

### Viewing Time

The program will take up to one hour to complete.

### Target Audience

This program is designed for primary care physicians.

Other health care professionals working with patients and their families may also find this program of interest.

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### Faculty Disclosure

**Sam Reid, MD** has disclosed no actual or potential conflict of interest in relation to this educational activity.

During this educational activity **Dr. Reid** will not be discussing the use of any commercial or investigational product not approved for any purpose by the FDA.

### Pediatric Emergency Medicine: Best Articles of 2008

**Sam Reid, MD**

Pediatric Emergency Medicine, Children's  
Hospitals and Clinics of Minnesota

### Pediatric Emergency Medicine: Best Articles of 2008

*A lecture about recent important studies  
published about acute illness and injury  
in children.*

## Program Objectives

*Upon completion of this program, participants should be able to:*

- Identify important recent contributions to the literature relevant to acute illness and injury in children
- Discuss the methodological strengths and weaknesses of the selected articles
- Incorporate, or make an informed decision not to incorporate, the findings of the selected articles into practice

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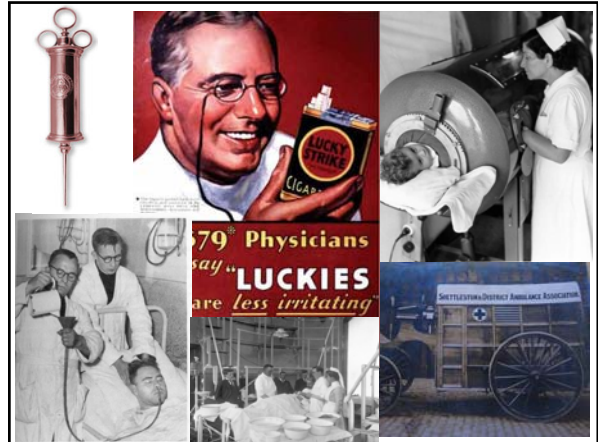
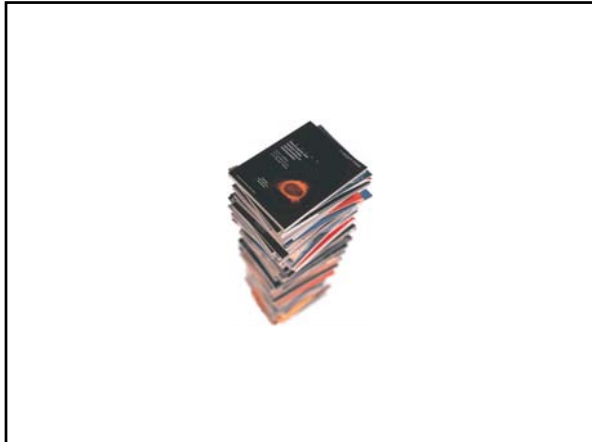
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To receive CME credit you must view the entire program and complete the evaluation form at the end.

## Acute Illness and Injury in Pediatric Patients: Best Articles of 2008

Samuel Reid, MD  
Pediatric Emergency Medicine  
Children's Hospitals and Clinics of Minnesota





### Objectives

- Identify important recent contributions to the literature relevant to acute illness and injury in children
- Discuss the methodological strengths and weaknesses of the selected articles
- Incorporate, or make an informed decision not to incorporate, the findings of the selected articles into practice

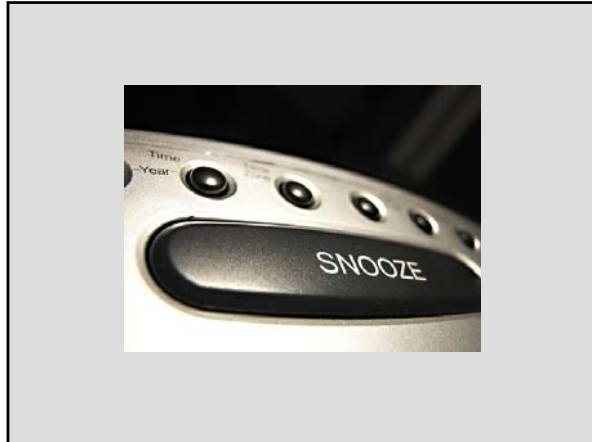
### Conflict of Interest

### Format

- Selection criteria
  - Original research
  - Published in 2008-9
  - Methodology high on EBM food chain
  - Potential to change practice in a way that matters to patients
  - Potential to change practice in near term
- "Executive" summaries
- Discussion

### Prerequisites

- Prospective design
- Validated instruments
- For comparison studies...
  - Randomized
  - Blinded observers when necessary and possible
  - Sample-size large enough to adequately power study to detect significant difference in primary outcome measure between study groups

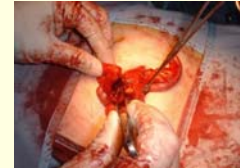


## Study # 1

Goldman RD, et al.

