COR PULMONALE

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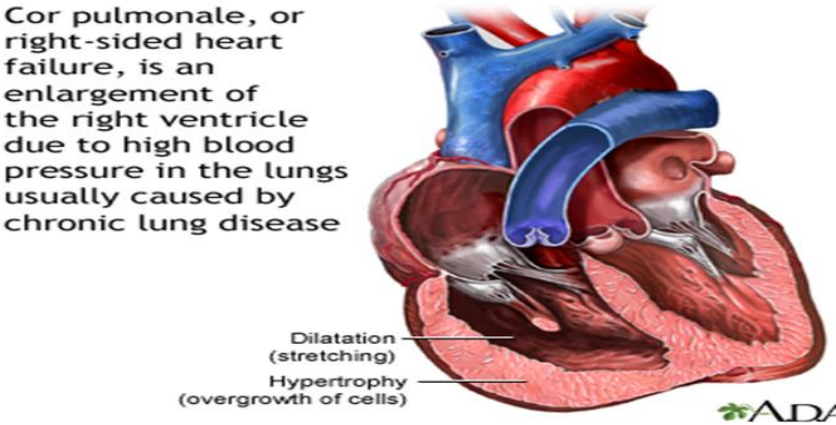
Definition

Cor pulmonale is also called right-sided heart failure, and is characterized by enlargement of the right ventricle, defined as an alteration in the structure and function of the right ventricle caused by a primary disorder of the respiratory system.



Major Causes of Cor Pulmonale

Lung disease
- Chronic obstructive pulmonary disease
- Cystic fibrosis
- Interstitial lung diseases

Disorders of the pulmonary circulation
- Pulmonary thromboembolism
- Primary pulmonary hypertension
- Tumor emboli
- Sickle cell anemia
- Schistosomiasis
- Pulmonary veno-occlusive disease

Neuromuscular diseases
- Amyotrophic lateral sclerosis
- Myasthenia gravis
- Poliomyelitis
- Guillain-Barré syndrome
- Spinal cord lesions
- Bilateral diaphragmatic paralysis

Thoracic cage deformities
- Kyphoscoliosis

Disorders of ventilatory control
- Primary central hypoventilation
- Sleep apnea syndromes

- Pulmonary hypertension is the common link between lung dysfunction and the heart in cor pulmonale.
- Right-sided ventricular disease caused by a primary abnormality of the left side of the heart or congenital heart disease is not considered cor pulmonale, but cor pulmonale can develop secondary to a wide variety of cardiopulmonary disease processes.
- Although cor pulmonale commonly has a chronic and slowly progressive course, acute onset or worsening cor pulmonale with life-threatening complications can occur.

Etiology and Pathophysiology of Cor Pulmonale

*Cor pulmonale usually presents chronically, but 2 main conditions can cause acute cor pulmonale: pulmonary embolism (more common) and acute respiratory distress syndrome (ARDS).

*The underlying pathophysiology in massive pulmonary embolism causing cor pulmonale is the sudden increase in pulmonary resistance.

*In ARDS, 2 factors cause right ventricular (RV) overload:

-the pathologic features of the syndrome itself,

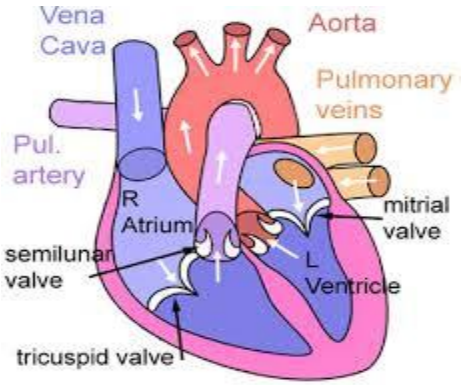
-mechanical ventilation.

Mechanical ventilation, especially higher tidal volume, requires a higher transpulmonary pressure.

Etiology and Pathophysiology of Cor Pulmonale

*In chronic cor pulmonale, RV hypertrophy (RVH) generally predominates.

*In acute cor pulmonale, right ventricular dilatation mainly occurs.



*In the case of ARDS, cor pulmonale is associated with increased possibility of right-to-left shunt through the patent foramen ovale and carries a poorer prognosis.

Etiology and Pathophysiology of Cor Pulmonale

Several different pathophysiologic mechanisms can lead to pulmonary hypertension and, subsequently, to cor pulmonale. These pathogenetic mechanisms include the following:

- Pulmonary vasoconstriction due to alveolar hypoxia or blood acidemia – This can result in pulmonary hypertension and if the hypertension is severe enough, it causes cor pulmonale.

Etiology and Pathophysiology of Cor Pulmonale

- Anatomic compromise of the pulmonary vascular bed secondary to parenchymal or alveolar lung disorders (eg, emphysema, pulmonary thromboembolism, interstitial lung disease, adult respiratory distress syndrome, and rheumatoid disorders) – These conditions can cause elevated pulmonary blood pressure.
- Chronic obstructive pulmonary disorder is the most common cause of cor pulmonale, and some connective tissue disorders with pulmonary involvement may result in pulmonary hypertension and cor pulmonale.

