

# Chronic Cough in Children

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FRCP (Edinburgh), AM (M'sia)



# Objectives

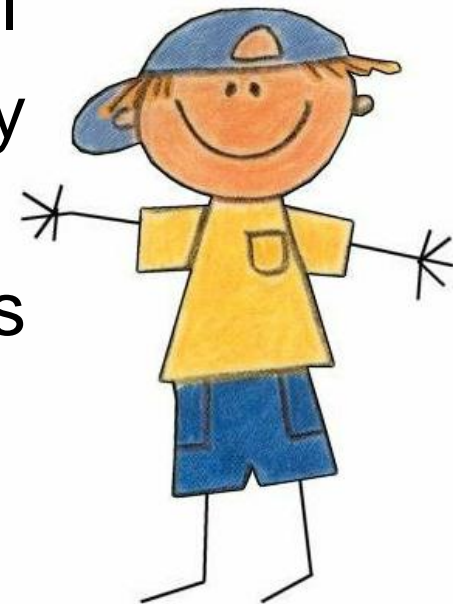
- Define cough in children
- Describe the etiologies of cough in children
- Review the common modalities of treatment for chronic cough in children





# Cough, cough, cough

- **Cough** may be the most frustrating to parents.
- keeps the child up at night
- parents and siblings lose sleep as well
- **cough** is a beneficial protective airway reflex.
- **Coughing** clears excessive secretions to maintain airway patency.





# Defining Cough

- time frame (*ie*, duration of cough)
- quality (*eg*, dry or wet, brassy, or staccato)
- suggested etiology (*ie*, specific and nonspecific)
- Chronic cough in children is defined as a cough of  $> 4$  weeks



# Children and Adult

- maturational differences in airway, respiratory muscle, and chest wall structure, sleep-related characteristics, respiratory reflexes, and respiratory control
- cough sensitivity is instead influenced by airway caliber (*ie*, FEV1) and age

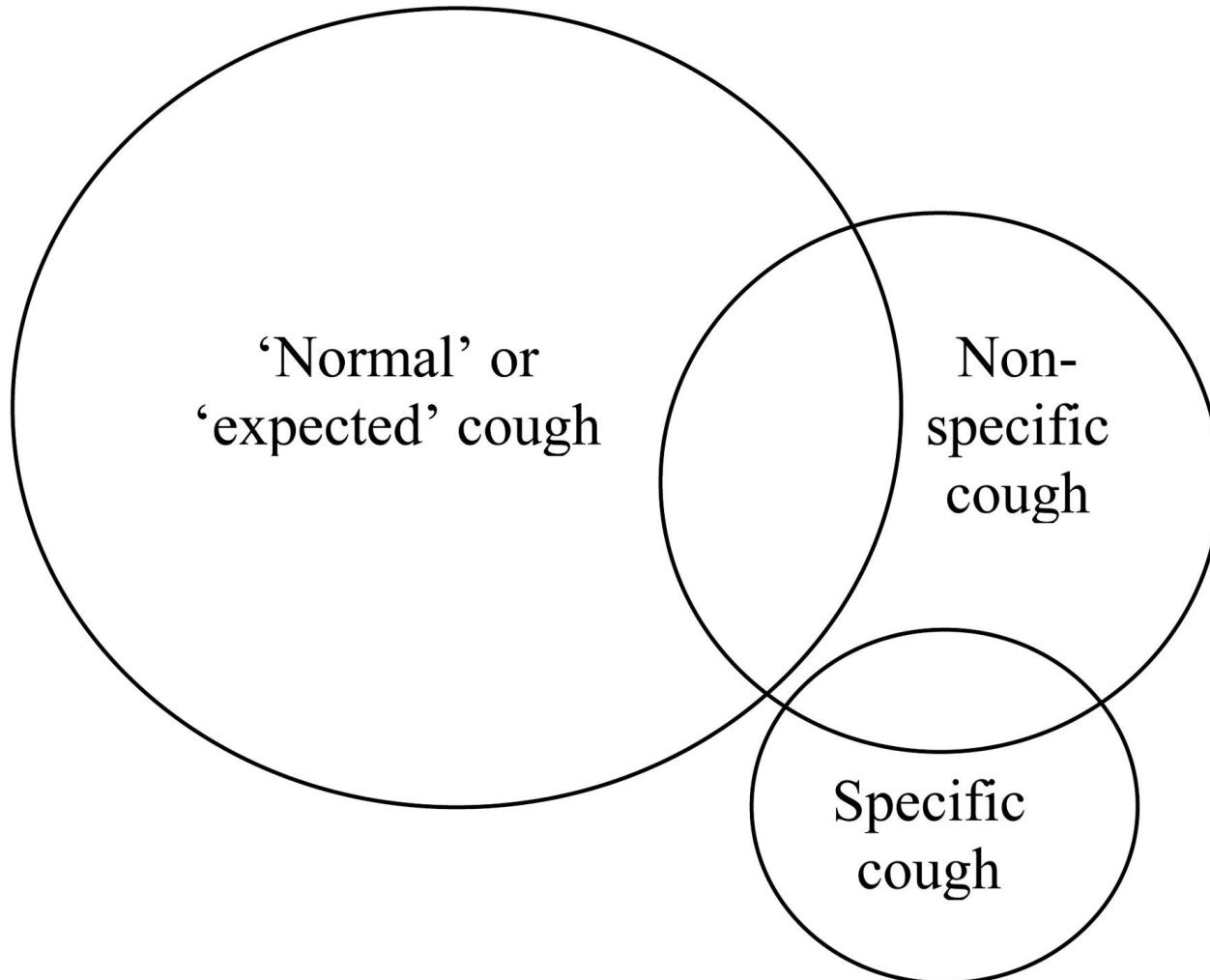


# Children and Adult

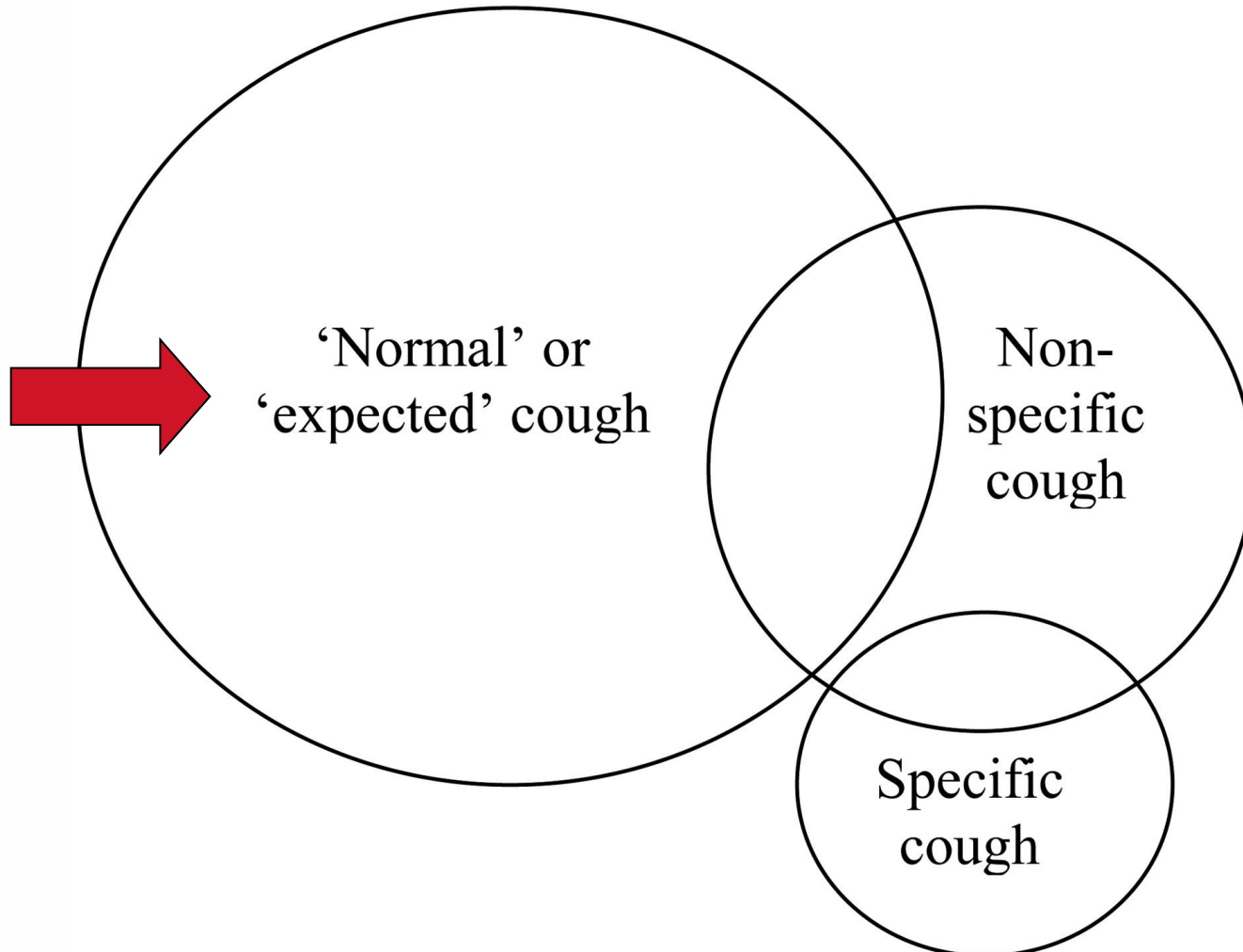
- children aged  $< 5$  years have 3.8 to 5 acute resp. infections per person per year while adults have only 2
- radiation from CXR in children, and high-resolution CT (HRCT) scans of the chest in children carry higher risks