### Prospective Validation of the Pediatric Appendicitis Score

*J Pediatr* 2008;153:278-282



## Methods

### Design

- Prospective cohort

### Subjects

- 849 children, age 1-17 years
- Chief complaint of abdominal pain < 7 days

### Exclusions

- Appendicitis diagnosed by CT or US prior to ED presentation
- History of appendectomy

## Methods

### Intervention

Pediatric Appendicitis Score (PAS)

- Samuel M. *J Pediatr Surg* 2002;37:877
- Retrospective validation

Component	Points
Pain migration	1
Anorexia	1
Nausea/vomiting	1
Fever > 38° C.	1
Percussion/cough/hopping tenderness	2
RLQ tenderness	2
WBC > 10,000	1
PMN > 7,500	1

## Methods

### Intervention

- Data collection form
- Pathology reports reviewed
- Phone F/U 5-7 days

### Outcome measure

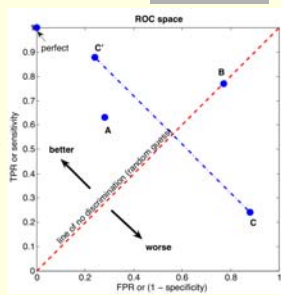
- Sensitivity and specificity of PAS for diagnosis of appendicitis

## Results

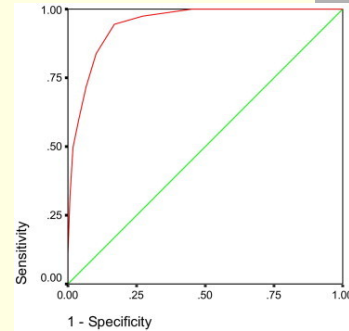
- 123/849 patients (14.5%) had appendicitis
- Mean PAS score
  - Appendicitis → 7
  - No appendicitis → 1.9
- If threshold for making diagnosis of **appendicitis** had been  $\geq 7$ , twenty-nine patients (4%) would have had unnecessary appendectomy.
- If threshold for making diagnosis of **no appendicitis** had been  $\leq 2$ , three patients (2.4%) with appendicitis would have been discharged from ED.
- Area under ROC curve = 0.95

## ROC Curves

- Plot of the sensitivity vs. (1 - specificity) for a binary classification system as its discrimination threshold is varied
- A point in the upper left corner (coordinate (0,1)) of the ROC space results in an area under ROC curve = 1.0
  - 100% sensitivity (all true positives are found)
  - 100% specificity (no false positives are found)



## ROC Curve: PAS Score



## Conclusion

- PAS is useful because:
  - A score  $\leq 2$  has a high validity for ruling out appendicitis.
  - A score  $\geq 7$  has a high validity for predicting the presence of appendicitis.
- Children with a score of 3-6 should undergo further investigation:
  - Observation
  - CT
  - US

## Context

- Brenner DJ, Hall EJ. **Computed tomography: An increasing source of radiation exposure.** *NEJM* 2008;357:2277-2284
  - There is direct evidence from epidemiologic studies that the organ doses [of radiation] corresponding to a common CT study result in an increased risk of cancer death. The evidence is reasonably convincing for adults and very convincing for children.

