Pulmonary hypertension

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PULMONARY HYPERTENSION (by Coiled) Draft 7.0

What you should know and say about PULMONARY HYPERTENSION.

Pulmonary system is low-pressure system. The mean arterial pressure in pulmonary artery (PAPm) is normally 11 – 17 mmHg; maximal limit of normal is 20 mmHg.

Definition: Pulmonary hypertension (PH) is when the PAPm at rest equals or raises over 25 mmHg.

(Other definitions, as that PH is when during exercise the PAPm temporarily increases over 30 mmHg, are not valid, because in some cases this happens in totally healthy people.)

Causes of PH:

There are new guidelines, which divide causes of PH into 7 CLINICAL groups (Table 4). But from the PATHOPHYSIOLOGICAL point of view, we want you to divide the causes in very similar manner as you do it with systemic hypertension; that there are primary and secondary causes. This sort of division is much more useful in understanding pathophysiological mechanisms behind it.

PATHOPHYSIOLOGICAL DIVISION: 1) Primary pulmonary hypertension (very rare): Under primary causes, you can mention idiopathic pulmonary arterial hypertension (IPAH) where cause is still not definitely known or heritable arterial pulmonary hypertension (HPAH) where the mutations are known. In both cases the problem is mainly in the wall of the distal arteries (< 500 um in diameter) where hypertrophy of media, intimal proliferation and fibrotic changes are seen. Inflammatory infiltrations and thrombotic changes are present as well. Pulmonary veins are unaffected. So to say it simple, the cause is primarily in the wall of the pulmonary arteries, they get thicker, more resistant and that is why the PAPm increases. Both of these examples belong in the CLINICAL DIVISION into the GROUP 1, the pulmonary ARTERIAL hypertension (PAH) GROUP (see below). Also these two examples belong to pre-capillary pulmonary hypertensions (see below)

2) Secondary pulmonary hypertension (common): As the term “secondary” tells us, in this case the primary cause is somewhere else then in the wall of the pulmonary arteries. And this is what you have to understand, because this is what the pathophysiologists will ask for: Secondary causes: a) PH due to left heart disease: Due to systolic or diastolic left ventricular dysfunction or due to valvular diseases. This type belongs to the post-capillary pulmonary hypertension (explained later) and thus pulmonary edema develops. This cause of PH is very common, e.g. 60% of all cases of severe left ventricular systolic dysfunction have PH. In this case the pulmonary veins are thickened and enlarged, capillaries are dilated, interstitial edema and blood in alveoli is present. Also lymphatic system is enlarged. Hypertrophy of tunica media of the distal pulmonary arteries can be present as well. The signs stem from the left heart failure: enlargement of the left atrium, pleural effusion, LUNG EDEMA and cardial asthma (asthma cardiale). In CLINICAL DIVISION this cause belongs to the GROUP 2.

Asthma cardiale: typical for failing left heart. It is paroxysmal night dyspnea cause by accumulation of transudate in the lungs (lung edema). This is due to horizontalization during sleep and thus increased blood returns from veins into the right heart and thus pulmonary circulation. Typically patient wakes up after several hours of sleep with dyspnea, wheezing and caught; verticalization helps him in breathing (orthopnea), because the blood will stay in veins and thus blood return is reduced. This is also why patients with left heart failure like to sleep with as many pillows as possible to simulate verticalization. The signs are pretty similar to bronchial asthma where the cause is totally different and that is inflammatory process causing narrowing of the lower airways. It is important to distinguish asthma cardiale from bronchial one, because the drugs for bronchial asthma can worsen the course of cardial asthma.

b) PH due to lung diseases and/or hypoxia: The mechanisms behind this are hypoxic vasoconstriction, loss of capillaries, inflammation etc. Thus diseases of lungs and also reflexes behind V/R ratio belong here. COPD, interstitial lung disease, sleep apnea syndromes, chronic stays in high altitudes. These all belong to pre-capillary causes of pulmonary hypertension, thus NO LUNG EDEMA is present. Hypertrophy of media and intimal proliferation is typically seen in distal pulmonary arteries. This cause is very common and e.g. in cases of interstitial lung diseases the PH develops in 39% of cases. Typically cor pulmonale develops. This cause is classified in the CLINICAL DIVISION as GROUP 3.

