

KIDZ 'N ALL CONFERENCE ABSTRACTS

ALLERGY SOCIETY OF SA PRESENTATIONS, CAPE TOWN

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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.

ALLSA INVITED PRESENTATIONS

THE CLINICAL RELEVANCE OF POLLEN MONITORING IN THE WESTERN CAPE

DM Berman,¹ S de Villiers,² C Motala¹

¹Allergy and Respiratory Unit, Red Cross Children's Hospital, Cape Town, ²Department of Environmental and Geographical Science, University of Cape Town, South Africa,

Pollen and fungal spore levels have been continuously monitored for 20 years at Red Cross Children's Hospital in Cape Town, a suburban area close to Table Mountain. In addition, airspora have been monitored at Table View, a town on the western coastline, since 1994. Two additional Burkard spore traps have been run for shorter periods in a semi-rural inland area, as well as in an urban area. The weather patterns in Cape Town and surrounding areas of the Western Cape vary widely, because of the long coastlines and mountainous terrain that exist within a relatively small area. It is therefore important to assess the different pollen and fungal loads in several areas, despite the fact that they might be in fairly close proximity to each other.

The asthma prevalence rate for 12-14 year olds resident in Cape Town was found to be 15% in 1995. Patients attending the Allergy Clinic at our hospital are skin-prick tested to a panel of inhalant allergens, which include locally occurring grasses, trees and fungal spores in accordance with the findings of the aerobiological data. Grass is an important inhalant allergen and in severe cases, immunotherapy is advised. Charts of the seasonality of the wild grasses are consulted in order to choose the months when the grass count is consistently <10 grains/m³. Most of these grasses have been introduced and naturalised, but the allergenicity of a limited number of African grasses has been studied.

Start times for flowering times for the major grasses and allergenic trees, as well as the total pollen count vary according to the area and are compared. In addition, a petro-chemical refinery is situated close to the monitoring site at Table View, where some pollutants are also continuously monitored and published in local newspapers together with pollen and fungal spore levels.

The allergologists in Cape Town at all the academic hospitals as well as those in private practice are assisted, not only by the reports of pollen and fungal spore levels but by the interpretation of these data., which should not be examined in isolation but against the background of other inhalant allergens that are known to occur in the area, such as house dust mite. Although pollen sensitivity is seasonal >80% of the allergic children attending our clinic are sensitive to *D. pteronyssinus*. As few of these are monosensitive, they frequently have severe rhinitis during the peak pollen months.

An interpretation of the pollen and fungal spore report as well as a bar chart showing these levels has assisted in the diagnosis and treatment of allergic rhinitis in the Western Cape and this service is currently being extended to other regions.

The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, rhinoconjunctivitis and atopic eczema: ISAAC. *Lancet* 35: 1225-1232.

Prescott RA, Potter PC. Allergenicity of the indigenous grasses of Southern Africa. *ACT* 2000; 12/6: 282-287.

ANTI-IgE THERAPY

EM Irusen

Lung Unit, Dept of Internal Medicine, University of Stellenbosch, Tygerberg Academic Hospital, Tygerberg, South Africa

Allergy is a significant triggering factor in the classic allergic disorders of both children and adults alike. In IgE-mediated reactions, sensitisation occurs when allergen-specific B cells are stimulated and switched to IgE antibody production by interleukin (IL)-4 and IL-13 produced by helper T cells type 2 (TH2). The IgE antibodies act by arming cells bearing either the high-affinity (FcεRI) or low-affinity (FcεRII or CD23) receptor. The subsequent interaction of allergen with IgE-FcεRI complexes on mast cells and basophils causes cross-linking of receptors that triggers the release of a variety of inflammatory mediators, cytokines and chemokines. Therefore, the ability to lower circulating free IgE levels is desirable because most individuals are exposed to multiple allergens to which they are sensitive at any given time. Anti-IgE represents an advanced form of immunomodulation – which directly targets IgE serum antibodies, thus inhibiting the central mechanism of immediate type hypersensitivity reactions.

Omalizumab (Xolair – formerly, rhuMAB-E25-, Genentech, Novartis) is a recently developed humanised monoclonal anti-IgE antibody directed at the FcεRI binding domain of human IgE. It reduces circulating free IgE, thus inhibiting the binding of IgE to mast cells without provoking mast cell activation.

Application of anti-IgE antibodies effectively reduces IgE serum levels regardless of allergen specificity. In mediating these effects, anti-IgE therapy was associated with:

- decreased sputum eosinophil counts
- significant reduction in tissue eosinophils, FcεRI+ cells, CD3+, CD4+ and -CD8+ T lymphocytes, B lymphocytes, and cells staining for IL-4+ but not with improvement in airway hyperresponsiveness to methacholine
- inhibition of both the early- and late-phase response to allergens.

This treatment has been successfully tested in patients with allergic rhinitis, asthma and food allergy, showing significant efficacy in reducing symptom scores and rescue medication use. In clinical trials of moderate to severe asthma, omalizumab allowed a reduction in inhaled corticosteroid dosage while improving peak flows and reducing exacerbations, particularly in patients at high risk of serious asthma-related morbidity and improved quality of life scores. When added to existing therapies of patients with more severe asthma, omalizumab also improved asthma control.

A combination of anti-IgE and allergen-specific immunotherapy was shown to be superior to each single treatment protocol in children and adolescents with allergic rhinitis, as demonstrated by efficacy of symptom scores and rescue medication use.

In perennial allergic rhinitis, omalizumab was safe and well tolerated in providing effective control of symptoms and improved RQoL while simultaneously minimising reliance on rescue antihistamines.

Additionally, in asthma patients with concomitant perennial allergic rhinitis, omalizumab provides improvement in these comorbid conditions. Patients who benefit most when omalizumab is administered as add-on therapy are those receiving high doses of BDP, those with a history of frequent emergency asthma treatment, and those with poor lung function. Patients should be treated with omalizumab for a minimum duration of 12 weeks to adequately assess their therapeutic responses.

