### 学位論文の要旨

Association between temporary housing habitation after the 2011 Japan earthquake and mite allergen sensitization and asthma development

(東日本大震災後の応急仮設住宅に入居歴のある住民を対象とした気管支喘息の有病率 およびアレルゲン感作と喘息の発症について)

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Introduction: It is unknown whether disasters such as earthquakes and tsunamis affect asthma development or exacerbation in adults. Since the 2011 Great East Japan Earthquake, levels of airborne fungi have increased in temporary housing in Ishinomaki, located in eastern Miyagi Prefecture, which was damaged by the large tsunami (1). We also previously reported a rare case of allergic bronchopulmonary mycosis in a patient who had been exposed to *Eurotium herbariorum* while residing in post-earthquake temporary housing in Ishinomaki (2). We investigated whether asthma prevalence increased in those aged  $\geq$ 15 years living in temporary housing after the Great East Japan Earthquake. The goal of the current study was to investigate changes in asthma prevalence and mite-specific IgE titers in temporary housing residents and we evaluated the prognosis of asthma in former residents of temporary housing after allergen avoidance.

**Methods:** We diagnosed asthma according to GINA guidelines from 2014 to 2019 in residents aged  $\geq 15$  years who were living, or had lived, in temporary housing in the city of Ishinomaki for at least 1 year. We analyzed serum antigen-specific IgE antibody levels to *Dermatophagoides farinae* (*Der f*), *Dermatophagoides pteronyssinus* (*Der p*), *Aspergillus fumigatus* (*Asp-f*). We analyzed the prognosis of asthma after the intervention of allergen avoidance in cases that were

followed for more than 3 years during the 6-year study period. We measured the *Der f*-specific IgE levels in serum and the amount of *Der* 1 antigen on their futons or mattresses. We instructed residents in an allergen avoidance strategy (3), including using microfiber bedding covers. The project was approved by the ethics committee of the University Hospital Medical Information Network (UMIN ID: UMIN000014376). The hospital ethics committee approved the study in accordance with the Helsinki Declaration. Human Subject Protection Committee approval in Hiratsuka city hospital was obtained (No 30-008).

Results: The prevalence of asthma exceeded 20% across all age groups from 2014 to 2019 of the study periods. The antigen-specific IgE antibody titer against Der f and Der p but not Asp-f, was significantly higher in asthmatic group than in non-asthmatics group (P < 0.01). Logistic regression in 2014 revealed that the risk factors for developing asthma after moving into temporary housing were allergic rhinitis or allergic conjunctivitis (P < 0.05), family asthma history (P < 0.05), never having smoked (P < 0.01), and peripheral airways disorder (low %  $V_{50}$ ) (P < 0.05) but not depression (4). The proportion of study participants with a "positive" antigen-specific IgE titer (i.e.,  $\geq 0.35~{
m IU}_{
m A}/{
m mL}$ ) was higher in asthmatics than in non-asthmatics for *Der f* and *Der p* but not for Asp-f. Among residents ≥50 years old who were diagnosed with asthma, the percentage with a *Der f*-specific IgE titer  $\geq 0.10$  IU<sub>A</sub>/mL was higher than the proportion with  $\geq 0.35$  IU<sub>A</sub>/mL. Among study participants, asthma onset occurred before the earthquake, during residence in shelters or temporary housing, and (starting in 2016) after moving out of temporary housing. The Der p-specific IgE level was positively correlated with the duration of temporary housing (P < 0.05, r = 0.41) and inversely correlated with the time elapsed since moving out of temporary housing (P < 0.05, r = -0.35)(5). Of the 202 examinees who were followed for at least 3 years during the 6-year study period, 72(35.6%) were asthmatic during at least one examination. After the allergen-avoidance intervention, both the Der 1 level on the futons or mattresses of residents who were diagnosed with asthma but who were non-asthmatic at the final screening and their serum *Der f*-specific IgE levels significantly decreased (p < 0.01) at the final examination (6).

**Discussion**: In the 2014 survey we reported (4), the rates of depression among victims of the Great East Japan Earthquake were more than double those among victims of the 1995 Great Hanshin-Awaji Earthquake, but there were no significant differences in mental stress-related illnesses between asthmatics and non-asthmatics. The development and exacerbation of asthma in our survey population may not have been directly related to the effects of post-earthquake mental stress.

Our results show that, compared with asthmatics, non-asthmatics showed greater weak sensitization to HDMs over the 6-year observation period. Furthermore, a greater proportion of asthmatic residents  $\geq$ 50 years of age had

"weakly positive" *Der* f serum IgE titers than "positive" titers in 2014, 2016, and 2017. These results indicate that both asthmatic and non-asthmatic adults  $\geq$ 50 years of age are more susceptible to weak sensitization to *Der* f than are adults  $\leq$ 49 years of age who are former or current residents of temporary housing.

The prevalence of asthma in our study population did not necessarily decrease after people moved out of temporary housing. In fact, new cases of asthma were diagnosed not only after examinees moved into temporary housing but also after they moved out; these latter cases occurred every year since 2016. This suggests that sensitization to mite allergens while living in temporary housing led to the development of asthma due to these environmental factors after residents had moved out. We considered that allergen sensitization could be increased, or asthma could newly develop, owing to the difference in mite allergen exposure in the living environment after moving out of temporary housing.

Mite allergen sensitization was found in both asthmatic and non-asthmatic temporary housing residents after the 2011 Japan earthquake and tsunami; asthma developed even after subjects moved out of temporary housing. Antigen avoidance ameliorated the mild asthma that was prevalent among residents of temporary housing after the earthquake.

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#### Main treatise

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