

ALLSA CONGRESS ABSTRACTS

ADVANCES IN ASTHMA AND FOOD ALLERGY

HOLIDAY INN DURBAN ELANGENI, 26-28 AUGUST 2005

Abstracts are listed alphabetically within each section according to the name of the presenter of the paper. Please consult the congress programme for more details.

INVITED PRESENTATIONS

CRITICAL REVIEW OF FIVE GREAT ALLERGY PAPERS

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- Arshad, SH, Bateman, B, Matthews, SM. Primary prevention of asthma and atopy during childhood by allergen avoidance in infancy: a randomized controlled study. *Thorax* 58: 489-493, 2003.

In genetically predisposed infants, allergen exposure during infancy plays a critical role in development of phenotypic manifestations, such as asthma and skin sensitivity. The findings of this study support aggressive avoidance measures of both allergenic foods and environmental allergens – especially dust mites during infancy.

- Sears, MR, Greene, JM, Willan, AR, *et al.* A longitudinal, population-based cohort study of childhood asthma followed to adulthood. *N Engl J Med* 349: 1414-1422, 2003.

This study was undertaken to determine outcomes of an unselected, population-based birth cohort of more than 1 000 children from New Zealand who were followed to adulthood. This study demonstrates that wheezing is common in developed countries. Almost three-quarters of subjects reported wheezing at some point in their lives. As well, most patients with chronic, persistent asthma have symptoms during their preschool years and lung function deficits are present early in the course of disease.

- Laubereau B, Brockow I, Zirngibl A, *et al.* Effect of breast-feeding on the development of atopic dermatitis during the first 3 years of life – results from the GINI-birth cohort study. *J Pediatr* 144: 602-607, 2004.

Previous studies by this group showed a protective effect of exclusive breast-feeding versus cow's milk formula in subjects at a higher atopic risk level at 1 year of life. This study shows that exclusive breast-feeding significantly decreases the risk of developing atopic dermatitis during the first 3 years of life in high-risk infants.

- Pumphrey R. Anaphylaxis: can we tell who is at risk of a fatal reaction? *Curr Opin Allergy Clin Immunol* 4: 285-290, 2004.

This paper provides a comprehensive analysis of anaphylactic fatalities in the UK and cases of non-fatal anaphylaxis seen in allergy clinics. A fatal reaction is often the first reaction, and it is therefore difficult to predict who is at risk. Some fatalities are unavoidable, but treatment is not optimal in other cases. To reduce the risk of a subsequent fatal reaction, management after recovery from a severe reaction should include accurate identification of the cause and effective avoidance measures, optimal asthma control for patients with food allergy, immunotherapy for venom allergy and training in self-treatment.

- Maestrelli P, Zanolla L, Pozzan M, *et al.* Effect of specific immunotherapy added to pharmacologic treatment and allergen avoidance in asthmatic patients allergic to housedust mite. *J Allergy Clin Immunol* 113: 643-649, 2004.

Specific immunotherapy benefits patients with perennial asthma caused by house-dust mite allergy, but patients receiving specific immunotherapy usually are also taking pharmacotherapy, and the added benefit of immunotherapy is unclear. This study demonstrates that immunotherapy can be safely administered to patients with perennial allergic asthma. However, it showed only modest evidence for a clinical benefit in patients receiving pharmacotherapy according to GINI guidelines.

INDOOR AIR QUALITY AND HEALTH: THE TOXIC MOULD ISSUE

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There is an increasing awareness that poor indoor air quality may generate a variety of deleterious effects on human health. In recent years this has become a major public health concern. This is not surprising when one considers that we spend a majority of our time travelling or working in a succession of indoor microenvironments.

Buildings have evolved with the purpose of protecting inhabitants from the elements. However, they do not protect dwellers from the effects of pollution. At times, home construction may even facilitate problems with indoor pollution. The quality of indoor air depends both on the quality of the outdoor air and the strength and nature of emissions of indoor sources. The sources of indoor pollution include the outdoor air quality, biologic exposures, chemical exposures and occupant activities.

Many investigations have indicated that the three major reasons associated with health complaints in building occupants are: 1) rapid new building occupancy; 2) building renovation, and 3) water or moisture incursion with subsequent microbial contamination, especially fungal proliferation.

Fungal contamination in buildings can vary greatly, and their presence in a dwelling does not necessarily constitute exposure. Measurement of mould spores and fragments varies depending on the methodology and instruments utilised. The presence of a specific immune response to a fungal antigen only confirms that exposure to one or more related species has occurred, but not that there is a symptomatic clinical state. The response of individuals to indoor bioaerosols is complex and depends on age, gender, state of health, genetic makeup, and degree and time of bioaerosol exposure.

When health effects occur as a result of fungal exposure, it more likely is related to transient annoyance or irritational reactions secondary to volatile organic compounds, glucans or proteases. Allergic symptoms may be related to mould proliferation indoors. However, because moulds are encountered both indoors and outdoors, it is difficult to determine where the sensitivity initially arose and if the adverse response is solely provoked by either an indoor or outdoor source. As an indoor allergen, mould is considered to be an infrequent participant in the induction of allergic symptoms when compared to house-dust mite, animal dander and cockroach allergen. Infection in healthy individuals is rare and usually caused by an outdoor source. Building-related disease caused by inhalation of mycotoxins in conventional dwellings has never been proven scientifically.

THE CHANGING RELATIONSHIP BETWEEN ACADEMIA AND THE PHARMACEUTICAL INDUSTRY – THE VIEW FROM ACADEMIA

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The relationship between academia and the pharmaceutical industry is increasingly coming under scrutiny. Academics and society in general are concerned about accountability and transparency, and the influence that industry may exert on academic freedom. The areas that may cause conflict are research, education, and influencing physicians' prescribing habits.

