

ALLSA CONGRESS ABSTRACTS

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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.

ORAL PRESENTATIONS – FREE PAPERS

PREDICTORS OF OBSTRUCTIVE LUNG DISEASE AMONG SEAFOOD-PROCESSING WORKERS ALONG THE WEST COAST OF SOUTH AFRICA

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Background: This study examines the patterns and the prevalence of obstructive lung disease (asthma and COPD) and associated risk factors in a working population of seafood-processing workers along the West Coast of the Western Cape.

Methods: A cross-sectional study was conducted on 643 currently employed workers in two fish processing plants working in fish canning and fishmeal processing. A modified version of the European Community Respiratory Health Survey (ECRHS) questionnaire was used. Skin-prick tests (SPT) used extracts of common airborne allergen. Lung function spirometry and methacholine challenge tests (tidal breathing method) were conducted using Vitalograph S-model bellows volume-time spirometers according to ATS guidelines. Serum omega-3 and omega-6 levels were also analysed to examine the association between dietary fatty acids and asthma outcomes.

Results: The overall prevalence of asthma symptoms (asthma attack/dyspnoea causing sleep disturbance/tight chest causing sleep disturbance in the past 12 months) was 11%. The prevalence of non-specific bronchial hyperresponsiveness (PC20 < 8 mg/ml or >12% increase in FEV1 post bronchodilator) was 26% while the prevalence of current asthma diagnosis, defined as recent wheeze and the presence of nonspecific bronchial hyperresponsiveness (NSBH) was 32%. Atopy (defined as a positive SPT to one or more common aeroallergens) was present in 37% of the population. The prevalence of COPD symptoms (reporting a chronic productive cough for 3 months in 2 consecutive years) was 3% while those with obstructive impairment on spirometry (FEV1/FVC <70%) comprised 5% of the population. There were 13% with evidence of both obstructive impairment and a post-bronchodilator FEV1 <80% predicted, providing a better reflection of the true prevalence of COPD. Logistic regression found that a history of chronic bronchitis, chest infections in childhood, work-related asthma or ocular-nasal symptoms were also significantly associated with all asthma outcomes. In the unadjusted analysis, atopy on its own, or specific sensitisation to house-dust mite (HDM) or one of the indoor allergens were also significantly associated with all asthma outcomes. Omega-6 series fatty acid levels of linolenic acid (18:2), dihomo-gamma linoleic acid (20:3) and total omega-6 were positively associated with NSBH or a diagnosis of current asthma. In the omega-3 series, eicosapentaenoic acid (20:5), and docosapentaenoic acid (22:5) were found to be negatively associated (protective effect) with NSBH and a diagnosis of current asthma. The predictors of COPD followed a similar pattern but were not consistently associated across all COPD outcomes.

PREDICTORS OF WORK-RELATED SYMPTOMS, ALLERGIC SENSITISATION AND OCCUPATIONAL ASTHMA AMONG SUPERMARKET BAKERY WORKERS

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Background: A recent study among British supermarket bakery workers reported a high risk of developing work-related asthma. This study aimed to determine the prevalence and predictors of work-related symptoms, allergic sensitisation, non-specific bronchial hyper-responsiveness (NSBH) and baker's asthma in small bakeries of a supermarket chain store in South Africa.

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) and measuring serum specific IgE to cereal flour allergens (wheat, rye, barley, soya, oats, corn flour), fungal alpha-amylase, peanut and storage mite. NSBH was assessed using the Medic Aid Pro Nebulizer Dosimeter method.

