

# Other Airway Conditions Involving the Distal Airway (Bronchiolitis) State-of-the-Art

MAYO  
CLINIC



Clayton T. Cowl, MD, MS, FCCP

President, CHEST

Chair, Division of Preventive, Occupational, and Aerospace Medicine

Joint Appointment, Division of Pulmonary & Critical Care Medicine

Mayo Clinic

Rochester, Minnesota USA

# Disclosures

Dr. Cowl has no financial or other COI disclosures related to the material in this presentation. There will be no discussion of off-label use for any drugs or devices.

# Learning Objectives

- Recognize naming and types of bronchiolitis and common causes
- Explain factors involved with diagnosing and treating bronchiolitis and similar airway conditions
- Recall key pathologic and radiographic features of various distal airway conditions

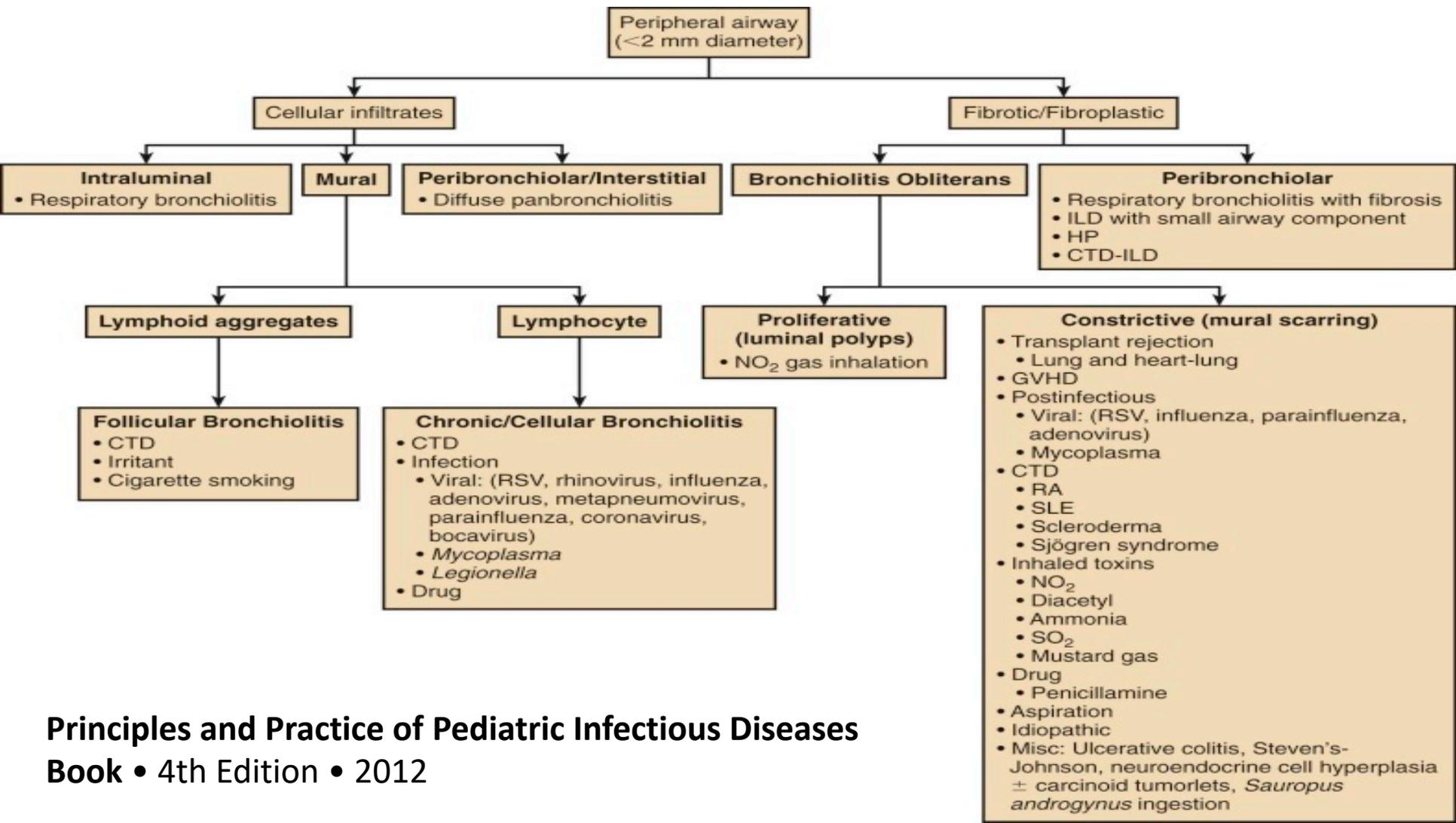


## Peripheral airways

- Defined as airways with less than 2 mm in diameter and no cartilage

## Membranous bronchioles

- Have full fibromuscular wall but this wall is very thin



	<b>Chronic Bronchitis</b>	<b>Bronchiectasis</b>	<b>Asthma</b>	<b>Emphysema</b>	<b>Bronchiolitis</b>
<b>Anatomic site</b>	Bronchus	Bronchus	Bronchus	Acinus	Bronchiole
<b>Pathology</b>	Mucous gland hyperplasia, hypersecretion	Airway dilatation, scarring	Smooth muscle hyperplasia, excess mucus, inflammation	Airspace enlargement, wall destruction	Inflammatory scarring, obliteration
<b>Etiology</b>	Tobacco smoke, air pollutants	Persistent or severe infections	Immunologic or undefined causes	Tobacco smoke	Tobacco smoke, air pollutants, miscellaneous
<b>Main symptoms</b>	Cough, sputum production	Cough, purulent sputum, fever	Episodic wheezing, cough, dyspnea	Dyspnea	Cough, dyspnea