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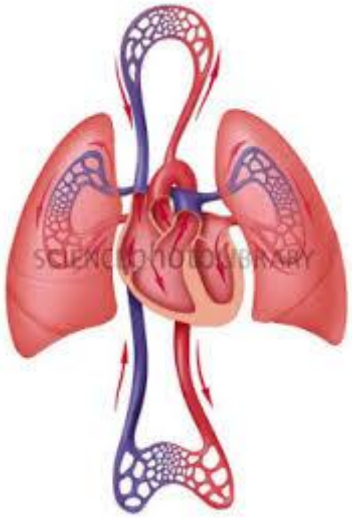
Etiology and Pathophysiology of Cor Pulmonale

- Increased blood viscosity secondary to blood disorders (eg, polycythemia vera, sickle cell disease, macroglobulinemia)

- Increased blood flow in pulmonary vasculature



- Idiopathic primary pulmonary hypertension

The result of the above mechanisms is increased pulmonary arterial pressure

Pathophysiology of Cor Pulmonale

* The RV is a thin-walled chamber that is more a volume pump than a pressure pump. It adapts better to changing preloads than afterloads.

*With an increase in afterload, the RV increases systolic pressure to keep the gradient.

* At a point, a further increase in the degree of pulmonary arterial pressure produces significant RV dilatation, an increase in RV end-diastolic pressure, and RV circulatory collapse.

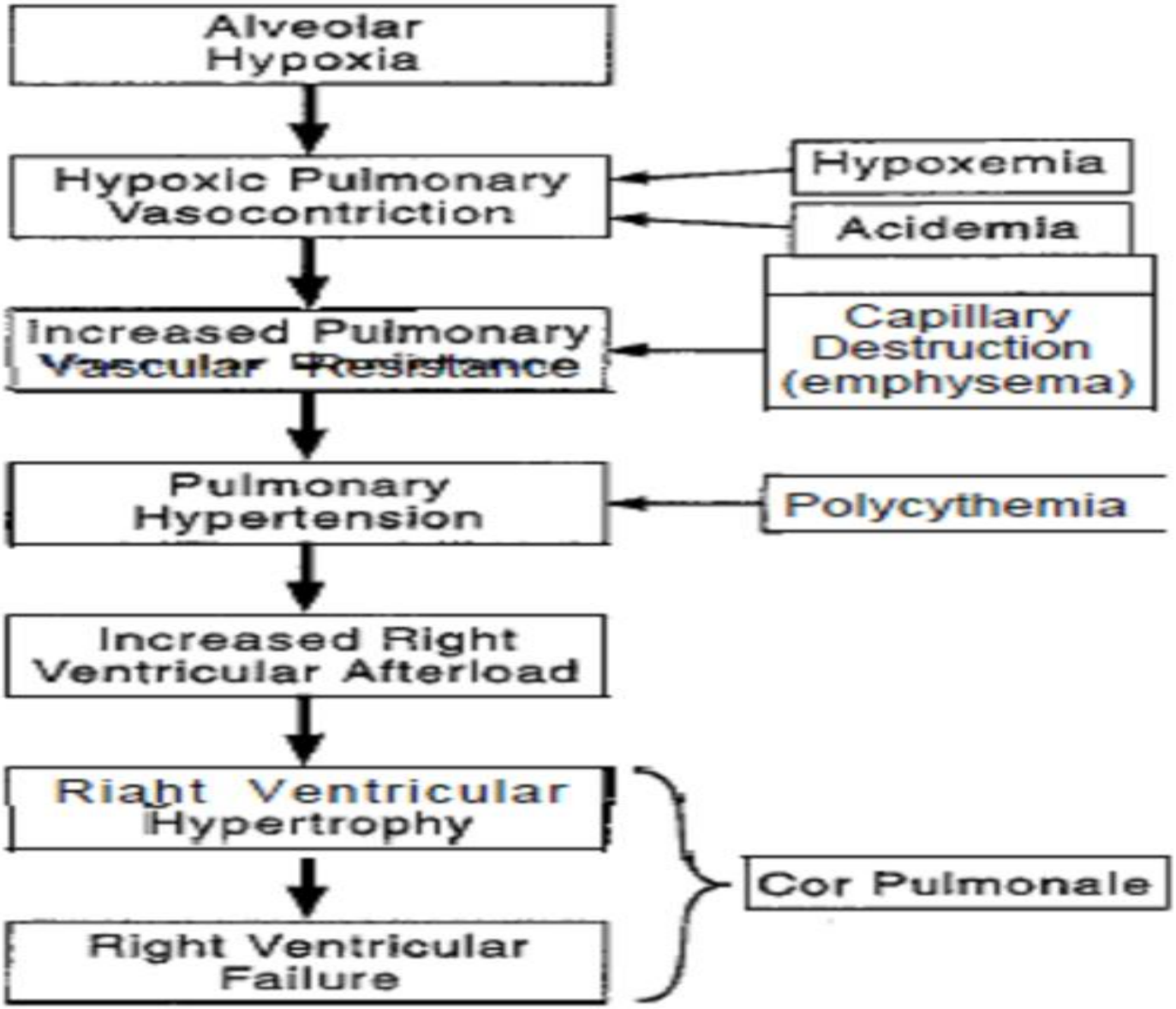
Pathophysiology of Cor Pulmonale

*A decrease in RV output with a decrease in diastolic left ventricle (LV) volume results in decreased LV output.