The current reality is that the pharmaceutical industry spends more on medical research in the United States of America than the National Institutes of Health.¹ More than half of all clinical research is industry funded. Most research is done in-house by the pharmaceutical company or by contract research organisations. In South Africa contract research constitutes an important source of income for universities. This type of research is often regarded as less important or prestigious by academics.

Problems with industry-sponsored research are: the trial data are considered proprietary by the companies; selective reporting of data (reporting only the per protocol analyses and ignoring the results of intention-to-treat analyses); selective publication of studies; and ghostwriting of the articles.² Conflict of interests may also arise if institutions are recipients of company sponsorship. The Nancy Olivieri case³ is an example of this conflict, in which the University of Toronto was in dispute with a clinical researcher who was concerned about the safety of an iron chelator in thalassaemia.

The role of the pharmaceutical industry in sponsoring continuing medical education may overlap with marketing of a product. The HPCSA has clear guidelines addressing funding for CPD activities. The funding should preferably be in the form of an educational grant payable to the health care provider arranging the activity, and should not be used for travel, accommodation or other expenses of attendees.⁴ Organisations such as No Free Lunch believe that drug company funding of education should be stopped, and that funding of such activities should be from independent sources.⁵

The majority of authors of clinical practice guidelines have some form of financial relationship with the pharmaceutical industry.⁶ This of course is not surprising as their expertise is derived in part from clinical trials experience. The pharmaceutical industry is virtually the only sponsor of new drug research and development. The problem is that the pharmaceutical industry is very powerful and influential: it is one of the most profitable industries, it is global and it has strong relationships with politicians, especially in the USA.⁷

The medical profession's close relationship with the pharmaceutical industry has the potential to undermine its independence and its ability to do what is best for the patient. It needs to look at putting a greater distance between itself and industry, refusing to accept gifts and declaring conflicts of interest. Universities will also have to carefully judge their relationship with the industry and monitor the effect that this relationship has on its research. Those of us who are in academic medicine will have to ensure that researchers are protected from interference with disclosure of results and are able to express their opinions in academic settings and journals.

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THE NIGHTMARE OF ALLERGY - ANAPHYLAXIS - PROPHYLAXIS AND MANAGEMENT

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Anaphylaxis is a multi-system immunologic reaction that occurs with re-exposure to an antigen previously processed. It is characterised as the massive release of chemical mediators including histamine, leukotriene C4, prostaglandin D2, and tryptase following antigen-specific cross-linking of IgE molecules or complement proteins on the surface of tissue mast cells and peripheral blood basophils. A grading system has been devised which may assist the practitioner in tailoring therapy and predicting biphasic reactions. A detailed office flow sheet for anaphylaxis simulation will be presented. Pre-treatment with anti-IgE will be discussed and clinical experience with anaphylaxis despite anti-IgE treatment will be shown. It is important for physicians engaged in immunotherapy, specifically RUSH or accelerated immunotherapy to understand the pathophysiology, know the treatment for, and recognise the clinical signs of anaphylaxis.

RETRO-FITTING FOR MEDICINE: HOW TO ADAPT STANDARD COMPUTER APPLICATIONS AND DEVICES TO IMPROVE PATIENT RECORDS AND COMMUNICATIONS WITH THE PATIENT AND THE REFERRING DOCTOR

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Medical applications for record keeping for many practitioners are extremely expensive both in outright purchase and in upgrade and maintenance. A system using standard off the shelf programs such as Microsoft Word integrated with digital cameras to produce an efficient system will be presented, as well as concepts for writing good consultant letters.

EXPERIMENTAL MODELS IN FOOD ALLERGY

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Identification of the offending allergen(s) and potentially cross-reactive structures is of paramount importance in order to practise appropriate allergen avoidance and eventually specific immunotherapy. Even a thorough clinical history is vital for any correct diagnosis, as it has been shown that in food allergy often only a small percentage of individuals with reported food hypersensitivity experienced symptoms when challenge with food. Therefore, objective *in vitro* and *in vivo* allergy tests are mandatory to confirm clinical suspicion. The clinicians rely in daily practice upon quantification of specific IgE to a range of available allergens to confirm their clinical suspicion. The recent development of a novel tool of coupling new (indigenous) allergens to the Streptavidin-ImmunoCAP makes it possible to compare the quantitative results directly with the conventional ImmunoCAP. Even though these automated *in vitro* techniques are of outstanding reproducibility and specificity; they can not give absolute diagnostic reliability. Recent efforts have increased the sensitivity of these automated assays and can now quantify IgE levels below 0.35 kU/l, which is of particular importance in patients with distinct clinical symptoms but negative serology. The other scenario is frequently observed in allergic reactions to plant allergens, where serological sensitisation is not confirmed by clinical manifestations. The reasons are often cross-reacting carbohydrate determinants (CCD) on glycol-proteins, causing mostly immunological problems during specific IgE detection. However, recent studies demonstrated clinical relevance in subgroups of patients sensitive to timothy grass and celery. The presence of specific IgE to CCDs on allergens can now be quantified using automated assays and might be of importance in non-conclusive diagnosis.

Hundreds of food allergens have already been identified and new ones are discovered almost weekly. Based on our current knowledge it seems to be clear that plant and animal food allergens belong to very few of the several thousand known protein families. However, several factors work together to result in the sensitisation of an atopic individual with any given allergen, such as the structure and biochemical/ biophysical properties of the allergen. Recent advances in the identification of molecular structure of allergens made it possible to generate recombinant (biotechnical produced) food allergens. These allergens, demonstrating comparable IgE binding to natural allergens, are recommended for so called 'component-resolved diagnosis' which is based on the specific antibody reactivity profile of an allergic patient. This knowledge is needed for patient-tailored allergen preparations to refine future immunotherapy. A very interesting example is the recent identification of the major allergen of strawberry, a lipid transfer protein (LTP). The recombinant allergen shows high cross-reactivity to LTP-allergens from apple and peach but seems to be less allergenic, as compared by functional cellular tests, making it very interesting for future immunotherapy. Recombinant allergens can also be used as additives to natural extracts to improve sensitivity of the assay (e.g. hazelnut) or used in automated assays to detect specific sensitivity (e.g. cherry). The activity of these generated allergens can also be compared with natural extracts *in vivo* using mouse models, which also address the differential response associated with the route of exposure.

