



Case report

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Acute effects after occupational endotoxin exposure at a spa

by Mathias Holm, MD,¹ Sandra Johannesson, MSc,¹ Kjell Torén, MD,^{1,2} Anna Dahlman-Höglund, PhD¹

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Objectives Two spa workers reported symptoms such as fever, shivering, palpitation, arthralgia, and diarrhea after performing seaweed massages on clients at a spa center. This study was carried out to determine whether the symptoms were related to exposure to endotoxin.

Methods Personal and stationary air sampling for the measurement of airborne endotoxin was carried out at the spa during the preparation of a bath and the following seaweed massage. In addition, the impact of storage time on the concentration of endotoxin in the seaweed was investigated.

Results The measurements confirmed exposure to aerosolized endotoxin at the spa (11 ng/m² and 22 ng/m³). The endotoxin concentration in the stored seaweed increased as the storage time increased, from 360 ng/g seaweed for fresh seaweed to 33 100 ng/g seaweed for seaweed stored for >20 weeks.

Conclusions Organic dust toxic syndrome was diagnosed for two workers who performed seaweed massages at a spa center at which aerosolized endotoxin was measured. In order to minimize endotoxin exposure during massages, it is important to use fresh seaweed or seaweed kept well cooled for no more than 2–3 weeks.

Key terms algae; case report; *Fucus serratus*; measurement; seaweed; work-related disease.

Exposure to organic dust or endotoxin is known to cause acute effects in humans (1–4). In this short report, we present two spa workers who described repeated symptoms including fever, shaking chills, palpitation, arthralgia, and diarrhea after performing seaweed massage on clients at a spa center. Aerosolized endotoxin was suspected to have caused the symptoms, which initiated further investigations, including measurements.

Case reports

Case 1

A healthy 40-year-old man visited his occupational health service after having worked at a spa for 1–2 years. He described problems after he had performed seaweed massages on clients. After 5–6 hours, he had fever with arthralgia and shivering. His symptoms went into complete remission approximately 12 hours after the massages. All told, he had experienced 15–20 episodes

with similar symptoms. He was referred to an occupational allergologist. At the visit he had no current symptoms. A standard skin prick test to common allergens, C-reactive protein, leucocytes, and precipitating antibodies against farmer's lung and *Aspergillus* were all negative. An X-ray examination of the lungs was normal, as were his spirometric values. Based on the clinical presentation, endotoxin exposure was strongly suspected to have caused the problem, and the patient was diagnosed as having inhalation fever.

Case 2

A 27-year-old woman had worked at the same spa as case 1 for approximately 3 months when she visited her occupational health service. Other than having celiac disease, she was healthy. She described episodes, each lasting 12–18 hours, of shivering, palpitation, and a sense of fever in combination with diarrhea. The symptoms went into complete remission between episodes. The patient had noted that she had treated the

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face of clients with a seaweed massage or algae treatment 5 hours prior to each episode. She was referred to a physician in the field of occupational medicine for evaluation and was given a diagnosis of fever. On the basis of the clinical presentation and knowledge from case 1, it was stipulated that her symptoms were due to the inhalation of endotoxin.

Investigation at the spa center

An occupational hygienist performed an investigation of the spa workers' exposure to different compounds at work. At the spa, 1 kg of brown seaweed (*Fucus serratus*) was placed in a bathtub with water heated to 38°C. Clients were normally treated in the bathtub for about 30 minutes, including 10 minutes of massage. The storage time and handling procedure for the seaweed used on this occasion were not known. A sample was taken from the water prepared with seaweed, and it was sent to the laboratory for analysis. The sample was found to contain an endotoxin concentration of 800 ng/ml.

On another occasion, the airborne endotoxin concentration around the bathtub was measured using active sampling with polycarbonate filters. Personal sampling on one of the employees was performed with a filter placed in the breathing zone. Sampling (2 l/minute) was started during the preparation of the bath and continued during the seaweed massage procedure.

Simultaneously with the personal monitoring, stationary sampling was carried out by placing a filter approximately 50 centimeters above the water surface. Both the personal and stationary sampling continued for 25 minutes. The personal air sample contained an endotoxin concentration of 11 ng/m³, and that of the stationary sample was 22 ng/m³. For a standardized analysis of endotoxin in water and air, we used an endpoint chromogenic test (limulus amoebocyte lysate—endosafe endochrome-K, standardized endotoxin method 1240, accreditation certificate number ISO 15189), delivered by Charles River Laboratories, Charleston, SC, USA.

Often the spa workers had several clients in succession, leading to extended exposure. However, there were no symptoms if exposure was avoided. Adding seaweed to the bath made the water somewhat turbid. It is likely that an aerosol was formed from small droplets or splashes being produced when the clients were massaged with the seaweed. It was concluded that the spa workers' symptoms had probably been caused by the aerosolized endotoxin they were exposed to during the massage procedure.

