Pediatric Pharmacotherapeutics: Children Are Not Little Adults!

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Disclosures

- Speaker Bureau: Novartis, GSK, Sanofi-Pasteur, Merck, Takeda, Vivus
- Consultant: Vivus, Sanofi-Pasteur, Takeda

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
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.


Medication development

- Until 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.


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.

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


Pediatric Medication Errors

Children: Are they different?

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

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 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)

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

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

Children: Drug clearance pathways

- Drug clearance pathways development 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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CYP450 pathways and children

<table>
<thead>
<tr>
<th>Activity in Enzyme</th>
<th>Fetus/Neonate</th>
<th>Age Adult Level Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>Nearly absent</td>
<td>4 months</td>
</tr>
<tr>
<td>CYP2C</td>
<td>Nearly absent</td>
<td>6 months</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>Nearly absent</td>
<td>3-5 years</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>Low</td>
<td>6-12 months</td>
</tr>
<tr>
<td>CYP3A7</td>
<td>High</td>
<td>Declines in first week of life; not present in adults</td>
</tr>
</tbody>
</table>


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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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Glucuronidation

- Neonates are less capable of this phase II reaction than older infants & children
  - Results in physiologic neonatal jaundice (bilirubin eliminated through glucuronidation)
  - Some medications (e.g. Ceftriaxone), displace bilirubin from albumin binding sites, and can worsen neonatal jaundice

Elimination

- Glomerular filtration rates (GFR) in newborns is only 30% to 40% of adult values
- GFR rises dramatically in the first 2 weeks of life in the term and preterm neonate
- By age 6 to 12 months, the GFR reaches adult values
- Drugs which are exclusively metabolized in the kidneys are more likely to cause systemic toxicity
  - Ampicillin
  - Aminoglycoside antibiotics (tobramycin, gentamicin)
  - Digoxin


What Medications Are Involved in Most Pediatric Outpatient Prescribing Errors?
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
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

Reasons for errors:
Recommended doses can differ

<table>
<thead>
<tr>
<th>Source</th>
<th>Recommended pediatric dose for oxycodone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harriet Lane Handbook</td>
<td>0.2 to 0.9 mg/kg/day q 4-6 hours</td>
</tr>
<tr>
<td>HMO Formulary</td>
<td>No weight-based dose provided.</td>
</tr>
<tr>
<td>Children’s Hospital Formulary</td>
<td>0.2 to 1.6 mg/kg/day q 3-4 hours</td>
</tr>
</tbody>
</table>

Doses may be higher in children: amoxicillin

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

Dr. Smart would like to treat with 90 mg/kg/day divided bid

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

Potential overdose??  Potential under-dose??
Narrow Therapeutic Index

- Many drugs have a narrow therapeutic index
- Therapeutic index:
  - Ratio of the dose of the drug lethal in 50% (LD50) of a tested population to the dose of the drug therapeutically effective in 50% (ED50) of the tested population
  - $\text{TI} = \frac{\text{LD50}}{\text{ED50}}$
- Drug with higher therapeutic index has a wider safety margin
  - Lithium
  - Valproate sodium
  - Theophylline
  - Digoxin
  - Carbamazepine
  - Clindamycin
  - Warfarin


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

DO NOT DEVELOP: EHR ALERT FATIGUE
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

Pediatric Medication Adherence

Factors affecting medication adherence

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


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

Flavoring is routinely available

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

- Liquid
- Pill
- Capsules
- Rectal administration
- IM vs. SC

Cost

- As medication costs rise, so too does reluctance to take medications
- This is particularly true for chronic medications
- Often by the time a drug is used in children, it is often generic or ending its patent
- Rarely, does a new drug come to market with a pediatric indication
  - After years of post-marketing information, drug then becomes FDA approved for children

Administration instructions

- If a drug has to be dosed without food or separated from other medications, this often affects adherence
- This becomes a significant issue in younger children who feed every few hours
Administration instructions