CT study	Newborn	10 years	20 years
Head	0.08%	0.03%	0.01%
Abdomen	0.14%	0.08%	0.06%

## Comments

- Strengths
  - Previous studies
    - Adults
    - Retrospective
    - Small samples
    - Combined clinical/radiographic modalities
    - Lack of validation on new cohort
  - No patients lost to follow-up
- Weaknesses
  - Convenience sample  $\rightarrow$  potential bias
  - Inter-rater variability

## Study # 2

Roslund G, et al.  
**The Role of Oral Ondansetron in Children With Vomiting as a Result of Acute Gastritis/Gastroenteritis Who Have Failed Oral Rehydration Therapy: A Randomized Controlled Trial**  
*Ann Emerg Med* 2008;52:22-29



## Methods

### Design

- Randomized, double-blind, placebo-controlled trial

### Subjects

- 106 children, age 1-10 years
- Clinical diagnosis of acute gastritis/ gastroenteritis
- Mild-moderate dehydration
  - Clinical scale
- Failed trial of oral rehydration in ED
  - Pedialyte popsicle or Pedialyte 5 ml Q3 minutes
  - Goal: 40 ml/kg in 2 hours

## Methods

### Exclusions

- Antiemetic during the 6 hours prior to presentation
- Chronic illness
- Severe dehydration/shock
- Ondansetron allergy

## Methods

### Intervention

- Ondansetron ODT, or

Weight	Dose
< 15 kg	2 mg
15-30 kg	4 mg
> 30 kg	6 mg

- Placebo
- 30 minutes later, trial of oral rehydration
  - Successful → discharged with phone F/U
  - Unsuccessful → IV rehydration

## Methods

### Primary outcome measure

- Proportion of children in each group requiring IV rehydration

### Secondary outcome measures

- Proportion of children admitted
- Number of episodes of vomiting and diarrhea in ED and after discharge
- Return ED visit for same illness within 72 hours

## Results

- Study groups statistically similar at baseline in terms of...
  - Age
  - Gender
  - Median days of vomiting
  - Median episodes of vomiting
  - Median days of diarrhea
  - Median episodes of diarrhea
- Patients in ondansetron group were more dehydrated than in placebo group

## Results

Outcome	Ondansetron n = 51	Placebo n = 55	Significant difference
Received IV rehydration	21.6%	54.5%	Yes
Admitted	5.9%	12.7%	Yes
Median number of vomiting episodes	0.71	0.5	No
Mean number of diarrhea stools	1.76	0.45	No
Bounce-back	2	1	No

## Conclusion

In children with acute gastritis/gastroenteritis and mild-to-moderate dehydration who failed initial oral rehydration therapy, the proportion of children who received intravenous rehydration was smaller in those who received ondansetron.

## Context

- “The small number of included trials provided some, albeit weak and unreliable, evidence which appeared to favor the use of ondansetron over placebo to reduce the number of episodes of vomiting due to gastroenteritis in children.”
  - Alhashimi D, et al. Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No. CD005506.

## Comments

- General
  - Half of patients receiving placebo tolerated second attempt at oral rehydration
- Strengths
  - 91% of patients contacted for phone follow-up
- Weaknesses
  - Convenience sample → selection bias
  - Unvalidated dehydration scale
    - Gorelick MH, et al. Validity and reliability of clinical signs in the diagnosis of dehydration in children. *Pediatrics* 1997;99:e6

## Study # 3

Martinón-Torres F, et al.

### **Nasal Continuous Positive Airway Pressure With Heliox Air Oxygen in Infants With Acute Bronchiolitis: A Crossover Study**

*Pediatrics* 2008;121:e1189-e1194



## Background

- Nasal CPAP
  - ↓Inspiratory muscle workload
  - Prevents/relieves atelectasis
  - Prevents airway collapse
  - Promotes gas distribution within obstructed airways
- Heliox
  - Reduces resistance to gas flow, thus reduces respiratory effort
  - Improves alveolar ventilation and CO<sub>2</sub> elimination

## Methods

### Design

- Prospective cross-over trial

### Subjects

- 12 children, age 1-24 months
- Severe RSV bronchiolitis
  - Modified Woods Clinical Asthma Score ≥ 5
- O<sub>2</sub> sat < 92% or tcPCO<sub>2</sub> > 50 mm Hg despite
  - Supportive therapy
  - Nebulized epinephrine
  - Heliox 10-15 L/min with NRB mask ≥ 1 hour

### Exclusions

- Chronic lung disease

## Methods

### Intervention

- Nasal CPAP with heliox for 30 minutes, then with air/oxygen for 30 minutes; *or*
- Vice versa
- Measurements at baseline, 30 and 60 minutes
  - Modified Wood's Clinical Asthma Score
  - SaO2
  - tcPCO2
  - RR