In a meta-analysis of the Cochrane Airways Group Asthma trials register, treatment with intravenous and subcutaneous omalizumab resulted in a 98-99% reduction in free IgE, reductions which were not observed following placebo treatment. Significant increases in the number of participants who were able to reduce (>50% reduction in daily corticosteroid use (four trials): odds ratio (OR) 2.50, 95% confidence interval (CI) 2.02-3.10; or completely withdraw their daily steroid intake (four trials): OR 2.50, 95%CI 2.00-3.13, were observed. Participants treated with omalizumab were less likely to suffer an asthma exacerbation (stable steroid phase (three trials): OR 0.46, 95%CI 0.35-0.61; steroid reduction phase (three trials) OR 0.46, 95% CI 0.36-0.59)

Omalizumab is well tolerated by asthma patients and represents a new approach to the treatment of moderate to severe asthma and other allergic manifestations. Anti-IgE therapy is limited by high costs and the necessity for permanent or every-season treatment; it is likely that it will first be used at the more severe end of the spectrum of the allergic diatheses.

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Hamelmann E, Rolinck-Werninghaus C, Wahn U. Is there a role for anti-IgE in combination with specific allergen immunotherapy? *Curr Opin Allergy Clin Immunol* 2003; **3**(6): 501-10.

Holgate ST, Chuchalin AG, Hebert J, *et al.* Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. *Clin Exp Allergy* 2004; **34**(4): 632-8.

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Bousquet J, Wenzel S, Holgate S, Lumry W, Freeman P, Fox H. Predicting response to omalizumab, an anti-IgE antibody, in patients with allergic asthma. *Chest* 2004; **125**(4): 1378-86.

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OCCUPATIONAL AND PARA-OCCUPATIONAL ALLERGIES: FOULING ONE'S OWN NEST?

Mohamed Jeebhay

Occupational and Environmental Health Research Unit, School of Public Health and Family Medicine, University of Cape Town, South Africa

Occupational allergies that result from immune hypersensitivity to substances encountered in the work environment constitute 15% of all occupational diseases. Occupational allergies are commonly caused by hazardous chemical substances (usually low molecular weight) or biological agents (usually high-molecular-weight proteins). The clinical manifestation of occupational allergies are no different from allergies caused by common inhalants. High-molecular weight agents usually cause an IgE-mediated response resulting in rhinitis, conjunctivitis, urticaria and asthma. Various studies on the social and economic impact of occupational allergies indicate that reactions such as occupational asthma are often severe enough to cause considerable inconvenience, discomfort, and even abandonment of trade.

While 10-15% of adult asthma can be attributable to occupational exposure, work-related factors are responsible for up to one third of cases (incidence rate of 17.4 cases/100,000). Worldwide, the most common causes of occupational asthma are cereal flours, enzymes, natural rubber latex, laboratory animals and low-molecular-weight agents (isocyanates and acid anhydrides). Occupational asthma is the third most common occupational lung disease reported in South Africa, originating mainly from health care (e.g. latex), food processing (e.g. grain, flour), motor (e.g. isocyanates) and mine metal refining industry (platinum salts).

Recent studies in various workplace settings in the Western Cape indicate a much higher prevalence of atopy among urban factory workers (45%) vs rural farm workers (25%). The prevalence of sensitisation to common aeroallergens was: house dust mite (16-41%), cockroach (11-22%), rye grass (11-14%) and bermuda grass pollen (5-9%). Sensitisation to occupational allergens varied: 6% to fish (seafood processors), 9% to latex (healthcare workers), 22% to spider mite (grape farmworkers) and 26% to wheat (grain mill workers).

As allergens become ubiquitous in the environment, allergic reactions encountered in the workplace closely mimic patterns in the broader community, resulting in an increasingly blurred distinction between work- and non-work-related disease. Adverse immunological reactions can occur as a result of worker exposure to commonly encountered food allergens in the home and workplace (e.g. seafood, wheat). Workers with known food allergy can become symptomatic as a result of cross-reacting workplace allergens (e.g. latex fruit allergy syndrome). Para-occupational exposures of spouses and children as a result of transport of allergens from the workplace to the home by workers (e.g. flour allergens, laboratory animal allergens, pesticides, spider mites) have emerged as an important issue in contexts of poor workplace hygiene conditions, home laundry of work clothes and home-based 'cottage industries'.

The cornerstones for the prevention of occupational allergies include the introduction of strict regulatory exposure standards, workplace

control measures and epidemiological surveillance. Manufacturer responsibility for product stewardship through detailed product labelling is important to ensure overall public health and safety. Finally, maintaining a high index of suspicion for recognising the contribution of common inhalant allergens as well as exposure to occupational and para-occupational allergens in symptomatic individuals is crucial to the long-term prevention of the morbidity associated with allergic disease.

KEYNOTE ADDRESS: THE RISE IN ALLERGY AND AUTOIMMUNITY: NEW CONCEPTS AND EMERGING MODELS

Susan L Prescott

School of Paediatrics and Child Health, University of Western Australia, Perth, Australia

Although there are clear parallels with the TH1/TH2 paradigm originally described in rodents, the role in human allergic disease development is much less clear. At an individual level, the presence of TH2 responses in allergic disease does not seem to represent a simple polarisation of responses along a TH1-TH2 continuum as previously supposed, and there is no conclusive evidence of impaired TH1 function in either asthma or atopy. In fact, many recent studies suggest that affected individuals are more generally responsive to allergens with increases in both TH1 and TH2 responses. This suggests a breakdown of more fundamental regulatory processes, likely to be common to many aspects of the immune response.