- In general, the following drugs are NOT affected by food:
  - Macrolides
  - Amoxicillin with or without clavulanate
  - Sulfonamides
  - Cephalosporins
- Drugs affected by food (take 1 hour before or two hours after meal)
  - Tetracyclines
  - Penicillin
  - Dicloxacillin
  - Ampicillin

Refrigeration

- Many antibiotics must be kept refrigerated
- Consideration for families who may not have access to adequate refrigeration or families who are going to be travelling
- In general, medications which are in a bottle, require refrigeration
- Medications not requiring refrigeration:
  - Sulfonamides (TMP/SMX)
  - Erythromycin
  - Clindamycin
  - Tetracycline

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
For instance: 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..0i22i30l2.1956.5384.0.5749.19.13.1.5.0.0.0.0.0.0.0.127.1021.1j2.13.0...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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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/postmarketdrugssafetyinformationforspatientsandproviders/drugsafetyinformationforhealthcareprofessionals/publichealthadvisories/jomug51137.htm accessed 07-01-2014

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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


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Stevens-Johnson Syndrome

- **FDA Warning/Regulatory Alert**
  - Note: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.
  - August 1, 2013: Acetaminophen (Acetaminophen is a common active ingredient in most pain and fever products). It is included in many prescription and over-the-counter (OTC) products. These adverse reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can occur. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fevers and pain/fever reductions (e.g., non-steroidal anti-inflammatory drugs, or NSAIDs, such as ibuprofen and naproxen) also carry the risk of causing similar adverse reactions, which is already described in the warning section of their Drug Label.

Accessed 07-01-2014

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
  - Clorpheneramine

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)

Asthma
Stepwise Approach for Managing Asthma in Patients Aged ≥ 12 Years

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 (B)

Intermittent Asthma
Intermittent Asthma
Persistent Asthma: Daily Medication
Consult with asthma specialist if Step 4 care or higher is required.
Consider consultation at Step 3.

Asthma exacerbation

Prednisone

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

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
    - OR... new otorrhea NOT due to otitis externa
  - Evidence: 1B
    - Mild bulging of TM and...
    - Recent (< 48 hours) onset of ear pain or...
    - Intense erythema of TM

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)

AAP Updated Guidelines (cont.)

- **Nonsevere bilateral AOM in children < 24 months without signs or symptoms:**
  - Antibiotics should be prescribed even in the setting of mild symptoms
    - Mild otalgia < 48 hours
    - Temperature < 39 degrees Celsius
AAP Updated Guidelines (cont.)

- Nonsevere unilateral AOM in children age 6 month – 23 months:
  - Two options:
    - Antimicrobial therapy
    - Observation as treatment option
  - Nonsevere
  - Follow-up must be ensured
  - Start antimicrobials if worsen or no improvement with 48 – 72 hours

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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AAP Updated Guidelines (cont.)

- Nonsevere AOM in older children (24 months or older):
  - Two options:
    - Antimicrobial therapy
    - Observation as treatment option
  - Nonsevere
  - Follow-up must be ensured
  - Start antimicrobials if worsen or no improvement with 48 – 72 hours

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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Summary: AAP Updated Guidelines (cont.)

<table>
<thead>
<tr>
<th>AGE</th>
<th>Otorrhea with AOM</th>
<th>Unilateral or Bilateral AOM with Severe Symptoms</th>
<th>Bilateral AOM without Otorrhea</th>
<th>Unilateral AOM without Otorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months – 2 years</td>
<td>Antibiotic</td>
<td>Antibiotic</td>
<td>Antibiotic or observation</td>
<td>Antibiotic therapy or observation</td>
</tr>
<tr>
<td>2 ≥ years</td>
<td>Antibiotic</td>
<td>Antibiotic</td>
<td>Antibiotic or observation</td>
<td>Antibiotic or observation</td>
</tr>
</tbody>
</table>

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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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

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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

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Initial Immediate or Delayed Antibiotic Treatment

