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## *Obliterative Bronchiolitis from Exposures in the Work Environment*

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There has been increased recognition of bronchiolar disease caused by occupational and environmental exposures (1). See Table I for a listing of the exposures reported in the literature, and the settings in which the exposures occurred. The medical documentation for the associations are typically case reports/case reviews, although some substances such as diacetyl and microwave popcorn have a more robust documentation including epidemiologic and animal studies. Initially bronchiolar disease was recognized in the setting of an acute exposure to irritants such as smoke and chemicals that caused acute pulmonary edema or chemical pneumonitis. If the patient survived then they went on to develop progressive shortness of breath from obliterative bronchiolitis. More recently the disease has been recognized without an acute event but rather after chronic exposure. This was highlighted among workers involved in the manufacture of microwave popcorn who were exposed to diacetyl and 2,3-pentanedione, which are chemicals used to manufacture artificial butter flavoring (2).

Variability in clinical presentation, pulmonary function test results and radiographic findings has hindered the diagnosis, particularly in distinguishing the condition from the more common disease of COPD. Changes in nomenclature and overlapping bronchiolar conditions have also hampered diagnosis. The pathology of obliterative bronchiolitis (bronchiolitis obliterans) is shown in Figure I. Table II adapted from a New England Journal of Medicine review article summarizes the bronchiolar disorders (3).

The most common finding in a patient with obliterative bronchiolitis is either normal spirometry or slightly reduced FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio with less than a 12% improvement in FEV<sub>1</sub> with administration of a bronchodilator. On lung volumes there will be normal TLC, increased RV and therefore an increased RV/TLC ratio. Diffusing capacity is typically normal but will become abnormal with progression of disease. A subset of patients will have restriction or a mixed obstructive/restrictive pattern. The definitive non-invasive test for obliterative bronchiolitis is a non-contrast high-resolution CT scan of the chest performed at full inhalation and then at full expiration. A mosaic perfusion pattern where on full expiration there is enhancement of decreased attenuation, which represents air trapping is found with obliterative bronchiolitis. There is a paucity of ground-glass opacities. These changes on high-resolution CT can be more sensitive than changes seen on pulmonary function tests.

Non-occupational/environmental causes of bronchiolar disease are: 1) rheumatoid arthritis; 2) in children, post adenovirus, measles or mycoplasma infection; 3) complication of allogeneic hematopoietic stem-cell transplantation; and 4) complications of lung transplant in long-term survivors.

The reports we have received from doctors in Michigan of patients with bronchiolitis obliterans from occupational exposures have all occurred after an acute exposure. We have not received any reports of bronchiolitis obliterans after chronic exposure. We know there are exposures occurring in Michigan, which have the potential for causing the

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disease. Diacetyl and 2,3-pentanedione, for example, the chemicals causing diacetyl obliterative bronchiolitis in microwave popcorn workers, are both added in the processing of coffee and also found as a natural ingredient in coffee (4). Elevated air levels of diacetyl and 2,3-pentanedione have been found during the roasting of coffee. Such roasting occurs at multiple locations in Michigan. These chemicals are also used in snack food production (potato and corn chips with nacho cheese and sour cream flavoring), cream cheese manufacture, buttermilk pancake mix production, pet food manufacture (hickory flavor) and commercial kitchens (butter flavored cooking oil).

**Table I. Examples of Known or Suspected Exposures Causing Bronchiolar Disorders**

<b>Exposure</b>	<b>Illustrative setting</b>
Acramin FWN	Textile printing
Ammonia	Chemical industry, refrigerant
Benzalkonium compounds	Floor polish spill
Bromine compounds	Flavoring research and development
Chlorine	Transportation spill, industrial leak
Chlorine-liberating disinfectant (powder)	Cleaning
Cooking oil fumes	Commercial cooking
Diacetyl and 2,3-pentanedione	Microwave popcorn, diacetyl manufacture, flavoring manufacture, coffee roasting
Dimethyl disulfide	
Dusts/gases/fumes	World Trade Center collapse
Flock (fibers of nylon, polyethylene, polypropylene, rayon)	Upholstery, greeting cards, fishing nets manufacture, artificial snow on movie set
Fly ash	Incineration of coal and oil
Food production dusts (possibly flavorings)	Animal feed manufacture
Humidifier disinfectant (polyhexamethylene guanidine)	Homes
Hydrochloric acid	
Hydrogen sulfide	Crude oil, natural gas, manure pits, toilets
Methyl isocyanate	Bhopal pesticide manufacture leak
Mineral dusts (aluminum oxide, asbestos, coal, iron oxide, silica, etc)	Coal mining, hard rock mining, photocopier toner
Oxides of nitrogen	Explosive detonation, silage decomposition, nitric acid use, nitrocellulose fires, welding gases
Phosgene	War gas, chemical manufacturing
Polymethylene polyphenol isocyanate	Plastics factory maintenance
Sauropus androgynous	Vegetable juice consumption for weight loss
Shoe dye	Shoe shining parlor
Smoke inhalation	Plastics factory fire, synthetic materials in house fire, Styrofoam combustion, photography processing fire (ammonia, nitrogen dioxide)
Sulfur dioxide	Paper mill bleaching, sulfur mine fire
Sulfur mustard	Chemical warfare
Thionyl chloride	Lithium battery manufacture

(Adapted from ref. 1)