## Assessment and treatment of acute toxic inhalations

Clayton T. Cowl

### Purpose of review

Acute toxic inhalation exposures affect thousands of individuals worldwide each year. The acute evaluation of these inhaled exposures is often fraught with difficulty in identifying a specific agent, may involve multiple compounds, and a wide variety of responses are seen depending on the physical properties of the specific toxicant, the length of time of inhalation, and the concentration of the exposure. Recognizing key aspects of the most common acute toxic inhalations is useful in developing a diagnosis and treatment strategy.

### Recent findings

Use of sequential observations with flexible bronchoscopy has been the standard of care for assessing airway injury, and virtual bronchoscopy using computed tomographic images in a three-dimensional reconstructed image can now better identify airway narrowing. Use of [ $^{18}$ F]-fluorodeoxyglucose uptake, as measured by PET, has the potential for early recognition of delayed acute lung injury in toxic inhalation exposures. Development of a standardized respiratory injury grading system is ongoing with a recent multicenter trial nearly complete, allowing for more accurate estimates of eventual outcomes and guide levels of intensity of care for patients with acute inhalation injury. Removal from the source of exposure and airway support remain the first critical aspect of treatment, and additional therapies have been studied recently that focus on altering molecular mechanisms of acute cellular injury, expanding potential treatments beyond other pharmacotherapeutic strategies utilized previously such as mucolytics, bronchodilators, and inhaled anticoagulants.

### Summary

Although a prevalent source of airway injury, exposure to acute toxic inhalants is often difficult to assess and prognosticate, and challenging to treat.

### Keywords

acute inhalation injury, acute toxic inhalants, gaseous inhalation, inhaled irritants, toxic inhalations

### INTRODUCTION

decades. Inhaled toxicants have been classified in a standard fashion into what has been termed the

## Which of the following statements regarding bronchiolitis is **MOST CORRECT**?

- A. Toxic inhalations make up the majority of cases of bronchiolitis.
- B. Bronchiolitis causes symptoms in all individuals with the condition.
- C. Lupus and rheumatoid arthritis have been associated with causing bronchiolitis.
- D. Finding small airways changes on the FEF25-75 of spirometry is pathognomonic for bronchiolitis.
- E. Azithromycin has been used in bronchiolitis for its anti-microbial rather than its anti-inflammatory effects on the small airways.

## Which of the following statements regarding bronchiolitis is **MOST CORRECT**?

- A. Toxic inhalations make up the majority of cases of bronchiolitis.
- B. Bronchiolitis causes symptoms in all individuals with the condition.
- C. **Lupus and rheumatoid arthritis have been associated with causing bronchiolitis.**
- D. Finding small airways changes on the FEF25-75 of spirometry is pathognomonic for bronchiolitis.
- E. Azithromycin has been used in bronchiolitis for its anti-microbial rather than its anti-inflammatory effects on the small airways.

## **Bronchiolitis obliterans (also known as obliterative bronchiolitis or constrictive bronchiolitis)**

- Common symptoms include dyspnea and cough;
- PFTs normal or show airflow limitation without bronchodilator reversibility;
- Has predisposing process (e.g., inhalational or drug exposure, rheumatic disease, lung or hematopoietic transplant);
- Expiratory air trapping (mosaic or diffuse) and bronchial wall thickening (e.g., "v" or "y" shaped branching linear opacities),
- Centrilobular nodules

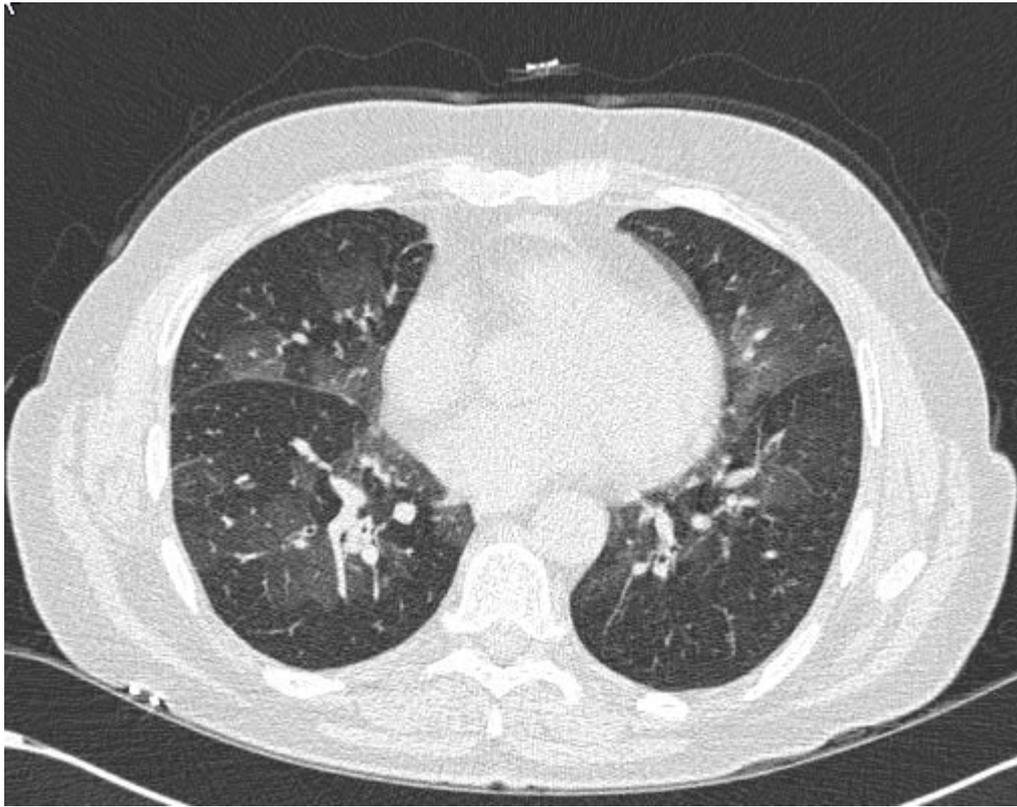
# Constrictive bronchiolitis (BO)

