

# Persistent Respiratory Symptoms following Prolonged Capsaicin Exposure

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## Abstract

Capsaicin causes direct irritation of the eyes, mucous membranes, and respiratory tract. It is used in self-defense, in crowd control, and as a less lethal weapon in police work. Controlled trials suggest that capsaicin has minimal serious acute effects. Herein, we report a woman who had a 20-minute exposure to capsaicin during a jail riot. She subsequently developed episodic dyspnea and cough, and increased sensitivity to scents, perfumes, and cigarette smoke. She has not had wheezes on physical examination or abnormal pulmonary function tests. Her response to inhaled steroids and long-acting beta-agonists has been incomplete. She appears to have developed airway sensory hyperreactivity syndrome after the inhalation of capsaicin, which likely injured sensory nerves and/or caused persistent neurogenic inflammation.

**Keywords:** Capsaicin; Toxicity; Dyspnea; Cough; Bronchial hyperreactivity; Neurogenic inflammation

## Introduction

Airway sensory hyperreactivity syndrome (SHR) is a newly recognized clinical syndrome with an estimated prevalence of 6.3% in the general population of Sweden.<sup>1</sup> These patients have increased sensitivity to environmental odors, such as perfumes, scents, cigarette smoke, and cleaning agents, and have chronic respiratory symptoms, including dyspnea, cough, and rhinorrhea. They have high scores on chemical sensitivity scales, have increased cough following the inhalation of capsaicin, but do not have bronchial obstruction or bronchial hyperreactivity.<sup>2</sup> This chemical sensitivity may reflect a genetic predisposition with alteration in sensory receptors or

an acquired characteristic that develops after environmental exposures or respiratory infections, which result in nerve injury. The differential diagnosis for SHR includes irritant-induced asthma, which can develop acutely after a single exposure to an irritant in high concentrations or chronically after multiple exposures to irritants in lower concentrations.<sup>3</sup> Herein, we report a patient who has developed persistent respiratory symptoms after a single intense exposure to capsaicin.

## Case Presentation

A 47-year-old woman presented to the pulmonary clinic for evaluation of chronic respiratory symptoms. The patient was in excellent health, with no history of

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chronic respiratory disease, until she was exposed to OC gas (capsaicin) at the correctional facility where she is employed. She was exposed to high concentrations of capsaicin for more than 20 minutes. Shortly after the exposure, she developed right-sided pleuritic chest pain, which increased over the next 24 hours, shortness of breath, and cough. She was treated at a local emergency center and discharged home. Over the next several months, she noted episodic wheezing and dyspnea. Four months after the capsaicin exposure, a large wilderness fire developed in the area near her home. This fire eventually covered at least 1000 km<sup>2</sup> and lasted at least six weeks. She had daily symptoms of wheezing and dyspnea during this period; these symptoms improved after the fires were extinguished and the level of soot in the air declined.

The first presentation of the patient to our clinic was nine months after her initial capsaicin exposure. She reported episodic symptoms of dyspnea and wheezing that occurred every 1–2 days and lasted up to 4–5 hours. The patient also had a chronic productive cough with thick white sputum. Her cough was triggered by noxious odors, such as cigarette smoke. She had been treated previously with budesonide/formoterol fumarate dihydrate, albuterol, montelukast sodium, and prednisone with some but incomplete resolution of her symptoms. She had stopped prednisone because of weight gain. She was a nonsmoker and her family history was negative for asthma.

Her physical examination was within normal limits; she had symmetrical thoracic expansion, normal percussion notes, normal vocal fremitus, and normal breath sounds. She had no wheezes or crackles. She underwent diagnostic studies with pulmonary function tests, including flow volume loops (normal configuration), spirometry (FEV<sub>1</sub>=2.53

L [112% predicted]; FVC=2.97 L [112% predicted]), lung volume measurements (TLC=4.76 L [120% predicted]; RV=1.78 L [120% predicted]), and diffusion capacity measurements (23.4 mL/min/mm Hg [113% predicted]). All these tests were within normal limits. She had a positive methacholine challenge test with greater than 20% reduction in FEV<sub>1</sub> after a total dose of 0.72 mg of methacholine using the Jaeger dosimeter (CareFusion Corp, Yorba Linda, CA, USA). A capsaicin provocation test was not performed because we did not want to risk any additional airway injury given the patient's initial response to capsaicin. Her chest x-ray was normal, without infiltrates or evidence of bronchial disease.

The patient was placed on budesonide/formoterol fumarate dihydrate (160/4.5 µg per inhalation, two puffs twice daily). At a follow-up visit two months later she noted improvement but continued to have episodic symptoms, especially shortness of breath. She reported sensitivity to fumes, such as smoke and perfume, but denied heartburn and postnasal drainage. At her next follow-up visit five months after her initial evaluation, she reported cough, white sputum production, and dyspnea. Her chest examination was within normal limits. She had a score of 43 on the chemical sensitivity scale for sensory hyperreactivity (score range 1–55, ≥43 cutoff for a high score).<sup>1</sup>

