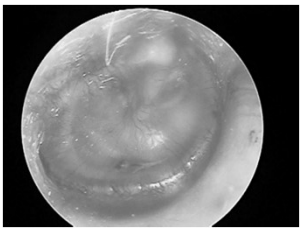
Otitis Media with Effusion

- Fluid in the middle ear
- No signs and symptoms of AOM
  - Air fluid levels
  - Dullness of TM
  - Decreased movement of TM

http://pediatrics.aappublications.org/cgi/content/abstract/113/5/1412 accessed 02-01-2010

57

OME



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58

OME

- Treatment:
  - Observation as a treatment option
  - Majority – up to 90% will resolve within 3 months without intervention
  - If still present at 12 weeks – may need hearing evaluation, referral to ENT
  - High risk individuals may be candidates for myringotomy

http://pediatrics.aappublications.org/cgi/content/abstract/113/5/1412 accessed 02-01-2010

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59

IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults Clinical Infectious Diseases Advance Access published March 20, 2012

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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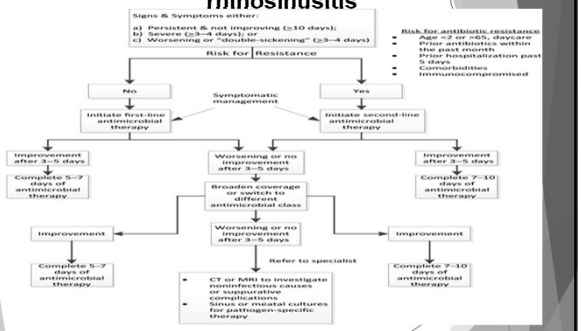
60

Algorithm for the management of acute bacterial rhinosinusitis



Chow A W et al. Clin Infect Dis. 2012;cid.cir1043

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Clinical Infectious Diseases

61

What Constitutes at Risk for Resistance?

- Age < 2 years or > 65 years
- Daycare
- Antimicrobial within past 1 month
- Hospitalization within past 5 days
- Comorbidities
- Immunocompromised

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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62

Goals of Treatment

- Restore integrity and function of osteomeatal complex
  - Reduce inflammation
  - Restore drainage
  - Eradicate bacterial infection

http://www.medscape.com/viewprogram/5621

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63

Treatment of Acute Bacterial Rhinosinusitis

- Nonpharmacologic Therapies
  - Increased water intake
  - Intranasal saline irrigations with either physiologic or hypertonic saline are recommended as an adjunctive treatment in adults with ABRS[1]

[1]http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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64

Management Strategies in ABRS

- Antihistamines or decongestants
  - No longer recommended
- Topical corticosteroids
  - Intranasal corticosteroids are recommended as an adjunct to antibiotics in the empiric treatment of ABRS, primarily in patients with a history of allergic rhinitis[1]
- Corticosteroids

[1]http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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65

Antimicrobial Regimens in Children

Table 9. Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children

Indication	First-line (Daily Dose)	Second-line (Daily Dose)
Initial empirical therapy	• Amoxicillin-clavulanate (45 mg/kg/day PO bid)	• Amoxicillin-clavulanate (90 mg/kg/day PO bid)
β-lactam allergy		
Type I hypersensitivity		• Levofloxacin (10–20 mg/kg/day PO every 12–24 h)
Non–type I hypersensitivity		• Clindamycin* (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)
Risk for antibiotic resistance or failed initial therapy		• Amoxicillin-clavulanate (90 mg/kg/day PO bid)
		• Clindamycin* (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)
		• Levofloxacin (10–20 mg/kg/day PO every 12–24 h)
Severe infection requiring hospitalization		• Ampicillin/sulbactam (200–400 mg/kg/day IV every 6 h)
		• Ceftriaxone (50 mg/kg/day IV every 12 h)
		• Cefotaxime (100–200 mg/kg/day IV every 6 h)
		• Levofloxacin (10–20 mg/kg/day IV every 12–24 h)

Abbreviations: bid, twice daily; IV, intravenously; PO, orally; qd, daily; tid, 3 times a day.

* Resistance to clindamycin (~31%) is found frequently among *Streptococcus pneumoniae* serotype 19A isolates in different regions of the United States [94].

