Childhood chronic respiratory diseases: important determinant of healthy aging

Bolesław Samoliński

Chairman of the Sub-Committee on Priorities of Polish Ministry of Health during Polish Presidency of the EU Council

Professor and Chairman of the Department of Prevention of Environmental Hazards and Allergology
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Impact of chronic respiratory diseases in healthy ageing

The problem
## GARD Book (September 2007)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year of estimate</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>2004</td>
<td>300 million</td>
</tr>
<tr>
<td>COPD</td>
<td>2007</td>
<td>210 million</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>1996 - 2006</td>
<td>400 million</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>1986 - 2002</td>
<td>&gt;100 million</td>
</tr>
<tr>
<td>Others</td>
<td>2006</td>
<td>&gt;50 million</td>
</tr>
</tbody>
</table>
Impact of chronic respiratory diseases in healthy ageing

The problem is known

The solutions in asthma and allergy

Can solutions be implemented at the EU level?

Can solutions be improved?
Impact of chronic respiratory diseases in healthy ageing

1- Lifelong impact of early life events

2- Prevention and control of chronic respiratory diseases

3- Knowledge gained from birth cohorts in allergy and asthma

4- Importance of the conclusions of The Polish Presidency
Impact of chronic respiratory diseases in healthy ageing

1- Lifelong impact of early life events
The Barker’s hypothesis
A foundation for lifetime

- David Barker showed in 1990 that people who had low birth weight are at greater risk of developing coronary heart disease.
- In 1995, the British Medical Journal named this the “Barker Hypothesis.”
- It is now widely accepted that fetal and early life events are strongly associated with chronic diseases later in life.
- In 2010 Time Magazine called it the “New Science.”
Successful prevention of chronic diseases
25 yr programme in Northern Karelia

P Pushka

CHD MORTALITY IN ALL FINLAND AND IN NORTH KARELIA 35-64 YEAR OLD MEN

-82%
-75%

start of the North Karelia Project
extension of the Project nationally

North Karelia
All Finland

Year

26.1.2006
Hypothesis paper

Is allergic asthma associated with delayed fetal maturation or the persistence of conserved fetal genes?

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Review article

Epigenetic inheritance of fetal genes in allergic asthma

Asthma has been associated with an exaggerated T-helper type 2 (Th2) over Th1 responses to allergic and nonallergic stimuli, which leads to chronic airway inflammation and airway remodeling. In the present article, we propose that many of the genes involved in IgE synthesis and airways (re)modeling in asthma are persistent or reminiscent fetal genes which may not be silenced during early infancy (or late pregnancy). Genes of the embryologic differentiation of ectodermic and endodermic tissues may explain some of the patterns of airway remodeling in asthma. In utero programming leads to gene expression, the persistence of which may be associated with epigenetic inheritance phenomena induced by nonspecific environmental factors. Clear delineation of these issues may yield new information on the mechanisms of asthma and new targets for therapeutic intervention and primary prevention.

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Key words: asthma; epigenetic; fetus; remodeling.

Prof. Jean Bousquet
Clinique des Maladies Respiratoires
Prenatal and passive smoke exposure in asthma
Systematic review

Burke et al, Pediatrics 2012

OBJECTIVES: Exposure to passive smoke is a common and avoidable risk factor for wheeze and asthma in children. Substantial growth in the prospective cohort study evidence base provides an opportunity to generate new and more detailed estimates of the magnitude of the effect. A systematic review and meta-analysis was conducted to provide estimates of the prospective effect of smoking by parents or household members on the risk of wheeze and asthma at different stages of childhood.

METHODS: We systematically searched Medline, Embase, and conference abstracts to identify cohort studies of the incidence of asthma or wheeze in relation to exposure to prenatal or postnatal maternal, paternal, or household smoking in subjects aged up to 18 years old. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were estimated by using random effects model.

