

Occupational Bronchiolitis **Obliterans in Food Flavoring**

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RAMAZZINI DAYS 2007 - JUBILEE CELEBRATION

25th Anniversary of the Collegium Ramazzini

25-28 October 2007

Carpi, Italy

Introduction

- Several recent studies reported severe occupational lung disease in workers exposed to materials used in food flavoring. In those cases, airborne dust from butter flavoring such as diacetyl were causative (not exclusive to only diacetyl).
- The Center of Disease Control (CDC) and the California OSHA issued a report (April 2007) indicating among others the need “to identify cases” and “reduce risk for lung disease” “from occupational exposure to flavoring”.

- We report here 4 patients, exposed to powders, vapors and mists in food flavoring industry, with chronic bronchiolitis obliterans.
- To our knowledge, at least one patient was initially misdiagnosed as “asthma”.
- Pulmonary function tests were done in accordance with the American Thoracic Society criteria [ATS/ACCP Statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med. 2003 Jan 15;167(2):211-77].

Case Report #1: 32-y.o. Male

- Occupation:
 - Machine operator and mixer at a food flavoring/powders company for 2 years.
- Exposure History:
 - Inhalation during mixing of heated flavoring powder;
 - Provided paper masks, described as ineffectual.
- Complaints and Symptomatology:
 - Suffocating symptoms and respiratory complaints upon exposure.
- Past Medical History:
 - Unremarkable.
- Physical Examination:
 - BP: 130/80;
 - Lung examination demonstrated diffuse wheezing.

Case Report #1

- Laboratory and Diagnostic Studies:
 - EKG, thyroid and urinalysis and chemistry panel were within normal limits;
 - Hematology panel: RDW of 11.3, eosinophils of 9, sedimentation rate of 18;
 - Allergy test: Immunoglobulin E of 684;
 - Chest x-ray: Normal
 - Spirometry: FVC of 43%, FEV₁ of 27%, diffusion capacity of 85%;
 - Repeat spirometry: FVC of 35%, FEV₁ of 22%;
 - Repeat spirometry: FVC of 46%, FEV₁ of 31%, diffusion capacity of 85%, bronchodilation did not improve the FEV₁ in all spirometric studies (effort was good; fixed obstructive airway disease).

Case Report #1

- Current Medications:
 - Proventil, Advair and Spiriva, with only a slight improvement.
- **Diagnosis:**
 - Bronchiolitis obliterans.

Case Report #2: 38-y.o. Male

- Occupation:
 - Production worker at food flavoring company for 5 months.
- Exposure History:
 - Inhalation during mixing of heated flavoring powder.
- Complaints and Symptomatology:
 - Shortness of breath, chest pain, cough and eye irritation by the end of the second week on the job;
 - Breathing problems worsened and was diagnosed with asthma;
 - Given inhalers and oral prednisone, which were ineffectual.
- Past Medical History:
 - Asthma at age 8, resolved at age 9.

Case Report #2

- Physical Examination:
 - BP: 104/58;
 - Lung examination exhibited positive diffuse wheezing.
- Laboratory and Diagnostic Studies:
 - EKG, urinalysis, chemistry panel, rheumatology and collagen vascular panels were within normal limits;
 - Hematology panel: Sedimentation rate of 33.
 - Allergy test: Immunoglobulin E of 217.
 - Spirometry: FVC of 29%, FEV₁ of 16% with no significant change post bronchodilator, bronchodilation did not improve FEV₁ in all spirometric studies (effort was good).

Case Report #2

- Current Medications:
 - Oral prednisone (60 mg per day) with no improvement, Proventil, Advair and home nebulizer, which are ineffectual, and 24-hour supplemental oxygen.
- **Diagnosis:**
 - Bronchiolitis obliterans.