At the population level, the search for an explanation for the recent epidemic increase in allergic disease has previously focused on potential pro-TH2 environmental influences. However, this approach makes it difficult to explain the paradoxical observation that 'TH1 autoimmune diseases' (such as type 1 diabetes) have also increased during the same period. Initially, the associated increase in TH2 allergic disease with progressively 'cleaner' environments was explained in terms of a shift in favour of TH2 responses because of reduced pro-TH1 inducing microbial exposure. An alternative emerging model proposes that altered exposure to bacterial elements (and other modern environmental changes) may be affecting regulatory systems such that they inadequately prevent over-expression of both inappropriate TH1 and TH2 responses in genetically predisposed individuals. This has led to investigation of pathways with known homeostatic and immunomodulatory effects, particularly of IL-10 and TGF- β regulatory pathways. Microbial exposure in early life appears to be important for the development of many cell populations that produce these regulatory cytokines (including CD4+25+ regulatory T cells, epithelial cells, CD8+ T cells and most classes of antigen-presenting cells). It is proposed that altered function of these cells (possibly in association with altered microbial exposure) may impair immune regulatory mechanisms and explain the general rise in many forms of immune disease. This may also explain experimental observations that animals raised in 'germ-free' environments have profound disorders of immune tolerance including both autoimmunity and allergy. Thus, while the 'hygiene hypothesis' may yet hold true, the proposed mechanisms are probably more complex than originally proposed.

Following this rationale, methods of enhancing 'regulatory' pathways are growing in popularity, and range from simple oral administration of probiotic bacteria, injection of mycobacteria to the administration of highly developed plasmid DNA vaccines. Rather than have a specific target in the immune cascade (which is still poorly understood), these strategies appear to act through enhanced regulatory TGF- β and IL-10 responses and may directly reduce airways inflammation in addition to atopic immune responses.

THE ROLE OF DIET AND DIETARY SUPPLEMENTS IN ALLERGY PREVENTION

Susan L Prescott

School of Paediatrics and Child Health, University of Western Australia, Perth, Australia

For many potential reasons, allergic disease appears to be one significant 'price' of modern living. There is a growing need to identify the aetiological factors and to design better prevention strategies to reduce the mounting disease burden. Although most current recommendations for disease prevention focus on allergen avoidance, other environmental factors such as dietary changes may be implicated in the recent increase in allergic disease and provide additional avenues for disease prevention.

Early diet and nutrition are important for many aspects of growth and

development, including immune responses. This presentation will give an overview of the potential influences of dietary and nutritional factors on the development of allergic immune responses in early childhood.

The significantly higher expression of allergic diseases in the 'modern' world suggests that environmental changes (some dietary) may favour 'TH2' allergic responses to allergens, which under other conditions may evoke 'TH1' responses in the same individuals. Early exposure to specific food allergens (in fetal and early postnatal life) has probably changed relatively little, and allergens are increasingly viewed as the 'target' of these responses, rather than the primary cause of allergic disease. It appears more likely that other poorly defined environmental changes may be directly affecting the increase of the 'TH2 propensity' of immune responses. Thus, as well as examining the role of dietary allergens, this discussion will also focus on other dietary factors which have the potential capacity to influence the immune development, including ingested organic pollutants, anti-oxidants, polyunsaturated fatty acids (PUFA), and probiotics. Some of these factors may provide future avenues for primary allergy prevention in pregnancy and early postnatal life, and are already under investigation by a number of groups.

UPDATE ON EARLY IMMUNE DEVELOPMENT

Susan L Prescott

School of Paediatrics and Child Health, University of Western Australia, Perth, Australia

With the disturbing increase in allergic disease, there is a pressing need to determine the aetiology, pathogenesis and safe avenues for disease prevention. This lecture examines new developments in the area of fetal and early postnatal immune maturation. It secondly addresses early predisposing influences and protective factors that may have a future role in allergy prevention.

Many aspects of immune function are less mature at birth. Although neonatal T cells can respond to antigens (including allergens) these responses are atypical and do not appear to represent classic memory responses. The pattern of cytokines produced during activation is also different from mature responses, with a relative dominance of Type 2 cytokines and a profound immaturity of Type 1 signalling. This is partly due to immaturity of APC function, but also appears to be due to intrinsic T cell factors. Reduced production of Type 1 cytokine interferon gamma (IFN- γ) appears to be regulated by hypermethylation of the IFN- γ gene promoter, particularly in CD4 T cells. The factors influencing this are unclear, but *in utero* exposures (such as infection) appear to modify IFN- γ expression, suggesting that the early environment is important in addition to genetic factors. Although immaturity of Type 1 IFN- γ responses appears to be relatively more pronounced in high risk neonates (of allergic parents), the underlying mechanisms are not known. There is growing recognition that this may be an early manifestation of immune dysregulation. In the early postnatal period, these individuals go on to develop increasing Type 2 cytokine responses to allergens, with parallel increases in allergen-specific IgE. However, they also show stronger Type 1 responses (and IgG responses) to allergens compared to non-allergic children. This further suggests that allergy is not simply due to a 'Type 2' polarisation of responses but rather a more fundamental failure of immune regulation, which leads to excessive and inappropriate responses to allergens.

There has also been increasing interest in environmental factors that could influence early immune development, as these may offer strategies for disease prevention. Complex multifactorial genetic and environmental interactions make research in this area difficult, and apparent associations with allergic disease may not be causal in nature. Many current targets for prevention such as early allergen exposure and infant feeding practices, are proving to be ineffective and may not be directly implicated in rising rates of disease. This is leading to new ways of modifying early immune development, including novel vaccination strategies and dietary modifications (which will be discussed in a separate lecture).