# Classification of types of cough in children



# Classification of types of cough in children



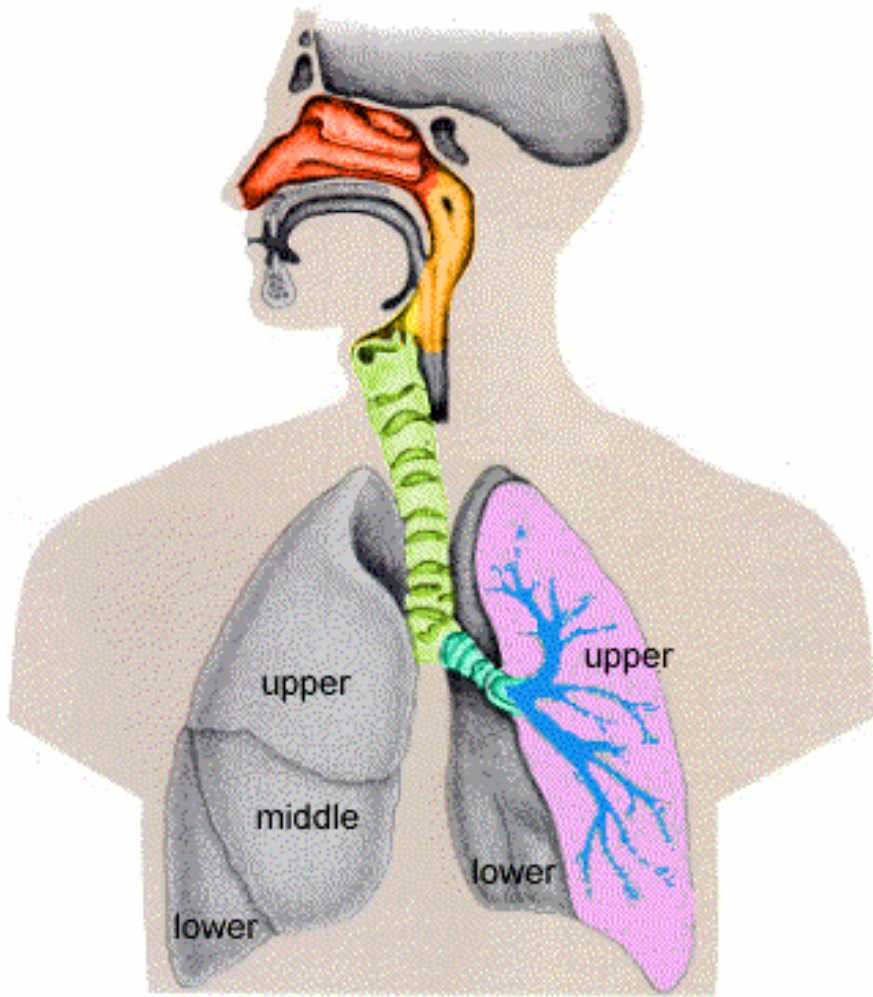


# Cough Characteristic Suggested Underlying Etiology or Contributing Factor

|                                    |  |
|------------------------------------|--|
| Barking or brassy cough            | Croup, laryngitis, tracheomalacia, habit cough |
| Cough productive of casts          | Acute bronchitis, pneumonia, asthma            |
| Honking                            | Psychogenic                                    |
| Paroxysmal (with or without whoop) | Pertussis and parapertussis                    |
| Staccato                           | Chlamydia in infants                           |



# Cough in Children - Location



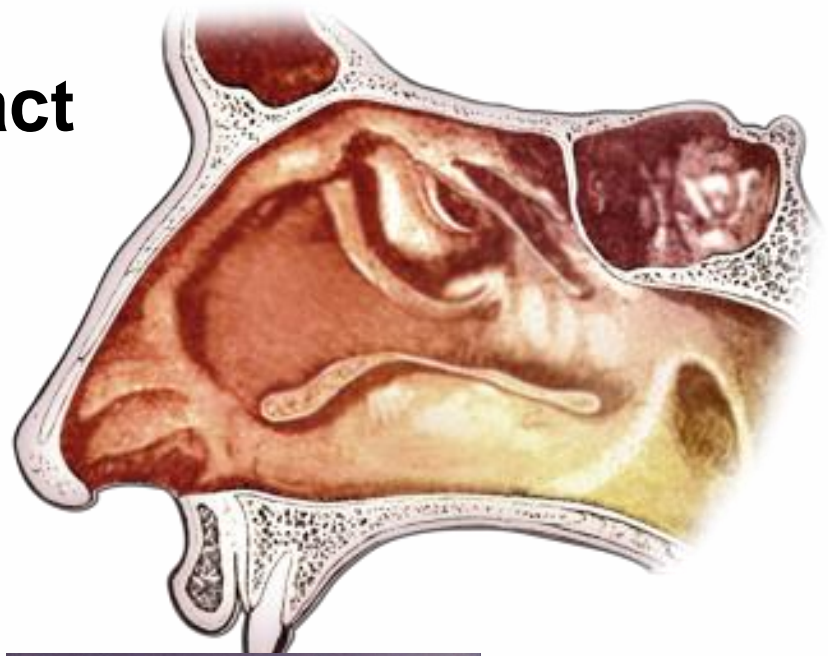
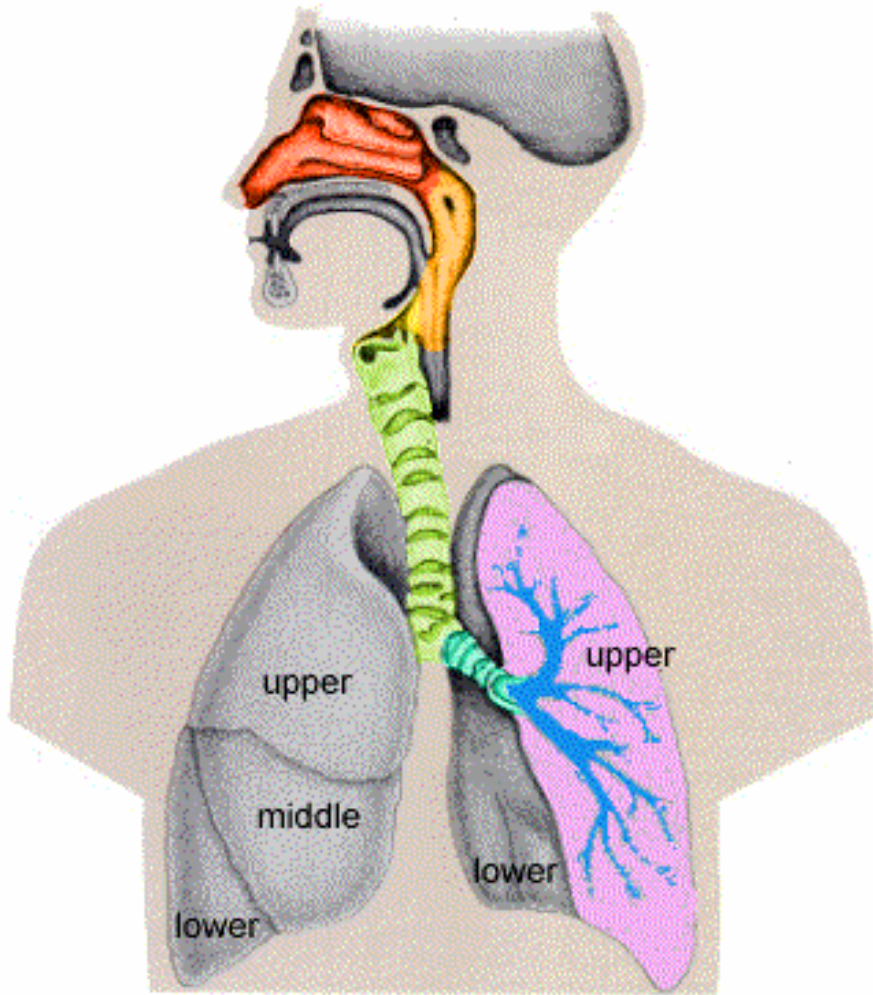
- Throat
- Nose
- Larynx
- Trachea
- Bronchus
- Bronchioles
- Lung
- Parenchyma
- Thoracic cavity
- Foreign bodies
- Cardiac causes