* Because the right coronary artery, which supplies the RV free wall, originates from the aorta, decreased LV output diminishes blood pressure in the aorta and decreases right coronary blood flow.

** What ensues is a vicious cycle between decreases in LV and RV output.

PATHOPHYSIOLOGY of Cor Pulmonale:



Cor Pulmonale Presentation

- *The clinical manifestations of cor pulmonale are generally nonspecific.*

- The symptoms may be subtle, especially in early stages of the disease, and they may be mistakenly attributed to the underlying pulmonary pathology.

Symptoms

- The patient may complain of **fatigue**, **tachypnea**, **exertional dyspnea**, and **cough.**
- **Anginal chest pain** can also occur and may be due to right ventricular ischemia (it usually does not respond to nitrates) or pulmonary artery stretching.

- A variety of **neurologic symptoms** may be seen due to decreased cardiac output and hypoxemia.

Symptoms

- Hemoptysis may occur because of rupture of a dilated or atherosclerotic pulmonary artery.

Other conditions, such as tumors, bronchiectasis, and pulmonary infarction, should be excluded before attributing hemoptysis to pulmonary hypertension.

- Rarely, the patient may complain of hoarseness due to compression of the left recurrent laryngeal nerve by a dilated pulmonary artery.

Symptoms

- In advanced stages, passive hepatic congestion secondary to severe right ventricular failure may lead to anorexia, right upper quadrant abdominal discomfort, and jaundice.
- In addition, syncope with exertion, which may also be seen in severe disease, reflects a relative inability to increase cardiac output during exercise with a subsequent drop in the systemic arterial pressure.

Symptoms

- Elevated pulmonary artery pressure can lead to elevated right atrial, peripheral venous, and capillary pressure
- By increasing the hydrostatic gradient, it leads to transudation of fluid and accumulation of peripheral edema.
- Although this is the simplest explanation for peripheral edema in cor pulmonale, other hypotheses explain this symptom, especially in a fraction of patients with chronic obstructive pulmonary disease (COPD) who do not show increase in right atrial pressure. A decrease in glomerular filtration rate (GFR) and filtration of sodium and stimulation of arginine vasopressin (which decreases free water excretion) due to hypoxemia play important pathophysiologic roles in this setting and may even have a role for peripheral edema in patients with cor pulmonale who have elevated right atrial pressure

Signs

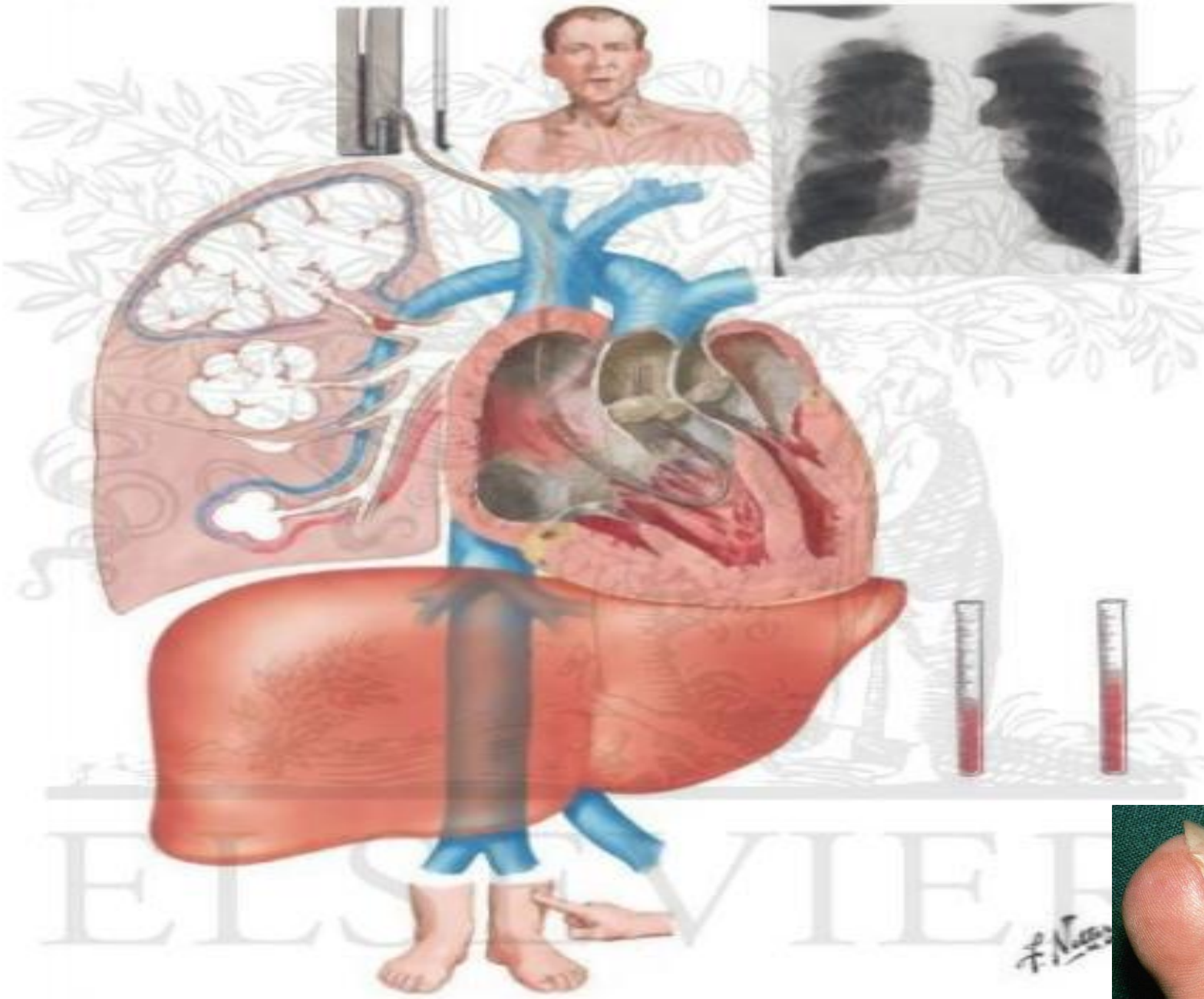
- Physical findings may reflect the underlying lung disease or pulmonary hypertension, right ventricular hypertrophy (RVH), and RV failure.
- An increase in chest diameter, labored respiratory efforts with retractions of the chest wall, distended neck veins and cyanosis may be seen.
- On auscultation of the lungs, wheezes and crackles may be heard as signs of underlying lung disease.
- Turbulent flow through recanalized vessels in chronic thromboembolic pulmonary hypertension may be heard as systolic bruits in the lungs.