Based on the previous findings functional *in vitro* assays have been recently developed which measure the activation of basophils. In addition to the CAST-assay, measuring released leucotrienes from activated cells, a flow cytometry test has been developed which quantifies the up-regulation of the cell-marker CD63. This assay has proven to be rapid (less than 3h) and a reliable diagnostic method that allows simultaneous testing of several putative allergens with a minimal amount of blood. This is particularly useful in cases where the

quantification of specific IgE is difficult or non-conclusive such as in food allergy.

Finally, as these techniques attempt to closely resemble the *in vivo* pathway leading to symptoms, it is anticipated that they will be further adapted to differentiate between clinically relevant and irrelevant serologies and assist in the quantitative evaluation of allergenicity (residual), component-resolved diagnosis (recombinant allergens) and importantly to select and monitor specific immunotherapy in the future.

MECHANISMS OF ALLERGEN-INDUCED ASTHMA

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Inhalation of environmental allergens is an important cause of asthma. Allergen inhalation into the lower airways results in the development of acute bronchoconstriction (the early response), and in more than half of subjects, the development of late bronchoconstriction (the late response) beginning 2-4 hours after inhalation, which can persist for up to 24 hours. These bronchoconstrictor responses are mainly mediated by cysteinyl leukotriene and histamine. The late response is associated with an influx of inflammatory cells into the airways, mainly eosinophils, mast cells and basophils. The increased number of eosinophils can persist for up to 1 week after allergen inhalation, and this is temporally associated with upregulation of mediators important in eosinophilopoiesis and trafficking, namely interleukin (IL)-5, eotaxin and RANTES, and with the persistence of allergen-induced airway hyper-responsiveness.

Eosinophils are produced in the bone marrow from eosinophil/basophil colony-forming units (Eo/B-CFU). These progenitors, in common with other marrow progenitors express the cell surface marker CD34. An important aspect of allergic inflammatory responses is the induction of increases in inflammatory cell progenitors, which contribute to disease through the continued production of inflammatory effector cells. We have demonstrated increases in bone marrow Eo/B-CFUs in asthmatic subjects after allergen inhalation. This study also indicated that after allergen challenge, the bone marrow is more responsive to IL-5, due to an upregulation of the IL-5 receptor on the surface of these cells. These results indicated that the responsiveness of the bone marrow to IL-5 after allergen is a determinant of the magnitude of the eosinophilic responses to inhaled allergen, and of the degree of the subsequent physiological abnormalities. Allergen-induced increases in bone marrow IL-5 also occur at these time points, mainly derived from an increase in bone marrow T-cells, possibly trafficking from the airways.

Inhaled corticosteroids inhibit the development of allergen-induced asthmatic responses and airway inflammation, an effect thought to be mediated through activity on airway cells. We have evaluated the ability of inhaled budesonide to attenuate allergen-induced increases in bone marrow Eo/B CFU in allergic asthmatics. This study has demonstrated that inhaled budesonide (400 µg/day for 1 week), significantly reduced allergen-induced airway inflammation and increases in blood eosinophils, as well as the baseline numbers of bone marrow CD34⁺ cells and Eo/B CFU. However, inhaled budesonide did not prevent the allergen-induced increases in Eo/B CFU or CD34⁺IL-5Rα⁺ cells. These results indicate that while the baseline production of bone marrow eosinophil progenitors is reduced by inhaled corticosteroids, the allergen-induced increases are insensitive to their action.

Cysteinyl leukotrienes, released following allergen inhalation, are important in causing airway eosinophilia. We have recently shown that treatment with the leukotriene receptor antagonist, montelukast, markedly attenuates allergen-induced airway eosinophilia, to a degree similar to inhaled budesonide and reduced the bone marrow's eosinophilopoiesis.

Dendritic cells (DCs) are the professional antigen-presenting cells in the airways. We have shown that there is a marked and rapid reduction in the numbers of circulating DCs within 3 h after inhaled allergen. This change is the largest in magnitude and most rapid of all the circulating cells measured. These findings suggest that trafficking of circulating DCs into the airways is a rapid event following allergen inhalation and that presentation of antigen in the airways may depend on the recruitment of DCs from the circulation, initiated by mediators released early after allergen inhalation. We subsequently demonstrated that a cys-LT1 receptor antagonist prevents this decline in circulating DCs, suggesting that cys-LTs are also involved in recruiting these cells into the airways.

Taken together, these studies have identified that both increased bone marrow production of IL-5 from T-cells and upregulation of its

receptor on Eo/B progenitors are necessary for increased production of eosinophils after allergen inhalation, which are involved in the persistence of allergen-induced airway physiological abnormalities. The upregulation of the IL-5 receptor may be caused by cysteinyl leukotrienes released following allergen inhalation. Cysteinyl leukotrienes also play a pivotal role in the migration of DCs to and from the airways in response to inhaled allergens.

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THE ROLE OF LEUKOTRIENE RECEPTOR ANTAGONISTS IN WHEEZY CHILDREN

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Wheezing (or asthma-like symptoms) occur in almost 50% of preschool children.¹ In some these symptoms are self-limiting, but the remainder will unfortunately experience a spectrum of recurrent or persistent morbidity. The underlying pathology comprises another spectrum of possible airway abnormalities that often includes airway inflammation. Viral infection, or allergy, or both could induce this airway inflammation. Cysteinyl-leukotriene mediators are released during allergic and respiratory syncytial virus (RSV) induced inflammation.²

RSV airway infection is a frequent initial cause for wheezing in young children and is also implicated in ongoing or recurrent post-bronchiolitis wheeze. The potential of RSV infection to further initiate allergy-related wheeze has also been debated. Other respiratory viruses (especially rhinovirus) also contribute significantly to the frequency and severity of acute asthma exacerbations in known asthmatic patients.