## Modified Wood's Clinical Asthma Score

	0	0.5	1	2
SaO2	≥ 95% (RA)	< 95% and ≥ 90% (RA)	≥ 90% (O2)	< 90% (O2)
Inspiratory breath sounds	Normal	Slightly unequal	Markedly unequal	Decreased/absent
Expiratory wheezing	None	Mild	Moderate	Marked
Accessory muscles	None	Mild	Moderate	Maximal
Cerebral function	Normal	Agitated when disturbed	Depressed/agitated	Markedly depressed/coma

## Methods

### Outcome measures

- Change in Modified Wood's Clinical Asthma Score
- Change in tcPCO2

## Results

Measurement	Baseline	Air-Oxygen	Heliox	Significant difference
M-WCAS	7.7	6.6	5.6	Yes
tcCO2 (mm Hg)	61.6	56.2	51.9	Yes
SaO2 (%) FIO2 = 0.35	88.6	95.5	96.5	No

## Conclusion

Nasal CPAP improves the clinical score and the CO2 elimination of infants with refractory bronchiolitis. These positive effects are significantly enhanced when heliox is used instead of air-oxygen.

## Comments

- General
  - Literature supports the use of both heliox and nasal CPAP in bronchiolitis.
  - No previous data examines the modalities together.
  - Small study but adequately powered to detect clinically significant changes.
- Weakness
  - Change in infant cry with heliox and different equipment noises made blinding not feasible → potential bias in assigning M-WCAS

## Most Interesting Meta-Analysis: 2008

Zhang L, et al. **Nebulized hypertonic saline solution for acute bronchiolitis in infants.** Cochrane Database of Systematic Reviews 2008(4).

- 4 randomized controlled trials, 254 infants
- Patients treated with nebulized 3% saline had...
  - Significantly shorter mean LOS
    - -0.94 days (95% CI: -1.48 to -0.40)
  - Significantly lower post-neb clinical severity scores on first 3 treatment days
- Current evidence suggests that nebulized 3% saline may significantly reduce hospital LOS and improve clinical severity scores in infants with bronchiolitis.

## Study #4

Lennon DR, et al.

### **Once-Daily Amoxicillin Versus Twice-Daily Penicillin V in Group A $\beta$ -Haemolytic Streptococcal Pharyngitis**

*Arch Dis Child* 2008;93:474-478



## Methods

### Design

- Randomized, non-inferiority trial

### Subjects

- 353 children, aged 5-12 years
- Signs and symptoms of acute pharyngitis/ tonsillitis
  - Sore throat *and* at least one of the following:
    - Fever  $\geq 38^{\circ}$  C.
    - HA
    - Nausea or abdominal pain
    - Difficulty swallowing
    - Inflamed throat
    - Tender cervical adenopathy
- Throat culture positive for GABHS

## Non-inferiority trials

- Non-inferiority trials are intended to show that the effect of a new treatment is not worse than that of an active control by more than a specified margin.
- In conditions for which proven effective treatment exists, placebo-controlled trials are often unethical. In these situations active-controlled trials are generally appropriate. The non-inferiority trial is appropriate for evaluation of the efficacy of an experimental treatment versus an active control when it is hypothesized that the experimental treatment may not be superior to a proven effective treatment, but is clinically and statistically not inferior in effectiveness.
- Smaller N required

## Methods

### Design

- Randomized, non-inferiority trial

### Subjects

- 353 children, aged 5-12 years
- Signs and symptoms of acute pharyngitis/ tonsillitis
  - Sore throat *and* at least one of the following:
    - Fever  $\geq 38^{\circ}$  C.
    - HA
    - Nausea or abdominal pain
    - Difficulty swallowing
    - Inflamed throat
    - Tender cervical adenopathy
- Throat culture positive for GABHS

## Methods

### Intervention

- Amoxicillin once daily x 10 days, *or*
  - $> 30$  kg: 1500 mg
  - $\leq 30$  kg: 750 mg
- PCN VK twice daily x 10 days
  - $> 20$  kg: 500 mg/dose
  - $\leq 20$  kg: 250 mg/dose
- Compliance
  - Supervised medication administration on school days
  - Drug diaries and return of medication bottles to assess weekend compliance
- F/U throat cultures and symptom evaluation on day 3-6, day 12-16, day 26-36
  - Positive cultures serotyped to detect treatment failures, relapses and new acquisitions