Results: The mean age of bakers was 32 years and 47% were current smokers. The prevalence of atopy (positive skin-prick test (SPT) to ≥ 1 common aeroallergen) was 42%. Common work-related symptoms were ocular-nasal (31%) and chest tightness/wheezing (17%). A quarter (27%) of bakers had positive SPT to ≥ 1 cereal flours/additives with the most common sensitisers being cereal flours such as wheat and rye (16%) and the lowest being alpha-amylase (3%). A higher proportion had elevated IgE levels to wheat (26%), rye (24%) and alpha-amylase (4%). There were 22% of workers who demonstrated evidence of bronchial responsiveness with two-thirds of these having airway obstruction and half of these having probable occupational asthma (11%). Doubling the employment duration was associated with an increased odds for specific IgE reactivity to wheat (OR: 1.28, CI: 1.01 – 1.62), rye (OR: 1.37, CI: 1.07 – 1.75), and allergic ocular-nasal symptoms due to wheat (OR: 1.32, CI: 1.00 – 1.83). Workers sensitised to wheat flour were three times more likely (OR: 3.75, CI: 1.79 – 7.84) to be bakers and six times more likely to be supervisors/managers (OR: 6.03, CI: 2.37 – 15.38). Stratification of the jobs per employment duration demonstrated a similar inverted U-shaped exposure response curve.

Conclusion: The overall 11% prevalence of baker's asthma in South African supermarket bakeries is higher than in British supermarket bakers (4%). Job title more so than employment duration is an important predictor of sensitisation among supermarket bakery workers.

LEVELS AND CONDITIONS ASSOCIATED WITH HIGHER INDOOR ALLERGENS IN BEDROOMS OF PRIMARY SCHOOL CHILDREN IN DURBAN HOMES

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Introduction: Evidence of indoor environment having a role in increased respiratory morbidity, especially in children, has been increasing in recent years. Allergens of indoor origin have been implicated in sensitisation, as causative factors and exacerbation of asthma and other respiratory illness.

Aim: In this study we investigated levels of biological allergens and home characteristics associated with levels equal or higher than levels associated with sensitisation.

Methodology: Home conditions data and dust samples were collected from 121 beds and/or sleep area floors. ELISA assays were used to quantify house-dust mite and mould allergens in collected dust. A median value of 0.47 µg/g Asp f 1 allergen level and 2.00 µg/g of Der p 1 and Der f 1 allergen level were used as cut-off points for categorising exposure.

Results and Discussion: Asp f 1 allergen was detected in all samples with mean levels of 0.59 µg/g of dust. Der p 1 and Der f 1 allergen had mean levels of 6.09 and 2.09 µg/g of dust respectively. Some home conditions were significant predictors of Asp f 1 levels equal or less than median value and house-dust mite allergen (Der) greater than the lower threshold limit. None of these conditions seem to be constant predictors of higher levels of biological allergens.

Conclusion: This study was able to quantify biological allergens in Durban homes using objective measurements and was also able to identify some home characteristics that are predictors of high allergen levels in these homes.

IL-4R α SIGNALLING IN SMOOTH MUSCLE CELLS IS NOT REQUIRED FOR THE DEVELOPMENT OF EXPERIMENTAL ALLERGIC ASTHMA

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Airflow in the lungs of patients with allergic asthma is impaired by excessive mucus production and airway smooth-muscle contractions. Elevated levels of the cytokines IL-4 and IL-13 are associated with this pathology. A large number of *in vitro* studies have suggested that signals from IL-4R α , the crucial receptor chain for IL-4 and IL-13, on smooth-muscle cells is critical for airway inflammation and airway hyperresponsiveness.

In order to define the contribution of IL-4 and IL-13 signalling in airway smooth-muscle cells to the onset of asthmatic pathology we have examined the role of their key receptor IL-4R α in smooth-muscle cells *in vivo*. Transgenic mice deficient for IL-4R α in smooth-muscle cells were used to investigate for the first time *in vivo* effects of impaired IL-4R α signalling in smooth-muscle cells on the outcome of asthmatic disease. Airway hyperresponsiveness, lung pathology, antibody and cytokine responses were analysed after sensitisation and challenge of mice with ovalbumin.

