Doi:10.1111/ina.12454

Online supporting information for the following article published in *Indoor Air*

DOI: TO BE ADDED BY THE PRODUCTION EDITOR

**Early age exposure to moisture damage and systemic inflammation at the age of 6 years**

Karvonen AM1\*, Tischer C2-4\*, Kirjavainen PV1,5, Roponen M6, Hyvärinen A1, Illi S7, Mustonen K1,  Pfefferle PI8, Renz H8, Remes S9, Schaub B7, von Mutius, E7,10,11, Pekkanen J1,12.

\*These authors contributed equally to this work.

1Department of Health Security, National Institute for Health and Welfare, Kuopio, Finland; P.O. Box 95, FIN-70701 Kuopio, Finland

2ISGlobal, Barcelona Institute for Global Health - Campus MAR, Barcelona, Spain; c/ Rosselló, 132, 5th 2nd. 08036, Barcelona, Spain

3Universitat Pompeu Fabra (UPF), Barcelona, Spain; Plaça de la Mercè, 10-12. 08002 Barcelona Spain

4CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain; Av. Monforte de Lemos, 3-5. Pabellón 11. Planta 0 28029 Madrid, Spain

5Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland; Yliopistonranta 1, FIN-70210 Kuopio, Finland

6Department of Environmental and Biological Sciences, University of Eastern Finland, Kuopio, Finland; Yliopistonranta 1, FIN-70210 Kuopio, Finland

7Dr. von Hauner Childrens Hospital, Ludwig Maximilians University Munich, Lindwurmstr. 4, D-80337, Munich, Germany

8Institute for Laboratory Medicine and Pathobiochemistry, Molecular Diagnostics, Philipps-University of Marburg, Germany; Baldingerstraße 35033, Marburg, Germany

9Department of Pediatrics, Kuopio University Hospital, Kuopio, Finland; P.O. Box 100, FI-70029 KYS, Finland

10Institute for Asthma and Allergy Prevention (IAP), Helmholtz Zentrum München, Munich, Germany; Ingolstaedter Landstrasse 1, 85764 Neuherberg, Germany

11Member of the German Centre for Lung Research

12Department of Public Health, University of Helsinki, Helsinki, Finland; P.O.Box 20, 00014 University of Helsinki, Finland

E-mail addresses: anne.karvonen@thl.fi, christina.tischer@med.uni-muenchen.de, pirkka.kirjavainen@thl.fi, marjut.roponen@uef.fi, anne.hyvarinen@thl.fi, Sabina.Illi@med.uni-muenchen.de, kmmuston@student.uef.fi, pfeffpet@staff.uni-marburg.de, renzh@med.uni-marburg.de, sami.remes@kuh.fi, Bianca.Schaub@med.uni-muenchen.de, Erika.Von.Mutius@med.uni-muenchen.de, and juha.pekkanen@helsinki.fi

Corresponding author:

Anne M. Karvonen, Department of Health Security, National Institute for Health and Welfare, P.O. Box 95, FIN-70701 Kuopio, Finland. E-mail: anne.karvonen@thl.fi. Tel: +358 (0) 29 524 6325.

**Supplementary Table 1: Study population and home characteristics (N=292\*)**

PASTURE (Protection against Allergy Study in Rural Environments), NA=the number of observations with missing values,
BMI Body mass index. \*Study population: data on home inspections in early age and either available CRP or cytokine measurements at 6 years of age.

**Supplementary Table 2A:** Adjusted associations between early age exposure to moisture damage in the child’s main living areas and systemic inflammation markers (CRP and leucocytes) at the age of 6 years, additionally adjusted for current exposure to moisture damage.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **N** | n(%) of **CRP** ≥ 75th percentile  | **aOR (95% CI)** | **N** | n(%) of **leucocytes** ≥ 75th percentile  | **aOR (95% CI)** |
| **Moisture damage**  |  |  |  |  |  |  |
| No damage | 137 | 37 (27%) | 1 | 139 | 34 (24%) | 1 |
| Minor | 54 | 13 (24%) | 0.67 (0.27-1.64) | 50 | 9 (18%) | 0.93 (0.37-2.39) |
| Major | 28 | 7 (25%) | 0.52 (0.16-1.68) | 26 | 10 (38%) | 2.59 (0.80-8.36) |

N number of observations, CRP C-reactive protein, aOR adjusted odds ratio, 95%CI 95% confidence interval

Models are adjusted for: gender, living on a farm, older siblings, maternal smoking during pregnancy, maternal allergy, body mass index, current exposure to moisture damage in child’s main living area, and study cohort.