THE BURDEN OF ASTHMA IN SOUTH AFRICA – AN UPDATE

Heather J Zar

School of Child and Adolescent Health, Red Cross Children's Hospital, University of Cape Town, South Africa

Asthma is common in South Africa. Measurement of the burden of disease can be assessed using (i) prevalence data and (ii) information on the incidence of fatal and near-fatal asthma. To coincide with

World Asthma Day on 14 May 2004, the Global Initiative for Asthma (GINA) released the *Global Burden of Asthma Report*, a comprehensive study of the prevalence and impact of asthma globally. In this, the prevalence of asthma in South Africa was reported as 8.1% in the general population, ranking 25th in the world. An early study of the prevalence of asthma in school children reported approximately 3% of urban and 0.1% of rural children to have asthma. More recent studies report a striking rise in the prevalence in both urban and rural children with a reduction in the urban-rural gradient. Comparison of the prevalence of self-reported asthma symptoms in 13-14-year-old schoolchildren in Cape Town using a questionnaire as part of the International Study of Asthma and Allergies in Childhood (ISAAC) study done in 1995 and repeated in 2001 also suggests an increasing prevalence in this 7-year period.

Measurement of the incidence of fatal and near-fatal asthma is useful for assessing the burden of disease as these represent a high proportion of the total costs of asthma care and can reflect the quality and accessibility of health services. South Africa is reported to have one of the highest rates of fatal asthma worldwide in the *Global Burden of Asthma Report*, in which the incidence of fatal asthma is reported as 18.5 per 100 000 asthmatics, the fifth highest rate globally. South Africa also ranked fourth highest globally for asthma mortality in the 5-34-year-old age group. Although the incidence of fatal asthma has declined in the past 20 years, the rate still remains much higher than those in developed countries. The incidence of near-fatal asthma in children as assessed by admission to intensive care units has also declined over this period. The incidence of fatal and near-fatal asthma has been strongly correlated with socio-economic deprivation.

The information on asthma prevalence and mortality suggest a considerable burden of disease in South Africa. Further study of the factors contributing to the rising prevalence of asthma is needed. Delineation of poverty-associated factors contributing to asthma mortality, such as poor access to care, inadequate treatment, smoke exposure or lack of appropriate asthma education, is important for development of improved management strategies.

ALLSA POSTER PRESENTATIONS

EVALUATION OF THE TEST FOR MAST CELL TRYPTASE IN ALLERGY TESTING

Bartha Fenenmore, Paul Potter

Allergology Unit, Division of Immunology, Groote Schuur Hospital and ADCRU Laboratory, UCT Lung Institute, Cape Town, South Africa

Objective: To review the utility of the Mast Cell Tryptase Test in the evaluation of serious allergic reactions.

Mast cells play a key role in allergic reactions and they may be found in increased numbers in inflammatory conditions. Upon activation, the mast cells release a variety of mediators that lead to the symptoms of allergic reactions such as systemic anaphylaxis. Among these mediators are histamine and tryptase. Tryptase is released into the circulation after a patient suffers an anaphylactic reaction. The half-life of tryptase released into the circulation is considerably longer than that of histamine. Increased levels of tryptase peak at about 1 hour and can be detected 3-6 hours after the anaphylactic reaction. Levels return to normal within 12-24 hours after release. Once the blood has been taken from the patient the tryptase remains stable in the serum. It is recommended that blood be taken immediately after a reaction, after about 30 minutes to 1 hour, after 2-3 hours, then 5-6 hours and a baseline specimen 14-24 hours later. An increase in tryptase levels followed by a sharp decrease indicates a probable allergic reaction. If the tryptase level remains elevated at high levels, other conditions such as mastocytosis may be indicated.

Method and Results: A total of 221 patients were tested at the Lung Institute and Groote Schuur Hospital from January 2001 to June 2004. 182 were found to have mast cell tryptase levels ranging from <1.0 $\mu\text{g/l}$ to 13.5 $\mu\text{g/l}$, which is considered to fall within the normal limits. 39 patients had levels greater than 13.5 $\mu\text{g/l}$. However, where serial tryptase levels at 2-3 hourly intervals after the event were compared with 'baseline' levels, levels of 2.98 $\mu\text{g/l}$ and 3.32 $\mu\text{g/l}$ suggested that tryptase had been released when levels rose to 8.84 $\mu\text{g/l}$ and 12.6 $\mu\text{g/l}$.

12 patients were tested post mortem and values from 7.0 $\mu\text{g/l}$ to 4275 $\mu\text{g/l}$ were found.

We have found that one of the most useful clinical indicators for tryptase levels is 'intra-operative anaphylaxis'.

The tryptase levels remain stable *in vitro* for many months after the blood has been taken. *In vivo* the levels rise for about 2 hours after the reaction and then return to normal 12-24 hours later. Even when only one specimen can be taken, as in the case of a postmortem specimen, it is a valuable indicator that anaphylaxis was a likely cause of death.

To request a determination of mast cell tryptase levels in serum, 2 ml of clotted blood should be sent to the laboratory.

EVALUATION OF THE CELLULAR ANTIGEN STIMULATION TEST (CAST) VS THE DBPCFC IN A COHORT OF PATIENTS WITH SUSPECTED ADVERSE REACTIONS TO SULPHITES

D Hawarden,¹ B Fenimore,¹ L Hill,² G Poggenpoel,¹ I Schloss,² K Hoffman,² P Potter¹ ¹Allergy Diagnostic and Clinical Research Unit (ADCRU), University of Cape Town Lung Institute, South Africa; ²Nutrition and Dietetics Unit, Groote Schuur Hospital, Cape Town, South Africa

Background: The US FDA defines a food additive as any substance that becomes part of a food product when added directly or indirectly. Sulphites were first used in 1664 as an additive in food. Sulphite sensitivity is difficult to confirm and patients are often placed onto a sulphite exclusion diet without formal confirmation of the diagnosis. We studied a subgroup of patients who consulted ADCRU having had adverse reactions to foods where sulphite seemed to be the most likely trigger. In this group we compared their cellular antigen stimulation tests (CAST) with double blind placebo controlled food challenges for sulphite.