In contrast to conclusions derived from *in vitro* studies the absence of IL-4R α on smooth-muscle cells had no effect on major aetiological markers of allergic asthma. Airway inflammation, airway hyperresponsiveness, mucus production, Th2 cytokine production and specific antibody response were unaffected in the transgenic mice when compared to control animals.

These findings suggest that the response of airway smooth-muscle cells to the cytokines IL-4 and IL-13 during the induction and acute phase of allergic asthma is not, as indicated by published *in vitro* data, critical for the outcome of the disease.

DIETARY AND ENVIRONMENTAL FACTORS ASSOCIATED WITH ASTHMA SYMPTOMS IN CAPE TOWN SCHOOL CHILDREN

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Background: The prevalence of current wheeze and asthma in school children in Cape Town has been reported to be increasing. The multicentre International Study of Asthma and Allergies in Childhood Phase 3 (ISAAC 3) offered an opportunity to investigate the relationship between environmental or dietary risk factors and asthma.

Methods: A cross-sectional survey of self-reported symptoms and diagnoses in 13- to 14-year-old school children using standardised ISAAC written and video questionnaires was performed in 2002. The associations between environmental and dietary predictors and the 12-month prevalence of wheeze and asthma diagnosis were estimated using logistic regression.

Results: A school-based sample of 5 037 pupils participated. The 12-month ('recent') prevalence of wheeze on written and video questionnaire was 20.3% and 11.2% respectively. On written questionnaire 14.4% of participants reported an asthma diagnosis. The following environmental and dietary variables were associated with a diagnosis of asthma or with the prevalence of recent wheeze:

Environmental variable	OR (95% CI) for Asthma	OR (95% CI) for wheeze on written questionnaire	OR (95% CI) for wheeze on video
Eating maize 3 or more times a week	0.69 (0.54- 0.89)	0.67 (0.54- 0.83)	0.85 (0.66- 1.09)
Eating pasta once or twice a week	1.18 (1.00- 1.39)	1.18 (1.02- 1.37)	1.26 (1.05- 1.51)
Exercise once or twice a week	1.61 (1.33- 1.95)	1.53 (1.29- 1.81)	1.42 (1.15- 1.76)
Taking paracetamol at least once a month	1.23 (1.05- 1.45)	1.48 (1.28- 1.71)	1.64 (1.37- 1.96)
Maternal smoking	1.11 (0.93- 1.33)	1.23 (1.04- 1.44)	1.41 (1.16- 1.72)
Respondent smoking	1.13 (0.86- 1.48)	1.51 (1.20- 1.90)	1.41 (1.06- 1.87)
Body Mass Index (BMI) > 95th centile for age	1.29 (0.94- 1.78)	1.79 (1.37- 2.35)	1.97 (1.43- 2.70)
Mother with tertiary education	1.41 (1.17- 1.70)	1.52 (1.29- 1.79)	1.22 (0.98- 1.50)
Using paraffin as cooking fuel	0.62 (0.46- 0.84)	0.73 (0.59- 0.92)	0.83 (0.60- 1.14)
Using wood as cooking fuel	1.93 (1.13- 3.30)	1.57 (0.96- 2.58)	2.24 (1.30- 3.86)

Conclusions: The study confirms the association in the Cape Town population of asthma with improved socio-economic status as reflected in diet, maternal higher education and paraffin use as cooking fuel. Maternal and respondent smoking, obesity and exposure to wood fumes may have more direct causal significance. The association with paracetamol is probably confounded by symptom severity. Although inferences are limited by the cross-sectional study design, the results add to the growing body of evidence on possible causes of asthma.

Funding: MRC, South Africa, an AstraZeneca Respiratory fellowship from South African Thoracic Society (HZ), and sponsorship from the following pharmaceutical companies: AstraZeneca, Boehringer-Ingelheim, 3M and Schering-Plough. We thank the International ISAAC Centre, New Zealand for a start-up grant.