This spectrum of airway pathology and asthma-like symptoms in wheezy children poses diagnostic and therapeutic dilemmas. Inhaled corticosteroids (ICS) play an important role in the prevention and treatment of asthma symptoms in patients suffering from allergic airway inflammation, but they do not contribute significantly to protection in those patients suffering from intermittent virus-induced exacerbations.³

The leukotriene receptor antagonists (LTRAs) - the first new class of anti-asthma medication in more than twenty years - offer documented efficacy in the management of chronic asthma.⁴ LTRAs were initially positioned as add-on therapy to inhaled ICS in patients not controlled on a medium dose of ICS alone. Emerging data now support their use as possible monotherapy in persistent asthma.⁵ The role of LTRAs as part of rescue therapy in acute asthma exacerbations is also being explored.

A recent randomised trial² initiated hope for the potential role that a LTRA (montelukast) could play in alleviating RSV postbronchiolitis symptoms. Another recent publication demonstrated montelukast (compared to placebo) to significantly reduce the rate of asthma

exacerbations in 2-5-year-old children suffering from intermittent viral-induced asthma exacerbations.⁶

These effects observed in viral-related wheezers – a large group of wheezy children with little guidance for treatment – suggest that the role of LTRAs may extend beyond that of chronic asthma.

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CHALLENGES IN THE MANAGEMENT OF ASTHMA IN SOUTH AFRICA

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Asthma is common in South African children, with approximately 10% of schoolgoing children experiencing symptoms. Furthermore, the prevalence appears to be increasing both in urban and rural areas. Asthma has therefore become one of the commonest chronic diseases and an important cause of health care utilisation. However, diagnosis and management of childhood asthma in South Africa poses unique challenges especially as the majority of South African children receive care in the public sector and are not covered by health insurance. South African guidelines for the diagnosis and management of childhood asthma, produced by the Allergy Society of South Africa and the South African Thoracic Society, provide a comprehensive guide to diagnosis and treatment. In addition, the South African essential drug list for primary care includes inhaled bronchodilators and corticosteroid metered dose inhalers. Nevertheless, implementation of such guidelines is difficult. Potential challenges to optimal asthma management in South Africa include:

Access and affordability of drugs. Inhaled therapy, the current standard of care for both prophylaxis of persistent asthma and relief of acute attacks, may be unavailable or unaffordable; lack of low-cost spacer devices further limits use of such therapy. The availability of effective new drugs such as combination inhalers or leukotriene receptor antagonists is likewise limited by cost. Even amongst those children who have health insurance, limitations on what medicines are covered and who may prescribe such therapy may impede access to effective asthma management.

Need for a low-cost spacer device. Underuse of inhaled therapy may also be due to lack of spacer devices, which are not included in the South African essential drug list. Homemade spacer devices such as a 500 ml plastic cold drink bottle have been developed for use when conventional spacers are unavailable or unaffordable. For young children, a mask needs to be attached to a bottle-spacer. Correct adaptation and use of such homemade devices need to be incorporated into asthma guidelines and educational initiatives to gain widespread acceptability and use.

Health system infrastructure. Poor access to care, particularly in impoverished rural communities may be a major obstacle to effective asthma management. Lack of transport, long distances to the nearest health facility and poor telecommunication facilities may further complicate management.

Cultural issues. Cultural barriers and misconceptions regarding the safety and efficacy of therapy may impact on patient or parent acceptability of such therapy. Language barriers may impede the ability to provide effective patient or parent education and lead to discordance in provider and patient/parent understanding. This can be especially challenging in places where multiple languages exist

and where no specific words for some of the asthma terminology such as 'wheeze' exist.

Use of traditional healers. In South Africa, patients/parents frequently seek help from traditional healers first; healers may be important educators. The place of traditional healers in asthma management deserves further consideration.

Education of health care professionals. Continuing medical education is necessary for health care providers to be informed as to the optimal and most effective asthma management strategies. Use of inhaled corticosteroids as preventative therapy is still widely underprescribed, similarly overuse of nebuliser therapy (rather than metered dose inhaler with spacer) is widespread.

Environmental determinants. Many children with asthma live in sub-optimal conditions with crowding, exposure to passive smoke and indoor fuels. Improvement of living conditions and caregiver education regarding smoking cessation remain formidable challenges.

POSTER PRESENTATIONS

NATURAL HISTORY OF MILK ALLERGY IN ATOPIC CHILDREN

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Background: Cow's milk (CM) exclusion diets are commonly used in the treatment of childhood CM allergy (CMA), but may adversely affect these children's quality of life (QOL), thus making unnecessary CM-exclusion diets undesirable.

Aim: To investigate the progression of childhood CMA children following CM-exclusion diets, as well as to evaluate the role of food challenges in reassessment of CMA.

Methods: A retrospective cohort study was conducted in which 21 CM-allergic children (13 boys and 8 girls) with ≥ 9 months CM-exclusion, underwent radioallergosorbent test (RAST) and skin prick tests (SPT). Parents completed a case history questionnaire. Children with CM-RAST <30 kU/l (age >2 years) or <10 kU/l (age <2 years) and without history of anaphylaxis or systemic disease underwent CM food challenges performed by a dietician.

Results: Fifteen subjects (71.4%) had had CM exposure since original diagnosis. Of these, 8 (53.3%) had no allergic response and proportionately these children showed no more new allergic symptoms than those without CM-exposure (Pearson χ^2 co-efficient = 0.0808, $p=0.776$). No immediate reactions and 1 delayed reaction followed CM-challenges. CMA impacted on QOL of child and family.

