360. New insights in the incidence, variation and risk factors of asthma

3223

Late-breaking abstract: Association of asthma with IgE to staphylococcal enterotoxins in a GA²LEN population based case-control study

Peter Tomassen[1], Claus Bachert[1], Peter Burney[2], Deborah Jarvis[2], on behalf of the GA²LEN Survey Follow-Up Working Group. *[1]Upper Airways Research Laboratory, Ghent University, Ghent, Belgium; [2]Respiratory Epidemiology and Public Health, Imperial College, London, United Kingdom*

Introduction: Presence of specific immunoglobulin E for staphylococcal enterotoxins (SE-IgE) in serum has been associated with severe asthma and nasal polyposis, but the prevalence and link to asthma in the general population has never been studied. We aimed to determine the prevalence of serum SE-IgE, and to study the association with asthma in the general population.
Methods: The GA²LEN Survey Follow-Up group conducted a multi-center case-control study in 18 centers across Europe. Subjects were sampled from a preceding cross-sectional survey in 4 groups (controls, asthmatics, chronic rhinosinusitis subjects, and those having both). Subjects answered questionnaires, underwent spirometry and skin prick testing for common allergens, and serum SE-IgE was measured. Analyses were weighted for sampling, using inverse probability weights.
Results: 3505 subjects participated, of which 2908 in 15 centers provided complete information and blood samples. The weighted overall prevalence of asthma was 10.6%, and the prevalence of SE-IgE >0.10 kU/L was 29.3%. SE-IgE was significantly associated with the presence of asthma, adjusting for age, sex, allergy and smoking history. The strength of the association was dependent of the SE-IgE concentration (odds ratio 1.01; 1.33; 1.54 in the first, second and third tertiles). The association was not modified by the presence of a positive skin prick test or tobacco smoking.
Conclusion: Presence of IgE to Staphylococcal enterotoxins is highly prevalent, and is associated with asthma in the general population across Europe. These findings open perspectives on a role for bacterial superantigens in the pathogenesis of asthma.

3224

Asthma incidence in a national sample of Canadian adolescents

Joshua Lawson[1], Ian Janssen[2], Alomgir Hossain[1], Mark Bruner[3], William Pickett[2]. *[1]Canadian Centre for Health and Safety in Agriculture, University of Saskatchewan, Saskatoon, SK, Canada; [2]Department of Community Health and Epidemiology, Queen's University, Kingston, ON, Canada; [3]School of Physical and Health Education, Nipissing University, North Bay, ON, Canada*

Background: Estimates of asthma incidence and its determinants have rarely been obtained from rural regions, especially in adolescent populations.
Objective: To compare the incidence of asthma among Canadian adolescents in rural and urban regions and to examine the determinants of asthma incidence.
Methods: We used data from the National Population Health Survey (NPHS), a nationally representative longitudinal survey of Canadians. The NPHS uses a complex survey design with data collected every 2 years since 1994/95. The NPHS collects information on socio-demographics and some health behaviours. All persons aged 12-18 years without asthma in Cycle 1 were followed until a reported diagnosis of asthma or censoring up to Cycle 7. Rural residence was defined by living in an area of <1000 people and >400 people/km². Incidence and Cox regression analyses were population weighted and bootstrapping procedures were used to estimate variances.
Results: This sample represented 2,482,610 adolescents of whom 293,445 developed asthma. Approximately 19% of the cohort was rural living at baseline. The incidence of asthma was approximately 10.2 per 1000 person-years and was higher in

urban dwellers than rural dwellers (10.9 vs. 7.7 per 1000 person-years). In adjusted analysis, rural residence was not associated with asthma development [Hazard ratio (HR)=0.58, 95%CI=0.25-1.32, p=0.19]. Being female and being exposed to passive smoking were both associated with the development of asthma ($p<0.01$).
Conclusions: Unlike results from younger children, a rural dwelling was not protective of developing asthma among adolescents, despite showing a trend. Asthma prevention initiatives for adolescents should target girls and focus on smoking exposure.