## Methods

### Primary outcome measure

- Bacteriological failure (persistence or relapse) on day 12-16
- Non-inferiority defined as 95% confidence that the eradication rate of amoxicillin was not more than 10% less than that of PCN VK

### Secondary outcome measure

- Symptom resolution

## Results

- Study groups statistically similar at baseline in terms of...
  - Age
  - Gender
  - Weight
  - Ethnicity
  - Temperature
  - Signs and symptoms

## Results: Bacteriological response

	Amoxicillin QD n = 177	Penicillin BID n = 176	Clinically significant difference
<b>Day 3-6</b>			
Persistence	9 (5.8%)	10 (6.2%)	No
<b>Day 12-16</b>			
Persistence	8 (5.1%)	7 (4.4%)	No
Relapse	12 (7.6%)	12 (7.6%)	No
<b>Day 26-36</b>			
Persistence	3 (1.9%)	3 (1.9%)	No
Relapse	14 (8.8%)	15 (9.4%)	No

## Results

- No difference in the degree of change in any symptom between the amoxicillin and PCN groups
- One child in the amoxicillin group with possible rheumatic fever at 1 week into treatment
  - Did not fulfill Jones criteria

## Conclusion

Once-daily amoxicillin is not inferior to twice-daily penicillin for the treatment and eradication of GABHS in children with pharyngitis.

## Comments

- Shorter antibiotic courses?
  - Broader spectrum agents
  - More expensive
- Strengths
  - Compliance

## Study # 5

Luck RP, et al.

### Cosmetic Outcomes of Absorbable Versus Nonabsorbable Sutures in Pediatric Facial Lacerations

*Pediatr Emerg Care* 2008;24:137-142



## Methods

### Design

- Prospective, randomized trial

### Subjects

- Patients aged 1-18 years
- Linear facial laceration, 1- 5 cm in length
- One or two-layered repair

### Exclusions

- Mammalian bite
- More than minimally contaminated
- > 8 hours old
- Amenable to closure with tissue adhesive

## Methods

### Intervention

- Surface repair with fast-absorbing surgical gut or nylon
- ED follow-up in 5-7 days
  - Wound infection and dehiscence noted
  - All visualized suture material removed
- ED follow-up in 3 months
  - Photographs reviewed by 3 blinded ED physicians
    - 100 mm VAS (worst scar = 0 to best scar = 100)
  - Parental questionnaire
    - 100 mm VAS
    - Convenience
    - Complications
    - Willingness to use same suture material in future

## Methods

### Primary outcome measure

- Physician observers' mean VAS
- Difference  $\geq 15$  mm defined as clinically significant

### Secondary outcome measures

- Infection rate
- Dehiscence rate
- Keloid rate
- Parental satisfaction

## Results

- 88 patients enrolled, 47 completed follow-up
- Study groups statistically similar at baseline in terms of...
  - Age
  - Gender
  - Ethnicity
  - Wound length
  - Number of layered repairs
  - Number of sutures placed

## Results

	Nylon n = 24	Gut n = 23	Clinically significant difference
Physician mean VAS	93.7 mm	92.3 mm	No
Parental mean VAS	91.2 mm	86.3 mm	No

- No patients developed wound infection
- 1 patient with gut closure developed wound dehiscence
- 1 patient with nylon closure developed keloid

## Results: Parental survey

	Nylon n = 24	Gut n = 23	Statistically significant difference
Felt material used was convenient	18 (75%)	21 (91%)	No
Prefer to use same material in future	19 (79%)	22 (96%)	No
Perceived complication of any kind	0	3 (13%)*	No

\* Premature unraveling (3), large scar (1)

## Conclusion

The use of fast-absorbing catgut suture is a viable alternative to non-absorbable suture in the repair of facial lacerations in children.

## Comments

- General
  - Wounds repaired by ED attendings
  - Follow-up at 3 months based on FDA standard for evaluating cosmetic outcome of wound repair products
  - Why did they remove absorbable suture material at 5-7 days?
    - Dehiscence
    - Karounis H, et al. *Acad Emerg Med* 2004;11:730-735
- Strengths
  - Large patient drop-out accounted for in sample-size calculation
- Weaknesses
  - Outcome of those lost to follow-up?

## Study #6

Chang AB, et al.