Conclusion: Reassessing CMA following ≥ 9 months CM-exclusion can prevent unnecessary CM-exclusion diets. Food challenges in combination with RAST and SPT should play an integral role in CMA diagnosis and reassessment.

SENSITISATION TO AERO-ALLERGENS AND FOOD ALLERGENS IN INFANTS WITH ATOPIC DERMATITIS IN SOUTH AFRICA

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Background: EPAACTM (Early Prevention of Asthma in Atopic Children), a multi-centre, multi-country study to investigate the potential of levocetirizine to prevent the development of asthma in high-risk infants with atopic dermatitis, has completed enrolment. An epidemiological analysis of the data recorded for all the children screened in the frame of the EPAACTM study has been performed. Very few sensitisation data in 1-2-year-old children with atopic parent(s) are available for South Africa as well as standardised comparison with other continents.

Methods: Children aged 1 to 2 suffering from atopic dermatitis and

with a family history of asthma were screened before potential inclusion in the EPAACTM study. Information and potential risk factors related to allergy as well as total and specific IgE were measured. Total and specific IgE were measured by the Pharmacia CAP system.

Results

1. 2 184 infants between 1 and 2 years of age with atopic dermatitis were screened in 12 countries and 514 randomised in the EPAACTM Study. 161 children from South Africa were screened.
2. The distribution was not very different to the distribution of sensitisation in the 301 infants screened in Australia: House-dust mite 33.5%, Grass Pollen GX1 10.3%, Cat 19.5%, Alternaria 7.4%, Egg 54.4%, Cow's milk 32.6%, Peanut 45.0%.
3. Peanut sensitisation in South Africa was lower than in Australia, but higher than for the EPAAC whole group. 11 infants (7.2%) in South Africa and 104 infants (4.9%) in the overall population had levels above 14 kU/l, predictive of challenge positive sensitisation (Sampson *et al.* 2002).
4. Only 2 infants were sensitised to GX2 (containing Bermuda Grass, an important South African aero-allergen) but not to GX1.

Conclusion: The prevalence of aeroallergen sensitisation in infants with eczema is very similar in the 2 southern hemisphere countries (RSA and Australia) participating in the EPAACTM study.

Concordant sensitisation to both of the 2 major sensitising grass pollen groups in South Africa (represented by Rye and Bermuda) occurs in infancy and monosensitisation to the Bermuda grass is relatively uncommon.

Identification of peanut sensitisation is important, particularly since 7.2% of the infants with eczema were found to have levels which are above the predicted threshold (15 kU/l) for challenge positive allergy to peanuts. This has important implications for patient management and follow-up.

FREE PRESENTATIONS

ENVIRONMENTAL EXPOSURE TO FLOUR DUST AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA: RESULTS OF A PRELIMINARY STUDY

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Background: Baker's asthma, caused by airborne allergens present in flour dust in the work environment, is the most commonly reported manifestation of occupational asthma among workers in South Africa. A preliminary study was performed as part of a larger epidemiological/intervention study, aimed at documenting environmental exposure to flour dust particulate and wheat allergen concentrations and to identify high exposure work processes/job types in bakeries of a large supermarket chain store.

Methods: Personal flour dust exposure assessments were conducted on randomly selected individuals within each job category (baker, baker controller, confectioner, counterhand, cleaner) in 3 bakeries of variable size. Sampling was conducted using a PAS6 sampling head, which samples the inhalable fraction of flour dust. The samples were analysed for particulate mass and specific flour allergens (wheat allergens and α -amylase). Exposure metrics were developed on the basis of individually measured exposures and average levels of these personal samples within each job category. The following variables were used in the ANOVA analysis to explain the variability in flour dust levels: job title, department, bakery size, and sampling day.

Results: A total of 42 full-shift personal samples were collected and analysed. Personal sampling revealed moderate variation across job titles in flour dust concentration (0.0-2.180 mg/m³). Bakers had the highest average (geometric mean) particulate dust concentration (0.904 mg/m³), followed by confectioners (0.539 mg/m³) and bakery controllers (0.289 mg/m³), with counterhands having the lowest aver-

age exposures (0.125 mg/m³). Similarly, in respect of the distribution of wheat allergen levels, bakers had the highest average (geometric mean) allergen concentration (16.504 ug/m³), followed by confectioners (7.307 ug/m³). There was a high degree of colinearity between inhalable dust and wheat allergen concentrations (Spearman $r=0.92$, $p<0.001$). Models with job title on its own explained the greatest variability in particulate concentration (adjusted $r^2=0.522$, $p<0.001$) as well as wheat allergen concentration (adjusted $r^2=0.692$, $p<0.001$). Adding bakery size (small, medium, large) into the model explained a greater variability in particulate concentration (adjusted $r^2=0.558$, $p<0.001$) and wheat allergen concentration (adjusted $r^2=0.701$, $p<0.001$). Sample day and bakery size, however did not explain any of the variability observed.

Conclusion: This study demonstrates that bakers have the highest 8-h average dust exposures, compared to confectioners and counterhands. Furthermore, job title explained the greatest variability in exposure observed over the working shift. The findings of this study are consistent with the 43-50% variability observed for job title as an explanatory variable in other international studies among bakery workers. The findings also suggest that flour dust particulate exposure could be used as a proxy for wheat allergen concentrations in this group of bakeries.

OCCUPATIONAL ALLERGY AND ASTHMA IN SMALL BAKERIES OF A SUPERMARKET CHAIN STORE IN SOUTH AFRICA

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Background: The food industry in South Africa employs 180 000 workers with 10%, mainly bakers, handling grain mill products. This sector reports over 25% of occupational asthma cases. This study aimed to determine the prevalence of work-related symptoms, allergic sensitisation, non-specific bronchial hyper-responsiveness (NSBH) and baker's asthma in small bakeries of a supermarket chain store.