PREVALENCE AND MOLECULAR EPIDEMIOLOGY OF HUMAN METAPNEUMOVIRUS, HUMAN CORONAVIRUS NL63 AND HUMAN BOCAVIRUS IN YOUNG CHILDREN WITH ACUTE WHEEZING

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Respiratory viruses have been temporally associated with the onset of acute wheezing episodes in young children. The role of recently

identified novel viruses, human metapneumovirus (hMPV), human coronavirus NL63 (HCoV NL63) and human bocavirus (HBoV) in wheezing is not well studied.

Aim: To investigate the prevalence and molecular epidemiology of hMPV, HCoV NL63 and HBoV in children presenting with acute wheezing.

Methods: A prospective study of consecutive preschool children presenting at Red Cross Children's Hospital with acute wheezing from May 2004 to November 2005. RNA and DNA was extracted from every sample, with hMPV and HCoV NL63 detected by RT-PCR and HBoV by PCR. Amplicons from positive samples were sequenced, aligned and phylogenetic trees constructed. A general shell viral and indirect immunofluorescence detected RSV, influenza A and B, parainfluenza 1, 2, 3 and adenovirus in every 5th nasal swab sample.

Results: 242 children, median (interquartile range) age 12 (6-25) months, were enrolled. A respiratory virus was found in 53/242 (21.9%) of nasal samples. hMPV, HBoV and HCoV NL63 was found in 20 (8.3%), 18 (7.4%) and 6 (2.5%) samples respectively. Of the 59 samples tested for the common respiratory viruses 15 (25%) were positive. Dual viral infections were uncommon, occurring in 6 cases (2.5%), 5 of which were associated with HBoV. There was a winter predominance of viral infections. Phylogenetic analysis confirmed the presence of both hMPV and HCoV NL63 lineages. HBoV isolates grouped with the ST2 prototype.

Conclusions: Respiratory viruses are commonly associated with acute wheezing in preschool children. The usual viral pathogens are more prevalent than hMPV, HCoV NL63 and HBoV.

Funding: Allergy Society of South Africa, GSK research award; World Health Organisation

ALLSA POSTER PRESENTATIONS

THE CHARACTERISATION AND GENERATION OF NATURAL AND RECOMBINANT PARVALBUMIN, THE MAJOR CROSS-REACTIVE ALLERGEN IN FISH

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Fish is the major cause of food-related allergic reactions, particularly in countries that contain large fish-processing communities. Parvalbumin is the major fish allergen, responsible for over 95% of hypersensitivities. This protein demonstrates characteristic cross-allergenicity that indicates its potential use as a diagnostic marker of fish allergies. At present, parvalbumin from a limited number of fish species has been characterised on a detailed molecular level. The aim of this study is to generate a recombinant marker allergen which may be utilised as a clinical diagnostic tool as well as to investigate the varying allergenic potential of parvalbumin by comparing fish species. In this study, the DNA sequence of parvalbumin from the fish species *Sardinops sagax* is currently being determined using specific primers designed by microsequencing, alignment of known parvalbumin sequences and 5'-rapid amplification of cDNA ends (RACE). Subsequently, a novel recombinant form of the protein will be generated. Using ammonium sulphate precipitation and ion-exchange chromatography, parvalbumin has been isolated from five economically relevant indigenous fish species, namely pilchard (*Sardinops sagax*), hake (*Merluccius capensis*), snoek (*Thyrsites atun*), yellowtail (*Sesiola lalandi*) and anchovy (*Engraulis japonicus*). Characteristic α and β isoforms of this protein have been identified using two-dimensional electrophoresis. Furthermore, serum from sensitised fish-processing factory workers was utilised to assess IgG and IgE-binding revealing specific binding to parvalbumin and several other allergens. This novel area of research could reveal properties that contribute to the allergenic potential of parvalbumin while the generation of a recombinant marker allergen would have clear benefits in a clinical setting.

ATOPY IN PRETORIA

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Introduction: Atopy in Gauteng and the Free State has been widely studied. However, all these studies reflect the allergy status of individuals living in Johannesburg and Bloemfontein. No study of this nature has been conducted in Pretoria.