| Age     | Pathogens  |
|---------|--|
| Newborn | <i>Group B streptococcus, E.coli, Klebsiella species, Enterobacteticeae</i>                                      |
| 1–3 mo  | <i>Chlamydia trachomatis, respiratory syncytial virus (RSV), other respiratory viruses, Bordetella pertussis</i> |
| 2-5 yo  | <i>Respiratory viruses, S. pneumoniae, Hib, M. pneumoniae, Chlamydia pneumoniae</i>                              |
| 6-18 yo | <i>M. pneumoniae, S. pneumoniae, C. pneumoniae, influenza A or B, adenovirus, other respiratory viruses</i>      |

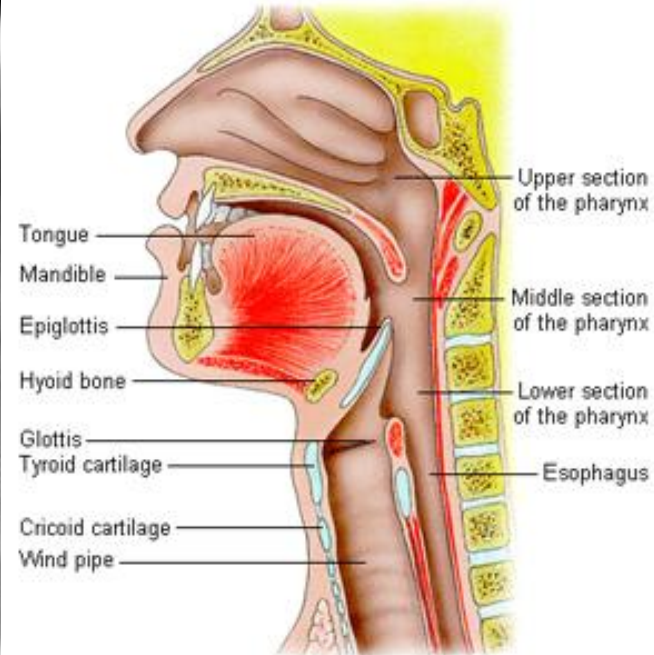
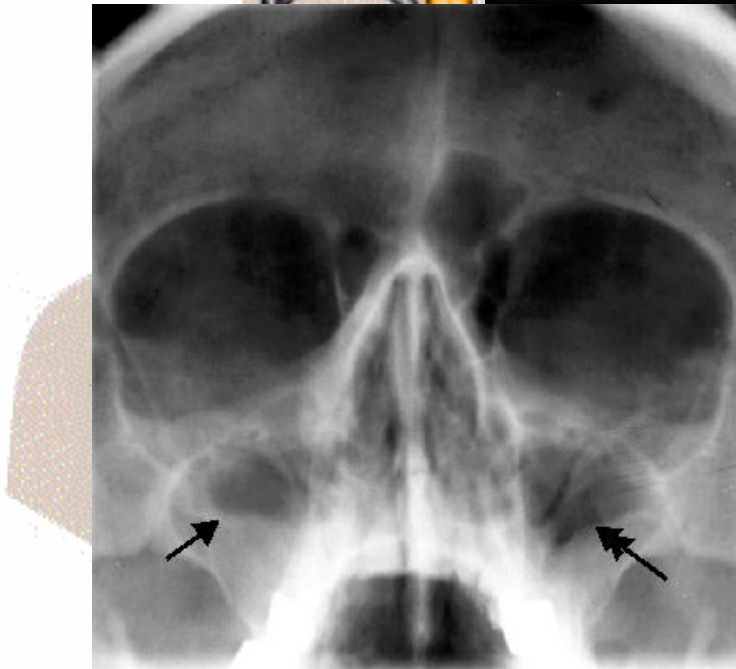
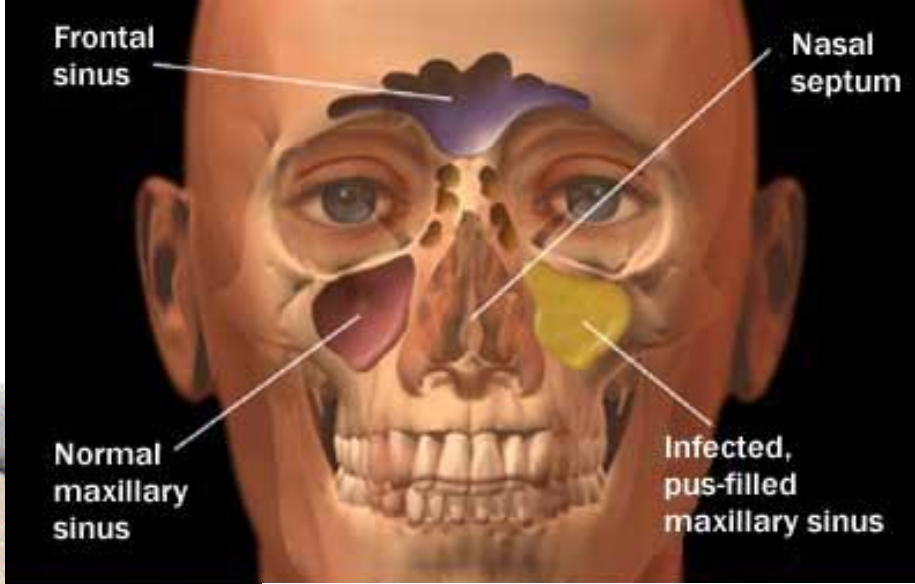


# Upper Respiratory Tract



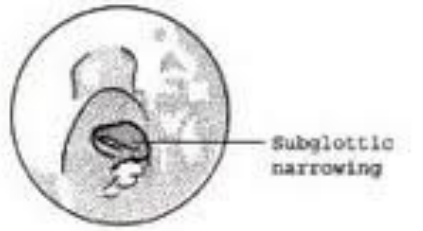
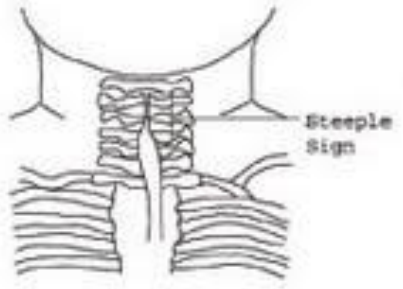
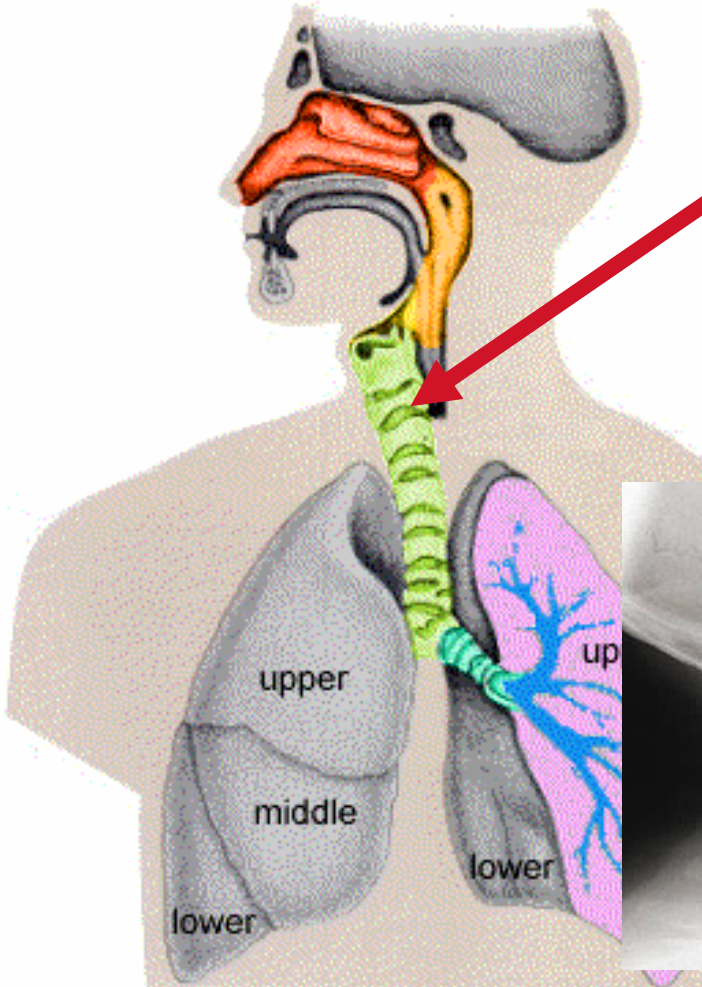
# Sinusitis

