*Case Reports and Literature Review*
*Volume 2*
*Article ID: 100006*

*Research Article*

# Acute Irritant-Induced Asthma Caused by Ozone

**Karl Færden[1*], Britt G Randem[1], Per A Lier[2], Bjørn Granhus[3], Per Søstrand[1], and Johny Kongerud[4,5]**

[1]Department of Environmental and Occupational Medicine, Oslo University Hospital, Norway

[2]Humana Sandvika AS, Norway

[3]Oslo Police District, Occupational Health Service, Norway

[4]Department of Respiratory Medicine, Rikshospitalet, Oslo University Hospital, Norway

[5]Faculty of Medicine, University of Oslo, Norway

***Corresponding author**: Karl Færden, Department of Environmental and Occupational Medicine, Oslo University Hospital, Postboks 4956 Nydalen, 0424 Oslo, Norway, Tel: +47-22-11-79-35; Fax: +47-22-11-99-75; E-mail: karl.faerden@ous-hf.no

**Received**: February 10, 2018; **Accepted**: March 22, 2018; **Published**: March 29, 2018



**Citation:** Færden K, Randem BG, Lier PA, Granhus B, Søstrand P, et al. (2018) Acute Irritant-Induced Asthma Caused by Ozone. Case Rep Lit Rev 2(1): 100006.

## Abstract

**Objective:** There is an increasing concern for negative health risks from ozone-generating devices sold as air cleaners. We present seven cases that developed asthma after an accident with ozone-producing UV-systems in a restaurant kitchen.

**Materials and Methods:** Out of a total of 127 possibly ozone-exposed employees, 55 employees reported symptoms, and seven employees were diagnosed with occupational asthma after the accident. These seven subjects were studied in relation to exposure, symptoms, lung function measurements, reversibility and bronchial hyper responsiveness (BHR) to methacholine, both shortly after the accidental exposure and at a follow-up two years later.

**Results:** Two years after cessation of exposure all seven subjects still needed treatment for asthma.

**Discussion:** Accidents involving ozone gas from air purifiers with UV-lamps may cause acute irritant-induced asthma. There is a need for greater awareness in the use of ozone-generating devices.

**Keywords:** acute irritant-induced asthma, UV-lamps, ozone, lung function, prognosis

## Abbreviations

BHR: Bronchial Hyper Responsiveness; IrIA: Irritant-Induced Asthma; ERS: European Respiratory Society; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in one second; TLC: Total Lung Capacity; RV: Residual Volume; DLCO: Diffusing Capacity for Carbon Monoxide; VA: Alveolar Volume; ATS: American Thoracic Society; FeNO: Exhaled Nitrogen Monoxide; ACT: Asthma Control Test

## Introduction

Epidemiological [1,2] and experimental human studies [3] have shown that short-term ozone exposure may be associated with adverse health effects on the respiratory tract in the form of inflammation [4] and airflow obstruction [5]. The inflammation appears to intensify with repeated exposure [6].

The degree of bronchoconstriction is determined by the $O_3$ concentration, duration of exposure and the level of physical activity of the exposed person [7]. In experimental situations, an $O_3$- concentration exceeding 0.3-0.5 ppm was shown to trigger bronchoconstriction at rest [8]. In ambient air, in Norway, levels are around 0.02-0.04 ppm $O_3$ [9,10].

There are significant individual variations in sensitivity to ozone. Genetic factors, age and pre-existing airway disease may be of importance [11].

The term irritant-induced asthma (occupational IrIA) is used to describe different clinical forms of asthma related to exposure to irritants at work. Examples of exposure that may cause IrIA are gases like chlorine, ozone, and sulfur dioxide, acids, alkalis, biocides, smoke, aerosol products, alkaline dust, and potentially sensitizing substances which may also have an irritant effect like isocyanates [12].

The use of ozone-generating UV lamps in restaurant kitchens with the aim to remove unwanted grease from ventilation systems has become common in Norway in the last decade.

There are a number of small-scale restaurant kitchens where an UV generator is placed by the fan for the ventilation system.