Method: CAST

The cellular antigen stimulation test (CAST) was first described in 1991 and is based on the production of sulphidoleukotrienes by blood basophils which are mediators of the immune response to an antigen. It measures sulphidoleukotriene production following isolation of basophils and antigen challenge *in vitro*. Sulphidoleukotrienes (sLT) LTC₄, LTD₄ and LTE₄ are metabolites of arachidonic acid, previously known as 'Slow Reacting Substances of Anaphylaxis (SRS-A)'. We used potassium metabisulphite (K₂S₂O₅)/E224 at a final concentration of 10 µg/ml as the stimulating antigen.

Method: Sulphite challenge

1. Sulphite elimination diet (including vitamin B₁₂) 48 hours prior to challenge.
2. 1, 5, 10, 15, 25, 50, 75, 100, 150 and 200 mg potassium metabisulphite diluted in preservative-free apple juice (30 ml) for each challenge.
Sulphite/Placebo Challenge → 24hrs → Placebo/Sulphite Challenge
3. Doses administered at 10-minute intervals. Vital signs including PEFR, BP, pulse and clinical symptoms were monitored with each dose.

Results:

1. 20 patients with CAST values below 200 pg/ml were selected. 14 subjects had values <40 pg/ml, and 6 subjects had CAST values of >40 pg/ml.
2. 10/14 patients with negative sulphite CASTs had a positive challenge. Some had more than one symptom.
3. 4/14 patients with a negative CAST did not react to the challenge.
4. 5/6 patients with a positive CAST had a positive food challenge.

Conclusion:

1. Careful history and clinical judgement gave an accurate diagnosis in 75% of cases confirmed by challenge.
2. Using a cut-off of 40 pg/ml an elevated CAST correctly identified 5/6 (83%) of challenge positive subjects as being sensitive to sulphites.
3. With a value below 40 pg/ml (negative CAST), 10/14 subjects (71%) had a positive challenge.

RELATIONSHIP BETWEEN *IN VIVO* AND *IN VITRO* MARKERS OF IgE REACTIVITY IN RELATION TO WORK-RELATED ALLERGIC SYMPTOMS AMONG SEAFOOD PROCESSING WORKERS

M Jeebhay,¹ T Robins,² I Swoboda,³ R Baatjies,⁴ N Balic,³ S Spitzauer,³ AL Lopata³

¹ University of Cape Town, Occupational and Environmental Health Research Unit; School of Public Health and Family Medicine, Cape Town, South Africa; ²University of Michigan, Department of Environmental Health Sciences, Michigan, United States; ³University of Vienna, Institute of Medical and Chemical Laboratory

Diagnostics, AKH, Vienna, Austria; ⁴University of Cape Town, Occupational and Environmental Health Research Unit, School of Public Health and Family Medicine, Cape Town, South Africa; ³University of Cape Town, Division of Immunology, Faculty of Health Sciences, NHLS, Cape Town, South Africa

Background: Fish and fish products are an important cause of IgE-mediated allergy in the domestic and occupational setting. Parvalbumins, small calcium-binding muscle proteins, have been identified as the major cross-reactive fish allergen. This study determined the association between work-related allergic symptoms, skin-prick test (SPT) to fish extract, specific IgE levels to fish and recombinant parvalbumin among seafood processors.

Methods: A cross-sectional study of 626 employed workers involved in fish canning (pilchard), fishmeal processing (anchovy) and rock-lobster processing was conducted. A modified ECRHS questionnaire and methacholine challenge tests were performed using ATS guidelines. SPT used common airborne allergens (ALK), fresh fish and rock lobster extracts. Serum specific IgE to carp and recombinant parvalbumin were quantified by ELISA.

Results: The average age was 36 years, 64% were women and 51% current smokers. The prevalence of atopy (positive SPT to ≥ 1 common aeroallergen) was 37%. Common work-related symptoms were ocular-nasal (27%), asthma (15%) and skin symptoms (13%). SPT revealed 3% of workers sensitised to either pilchard or anchovy (6% to 1 fish species) and 2% to rock lobster. Furthermore, 22% of workers demonstrated NSBH (PC₂₀ ≤ 8 mg/ml). Sensitisation to fish on SPT was significantly associated with self-reported allergy to seafood (OR=3.2; CI: 1.1-8.8; p=0.027) and work-related ocular-nasal symptoms (OR=2.1; CI: 1.1-4.2; p=0.034). The prevalence of elevated IgE (defined as 1.5 times the negative control) to recombinant parvalbumin was 24% and to carp 26%. Among the 32 workers with positive SPT to fish, 16% had elevated IgE levels to parvalbumin and 19% to carp. There was a significant degree of concordance (kappa=0.35; p<0.001) between carp and parvalbumin. A borderline association (OR=4.1; CI: 0.9-18.6; p=0.068) was demonstrated between elevated IgE levels to parvalbumin and fish allergic asthma (positive SPT to any fish and NSBH).

Conclusion: Among fish processors SPT using fresh fish extracts appear to be reliable predictors of self-reported seafood allergy and work-related ocular-nasal allergic symptoms. Furthermore, the presence of elevated IgE antibody levels to recombinant parvalbumin could possibly be used as a marker for fish allergic asthma.