## Allergic rhinitis

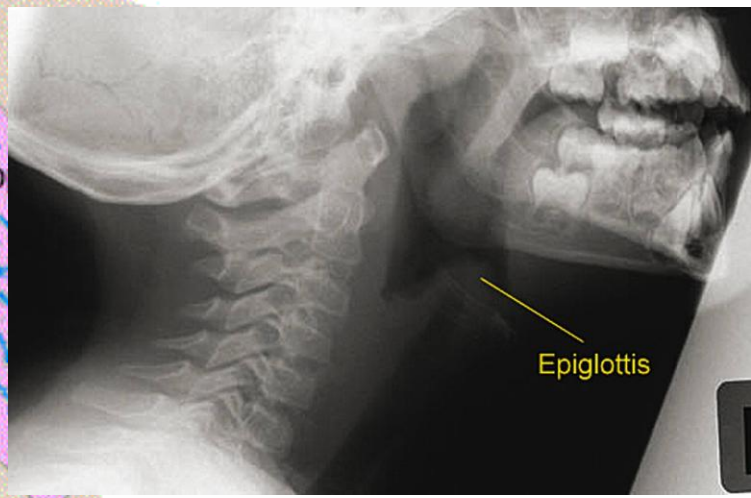


## Post-nasal drip





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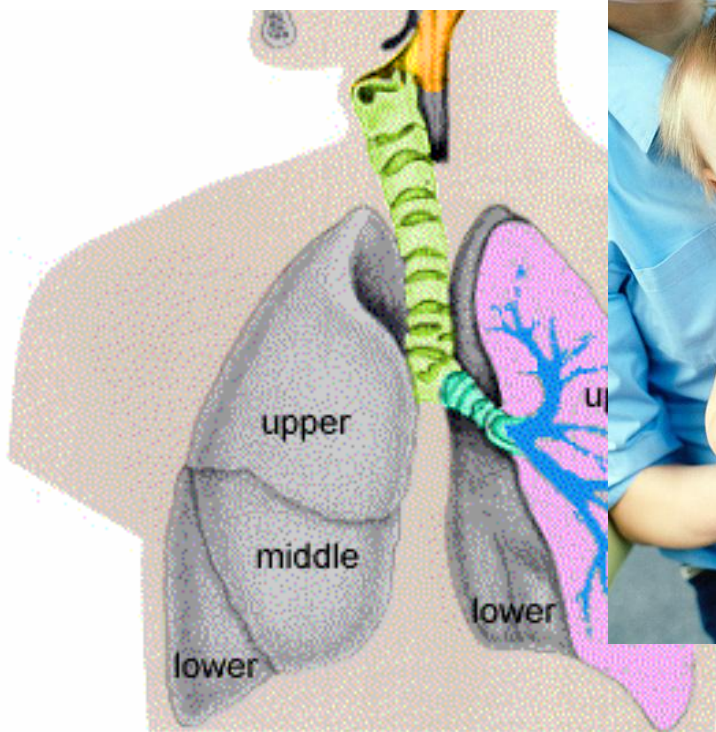
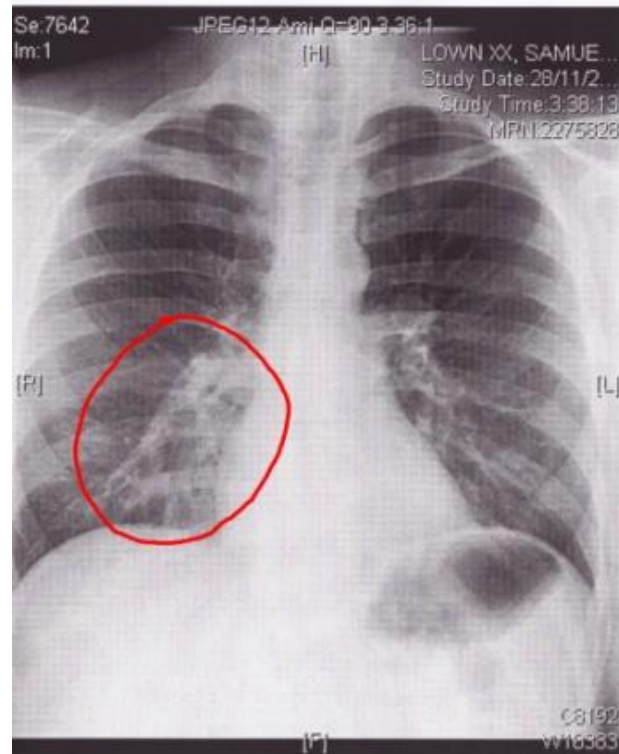


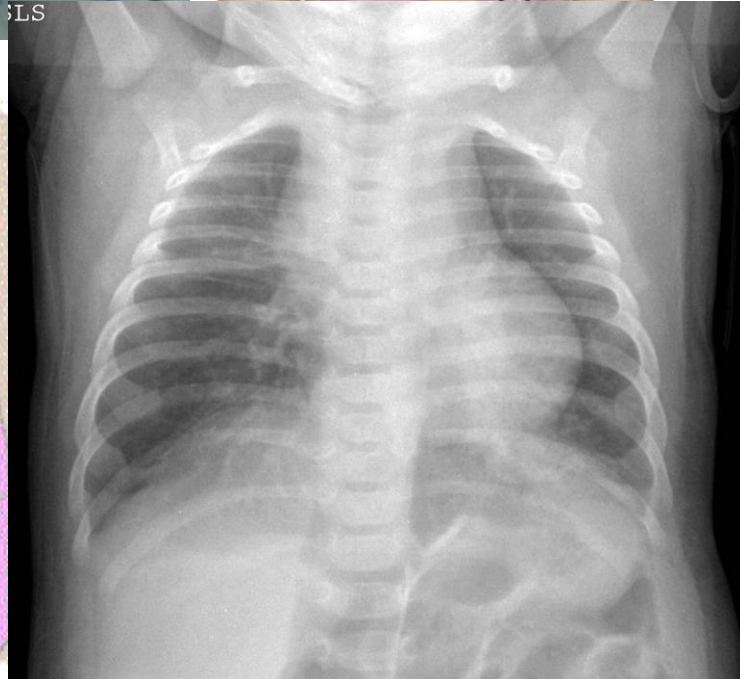
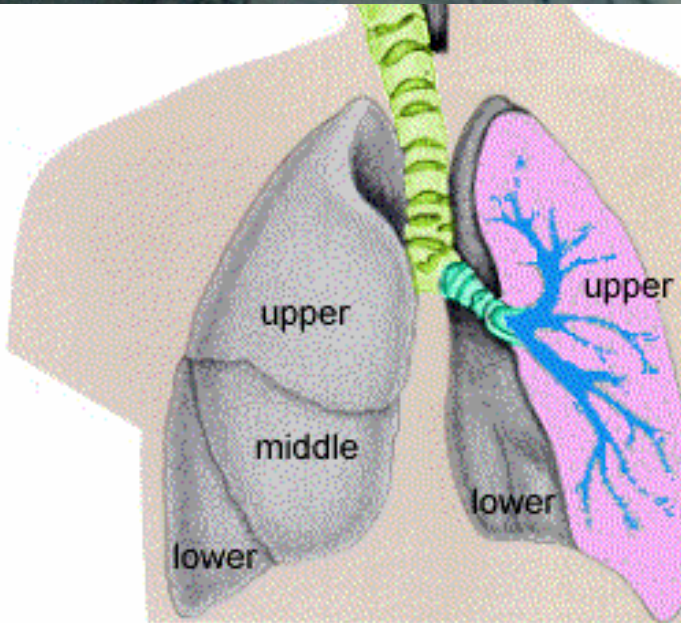
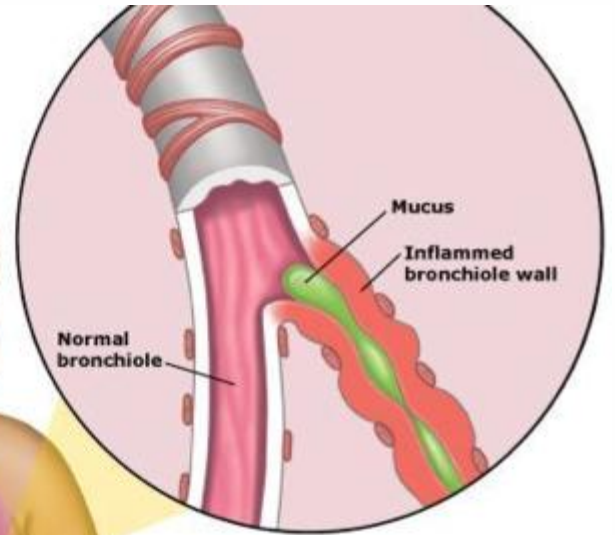
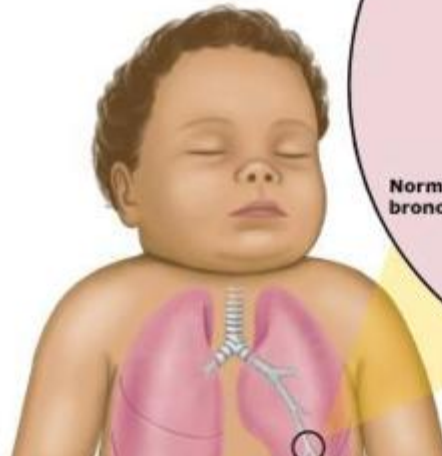
Normal