A recent study (2017) that evaluated emission of ozone from 17 different consumer products and appliances, warns against the increasing risk of adverse health effects of ozone from such products [13]. The United States Environmental Protection Agency also warns about the possible negative effects of ozone generators sold as air cleaners [14].

There are few studies regarding work-related ozone exposure. In a longitudinal study in the Swedish paper industry, repeated exposure to levels above 0.30 ppm $O_3$ was reported to be associated with an increased risk of experiencing asthma-like symptoms [15,16]. In two recently published case reports from a Norwegian fish hatchery and a Norwegian sewage plant, four cases of IrIA after accidents involving ozone were described [17,18].

In the present study ozone gas leaked into the indoor air of a home care services over a two-week period in July 2013 via the ventilation system. The gas was emitted from an air purifier in a restaurant kitchen on the ground floor, one floor below the company premises. Ozone was produced by a lamp with ultraviolet radiation, UV-C (100-280 nm) placed in the ventilation fan to remove grease.

Due to a concurrence of circumstances including: arrest of the ventilation system, a fan placed at the bottom of the ventilation system automatically starting to blow when the system stopped, lack of information from the firm that installed the device, and the fact that leaders and technicians who could have handled the situation were on summer vacation, ozone gas probably diffused into the company offices for 14 consecutive days.

The aim of the study was to examine the natural course of acute irritant-induced asthma occurring after ozone exposure. We wanted to know if the subjects' asthma would heal spontaneously.

## Materials and Methods

### Exposure

The rooms exposed to ozone leakage were among others, the cafeteria kitchen, the cafeteria and several offices.

Measurements with Heated Metal Oxide Sensor (A-22 Ozone Sensor) ten days after the ozone device was installed showed morning values of 0.726 ppm $O_3$ in the kitchen on the first floor, 0.260 ppm $O_3$ in the hallway outside the cafeteria, 0.250 ppm $O_3$ in a meeting room after this was aired for 0.5 hours, and 0.016 ppm $O_3$ at the bottom of a corridor. The ozone levels when cooking activity was started in the kitchen on the first floor around 16:00 pm, were under detection levels.

**Subjects**

A total of 127 persons were at work in the premises when the relevant exposure occurred in July 2013. Information from the local occupational health service about the event and a standardized questionnaire [19] for identifying respiratory symptoms, past illnesses and smoking habits were sent to all of them. Fifty-five persons reported symptoms that could be related to the ozone exposure. These included stinging and watery eyes, chest pain, increased mucus production, pain and tightness in the chest, shortness of breath, headache, nausea and abdominal pain. For selecting those who should be referred to a pulmonary physician, emphasis was put on who might have been exposed in the specific time period, as well as selecting those reporting symptoms of cough, shortness of breath and wheezing.

Of the 45 exposed employees examined by a pulmonary physician during August and September 2013, eleven employees were reported to The Norwegian Labour Inspection Authority due to suspected work-related asthma.

Eight subjects, including seven referred to our Department of Occupational medicine, had by the first of November 2015 their asthma recognized as an occupational disease by the Norwegian Labour and Welfare Administration. These were invited to participate in a follow-up two year after cessation of exposure. One subject was excluded due to other serious illness. The follow-up consisted of a consultation with a pulmonary physician during the period December 2015 to January 2016, with lung function measurements, reversibility test and BHR to methacholine.

Five of the subjects were women and two were men, aged 24-45 (mean 34) years (Table 1). They worked in home care services, three nurses, three assistants, and one kitchen assistant. None of them were daily smokers at the time the asthma diagnosis was made (Table 1). One subject reacted with hay fever to dust mites. The others had no known allergies. One of the subjects had four years before the event been examined for asthma-like symptoms, but asthma diagnosis was not confirmed. The other six had no earlier airway symptoms.

