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Dampness and mold hypersensitivity syndrome and vaccination as risk factors for chronic fatigue syndrome

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Dear Editor,

Dampness and Mold Hypersensitivity Syndrome (DMHS) associates with several other neglected medical conditions such as the Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) [1] and Multiple Chemical Sensitivity (MCS) [2]. In DMHS 5 criteria have been proposed: *1)* exposure to dampness microbiota (DM); *2)* recurrent and/or unusual infections; *3)* Sick Building Syndrome (SBS); *4)* development of MCS and *5)* sensitized olfactory scenting [3]. We hypothesized that previous exposure to DM could be a risk factor for vaccination to trigger disability with/or without neurological sequelae. Therefore we investigated the potential combined risks of DMHS and Pandemrix®, Gardasil® or Cervarix® (PGC) to cause severe disability. Conditions such as Ehlers-Danlos Syndrome (EDS) [4], ME/CFS [5], Postural Orthostatic Tachycardia Syndrome (POTS) [6], Complex Regional Pain Syndrome (CRPS), Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) were considered.

Families of 100 children, who developed disabilities, responded within a closed Facebook group to our questionnaire. The parents used self-assessment that was blinded to the principle investigator [TT] and were interviewed by another investigator [TJ]. Groups 1–4 were study groups, and Groups 5–8 served as controls. Three cases were excluded as not fulfilling the criteria. The parents of 16 cases were too exhausted to participate. Finally, 81 cases were included. The cases were asked to allocate themselves into one of the following groups:

Group1: Exposure to DM at home and school and vaccination with PGC.

Group2: Exposure to DM only at home and vaccination with PGC.

Group3: Exposure to DM only at school and vaccination with PGC.

Group4: Questionable exposure to DM at home or school and vaccination with PGC.

Group5: Definitely no exposure to DM and vaccination with PGC.

Group6: Definite exposure to DM at home or at school but no PGC vaccination.

Group7: Questionable exposure to DM but no PCG vaccination.

Group8: Questionable exposure to DM, no PGC vaccination but vaccination with other vaccines within the 5 years before the onset of the disease.

The study did not require ethical clearance, because it was based on a questionnaire initiated by parents of sick children.

The diagnoses reported by participants are collected in the Table 1. The reported symptoms were: Migraine; fatigue; headache; dizziness; balance, visual, hearing or speech disturbance; cognitive problems; problems in the perception of the environment; hyperactivity when tired; difficulty falling asleep; sensory hypersensitivity; *petit mal* epilepsy; insomnia, nightmares, abnormal sleep (waking up, not deep sleep); tachycardia when sitting; irritability; adaptation difficulties in the change of situations; impulsiveness; concentration problems, hyperactivity, occasional dizziness during infection.

The disabilities appeared during the years of 2009–2016 at the ages from 8 to 14 years. The majority of cases were allocated to the Groups 1–4. ME/CFS proportion in the Groups 1–4 was in 52/74 cases (70%). If POTS alone or in combination with other symptoms is a feature of ME/CFS, then the prevalence of ME/CFS was 72/81 (89%). Unexpectedly, there were no children in the Group 5.

Depending on the assessment when calculated from the Groups 1–3 or the Groups 1–4, 46/81 (57%) or 74/81 (91%) had been exposed to indoor air DM, respectively. Furthermore, 32/81 (40%) of cases presented with recurrent infections (≥ 3 episodes/year requiring medical treatment). As much as 15/76 (20%, Groups 1–4 & Group 8) reported various neurological symptoms prior the vaccination.

After vaccination, MCS developed in 15/76 (20%) of the respondents. In 6 cases MCS developed within one year and in 6 cases within 1–5 years after the vaccination. The incidence of MCS was the highest in the Group 1 (5/15; 33%); in the Groups 2–4 this incidence was 1/6 (17%), 4/25 (16%) and 4/28 (14%), respectively. Two cases reported MCS in the Group 6, none in the Groups 7 and one case in the Group 8.

Severe stress (parents' divorce or death of a close person) as a potential trigger was reported in 21/77 (27%) of the cases; 3/81 (3.7%) reported exposure to herbicides and 8/81 (9.9%) to 2-ethylhexanol. Prior to the onset of disabilities, all children had either high or moderate level of physical activity. By the time of this investigation

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Table 1
The distribution of diagnoses in the study cohort.

Diagnoses	All cases	Girls	Boys
ME/CFS	19	14	5
ME/CFS + POTS	30	19	11
ME/CFS + POTS +CRPS	1	1	0
ME/CFS + PANS + POTS	2	2	0
ME/CFS + PANS	3	2	1
ME/CFS + CRPS	1	1	0
POTS	10	7	3
POTS + PANS	6	2	4
PANS	4	1	3
PANS + PANDAS	1	1	0
CRPS	1	0	1
No diagnoses #	3	3	0
n	81	53	28

#These cases were enrolled into the study. Two girls had neurological symptoms but their parents were unable to allocate them to any Group. One 11-year old girl had a stroke after the vaccination.

disability did not improve in 42/81 (52%); partial recovery was found in 31/81 (38%); disability after physical or psychological activity was documented in 5/81 (6.1%) and only 3/81 (3.7%) reported full recovery. Physical activity of the children now is the following: 3 children have a little limitations of everyday life (partly recovered); 18 girls and 15 boys experience limitations of everyday life; 17 girls and 7 boys have limitations in sports activities; 4 girls need aide or a wheelchair when moving; 7 girls and 4 boys are partly and 3 girls are fully bedridden, and 3 recovered completely. The majority 48/81 (59%) reported hypermobile joints, including 13/81 (16%) patients with EDS.

