Snippets from the journals

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In this year's first edition of Snippets from the Journals, I continue to review articles from the *Journal of Allergy and Clinical Immunology (JACI)*. This journal is the most cited journal in allergy and asthma. It is the official journal of the American Academy of Allergy Asthma and Immunology (AAAAI). The AAAAI has close ties with South Africa and many South Africans are members and fellows. The AAAAI offers special member rates to international members and fellows ($25) with its E-membership program. A handful of travel grants are offered each year to younger members and/or fellows in training (FIT), to present abstracts and attend the annual meeting. Also, fellows in training can participate in the AAAAI FIT program at these meetings and throughout the year.

Each edition of *JACI* starts with a themed clinical review. The January 2010 edition (Vol 125, No.1) concentrates on recent insights into atopic dermatitis and implications for management of infectious complications. Needless to say, these reviews are too comprehensive for snippets and are available online at www.jacionline.org.

The first article for review has a strong South African flavour with work done in our country by James Calvert and Peter Burney from Imperial College with assistance from the Wellcome Trust. The article **'Ascaris, atopy, and exercise-induced bronchoconstriction in rural and urban South African children'** features in the January 2010 edition, p.100.

Calvert and Burney conducted an extensive study among schoolgoing children in Khayelitsha and the Ketani district of the rural Eastern Cape. This was a massive study involving 1671 children in rural schools and 1651 urban children. Each child had an exercise test to identify exercise-induced bronchoconstriction (EIB), with a positive result defined as a decrease in FEV_1 of 15% or decrease in F_{25-75} of 26% or greater. The children with EIB were then matched to equivalent controls and additional total and specific IgE, and stool geohelminth levels were tested, and skin atopy tests performed. A household questionnaire was also completed. The results are quite complex and can be accessed for many local pearls. EIB was identified in 8.7% (146/1671) of rural children and 14.9% (246/1651) of urban children. While the urban figure is not surprising, the rural figure is higher than in previous studies.

A total of 380 of the 392 children with EIB and 393 control subjects underwent the additional investigations. Observations were made between subjects and controls as well as between urban subjects and rural subjects. The difference in risk of EIB between the urban and rural children and controls could be partly explained by a combination of positive skin test responses, infection with *Ascaris* and increasing fatness. The difference in risk is fully explained when household affluence is included in the model. Interestingly, household affluence has been implicated in previous studies.

No difference in the effect of atopy or *Ascaris* infection on EIB was demonstrated between the rural and urban areas. The authors point out that the increased risk of EIB associated with *Ascaris* infection might reflect non-atopically mediated inflammation in the lung (*Ascaris* larvae) leading to increased bronchial reactivity.

This article is followed by an editorial written by Thomas Platts-Mills and Philip Cooper (p.106) trying to tie in these results with findings from other countries. The conclusion is worth noting: 'In Africa, there have been major increases in the prevalence of "wheezing". However this does not necessarily translate into the severe asthma that is now so common amongst children in Western countries. Thus we still need to understand the factors that leave some rural villages with no significant asthma compared with the increased prevalence of wheezing that has appeared with urbanization.'

Ironically, in the same journal (p. 123) **Peter Bager *et al.*** from Denmark report on their study in which they infected allergic rhinitis patients with *Trichuris* ova in the hope of alleviating their rhinitis symptoms. There was a substantial clinical and immunologic response (diarrhoea and eosinophilia) but no therapeutic effect on allergic rhinitis.

An interesting article adds to the many publications already confirming the efficacy of sublingual immunotherapy. **Long-term clinical efficacy in grass pollen–induced rhinoconjunctivitis after treatment with SQ-standardized grass allergy immunotherapy tablet. Stephen Durham *et al*. p 131-138.e7.**

This study involved 257 patients with moderate to severe grass pollen induced rhinoconjunctivitis undergoing sublingual immunotherapy (SQ-standardised grass allergy immunotherapy tablet). The aim was to determine if improvement after 3 years of therapy would be sustained 1 year after treatment was completed. End points included symptom scores, quality of life questionnaires and IgG4 measures. Encouragingly, the conclusion confirmed clinical and immunological improvement was sustained 1 year after treatment. This is indicative of disease modification and associated long-term benefits.