Bronchitis



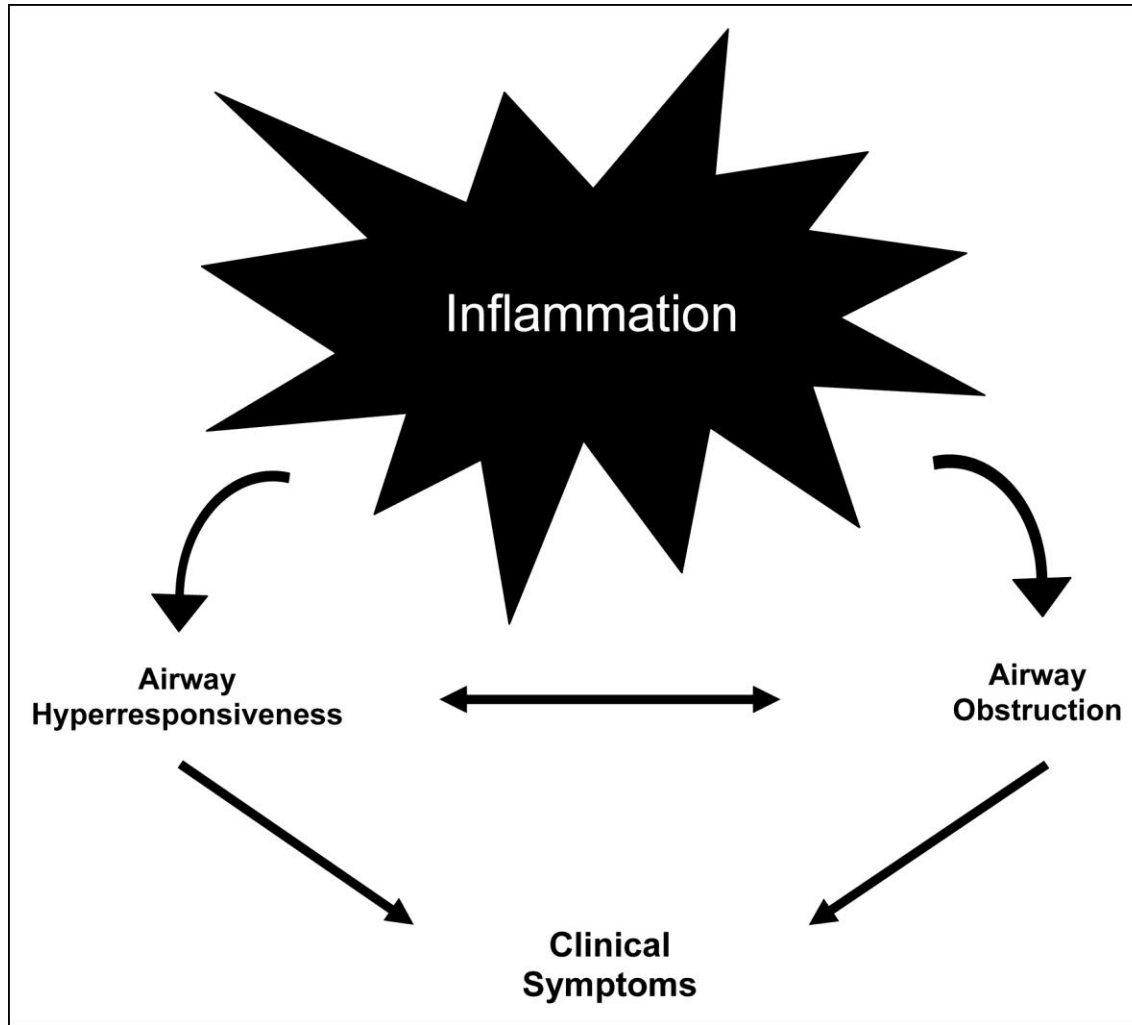
Tertiary bronchi







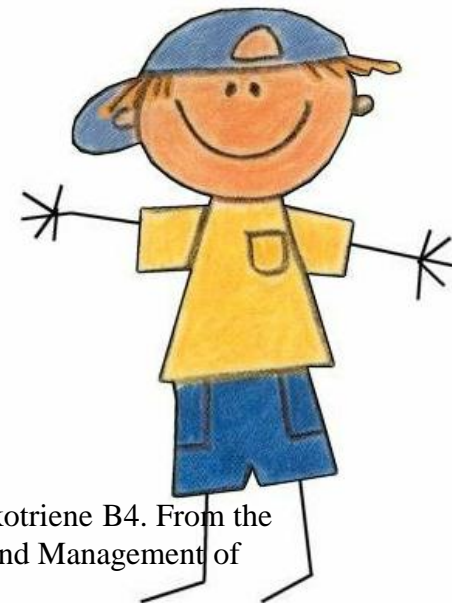
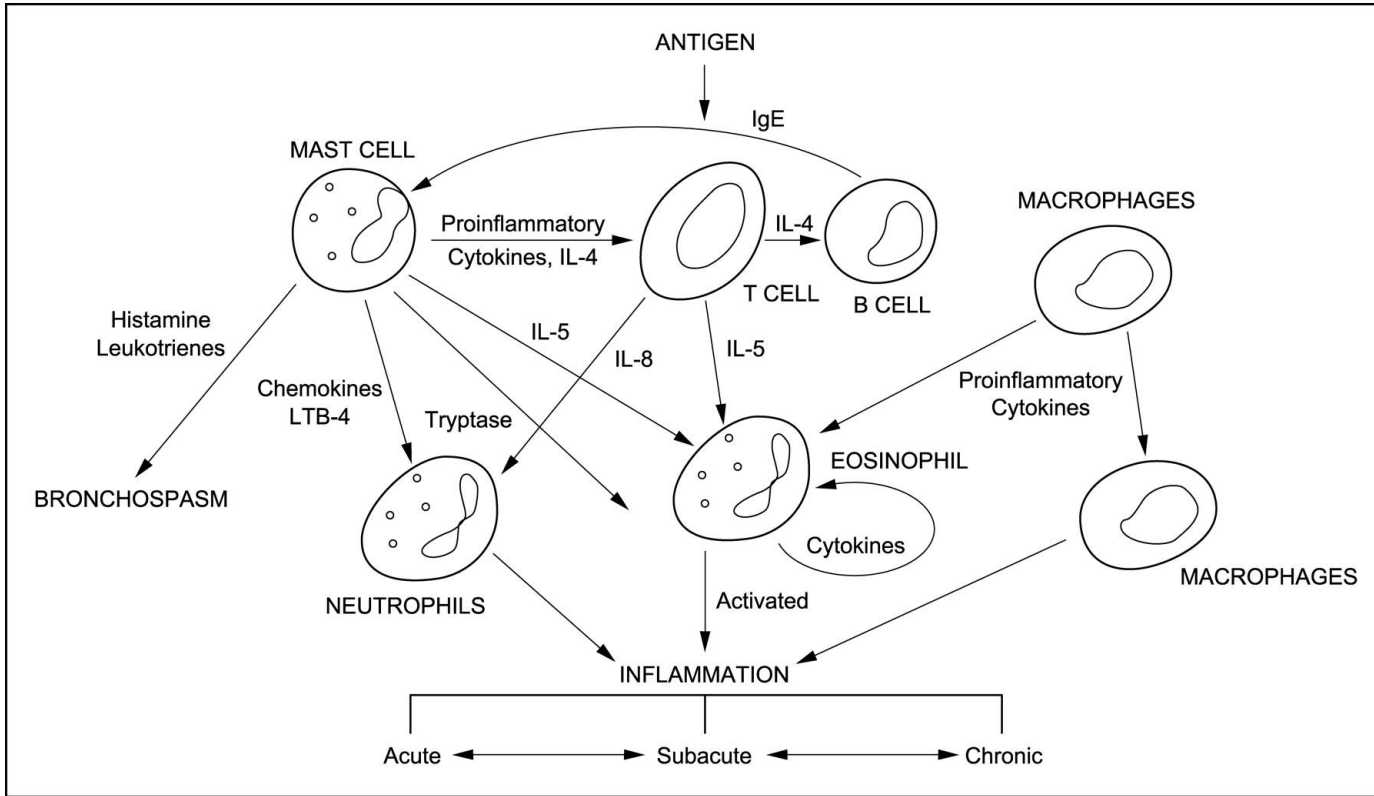
# Mechanisms underlying the clinical symptoms of asthma