- Airway disease that surrounds the lumen with fibrotic concentric narrowing and obliteration.
- Mosaic pattern seen on the expiratory high-resolution chest CT scan is diagnostic in an individual with shortness of breath, early inspiratory crackles, and irreversible airflow obstruction.
- Swyer-James-MacLeod syndrome is no longer considered a congenital disorder but as constrictive bronchiolitis detected in young adults who had infectious pneumonia during infancy.
- Azithromycin may be effective in some lung transplant recipients for treatment of bronchiolitis obliterans syndrome for prevention of constrictive bronchiolitis.

# Bronchiolitis obliterans – CONT.

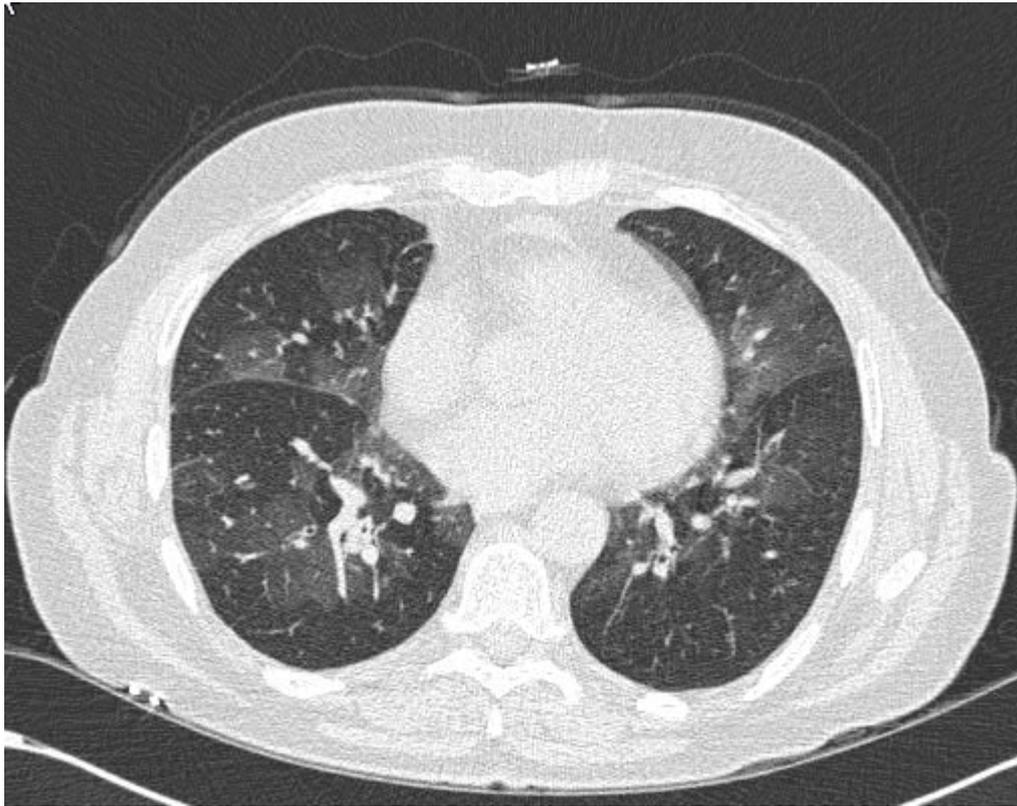
Optimal treatment unknown:

- Stop exposure to potential inciting agents
- Symptomatic treatment with inhaled bronchodilators and oxygen;
- Other options: macrolides, glucocorticoids, immunosuppressive agents, anti-reflux therapy, lung transplantation