**A 5- versus 3-day course of oral corticosteroids for children with asthma exacerbations who are not hospitalised: a randomised controlled trial.**

*Med J Austral* 2008;189:306-310



## Methods

### Design

- Randomized, double-blind, controlled trial

### Subjects

- Children 2-15 years old
- Acute asthma exacerbation managed as outpatient
- Asthma
  - >2 prior episodes of wheezing and/or dyspnea with a clinical response to albuterol
- Exacerbation
  - Acute deterioration in asthma control requiring more than one dose of albuterol per hour

## Methods

### Exclusions

- Underlying respiratory disease (e.g. bronchiectasis)
- Severe neurodevelopmental abnormality
- Immunodeficiency
- Steroid treatment before presentation
- Severe asthma exacerbation requiring hospitalization

## Methods

### Intervention

- Australasian Triage and Asthma Severity Scales recorded
- Prednisolone 1 mg/kg for 5 days, *or*
- Prednisolone 1 mg/kg for 3 days + placebo for 2 days
- Paediatric Asthma Caregiver's Quality of Life Questionnaire and validated daily diary scores for asthma and cough recorded at baseline and weekly through day 28

## Methods

### Primary Outcome Measure

- Proportion of children symptom-free on day 7 (asthma score < 0.2)

### Secondary Outcome Measures

- Quality of life scores on days 7 and 14
- Asthma scores on days 5, 10, 14
- Unscheduled medical care

## Results

- Study groups statistically similar at baseline in terms of...
  - Age
  - Gender
  - Days unwell
  - Tobacco smoke exposure
  - Asthma Severity Scale
  - Australasian Triage Scale
  - PACQLQ score
  - Inhaled steroid use
  - Regular medication use
  - Number of steroid courses past 12 months

## Results

- No difference between groups
  - Proportion of children symptom-free at 7 days
  - Quality of life and daily asthma scores
  - Hospitalization
  - Adverse events

## Conclusion

A 5-day course of prednisolone confers no advantage over a 3-day course for outpatients with asthma exacerbation.

## Comments

- General
  - Dosing lower than standard U.S. practice
  - Decadron
    - Gordon S, et al. Randomized trial of single-dose intramuscular dexamethasone compared with prednisolone for children with acute asthma. *Pediatr Emerg Care* 2007;23:521-527
- Strengths
  - Sample size calculated to account for adequate power for all outcome measures, not just primary outcome.
  - Data analyzed on both intention-to-treat analysis and per-protocol basis → same results

## Study #7

Panickar J, et al.

### Oral Prednisolone for Preschool Children with Acute Virus-Induced Wheezing.

*N Engl J Med* 2009;360:329-338



## Methods

### Design

- Randomized, double-blind, placebo-controlled trial

### Subjects

- 687 children, age 10-60 months
- Wheezing preceded by signs/symptoms of viral URI

### Exclusions

- Shock
- Evidence of bacterial sepsis
- Known heart or lung disease
- Immunodeficiency
- Immunosuppression
- Varicella exposure or infection

## Methods

### Intervention

- Albuterol
  - 10 puffs with spacer/face mask or,
  - Neb (2.5 mg for age < 3 yrs; 5 mg for age ≥ 3 yrs)
- Preschool Respiratory Assessment Measure (PRAM) score assigned at 0, 4, 12, 24 hours

## Preschool Respiratory Assessment Measure (PRAM score)

	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle contraction	Absent		Present	
Air entry	Normal	Decreased at bases	Decreased throughout	Absent or minimal
Wheezing	Absent	Expiratory	Expiratory and inspiratory	Audible or minimal air movement
O2 sat (RA)	≥ 95%	92-94%	< 92%	

## Methods

### Intervention

- Structured history
  - Details of previous wheezing episodes
- Previous diagnoses
  - Asthma
  - Eczema
  - Hay fever
  - Food allergy
  - Bronchiolitis
- Home treatments for wheezing
- FH of asthma
- Smoke exposure

## Methods

### Intervention

- Prednisolone or placebo
  - ≤ 24 months → 10 mg once daily x 5 days
  - > 24 months → 20 mg once daily x 5 days
  - British Thoracic Society recommendations
- Patients discharged when...
  - Minimal wheezing post-albuterol
  - RA O2 sat > 92%
  - Judgment that child will not require albuterol no more often than Q4 hours
- Symptom diary (daily score, 0-3)