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
accessed 12-29-2012

66

Important Changes

- Macrolides (clarithromycin and azithromycin) are not recommended due to high rates of resistance among *S. pneumoniae* (30%)
- TMP/SMX is not recommended due to high rates of resistance among both *S. pneumoniae* and *H. influenzae* (30%–40%)
- Second and third-generation cephalosporins are no longer recommended due to variable rates of resistance among *S. pneumoniae*.

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html accessed 12-29-2012

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67

Length of treatment

- The recommended duration of therapy for uncomplicated ABRS in adults is 5–7 days
- In children with ABRS, the longer treatment duration of 10–14 days is still recommended

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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68

When to Change Treatments

- An alternative treatment should be considered if symptoms worsen after 48–72 hours of initial empiric antimicrobial therapy, or when the individual fails to improve despite 3–5 days of antimicrobial therapy

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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69

When to Refer

Table 14. Indications for Referral to a Specialist

- Severe infection (high persistent fever with temperature >39°C [>102°F]; orbital edema; severe headache, visual disturbance, altered mental status, meningeal signs)
- Recalcitrant infection with failure to respond to extended courses of antimicrobial therapy
- Immunocompromised host
- Multiple medical problems that might compromise response to treatment (eg, hepatic or renal impairment, hypersensitivity to antimicrobial agents, organ transplant)
- Unusual or resistant pathogens
- Fungal sinusitis or granulomatous disease
- Nosocomial infection
- Anatomic defects causing obstruction and requiring surgical intervention
- Multiple recurrent episodes of acute bacterial rhinosinusitis (ABRS) (3–4 episodes per year) suggesting chronic sinusitis
- Chronic rhinosinusitis (with or without polyps or asthma) with recurrent ABRS exacerbations
- Evaluation of immunotherapy for allergic rhinitis

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012
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70

Pharyngitis

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Pharyngitis

- Epidemiology
  - Group A Beta Hemolytic Strep
    - Most interest because of its association with severe complications
    - Peritonsillar abscesses, rheumatic fever, post-streptococcal glomerulonephritis - complications

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72

Exudative pharyngitis

Exudative pharyngitis
Differentials include:
Strep pharyngitis
Peritonsillar abscess
Mononucleosis
Viral pharyngitis

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73

Strep pharyngitis treatment

- Penicillin VK 250-500 mg BID X 10 days
  - 250 mg two times daily (children)
  - 500 mg two times daily (adolescents)
  - Amoxicillin 50 mg/Kg/day divided BID X 10 days is acceptable and tastes better in liquid form, but broader spectrum than needed
    - ONCE DAILY is okay option
    - Not to exceed 1000 mg daily of amoxicillin
- Penicillin allergy
  - Past urticaria/anaphylaxis-
    - Erythromycin 50 mg/kg/day, divided BID- 4xDay X 10 days (possible alternatives: Azithromycin X 5 days, clindamycin X 10 days)
  - NOT urticaria/anaphylaxis - Cephalexin possible

Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 Nov;55(10):e86-e102 accessed 07-01-2014

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74

Miscellaneous Pediatric Prescribing Information

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75

Miscellaneous

- Albuterol inhalers
  - All contain 200 inhalations
  - Well-controlled patients should need < 1 inhaler per year
  - Closely monitor utilization of these inhalers

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76

Tetracycline/Doxycycline

- Tetracycline should never be administered to children < 8 years of age
  - Due to graying of the teeth
- Children > 8 years of age
  - 25 – 50 mg/kg/day in two divided dosages
- Doxycycline:
  - > 8 years of age 4-5 mg/kg/day in two divided dosages every 12 hours
- In general, vitamins, milk, calcium will chelate TCN and therefore should not be taken at the same time

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Herbal preparations

- Resurgence of usage of herbal or complementary therapies
  - N-acetyl-methoxytryptamine (Melatonin)
  - Hypericum (St. John's Wort)
  - Echinacea purpurea (Echinacea)
- Significant number of drug/drug interactions
- Many are unsafe in pediatrics
  - Hypericum (St. John's Wort) interacts with a significant number of other medications
  - CYP3A4 inducer

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78

Miscellaneous Pediatric Approvals

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ADHD Treatment

- Single entity amphetamine product (Mydayis)
  - Three different types of coated beads
  - Released at separate intervals
  - Duration of symptom control (16 hours)
  - 13 years of age and older
  - 12.5 or 25 mg once daily dosage
- Once daily extended release ODT formulation of methylphenidate (Contempla XR-ODT)
  - Ages 6 – 17 years
  - 12 hour of symptom control
  - 8.6 mg, 17.3 mg, and 25.9 mg strengths