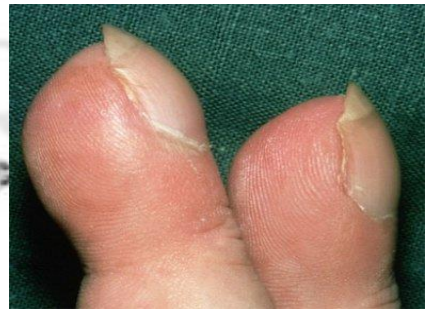
Signs

- Splitting of the second heart sound with accentuation of the pulmonic component can be heard in early stages.
- A systolic ejection murmur with sharp ejection click over the region of the pulmonary artery may be heard in advanced disease, along with a diastolic pulmonary regurgitation murmur.
- Other findings upon auscultation of the cardiovascular system may be third and fourth sounds of the heart and systolic murmur of tricuspid regurgitation.

Signs

- RVH is characterized by a left parasternal or subxiphoid heave.
- Hepatojugular reflux and pulsatile liver are signs of RV failure with systemic venous congestion.
- On percussion, hyperresonance of the lungs may be a sign of underlying COPD; ascites can be seen in severe disease.
- Examination of the lower extremities reveals evidence of pitting edema. Edema in cor pulmonale is strongly associated with hypercapnia.





Diagnostic Considerations

- A general approach to diagnose cor pulmonale and to investigate its etiology starts with routine laboratory tests, chest radiography, and electrocardiography.
- Echocardiography gives valuable information about the disease and its etiology.
- Right heart catheterization is the most accurate but invasive test to confirm the diagnosis of cor pulmonale and gives important information regarding the underlying diseases.

Diagnostic Considerations

- Making a diagnosis of cor pulmonale should be followed by further investigation to determine the underlying lung pathology. Sometimes a common lung disease such as chronic obstructive pulmonary disease (COPD) is not the only lung pathology as the cause of cor pulmonale; other lung diseases may coexist. Thus, pulmonary function tests may become necessary to confirm the underlying lung disease.
- Ventilation/perfusion (V/Q) scanning or chest computed tomography (CT) scanning may be performed if the patient's history and physical examination suggest pulmonary thromboembolism as the cause or if other diagnostic tests do not suggest other etiologies.

Diagnostic Considerations

- Any abnormal result in each of the above tests may need further diagnostic evaluation in that specific direction.

- Imaging studies may show evidence of underlying cardiopulmonary diseases, pulmonary hypertension, or its consequence, right ventricular enlargement.

Diagnostic Tests

Laboratory investigations are directed toward defining the potential underlying etiologies as well as evaluating complications of cor pulmonale.

In specific instances, appropriate laboratory studies may include the following:

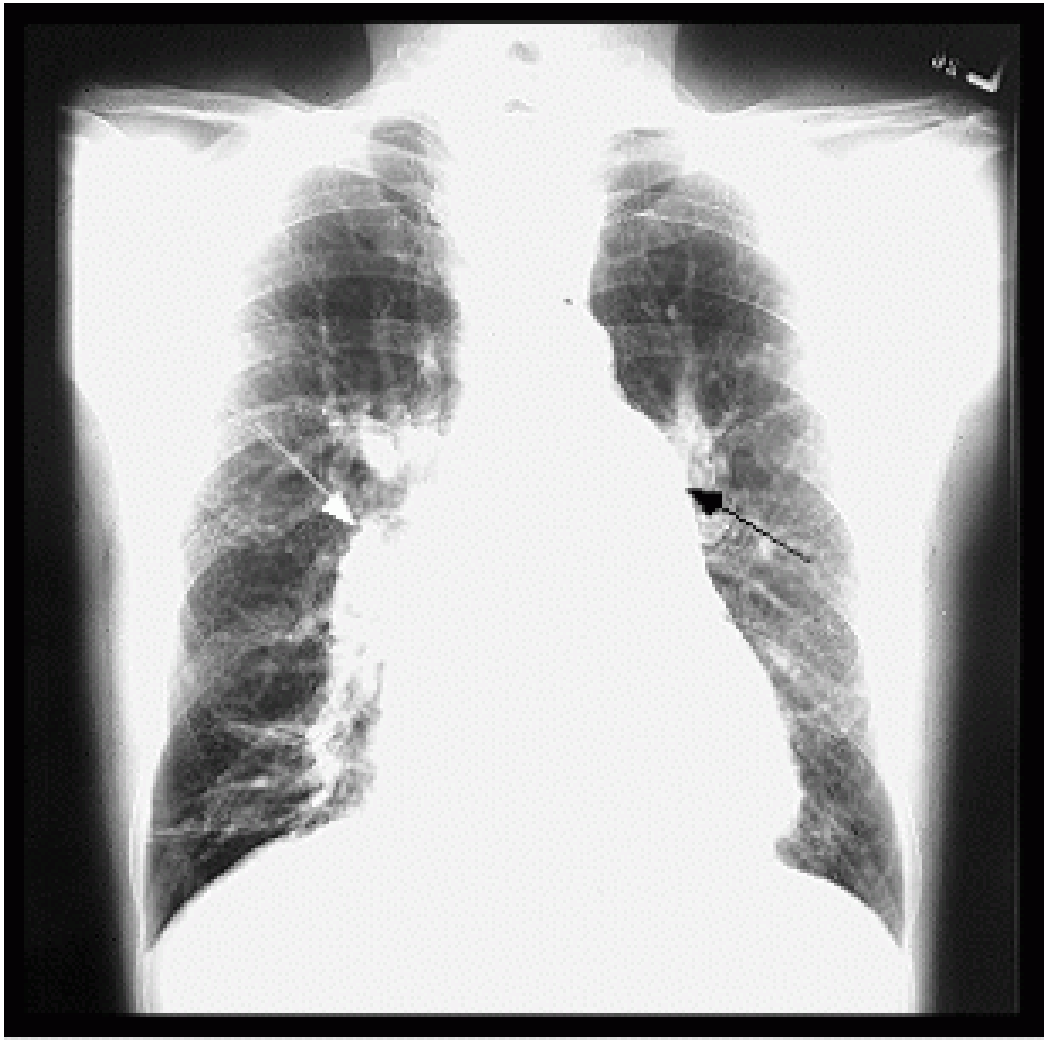
- Hematocrit for polycythemia, which can be a consequence of underlying lung disease but which can also increase pulmonary arterial pressure by increasing viscosity
- Serum alpha1-antitrypsin, if deficiency is suspected
- Antinuclear antibody level for collagen vascular disease, such as scleroderma
- Coagulations studies to evaluate hypercoagulability states (eg, serum levels of proteins S and C, antithrombin III, factor V Leyden, anticardiolipin antibodies, homocysteine)

Arterial Blood Gas Analysis

Arterial blood gas measurements may provide important information about the level of oxygenation and type of acid-base disorder.

Chest Radiography

- In patients with chronic cor pulmonale, the chest radiography may show enlargement of the central pulmonary arteries with oligemic peripheral lung fields.
- Pulmonary hypertension should be suspected when the right descending pulmonary artery is larger than 16 mm in diameter and the left pulmonary artery is larger than 18 mm in diameter.
- Right ventricular enlargement leads to an increase of the transverse diameter of the heart shadow to the right on the posteroanterior view and filling of the retrosternal air space on the lateral view.
- These findings have reduced sensitivity in the presence of kyphoscoliosis or hyperinflated lungs.



Pulmonary artery hypertension Chest radiograph in PA view showing enlarged pulmonary arteries (arrows) due to pulmonary hypertension induced by anomalous pulmonary venous drainage. Courtesy of Sven Paulin, MD, Beth Israel Hospital, Boston.

Electrocardiography

Electrocardiographic (ECG) abnormalities in cor pulmonale reflect the presence of right ventricular hypertrophy (RVH), RV strain, or underlying pulmonary disease. Such ECG changes may include the following:

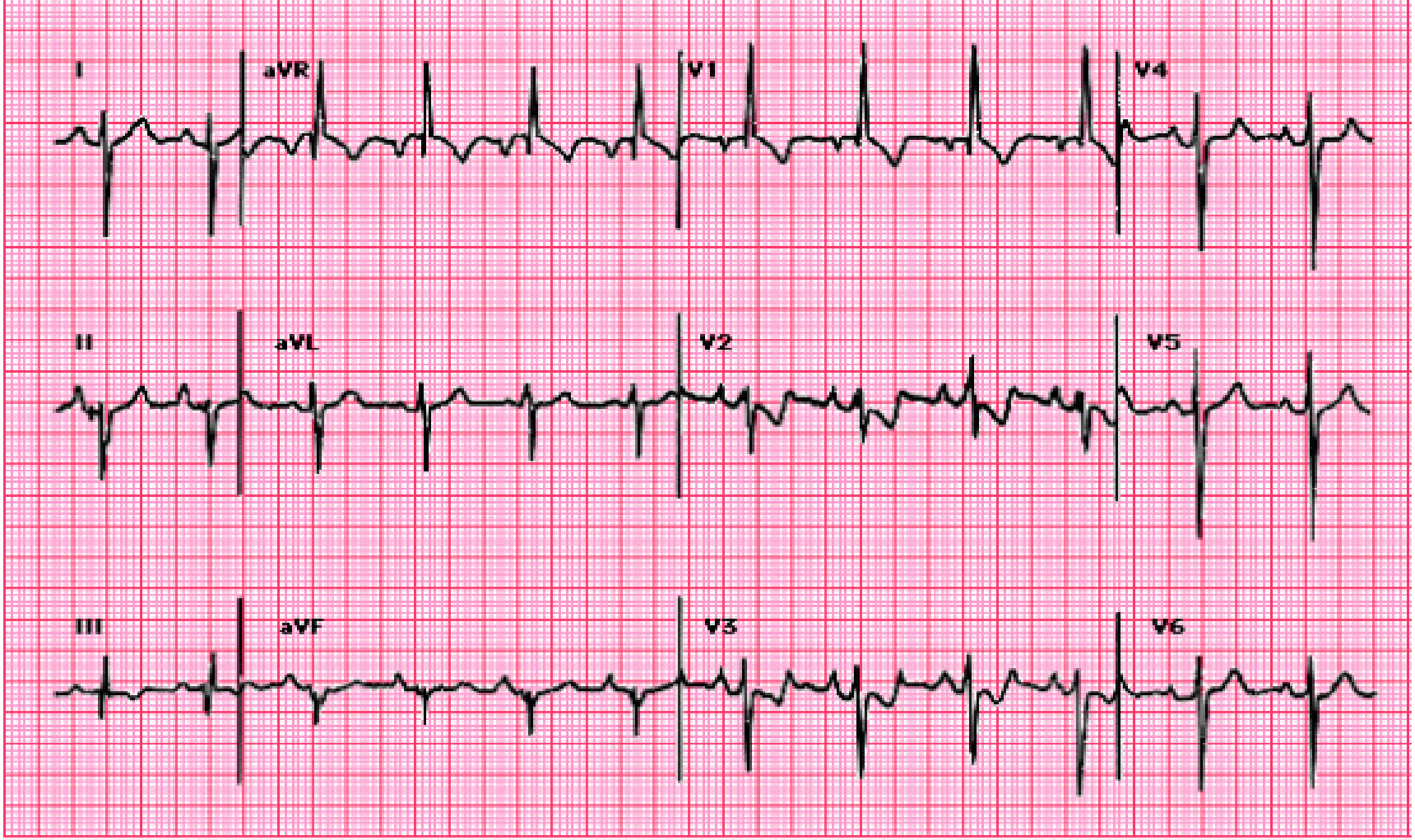
- Right axis deviation
- R/S amplitude ratio in V1 greater than 1 (an increase in anteriorly directed forces may be a sign of posterior infarction)
- R/S amplitude ratio in V6 less than 1
- P-pulmonale pattern (an increase in P wave amplitude in leads 2, 3, and aVF)
- S_1 Q_3 T_3 pattern and incomplete (or complete) right bundle branch block, especially if pulmonary embolism is the underlying etiology
- Low-voltage QRS because of underlying COPD with hyperinflation

Electrocardiography

Severe RVH may reflect as Q waves in the precordial leads that may be mistakenly interpreted as an anterior myocardial infarction (however, as electrical activity of the RV is significantly less than the left ventricle [LV], small changes in RV forces may be lost in the ECG).

Additionally, many rhythm disturbances may be present in chronic cor pulmonale; these range from isolated premature atrial depolarizations to various supraventricular tachycardias, including paroxysmal atrial tachycardia, multifocal atrial tachycardia, atrial fibrillation, atrial flutter, and junctional tachycardia.

These dysrhythmias may be triggered by processes secondary to the underlying disease, (eg, anxiety, hypoxemia, acid-base imbalance, electrolyte disturbances, excessive use of bronchodilators, heightened sympathetic activity). Life-threatening ventricular tachyarrhythmias are less common.



Right ventricular hypertrophy Right ventricular hypertrophy due, in this case, to primary pulmonary hypertension. The characteristic features include marked right axis deviation (+210° which is equal to −150°), tall R wave in V1 (as part of a qR complex), delayed precordial transition zone with prominent S waves in leads V5 and V6, inverted T waves and ST depression in V1 to V3 consistent with right ventricular "strain", and peaked P waves in lead II consistent with concomitant right atrial enlargement. Courtesy of Ary Goldberger, MD.

2-D and Doppler Echocardiography

Two-dimensional (2-D) echocardiography usually demonstrates signs of chronic right ventricular (RV) pressure overload.

As this overload progresses, increased thickness of the RV wall with paradoxical motion of the interventricular septum during systole occurs.

