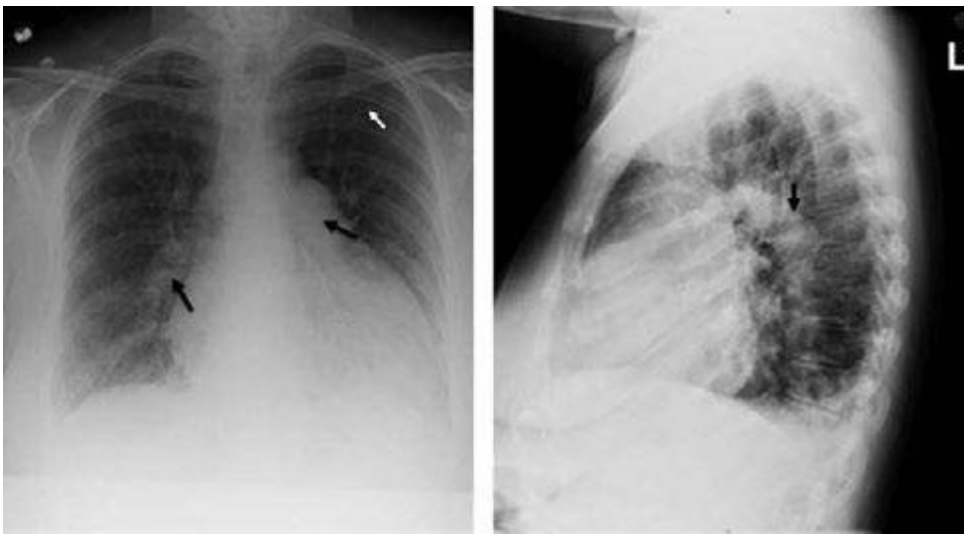

FIGURE 304-3 Posteroanterior (*left*) and lateral (*right*) chest radiograph showing enlarged pulmonary arteries (*black arrows*) and pruning of the distal pulmonary vasculature (*white arrow*) commonly seen with advanced pulmonary arterial hypertension.

PULMONARY HYPERTENSION AS A COMORBID DISEASE

PAH is just one of a number of disease classifications that affect the pulmonary vascular bed. PH was previously classified as primary or secondary, but as understanding of the various contributing diseases has increased, classification systems have attempted to group these diseases by clinical features to aid in diagnosis. The World Health Organization (WHO) formulated a clinical classification of the various manifestations of PH, of which PAH is a subgroup, according to similarities in pathophysiologic mechanisms and clinical presentation. PH is a diverse mix of pathologies in which the only unifying theme is elevated PAP relative to left atrial pressure. The categorization of PH was designed by convenience for the purpose of facilitating novel treatments to be tested across different presentations and is not based on a molecular understanding of the pathology and is not a guide for management decisions.