An important study from Manchester includes Ashley Woodcock and Adnan Custovic among the authors. This study, **Allergy or tolerance in children sensitized to peanut: Prevalence and differentiation using component-resolved diagnostics. Nicolaos Nicolaou *et al*. p.191,** sheds light on why sensitised children are not necessarily allergic. About 10% of children from a birth cohort had skin test or RAST sensitivity to peanut. Most of these children underwent oral challenge. Interestingly only 2% had actual symptoms during the oral challenge. A specific predictor was an IgE response to the Ara h 2 specific allergen.

The February issue of *JACI* is the congress issue with a supplement including all the abstracts presented at the conference. The review theme covers articles with a pharmacogenomic interest including articles on variable responses in clinical trials and the need for personalised medicine.

This issue also highlights the recent FDA statements on long-acting beta-agonists (LABAs). In February 2010 the FDA extended its previous black box warning on safety concerns with LABAs.

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'The new FDA requirement is that manufacturers must state:

That asthma patients must not take LABAs on a long-term basis unless their condition cannot be adequately controlled with other medications such as inhaled corticosteroids.'

The labels must also state that the LABAs should never be used alone in the treatment of asthma in adults or children. Instead, they should be combined with an asthma 'controller' medication.

As a result of the new warning labels required by the agency, patients who gain control of their asthma through these combination corticosteroid products need to be switched to a corticosteroid alone or some other controller medication, with no LABA added.

These recommendations certainly caused a stir at the AAAAI meeting with most of the leadership speaking out against them. The recommendations do contradict most current asthma guidelines and experts queried the logic of withdrawing effective treatment once control is achieved 'without good literature experience to back it up' (Dr William Busse).

Effects of budesonide and formoterol on allergen-induced airway responses, inflammation, and airway remodeling in asthma. Margaret M Kelly *et al.* from McMaster University, Canada (p.349)

The authors have timeously produced a paper that clearly shows that 'Allergen-induced sputum eosinophilia was significantly reduced by combination treatment to a greater extent than by budesonide alone. Allergen inhalation resulted in a significant increase in submucosal tissue myofibroblast numbers and produced a significant decrease in percentage smooth muscle area. Combination therapy, but not budesonide monotherapy, significantly attenuated these changes in myofibroblast numbers and smooth muscle area.'

The authors conclude 'The effects on allergen-induced changes in sputum eosinophils, airway myofibroblast numbers, and smooth muscle seen with combination therapy suggest that the benefits associated with this treatment might relate to effects on airway inflammation and remodeling. The attenuation of early asthmatic responses and airway hyperresponsiveness by combination treatment was likely due to the known functional antagonistic effect of formoterol.'

This article is followed by an editorial comment entitled **Long-acting β-agonists and inhaled corticosteroids: Is the whole greater than the sum of its parts? (p.357)** Shamsah Kazani and Elliot Israel give a very erudite account of how β-agonists work at a cellular and receptor level and how it is possible that inhaled corticosteroids work better when in combination with β-agonists.

'There is a fair amount of *in vitro* data to suggest that ICSs and LABAs might interact synergistically. β-agonists have been shown to stimulate the glucocorticoid receptor and the CCAAT enhancer–binding protein. CCAAT enhancer–binding protein α and the glucocorticoid receptor translocate to the nucleus and inhibit smooth muscle cell proliferation. Furthermore, addition of β-agonists to corticosteroids has been shown to enhance the antiproliferative effect of the corticosteroid on smooth muscle *in vitro*.'

This is certainly not the last word on this matter and it will be interesting to see how it affects local and international guidelines.

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