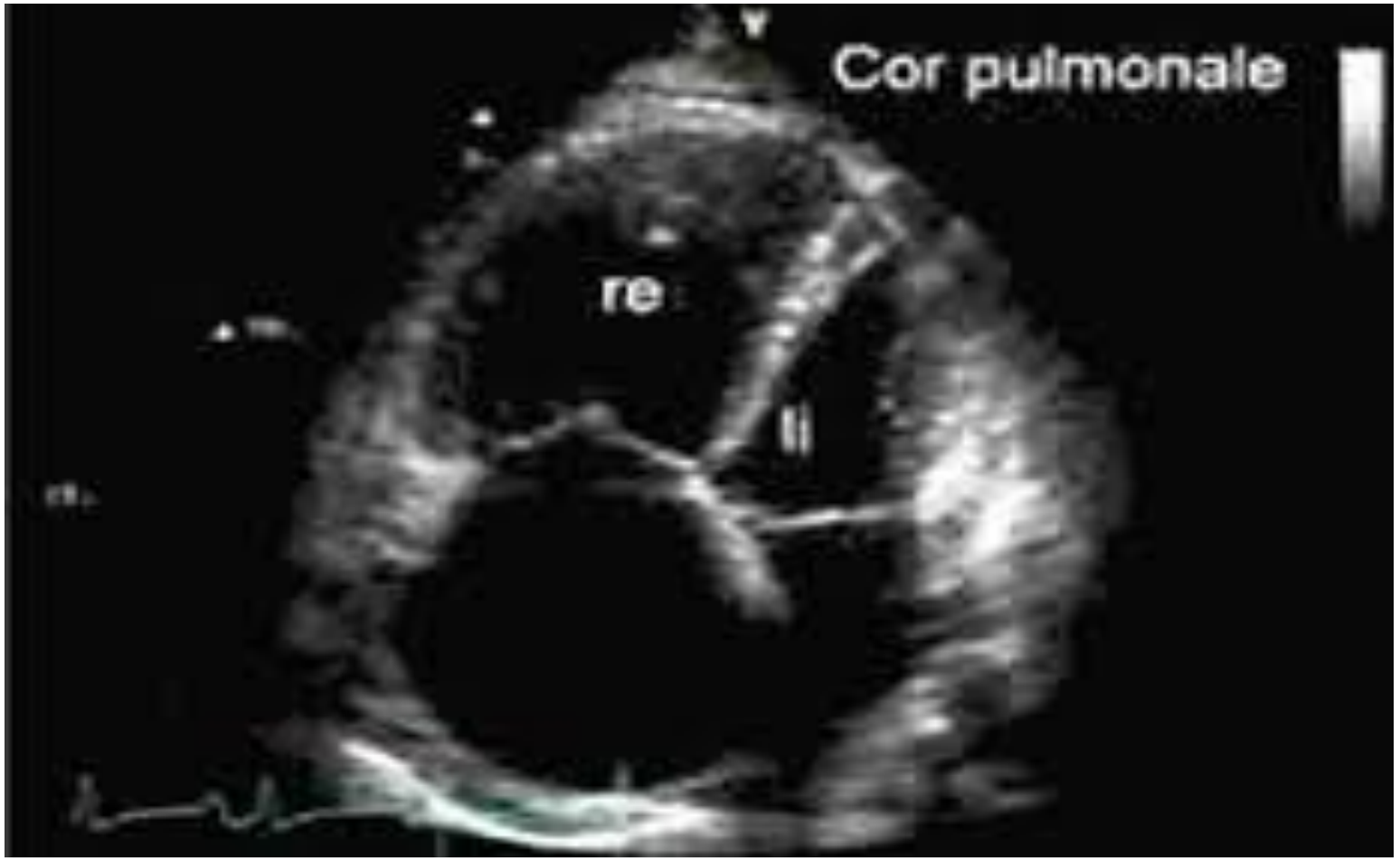
At an advanced stage, RV dilatation occurs, and the septum shows abnormal diastolic flattening.

In extreme cases, the septum may actually bulge into the left ventricular (LV) cavity during diastole, resulting in decreased LV diastolic volume and reduction of LV output.

2-D and Doppler Echocardiography

- Doppler echocardiography is used to estimate pulmonary arterial pressure, taking advantage of the functional tricuspid insufficiency that is usually present in pulmonary hypertension.
- This imaging modality is considered the most reliable noninvasive technique to estimate pulmonary artery pressure.
- However, the efficacy of Doppler echocardiography may be limited by the ability to identify an adequate tricuspid regurgitant jet, which may be further enhanced by using saline contrast.

Echocardiography



Magnetic Resonance Imaging

Magnetic resonance imaging of the heart is another modality that can provide valuable information about right ventricular mass, septal flattening, and ventricular function

Differentials

When diagnosing cor pulmonale, it is important to consider the possibility of thromboembolic disease and primary pulmonary hypertension as possible etiologies.

In addition, also assess for the following conditions:

- Atrial myxoma
- Blood disorders that are associated with increased blood viscosity
- Congestive (biventricular) heart failure
- Constrictive pericarditis
- High-output heart failure
- Infiltrative cardiomyopathies
- Primary pulmonic stenosis
- Right heart failure due to right ventricular infarction
- Right-sided heart failure due to congenital heart diseases
- Ventricular septal defect

Overview of Cor Pulmonale Management

Medical therapy for chronic cor pulmonale is generally focused on treatment of the underlying pulmonary disease and improving oxygenation and right ventricular (RV) function by increasing RV contractility and decreasing pulmonary vasoconstriction.

However, the approach might be different to some degree in an acute setting, with priority given to stabilizing the patient.

Overview of Cor Pulmonale Management

Cardiopulmonary support for patients experiencing acute cor pulmonale with resultant acute RV failure includes fluid loading and vasoconstrictor (eg, epinephrine) administration to maintain adequate blood pressure.