c) PH due to chronic pulmonary thromboembolism: Pathophysiology: Remodeling of pulmonary arteries due to major vessel thromboembolism. The thrombi are getting organized and are attached straight to the media of the pulmonary arteries replacing the intima. This results in partial stenosis or total occlusion of pulmonary arteries. Also collaterals from SYSTEMIC circulation sometimes grow to reperfuse the regions behind the total occlusion from the pulmonary arterial side. That is also why lung infarction is less common, because rather both perfusion systems (pulmonary and systemic) have to be occluded to get lung infarction. In 0,5 – 2% of acute pulmonary embolism PH later develops. Also typically cor pulmonale develops. Again NO LUNG EDEMA is present, because this cause is pre-capillary. Pulmonary embolism is classified in the CLINICAL DIVISION AS GROUP 4.

Cor pulmonale (chronicum): It is a hypertrophy of the right ventricle due to pre-capillary pulmonary hypertension (explained below) caused by lung disease (COPD, interstitial lung diseases etc.) or successive pulmonary embolism. CAVE: Hypertrophy of the right ventricle caused by post-capillary hypertension or due to left-to-right intracardial shunts is NOT considered as cor pulmonale. The cause of pre-capillary hypertension must by due to lung pathology or due to embolism. Cor pulmonale chronicum is rather isolated hypertrophy of the right heart.

Cor pulmonale (acutum): Acute massive pulmonary embolization causes immediate dilation of right ventricle and immediate right heart failure. Thus it is a very acute cause of pre-capillary PH.

d) PH due to systemic to pulmonary shunts (LEFT to RIGHT shunts) Due to congenital heart defects there is a opening between atria or ventricles. This causes systemic-to-pulmonary shunts. This slowly progresses and the pulmonary pressure increases. We call this sometimes also hyperkinetic pulmonary hypertension. There are rather NO LUNG EDEMAS present in this case because the cause is rather pre-capillary. The pulmonary pressure can increase so high that it goes over the systemic pressure and thus the shunting reverses to pulmonary-to-systemic (righ-to-left) shunting. When this reverse happens (Eisenmenger’s syndrome) the central cyanosis and hypoxemia develops. This cause is classified in CLINICAL DIVISION under the GROUP 1 = PAH.

Pulmonary Capillary Wedge Pressure (PCWP) = Pulmonary Artery Wedge Pressure (PAWP) = Pulmonary Wedge Pressure (PWP): Is measured by Swan-Ganz catheter. The idea is that the pressure behind the wedged balloon of the catheter placed at the farthest end of the arterial pulmonary tree equals the pressures in the left atrium. Normally this pressure is below 15 mmHg, if it is over 15 mmHg, we think of left heart failure or mitral valve disease. Thus by measuring the PCWP, we can divide the causes of pulmonary hypertension into two groups: pre-capillary and post-capillary pulmonary hypertension.

Pre-capillary pulmonary hypertension: The PCWP is low and thus the causes of PH can be: lung diseases (COPD, interstitial lung disease, hypoxic vasoconstriction (high altitudes or sleep apnea), pulmonary embolism, left-to-right shunting. Because the cause is pre-capillary, there is NO LUNG EDEMA, cor pulmonale and failure of the RIGHT heart with the signs typical for it are the clinical hallmarks of this type of PH.

Post-capillary pulmonary hypertension: The PCWP is over 15 mmHg and thus the cause is left heart failure or mitral valve diseases. Typical signs are LUNG EDEMA, asthma cardiale and later, when the right heart will start to fail ALSO, signs connected with right heart failure will arise.