<table>
<thead>
<tr>
<th>Recommended First Line Treatment</th>
<th>Alternative Treatment (if Penicillin Allergy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin (80-90 mg/kg/day) in two divided doses OR</td>
<td>Cefdinir (14 mg/kg/day) in one – two divided doses</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate (90 mg/kg/day or amoxicillin) with 6.4 mg/kg/day of clavulanate) in two divided doses</td>
<td>Ceftriaxime (50 mg IM or IV) daily for 1 or 3 days</td>
</tr>
</tbody>
</table>

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

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

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

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
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

Otitis Media (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 Wright, 2014
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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Goals of Treatment

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


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

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

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
- Corticosteroids

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

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
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.

When to Refer

Table 14: Indications for Referral to a Specialist

- Severe oropharyngitis (high febrile illness with temperature >39°C, rapidly evolving tonsillar exudate, severe headache, visual disturbances, severe malaise, and meningismus).
- Recurrent oropharyngitis with failure to respond to extended courses of antimicrobial therapy.
- Impaired swallowing or aspiration.
- Multiple medical problems that might complicate response to treatment, e.g., surgical or medical requirement, immunosensitivity to antimicrobial agents, organ transplant.
- Unusual or resistant organisms.
- Fungal etiologies or granulomatous disease.
- Neoplastic infiltration.
- Anatomic defects causing obstruction and requiring surgical intervention.
- Multiple recurrent episodes of acute bacterial tonsillitis.
- Chronic oropharyngitis with or without pharyngitis or unexplained or recurrent sinusitis.
- Recurrent oropharyngitis with recurrent adenotonsillar hypertrophy.

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

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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

Exudative pharyngitis

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

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 40 mg/Kg/day divided BID X 10 days is acceptable and tastes better in liquid form, but broader spectrum than needed
- Penicillin allergy
  - Past urticaria/anaphylaxis-
    - Erythromycin 40 mg/kg/day, divided BID- 4xDay X 10 days (possible alternatives: Azithromycin X 5 days, clindamycin X 10 days)
  - NOT urticaria/anaphylaxis - Cephalexin possible

References:

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**Miscellaneous Pediatric Prescribing Information**

**Miscellaneous**

- To instill ear drops:
  - Children < 3 years of age: pull pinna down and back
  - Children > 3 years of age: pull pinna up and back
- Oral medication:
  - Should never use teaspoon or tablespoons
  - Should use syringes, nipples or droppers
- Suppositories
  - Place child in side lying position
  - Lubricate suppository with vaseline or K-Y jelly like products

**Miscellaneous**

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

- **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

### 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

### Miscellaneous Pediatric Approvals
**Mometasone and Formoterol**

- Mometasone/formoterol inhaler (Dulera)
- ICS/LABA
- New box warning
  - Short term therapy with LABA if possible
  - Step down when able
- Dosage:
  - 12 years of age and older
  - 100/5 and 200/5: 2 inhalations two times daily

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**Triamcinolone nasal**

- Triamcinolone nasal
  - 2-5 years: 1 spray into each nostril once daily
  - 6-11 years: 1-2 sprays into each nostril once daily
  - > 12 years: 1-2 sprays into each nostril once daily
- Now available OTC

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**Azelastine hydrochloride and fluticasone propionate**

- Brand name: Dymista
- Indication:
  - Seasonal allergic rhinitis in patients 12 years of age and older
- Class:
  - Antihistamine and corticosteroid
- Pharmacology:
  - Azelastine HCl is an antihistamine that antagonizes H1-receptor activity by interfering with the inflammatory response to the allergens
  - Fluticasone propionate is a corticosteroid with anti-inflammatory activity

Azelastine hydrochloride and fluticasone propionate

- Dosage:
  - 137 mcg of azelastine hydrochloride
  - 50 mcg of fluticasone propionate
  - 1 spray into each nostril; two times daily
- Adverse reactions:
  - Somnolence
    - Avoid concurrent use of alcohol due to risk of somnolence
  - Epistaxis
  - Glaucoma and cataracts
  - Growth velocity in children