**Table 1:** Demographic characteristics of the seven subjects with IrIA

| | Age (yrs) | Gender | | Smoking habits | | Ethnicity | |
|---|---|---|---|---|---|---|---|
| | | Male | Female | Neversmoker | Ex-smoker, pack yrs | Asian | White |
| 1 | 36 | | • | | 6 | | • |
| 2 | 42 | | • | | 3 | | • |
| 3 | 24 | | • | | 0.5 | | • |
| 4 | 42 | • | | • | | | • |
| 5 | 35 | | • | • | | • | |
| 6 | 45 | | • | • | | | • |
| 7 | 34 | • | | | 3 | | • |

**Lung function measurements**

Testing of lung function included dynamic spirometry, determination of static lung volumes and gas diffusion. All tests were performed by the European Respiratory Society (ERS) Task Force Guidelines using Jaeger Master Screen PFT and Master Screen Body with integrated software for spirometry, diffusion and body box (CareFusion SentrySuite) [20].

The measured spirometry variables were forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and FEV1/FVC. The static lung volume variables were total lung capacity (TLC) and residual volume (RV).

Gas diffusion variables were diffusing capacity for carbon monoxide (DLCO) and DLCO divided by alveolar volume (DLCO/VA). Values recommended by the ERS was used as reference [21,22].

Reversibility was tested by inhalation of 0.4 mg salbutamol by the National Asthma Education and Prevention Program guidelines [23]. An increase in FEV1 of 12% from baseline or more, accompanied by an absolute increase in FEV1 of at least 200 ml, was considered a positive test.

Nonspecific BHR to methacholine was tested in accordance with principles of the American Thoracic Society (ATS) Guidelines [24], but with a simplified dosimeter method (Jaeger Aerosol Provocation System) with a computerized nebulisation using Jaeger ABS pro with Omron Comp Air nebulizer [25]. The cumulative dose of methacholine (PD20) which triggered a 20% fall in FEV1 was calculated and entered as a measure of BHR.

A response to PD20 methacholine <0.4 mg was classified as "severe BHR", 0.4- 0.8 mg as "moderate BHR", 0.8- 1.6 mg as "mild BHR" and 1.6-3.3 mg as "very mild BHR".

The fraction of exhaled nitrogen monoxide (FeNO) expressed as parts per billion (ppb) was measured by ERS criteria using Niox Mino, Aerocrine [26]. The values published by Olin et al. were used as reference [27].

**Allergy tests**

All subjects underwent a skin prick test for 10 commonly occurring respiratory allergens (hazel, alder, birch, timothy, mugwort, dog, cat, house dust mite, and fungi).

The diagnosis of acute IrIA was based on criteria proposed by Vandenplas et al. [12]; Absence of preexisting asthma symptomatology, onset of asthma symptoms after a single specific inhalational exposure or accident, exposure to an irritant vapor, gas, fume, or smoke in very high concentration, onset of asthma symptoms within minutes to hours and <24 h after the exposure, presence of airflow limitation with a significant bronchodilator response or nonspecific BHR to histamine/methacholine, and exclusion of other pulmonary disorders that could explain the symptoms or simulate asthma.

The Asthma control test (ACT) was used to assess asthma control [28]. The test consists of five questions about the last four weeks of respiratory symptoms and daily functioning. Score results ranged from 5 (poor asthma control) to 25 (complete asthma control), where higher scores reflect better control of asthma. An ACT score ≥ 19 indicates good asthma control.

Work history, exposure during leisure time, and lifestyle factors were assessed by an occupational physician at 6-14 months after cessation of exposure.

The study was approved by the Regional Ethics Committee REK No. 2015/2365 and of the Data Protection Officer at Oslo University Hospital No. 2015/8820.

## Results

Five of seven subjects diagnosed as IrIA described a rapid onset of asthma symptoms while noticing the smell of ozone gas, while two subjects had a delayed reaction with asthma symptoms 2-4 weeks after the incident (Table 2). These consisted of a burning sensation in the airways, coughing, shortness of breath, wheezing, pain in the chest and unusual fatigue.

At the time of determination of asthma diagnosis, six of the seven subjects had either positive reversibility and /or positive BHR tests (Table 3).

FVC, FEV1, FEV1/FVC ratio and FeNO values were within normal range in all cases (Table 2 and 3). None of the seven experienced symptoms so severe that they had to seek immediate help from a doctor.