Case Report #3: 50-y.o. Male

- Occupation:
 - Compounder for food flavoring company for 6 years.
- Exposure History:
 - Inhalation during mixing of flavoring powders and liquids for 5 to 6 hours day;
 - Provided paper masks, described as ineffectual.
- Complaints and Symptomatology:
 - Headaches upon inhalation of powder and fumes;
 - Cough after one year on the job, given diagnosis of asthma by private physician and prescribed inhalers.
- Past Medical History:
 - Unremarkable.
- Physical Examination:
 - BP: 130/80.

Case Report #3

- Laboratory and Diagnostic Studies:
 - Urinalysis revealed moderate leukocytes;
 - Hematology panel: Neutrophils of 40, eosinophils of 7 and sedimentation rate of 20;
 - Allergy test: Immunoglobulin E was normal
 - EKG and chest x-ray were normal;
 - Spirometry: FVC of 50%, FEV₁ of 37%, diffusion capacity of 102, FEV₁ did not improve on bronchodilation;
 - Repeat spirometry: FVC of 48%, FEV₁ of 37% and increased to 39% post-bronchodilator, bronchodilation did not improve FEV₁ in all spirometric studies (effort was good).

Case Report #3

- Current Medications:
 - Albuterol, Spiriva and Singular (with some improvement).
- **Diagnosis:**
 - Bronchiolitis obliterans.

Case Report #4: 44-y.o. Female

- Occupation:
 - General laborer at food powder company for 10 years.
- Exposure History:
 - Inhalation of fumes and dust while mixing chemicals for concentrated fruit juices and candies.
 - Provided paper masks, described as ineffectual.
- Complaints and Symptomatology:
 - Shortness of breath, watery eyes and nasal congestion after four years on the job.
- Past Medical History:
 - Unremarkable.
- Physical Examination:
 - BP: 120/80.

Case Report #4

- Laboratory and Diagnostic Studies:
 - EKG: sinus bradycardia;
 - Chemistry panel, hematology panel and thyroid panel were within normal limits;
 - Chest x-ray was within normal limits;
 - Methacholine challenge test (sometime in 2003): FEV1 was 103% and decreased to 63% after methacholine, complained of worsening shortness of breath;
 - Diagnosis at that time: occupational asthma
 - Her symptoms deteriorated and was re-evaluated in 2007
 - Repeat spirometry (about 3 years later): FVC of 36%, FEV1 of 42% with good effort and no improvement post-bronchodilation.

Case Report #4

- Current Medications:
 - Proventil.
- **Diagnosis:**
 - Initial diagnosis: reactive airway disease;
 - Diagnosis three years later: bronchiolitis obliterans.

Summary of Case Reports

Patient ID	Age (years)	Sex	Duration of exposure	Symptoms	Pulmonary function test, FEV ₁ (before → after)	Chest x-ray	Chest CT scan	Biopsy	Treatment
1	32	Male	2 years	Suffocation, eye irritation	27% → 36%; 22% → 23%; 31% → 29%	Normal	Diffuse patchy bilateral ground glass opacities	N/A	Proventil, Spiriva, Advair
2	38	Male	5 months	Shortness of breath, chest pain, cough, eye irritation	16% → 17%; 13% → 17%; 12% → 14%	N/A	Incidental small pulmonary nodules at the right lung base	Bronchiolitis obliterans	Proventil, Spiriva, Advair, 24-hour supplemental oxygen
3	50	Male	6 years	Cough	37% → 37%; 40% → 35%; 37% → 39%	Normal	Minimal pleural-based markings bilaterally	N/A	Albuterol, Spiriva, Singular
4	44	Female	10 years	Shortness of breath, watery eyes, nasal congestion	Positive methacholine; 42% → 42%	Normal	Pending	N/A	Proventil

Discussion

The key diagnostic feature in our patients were:

1. History of exposure to food flavoring materials, including diacetyl;
2. Obstructive airway disease ($FEV_1 \downarrow$) with no improvement upon bronchodilation (fixed obstruction);
3. Absence of other known causes;
4. Failure to respond to conventional treatment for asthma.