RESULTS: We identified 79 prospective studies. Exposure to pre- or postnatal passive smoke exposure was associated with a 30% to 70% increased risk of incident wheezing (strongest effect from postnatal maternal smoking on wheeze in children aged ≤2 years, OR = 1.70, 95% CI = 1.24-2.35, 4 studies) and a 21% to 85% increase in incident asthma (strongest effect from prenatal maternal smoking on asthma in children aged ≤2 years, OR = 1.85, 95% CI = 1.35-2.53, 5 studies).

CONCLUSIONS: Building upon previous findings, exposure to passive smoking increases the incidence of wheeze and asthma in children and young people by at least 20%. Preventing parental smoking is crucially important to the prevention of asthma.
Impact of chronic respiratory diseases in healthy ageing

1- Lifelong impact of early life events

2- Prevention and control of chronic respiratory diseases
Efficiency of the Finnish asthma plan
Haahtela et al, Thorax 2006

% change 1993-2003

-80
-60
-40
-20
0
20
40
60

asthma prevalence
hospital days
disability pension
total costs
cost per pt per year

World Health Organization
A world where all people breathe freely
Rapid reduction in asthma hospitalizations in Salvador da Bahia, Brazil (2.7 million inhabitants)

Souza-Machado et al Eur Respir J 2010
However, only 7 countries in the EU have a national asthma plan lead by the Ministry of Health
Asthma Programme 1994-2004
Focus: (1) inflammation, (2) early intervention, (3) guided self-management, and (4) networking

National Allergy Programme 2008 -2018
– current status and patient involvement

In association with the WHO GARD Programme = Global Alliance against Respiratory Diseases

Focus: (1) children, young people, (2) from treatment to prevention, (3) tolerance, (4) diagnostic quality, and (5) early intervention to control severe allergies

Ministry of Health; National Public Health Institute; NGOs: Allergy & Asthma Federation, Finnish Lung Health Association, Finnish Pulmonary Association HELI
PAPA-EU
Prevention of asthma, prevention of allergy in Europe

1. Combine the Finnish asthma and allergy programmes in a single programme
2. Translate/customize the programme in all EU languages
3. Adapt the national programme to GPs (IPCRG)
4. Assess the Norwegian government project of adaptation
5. Assess how Polasthma is implemented in Poland
6. Disseminate to patients (EFA, EAACI)
Impact of chronic respiratory diseases in healthy ageing

1- Lifelong impact of early life events

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3- Knowledge gained from birth cohorts in allergy and asthma
Childhood asthma followed to adulthood
Dunedin cohort

Males study members
613 subjects (both sexes)
51.4% followed
Multicenter Allergy Study
M Rochat et al, J Allergy Clin Immunol 2010

Atopy and rhinitis versus new onset wheeze in children

Stratification at the age of 5 years:
- Control group
- Atopy, no rhinitis
- Non-allergic rhinitis
- Allergic rhinitis

Probability of remaining free of wheezing

Years until new onset
Need to pool birth cohorts

Bousquet J et al, Int Arch Allergy Immunol 2012

• Long-term birth cohort studies are essential to understanding the life course, early predictors, risk and protective factors of allergy and the complex interplay between genes and environment (including life style and socio-economic determinants) and future determinants of ageing.

• Over 130 cohorts focusing on asthma and allergy have been initiated around the world and some have followed subjects up to adulthood.

• The information gathered by these birth cohorts has already made a significant advance in our understanding of allergy and asthma (and predictors of COPD).

• However, these data are scattered.
Need to pool birth cohorts

Bousquet J et al, Int Arch Allergy Immunol 2012

• To broaden the diversity of environmental exposures in Europe (dietary, inhalant, socio-economic factors),

• To achieve the statistical power needed to assess genetic and environmental determinants and their interactions,

• To assess the life course of allergic and asthmatic phenotypes including economic burden and quality of life of very severe phenotypes

• To determine gender-specific differences across different cultures and regions in Europe

• To facilitate research on mechanisms of allergy and asthma.
Need to pool birth cohorts

Bousquet J et al, Int Arch Allergy Immunol 2012

Since 2004, several research initiatives funded under the EU Framework Program for Research and Technological Development FP6-FP7 have identified, compared and evaluated pooling data from existing European birth cohorts.