**Table 2:** Spirometry results of the seven subjects with IrIA

| | FVC (l) (% predicted) | | FEV1 (l) (% predicted) | | FEV1/FVC ratio | |
|---|---|---|---|---|---|---|
| | **Baseline** | **Follow-up** | **Baseline** | **Follow-up** | **Baseline** | **Follow-up** |
| 1 | 3.4 (102) | 3.5 (107) | 2.7 (95) | 2.8 (98) | 0.79 | 0.79 |
| 2 | 4.3 (121) | 4.2 (120) | 3.5 (115) | 3.4 (115) | 0.81 | 0.80 |
| 3 | 4.0 (92) | 4.6 (106) | 3.2 (84) | 4.1 (109) | 0.79 | 0.90 |
| 4 | 5.0 (104) | 4.6 (96) | 3.7 (93) | 3.5 (90) | 0.74 | 0.76 |
| 5 | 2.8 (81) | 3.3 (96) | 2.3 (76) | 2.7 (90) | 0.82 | 0.81 |
| 6 | 2.0 (91) | 2.1 (96) | 1.6 (90) | 1.6 (90) | 0.76 | 0.78 |
| 7 | 5.4 (105) | 4.7 (97) | 4.0 (95) | 3.2 (78) | 0.75 | 0.67 |

**Table 3:** Other indicators of asthma

| | Reversibility (FEV1) | | *Methacholine challenge* test (mg) | | FeNO (ppb) | Medication use # | | Asthma control test |
|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **Follow-up** | **Baseline** | **Follow-up** | **Baseline** | **Baseline** | **Follow-up** | **Follow-up** |
| 1 | 310 ml, 11% | 290 ml, 10% | neg | neg | 26 | o | a+c | 19 |
| 2 | 60 ml, 2% | 90 ml, 3% | 0.5 | neg | 20 | o | a+c+l | 16 |
| 3 | 440 ml, 14% | 20 ml, 1% | 2.0 | neg | 18 | o | a+c+l+t | 15 |
| 4 | 260 ml, 7% | 160 ml, 5% | 0.4 | 1.6 | 10 | o | a+c+l | 10 |
| 5 | 180 ml, 8% | 20 ml, 1% | 2.1 | neg | 14 | o | a+c | 25 |
| 6 | 210 ml, 14% | 50 ml, 3% | neg | 2.1 | 7 | o | a+c | 11 |
| 7 | 60 ml, 2% | 320 ml, 10% | 0.5 | 1.8 | 14 | o | a+c | 21 |

# o = no medication; a = adrenergic; c = corticosteroid; l = leukotriene receptor agonist; t = theophylline

Five of the subjects stayed mainly inside the premises during the two weeks that the ozone exposure lasted, while two also occasionally worked with clients outside the premises and were then out of exposure. One was away on summer vacation during the first week. We were informed that the staff opened the windows to get rid of the smell, which may indicate that exposure has been uncomfortable, but at the same time not so high that they were forced to leave the premises.

Two years after cessation of exposure, several of the subjects still suffered from not well controlled asthma, and all required medical treatment for asthma (Table 3). Three out of seven subjects experienced wheezing 3-6 times or more during the week, four out of seven reported being woken up by asthma symptoms at least once a night, and six of seven had used extra medication 2-3 times or more during the week. Four experienced unsatisfactory asthma controls from Asthma Control Test score <19 (Table 3). One subject (no 7) had a moderate fall in lung function values and may have developed chronic obstructive pulmonary disease (COPD). The other six had unchanged or better lung function values compared to baseline. Three of the subjects still had BHR despite the use of inhaled corticosteroids, all graded as "very mild BHR".

None had long absence from work or needed emergency treatment in hospital for their asthma during the two years follow-up. All were in full employment.

## Discussion

As far as we know, this is the first time that IrIA is reported after exposure to ozone from an UV lamp in a restaurant kitchen, and the first time that the natural course of IrIA from accidental ozone exposure has been followed up two years after the incident.

The level of exposure and the clinical development of respiratory symptoms were similar to what was reported in the three studies that have described IrIA after accidental exposure to ozone [15,17,18].

In the accidental IrIA case from the Norwegian fish hatchery, peak values above 1 ppm $O_3$ was measured with an ozone sensor carried by one of the workers [17]. In the sewage plant, exposure levels measured by a stationary ozone sensor were repeatedly above 0.5 ppm $O_3$ [18].