HDM-STIMULATED IL13 RELEASE IN ATOPIC ASTHMATIC CHILDREN WITH A HIGH PREVALENCE OF ASCARIS INFESTATION

B Nurse,¹ C Motala,² PC Potter³

¹Allergy Unit¹ & Allergy Clinic,² NHLS,¹ Groote Schuur³ & Red Cross Children's Hospital,² University of Cape Town, Western Cape, South Africa

Background: Raised levels of the TH2 cytokine IL13, which is implicated in mucus production and bronchial hyperresponsiveness in atopic respiratory disease, is also induced in response to helminth infections. Infestation with the intestinal helminth *Ascaris lumbricoides* is high in children of low-income communities in the Western Cape, while atopic diseases appear to be increasing in both high- and low-income communities. House dust mite (HDM) is the major allergen affecting children in the area. We characterised HDM-stimulated IL13 release from peripheral blood mononuclear cells (PBMC) in children with a high incidence of *Ascaris* infestation.

Method: Patients (n=46; mean age 11.8 years) with chronic atopic asthma, and 27 asymptomatic controls (mean age 10.5) were assessed. The controls* were divided into Sensitised Controls (n=11; with allergen IgE) and Normal Controls (n=16; no allergen IgE). Specific IgE to 10 common allergens and *Ascaris* were measured (Pharmacia UniCAP; specific IgE levels >0.35 kU/L are positive). HDM-stimulated lymphocyte proliferation and IL13 release was analysed. PBMC (2 x 10⁵/200 µl RPMI with 10% AB serum/well) were stimulated for 7 days with HDM.

Results: HDM-stimulated IL13 release in the Atopic Asthmatics (median 113 pg/ml) was not significantly different to that in the Sensitised Controls (83 pg/ml; p=1.0) and significantly increased relative to the Normal Controls (12 pg/ml; p=0.005). Proliferation was not significantly different between the groups (p=0.5). *Ascaris* IgE (range 0.4 -37 kU/L) was detected in 61% of Atopic Asthmatics, 82% of Sensitised Controls and 19% of Normal Controls. The Atopic Asthmatics with and those without *Ascaris* IgE had no significant difference in HDM-stimulated proliferation (p=0.7) or IL13 release

($p=0.3$). Both groups had a similar profile of allergen sensitisation. There was also no correlation between *Ascaris* IgE levels and HDM-stimulated IL13 release (Atopic Asthmatics $r=-0.2$; $p=0.2$).

Conclusions: IL13 release was significantly increased in the Atopic Asthmatics versus the Normal Controls but was not different from that in the Sensitised Controls. This finding agrees with recent evidence that increased IL13 release is associated with allergen IgE sensitisation not with atopic disease per se. There was no evidence that the presence of relatively low levels of *Ascaris* IgE, as evidence of past or recent infestation, influenced allergen-stimulated release of IL13.

*Combined control group:

Those with and without *Ascaris* IgE didn't have similar atopic profile.

The majority of those with *Ascaris* IgE also had allergen IgE (9/12) (9 sensitised controls & 3 normal controls), (ie 2 differences between the groups, ie allergen & *Ascaris* IgE) (too few in each control group to divide each into +/- *Ascaris*)

LEVOCETIRIZINE RELIEVES SYMPTOMS OF PERENNIAL ALLERGIC RHINITIS IN CHILDREN

Paul C Potter,¹ and the Paediatric Rhinitis Study investigators

¹Allergy Unit, Groote Schuur Hospital, Observatory, Cape Town, South Africa

Background: Perennial allergic rhinitis (PAR) is difficult to treat and affects Health-Related Quality of Life (HRQoL) in adults. Few data are available in children. Levocetirizine (LCTZ) is a new antihistamine approved in Europe for the treatment of PAR as from 6 years of age.

Methods: A 4-week double-blind placebo-controlled (PB) study was performed including, at some centres, a measurement of nasal resistance. A HRQoL assessment, using the Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) was performed in all children. Children, using an electronic diary, and investigators gave their appreciation of the evolution of the disease.

Results: 306 children (61% boys), aged 6-14 years (mean age 9.9), were randomised. All were sensitised to house dust mite and 47.4% were asthmatic. Over the first 2 weeks of treatment, LCTZ patients showed a relative improvement of 90.9% as compared to PB ($p=0.001$), i.e. the effect of LCTZ was almost twice the PB effect. This reduction remained statistically significant over the whole study duration ($p=0.008$). PRQLQ results confirmed this improvement, with LCTZ being constantly superior to PB. Rhinomanometry measurements showed an effect in nasal congestion that needs further analysis. Investigators considered that 57% of the LCTZ group patients were moderately or markedly improved. No serious unexpected adverse event occurred.

Conclusion: This study demonstrates the efficacy of LCTZ in 6-12-year-old children on symptoms score and quality of life. LCTZ is very well-tolerated and provides a global relief to PAR symptoms in children.

LONG-TERM CONTROL OF ATOPIC DERMATITIS WITH PIMECROLIMUS CREAM 1% IN INFANTS: A 2-YEAR COHORT STUDY

K Papp,¹ Paul C Potter,² A Kapp,³ Y de Prost,⁴ HP Goertz,⁵ C Paul⁵

¹Probit Medical Research, Waterloo, Ontario, Canada

²Allergy Diagnostic and Clinical Research Unit, Cape Town, South Africa

³Hannover Medical University, Hanover, Germany

⁴Necker Hospital for Sick Children, Paris, France

⁵Novartis Pharma AG, Basel, Switzerland

Data are presented from an 18-month interim analysis (part of a 1-year extension to a double-blind study) of 91 infants, aged 3-23 months (at inclusion), with mild to severe atopic dermatitis, who received pimecrolimus cream 1% (Elidel®) bid at the first signs and symptoms of disease. Response to vaccination was assessed by measuring antibody titre levels for tetanus, diphtheria, rubella and measles. The median change in the Eczema Area and Severity Index (EASI) from baseline to the 18-month analysis showed a reduction of 89%. Most patients had minimal residual disease as assessed by EASI and body surface area (BSA) involvement at 18 months. The mean BSA affected was 8.8% at 18 months vs 27.6% at inclusion. 57% of patients had an Investigators' Global Assessment score of 0 or 1 (clear or almost clear) at the 18-months analysis. Pimecrolimus cream 1% was well tolerated: no patients discontinued as a result of adverse events. There was no relationship between exposure to pimecrolimus and immune response to any of the four vaccinations assessed. In total, 82% (rubella), 83% (diphtheria), 89% (measles)

and 91% (tetanus) of patients had protective antibody titres to vaccination vs 61-80% (rubella), 79-92% (diphtheria) and 76-82% (measles) in the general population (no comparison was available for tetanus). Atopic dermatitis continues to improve over time under long-term treatment with pimecrolimus, while safety is maintained with no effect on the ability of atopic infants to generate an immune response to vaccination.