## Methods

### Outcome measures

- Primary
  - Time from enrollment to discharge order
  - Time from enrollment to actual discharge
  - Powered to detect 5 hour difference in LOS
- Secondary
  - PRAM score at 4, 12, 24 hours
  - Total albuterol dose
  - Mean 7-day symptom score
  - Time to "back to normal"
  - Hospital readmission within 1 month

## Results

- No significant difference in baseline characteristics or PRAM score
  - Prednisolone → 4.32
  - Placebo → 4.27

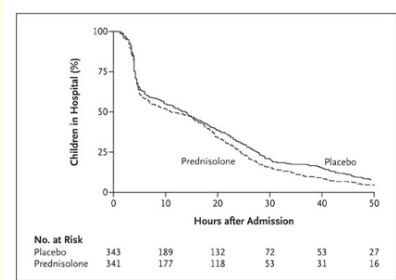
## PRAM

	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle contraction	Absent		Present	
Air entry	Normal	Decreased at bases	Decreased throughout	Absent or minimal
Wheezing	Absent	Expiratory	Expiratory and inspiratory	Audible or minimal air movement
O2 sat (RA)	≥ 95%	92-94%	< 92%	

## Results

	Placebo n = 344	Prednisolone n = 343	Significant?
Median time to D/C order	12 hrs	10.1 hrs	No
Median time to D/C	13.9 hrs	11 hrs	No
Albuterol puffs	66.7	52.8	No
PRAM 4 hrs	2.74	2.48	No
PRAM 12 hrs	2.28	2.49	No
PRAM 24 hrs	1.58	1.52	No
Respiratory symptom score at 7 days	1.10	1.00	No

## Results



## Results: Subgroup at High Risk for Asthma

- High risk for asthma (n = 124)
  - History of > 3 prior episodes of wheezing
  - Parent with asthma
  - Physician diagnosed eczema
- No difference between prednisolone or placebo patients in terms of LOS

## Conclusion

- We found no evidence that a short course of oral steroids significantly shortened the duration of hospitalization or significantly reduced markers of symptom severity as assessed by physicians or parents.
- Our results suggest that oral prednisolone should not be routinely given to preschool children presenting to the hospital with acute, mild-to-moderate virus-induced wheezing.

## Comments

- Editorial
  - "There can no longer be any justification for the administration of prednisolone to preschoolers without atopy who have episodic (viral) wheezing...unless a severe clinical course is anticipated."
  - Beta agonists and possibly, leukotriene receptor antagonists (prophylactic or intermittent)
- Pathophysiology similar to bronchiolitis?
- Strengths
- Weaknesses
  - Discharge criteria largely subjective
  - Parent-assessment of symptom severity unvalidated

## Study # 8

Nurko S, et al.

### **PEG3350 in the Treatment of Childhood Constipation: A Multicenter, Double-Blinded, Placebo-Controlled Trial**

*J Pediatr* 2008;153:254-261



## Methods

### Design

- Randomized, double-blinded, placebo-controlled trial

### Subjects

- Children, 4-16 years-old
- Chronic functional constipation
  - More than 3 month history of < 3 spontaneous BM/wk plus 1 or more of the following
    - Straining
    - Hard stool
    - Sensation of incomplete evacuation
    - Large stools obstructing toilet
    - Painful defecation

## Methods

### Exclusions

- Organic cause of constipation
- Fecal impaction at beginning of treatment
  - Hypogastric mass
  - Hard stool on rectal exam

## Methods

### Intervention

- Laxative-free period of 1 week with symptom diary, then,
- 14 day treatment period with...
  - Placebo or,
  - PEG3350 0.2 mg/kg/day (max 8.5 g) or,
  - PEG3350 0.4 mg/kg/day (max 17 g) or,
  - PEG3350 0.8 mg/kg/day (max 34 g)
- Behavior modification
- Daily stooling/symptom records
- Return visits on day 7 and 14

## Methods

### Primary outcome measure

- Proportion of children who responded to treatment
  - $\geq 3$  BM during second week of treatment

### Secondary outcome measures

- Weekly number of BM
- Fecal incontinence
- Change in scores of...
  - Stool consistency
  - Straining
  - Cramping

## Results

- Study groups statistically similar at baseline in terms of...
  - Age
  - Gender
  - Weight
  - Age at constipation onset
  - Age of toilet training
  - Duration of constipation
  - Previous laxative use
  - # BM/week
  - Fecal incontinence
  - Abdominal pain
  - Stool in rectum