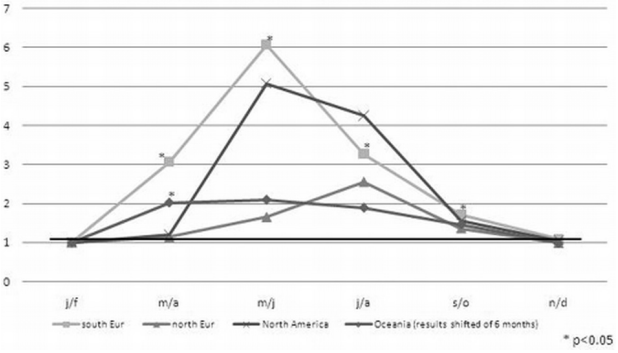
3225
Temporal patterns of wheeze during the school ages in a population-based cohort
Anders Bjerg, Linnea Hedman, Sigrid Sundberg, Martin Andersson, Eva Rönmark. *The OLIN Studies, Dept of Medicine, Sunderby Central Hospital of Norrbotten, Luleå, Sweden*

Introduction: Wheeze, as suggestive of asthma, may follow various time courses during childhood. Incidence, remission and relapse rates are high. Compared to the pre-school ages, school age and adolescence have been less studied. The aim was to characterize temporal patterns of wheeze in school children.
Methods: At age 7-8 years, 3,430 (97% of invited) children in Northern Sweden completed ISAAC questionnaires. The same questions were used in 10 yearly follow-ups until age 17-18. Data from the 2,622 (76.4%) subjects that participated at 5 or more occasions were analysed.
Results: From age 7-8 to 17-18 one third reported wheezing at some occasion. Persistent wheeze from age 7-8 was reported by 2.9%. It was closely associated with rhino-conjunctivitis and parental asthma at age 7-8, RR 10 (6.6-15) and 5.3 (3.5-8.2). Incident wheeze persisting until age 17-18 was reported by 7.6%, while 2.6% had remittent wheeze, i.e. wheeze at age 7-8 but not at study end. Remittent wheeze was associated with respiratory infections before age 7-8, RR 4.1 (2.2-7.8). Transient wheeze for 1 years or more, not persisting until age 17-18, was seen in 8.7%. Of the 12.0% reporting intermittent periods of wheeze with no clear pattern, nearly half wheezed only at 1 or 2 occasions.
Discussion: In this large cohort of school children followed yearly by questionnaires, the majority of children with any wheeze during the school years were neither wheezing at age 7-8, nor at age 17-18. Half of the children wheezing at age 7-8 were in remission by age 17-18. Whereas wheeze associated with respiratory infections has a good probability of remission, heritability and concomitant allergic rhinitis predict persistence of wheeze.

3226
Seasonal variations in asthma attacks and grass sensitisation
Cristina Canova, Peter Burney, Deborah Jarvis, on behalf of the European Community Respiratory Health Survey I. *Respiratory Epidemiology and Public Health, NHLI, Imperial College, London, United Kingdom*

Seasonal variation in asthma mortality and hospitalization has been reported. In this study we describe seasonal variation in asthma symptoms and assess whether this was modified by SPT sensitisation. Asthmatics aged 20-44 years (n=2573) taking part in the European Community Respiratory Health Survey I are included. Participants identified bi-monthly periods they usually experienced attacks of asthma. Effect modification of sensitization to grass, cat, dust, birch, Alternaria on asthma attacks in each bi-monthly period was assessed within each country, using marginal logistic regressions, based on generalised estimating equations. Interaction coefficients were then combined using random effects meta-analysis.
Seasonal variation in asthma attacks was seen in most countries, although with different patterns. Seasonal variation was not modified by sensitisation to indoor allergens (cat, dust) but was modified by sensitisation to grass.

Figure 1) Grass bi-months interaction risk of on asthma attacks



In Southern Europe the risk of asthma in May/June compared to Jan/Feb in those with IgE to grass was six times that seen in asthmatics not sensitised to grass. Overall sensitisation to Alternaria increased the risk of attacks in Jul/Aug compared to Jan/Feb (OR 2.3).
Asthmatics sensitised to grass and Alternaria experience seasonal exacerbations likely triggered by allergen exposure. The effect of pollen on asthma severity in a sub group of susceptible asthmatics may be much greater than previously documented.