Hill, V. L. et al. *Pediatrics in Review* 2009;30:331-336



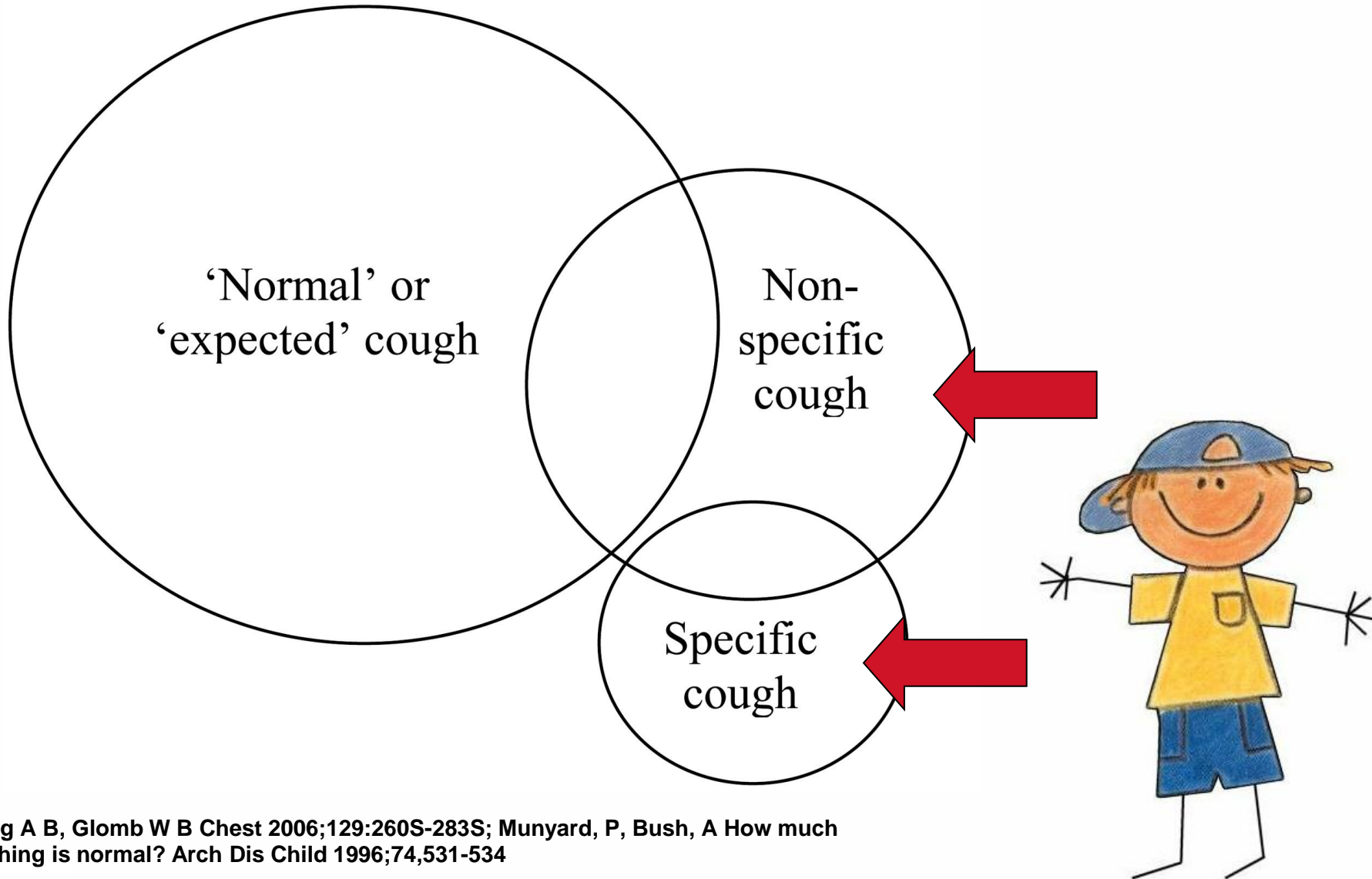
# Cellular mechanisms involved in airway inflammation



Hill, V. L. et al. *Pediatrics in Review* 2009;30:331-336

Cellular mechanisms involved in airway inflammation. IL=interleukin, IgE=immunoglobulin E, LTB4=leukotriene B4. From the National Asthma Education and Prevention Program. Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. 1997.

# Classification of types of cough in children



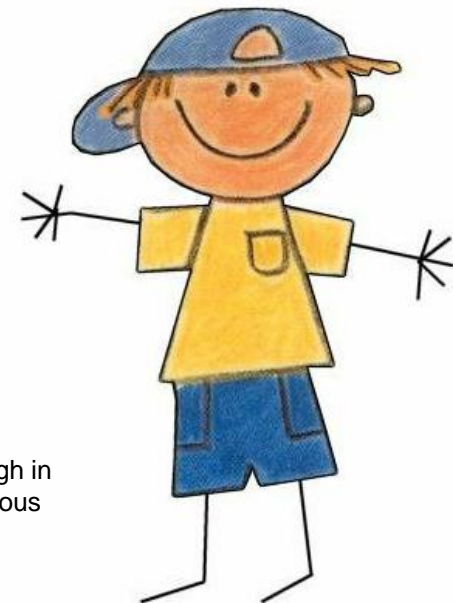
# Chronic Cough in Children

- specific cough, the etiology and necessity of further investigations is usually evident from the presence of coexisting symptoms and signs
- nonspecific cough, the etiology is ill-defined (post-viral cough and/or increased cough receptor sensitivity)