Evaluation of the seaweed-handling procedure

We contacted the supplier of the seaweed to analyze it for endotoxin. The supplier harvested fresh brown seaweed (*Fucus serratus*) from the sea. For it to become slimy, he thereafter placed it in 75°C water with 6–7% salt for 10 minutes. The warm seaweed was then cooled and placed in a plastic bag, which was sealed. It was recommended that the seaweed be stored at +4°C for a maximum of 2–3 weeks before use.

We received several such sealed plastic bags with seaweed with a controlled storage time. The seaweed was analyzed for endotoxin while it was fresh and after 4 or 14 weeks of storage. In addition, seaweed aged >20 weeks, returned by the spa to the supplier, was also analyzed for endotoxin. [The storage time of this specific seaweed was unknown.] Just before the analysis, the sealed bags with seaweed of different ages were placed at room temperature. The seaweed was sent to the laboratory for the aforementioned standardized endotoxin analysis. [See the section Investigation at the spa center.] The results showed an increase in the endotoxin levels after 14 weeks of storage (9180 ng/g seaweed) when compared with the levels of fresh (360 ng/g seaweed) and 4-week-old (480 ng/g seaweed) seaweed. The seaweed with a storage time of >20 weeks showed an endotoxin concentration of 33 100 ng/ng seaweed. A bacterial analysis showed unfermented gram-negative bacteria.

Discussion

These case reports highlight a previously unpublished exposure to aerosolized endotoxin. The symptoms and course of events described by the spa workers are in line with previously reported acute effects of exposure to organic dust or endotoxin (1–4).

The organic dust toxic syndrome (ODTS) includes conditions such as inhalation fever (mill fever, humidifier fever, grain fever), mycotoxicosis, atypical farmer's lung, and silo unloader's lung. The inhalation of aerosols containing large amounts of micro-organisms can result in ODTS (5). Endotoxins (lipopolysaccharide), derived from gram-negative bacteria or cyanobacteria, are known to cause acute effects similar to ODTS in humans (2). However, ODTS has been reported when inhaled endotoxin levels have been assumed to be too low to induce symptoms. This finding suggests the presence, in some cases, of a combination of factors that give rise to ODTS (6). Exposure to endotoxin has been identified in a variety of occupational environments, including cotton factories, fiberglass wool manufacturing, the repulping and de-inking in paper waste industries, swine enclosures, poultry farming, milking barns, work close to swimming pools, and workplaces with humidifiers (3, 7).

In the water prepared with seaweed at the spa, the endotoxin concentration was 800 ng/ml, which is about 100–1000 times that found in normal drinking water (3). However, it is the fraction aerosolized that normally enters the human body via the airways that can have a deleterious effect. One limitation of this study was the lack of information on both the storage time and the handling procedure of the specific seaweed used during the measurement. However, it does show that endotoxin was released into the air during the spa treatment with seaweed. Unfortunately, we were only able to perform a very limited number of measurements because the patients no longer worked at the spa center (and we therefore had no further access to the spa). It may, therefore, be that the measured levels of endotoxin at the spa center on this single occasion did not represent levels at which the patients had experienced symptoms.

It is unclear whether lung-function parameters or clinical symptoms are the most sensitive in assessing the adverse effects of endotoxin inhalation, and there is no precise information about the relation between systemic effects and endotoxin levels (8). Using a pooled set of data, Castellán et al calculated a threshold level of 9 ng/m³ for an acute effect of endotoxin on lung function, and even lower threshold levels for such an effect have been presented (8, 9).

Alginate, a polysaccharide extracted from seaweed for use in the food industry and healthcare, has been shown to be contaminated with endotoxin (10, 11). This finding is in line with the results of our study, in which endotoxin was found in fresh seaweed. Moreover, the concentration of endotoxin seems to increase markedly as the storage time of seaweed increases. This circumstance could result in big differences in endotoxin exposure at the spa center, depending on the storage and handling of the seaweed used.

Fever after endotoxin exposure is thought to be mediated by tumor necrosis factor alpha (TNF- α), which is known to be stimulated by lipopolysaccharide (12). There are data indicating that some alginates, apart from the effect caused by endotoxin contamination, can stimulate TNF- α by a mechanism similar to that used by lipopolysaccharide (13). Consequently, it may be that seaweed contains components capable of inducing symptoms similar to those found after endotoxin exposure.

In conclusion, ODTS was diagnosed for two staff members performing seaweed massages at a spa center at which aerosolized endotoxin was measured. Endotoxin was found in fresh seaweed, and the concentration

increased markedly with an increase in the length of storage of the seaweed. In minimizing endotoxin exposure, it is important to use either fresh seaweed or seaweed kept well cooled for no more than 2–3 weeks in a refrigerator.

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