Methodology: Standard allergen extracts (Alk Abelló) with negative and positive control were used for testing. The allergen extracts used

were: Bermuda grass, 5 grass mix, tree mix, corn culture *Zea Mays* (pollen), dog hair dander, cat hair dander, standardised mite *Dermatophagoides pteronyssinus* (HDM), *Blattana* sp (cockroach), horse, cow's milk, whole grain, soybean, peanut mix, whole egg, fish mix and wheat. Reactions were measured according to wheal size at 10 minutes, and wheal 3 mm greater than the negative control was regarded as a positive reaction for inhalants. The cut-off points of Sporok were used for positive food reactions.

Results: 50 asthmatic children were studied. Skin-prick test (SPT) positivity was commonest to Bermuda grass (24%) while grass mix was the next most common aeroallergen sensitivity. HDM sensitivity occurred in 10% of patients. Food allergens were uncommon but potato sensitivity was displayed in 14%.

Conclusion: Grass sensitivity reflects the prevailing aero-allergen exposure in a typical highveld city. However it appears that HDM sensitivity is uncommon suggesting that the climate in this area is significantly adverse to mite growth. This may be the first Highveld town where micro-climate does not favour mite survival. Mite studies are required from Pretoria. All children with potato sensitivity had atopic eczema. This requires investigation.

EXACERBATION OF ASTHMA CHANGES: MECHANICAL PROPERTIES OF SYSTEMIC VESSELS

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In asthma pathogenesis the essential role belongs to vascular infringements. Now for an estimation of functional condition of the cardiovascular system special interest gets research of mechanical properties of vessels, in particular of arterial stiffness. It is not clear whether increased arterial stiffness is observed at asthma and what role it can play in its pathogenesis. We examined 54 patients with severe and medium asthma by noninvasive arteriography (arteriograph TensioClinic TL1 (TensioMed, Hungary)) with the purpose of studying the role of arterial stiffness in pathogenesis of asthma.

During exacerbation of asthma the aortal stiffness was authentically more than in healthy persons. It was expressed in increase of aortic pulse wave velocity (aPWV) and augmentation index (IA). Thus aPWV in patients with severe asthma almost by 2 times surpassed aPWV in healthy persons and was $10,5 \pm 1,3$ m/s. IA in such patients was $14,4 \pm 5,8\%$, that by 6 times exceeded control level. Authentically raised ($p < 0,001$) arterial stiffness causes substantial increase cardiovascular risk during exacerbation of asthma. This condition can explain amplification of cardiovascular events in patients with exacerbation of asthma. Irrespective of expressiveness of increase of arterial stiffness at exacerbation, during remission of asthma aPWV and IA essentially improved and came nearer to control level. That testifies about the transitory character of the described changes. Increased arterial stiffness in asthma mainly correlates to the degree of lung ventilation dysfunction and hypoxia, as with duration and severity of disease. Further research work in this direction will allow opening more pathophysiological mechanisms of vascular dysfunction in asthma.

A PRIMARY IMMUNODEFICIENCY DISEASES (PID) REGISTRY FOR SOUTH AFRICA – PROBLEMS AND PROGRESS

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A recently introduced SA PID registry was announced at the All 4 Kids Paediatric Congress in September 2006 at the Sun City Congress, subsequent to a presentation by Dr Helen Chapel, clinical immunologist from Oxford, on the management of the commoner B-cell-related deficiencies. Clearly early identification and meticulous follow-up of these patients influences the outcome of these potentially treatable conditions positively. For South Africa there are no statistics available documenting prevalence or outcome for PIDs. General awareness for these conditions is poor, judging by delayed diagnosis and suboptimal therapy. Funding was obtained for a part-time secretary and a registry with informed consent was started on 1 November 2006. The registry records SA patients initially and aims to expand to include neighbouring states at a later stage. Affiliation with the European Society for Immunodeficiency Diseases (ESID) has been proposed and accepted. Parental and patient motivation has been uniformly positive. Data regarding laboratory information are not uniform and definitive molecular diagnosis is not available in all but a few. Entries from across the country will be discussed.