GENERAL SIGNS/SYMPTOMS OF PH:

The signs/symptoms of PH are non-specific and are mostly related to progression of RIGHT ventricular dysfunction (this accounts for all the pre-capillary causes; in post-capillary causes, naturally also signs connected with LEFT ventricular dysfunction, e.g. lung edema, asthma cardiale etc., will occur). In the initial stage of PH, there are no obvious signs/symptoms at rest, only EXERCISE reveals dyspnea, tiredness, weakness, syncope and angina (pain could be explained by increased demands on the hypertrophic right heart and thus myocardial ischemia, or in rare cases myocardial ischemia due to external compression of the left coronary artery by dilated pulmonary artery (check below). Less commonly dry cough and nausea and vomiting during exercise can be seen.

Abdominal distension and peripheral edema (ankle edema) are signs of progression where the right ventricle already fails.

Only in some patients, hemoptysis due to rupture of hypertrophied bronchial artery can occur. Also external compression by dilated pulmonary arteries can cause compression of nerves (compression of left n. laryngeus recurrens causes hoarseness) or coronary arteries (compression of main left coronary artery causes angina). Severe dilation of pulmonary artery can end with rupture and heart tamponade.

On auscultation a pan-systolic murmur due to tricuspid regurgitation and diastolic murmur due to regurgitation through pulmonary valves are present.

Jugular vein distention, hepatomegaly, ascites, peripheral edema, cold extremities are typical for worsening of the disease.

Note a side: Atherosclerosis in pulmonary system: Although the pressure is lower, atherosclerosis occurs in pulmonary arteries as well, but NOT VEINS!

CAVE: DO NOT LEARN CLINICAL CLASSIFICATION OF PH – only if you would be bored before the exam.)

CLINICAL DIVISION:

PH is divided into 7 clinical GROUPS:

GROUP 1 – Pulmonary Arterial Hypertension = PAH (very rare) GROUP 1’ – Pulmonary Veno-Occlusive disease and/or capillary hemangiomatosis = PVOD (very rare) GROUP 1’’ - Persistent Pulmonary Hypertension of the Newborn (very rare) GROUP 2 – Pulmonary Hypertension due to Left Heart Failure (common) GROUP 3 – Pulmonary Hypertension due to Lung Disease or Hypoxia (common) GROUP 4 – Pulmonary Hypertension due to Chronic Thromboemboly (common) GROUP 5 – Pulmonary Hypertension due to unclear or multifactorial causes (due to heterogenicity of the group the prevalence is unknown)

Table 3 (see below) divides PH according to hemodynamic features (PWP=PCWP=PAWP, PVR, CO) into 2 groups, pre-capillary and post-capillary. In the pre-capillary group (NO LUNG EDEMA) GROUP 1, 3, 4 and 5 are placed. In post-capillary group (progression is marked by LUNG EDEMA) GROUP 2 and some representatives of GROUP 5 are placed.

CAVE: Realize hear that all the groups are PULMONARY HYPERTENSIONS, but the first group has adjective ARTERIAL in it (PAH). Also realize, that this is a different division then to primary and secondary, because the group 1 = PAH encompasses of not only unknown causes as IPAH, but also known causes as e.g. congenital heart diseases.

GROUPS IN MORE DETAIL:

GROUP 1 = PAH (very rare – 5 to 10 per 1 million of cases) To be listed under PAH the cause of PH has to be pre-capillary, but also cannot fit into the other GROUPS, i. e. GROUP 2 – 5. In other words, the PH cannot be caused be left heart failure, lung disease, thromboembolism or by rare diseases listed in GROUP 5 (check Table 5).

o Idiopathic PAH = IPAH (the rarest out of all PAH) o Heritable PAH o Associated PAH (about half of all PAH) – same clinical signs can be present as in IPAH. All congenital heart diseases with left-to-right shunts belong here (check Table 6): • Eisenmenger's syndrome • PAH associated with systemic-to-pulmonary shunts • PAH with small defects • PAH after corrective cardiac surgery Schistosomiasis – together with portal hypertension; it is rather generalized problem; possibly cause by local inflammation due to oocytes of the parasite.