POLLEN AEROALLERGEN SENSITISATION AND EFFICACY OF FEXOFENADINE IN CHILDREN FROM THE SOUTHERN HEMISPHERE

Paul C Potter,¹ Lisanti M,² Groenewald M,³ Portes R,⁴ Weinberg E,⁵ Vucovich P,⁶ Puterman A,⁷ Baena-Cagnani C,⁸ Hardy P,⁹ Ruuth E⁹

¹Allergy Diagnostic and Clinical Research Unit, Cape Town, South Africa

²Institute of Allergy and Immunology, Mendoza, Argentina

³1 Military Hospital, Pretoria, South Africa

⁴Center for Asthma, Allergy and Immunology, Buenos Aires, Argentina

⁵Allergy Clinic, Red Cross Children's Hospital, South Africa

⁶Hospital Italiano, Córdoba, Argentina

⁷Kingsbury Hospital, Cape Town, South Africa

⁸Division of Respiratory Medicine, Paediatric Hospital, Catholic University of Córdoba, Argentina

⁹Aventis Pharma, Cedex, France

Rationale: Allergen sensitisation is an important risk factor for allergic diseases, including allergic rhinitis. This study reports the sensitisation status, and efficacy of fexofenadine (FEX), in a subset of children (aged 6-11 years) from the Southern Hemisphere with seasonal allergic rhinitis (SAR) enrolled into a large, placebo-controlled, randomised, parallel-group study.

Methods: For randomisation, children required a positive skin-prick test to at least one pollen allergen for the current season and concordance to that specific allergen in *in vitro* IgE testing. Specific IgEs were determined by the fluoro enzyme immuno assay; positive IgE was defined as IgE class =2 (>0.7 kUA/L). Analysis was performed on the modified intention-to-treat (mITT) population, treated with either FEX HCl 30 mg BID or placebo. Efficacy was evaluated as the overall mean change from baseline in 12 hour reflective total symptom score (TSS).

Results: A subset of 303 subjects (FEX, n=146; placebo, n=157), from 40 centres in Argentina, Australia, Chile, Uruguay and South Africa, was analysed. Sensitisation to pollen allergens assessed by plant category showed that grasses were the most common group of allergens (>93%); sensitisation to weeds was 8.9% for FEX and 17.8% for placebo; sensitisation to trees was 20.5% for FEX and 20.4% for placebo. FEX significantly improved the mean change from baseline in TSS compared with placebo ($p<0.05$).

Conclusions: In this subset of children from the Southern Hemisphere, grasses were the most common groups of sensitising allergens. Furthermore, FEX significantly improved the symptoms of SAR in this population of children.

ALLSA ORAL PRESENTATIONS

PROLONGED BREASTFEEDING AND MATERNAL SMOKING INFLUENCE ATOPY IN CHILDREN FROM A POOR URBAN COMMUNITY

^{1,2}Obihara CC, ¹Marais BJ, ¹Gie RP, ³Potter P, ³Bateman E, ⁴Lombard CJ, ¹Beyers N, ³Kimpen JLL

¹Centre for TB Research and Education (CENTRE), Department of Paediatrics and Child Health, Faculty of Health Sciences, Stellenbosch University, Stellenbosch, South Africa

²Wilhelmina Children's Hospital, University Medical Center, Utrecht, The Netherlands

³University of Cape Town, Cape Town, South Africa

⁴Medical Research Council of South Africa, Cape Town, South Africa

Background: The protective effect of breastfeeding against the development of atopic disease in children remains controversial, with few reports from developing countries. We investigated the association between atopy in children and breastfeeding duration, maternal smoking and parental atopic history in a poor urban community.

Methods: The study area is an epidemiological field site with a population of 39 000, in the Western Cape Province of South Africa. The notification rate of tuberculosis (total cases) is 900 per 100 000. The prevalence of asthma and allergic rhinitis in children is about 16%, and eczema 9%. A 15% random sample of the population was studied. Data on 861 children aged 6-14 years were collected. The children received a tuberculin skin test (TST) and completed the ISAAC questions on atopy and questions on breastfeeding duration, maternal smoking during and after pregnancy and parental atopic history. The results were corrected for the effect of clustering due to the sampling method and for possible confounders.

Findings: The prevalence of any atopy (adjusted OR= 0.57; 95% CI 0.38-0.86) and hay fever (adjusted OR= 0.58; 95% CI 0.33-1.00) was significantly lower in the children with prolonged (= 6 months) breastfeeding and there was a trend towards lower prevalence of asthma (adj. OR= 0.92; 95% CI 0.59-1.43) and eczema (adj. OR= 0.72; 95% CI 0.44-1.18), but these were not statistically significant. Breastfeeding for 12-24 months was associated with less atopy (any atopy) than breastfeeding for 6-12 months when compared with breastfeeding less than 6 months; for any atopy ([OR 0.52, 95% CI 0.28-0.97] vs. [0.49; 0.28-0.87]) and hay fever ([OR 0.73; 0.34-1.59] vs. [0.40; 0.17-0.90]). Children with a parental atopic history reported significantly more atopy. The protective effect of prolonged breastfeeding was significant in children without a parental history of atopy, but this effect disappeared in children with a parental atopic history.