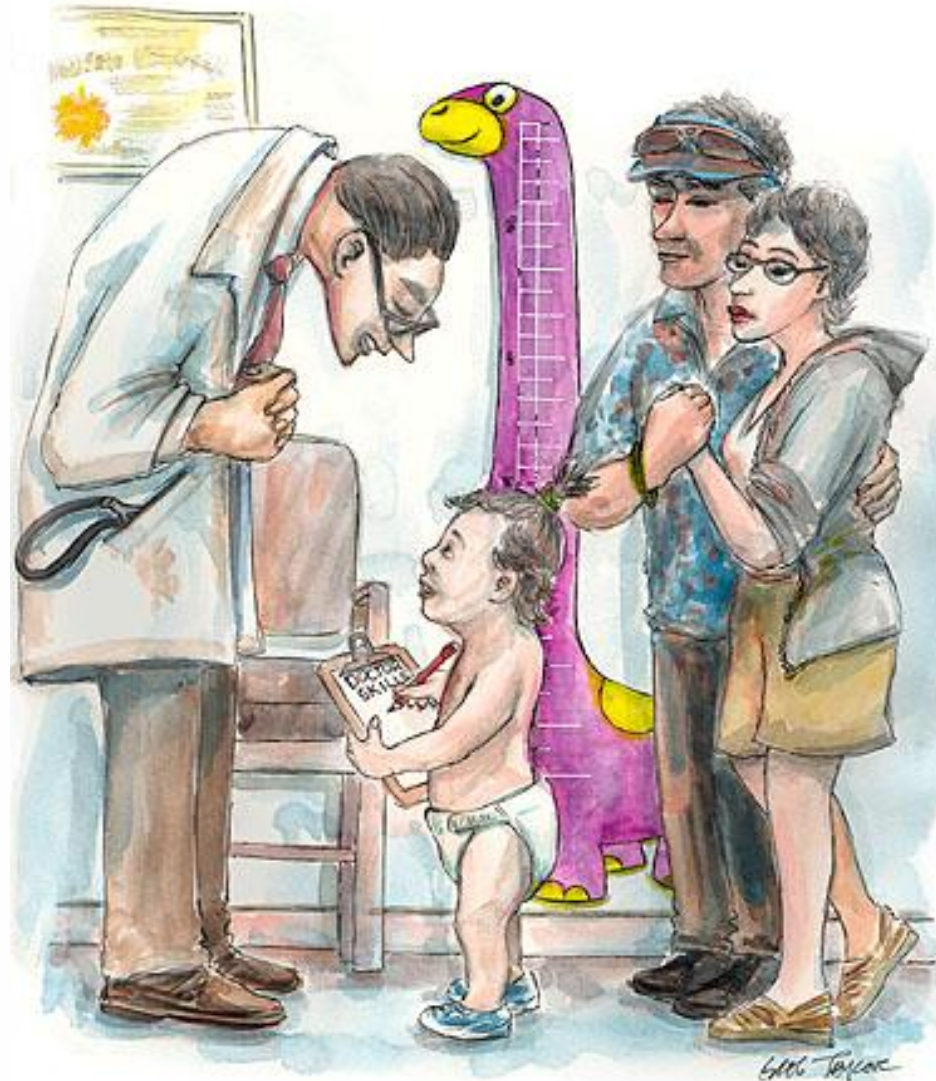


# Psychological Cough in Children

- In older children, cough is also subjected to psychological influences
- children were more likely to cough under certain psychological settings



# Review of Cough Treatment Modalities



# Treatment Modalities for Cough in Children

- Cough mixtures



# Use of Cough Mixtures



- Narcotic and non-narcotic **cough** medicines.
- Narcotic **cough** medicines typically contain codeine or hydrocodone, which act on the medullary **cough** center in the brainstem.
- Non-narcotic **cough** medicines is dextromethorphan, which is a narcotic analog.





# Codeine

- Side effects of codeine include lightheadedness, dizziness, sedation, GI effects, and sweating
- overdose are respiratory depression and a decreased level of alertness or consciousness
- Dosage: 2mg/kg



# Dextromethorphan

- Dextromethorphan include drowsiness, dizziness, nausea, GI upset, and abdominal discomfort
- Dextromethorphan may cause behavioral disturbances and respiratory depression when overdose occurs.



# Combination

- antihistamine/decongestant
- antihistamine/antitussive
- antitussive/expectorant
- decongestant/expectorant
- antihistamine/antitussive/decongestant
- antitussive/decongestant/expectorant



# Over-the-counter medications for acute cough in children and adults in ambulatory settings

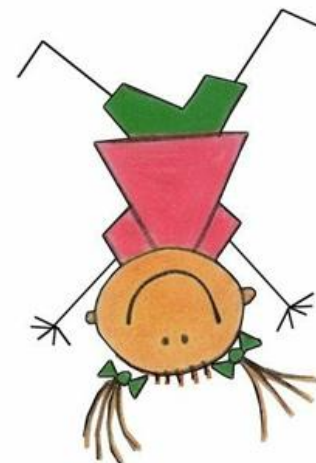
Susan M Smith, Knut Schroeder, Tom Fahey

Department of Family Medicine and General Practice, Royal College of Surgeons in Ireland Medical School, Dublin, Ireland.

Department of Public Health and Primary Care, Trinity College Centre for Health Sciences, Dublin, Ireland.

Academic Unit of Primary Health Care, Department of Community Based Medicine, Cotham Hill, UK

*Cochrane Database of Systematic Reviews*, Issue 4, 2009



# Over-the-counter medications for acute cough in children and adults in ambulatory settings

Susan M Smith, Knut Schroeder, Tom Fahey

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***The results of this review suggest that there is no good evidence for or against the effectiveness of OTC medications in acute cough.***



# Adverse Events Attributable to Cough and Cold Medications in Children

Melissa K. Schaefer, MD<sup>a,b</sup>, Nadine Shehab, PharmD<sup>a</sup>, Adam L. Cohen, MD, MPH<sup>c</sup> and Daniel S. Budnitz, MD, MPH<sup>a</sup>

Division of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases

Epidemic Intelligence Service, Office of Workforce and Career Development

Division of Bacterial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Pediatrics. 2008 Apr;121(4):783-7. Epub 2008 Jan 28.



# Adverse Events Attributable to Cough and Cold Medications in Children

Melissa K. Schaefer, MD<sup>a,b</sup>, Nadine Shehab, PharmD<sup>a</sup>, Adam L. Cohen, MD, MPH<sup>c</sup> and Daniel S. Budnitz, MD, MPH<sup>a</sup>

- *Annually, an estimated **7091 patients aged <12 years** were treated in emergency departments for adverse drug events attributable to cough and cold medications, accounting for **5.7%** of emergency department visits for all medications in this age group.*
- *Most visits were for children aged **2 to 5 years** (64%).*
- ***Unsupervised ingestions** accounted for **66%** of estimated emergency department visits*
- *most of these ingestions involved children aged **2 to 5 years** (77%).*
- *Most children did not require admission or extended observation (**93%**).*



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines





# Use of Antihistamines

- block H1 receptors on nasal vasculature and compete with histamine for receptor sites.
- The first-generation antihistamines, commonly diphenhydramine, hydroxyzine, chlorpheniramine, brompheniramine, and clemastine,
- cross the blood-brain barrier and affect the central nervous system (CNS).



# Use of Antihistamines

- The second-generation antihistamines include terfenadine, astemizole, loratadine, and cetirizine.
- do not cross the blood-brain barrier to any great extent, they cause fewer CNS effects.
- do not possess anticholinergic properties and have little drying effect.
- not as effective as the first-generation antihistamines



# Side effects of antihistamines

- Sedation
- Paradoxical excitability
- Dizziness
- Respiratory depression
- Hallucinations
- Tachycardia
- Heart block
- Arrhythmia
- Dry mouth
- Blurred vision
- Urinary retention



# Anti-histamines for prolonged non-specific cough in children

Anne B Chang, Jane Peake, Margaret S McElrea

Queensland Children's Respiratory Centre and Queensland Medical Research Institute, Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Brisbane, Australia.

Immunology and Allergy, Royal Children's Hospital, Brisbane, Australia.

Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia

Cochrane Database of Systematic Reviews, Issue 4, 2009



# Anti-histamines for prolonged non-specific cough in children

Anne B Chang, Jane Peake, Margaret S McElrea

Cochrane Database of Systematic Reviews, Issue 4, 2009

*However the use of anti-histamines in children with non-specific cough has to be balanced against the well known risk of adverse events especially in very young children*



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist



# Leukotriene receptor antagonist for prolonged non-specific cough in children

Anne B Chang, Donna Winter, Jason P Acworth

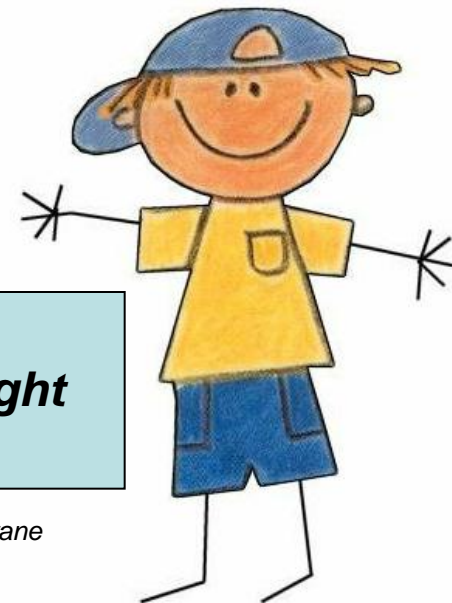
Queensland Children's Respiratory Centre and Queensland Medical Research Institute, Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Brisbane, Australia.

Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia.

Emergency Medicine, Royal Children's Hospital, Brisbane, Australia

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***The leukotriene pathway is reported to be involved in the sensory (neurogenic) pathway, which is a mechanism thought to be involved in the pathogenesis of chronic cough.***



# Leukotriene receptor antagonist for prolonged non-specific cough in children

Anne B Chang, Donna Winter, Jason P Acworth

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***There is no RCT evidence to support the routine use of leukotriene receptor antagonist for the symptom of non-specific cough in children***





# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs



# Non-steroidal anti-inflammatory drugs for the common cold

Soo young Kim, Yoon-Jung Chang, Hye Min Cho, Ye-won Hwang, Yoo Sun Moon

Department of Family Medicine, Kangdong Sacred Heart Hospital, Seoul, Korea, South.