Pathophysiology of PAH: not definitely known, vasoconstriction, proliferative and obstruction mechanisms are present, inflammation and thrombosis. There is a connection with endothelial dysfunction. Reduced production of NO and prostacyclin and overproduction of thromboxane A2 and endothelin 1. This all leads to increased arterial tone in pulmonary system.

GROUP 1’ (actually it belongs under PAH, but not purely) = PVOD = Pulmonary veno-occlusive disease is similar to IPAH, but the problem is POSTCAPILLARY (exception) in small septal veins and pre-septal venules. There are occlusive lesions. Thus for this type of PAH, LUNG EDEMA IS PRESENT (exception). Occult alveolar hemorrhage and lymphatic dilation is present as well (this resembles left ventricular failing). Distal pulmonary arteries are then affected as well with medial hypertrophy and intimal fibrosis.

GROUP 1’’(actually it belongs under PAH, but not purely) - Persistent Pulmonary Hypertension of the Newborn (very rare)

GROUP 2 – left heart failure (check PH due to left heart disease in the pathophysiology section above)

GROUP 3 – lung diseases or hypoxia (check PH due to lung diseases and/or hypoxia in the pathophysiology section)

GROUP 4 – chronic thromboembolic pulmonary hypertension (check PH due to chronic pulmonary thromboembolism in the pathophysiology section)

GROUP 5 – disease with unclear pathophysiology o Hemolytic anemias (from PAH newly moved over here) – sickle cell anemia, spherocytosis, thalassemias – chronic hemolysis in connection with large consumption of NO. This causes lower cGMP levels and thus this vasodilator is not activated. o Sarcoidosis, histiocytosis.

Pulmonary hypertension is a chronic increase in mean capillary pressure in the pulmonary artery above 22 torr (mmHg). This happens due to increased resistance or flow in the pulmonary basin.

Division

- precapillary vs. postcapillary
- acute vs. chronic

Content

Physiology of the pulmonary canal [edit | edit source]

The pulmonary canal is a low-pressure system into which the heart pumps blood at a pressure of 25 torr from the right ventricle through the pulmonary artery. In diastole, the pressure drops to about 5 torr; therefore, the mean pressure in the lung is 15 torr. On the venous side of the river bed, the pressure is equal to the pressure in the left heart atrium. Since direct pressure measurement in the left atrium is difficult to implement for practical reasons, an approximation is used, the so-called wedging pressure (direct pressure measurement at the level of the last arteriole in which the catheter is "wedged"). Under physiological circumstances, the wedging pressure reaches about 5 torr. If there is an increase in pressure in any (arterial or venous) part of the riverbed, we speak of pulmonary hypertension . This condition tends to spread to the entire river basin. Unlike the systemic circulation, where hypoxia leads to vasodilation, the pulmonary vessels contract in response to the reduced partial pressure of O 2 , thereby increasing the resistance to blood flow in the given area, and this is subsequently redirected to the part with a higher p O 2 (hypoxic pulmonary vasoconstriction).

Precapillary pulmonary hypertension [edit | edit source]

Acute

- pulmonary embolism

Chronic

- developmental defects of circulation (defects with left-right shunt)
- obstructive and restrictive lung diseases (combination of changes in the mechanical properties of the lungs, destruction of the pulmonary bed, alveolar hypoxia → hypoxic pulmonary vasoconstriction, alveolar hypercapnia , increased blood viscosity − compensatory polyglobulia at chronically reduced p O2)
- morphological changes of pulmonary vessels
- compensatory formation in postcapillary pulmonary hypertension

Postcapillary pulmonary hypertension [edit | edit source]

- left heart failure
- venous congestion in the lungs (pulmonary edema)
- asthma cardiale: attacks of shortness of breath (especially at night) in patients with heart failure

Consequences of pulmonary hypertension on the systemic circulation [edit | edit source]

Cor pulmonale : hypertrophy and dilatation of the right heart caused by chronic arterial hypertension in the pulmonary artery as a result of lung disease (cor pulmonale chronicum). Cor pulmonale acutum : pulmonary embolism leads to acute failure of the right heart, which is unable to "push" blood through the obstruction.

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