



**Figure 15-52** Histologic variants of malignant mesothelioma. **A**, Epithelioid type. **B**, Mixed type, stained for calretinin (immunoperoxidase method). The epithelial component is strongly positive (dark brown), while the sarcomatoid component is less so. (Courtesy Dr. Thomas Krausz, Department of Pathology, The University of Chicago, Pritzker School of Medicine, Chicago, Ill.)

with the fact that mesothelial cells have the potential to develop as epithelium-like cells or mesenchymal stromal cells.

The **epithelioid type** of mesothelioma consists of cuboidal, columnar, or flattened cells forming tubular or papillary structures resembling adenocarcinoma (Fig. 15-52A). Immunohistochemical stains are very helpful in differentiating it from pulmonary adenocarcinoma. Most mesotheliomas show strong positivity for keratin proteins, calretinin (Fig. 15-52B), Wilms tumor 1 (WT-1), cytokeratin 5/6, and D2-40. This panel of antibodies is diagnostic in a majority of cases when interpreted in the context of morphology and clinical presentation. The mesenchymal type of mesothelioma (**sarcomatoid type**) appears as a spindle cell sarcoma, resembling fibrosarcoma. Sarcomatoid mesotheliomas tend to have lower expression of many of the markers described previously and some may be positive only for keratin. The **mixed (biphasic) type** of mesothelioma contains both epithelioid and sarcomatoid patterns (Fig. 15-52B).

**Clinical Course.** The presenting complaints are chest pain, dyspnea, and, as noted, recurrent pleural effusions. Concurrent pulmonary asbestosis (fibrosis) is present in only 20% of individuals with pleural mesothelioma. The lung is invaded directly, and there is often metastatic spread to the hilar lymph nodes and, eventually, to the

liver and other distant organs. Fifty percent of patients die within 12 months of diagnosis, and few survive longer than 2 years. Aggressive therapy (extrapleural pneumonectomy, chemotherapy, radiation therapy) seems to improve this poor prognosis in some patients.

Mesotheliomas also arise in the peritoneum, pericardium, tunica vaginalis, and genital tract (benign adenomatoid tumor; see Chapter 21). *Peritoneal mesotheliomas* are related to heavy asbestos exposure in 60% of male patients (the number is much lower in females). Although in about half cases the disease remains confined to the abdominal cavity, intestinal involvement frequently leads to death from intestinal obstruction or inanition.

## SUGGESTED READINGS

### Acute Lung Injury

Dushianthan A, et al: Acute respiratory distress syndrome and acute lung injury. *Postgrad Med J* 87:612, 2011. [Succinct review of definitions, etiology, diagnosis and treatment of acute respiratory distress syndrome and acute lung injury.]

Matthay MA, Zemans RL: The acute respiratory distress syndrome: Pathogenesis and treatment. *Annu Rev Pathol* 16:147, 2011. [Updated view of the pathogenesis of acute respiratory distress syndrome]

### Obstructive Pulmonary Diseases

Hogg JC: A pathologist's view of airway obstruction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 186:v, 2012. [A succinct editorial reviewing current knowledge about small airway involvement in COPD.]

Mitzner W: Emphysema—a disease of small airways or lung parenchyma? *N Engl J Med* 365:1637, 2011. [An editorial on the alveolar and small airway changes in emphysema.]

### Emphysema

Agusti A, Vestbo J: Current controversies and future perspectives in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 184:507, 2011. [Review of advances over the last decade in understanding COPD and remaining areas of uncertainties.]

Huang YJ, et al: From microbe to microbiota: Considering microbial community composition in infections and airway diseases. *Am J Respir Crit Care Med* 185:691, 2012. [Discussion of the role of the lung microbiome in health and in asthma, COPD and cystic fibrosis.]

Tuder RM, et al: Lung disease associated with alpha1-antitrypsin deficiency. *Proc Am Thorac Soc* 7:381, 2010. [Review of the broad range of activities of alpha1-antitrypsin and how its deficiency causes emphysema.]

Tuder RM, Petrache I: Pathogenesis of chronic obstructive pulmonary disease. *J Clin Invest* 122:2749, 2012. [Review article with emphasis on the pathogenesis of emphysema and how it is similar to aging.]

### Chronic Bronchitis

Kim V, Criner GJ: Chronic bronchitis and COPD. *Am J Respir Crit Care Med* (ePub ahead of print) 2012. [Concise review of epidemiology, pathogenesis, clinical sequelae of mucous hyperplasia, and therapy of chronic bronchitis.]

### Asthma

Corren J, et al: Lebrikizumab treatment in adults with asthma. *N Engl J Med* 365:1088, 2011. [Data from this study provide proof of the concept that anti-interleukin-13 therapy can be targeted to susceptible patients—a step forward in personalized therapy for asthma.]

Fahy JV, Locksley RM: The airway epithelium as a regulator of Th2 responses in asthma. *Am J Respir Crit Care Med* 184:390, 2011. [Summarizes and explains how epithelial cells regulate both innate and adaptive immune responses in the airway.]

Galli SJ, Tsai M: IgE and mast cells in allergic disease. *Nat Med* 18:693, 2012. [This review discusses the roles IgE and mast cells in immune responses that manifest clinically as asthma and other allergic disorders.]

Holt PG, Sly PD: Viral infections and atopy in asthma pathogenesis: New rationales for asthma prevention and treatment. *Nat Med*