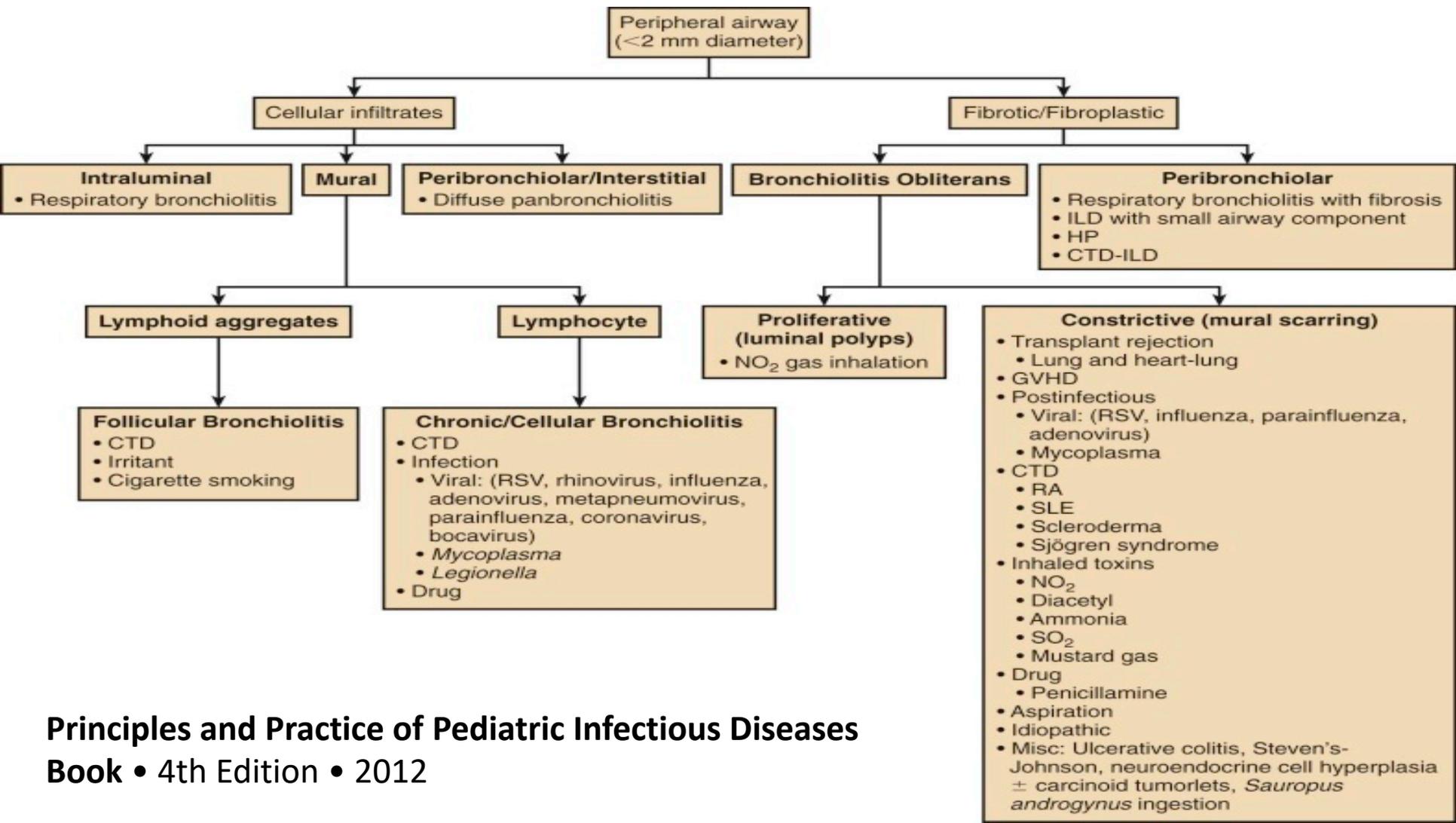
What findings are noted in this CT image seen commonly in constrictive bronchiolitis?

- Pulmonary nodules
- Tram track lines
- Mosaic attenuation
- Vascular injection



What findings are noted in this CT image seen commonly in constrictive bronchiolitis?

- Pulmonary nodules
- Tram track lines
- Mosaic attenuation
- Vascular injection



# Airway-centered interstitial fibrosis

- Associated with chronic nonproductive cough;
- Usually seen in smokers;
- PFTs restrictive or obstructive;
- Percentage of lymphocytes on bronchoalveolar lavage is less than 40%
- See peribronchovascular ground glass opacities, traction bronchiectasis, and thickening of bronchial walls
- Centrilobular and bronchiolocentric inflammatory infiltrate with peribronchiolar fibrosis and an absence of granulomas
- Treat with systemic or inhaled glucocorticoids