GA²LEN: Global Allergy and European Network, FP6

ENRIECO: Environmental Health Risks in European Birth Cohorts, FP7

CHICOS: Developing a Child Cohort Research Strategy for Europe, FP7

MeDALL: Mechanisms of the Development of ALLergy, FP7
MeDALL is a collaborative project supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework programme.
MeDALL achievements

NIH-MeDALL meeting – September 11-12, 2012
J Bousquet, JM Anto, T Keil, J Sunyer

• Harmonized questionnaire for prospective birth cohorts available (web-based version in 4 languages).
• To compare prospective data across all participating MeDALL birth cohorts.
• A pooled database of recent ongoing longitudinal birth cohorts in allergy and asthma data from 14 birth cohorts in Europe, making this study unique in terms of geographical variability.
• The data of over 44,000 children have been included: 22,417 aged around 4-6 years and 18,975 aged around 8-10 years.
IgE-associated phenotypes in 8-year old children.
Cluster analysis of European birth cohorts

Judith Garcia-Aymerich, Marta Benet, Jean Bousquet, Joachim Heinrich, Thomas Keil, Henriette A Smit, Jordi Sunyer, Magnus Wickman, Josep M Antó, on behalf of the MeDALL Consortium

Sept 2, 2012 / Vienna
Methods

- Pooled analysis of cross-sectional and longitudinal data from 11 European birth cohorts.
Methods

• Pooled analysis of cross-sectional and longitudinal data from 11 European birth cohorts.

• Data at 4 years and 8 years of age:
  • From standardised questionnaires:
    - Clinical phenotypes of wheezing/asthma, rhinitis, dermatitis: symptoms, self reported diagnosis, atopy…
    - Sociodemographic data: age, gender, socioeconomic status…
    - Risk factors: smoking, siblings…
  • Clinical data: weight, height, IgE…

• Database harmonisation of 83 variables.

• Multiple (20) imputation using chained equations of missing data (approx. 10% person·variables)
Results – number of clusters

Two groups emerged as the best separation maximizing between- and minimizing within- groups distances,
also in sensitivity analyses
Two groups emerged as the best separation maximizing between- and minimizing within- groups distances,
also in sensitivity analyses

This study suggests that the atopic march is a reality.
MeDALL future

• **Scale up of existing birth cohorts**
  • Size:
    • Largest cohort: 14,000 children
    • MeDALL: 44,000 children
    • Expectation: >100,000 children (all data available)
  • Geographic diversity:
    • Developed and developing countries
    • Environmental exposure
  • Duration: most children are already > 12 yrs

• **Common protocol for ongoing and new cohorts**
  • Interoperable with historical data
  • New research questions

• **Difficulty to initiate new birth cohorts**

• **To understand links between early life and ageing**
Impact of chronic respiratory diseases in healthy ageing

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4- Importance of the conclusions of The Polish Presidency
Council conclusions on prevention, early diagnosis and treatment of chronic respiratory diseases in children

3131st EMPLOYMENT, SOCIAL POLICY, HEALTH and CONSUMER AFFAIRS Council meeting

Brussels, 1 and 2 December 2011

The Council adopted the following conclusions:
POSITION PAPER

Prevention and control of childhood asthma and allergy in the EU from the public health point of view: Polish Presidency of the European Union

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Debate on “Impact of early diagnosis and control of chronic respiratory diseases on active and healthy ageing”

Following your application dated 29/4/2012, regarding the placing of the Debate on “Impact of early diagnosis and control of chronic respiratory diseases on active and healthy ageing”, under the auspices of the Cyprus Presidency of the Council of EU, I am pleased to inform you that your request has been approved.

2. Please note that the logo of the Cyprus Presidency will be available at a later stage, remain at your disposal for any further information.

(Elena Stavrou)  
for Head  
of Cyprus EU Presidency Secretariat

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