

## SNIPPETS FROM THE JOURNALS

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The 22 January 2009 edition of the *New England Journal of Medicine* carries two articles related to the wheezy infant that are important in understanding this condition. Ironically the two articles are broadly contradictory although this is not so when read in depth.

The first article is titled '*Oral prednisolone for pre-school children with acute virus-induced wheezing*' (J Panicker and others). The authors comment that attacks of wheezing induced by upper respiratory viral infections are common in children aged 10 months till 6 years. Oral prednisolone is widely used to treat these children with wheezing who present to hospital and there is conflicting evidence regarding its efficacy.

The authors conducted a randomised, double-blind, placebo-controlled trial comparing a 5-day course of oral prednisolone with placebo. The dose of prednisolone was 10 mg per day for children 24 months or younger and 20 mg per day for children over 24 months of age. These doses were in accordance with British Thoracic Society guidelines. (These doses are far less than the 2 mg/kg dose used in South Africa.) Further, the authors state that they enrolled children between the ages of 10 months and 60 months who had an attack of wheezing that 'a physician judged to be preceded by the symptoms and signs of a viral infection of the upper respiratory tract'. The authors also tried 'to reduce the recruitment of infants with wheezing associated with bronchiolitis'.

The primary outcome was the duration of hospitalisation. Secondary outcomes were the score on the Preschool Respiratory Assessment Measure (PRAM), albuterol use, and a 7-day symptom score.

Of the 700 children enrolled there was no significant difference in the duration of hospitalisation between the placebo group and the prednisolone group [13.9 hours vs. 11.0 hours]. In addition, there was no significant difference between the two study groups for any of the secondary outcomes or for the number of adverse events.

In the discussion, the authors report on the Csonka and Tal studies that did show benefits of systemic corticosteroids. Csonka used 2 mg/kg of oral prednisolone and Tal used 4 mg of intramuscular methylprednisolone. The children in this (Panicker *et al.*) study had mild to moderate wheeze rather than severe wheezing and the majority of children who were recruited 'did not have the classic atopic asthma phenotype that is responsive to a short course of oral corticosteroids'.

The second article is titled '*Preemptive use of high dose fluticasone for virus-induced wheezing in young children*' by FM Ducharme and others.

These Canadian authors studied 129 children aged 1 to 6 years. These children had previously had moderate to severe wheezy episodes with upper respiratory tract infections. The children were now randomly assigned to receive 750 µg inhaled fluticasone or placebo twice daily for up to 10 days after the first signs of an upper respiratory tract infection. This was a home-based study and parents started treatment at their discretion. The children eligible for this study would have already

had 3 episodes or more of wheezing. Children excluded from this study included those with allergic rhinitis and documented positive skin tests or elevated specific IgE levels. The primary outcome was rescue with oral corticosteroids.

Of 2 243 children screened, 1 860 were ineligible. Of the 383 eligible children, the parents of 199 declined participation leaving 62 in the fluticasone group and 62 in the placebo group.

The results showed that 8% of upper respiratory tract infections in the fluticasone group led to treatment with rescue corticosteroids as compared with 18% in the placebo group. A concern was that the children in the fluticasone group had a smaller gain in height and weight.

It is important to be aware that the efficacy of oral and inhaled cortisone is being studied in different cohorts of wheezy children. These cohorts include children with bronchiolitis or children with wheeze following upper respiratory tract infections, or children with asthma or children with predictive scores for asthma. These groups are further subdivided into mild or moderate or severe wheezers. Finally, the dose and route of the corticosteroid can range widely. One needs to read these articles very carefully.

Finally I would like to draw readers attention to a seminal article in the April 2009 *Journal of Allergy and Clinical Immunology*. The article is titled '*An interaction between filaggrin mutations and early food sensitization improves the prediction of childhood asthma.*' (Ingo Marenholz *et al.*).

In this article the authors evaluated whether filaggrin gene (FLG) mutations identified in people with eczema can predict the development of asthma.

Loss of function mutations in the gene encoding filaggrin, which is important for skin barrier function, were identified to be strong genetic risk factors for eczema and eczema-associated asthma.

FLG mutations were identified in the German Multicenter Allergy Study (MAS) birth cohort. This cohort of 1 314 German children was selected in 1990 and followed intensively in respect of allergy symptoms, eczema, allergen sensitisation and asthma; 871 of these children had donated DNA samples and formed the study population.

Of the study population, 236 children had eczema before the age of 3 years and 168 had asthma till age of 13 years. Within the first 3 years of life, 104 children had detectable food allergen sensitisation.

FLG mutation alone in this cohort had a positive predictive value for asthma of 32.5%. Early sensitisation to food allergen alone had a positive predictive value for asthma of 43.0%. FLG mutation plus early food allergen sensitisation increased the positive predictive value to 73%. The combination of FLG mutation, early food allergen sensitisation and eczema yielded a positive predictive value for asthma of 100%.

The clinical implication of this finding is that FLG mutations can be used for the prediction of childhood asthma and might facilitate the development of early preventive subgroup-specific interventions.

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