## Which of the following pathogens is most commonly associated with the development of bronchiolitis in children?

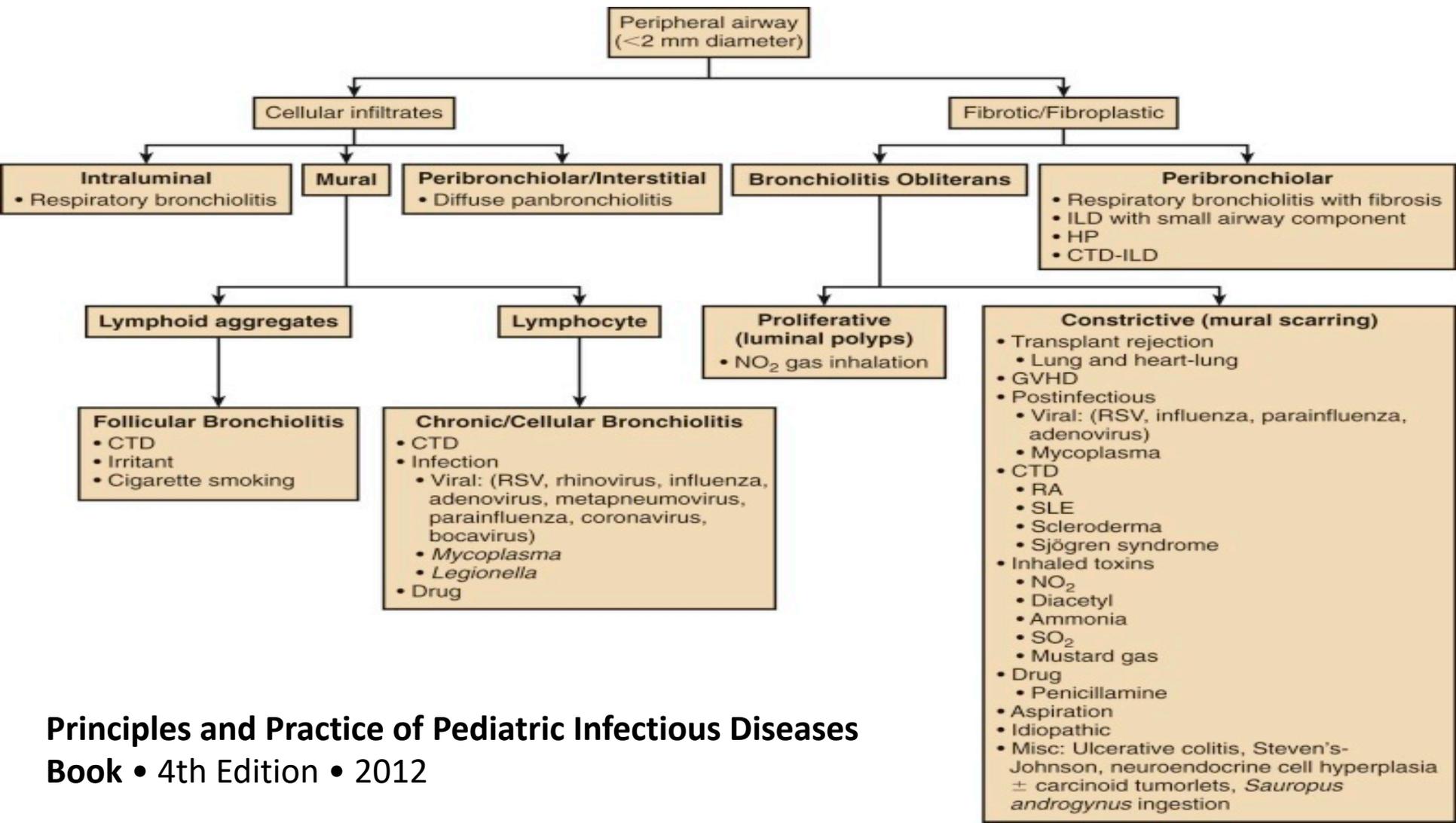
- A. Respiratory syncytial virus (RSV)
- B. Noravirus
- C. Strongyloides
- D. Streptococcus pneumoniae
- E. Cladosporidium

## Which of the following pathogens is most commonly associated with the development of bronchiolitis in children?

- A. Respiratory syncytial virus (RSV)
- B. Noravirus
- C. Strongyloides
- D. Streptococcus pneumoniae
- E. Cladosporidium

# Acute Bronchiolitis

- Seen most commonly as a result of viral infectious diseases in the first two years of life
- 2-3% of children in the first 12 months of life are hospitalized with bronchiolitis, resulting in 125,000 hospitalizations and 200 to 500 deaths each year in the United States alone
- CDC data show the prevalence of bronchiolitis more than doubled between 1980 and 1996