AGE OF INTRODUCTION, FREQUENCY AND QUANTITY OF PEANUT AND PEANUT PRODUCT CONSUMPTION AMONG 4-36-MONTH-OLD BLACK INFANTS IN THE CAPE METROPOLE REGION

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Objective: To determine trends of peanut and peanut product consumption in black infants in the Cape Metropole Region, quantifying mean daily intake of peanut products, determining the mean age of introduction of peanut products and comparing consumption patterns of peanut products between different socio-economic groups.

Study design & methods: Cross-sectional, descriptive and exploratory study. Mothers ($n = 198$) of black infants aged 4-36 months were interviewed about their infants' peanut intake using a peanut consumption questionnaire.

Results: It was found that the majority of subjects ($n = 159$, 79%) had consumed peanuts and/or peanut products by the time of the survey. The mean age of introduction of peanuts and peanut products was 10 months and 127 (64%) of subjects started eating these before 1 year of age. Peanut butter is the most commonly consumed peanut containing product. It is most commonly consumed added to porridge for the 4-11- and the 12-23-month age groups. However, for the 24-36-month age group, peanut butter is more commonly consumed on bread than in porridge.

The median total intake of peanut butter and peanuts was 12 g/day. Significantly higher percentages of peanut and peanut product consumers were from households earning incomes below the poverty index.

As far as symptoms of peanut allergy are concerned, no infants had ever presented with any of the listed symptoms after ingestion of peanuts or peanut products.

Conclusions: Peanut consumption among black infants in the Cape Metropole Region is higher than previously recorded in food consumption surveys of South African infants and children. Peanut products are introduced into the diets of black infants at an early age. Peanut consumption (ever and current) and early introduction of peanut products are significantly correlated with lower socio-economic class. Knowledge of this consumption pattern may be useful in future studies to assess the possibility of a link between high consumption rates and low prevalence of diagnosed peanut allergic infants in the Cape Metropole Region.

ATOPY IN HIV-POSITIVE CHILDREN IN PRETORIA

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Introduction: The relationship between the development or aggravation of a pre-existing atopic state and HIV has not been thoroughly investigated in the South African context. HIV-positive patients have been shown to have a higher prevalence of atopy in the early stage of their disease.

Methodology: A random sample of children attending an HIV clinic were enrolled. They had skin-prick testing (SPT), recording of CD4 count, HIV staging, and evidence of atopy recorded. Alk Abelló allergen extracts (Laboratory Specialities) with negative and positive controls were used for testing. A panel of common aero-allergen extracts were used. Reactions were measured by standard protocol.

Results: Forty-five (90%) of the 50 children tested showed no reaction to SPT. 26% of the children tested had a positive family history of atopy and 38% of these children with a positive family history of atopy had a reactive SPT. These children were all known asthmatics and gave a positive history of dermatitis and allergic rhinitis. 80% of these children had a CD4 count of less than 20% and were HIV stage 3 and 4. 20% were HIV stage one and had a CD4 count of above 20%.

Conclusion: The children who had a non-reactive SPT all had a negative family history of atopy and in contrast, all the children who showed evidence of atopy, had a positive family history of atopy. It appears that the stage of the HIV disease does not influence the development of allergy. The dermatitis and allergic rhinitis that is prevalent among these individuals is probably due to some other factor.

MECHANISMS OF ANISAKIS-INDUCED CONTACT DERMATITIS AND ASSOCIATED SYSTEMIC SENSITIZATION

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Background: *Anisakis* larvae are commonly found parasitising fish, and can cause dermatitis in people frequently exposed to fish, such as seafood-processing workers.