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80

Additional New Approvals

- Cetirizine ophthalmic solution (Zerviate)
  - Allergic conjunctivitis
  - First cetirizine ophthalmic product
  - 0.24% once daily
  - 2 years of age and older

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81

New Labeling

- Budesonide/Formoterol (Symbicort)
  - Ages 6 – 12 years of age with asthma
- Fluticasone and salmeterol (AirDuo RespiClick)
  - Ages 12 years and older with asthma
- Lisdexamfetamine (Vyvanse)
  - Ages 6 years and older
  - Available in a chewable tablet
  - 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg
- Lurasidone Hydrochloride (Latuda)
  - Adolescents ages 13 – 17 years
  - Indication: schizophrenia or irritability associated with autistic disorder

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82

Additional Approvals

- Tiotropium Bromide (Spiriva Respimat)
  - Indicated for asthma ages 6 – 11 years
- Ciprofloxacin and Gatifloxacin Ophthalmic
  - Bacterial conjunctivitis
  - Ages 1 month and older
  - Previously approved for 1 year of age and older

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83

Baloxavir marboxil (Xofluza)

- Indication:
  - Treatment of acute, uncomplicated influenza in patients aged ≥ 12 years who have been symptomatic for no more than 48 hours
- Class:
  - Polymerase acidic (PA) endonuclease inhibitor
    - Inhibits influenza virus replication

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

84

Baloxavir marboxil

- Dosage:
  - 20 mg and 40 mg dosages available
  - Weight based:
    - 40 kg to < 80 kg: Single dose of 40 mg
    - ≥ 80 kg: 80 mg dose
  - With or without food
  - Avoid co-administration with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids, or oral supplements

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

85

Efficacy

- Primary endpoint of both trials was:
  - Time to alleviation of symptoms,
    - Time when all seven symptoms (cough, sore throat, nasal congestion, headache, feverishness, myalgia, and fatigue) had been assessed by the subject as none or mild for a duration of at least 21.5 hours
  - Results Trial 1: 50 hours vs. 78 hours (placebo)
  - Results Trial 2: 54 hours vs. 80 hours (placebo)
  - Also looked at oseltamivir comparison: No difference between oseltamivir and baloxavir marboxil

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

86

Baloxavir marboxil

- Warnings and precautions:
  - Limited data on pregnancy and lactation
- Contraindications:
  - Known hypersensitivity to one of the ingredients

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

87

Baloxavir marboxil

- Side effects:
  - Diarrhea (3%), bronchitis (2%), nasopharyngitis (1%), headache (1%) and nausea (1%)
- Advantages
  - Unique mechanism of action
  - Single dose, oral medication
  - Targets influenza A and B, including those resistant to oseltamivir and avian strains
  - Well-tolerated

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

88

Baloxavir marboxil

- Competition:
  - Oseltamivir
- Cost:
  - $150.00
  - Have found coupons on-line for no more than $30.00

https://www.gene.com/download/pdf/xofluza_prescribing.pdf accessed 01-02-2019

89

Glucopyrronium (Qbrexza)

- Treatment of primary axillary hyperhidrosis in children 9 years of age and older and adults
- Single-use cloth
- Anti-cholinergic
- Apply once every 24 hours to axillary regions

90

OTC Option

- Epinephrine inhalation aerosol bronchodilator suspension (Primatine MIST) for the temporary relief of mild symptoms of intermittent asthma (eg, wheezing, tightness of chest, shortness of breath) in patients aged ≥12 years
- Launch: first quarter of 2019

91

Additional Pediatric Indication

- Sweet Vernal, Orchard, Perennial Rye, Timothy, Kentucky Blue Grass Mixed Pollens Extract (Oralair)
  - Indication previously: 10 – 65 years
  - Additional indication: 5 – 9 years
- Sublingual tablet:
  - 100 and 300 mg

wwww.eMPR.com/news accessed January 2019

92

Hexavalent Pediatric Vaccine Approved

- Vaxelis:
  - diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, haemophilus b conjugate [meningococcal protein conjugate] and hepatitis B [recombinant] vaccine
    - Active immunization in children aged 6 weeks through 4 years (prior to the 5th birthday)
    - 3-dose series given at 2, 4, and 6 months of age
  - It may be used to complete the hepatitis B series
  - The 3-dose series does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the primary series

93


Thank You!
I Appreciate Your Attention!
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94


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95