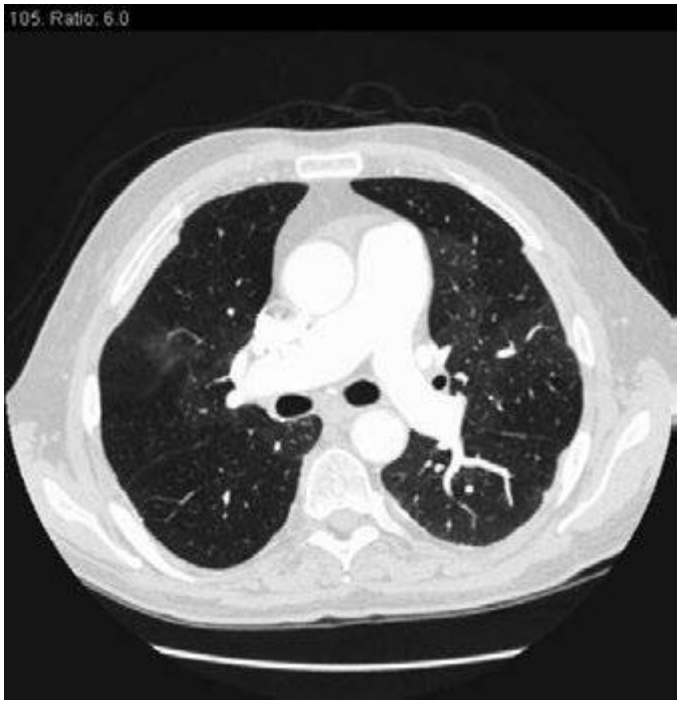

FIGURE 304-4 Representative computed tomography scan of the chest demonstrating enlarged main pulmonary arteries. There is also a mosaic pattern evident in both lungs.

The current classification system, last revised in 2013 during the Fifth World Symposium on Pulmonary Hypertension, recognizes five categories of PH, including PAH, PH due to left heart disease, PH due to chronic lung disease, PH associated with chronic thromboemboli, and a group of miscellaneous diseases that only rarely cause PH.

Pulmonary Arterial Hypertension WHO Group I PH, pulmonary arterial hypertension (PAH), is a relatively rare cause of PH. PAH includes a group of diseases that result in pulmonary arterial precapillary remodeling marked by intimal fibrosis, increased medial thickness, pulmonary arteriolar occlusion, and classic plexiform lesions. PAH is defined as a sustained elevation in resting mPAP ≥25 mmHg, PVR>240 dyne·s/cm^5, and PCWP or left ventricle end-diastolic pressure of ≤15 mmHg based on a right heart catheterization. With a normal PCWP and an elevated mPAP, these diseases demonstrate an increased transpulmonary gradient (mPAP – PCWP); in addition, the PVR is elevated.

Idiopathic pulmonary arterial hypertension (IPAH) is a progressive disease that leads to right heart failure and death. It is typically seen in young women. The National Institutes of Health registry, the first large registry of patients with PAH, reported that the average age at diagnosis was 36 years, with only 9% of patients with IPAH over the age of 60 at diagnosis. However, the more current clinical data suggest that the patient demographics are changing. The Pulmonary Hypertension Connection registry found that the average age of diagnosis for IPAH was 45 years, with 8.5% of patients older than 70 years at diagnosis. This finding is supported by data from the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL), the largest cohort of PAH to date, which reported that the average age at diagnosis of IPAH was 44.9±0.6 years.

Other forms of PAH that deserve specific consideration in patients are those associated with HIV, connective tissue disease, and portal hypertension. Although HIV is a rare cause of PAH, this form of PAH is indistinguishable from IPAH and is an important cause of mortality in the HIV-infected population. Importantly, there is no correlation between the stage of HIV infection and the development of PAH.

Among connective tissue diseases, the prevalence of PAH has been established only for systemic sclerosis, especially in those with limited cutaneous scleroderma. Although the average age of scleroderma onset is 30 to 50 years old, patients who eventually develop scleroderma-associated PAH tend to be older at the time of scleroderma diagnosis. Outcomes of scleroderma are closely linked to the development of PAH and are associated with a poor prognosis, although modern therapies have improved outcomes.

Portopulmonary hypertension occurs in 2–10% of patients with established portal hypertension. Its occurrence appears to be independent of the cause of liver disease and is observed in patients with nonhepatic causes of portal hypertension. A hyperdynamic circulatory state is common, as in most patients with advanced liver disease; however, the same pulmonary vascular remodeling observed in other forms of PAH is seen in the pulmonary vascular bed in portopulmonary hypertension. It is important to distinguish this process from hepatopulmonary syndrome, which can also manifest with dyspnea and hypoxemia but is pathophysiologically distinct from portopulmonary hypertension in that abnormal vasodilation of the pulmonary vasculature leads to intrapulmonary shunting.

Pulmonary Hypertension Associated with Left Heart Disease WHO Group II PH includes patients with left heart systolic failure, aortic and