## Table II. Disorders of the Bronchioles

### Overlapping or related constrictive disorders

**Bronchiolitis obliterans:** synonymous with obliterative bronchiolitis

**Constrictive bronchiolitis:** characterized by constrictive fibroproliferative narrowing of small-airway walls

**Bronchiolitis obliterans syndrome:** clinical manifestations of obliterative bronchiolitis in patients who have undergone lung transplantation or hematopoietic stem-cell transplantation

### Other disorders

**Panbronchiolitis:** seen mainly in Asia; follows infection; responds well to macrolides

**Follicular bronchiolitis:** constriction of bronchioles by surrounding lymphoid tissue; autoimmune disorders

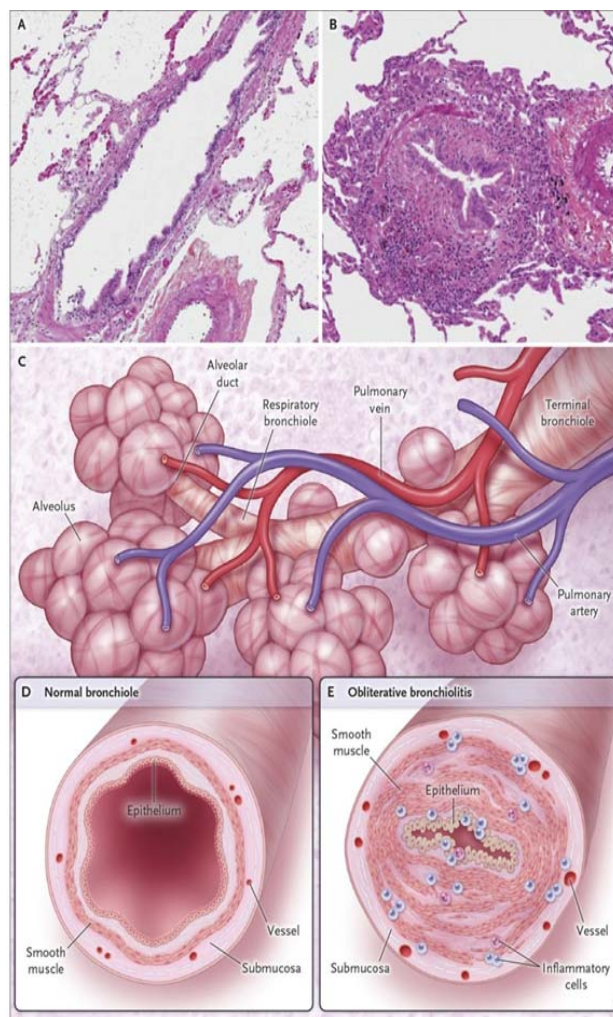
**Respiratory bronchiolitis-interstitial lung disease:** uniformly associated with cigarette smoking

**Bronchiolitis obliterans with organizing pneumonia (BOOP), also known as cryptogenic organizing pneumonia:** clinically and histologically distinct from obliterative bronchiolitis; with proliferation of polypoid fibroblasts in airway lumen; sometimes occurs after bacterial pneumonia, but inciting insult often unknown

**Hypersensitivity pneumonitis:** can be associated with small-airway narrowing from granuloma; caused by immune reaction to an antigen

(Adapted from ref. 3)

Figure I. Histologic and Schematic View of Normal Bronchioles and Biopsy Specimen from Patient with Obliterative Bronchiolitis



Ref. 3

**Please let us know if you have patients with known or suspected bronchiolitis obliterans from an occupational/environmental exposure. As always, Kenneth Rosenman, MD is available to assist with diagnostic and management issues on individual patients, 1-800-446-7805.**

### References

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\*Project  
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# News

Michigan State University  
College of Human Medicine  
West Fee Hall  
909 Fee Road, Room 117  
East Lansing, MI 48824-1316  
Phone (517) 353-1846

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\*PS Remember to report all cases of occupational disease!

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James Blessman, M.D., M.P.H.  
President, Michigan Occupational  
& Environmental Medical Association  
Wayne State University  
Razi Rafiq, M.D.  
President, Michigan Allergy and  
Asthma Society  
Darryl Lesoski, M.D., M.P.H.  
Munson Medical Center  
Traverse City, MI  
Thomas G. Robins, M.D., M.P.H.  
University of Michigan  
School of Public Health  
Division of Occupational Medicine  
Timothy Damm M.D.  
President, Michigan Thoracic Society  
Eric J. Rose, D.O.  
Marquette General Health System  
Marquette, MI

### Advisory Board

(517) 353-1846  
MSU-CHM  
West Fee Hall  
909 Fee Road, Room 117  
East Lansing, MI 48824-1316

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*At the Michigan Occupational  
Safety & Health Administration  
(MIOSHA)*

Barton G. Piekelman  
Acting Director MIOSHA

*At Michigan State University—  
College of Human Medicine*

Kenneth D. Rosenman, M.D.  
Professor of Medicine  
Project SENSOR, Director  
Mary Jo Reilly, M.S.  
Project SENSOR Coordinator  
Melissa Millerick-May, M.S., Ph.D.  
Project SENSOR Office Staff:  
Tracy Carey  
Ruth VanderWaal  
Patient Interviewers:  
Steve Cross  
Nikolette Jones  
Alison Karadoff  
Mukti Patel  
Shayna Vega

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Health Administration (MIOSHA)

Management and Technical  
Services Division  
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Lansing, MI 48909-8149

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Project SENSOR Staff