Methods: A cross-sectional study of 517 (current and previously employed) bakers was conducted in 31 Cape Town bakeries using a modified European Community Respiratory Health Survey (ECRHS) questionnaire. Skin prick tests (SPT) used extracts of common aeroallergens (ALK) and cereal flour allergens (Bencard) (wheat, rye, barley, soya, oats, corn flour), fungal alpha-amylase, peanut and storage mite (*L. destructor*). ImmunoCAP (UniCAP Pharmacia) for wheat, rye and fungal alpha-amylase were also used. NSBH was assessed using the Medic Aid Pro Nebulizer Dosimeter method.

Results: The mean age of bakers was 32 years. The prevalence of atopy (positive SPT to ≥ 1 common aeroallergen and allergic symptoms) was 29%. Common work-related symptoms were ocular-nasal (31%), chest tightness/wheezing (17%) and skin symptoms (11%). 27% of bakers had positive SPT ≥ 1 cereal flours/additives. Most common sensitisers were cereal flours: rye (16%), wheat (16%), corn (14%), barley (12%), oats (8%), soya (8%) and storage mites (14%). SPT sensitisation to peanut (6%) and fungal alpha amylase (3%) was lower. A higher proportion had elevated IgE levels to wheat (26%) and rye (24%). The prevalence of work-related allergic rhino-conjunctivitis (symptoms and wheat/rye sensitisation) was much higher (16%) than chest symptoms (8%). NSBH (defined as $PD_{20} < 0.4$ mg) was present in 22% (n=419) of bakers. Overall, 11% demonstrated occupational asthma (NSBH and sensitisation to flour products/additives). Occupational asthma associated with rye/wheat (9-10%) was more common than with fungal alpha-amylase (2%). Atopy was significantly associated with sensitisation (OR: 5.1, CI: 3.4-7.9) and occupational asthma due to cereal flours/additives (OR: 9.4, CI: 4.5-19.5).

Conclusion: The overall 11% prevalence of baker's asthma in South African chain store bakeries is lower than the 15-21% reported for traditional and industrial bakeries. Cereal flours such as wheat and

rye appear to be more important in causing asthma than additives such as fungal enzymes.

WORK-RELATED RESPIRATORY ALLERGY ASSOCIATED WITH STORAGE PESTS AND MITES AMONG GRAIN MILL WORKERS IN THE WESTERN CAPE

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Background: Exposure to grain dust is associated with a number of adverse allergic health outcomes including conjunctivitis, rhinitis, urticaria/dermatitis and asthma. These clinical manifestations are the result of a multitude of allergens and bioactive materials present in the grain dust. The aim of this study was to assess the patterns of sensitivity to various storage pests among grain mill workers and their relationship to work-related respiratory symptoms and asthma.

Methods: This is a sub-study of the cross-sectional study previously conducted on 111 workers employed in a grain mill in Cape Town. The study instruments included a questionnaire based on the American Thoracic Society (ATS) questionnaire, and specific IgE determinations on serum obtained from workers. Blood samples were analysed by ImmunoCAP using the UniCAP® System (Pharmacia Diagnostics AB, Uppsala, Sweden) for house-dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*), storage mites (*Blomia tropicalis* (d201), *Lepidoglyphus destructor* (d71) and *Tyrophagus putrescentiae* (d72)), cockroaches (*Blattella germanica*, *Periplaneta americana*, *Blatta orientalis*), beetles (*Tenebrio molitor* (Ro212), *Sitophilus granarius* (Ri202)) and mould (mouldmix1 containing *Penicillium notatum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Alternaria alternata*). According to the ImmunoCAP scoring system, a positive score was any value greater than 0.35 kU/l.

Results: Among this group of 111 workers, the majority (89%) were men and 49% smokers. The prevalence of IgE reactivity to house-dust mite (41%) was very similar to reactivity to at least one grain-dust allergen (42%) viz. cereal grains, insects and mites. Reactivity patterns to storage mites were similar to wheat (26%), while the prevalence of reactivity to cockroach (*B. germanica*) similar to rye (22%). Storage mite, *Blomia tropicalis*, produced the strongest IgE response (mean IgE = 7.85 kU/l). Beetles such as grain weevil (16%) and mealworm (13%) produced a lower proportion of sensitised individuals, with the latter producing a stronger immune response (mean IgE = 2.32 kU/l). Among the cockroaches, *B. orientalis* appeared to generate the strongest immune response. Very high statistically significant linear correlations (Spearman $r = 0.75-0.9$) were found between dust mites and storage mites, and between cockroaches and beetles, indicating the existence of similar allergens. Among the group of grain mill workers studied, the prevalence of work-related asthma symptoms such as wheeze and tight chest was 13% and 5% respectively, while 7% of workers were being treated for doctor-diagnosed asthma. IgE reactivity to mealworm (*T. molitor*) was significantly ($p < 0.05$) associated with work-related asthma (wheeze) as were cockroach species (*B. orientalis*) in atopic workers (workers with elevated IgE reactivity to house dust mite).

Conclusion: Allergens from storage pests (mealworm and cockroach) in grain mill dust is a significant predictor of work-related asthma symptoms. This is particularly evident in atopic workers who demonstrated increased IgE reactivity to mealworm (*Tenebrio molitor*) and cockroach (*B. orientalis*) associated with work-related asthma symptoms.

THE ASSOCIATION OF BRONCHIAL HYPER-RESPONSIVENESS AND AERO-ALLERGEN SENSITISATION IN URBAN BLACK AFRICAN SCHOOL CHILDREN IN SOUTH AFRICA

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Background: There are not many data on the correlation between specific allergen sensitisation and bronchial hyper-responsiveness (BHR) in Black African children.

Aim: A study was conducted to ascertain the prevalence of bronchial hyper-responsiveness in an urban black African population and its correlation with specific allergen sensitization.