## Discussion

This patient had a single intense exposure to capsaicin and developed chronic respiratory symptoms, including dyspnea and cough. The development of her clinical syndrome may have been facilitated by prolonged exposure to environmental smoke related to forest fires near her home. She has had persistently increased sensitivity to environmental irritants,

such as scents and cigarette smoke, following her initial exposure to capsaicin. She has had normal pulmonary function tests but did have an abnormal response to methacholine. Except for the latter feature, she appears to have an acquired airway sensory hyperreactivity syndrome. Shortly after her exposure she had pleuritic chest pain; this probably represented a transient pneumonitis with pleuritis. Patients with airway SHR have increased sensitivity to environmental irritants and odors and typically note dyspnea, cough, and upper airway symptoms when exposed to relatively innocuous agents, such as perfume. They have high scores on the chemical sensitivity scale for sensory hyperreactivity and increased cough responses to inhaled capsaicin.<sup>2</sup> A population-based study in Sweden demonstrated that approximately 6% of the population has this syndrome. These symptoms tend to persist, at least five years in one longitudinal study, and cause significant reductions in quality of life. Response to treatment appears to be limited, and one study demonstrated that most patients had reduced their use of medications during follow-up even though the symptoms persisted.<sup>4</sup> The etiology of this syndrome is unclear. It could reflect mutations in sensory receptors or nerves with a gain in function or an acquired injury to receptors and/or nerves.<sup>5</sup>

Capsaicin (8-Methyl-N-vanillyl-trans-6-nonenamide,  $C_{18}H_{27}NO_3$ , molar mass 305.41 g/mol) is a neurotoxin derived from chili peppers. It is used in the food industry to add spice/heat, in wildlife management as a pest deterrent, in topical ointments and dermal patches for the treatment of neuropathic pain, arthritis, and ligament sprains, and in law enforcement as a less than lethal force to control violent subjects.<sup>6</sup> Acute exposures to capsaicin irritate the skin, mucus membranes, the gastrointestinal tract, and

the respiratory system; inhaled capsaicin temporarily causes shortness of breath, coughing, nasal discharge, and lacrimation. Chan and coworkers exposed 35 law enforcement trainees to one spray of capsaicin using an exposure chamber and measured spirometry, oxygen saturation, and end-tidal  $CO_2$  for 10 minutes.<sup>7</sup> These controlled exposures had no effect on spirometry and did not cause hypoxemia or hypercapnia. Busker and van Helden reviewed the literature on the toxicology of pepper spray when used as a police weapon and concluded it was relatively safe and effective.<sup>8</sup> Miller reported a police officer who developed a pneumomediastinum after exposure to pepper spray which caused dyspnea, severe cough, and chest pain.<sup>9</sup> Our search of PubMed identified one report of acute airway disease associated with inhaled capsaicin (discussed below).<sup>10</sup> Animal experiments indicate that ingestion of less than 40 g of capsaicin may be fatal.<sup>11,12</sup> Common pepper spray preparations can contain up to 120 g in a unit.

Capsaicin binds to the transient receptor potential vanilloid 1 (TRPV1). This is an excitatory cation channel in nociceptive, primary sensory neurons found in the trigeminal nerve, the vagus nerve, and dorsal root ganglia with C- and A- $\delta$  fibers. These channels respond to temperature, noxious stimuli, pain, and stretching and are regulated by diverse G protein-coupled and tyrosine kinase receptors. Capsaicin lowers the receptor threshold for response to cold and possibly other stimuli. Activation of the receptors can cause bronchoconstriction and neurogenic inflammation by the release of neuropeptides, such as substance P, neurokinin A, and calcitonin gene-related peptide (CGRP).<sup>13</sup> These peptides can cause vasodilatation, plasma leak from capillaries, and leukocyte adherence to capillary endothelium, and this could cause persistent

inflammation in the airways, especially if repeated environmental exposures cause recurrent receptor stimulation. Repeated exposures to capsaicin can elicit immune responses, but this possibility does not directly apply to our patient.<sup>14,15</sup>

Occupational asthma accounts for 25% or more of *de novo* adult asthma.<sup>16</sup> Reactive airways dysfunction syndrome (RADS) is a subtype of occupational asthma which develops after a single exposure to chemicals such as ammonia and chlorine.<sup>3,17</sup> The diagnostic criteria include the absence of any preexisting respiratory disorder, the acute onset of asthma after a single exposure to an irritant gas or fume in very high concentrations, the onset of symptoms within 24 hours after exposure, a positive methacholine challenge test following exposure, and the presence of airflow obstruction on pulmonary function testing. Common causes for this syndrome include acids, chlorine gas, ammonia, paint sprays, fires with various pyrolysis products, and exposure to solvents. There is one reported case of RADS following exposure to a riot control agent (Deep Freeze).<sup>10</sup> This patient had persistent symptoms, wheezes and rales, and a partially reversible obstructive defect. We suggest that our patient has the operational equivalent of RADS and that her presentation represents the acute onset of persistent SHR after a single exposure to capsaicin. This chemical binds to TRPV1 receptors and can cause neurogenic inflammation which may have altered receptor function in her airways. Her symptoms and serial pulmonary function tests support this diagnosis. She did have an increased response to methacholine which may reflect the intensity of her initial exposure with pronounced injury to sensory nerves. She has had an incomplete response to medication used in patients with asthma. Ternesten and Hasseus's report also indicates that pa-

tients with SHR have a poor response to drugs used for asthma.<sup>4</sup> Current research is focused on the modulation of TRPV1-receptor activity which represents a potential target for pharmacological therapy in airway disease and SHR.<sup>2,5,18</sup>

In summary, capsaicin is commonly used as a non-lethal alternative in riot control and for subduing of aggressive assailants. Our patient had a single prolonged exposure to capsaicin OC spray and appears to have developed SHR. Since this patient had no prior history of chronic cough, asthma, chronic rhinosinusitis, or gastro-esophageal reflux, this single intense capsaicin exposure likely caused sensory nerve injury, which in turn lowered the cough threshold through up regulation in TRPV1. This case demonstrates that adverse effects can occur with intense exposures to capsaicin, that chronic respiratory symptoms may develop, and that these symptoms respond poorly to therapy. In addition, it seems worthwhile to establish precise timelines for possible environmental exposure(s) and development of symptoms in patients with airway SHR to better understand the pathogenesis of this disorder.

**Conflicts of Interest:** None declared.

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