We found only one epidemiological study in the international literature calculating ozone exposure levels and respiratory symptoms in a factory; a longitudinal study from the Swedish paper industry [15,16]. They reported an increased risk of asthma-like symptoms by repeated exposure to levels above 0.30 ppm $O_3$.

Generally, from human chamber studies, the $O_3$- concentrations must exceed 0.3-0.5 ppm to trigger bronchoconstriction in resting subjects [8]. In our case study, the subjects reported a burning sensation in the airways, coughing, shortness of breath, and chest pain at the same time they smelled he ozone.

It is difficult to measure ozone because of its highly reactive, volatile and unstable properties. Ozone gas is consumed by reacting with other agents, e.g. to oxidize fat. Supported by measurements of ozone levels on the premises, that ranged 0.016 to 0.760 ppm $O_3$, this might indicate an ozone level exposure of at 0.30 ppm, or higher.

Based on a report from the employer showing that the ozone producing device was not turned off before two weeks later, and subjects presenting with repeated IrIA attacks during ozone exposure, we assume that the subjects most likely were exposed to several peaks of ozone over a number of consecutive days. Diagnosing the subjects with acute irritant-induced asthma is in line with the diagnostic algorithms proposed by the European Academy of Allergy and Clinical Immunology (EAACI) position paper 2014 for irritant-induced asthma [12].

The differential diagnosis of IrIA with patients presenting with persistent symptoms includes worsening of underlying asthma that has been exacerbated by an irritant exposure, immunological reactions of respiratory allergens, paradoxical dysfunction of the vocal cord, non-asthmatic eosinophilic bronchitis, as well as other diseases or influence that can simulate asthma. We found that one of the subjects four years before the incident had been referred to an out-patient clinic for asthma-like symptoms, but asthma diagnosis was not confirmed. The other six had no earlier symptoms from the airways. All subjects had FeNO values within normal variation, which makes eosinophilic asthma and non-asthmatic eosinophilic bronchitis less probable [29].

At the two-year follow-up, we found that none of the subjects had long absence from work or needed emergency treatment in hospital, and all were in full employment in their field. However, all required asthma medical treatment.

The prognosis of acute IrIA has not been well described and there are only a few studies with longitudinal and/or prospective data. The present knowledge suggests a wide degree of response that goes from complete healing of the symptoms to persistent respiratory disability [30,31].

Ozone has at present found important applications as a water disinfectant, to increase the shelf life of foods and flowers, as well as odor-enhancing properties, but we need to keep in mind that ozone is a highly toxic gas for the lungs, and that we therefore need to implement measures to prevent accidental exposures. Recent studies have demonstrated that ozone gas in commercial use can cause serious chronic respiratory disease. There is a need for

greater awareness and knowledge about the use of ozone-generating plants. The emissions from ozone producing UV systems in kitchens should not be connected to the general ventilation system.