Methods: Xhosa children were selected from an urban school in Mowbray, Cape Town. Subjects were tested for an exaggerated response to methacholine administered by the Yann method. A positive response was defined as a fall in FEV1 of 20% or greater following challenge. Sensitisation to Der P, Der F, Grass mix, Bermuda grass, Mould mix, Cat, Dog, Cockroach, Egg, Milk, Peanut and Potato was assessed using skin prick testing (ALK®) with a positive result being wheal size >3mm larger than a negative control. Correlations were assessed by the Chi squared test utilising the Yates correction.

Results: 212 urban children, aged 17-21 years underwent testing. 33 (15.6%) children had a positive methacholine challenge. The prevalence of skin sensitivity to allergens was as follows:

There was a significant correlation between positive methacholine challenge and sensitivity to any aeroallergen ($p=0.0000$). This association was strongly significant for Der P, Der F, Cockroach (all $p=0.0000$) and Cat ($p=0.0007$). There was no association between positive methacholine challenge and sensitivity to any food.

Aeroallergen	SPT positive number (%)	BHR number (%)
Any	68 (32.1)	24 (72.7)
Der P	52 (24.5)	22 (66.7)
Der F	49 (23.1)	21 (63.6)
Cockroach	37 (17.5)	15 (45.5)
Grass	11 (5.2)	3 (9.1)
Bermuda Grass	9 (4.2)	4 (12.1)
Dog	6 (2.8)	1 (3.0)
Cat	5 (2.4)	4 (12.1)
Mould	2 (0.9)	1 (3.0)

Allergen	SPT positive number (%)	BHR number (%)
Any	12 (5.7)	3 (9.1)
Egg	7 (3.3)	2 (6.1)
Peanut	4 (1.9)	1 (3.0)
Milk	4 (1.9)	1 (3.0)
Potato	3 (1.4)	0 (0)

Conclusions: Bronchial hyper-responsiveness is associated with aeroallergen sensitization in an urban Black African population. Housedust mite and cockroach sensitivities are the dominant prevalent allergens in this subgroup of children, similar to that in inner city children in the USA. Skin prick tests may be a useful investigation in the assessment of asthma and bronchial hyper-reactivity in such subjects.

Acknowledgements: Glaxo-SmithKline, the Allergy Society of South Africa, the UCT School of Child and Adolescent Health, Labspec and Pharmacia.

TOTAL IgE AND SPECIFIC ALLERGEN PROFILE IN URBAN BLACK AFRICAN SCHOOL CHILDREN IN CAPE TOWN

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Background: The usefulness of total IgE level in the assessment of atopy has been disputed in black Africans, due to possible confounding with parasitic infestation and ethnic variation in IgE levels. Prior research in this cohort shows an association between higher total IgE levels with other measures of allergy such as a history of asthma and current bronchial hyper-responsiveness. However recent research (Calvert *et al*, 2004) shows high prevalence of infection >60% with *Ascaris* in a similar population, which is significantly associated with a raise in total IgE.

Aim: A study was conducted to ascertain the total IgE levels and their correlation with specific allergen sensitisation (skin prick tests) and *Ascaris* sensitisation (CAP-RAST) in an urban black African population.

Methods: 220 urban Xhosa (mean age 17 years) attending a high

school in Mowbray, Cape Town were studied by ascertaining total IgE levels and Ascaris specific IgE (Pharmacia diagnostics) and skin test reactivity to Der P, Der F, Grass mix, Bermuda grass, Mould mix, Cat, Dog, Cockroach, Egg white, Milk, Peanut and Potato (ALK®). Skin-prick tests were deemed positive if wheal size was 3mm or more greater than the negative control.

Results: Mean total IgE was 307.7 kU/l (confidence intervals 232.1-383.2). The median was 106 kU/l and the interquartile range 50.4 kU/l to 288 kU/l.

Skin-prick tests were positive for aeroallergens in 71 (32.3 %) subjects. The most common positive tests were Der P (24.5 %), Der F (23.2 %) and cockroach (17.3 %). Skin-prick tests were positive for food allergens in 12 (5.4 %) subjects, the most common positive test being egg white (7, 3.2 %). Total IgE significantly correlated with an increasing number of positive skin-prick tests (Kruskall Wallis ANOVAR = 0.0000). Total IgE was significantly higher in those subjects with positive skin-prick tests to Der P (p=0.0000), Der F (p=0.01), Cockroach (p=0.0000), Grass mix (p=0.0001), Bermuda grass (p=0.0001) and Cat (p=0.02). Of note, total IgE was lower (not statistically significant) in those subjects with a positive skin test to Dog (n=6). Total IgE was significantly higher in subjects with a positive skin-prick test to milk (n=4, p=0.02), but not in those with positive skin tests to Egg white (n=7) or Peanuts (n=4).

Ascaris IgE was negative (<0.35 kU/l) in 145 (69 %) subjects. Of the remaining subjects who had elevated (>0.35 kU/l) ascaris IgE, in 58 (28 %) the levels were class 1 (0.35 – 3.5) and class 2 (3.5 – 17.5) in only 7 (3 %). In those with detectable levels of Ascaris specific IgE, the mean was only 0.58 kU/l (standard deviation 1.69) and the highest level was 17.5 kU/l. In those with undetectable ascaris specific IgE, the median total IgE was 77.1 (interquartile range 32.1-139), within the “normal” range for age. Total IgE was significantly higher in those with raised Ascaris IgE (Kruskall Wallis p=0.0000); 397.5 (142-782) for class 1 and 1019 (417-3330) for class 2.

Conclusions and Discussion: In this cohort, total IgE correlated well with positive skin-prick tests to aeroallergens. There was a low incidence of subjects with raised Ascaris IgE, but in these subjects total IgE was raised out of the “normal” range. The usefulness of total IgE estimation in the assessment of an individual’s atopic status may thus depend on the likelihood of Ascaris infection, rather than on genetic variation in IgE levels.