Schenkel, E. et. al

- 98 patients randomized to either placebo or mometasone furoate aqueous nasal spray
- Ages: 3 - 9 years
- After 1 year, there was no suppression of height in the children using the nasal corticosteroid when compared with the child using placebo

Pediatrics Vol 105 No. 2 February 2000, p. 22

Another Approval

- Adapalene and benzoyl peroxide Gel (Epiduo)
  - 0.1%/2.5%
- Indications:
  - Acne
  - Approved as young as 9 years of age
January 2013 Approval

- Methylphenidate (Quillivant XR)
- Liquid methylphenidate
- Long-acting once daily which can last up to 14 hours
- 5mg/mL suspension
- Starting dose: 20 mg in am

Rosuvastatin

- Rosuvastatin (Crestor) Approved to treat elevated LDL in children age 10 – 17 years of age
- Added to additional options
  - Atorvastatin (Lipitor)
  - Metformin

Almotriptan

- Almotriptan (Axert): Approved for treatment of migraines in adolescents (age 12 – 17)
Rizatriptan
- Maxalt and Maxalt MLT
- Approved for acute treatment of migraine in children 6-17 years of age

Telmisartan
- Telmisartan (Micardis): Approved for children age 6 – 16 years of age to treat hypertension

Colesevelam
- Powdered formulation
  - Colesevelam (Welchol)
  - Indicated for boys and postmenarchal girls age 10 – 17 years with familial hypercholesterolemia
  - May be used in this age in combination with a statin also
Auto-injector epinephrine

- **Epinephrine (Auvi-Q)**
  - Approved down to 15 kg
  - 15-30 kg
    - 0.15 mg SC/IM x 1; may repeat x 1
  - > 30 kg
    - 0.3 mg SC/IM x 1; may repeat x 1

Additional Updates

- **Loratadine (Claritin) syrup**:
  - Patients ages 2 to 5 years require a lower dose (5 milligrams) compared to a 10-milligram dose in older children and adolescents.

- **Fentanyl transdermal (Duragesic transdermal patch)**
  - Used to manage chronic pain.
  - It is now only to be used in patients older than 2 years who have been on opioids and are opioid tolerant

- **Fluvoxamine maleate (Luvox) tablets**
  - Indications: obsessive-compulsive disorder
  - The dose of the drug may need to be increased to the recommended adult dose in adolescents, but girls ages 8 to 11 years may need lower than the recommended dose

Additional Updates

- **Gabapentin (Neurontin) capsules, tablets, and oral solution**.
  - Used as adjunctive therapy in the treatment of partial seizures in pediatric patients ages 3 to 12 years
  - Neuropsychiatric adverse events were identified in 3- to 12-year-olds

- **Famotidine (Pepcid) tablets, injection, and oral suspension**.
  - Used to treat gastroesophageal reflux disease.
  - Patients up to 3 months of age require a lower dose because their ability to get rid of the drug is less than that of older children and adults
Levothyroxine

- Ideally, take 1 hour before first meal of day
- Empty stomach
- Bedtime dosage is also okay: 4 hours after last meal
- Key: consistency


Azithromycin

- Small increase in cardiovascular death, and in the risk of death from any cause, in patients treated with a 5-day course of azithromycin compared to persons treated with amoxicillin, ciprofloxacin, or no drug.
- FDA is reviewing the results from this study and will communicate any new information on azithromycin and this study or the potential risk of QT interval prolongation after the agency has completed its review

http://www.fda.gov/drugs/drugsafety/ucm341822.htm accessed 07-01-2014

New Warnings

- Recommended that dexmethylphenidate (Focalin) have additional warnings added to package insert
  - Suicidal ideations
  - Angioedema
  - Anaphylaxis risk
Ondansetron

- High dose ondansetron (Zofran) pulled from market
- 32 mg dose; intravenous dosage
- Increased risk of QT prolongation, increasing risk for torsades de pointes

Thank You!
I Appreciate Your Attention!

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