Depending on the assessment, 57–91% of responders were exposed to bad indoor air. This exceeds the national epidemiologic data on the exposure to DM at homes (6–10%) or at daycare or school (12–18%) [7]. Our data support a dose-dependent association between DMHS and MCS [3]. Indeed, the incidence of MCS in the highly exposed Group 1 was double (33%) compared to that of the less exposed, Groups 2 and 3 (16.5%). In line with earlier reports, hypermobile joints and EDS were common also in our study cohort. Surprisingly, there were no cases with definitely no exposure to DM who received PGC vaccination. Lack of sufficient size control groups and inclusion of subjective self-assessments are acknowledged as the major limitations of this study.

Although the vaccines as plausible triggers of disabilities did not come up clearly in this investigation, a temporal association could not be excluded. None of the disabilities appeared before the Pandemrix® vaccination that was started in 2009. The national Human Papilloma Virus (HPV) vaccination program started in late 2013. HPV vaccines have been reported to associate with POTS, CRPS and fibromyalgia [8]. Also, other reports raise concerns about the safety of HPV vaccines: *a)* peptides used in HPV vaccines possess sequence homology with human proteins (Y Segal, oral presentation, 11th Congress of Autoimmunity), *b)* molecular mimicry can cause ASIA (Autoimmune Syndrome Induced by Adjuvants) [9]), and *c)* alike mycotoxins [10], aluminum hydroxide activates NLRP3 inflammasome resulting in IL-1β production, and activates the complement system cascade [11]. Combined, these factors may exert a synergic effect and be detrimental to cause ME/CFS.

The conclusions of this study are the following. Firstly, presented data confirm the linkage between DMHS and MCS. Secondly, DMHS may predispose to the development of ME/CFS which may require an additional trigger, such as vaccination. Our data are an alert for consideration that preceding DMHS with or without MCS or joint hypermobility/EDS should be acknowledged as contraindications for PGC vaccination. Proper assessment of risk factors would increase the safety profile of these vaccines without compromising herd immunity.

Conflict of interest

OP has examined and treated some of the children at his private consultation.

Authors' contribution

TT and TJ designed the study; TJ interviewed the families and calculated the data. TT wrote the first draft. KV and OP actively participated to the scientific writing of the manuscript and reviewed the contemporary literature regarding ME/CFS and presented hypothesis of the mechanisms. All authors contributed to the writing of the manuscript and accepted the final version.

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References

[1] Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. The National Academies Collection: Reports funded by National Institutes of Health (Washington (DC)). 2015.
[2] Dantoft TM, Andersson L, Nordin S, Skovbjerg S. Chemical intolerance. Curr Rheumatol Rev 2015;11(2):167–84.
[3] Valtonen V. Clinical Diagnosis of the Dampness and Mold Hypersensitivity Syndrome: Review of the Literature and Suggested Diagnostic Criteria. Front Immunol 2017;8:951.
[4] Roma M. Postural tachycardia syndrome and other forms of orthostatic intolerance in Ehlers-Danlos syndrome. Auton Neurosci: Basic and Clin 2018. https://doi.org/10.1016/j.autneu.2018.02.006.
[5] Morris G, Berk M, Walder K, Maes M. The Putative Role of Viruses, Bacteria, and Chronic Fungal Biotoxin Exposure in the Genesis of Intractable Fatigue Accompanied by Cognitive and Physical Disability. Mol Neurobiol 2016;53(4):2550–71.
[6] Sharif K, Watad A, Bragazzi NL, Lichtbroun M, Martini M, Perricone C, et al. On chronic fatigue syndrome and nosological categories. Clin Rheumatol 2018;37(5):1161–70.
[7] Reijula K, Ahonen G, Alenius H, Holopainen R, Lappalainen S, Palomäki E, et al. Rakennusten kosteus- ja homeongelmat. 2012. Eduskunnan tarkastusvaliokunnan julkaisu https://www.eduskunta.fi/FI/tietoaeduskunnasta/julkaisut/Documents/trvj_1+2012.pdf.
[8] Martinez-Lavin M. Hypothesis: Human papillomavirus vaccination syndrome–small fiber neuropathy and dysautonomia could be its underlying pathogenesis. Clin Rheumatol 2015;34(7):1165–9.
[9] Watad A, Quaresma M, Brown S, Cohen Tervaert JW, Rodriguez-Pint I, Cervera R, et al. Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome) - An update. Lupus 2017;26(7):675–81.
[10] Tavares AH, Burgel PH, Bocca AL. Turning Up the Heat: Inflammasome Activation by Fungal Pathogens. PLoS Pathog 2015;11(7):e1004948.
[11] Kooijman S, Brummelman J, van Els C, Marino F, Heck AJR, Mommen GPM, et al. Novel identified aluminum hydroxide-induced pathways prove monocyte activation and pro-inflammatory preparedness. J Proteomics 2018;175:144–55.

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