Maternal smoking during and after pregnancy was associated with a higher asthma prevalence in the children with this exposure (OR = 3.38, 95% CI 1.45-7.89 and OR= 1.96; 95% CI 1.24-3.08 respectively), irrespective of parental history of atopy.

Interpretation: These results, obtained from the study of children in a poor urban setting in a developing country, confirm the protective effect of prolonged breastfeeding on the development of atopic diseases and in particular hay fever. However, the over-riding influence of both genetic and other environmental factors, in particular the importance of maternal smoking as a risk factor of asthma is confirmed.

Recommendations: Advice would be to encourage prolonged breastfeeding to reduce atopic diseases in children and to intensify the campaign against maternal smoking (during and after pregnancy) particularly in developing countries.

PREVALENCE OF ATOPIC DERMATITIS IN XHOSA CHILDREN LIVING IN RURAL, PERI-URBAN AND URBAN AREAS

G Todd,¹ N Saxe,¹ J Milne,¹ S Tolosana,¹ H Williams²

¹Division of Dermatology, University of Cape Town and Grootte Schuur Hospital

²University of Nottingham, United Kingdom

Aim: It is still unclear if a true urban/rural gradient exists for the occurrence of atopic dermatitis AD.¹ The objective of this study was to determine the prevalence of AD in Xhosa children living in the Transkei (rural), informal migrant settlements around Cape Town (peri-urban) and in stable urban Langa. This was done in an attempt to establish if an urban/rural gradient exists for the occurrence of AD.¹

Method: Three cross-sectional surveys of at least 1 000 children aged 3-11 years in each of the settings using sampling frames based on local maps. Because of difficulties in translating some commonly used questions about AD into the Xhosa language, AD prevalence was determined by the presence or absence of typical signs based on the direct examination of the skin by trained dermatologists. The UK diagnostic criteria were also used and compared with the clinical.

Results: In all, 3 058 children participated in the study, representing an overall response rate of 99.9%. All of the children were black Africans. The point prevalences of AD according to a dermatologist were 0.7%, 1.1% and 3.7% in rural, peri-urban and urban settings respectively, representing an increased risk of AD for those living in urban Cape Town of 3.95 (95% CI 2.28-6.83, p<0.0001) when compared with the other locations.

This study provides evidence to suggest that moving from a rural area characterised by open housing and subsistence farming to an urban location is associated with a modest increased risk of AD. Another striking finding of the study is that AD is very rare indeed in Xhosa children living in rural settlements. Further study of these communities may identify important protective factors in the environment that could lead to disease prevention.

A comparison between clinical findings and UK diagnostic criteria

revealed similar differences, although the UK criteria overestimated the point prevalence, probably because of the high prevalence of other itchy skin diseases in these communities.

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THE PREVALENCE OF ASTHMA, ALLERGIC RHINITIS AND ATOPIC ECZEMA (ISAAC PHASE 3 STUDY) IN ADOLESCENTS IN CAPE TOWN AND COMPARISON WITH ISAAC 1

HJ Zar,¹ RI Ehrlich,² EG Weinberg¹

¹School of Child and Adolescent Health, Red Cross Childrens Hospital and ²School of Public Health, University of Cape Town, South Africa

Aim: The prevalence of asthma and allergic disease in children has been increasing globally. The aim of this study was to investigate the prevalence of asthma, allergic rhinoconjunctivitis and atopic eczema in South African adolescents and to compare this to the prevalence measured 7 years earlier.

Methods: Cross-sectional survey of self-reported symptoms in 13-14-year-old schoolchildren using a standardised ISAAC written and video questionnaire as part of the multicentre International Study of Asthma, Allergic rhinitis and Eczema (ISAAC) phase 3. A random sample of schools within the Cape Metropole area was selected; the study was conducted from March to September 2002. Prevalence rates were compared with those obtained in ISAAC phase 1 done in 1995 in the same geographical area.

Results: 6 036 pupils from 53 schools participated in the study; of these 5 165 (85.6%) and 5 136 (85.1%) completed the written and video questionnaires respectively. Within the prior 12 months, wheezing was reported by 15.5%, exercise-induced wheeze by 32% and severe wheezing by 7.6% on the written questionnaire. The prevalence of these symptoms, as reported from the video questionnaire was 8.2%, 12.8% and 6% respectively; these rates were higher than those reported in ISAAC 1 (table). The prevalence of nasal symptoms within the prior 12 months (34.4%) and eczema symptoms (21.6%) also increased (table). However, a diagnosis of asthma ever had been made in 11.1% which was lower than that in ISAAC 1 (13.3%), p<0.001. Thirty-four per cent of respondents reported that nasal symptoms had limited their activity within the past 12 months of which 12.8% had moderate or severe impairment. Sleep disturbance within the prior 12 months attributable to eczema was reported in 19.2%; 7.1% had this once or more a week.

Conclusion: The prevalence of asthma and atopic eczema in adolescents has increased over the past 7 years in this geographical area. Allergic diseases are common in this group of adolescents and may significantly impair their quality of life.

Table: Prevalence of asthma, rhinitis and eczema symptoms in the prior 12 months and comparison between ISAAC 3 and ISAAC 1

	ISAAC 3 (2002)	ISAAC 1 (1995)	p
Written questionnaire			
Wheezing	15.5%	16.0%	0.5
Exercise-induced wheeze	32.0%	21.5%	<0.001
Severe wheeze	7.6%	5.2%	<0.001
Nasal symptoms	34.4%	33.2%	0.17
Flexural rash*	21.6%	8.9%	<0.001
Video questionnaire			
Wheezing	8.2%	6.4%	<0.001
Exercise-induced wheeze	12.8%	11.5%	0.048
Severe wheeze	6.0%	5.1%	0.032

* at any time