## References


1. Cody RP, Weisel CP, Birnbaum G, Lioy PJ (1992) The effect of ozone associated with summertime photochemical smog on the frequency of asthma visits to hospital emergency departments. Environ Res 58: 184-194.
2. Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F (2004) Ozone and short-term mortality in 95 US urban communities, 1987-2000. JAMA 292: 2372-2378.
3. Sandström T (1995) Respiratory effects of air pollutants: experimental studies in humans. Eur Respir J 8: 976-995.
4. Stenfors N, Pourazar J, Blomberg A, Krishna MT, Mudway I, et al. (2002) Effect of ozone on bronchial mucosal inflammation in asthmatic and healthy subjects. Respir Med 96: 352-358.
5. Metha AJ, Henneberger PK, Torén K, Olin AC (2005) Airflow limitation and changes in pulmonary function among bleachery workers. Eur Respir 26: 133-139.
6. Christian DL, Chen LL, Scanell CH, Ferrando RE, Welch BS, et al. (1998) Ozone-induced inflammation attenuated with multiday exposure. Am J Respir Crit Care Med 158: 532-537.
7. Folinsbee LJ, Drinkwater BL, Bendi JF (1978) The influence of exercise on the pulmonary changes due to lower concentrations of ozone. Folinsbee LJ, Wagner JA, Borgia JF, editors. In: Environmental stress: Individual Human Adaptions. Academic Press, New York, USA *pp: 125-145*.
8. Goldsmith JR, Nadel JA (1969) Experimental exposure of human subjects to ozone. J Air Pollut Contro Assoc 19: 329-331.
9. Bylin G, Cotgreave I, Gustafsson L, Nyberg F, Pershagen G, et al. (1996) Health risk evaluation of ozone. Scand J Work Environ Health 22 suppl 3: 1-104.
10. The Norwegian Environment Agency (2010) Ground-level ozone.
11. Vinikoor-Imler LC, Owens EO, Nichols JL, Ross M, Brown JS, et al. (2014) Evaluating potential response-modifying factors for associations between ozone and health outcomes: a weight-of-evidence approach. Environ Health Perspect 122: 1166-1176.
12. Vandenplas O, Wiszniewska M, Raulf M, de Blay F, Gerth van Wijk R, et al. (2014) EAACI position paper: irritant-induced asthma. Allergy 69: 1141-1153.
13. Zhang Q, Jenkins PL1 (2017) Evaluation of ozone emissions and exposures from consumer products and home appliances. Indoor Air 27: 386-397.
14. EPA United States Environmental Protection Agency (2017) Indoor Air Quality. Ozone Generators that are Sold as Air Cleaners.
15. Olin AC, Granung G, Hagberg S, Adriansson M, Brisman J, et al. (2002) Respiratory health among bleachery workers exposed to ozone and chlorine dioxide. Scand J Work Environ Health 28: 117-123.
16. Henneberger PK, Olin AC, Andersson E, Hagberg S, Torén K (2005) The incidence of Respiratory Symptoms and Diseases Among Pulp Mill Workers with Peak Exposures to Ozone and Other Irritant Gasses. Chest 128: 3028-3037.
17. Aas O (2014) Når et nyttig desinfeksjonsmiddel kommer på avveie. To arbeidstakere med akutte luftveisplager etter eksponering for ozon. Ramazzini 2: 11.
18. Tjalvin G, Hag R, Skorge TD, Aasen TB, Moen BE, et al. (2012) Two men who acquired acute respiratory symptoms while working at a sewage plant. Tidskr Nor Laegeforen 132: 1763-1766.

19. Fletcher CM (1960) Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). BMJ 2: 1665.
20. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, et al. (2005) General considerations for lung function testing. Eur Respir J 26: 153-161.
21. Cotes JE, Chinn DJ, Quanjer PH, Roca J, Yernault JC (1993) Standardization of the measurement of transfer factor (diffusing capacity). Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J Suppl 16: 41-52.
22. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, et al. (1993) Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J Suppl 16: 5-40.
23. National Asthma Education and Prevention Program: Expert panel report III: Guidelines for the diagnosis and management of asthma (2007).
24. Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, et al. (2000) Guidelines for methacholine and exercise challenge testing-1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med 161: 309-329.
25. Schulze J, Rosewich M, Riemer C, Dressler M, Rose MA, et al. (2009) Methacholine challenge - Comparison of an ATS protocol to a new rapid single concentration technique. Respir Med 12: 1898-1903.
26. American Thoracic Society; European Respiratory Society (2005) ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am J Respir Crit Care Med 171: 912-930.
27. Olin AC, Bake B, Torén K (2007) Fraction of exhaled nitric oxide at 50 mL/s: reference values for adult lifelong never-smokers. Chest 131: 1852-1856.
28. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, et al. (2004) Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol 113: 59-65.
29. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, et al. (2011) An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med 184: 602-615.
30. Malo JL, L'archevêque J, Castellanos L, Lavoie K, Ghezzo H, et al. (2009) Long-term outcomes of acute irritant-induced asthma. Am J Respir Crit Care Med 179: 923-928.
31. Takeda N, Maghni K, Daigle S, L'Archevêque J, Castellanos L, et al. (2009) Long-term pathologic consequences of acute irritant-induced asthma. J Allergy Clin Immunol 124: 975-981.