Problem Based Learning: Balancing Safety and Efficacy of Asthma Therapy

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LEARNING OBJECTIVES

1) Identify knowledge gaps related to ICS dosing and side effect recognition and treatment.

2) Identify key clinical decisions that contributed to the development of a rare systemic side effect of ICS in a child with possible asthma.

3) Discuss methods to promote prevention and early recognition of systemic side effects of ICS.
History – ML, 6 Years, 7 Months Old

- Presented to Pediatric Allergist on 11/23/09.
- 3-year history of runny nose, nasal congestion, posterior nasal drainage.
- Cough bouts during colds and occasionally with exercise.
- No recent shortness of breath or wheezing.
- One oral steroid course at about 3 years of age.
- No oral steroids or ER visits in the past year.
• Recurrent sinusitis, otitis media and two sets of tympanostomy tubes, osteomyelitis, and gastroenteritis.

• RSV at 18 months, not hospitalized, received a short (~1 month) course of nebulized Pulmicort and albuterol p.r.n., but not needed in last 3 years.

• Smoke free environment, no indoor pets.

• Family history was positive for allergy/asthma in Mother.

• ROS was otherwise negative.
CURRENT MEDICATIONS (can’t tell if they helped):

- Zyrtec® 10 mg qd
- Singulair® 5 mg qd.
- Veramyst® – 2 sprays qd, started 1/09.
- Albuterol inhaler p.r.n.
- Multivitamin daily.
Physical Examination

- HR 118, RR 20, *Ht 43.5 in (5th %ile), Wt 41lbs (10th %ile).*
- Well-developed and well-nourished.
- Allergic shiners, pale, edematous nasal turbinates, watery nasal discharge, and lymphoid hyperplasia of the posterior pharyngeal wall.
- Remainder of exam normal.
Allergy Skin Testing/Other

- Puncture skin tests positive to tree and grass pollen, mold and house dust mite.
- Chest Radiograph – not done.
# Spirometry Report

**Puritan-Bennett Renaissance II**

**S/N:** G060701489  
**Version:** 1.1.11

**ALLERGY AN**  
**ASTHMA CLINIC, P.A.**  
**Session Date:** 23NOV2009  
**Session Time:** 02:12PM  
**Last Cal Check:** 23NOV2009

**BEST FVC/FVL REPORT**

- **Height:** 44"  
- **Physician:**  
- **Sensor Code:** 442087  
- **Temperature:** 70F  
- **Barometric Press:** 763mmHg

<table>
<thead>
<tr>
<th>Measurement</th>
<th>O2</th>
<th>BEST</th>
<th>Trial</th>
<th>%Pred</th>
<th>Pred</th>
<th>LLN</th>
<th>O2</th>
<th>BEST</th>
<th>Trial</th>
<th>%Pred</th>
<th>%Chg</th>
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<td>F</td>
<td>0.81</td>
<td>2</td>
<td>&lt;</td>
<td>65</td>
<td></td>
<td>F</td>
<td>0.77</td>
<td>1</td>
<td>&lt;</td>
<td>62</td>
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<tr>
<td>FEV1 (L)</td>
<td>F</td>
<td>0.64</td>
<td>6</td>
<td>&lt;</td>
<td>55</td>
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<td>F</td>
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<td>&lt;</td>
<td>64</td>
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<td>FEV1%</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
<td>85</td>
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<td>93</td>
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<tr>
<td>FEF25-75 (L/S)</td>
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<td>49</td>
<td></td>
<td>1.43</td>
<td></td>
<td>1.10</td>
<td></td>
<td>1</td>
<td>77</td>
<td>54</td>
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<td>PEF (L/M)</td>
<td>58.1</td>
<td>6</td>
<td>35</td>
<td></td>
<td>161.6</td>
<td></td>
<td>83.4</td>
<td>1</td>
<td>51</td>
<td>43</td>
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<td>FIVC (L)</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>1.24</td>
<td></td>
<td></td>
<td>0.58</td>
<td>1</td>
<td>47</td>
<td>***</td>
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**Report Summary:**

- **Pre Med:** Tests 7  
  Acceptable 0  
  Reproducible 5  
  FVC VAR: 27ML  
  FEV1 VAR: 10ML

- **Post Med:** Tests 4  
  Acceptable 0  
  Reproducible 2  
  FVC VAR: 87ML  
  FEV1 VAR: 92ML

**NONE Interpretation:**

- **PREMED - Undetermined**  
- **POSTMED - No Sig. Improv. in FVC FEV1**

**Comment:**
Spirometry

Pre PF: 130
Post PF: 110

Bronchodilator Used: 4 Puffs Xopenex

Effort/Technique: Good / Fair

Initials: CLR

Legend:
- Pre
- Post
- Pred
Diagnoses by the Allergist

- Allergic rhinitis.
- Asthma (cough-variant).
- Cough.
- Recurrent sinusitis.
Recommendations and Dosages

- Nasonex® - 2 sprays in each nostril qd.
- Flovent® 110 mcg 2 puffs bid with Aerochamber.
- Zyrtec® 10 mg qd.
- Singulair® 5 mg qhs.
- Ventolin® HFA 2-4 puffs q4-6 hours p.r.n.
- Asthma action plan using symptoms.
- Follow-up visit in 6 weeks.

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Followup

Next Office Visit (1/14/10, age 6 years, 9 months, month #2)

• No interval asthma symptoms or albuterol use.
• Medication compliance good.
• Physical examination unchanged.
• ACT score 23.
• FVC 60%, FEV1 63%, FEF25-75 95%, PEF 67% predicted, interpreted as poor technique.
• Continue medications.
• Return visit 6 months.
Next Office Visit (8/3/10, age 7 years, 4 months, **month #9**).