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SENSITISATION TO THREE COCKROACH SPECIES IN SOUTHERN AFRICA

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Background: Cockroaches are important allergen sources in many countries, especially in the tropics. Cockroaches produce several allergens that are major risk factors for rhinitis and asthma. Worldwide, the prevalence of cockroach sensitivity varies between 30% and 70%. Geographical differences exist with regard to cockroach allergen exposure and sensitivity within countries and between countries. No data are available for Africa in this regard. Currently the diagnosis of cockroach sensitivity in southern Africa relies mainly on the detection of specific IgE to *Blattella germanica* (German cockroach), while a number of other species are found close to human dwellings. The aim of this study was to investigate the prevalence and distribution of sensitisation to three different cockroach species among subjects residing in four different geographical regions in southern Africa.

Method: The patient cohort was selected from allergic children test-

ed skin-prick test positive to *B. germanica*. Twenty children (age 2-17 years) each from Cape Town (Red Cross Hospital), Durban (Westville Hospital) and Pretoria (Military Hospital) were analysed for specific IgE antibodies to three different cockroach species. The specific IgE response in serum samples was quantified by using the UniCAP® System for *Blattella germanica* (i6), *Periplaneta americana* (Ri206) and *B. orientalis* (Ri207). In addition 40 adult allergic patients from Harare (Zimbabwe) were analysed for cockroach specific IgE antibodies. Cross-reactivity studies on selected subjects were performed by Cockroach-ImmunoCAP (*B. germanica*)-inhibition assay with house-dust mite extract, as previously described.

Results: Strong IgE reactivity particular to *B. germanica* was found among subjects residing in Pretoria and Harare. By contrast strong IgE responses to other cockroach species, *Periplaneta americana* and *Blatta orientalis*, were observed in subjects living in Cape Town and Durban. The levels of specific IgE antibodies to all three cockroach species appeared to be higher in Cape Town than those from the other three cities investigated. Monosensitivity to all three cockroach species was observed and minimal crossreactivity to house-dust mite.

Conclusions: These data show that allergy to *P. americana* and *B. orientalis* are an important diagnostic consideration in temperate and coastal regions of southern Africa, whereas sensitisation to *B. germanica* appears to predominate in regions of higher altitude such as Pretoria and Harare.

ANISAKIS PEGREFFII CONTAINS POTENT SENSITISING ANTIGENS

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Background: *Anisakis pegreffii*, a nematode that infests fish, is able to cause both infection and allergies in man. The present study examines allergic responses against *A. pegreffii* in South African fish processing workers, and uses gene deficient mice to investigate the immunology of *A. pegreffii*.

Methods: 578 fish processing workers were tested for *Anisakis* sensitivity and specific IgE levels using skin-prick testing and RAST. Western blots were performed against *A. pegreffii* crude extract using serum from sensitised workers, non-sensitised controls and infected mice. Wildtype, IL-4 knockout and IL-4Rα knockout mice were infected with live *A. pegreffii* larvae and the cytokine and antibody responses measured by ELISA. Sensitised mice were challenged orally with *A. pegreffii* extract and examined for symptoms, histopathology and mast cell proteases.

Results: 8% of workers were sensitised to *Anisakis*, producing specific IgE against a wide range of allergens. A similar pattern of allergen recognition was found in mice infected intraperitoneally with *A. pegreffii*. The worm induced a strong Th2/type 2 response with IL-4, IL-5, IL-9, IL-13 and antigen specific IgG1/IgE, typical for many gastrointestinal helminth infections. Importantly, when challenged orally with *A. pegreffii* extract, mice produced a response typical of food allergy, with itching, diarrhoea and airway mucus hypersecretion. IL-4 knockout mice had reduced symptoms, while symptoms were completely abrogated in IL-4 receptor-alpha knockout mice. Surprisingly, oral dosing of mice with *A. pegreffii* alone and no adjuvants resulted in production of type 2 antibodies IgG1 and IgE.

Conclusions: These data show that *A. pegreffii* contains potent sensitising allergens, and that both IL-4 and IL-13 play a role in *Anisakis* allergy.

ALLERGEN SENSITIVITIES OF PATIENTS WITH ALLERGIC RHINITIS PRESENTING TO THE ENT CLINIC AT UNIVERSITAS ACADEMIC HOSPITAL, BLOEMFONTEIN

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Aims: The aims of the study were to review the presenting symptoms and allergen sensitivities as determined by skin-prick testing of patients with allergic rhinitis presenting to the ENT clinic at Universitas Academic Hospital, Bloemfontein.

Methods: The records of all patients with allergic rhinitis confirmed

by skin-prick testing at the ear, nose and throat clinic at Universitas Academic Hospital between 1 January 2004 and 31 January 2005 were reviewed.

Results: A total of 97 patients were identified. The age of the patients ranged between 4 and 71 years (median 26 years). There were 65 (67%) females and 32 (33%) males. Nasal obstruction was the most common symptom, being present in 78% of patients, followed by watery rhinorrhoea (57%) and sneezing (40%). Allergen sensitivities were: Bermuda grass (55%), maize pollen (55%), Rye grass (36%), *Alternaria alternata* (25%), *Platanus acerifolia* (24%), *Dermatophyoides pteronyssinus* (23%), dog epithelia (20%), cat epithelia (14%), *Lepidoglyphus destructor* (13%) and *Olea europaea* (13%). Bermuda grass was a significantly more common allergen in

patients living in an urban environment compared to a rural environment, while there was no significant difference in the prevalence of the other allergens when comparing patients from an urban as opposed to a rural environment. Sensitisation to *Lepidoglyphus destructor* was not significantly more common in patients living on farms. There was no association between sensitisation to *Lepidoglyphus destructor* and sensitisation to *Dermatophyoides pteronyssinus*. 16 patients (16.4%) had asthma and 8 patients (8.2%) had eczema.

Conclusions: Nasal obstruction is the most common presenting symptom of allergic rhinitis. Bermuda grass, maize pollen and Rye grass are the most common causative allergens in the Free State.

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