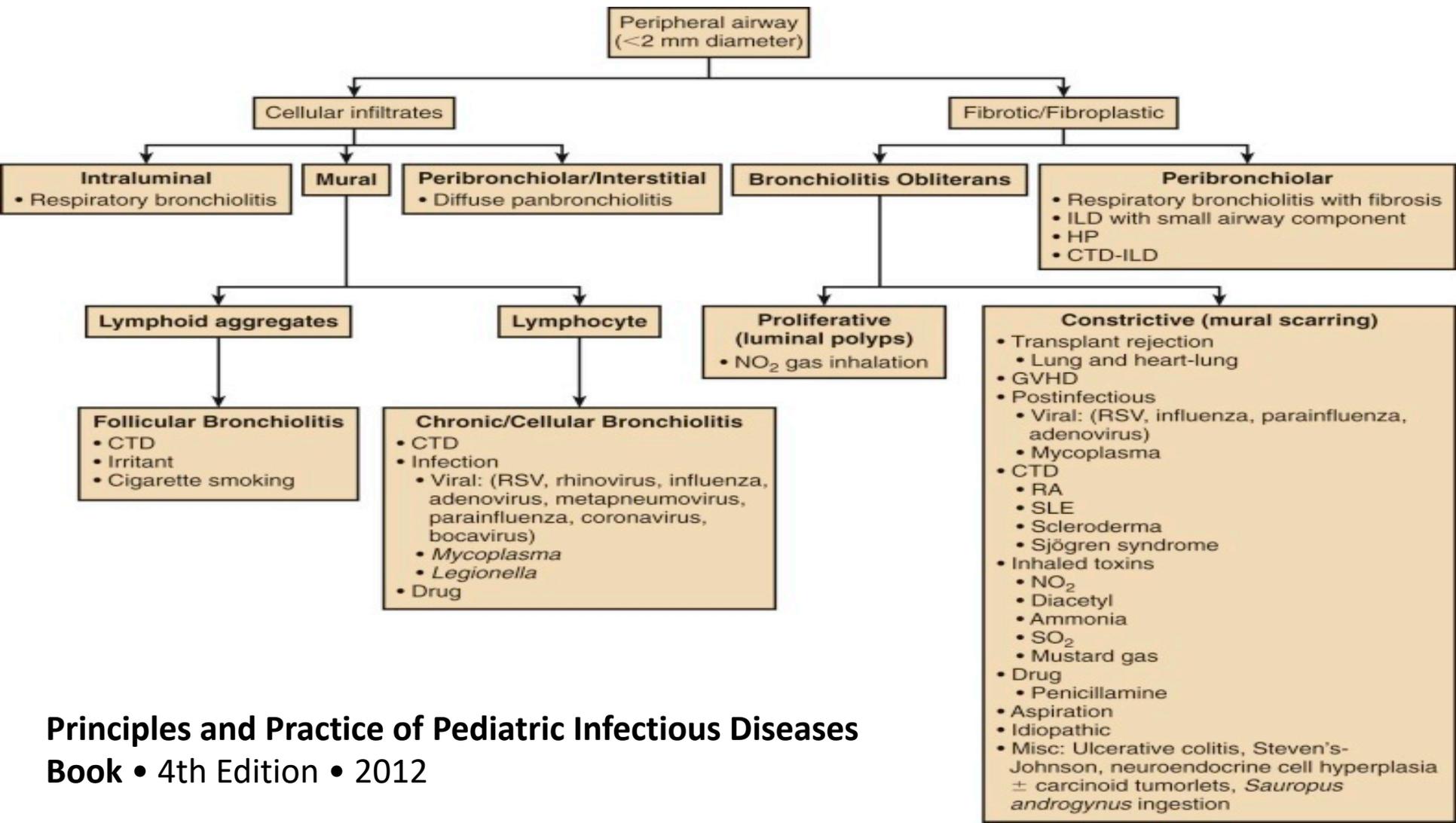


# Proliferative bronchiolitis

- Distinctive histopathological pattern in which characteristic intraluminal fibrotic buds, called Masson bodies, extend beyond alveolar ducts to alveoli
- When proliferative bronchiolitis is associated with extension of inflammatory cells into the more distal pulmonary parenchyma, the process is called organizing pneumonia
- It is not uncommon to identify foamy macrophages in the alveolar spaces
- Associated with NO<sub>2</sub> inhalations

# Proliferative bronchiolitis

- Usually seen in the context of cryptogenic or secondary organizing pneumonia or nitrogen dioxide (NO<sub>2</sub>) exposure
- Diffuse or patchy ground glass or consolidative opacities
- Fibroblast proliferation and an organizing, polypoid intraluminal exudate in respiratory bronchioles and alveolar ducts
- Stop any inciting exposure
- Start systemic glucocorticoid trial



# Follicular bronchiolitis (mural)

- Characterized by progressive dyspnea
- Associated with rheumatic diseases, immunodeficiency, hypersensitivity pneumonitis
- Centrilobular nodules; may have patchy ground glass opacity
- Polyclonal hyperplasia of bronchiolar associated lymphoid tissue (BALT) produced by antigen stimulation (lymphoid aggregates), with reactive germinal centers distributed along the bronchioles and less frequently more proximal to the bronchi
- Treat underlying disease

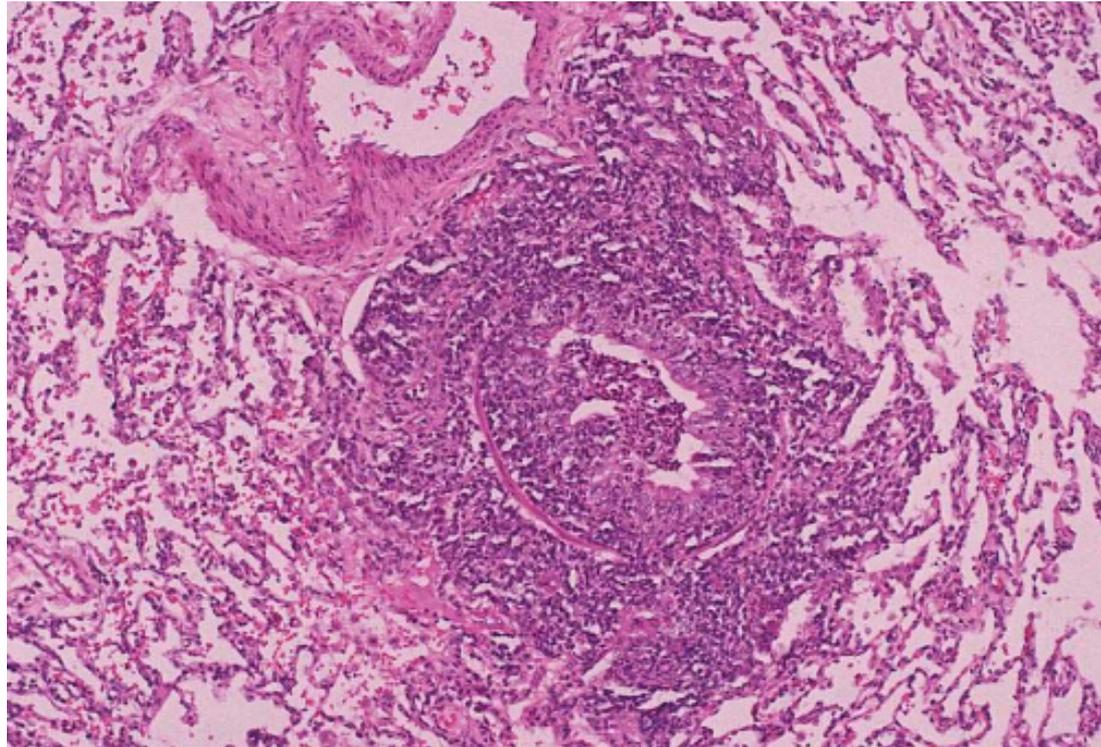
# Respiratory bronchiolitis (intraluminal)