3227
Initiation of controller medication in newly diagnosed asthma patients: Impact on economic resource utilization
Pierrick Bedouch[1], Mohsen Sadatsafavi[1], J. Mark FitzGerald[2], Carlo Marra[1], Larry Lynd[1]. [1]*Collaboration for Outcomes Research and Evaluation (CORE), Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada;* [2]*Department of Medicine & Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Vancouver, BC, Canada*

Introduction: To better understand the economic burden of asthma, we compared asthma-related direct costs among adults prescribed controller regimens.
Methods: A cohort of newly diagnosed asthma patients (14-65 y/o), initiating a controller therapy for the first time between 1997 to 2007, was created from the health administrative database of British Columbia, Canada. Five cohorts of patients were created according to the way controller therapy was initiated: inhaled corticosteroid (ICS group), ICS/long-acting beta-agonist combination (ICS/LABA group), ICS+LABA in separate formulations (ICS+LABA group), leukotriene receptor antagonist (LRA group) or ICS+LRA in separate formulations (ICS+LRA group). Index Date (ID) was defined as the date controller medication prescribed. Direct cost of asthma in the post-ID year (2008 Canadian dollars) was calculated from the hospital, physician visits, and prescription records, adjusted for multiple covariates estimated from the pre-ID year.
Results: 153,224 patients were included: 109,601 ICS; 34,184 ICS/LABA; 2,249 ICS+LABA; 6,289 LRA; 901 ICS+LRA. The average age was 37.7 and 61.0% were female. The average direct costs of asthma for the post-ID year for the ICS group was 265.2$. All other groups had higher incremental costs: ICS/LABA +$125.9, ICS+LABA +$218.2, LRA +$198.4, and ICS+LRA +$322.4 (all $p<0.01$). Older age, higher resource, and higher cumulative dose of rescue medicine use in the pre-ID year were predictors of resource use in the post-ID year ($p<0.01$).
Conclusions: Initiation of ICS, as recommended by guidelines, was associated with the lowest costs than initiation of other controller or combination therapies.

3228
A longitudinal study investigating factors associated with changes in lung function over time in early life (age 3 to 11)
Danielle Belgrave, Lesley Lowe, Angela Simpsonn, Adnan Custovic. *Respiratory Medicine, University Hospital South Manchester, University of Manchester, Manchester, United Kingdom*

Background: Previous studies have investigated factors associated with poor lung function in children. However, these studies use a cross-sectional approach which ignores changes in lung function over time. In this study, we develop multilevel longitudinal models in order to investigate factors affecting developmental change in lung function in early life.
Methods: In a population-based birth cohort 1185 participants were recruited prenatally and followed prospectively (1, 3, 5, 8 and 11 years). At each time point, a validated questionnaire was administered to collect information on asthma-related symptoms, height and weight. We assessed atopy and lung function (Specific Airway Resistance (sRaw), plethysmography) at each follow-up.We use a longitudinal linear mixed models approach to determine predictors of change in sRaw over time.
Results: Univariate longitudinal analyses revealed marked deterioration in sRaw among children who were atopic (mean difference 2.85%, 95% CI 1.05%-9.84%, p=0.003). Children who wheezed also had poorer lung function (mean difference 5.20%, 95% CI 0.87%-2.54%, $p<0.001$). Boys had poorer lung function compared to girls (mean difference 3.48%, 95% CI 0.87%-6.52%, p=0.03) and also had a higher rate of deterioration of sRaw over time which increased by 0.011 units (p=0.012) per year. In a multivariate longitudinal model, the factors which best predicted diminished lung function were atopy, increased BMI, paternal atopy, gender and current wheeze.
Conclusion: Multilevel longitudinal models allow us to predict factors associated with diminished lung function as well as factors associated with change in lung function over time.