Methods: A cross-sectional study on 594 fish-processing workers investigated environmental and host-associated factors for occupational dermatitis. Skin examination, skin-prick test (SPT) and patch-testing was performed on all 120 symptomatic workers and randomly selected controls ($n = 134$).

A murine model was established to study local pathology and systemic sensitisation following epicutaneous exposure to *Anisakis* larval antigens. Biologically relevant sensitisation was assessed by intravenous challenge with *Anisakis* proteins. Knockout and cell-specific knockout mice were used to characterise the roles of IL-4, IL-13 and the IL-4R α and the cell-specific requirements for IL-4/IL-13 responsiveness.

Results: Skin symptoms were reported by 27% of the workforce. Workers sensitised to *Anisakis* were almost twice as likely (OR = 1.9) to report skin symptoms.

Epicutaneous sensitisation with *Anisakis* larval antigens induced local skin inflammation, Th2 responses and production of anti-*Anisakis* IgE and IgG1. Intravenous challenge of sensitised mice resulted in anaphylactic shock. Skin pathology was IL-4 independent but IL-13 dependent, while systemic anaphylaxis reactions were primarily IL-4 mediated. Macrophage/neutrophil specific expression of the IL-4R α was not required for pathology or anaphylaxis. T-cell deficient IL-4R α mice experienced partial inhibition of systemic anaphylaxis, despite showing enhanced epidermal hyperplasia. This illustrates the necessity for cell-specific evaluation of IL-4/IL-13 responsiveness during allergic responses.

Conclusions: IL-4, IL-13 and the IL-4R α play important and distinct roles in *Anisakis*-induced contact dermatitis and associated systemic sensitisation in mice.

RAISED HOUSE DUST MITE-STIMULATED IL13/IFN γ RELEASE: ASSOCIATION WITH ALLERGEN-SENSITISATION RATHER THAN ATOPIC DISEASE

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Background: T-helper (TH) lymphocyte responses are polarised toward a TH2 cytokine response in atopic disease. A recent study suggested increased TH2 cytokine release is associated with allergen sensitisation rather than atopic disease. We therefore compared TH2/TH1 cytokine responses to allergen between atopic asthmatic, asymptomatic but allergen-sensitised, and normal children.

Method: IL-13/IFN γ release and proliferation of house-dust mite (HDM)-stimulated PBMC from 20 severe and 25 moderate asthmatics, 11 allergen-sensitised and 16 normal controls were studied. PBMC (2×10^5 /200 μ l medium) were stimulated for 7 days with HDM.

Results: IL-13 release was significantly increased in the severe asthmatic (median 150 pg/ml), moderate asthmatic (67 pg/ml) and sensitised (95 pg/ml) groups compared with the normals (16 pg/ml; $P < .02$). IFN γ release was: 60 pg/ml (severe asthma), 20 pg/ml (moderate asthma), 1 pg/ml (sensitised) and 127 pg/ml (normal). The IL-13/IFN γ ratio was significantly increased in the severe asthmatic (median 1.96), moderate asthmatic (3.18) and sensitised (59.00) groups compared with the normals (0.14; $P < .005$). There was no significant difference in IL-13, IFN γ or IL-13/IFN γ ratio between the asthmatic groups and the sensitised group. Proliferation did not differ significantly between any of the groups.

Conclusion: T-cell responses to allergen in asymptomatic but allergen-sensitised subjects is similar to subjects with atopic asthma, polarised toward a more extreme TH2 type cytokine response than in normal subjects. Thus allergen sensitisation and a polarised TH2 cytokine response to allergen are not sufficient to account for the development of atopic disease.

INFLAMMATORY MARKERS IN THE NOSE IN RESPONSE TO INTRANASAL GLUCOCORTICOID THERAPY IN CHILDREN AT THE RED CROSS CHILDREN'S HOSPITAL

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Background: Enhanced levels of total and specific IgE, and elevated numbers of eosinophils, lymphocytes (TLC) and mast cells are implicated in the pathogenesis of allergic rhinitis in children.