- No interval asthma symptoms or albuterol use.
- Physical examination unchanged.
- FVC 74%, FEV1 75%, FEF25-75 97%, PEF 75% predicted, interpreted as improved effort and mild obstruction.
Outcomes Of Stepping Down Asthma Medications In A Guideline-Based Pediatric Asthma Management Program (Mayo Clinic)

- Retrospective study of 5-18 year-old children (n=477) in an integrated primary care practice.
- Only 34% of 264 who were eligible* were stepped-down.
- Step-down was successful* 80% of the time.

* Criteria based on NAEPP-3 guideline definition of control (≥ 3 months)

Ann Allergy Asthma Immunol 110 (2013) 354e358
Office Visit (8/3/10), continued.

- Recommendation made to continue medications.
- Return visit 6 months.
Followup

Next Office Visit (2/21/11, age 7 years, 10 months, month #15).

- No interval asthma symptoms (except slight cough today) or albuterol use and no nasal symptoms.
- Mother worried about weight gain and easy bruising of skin.
- Physical examination unchanged. **Ht 45.5 in (3rd %ile compared to 5th %ile on 11/23/09), Wt 52 lbs. (slightly >25th %ile compared to 10th %ile on 11/23/09).**
- ACT score 25.
- PFT (14 total attempts): FVC 66%, FEV1 66%, FEF25-75 99%, PEF 58% predicted, interpreted as poor technique.
Height/weight Plot Changes Not Viewed as Significant
Followup

Office Visit (2/21/11, continued).

• Considering Mom’s concerns and ML’s improvement, “it was time to wean the Flovent® anyway”.

• Continue medications, except decrease Flovent® 110 mcg to 2 puffs qhs after the cough resolves.

• Rinsing, gargling, spitting and brushing after use appeared for the first time in the asthma action plan.

• Return visit 6 months.

BUT, SHE NEVER MADE IT TO THAT FOLLOW-UP VISIT!
What Can We Do About This?

• Raise awareness
• Carefully and thoughtfully balance efficacy and safety
INTRODUCING A NON-PROFIT!

*Macci’s TEAMS*

T = Teaching
E = Everyone
A = About
M = Medication
S = Safety

www.macisteamsonline.org
BALANCING SAFETY AND EFFICACY OF ICS in Children


- Make safety a priority, especially if pre-pubertal, mild disease, also using INCS, high adherence.
- Choose ICS with the best safety profile, low systemic activity and at least one negative robust growth study (per FDA guidance)
- Use spacer/chamber and rinse mouth
- Use lowest effective dose
- Optimize steroid-sparing strategies
- Be proactive and have a safety discussion with parent.
- Monitor:
  — Growth in all children
  — Other SSEs at high doses
## Do All ICS Have The Same Systemic Activity? Key One-Year Growth Studies

<table>
<thead>
<tr>
<th>ICS MOLECULE</th>
<th>ICS BRAND</th>
<th>GROWTH PRIMARY OUTCOME?</th>
<th>ROBUST*?</th>
<th>EFFECT ON GROWTH?</th>
<th>APPROVED IN CHILDREN?</th>
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<tbody>
<tr>
<td>BDP CFC¹</td>
<td>Beclovent</td>
<td>Yes</td>
<td>Yes</td>
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<td>BDP HFA²</td>
<td>Qvar</td>
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<td>No</td>
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<td>BUD³</td>
<td>Pulmicort</td>
<td>No</td>
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<td>TAA⁴</td>
<td>Azmacort</td>
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<td>MF⁵</td>
<td>Asmanex</td>
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<td>Flovent</td>
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<td>CIC⁷</td>
<td>Alvesco</td>
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<td>FLUN⁸</td>
<td>Aerospan</td>
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3. CAMP study, NEJM. 2000;343:1054-1063

* Designed per FDA Guidance
# Summary of ICS PK/PD Features

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<tr>
<th></th>
<th>BDP/17-BMP</th>
<th>BUD</th>
<th>FP</th>
<th>MF</th>
<th>CIC/des-CIC</th>
<th>Flunisolide HFA</th>
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<td>Oral bioavailability (%)</td>
<td>High &lt;1/26</td>
<td>Moderate 11</td>
<td>Low &lt;1</td>
<td>?</td>
<td>Low &lt;1/&lt;1</td>
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<td>Clearance (L/h)</td>
<td>High 120 (BMP)</td>
<td>High 84</td>
<td>High 67–90</td>
<td>?</td>
<td>Very high 228 (des-CIC)</td>
<td>High 83-167</td>
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<td>Free fraction (not protein bound) (%)</td>
<td>Moderate 13 (BDP)</td>
<td>Moderate 12</td>
<td>Moderate 10</td>
<td>Low &lt;1 SD Mod 11 MD</td>
<td>Low 1/1</td>
<td>20%</td>
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<td>Receptor binding affinity</td>
<td>Low/High 53/1345</td>
<td>Moderate 935</td>
<td>High 1800</td>
<td>High 2200</td>
<td>Low/High 12/1200</td>
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<td>Formulation</td>
<td>Solution</td>
<td>Suspension</td>
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<td>DPI</td>
<td>Solution</td>
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<tr>
<td>Pulmonary deposition (%)</td>
<td>High 53 (BDP)</td>
<td>Moderate 28</td>
<td>Moderate 16</td>
<td>Moderate 14</td>
<td>High 52 (des-CIC)</td>
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<td>Lipid conjugation</td>
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Save the Date

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