3229
Transforming growth factor beta-1 gene polymorphisms and course of asthma
Despo Ierodiakonou[1], Dirkje S. Postma[2], Gerard H. Koppelman[3], Jorrit Gerritsen[3], Wim Timens[4], H. Marike Boezen[1], Judith M. Vonk[1]. [1]*Epidemiology, University Medical Center Groningen. University of Groningen, Groningen, Netherlands;* [2]*Pulmonology, University Medical Center Groningen. University of Groningen, Groningen, Netherlands;* [3]*Pediatric Pulmonology and Pediatric Allergology-Beatrix Children's Hospital, University Medical Center Groningen. University of Groningen, Groningen, Netherlands;* [4]*Pathology and Medical Biology, University Medical Center Groningen. University of Groningen, Groningen, Netherlands*

$TGF\beta_1$ is a cytokine with a potent role in asthma, in particular in airway remod-

eling. We investigated the role of $TGF\beta_1$ gene single nucleotide polymorphisms (SNPs) in the course of asthma.
Four haplotype tagging SNPs (rs7254679, rs4803455, rs1800469, rs10417924) were genotyped in 215 asthmatics with a 30-year follow up (population 1) and in 99 asthmatics who provided bronchial biopsies (population 2). Associations of SNPs with lung function, bronchial hyperresponsiveness (BHR i.e. $PC_{20} \leq 16$mg/ml), complete remission (pre bronchodilation FEV_1% predicted $\geq$ 80% & absence of BHR, symptoms, medication), basement membrane (BM) thickness and number of submucosal vessels were investigated using linear or logistic regression. Associations of SNPs with FEV_1 decline were estimated using mixed effect models, and associations with area covered with smooth muscle and collagen were tested non parametrically.
Population 1: the G-allele of rs7254679 was associated with lower FEV_1 (b (95%CI)=-21.2ml (-40.8;-2.0) and VC (b=-29.8ml (-49.3;-10.4)), increased risk for BHR (OR (95%CI)=2.7 (1.02-6.5)) and less remission (OR=0.3 (0.09-0.99)) The A-allele of rs4803455 was associated with accelerated FEV_1 decline (b=-13.8ml/year (-20.9;-6.7)) and the T-allele of rs1800469 with less FEV_1 decline (b=7.2ml/year (0.8;13.7). Population 2: the G-allele of rs7254679 tended to be associated with increased BM thickness (b=0.7 (-0.1;1.4 p=0.09)).
This is the first study indicating that $TGF\beta_1$ SNPs play a role in the course of asthma. Further analysis of data of another 40 subjects with bronchial biopsies will allow us to investigate the associations between $TGF\beta_1$ SNPs and airway remodeling in asthma in more detail.

3230

A nested case-control study of serum 25-hydroxyvitamin D levels and risk of adult-onset asthma – The HUNT study

Xiao-Mei Mai[1], Arnulf Langhammer[1], Carlos A. Camargo Jr.[2], Yue Chen[3].
[1]Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway; [2]Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States; [3]Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada

Background: The impact of low vitamin D status on the development of asthma is not clear. We conducted a nested case-control study to investigate the relation of baseline serum 25-hydroxyvitamin D [25(OH)D] levels and adult-onset asthma.
Methods: A total of 25,616 adults aged 19-55 years who participated in the second Norwegian Nord-Trøndelag Health Study (HUNT), were followed-up for 11 years. A nested case-control study consisted of all the new onset asthma cases during the follow-up (n=600) and a random sample of non-asthma controls (n=2013). Baseline blood samples were available in 584 asthma cases and 1958 non-asthma controls. Baseline serum 25(OH)D levels were measured by automated antibody-based chemiluminescence assay.
Results: The mean level of baseline serum 25(OH)D was slightly lower in asthma cases compared with controls in both men (geometric mean: 51 vs. 54 nmol/L, p=0.04) and women (geometric mean: 52 vs. 55 nmol/L, p=0.02). Men with a serum 25(OH)D levels <50 nmol/l at baseline had a significantly higher risk of asthma (crude OR 1.75, 95%CI 1.14-2.68) compared with those with a serum 25(OH)D level of 75 nmol/l or higher. After adjustment for age, smoking, family history of asthma, education, physical activity, social benefit, and economic difficulties, the OR was 1.60 (95% CI 1.02-2.50). Further adjustment for body mass index (BMI) yielded an OR of 1.47 (95%CI 0.93-2.32). In women, baseline serum 25(OH)D level was not associated with the risk of asthma in either unadjusted or adjusted models.
Conclusions: After adjustment for BMI and other covariates, baseline levels of serum 25(OH)D were not independently associated with adult-onset asthma.