- Almost exclusively in smokers
- Often seen as asymptomatic finding on biopsy performed for another reason
- Diffuse or patchy ground glass opacities or fine centrilobular nodules and air trapping; bronchial wall thickening
- Mild bronchiolar inflammation, tan-pigmented macrophages within the lumens of first and second order respiratory bronchioles
- Treatment is cigarette smoking cessation

# Respiratory bronchiolitis

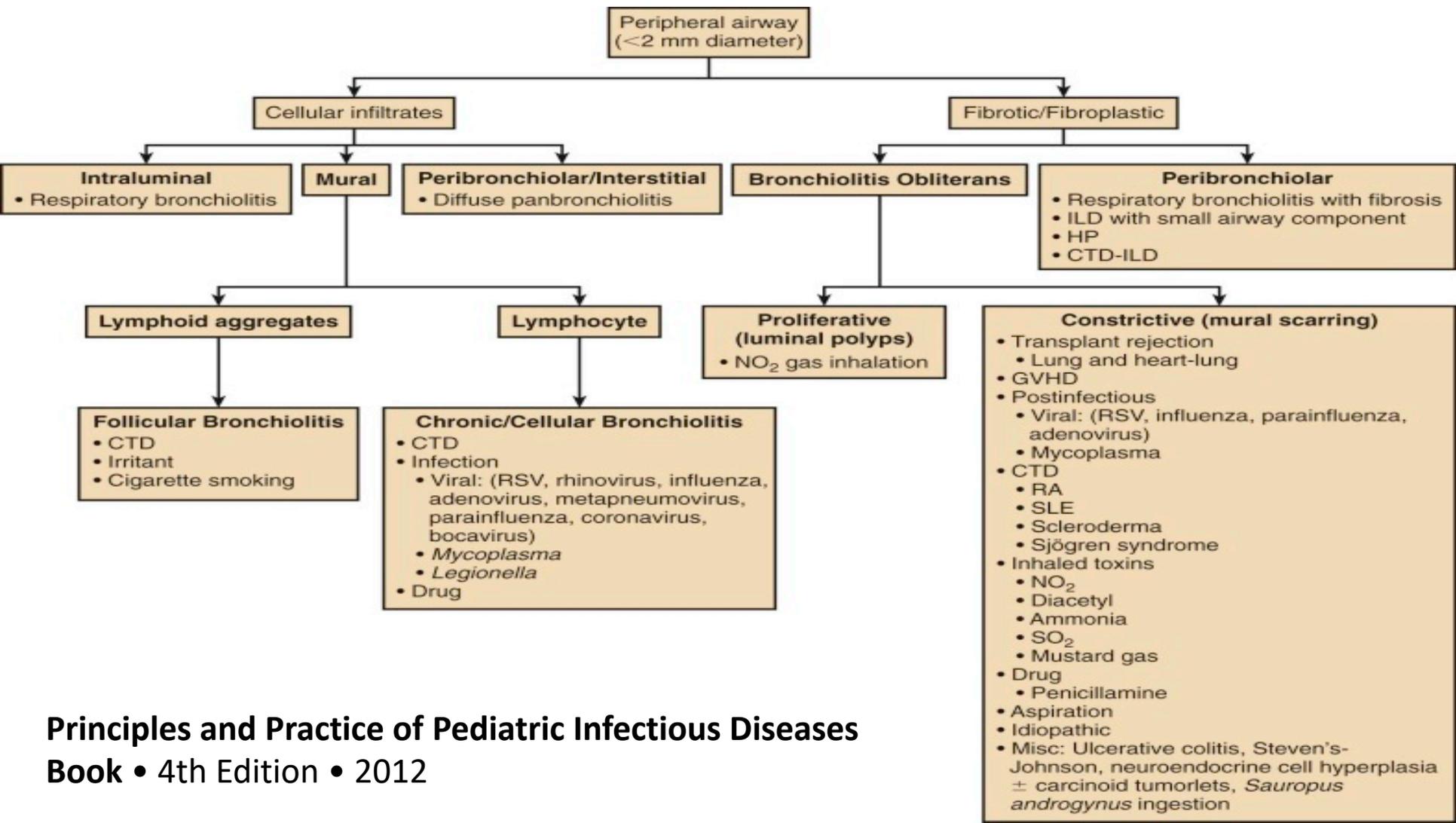
 CHEST<sup>®</sup>  
Congress  
2019

Thailand  
Bangkok | 10-12 April



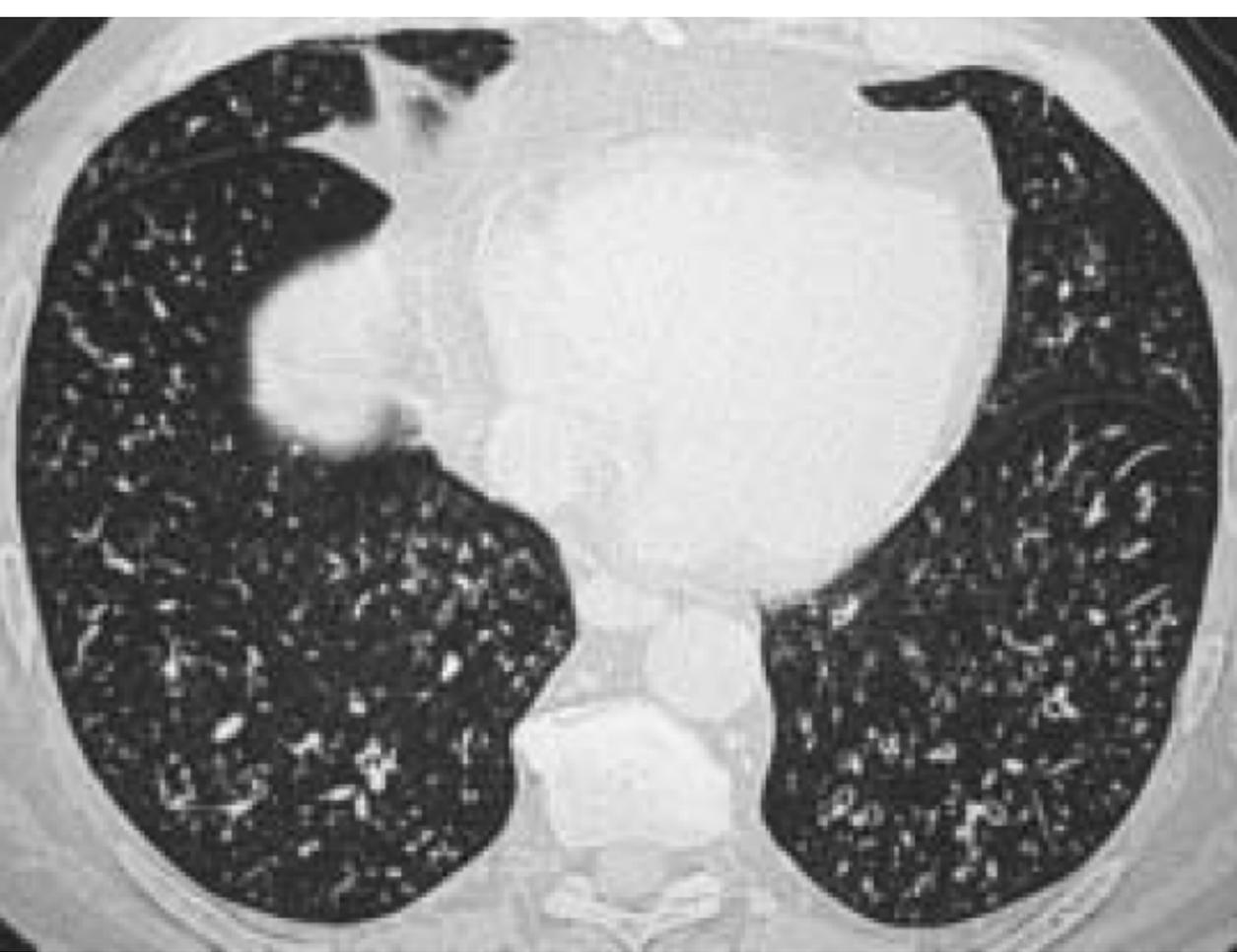
Register now at [congress.chestnet.org](https://congress.chestnet.org)

Connecting a Global Community  
in Clinical Chest Medicine



# Diffuse panbronchiolitis

- History of sinusitis (75%) and productive cough;
- Generally limited to patients in Japan or other areas in SE Asia
- Diffuse centrilobular opacities, nodular and linear (tree-in-bud) opacities, thickened and dilated bronchiolar walls, and large cystic opacities with dilated proximal bronchi (in advanced disease)
- Bronchiolar transmural infiltrate composed of lymphocytes, plasma cells, and distinctive lipid-laden "foamy" macrophages
- Diagnose through compatible clinical findings in a patient in Japan; otherwise lung biopsy
- Macrolide antibiotic for six months or longer



 **CHEST**<sup>®</sup>  
Congress  
2019

**Thailand**  
Bangkok | 10-12 April

Eur Respir J 2006; 28: 862–871

Register now at [congress.chestnet.org](http://congress.chestnet.org)

Connecting a Global Community  
in Clinical Chest Medicine

# Summary

- Bronchiolitis is one category of conditions affecting the distal airways -- with acute forms associated with viral infections in infants (RSV)
- Nomenclature was modified to describe pathological features (cellular v. fibrotic -- proliferative v. constrictive bronchiolitis)
- May be a continuum of airway inflammation that is similar in other inflammatory airway conditions causing asthma and COPD
- Toxic inhalations in addition to connective tissue diseases and infections are etiologies to consider in adult bronchiolitis

Join colleagues from around the region to gain access to the CHEST learning and training experience at our regional congress. This unique program will go beyond the classroom-style setting to connect you to leading experts who will teach and develop you and your team.

**Learn More: [athens.chestnet.org](http://athens.chestnet.org)**



**ATHENS 2019**  
GREECE | 27-29 JUNE