Of course, the primary problem should be corrected, if possible. For example, for massive pulmonary embolism, consider administration of anticoagulation, thrombolytic agents or surgical embolectomy, especially if circulatory collapse is impending; consider bronchodilation and infection treatment in patients with chronic obstructive pulmonary disease (COPD); and consider steroid and immunosuppressive agents in infiltrative and fibrotic lung diseases.

Patient education

Patient education regarding the importance of adherence to medical therapy is vital, because appropriate treatment of both hypoxia and underlying medical illness can improve mortality and morbidity.

Oxygen Therapy

Oxygen therapy is of great importance in patients with underlying chronic obstructive pulmonary disease (COPD), particularly when administered on a continuous basis. With cor pulmonale, the partial pressure of oxygen (PaO_2) is likely to be below 55 mm Hg and decreases further with exercise and during sleep.

Pharmacotherapy
Diuretic agents

- Diuretics are used in the management of chronic cor pulmonale, particularly when the RV filling volume is markedly elevated and in the management of associated peripheral edema.
- These agents may result in improvement of the function of both the right and left ventricles; however, diuretics may produce hemodynamic adverse effects if they are not used cautiously.
- Excessive volume depletion can lead to a decline in cardiac output.

Diuretic agents

Another potential complication of diuresis is the production of a hypokalemic metabolic alkalosis, which diminishes the effectiveness of carbon dioxide stimulation on the respiratory centers and lessens ventilatory drive.

The adverse electrolyte and acid-base effect of diuretic use can also lead to cardiac arrhythmia, which can diminish cardiac output.

Therefore, diuresis, while recommended in the management of chronic cor pulmonale, needs to be used with great caution.

Vasodilator drugs

Vasodilators have been advocated in the long-term management of chronic cor pulmonale with modest results. Calcium channel blockers, particularly oral sustained-release nifedipine and diltiazem, can lower pulmonary pressures, although these agents appear more effective in primary rather than secondary pulmonary hypertension.

Vasodilator drugs

Other classes of vasodilators, such as beta agonists, nitrates, and angiotensin-converting enzyme (ACE) inhibitors have been tried but, in general, vasodilators have failed to show sustained benefit in patients with COPD, and they are not routinely used.

A trial of vasodilator therapy may be considered only in patients with COPD with disproportionately high pulmonary blood pressure.

Beta-selective agonist drugs

Beta-selective agonists have an additional advantage of bronchodilator and mucociliary clearance effect.

The FDA approved epoprostenol, treprostinil, bosentan, and iloprost for the treatment of PPH. Epoprostenol, treprostinil, and iloprost are prostacyclin (PGI2) analogues and have potent vasodilatory properties. Epoprostenol and treprostinil are administered intravenously (IV) and iloprost is an inhaler. Bosentan is a mixed endothelin-A and endothelin-B receptor antagonist indicated for PAH, including PPH. In clinical trials, bosentan improved exercise capacity, decreased rate of clinical deterioration, and improved hemodynamics.

There are not enough data available yet regarding the efficacy of these drugs in patients with secondary pulmonary hypertension, such as in patients with COPD.

Cardiac glycoside agents

*The use of cardiac glycosides, such as digitalis, in patients with cor pulmonale has been controversial, and the beneficial effect of these drugs is not as obvious as in the setting of left heart failure. Nevertheless, studies have confirmed a modest effect of digitalis on the failing right ventricle in patients with chronic cor pulmonale.

*This drug must be used cautiously, however, and should not be used during the acute phases of respiratory insufficiency when large fluctuations in levels of hypoxia and acidosis may occur. Patients with hypoxemia or acidosis are at increased risk of developing arrhythmias due to digitalis through different mechanisms, including sympathoadrenal stimulation.

Theophylline

In addition to bronchodilatory effects, theophylline has been reported to reduce pulmonary vascular resistance and pulmonary arterial pressures acutely in patients with chronic cor pulmonale secondary to COPD.

Theophylline has a weak inotropic effect and thus may improve right and left ventricular ejection. Low doses of theophylline have also been suggested to have anti-inflammatory effects that help to control underlying lung diseases such as COPD.

As a result, considering the use of theophylline as adjunctive therapy in the management of chronic or decompensated cor pulmonale is reasonable in patients with underlying COPD.

Warfarin

Anticoagulation with warfarin is recommended in patients at high risk for thromboembolism.

The beneficial role of anticoagulation in improving the symptoms and mortality in patients with primary PAH has been demonstrated in several studies.

The evidence of benefit, however, has not been established in patients with secondary PAH. Therefore, anticoagulation therapy may be used in patients with cor pulmonale secondary to thromboembolic phenomena and with underlying primary PAH

Outpatient Monitoring

Patients with cor pulmonale generally require close attention in the outpatient setting. It is appropriate to regularly assess the patient's oxygen needs and pulmonary function. Consider a formal program of pulmonary rehabilitation, as many patients benefit from this therapy.

Prognosis of Cor Pulmonale

*The prognosis of cor pulmonale is variable depending upon the underlying pathology. Development of cor pulmonale as a result of a primary pulmonary disease usually heralds a poorer prognosis.

*For example, patients with chronic obstructive pulmonary disease (COPD) who develop cor pulmonale have a 30% chance of surviving 5 years.

*However, whether cor pulmonale carries an independent prognostic value or is simply reflecting the severity of underlying COPD or other pulmonary disease is not clear.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