Objective: Allergic rhinitis (AR) in children is associated with elevated Th2-type cytokines and chemokines, leading to inflammation and obstruction in the nasal cavity. IGC therapy may act by reducing the expression of such inflammatory markers and thus TLC activation, and increase the production of counter-regulatory cytokines, such as IL-10.

We sought to measure the chemokines CXCL8 (IL-8) and CC (eotaxin in the nose), and circulating eosinophil cationic protein (ECP). These measurements were made prior to and after 4 weeks of IGC therapy (fluticasone propionate). Possible factors associated with failure to respond to therapy were noted.

Methods:

Patients: 25 children with PAR (perennial), some with seasonal exacerbations, aged 6-12 years, with one or more positive skin-prick tests (SPT) to 10 common aeroallergens.

Exclusion criteria: Children with asthma or other chronic illness, other than rhinitis, oral corticosteroids and antihistamines within the last two months, and non-compliance.

Study design: Initial assessment was by questionnaire and history, clinical examination, SPT and nasal smear. Nasal lavage was performed using 3 ml physiological buffered saline in one nostril, and the recovered wash-out was filtered through 3 layers of muslin. The

resultant supernatant was frozen at -80°C and kept for chemokine measurements.

A blood sample was taken for measurement of:

- Total and specific IgE to aeroallergens and *Ascaris lumbricoides*.
- ECP
- IL-5 and IL-10 following stimulation of peripheral blood mononuclear cells with PHA and aeroallergen extract.

IGC regimen was instituted after a 2-week wash-out period, and the weight of the containers were taken at the start and end of the 4-week period.

Reassessment: Nasal lavage and blood sample were repeated after the 4-week period.

Results: A significant reduction in eotaxin and ECP were obtained following IGC therapy. IL-8 levels were significantly increased in the nose, with some exceptions. IL-5 levels declined significantly overall. Levels of IL-10 were variable. A good response to IGC therapy was noted after the 4-week period in 7/25 (27%), a moderate response in 10/25 (39%), and a poor/no response in 9/25 (35%) of children. 7/10 of the poor responders were subject to passive smoke inhalation, 7/9 of the moderate responders and only 2/7 of the good responders.

Conclusions: IGC therapy was associated with a decline in nasal eotaxin and ECP, an increase in intranasal IL-8, and a reduction in IL-5 production from stimulated PBMCs.

Enhanced IL-10 levels, possibly from T regulatory cells, may be associated with a good response to IGC.

Exposure to smoke may result in an enhanced proinflammatory response.

PRODUCT NEWS



MSD (Pty) Ltd is proud to announce the introduction of SINGULAIR 4 mg. Studies have shown that asthma in children under the age of six is on the increase worldwide.¹ SINGULAIR 4 mg is the first asthma controller therapy, that is not a steroid, to be approved in South Africa for children as young as 2 years old.²

Studies have shown improvements in symptom and activity scores from as early as day one, affirming the efficacy of SINGULAIR 4 mg in this age group.³ The current guidelines for treatment of asthma in children, as compiled by the Allergy Society of South Africa (ALLSA), call for the introduction of a leukotriene antagonist as a controller agent in this age group at step 2, after the use of short-acting reliever medication has proven to be inadequate in controlling asthma symptoms. In other words using leukotriene antagonist as a first line controller agent.⁴ At present, of the leukotriene receptor antagonists, only SINGULAIR is indicated for use in children under the age of 12.²

SINGULAIR 4 mg is indicated for the prophylactic treatment of mild to moderate asthma in the 2-5 year old age group. SINGULAIR 4 mg is presented in a 28-day pack and one tablet should be taken once daily at bedtime.² To date worldwide use is more than 2.2 million children in more than 90 countries. This puts SINGULAIR in the unique position of being the only controller therapy to be registered and indicated for asthmatic patients from 2 years old and up.²



The FREEDOM to be a Child!

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