## Results

	Placebo n = 24	PEG3350 0.2 g/kg/d n = 26	PEG3350 0.4 g/kg/d n = 27	PEG3350 0.8 g/kg/d n = 26
Successful treatment	10 (42%)	21 (81%)	20 (74%)	20 (77%)

- Children receiving PEG3350 at all doses had significantly more stools and less straining than those receiving placebo.
- Children receiving PEG3350 at doses  $\geq 0.4$  g/kg/day had significantly better stool consistency.
- Children receiving PEG3350 at 0.8 g/kg/day had a *tendency* toward more abdominal pain and fecal incontinence.

## Conclusion

This study confirms the efficacy of PEG3350 for the short-term treatment of children with functional constipation. We recommend a starting dose of 0.4 g/kg/day.

## Comments

- General
  - Little data guiding laxative use in childhood constipation
  - First randomized-placebo controlled study examining efficacy and dosing of PEG3350 in children
  - Does the 42% response rate in placebo group indicate the efficacy of behavior modification?
- Weakness
  - Patients at tertiary care center  $\rightarrow$  generalizability?

## Study #9

Hsu HE, et al.

### Effect of Pneumococcal Conjugate Vaccine on Pneumococcal Meningitis.

*N Engl J Med* 2009;360:244-256



## Methods

### Design

- Prospective population-based surveillance study: 1998 - 2005

### Subjects

- 1379 cases of pneumococcal meningitis
  - S. pneumoniae* isolated from CSF
  - Clinical diagnosis of meningitis + *S pneumoniae* isolated from blood

## Methods

### Intervention

- Regular communication with clinical labs in each of eight catchment areas
- Periodic audits of laboratory records
- Standardized case-report forms

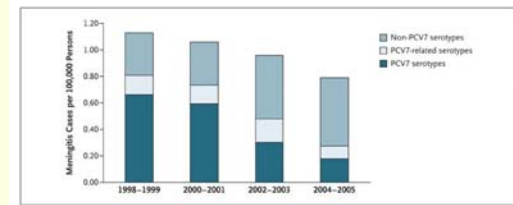
### Outcome measures

- Changes in incidence of pneumococcal meningitis
  - PCV-7 serotypes
  - PCV-7-related serotypes
  - Non-PCV7 serotypes
- Changes in rates of antibiotic nonsusceptibility

## Results: Incidence

- All serotypes
  - Overall rate ↓30.1%
  - For patients < 2 years old, rate ↓64%
- PCV7 serotype disease
  - Overall, ↓73.3%
  - For patients < 2 years old, ↓92.8%
- PCV7-related serotype disease
  - Overall, ↓32.1%
  - For patients < 2 years old, ↓83.5%
- Non-PCV7 serotype disease
  - Overall, ↑60.5%
  - For patients < 2 years old, ↑275%

## Results

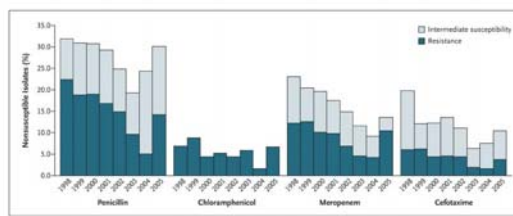


Mean annual incidence of pneumococcal meningitis by serotype group and time period

## Results: Rate of Antibiotic Resistance

- Rate of penicillin resistance decreased 41.1% between 1998-1999 and 2004-2005
- Rate of cefotaxime resistance decreased 60% between 1998-1999 and 2004-2005
- All isolates were sensitive to vancomycin

## Results



Percentage of Pneumococcal Isolates that were Resistant to Various Antibiotics According to Year and Degree of Resistance

## Conclusion

- Rates of pneumococcal meningitis have decreased since PCV7 was introduced.
- Although the overall effect of the vaccine remains substantial, a recent increase in meningitis caused by non-PCV serotypes, including strains resistant to antibiotics, is a concern.

## Comments

- Similar findings as studies of other forms of invasive pneumococcal disease
- Vaccines in development
  - PCV10 would have covered 27.4% of cases in 2004-2005
  - PCV13 would have covered 50.0% of cases in 2004-2005

## Comments and Questions

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