Impact of Exposure to Air Pollution on Asthma: A Multi-Exposure Assessment

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Background

Asthma is the most common chronic disease in children.[1] Exposure to ambient air pollution from motor vehicles may not only exacerbate existing asthma, but also may contribute to the development of asthma.[2-7]

Studies that focus on exposure contrasts within urban areas related to traffic, including my own and studies from Denmark, demonstrate that maternal exposure to traffic-related air pollution during pregnancy reach the fetal blood circulation and induce DNA damage,[8,9] restricts fetal growth,[10,11] and doctor-diagnosed lower respiratory tract infections in the first year of life,[12] and short-term exposure to traffic-related air pollution triggers wheezing in the first 3 years of life[13] and hospital admission for asthma in children up to 18 years of age.[14]

Asthma has a complex etiology, which is still not well understood, as multiple factors, including prenatal exposure, may be involved.[15,16] Some of these factors may be correlated, share sources and pathways resulting in joint effects that are greater than additive. Thus, the potential for confounding and effect modification of the ambient air pollution exposure effects on asthma is very high. The role of early-life exposure to ambient air pollution on the asthma pandemic remains poorly understood due to the lack of large birth cohort studies with sufficient long follow-up and assessment of multiple exposures.

Objectives

We aim to evaluate the risk of developing asthma associated with early-life exposure to air pollution from multiple outdoor and indoor sources such as motorized vehicles, wood stove combustion, smoking, secondary formation, farming and other relevant risk factors through large longitudinal studies of children born in Denmark (Fig.1).

Furthermore, we seek to determine a mechanistic basis for these effects by studying lung function and biomarkers of inflammation, immunological and DNA methylation changes measured in children of asthmatic mothers.

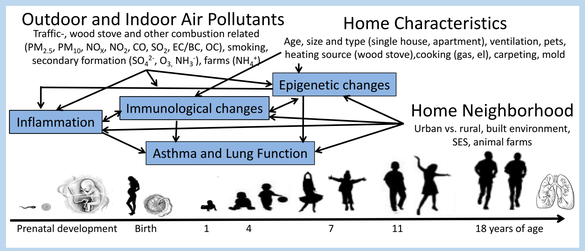

Fig. 1. Relationships between the proposed exposures and outcomes to be studied.

The proposed work will benefit from the internationally-unique access to multiple high-quality environmental exposure, health outcome and individual data available in Denmark including: results from advanced exposure modeling, nation-wide data on asthma, smoking and other personal, home and neighborhood characteristics along with extensive birth cohort data (Fig. 2 & 3).

Drawings by Heather Spears

References

[1] WHO 2016
[2] Andersen et al. 2013
[3] Bowatte et al. 2015
[4] BråBack and Forsberg 2009
[5] Gasana et al. 2012
[6] HEI 2010
[7] Shibi et al. 2016
[8] Pedersen et al. 2009
[9] Pedersen et al. 2015
[10] Pedersen et al. 2013
[11] Pedersen et al. 2016
[12] Aiguilera et al. 2013
[13] Andersen et al. 2008
[14] Iskander et al. 2011
[14] Beasley et al. 2015
[15] Peat et al. 2002

Acknowledgement

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Study Design

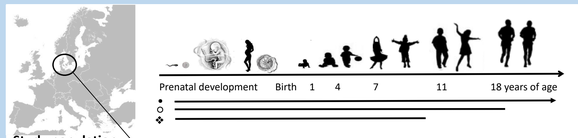
Three populations of children will be studied in a comprehensive manner (Fig. 3). First, to ensure power and avoid potential selection bias, all children born in Denmark since 1997 (N≈1,150,000) will be evaluated. Secondly, we will study a subset of ≈90,000 of these children who participate in the Danish National Birth Cohort (DNBC). Extensive data on individual risk factors, asthma as well as indoor sources are available from early pregnancy and after birth at 1.5, 7, 11 and 18 years of age. Lastly, effects on lung function and biomarkers will be studied in a subset of ≈1,000 of these children who participate in the COPenhagen Prospective Studies on Asthma in Childhood Cohort (COPSAC). The combination of register-, cohort-, clinical- and biomarker based studies allow us to conduct studies that complement each other in terms of size and bias related to selection, misclassification of outcomes or exposures and confounding by e.g. breastfeeding, postnatal smoking, indoor sources of air pollution.

Personal identification number

- Land-use, road and building characteristics
- Home address(es)
- Pregnancy and birth characteristics
- Family
- Diseases
- Prescribed medication
- Vaccinations
- Hospital and GP visit
- School performance
- Education, income and job
- Biological samples
- Questionnaire data from cohort studies etc.
- Mortality and emigration

Fig. 2. The personal identification (CPR) number permits tracking of individuals in the Danish population over time and accurate linkage of individual-level information from Denmark's nationwide population-based registers and cohort studies.

Study Design – cont.



Study population:
- All children born in Denmark since 1997 (N≈1,150,000)
- ○ Danish National Birth Cohort (DNBC, N ≈ 90,000)
- ❖ COPenhagen Prospective Studies on Asthma in Childhood Cohort (COPSAC, N ≈ 1,000)

Exposures:
- Ambient air pollution ($PM_{2.5}$, PM_{10}, NO_x, NO_2, O_3, CO, SO_2, EC/BC, OC, SO_4^{2-}, NH_3^-, NH_4^+)
- Residential neighborhood (built environment, urban vs. rural, animal farms, SES)
- Home characteristics (age, size, type (single house vs. flat), wood stove heating, gas cooking)
- Personal characteristics (prenatal smoking, SES)
- ○ Personal characteristics (postnatal smoking, lifestyle, indoor home environment, daycare)
- ❖ Personal characteristics as above

Outcomes:
- Asthma hospitalization
- Prescription of asthma medicine
- ○ Parental-reports of doctor diagnosed asthma and other asthma-related outcomes
- ❖ Parental-reports of doctor diagnosed asthma and other asthma-related outcomes, clinical assessment of lung function and biomarker measurements in blood and airway epithelial cells

Fig. 3. Populations, exposures and outcomes to be studied.

Potential confounding and effect modification will be considered. Traditional and more efficient advanced statistical methods will be used to study the individual and joint effects of multiple exposures.

Further information

Please feel welcome to contact Marie Pedersen for further questions and/or in case you are interested in collaborating on these studies here at the HEI meeting or via e-mail: mp@sund.ku.dk