Division of Cancer Control, National Cancer Center, Goyang-si, Korea, South. 3

Medical Library, Sungkyunkwan University, Samsung Medical Center, Seoul, Korea, South.

Department of Family Medicine, Korea University Ansan Hospital, Gyeonggi-Do, Korea, South.

Department of Family Medicine, Hallym University College of Medicine, Chunchon Sacred Heart Hospital, Chunchon, Korea, South

*Cochrane Database of Systematic Reviews*, Issue 4, 2009



Kim SY, Chang YJ, Cho HM, Hwang YW, Moon YS. Non-steroidal anti-inflammatory drugs for the common cold.

*Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD006362. DOI:10.1002/14651858.CD006362.pub2.

# Non-steroidal anti-inflammatory drugs for the common cold

Soo young Kim, Yoon-Jung Chang, Hye Min Cho, Ye-won Hwang, Yoo Sun Moon

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***Our findings conclude that NSAIDs improved most analgesia-related symptoms caused by the common cold, but there is no clear evidence that NSAIDs are effective in improving coughs and runny noses caused by the common cold.***



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist



# Inhaled beta2-agonists for non-specific chronic cough in children

Ahmed AT Tomerak, Harish HV Vyas, Monica Lakhanpaul, Julian McGlashan, Michael C McKean

Department of Child Health, Queen's Medical Centre, Nottingham, UK.

Paediatric Intensive Care, University Hospital, Queen's Medical Centre, Nottingham, UK.

National Collaborating Centre for Women's and Children's Health, London, UK.

Department of Otolaryngology, Queen's Medical Centre, Nottingham, UK.

Paediatrics, Newcastle upon Tyne NHS Trust, Newcastle upon Tyne, UK

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Tomerak AAT, Vyas HHV, Lakhanpaul M, McGlashan J, McKean MC. Inhaled beta2-agonists for non-specific chronic cough in children. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD005373. DOI: 10.1002/14651858.CD005373.



# Inhaled beta2-agonists for non-specific chronic cough in children

Ahmed AT Tomerak, Harish HV Vyas, Monica Lakhanpaul, Julian McGlashan, Michael C McKean

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***The existence of cough variant asthma (cough as the only respiratory symptom without any evidence of airway obstruction) is controversial.***

***This review raises the appropriateness of the common practice of using inhaled  $\beta_2$  agonists in the treatment of children with cough without any other evidence of airway obstruction.***

***The review found that there is nothing at present to suggest that treatment with  $\beta_2$  agonists will be beneficial in treating nonspecific isolated cough in children.***

Tomerak AAT, Vyas HHV, Lakhanpaul M, McGlashan J, McKean MC. Inhaled beta2-agonists for non-specific chronic cough in children. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD005373. DOI: 10.1002/14651858.CD005373.



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist
- Inhaled corticosteroids



# Inhaled corticosteroids for non-specific chronic cough in children

Ahmed AT Tomerak, Julian McGlashan, Monica Lakhanpaul, Harish HV Vyas, Michael C McKean

Department of Child Health, Queen's Medical Centre, Nottingham, UK.

Department of Otolaryngology, Queen's Medical Centre, Nottingham, UK.

National Collaborating Centre for Women's and Children's Health, London, UK.

Paediatric Intensive Care, University Hospital, Queen's Medical Centre, Nottingham, UK.

Paediatrics, Newcastle upon Tyne NHS Trust, Newcastle upon Tyne, UK

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

Tomerak AAT, McGlashan J, Lakhanpaul M, Vyas HHV, McKean MC. Inhaled corticosteroids for non-specific chronic cough in children. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD004231. DOI: 10.1002/14651858.CD004231.pub2.



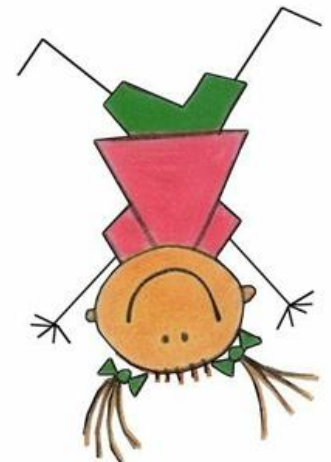


# Inhaled corticosteroids for non-specific chronic cough in children

Ahmed AT Tomerak, Julian McGlashan, Monica Lakhanpaul, Harish HV Vyas, Michael C McKean

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***The review found that there is currently no good evidence to suggest that treatment with standard doses of inhaled corticosteroids will be beneficial.***



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist
- Inhaled corticosteroids
- Antibiotics



# Antibiotics for prolonged moist cough in children

Julie M Marchant, Peter S Morris, Justin Gaffney, Anne B Chang

Dept. of Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia.

Ear Health and Education Unit, Menzies School of Health Research, Darwin, Australia.

Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia.

Respiratory Medicine Level 3 Woolworths Bldg, Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Brisbane, Australia

Cochrane Database of Systematic Reviews, Issue 4, 2009

*Chronic cough is reported in up to 9% of preschool aged children. American general practice guidelines suggest antimicrobial treatment may be indicated in children with cough lasting > 10 days.*

Marchant JM, Morris PS, Gaffney J, Chang AB. Antibiotics for prolonged moist cough in children. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD004822. DOI: 10.1002/14651858.CD004822.pub2.



# Antibiotics for prolonged moist cough in children

Julie M Marchant, Peter S Morris, Justin Gaffney, Anne B Chang

Cochrane Database of Systematic Reviews, Issue 4, 2009

*Two small RCTs were available for analysis although both have methodological flaws. They found that treatment with antibiotics for prolonged moist cough in children was beneficial with one clinical cure for every three children treated. Antibiotics resulted in the prevention of illness progression for one in every four patients treated.*



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist
- Inhaled corticosteroids
- Antibiotics
- Honey and lozenges



# Honey and lozenges for children with non-specific cough

Selamawit Mulholland, Anne B Chang

Queensland Respiratory Centre, Royal Children's Hospital, Herston, Australia.

Queensland Children's Respiratory Centre and Queensland Children's Medical Research Institute, Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Brisbane, Australia

*Cochrane Database of Systematic Reviews*, Issue 4, 2009



# Honey and lozenges for children with non-specific cough

Selamawit Mulholland, Anne B Chang

*Cochrane Database of Systematic Reviews*, Issue 4, 2009

***Clinically, this review was unable to provide any justifiable recommendation for or against honey and/or lozenges due to the lack of evidence***



# Treatment Modalities for Cough in Children

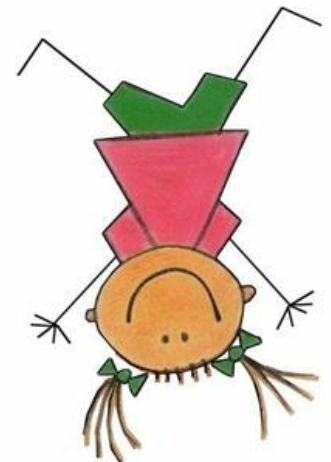
- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist
- Inhaled corticosteroids
- Antibiotics
- Honey and lozenges
- Education





# Use of Education

- educate parents about the cause of their child's illness
- how long they can reasonably expect symptoms to last
- signs and symptoms of complications
- the lack of efficacy of medications in **children**
- associated adverse effects



# Treatment Modalities for Cough in Children

- Cough mixtures
- Antihistamines
- Leukotriene receptor antagonist
- Non-steroidal anti-inflammatory drugs
- Inhaled beta2-agonist
- Inhaled corticosteroids
- Antibiotics
- Honey and lozenges
- Education
- What else?



# Placebo effect

Schroeder, K, Fahey, T Should we advise parents to administer over the counter cough medicines for acute cough? Systematic review of randomised controlled trials. Arch Dis Child 2002;86,170-175

Paul, IM, Yoder, KE, Crowell, KR, et al Effect of dextromethorphan, diphenhydramine, and placebo on nocturnal cough and sleep quality for coughing children and their parents. Pediatrics 2004;114,e85-e90

Chang AB, Gaffney J, Connor FC, et al. Gastro-oesophageal reflux treatment for prolonged non-specific cough in children and adults. Cochrane Database Syst Rev (database online). Issue 2; 2005



The therapeutic benefit of placebo treatment for cough has been reported to be as high as 85%.



**The Pediatrician is in!**



# Chronic Cough in Children

Light at the end of the tunnel?



# Chronic Cough in Children

- Define cough in children
- Describe the etiologies of cough in children
- Review the common modalities of treatment for chronic cough in children