**Supplementary Table 2B:** Adjusted associations between early age exposure to moisture damage in the child’s main living areas and the production of unstimulated and stimulated cytokines at the age of 6 years, additionally adjusted for current exposure to moisture damage.

|  |
| --- |
| **Unstimulated** |
| **Moisture damage**  | **N** | n(%) of **TNF-α** ≥ 75th perc  | **aOR (95% CI)** | n(%) of **IL-1β**  ≥ 75th perc | **aOR (95% CI)** | n(%) of **IL-6** ≥ 75th perc | **aOR (95% CI)** |
| No damage | 137 | 37 (27%) | 1 | 36 (26%) | 1 | 40 (29%) | 1 |
| Minor | 49 | 13 (26%) | 0.72 (0.29-1.81) | 11 (22%) | 0.52 (0.23-1.54) | 10 (20%) | 0.48 (0.18-1.28) |
| Major | 26 | 5 (16%) | 0.44 (0.12-1.64) | 8 (31%) | 0.93 (0.29-3.02) | 6 (23%) | 0.39 (0.10-1.49) |
| **PI-stimulated** |
| No damage | 139 | 36 (26%) | 1 | 39 (28%) | 1 | 39 (28%) | 1 |
| Minor | 50 | 14 (28%) | 0.94 (0.34-2.55) | 9 (18%) | 0.41 (0.15-1.16) | 12 (24%) | 0.58 (0.22-1.53) |
| Major | 26 | 6 (23%) | 0.81 (0.22-3.03) | 6 (23%) | 0.32 (0.08-1.28) | 5 (19%) | 0.35 (0.09-1.37) |
| **LPS-stimulated** |
| No damage | 139 | 32 (23%) | 1 | 37 (27%) | 1 | 38 (27%) | 1 |
| Minor | 50 | 12 (24%) | 0.68 (0.26-1.74) | 9 (18%) | 0.57 (0.22-1.47) | 11 (22%) | 0.59 (0.23-1.55) |
| Major | 41 | 8 (20%) | 0.84 (0.26-2.70) | 7 (17%) | 0.85 (0.26-2.77) | 3 (7%) | 0.24 (0.05-1.07) |
| **PPG-stimulated** |
| No damage | 139 | 38 (27%) | 1 | 35 (25%) | 1 | 37 (27%) | 1 |
| Minor | 49 | 13 (27%) | 0.82 (0.34-1.97) | 11 (22%) | 1.06 (0.43-2.59) | 14 (29%) | 1.36 (0.58-3.22) |
| Major | 25 | 6 (24%) | 0.74 (0.23-2.44) | 6 (24%) | 0.77 (0.22-2.66) | 3 (12%) | 0.44 (0.10-1.83) |

N number of observations, CRP C-reactive protein, aOR adjusted odds ratio, 95%CI 95% confidence interval, TNF-α tumor necrosis factor alpha, IL-1β Interleukin 1-beta, IL-6 Interleukin 6, PI phorbol 12-myristate 13-acetate and ionomycin stimulated, LPS lipopolysaccharide stimulated, PPG peptidoglycan stimulated. Models are adjusted for: gender, living on a farm, older siblings, maternal smoking during pregnancy, maternal allergy, body mass index, current exposure to moisture damage in child’s main living area, and study cohort.

**Supplementary Table 2C:** Adjusted associations between early age exposure to moisture damage in the child’s main living areas and combined levels of stimulated cytokines at the age of 6 years, additionally adjusted for current exposure to moisture damage.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Unstimulated** |  |
|  | **N** | n(%) of cytokines ≥ 75th percentile  | **aOR (95% CI)** | **N** |
| **Moisture damage**  |  |  |  |  |
| No damage | 137 | 38 (28%) | 1 | 139 |
| Minor | 49 | 11 (22%) | 0.55 (0.21-1.43) | 50 |
| Major | 26 | 5 (19%) | 0.42 (0.11-1.59) | 26 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **PI-stimulated** | **LPS-stimulated** |  | **PPG-stimulated** |
|  | **N** | n(%) of cytokines ≥ 75th percentile  | **aOR (95% CI)** | n(%) of cytokines ≥ 75th percentile  | **aOR (95% CI)\*** | **N** | n(%) of cytokines ≥ 75th percentile  | **aOR (95% CI)\*** |
| **Moisture damage**  |  |  |  |  |  |  |  |  |
| No damage | 139 | 39 (28%) | 1 | 34 (24%) | 1 | 139 | 39 (28%) | 1 |
| Minor | 50 | 12 (24%) | 0.48 (0.18-1.32) | 9 (18%) | **0.33 (0.11-0.99)** | 49 | 13 (27%) | 0.81 (0.32-2.02) |
| Major | 26 | 5 (19%) | 0.29 (0.07-1.17) | 6 (23%) | 0.39 (0.11-1.44) | 25 | 4 (16%) | 0.28 (0.07-1.17) |

N number of observations, CRP C-reactive protein, aOR adjusted odds ratio, 95%CI 95% confidence interval, TNF tumor necrosis factor, IL-1b Interleukin 1-beta, IL-6 Interleukin 6, PI phorbol 12-myristate 13-acetate and ionomycin stimulated, LPS lipopolysaccharide stimulated, PPG peptidoglycan stimulated. Combination variables for IL-1β, IL-6, and TNF-a were created by taking the ranks of the three cytokines without stimulant (unstimulated) and within each stimulates (PI, LPS and PPG). Models are adjusted for: gender, living on a farm, older siblings, maternal smoking during pregnancy, maternal allergy, body mass index, current exposure to moisture damage in child’s main living areas, and study cohort.