- In California, since April of 2006 a total of additional 5 cases were discovered.
- The common denominator is fixed obstructive airway disease, exposure to chemicals used in the food flavoring industry, lack of adequate protective devices and absence of other causes (i.e., preexisting asthma, cigarette smoking) and a mean age of 34 (range 27-44).

- Our findings in these 4 patients are compatible with other studies (e.g., Kreiss, K. et al. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. N Engl J Med. 2002 Aug 1;347(5):330-8):
 - “Our findings of excess rate of lung disease and associations between indexes of exposure to volatile organic chemicals and obstructive lung disease supports the conclusion that an agent in butter flavoring caused occupational bronchiolitis obliterans in exposed workers at this popcorn plant.”

Summary

1. Workers in food flavoring industry (probably not limited to production) are at increased risk for severe and progressive lung disease, bronchiolitis obliterans.
2. The condition is probably under-diagnosed (lack of occupational history by clinicians) and underreported (NIOSH and California OSHA hearings 2006, 2007).
3. Shortness of breath and obstructive airway disease in food flavoring industry and chain of distribution, i.e., bakeries, movies, etc., must be evaluated with a detailed occupational history and pulmonary function tests based on the American Thoracic Society criteria (CT scan of the chest may be important).
4. Meticulous follow-up and reporting to OSHA.NIOSH is mandatory.
5. Treatment: no evidence that steroids and immunosuppressive therapy is helpful.

Conclusion

- Recent onset of shortness of breath, followed by “asthma” in workers with a history of exposure to powders, vapors and mist used in the food flavoring industry should be **a red flag** for bronchiolitis obliterans, asthma, bronchiolitis obliterans with organizing pneumonia, and pulmonary fibrosis.
- Fixed obstructive airway disease is a prime diagnostic feature. CT scan of the chest is helpful. Lung biopsy is probably not helpful and it may not change the treatment nor the clinical outcome..
- In some patients who were diagnosed as “occupational asthma” resistant to treatment, reevaluation of occupational history and spirometry with bronchodilation is mandatory (Case #4).

Literature

- A cluster of severe bronchiolitis obliterans cases in a small rural microwave popcorn plant (Kreiss, K.; et al. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. *N Engl J Med.* 2002 Aug 1;347(5):330-8).
- Kanwal, R.; et al. Evaluation of flavorings-related lung disease risk at six microwave popcorn plants. *J Occup Environ Med.* 2006 Feb;48(2):149-57.
- Centers for Disease Control and Prevention (CDC). Fixed obstructive lung disease among workers in the flavor-manufacturing industry--California, 2004-2007. *MMWR Morb Mortal Wkly Rep.* 2007 Apr 27;56(16):389-93.

Literature

- The spectrum of lung disease in flavoring workers may be broader: asthma, bronchiolitis obliterans with organizing pneumonia, fibrosis, granulomatosis, pneumonia. “Perhaps bronchiolitis obliterans is a much more common finding than we think” -- Kreiss, K. Occupational Bronchiolitis Obliterans Masquerading as COPD. Am J Respir Crit Care Med. 2007 Sep 1;176(5):427-9.
- Exposure levels as low as 0.2 to 0.6 ppm -- Kreiss, K. Flavoring-related bronchiolitis obliterans. Curr Opin Allergy Clin Immunol. 2007 Apr;7(2):162-7.
- Federal agencies knew about diacetyl dangers and kept quiet. -- OMB Watch. Federal Agencies Knew of Diacetyl Dangers and Kept Silent. Published: 9/11/2007. <http://www.ombwatch.org/article/articleview/3970>.

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- Industrial sputum evaluation in microwave popcorn production workers demonstrate neutrophilic airway inflammation. -- Akpinar-Elci, M.; et al. Induced sputum evaluation in microwave popcorn production workers. Chest. 2005 Aug;128(2):991-7.