

Pulmonary hypertension:

a guide for GPs

INTRODUCTION

Dyspnoea on exertion, impaired exercise tolerance, and fatigue are most often due to common cardiac and pulmonary diseases such as heart failure or COPD, but may be also due to pulmonary hypertension, a pathophysiological state of diverse aetiology that is frequently misdiagnosed or recognised late. Pulmonary hypertension has a poor prognosis; patients often take a long time to present and appropriate referral and treatment can be delayed.¹

DEFINITION OF PULMONARY HYPERTENSION

Pulmonary hypertension is an umbrella term which describes a pathophysiological state characterised by the elevation of pulmonary artery pressure (PAP). It is diagnosed when the mean PAP is ≥ 25 mmHg at rest.²

PRESENTATION AND EXAMINATION

The most important challenge is to think of the condition, as its signs and symptoms are non-specific. The presenting complaint in about 60% of cases is shortness of breath on exertion, and is nearly always present at diagnosis. Another common presentation is fatigue. Dyspnoea at rest or syncope usually occur late. Clinical examination in the early stage may be unremarkable or may reveal a loud pulmonary component of the second heart sound and a pan-systolic murmur. A raised jugular venous pressure and pedal oedema indicate right heart failure in the advanced stage.

CLASSIFICATION OF PULMONARY HYPERTENSION

Five groups of pulmonary hypertension are recognised,³ each reflecting the underlying aetiology. Group 1 comprises a rare pulmonary vascular disease called pulmonary arterial hypertension (PAH), which is characterised by progressive vascular remodelling. PAH can be

idiopathic, heritable, induced by drugs or toxins, or associated with conditions, such as connective tissue disease, congenital heart disease, portal hypertension, or HIV. Rare conditions such as pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis share some characteristics with the PAH group and are classified as group 1. Group 2 is associated with left ventricular dysfunction or valve disease. The past medical history is usually significant for myocardial infarction, severe arterial hypertension, atrial fibrillation, or rheumatic heart disease. Group 3 is related to lung disease or chronic hypoxia, for example, COPD, interstitial lung disease, or sleep apnoea. The chief aetiology of group 4 is recurrent pulmonary embolism (PE) and is therefore termed chronic thromboembolic pulmonary hypertension (CTEPH). Lastly, group 5 is associated with unclear or multifactorial mechanisms.

EPIDEMIOLOGY

PAH has a prevalence of 15–60 cases/million and an annual incidence of 7.6 cases/million. The average age of PAH patients at diagnosis is 53 ± 14 years⁴ and females outnumber males by almost 2:16. Special attention should be paid to patients with systemic sclerosis (SSc) since PAH is a feared and potentially fatal complication of this condition. Groups 2 and 3 are the commonest forms of pulmonary hypertension. Accordingly, a mild pulmonary hypertension is often found in left heart disease and may be diagnosed in ~50% of cases of chronic lung disease. CTEPH may be observed in 1–4% of patients following acute PE.

INVESTIGATIONS

The ECG may show right axis deviation and incomplete RBBB. A normal ECG, however, does not exclude pulmonary hypertension. The chest X-ray may show dilated pulmonary arteries (Figure 1) and an enlarged right

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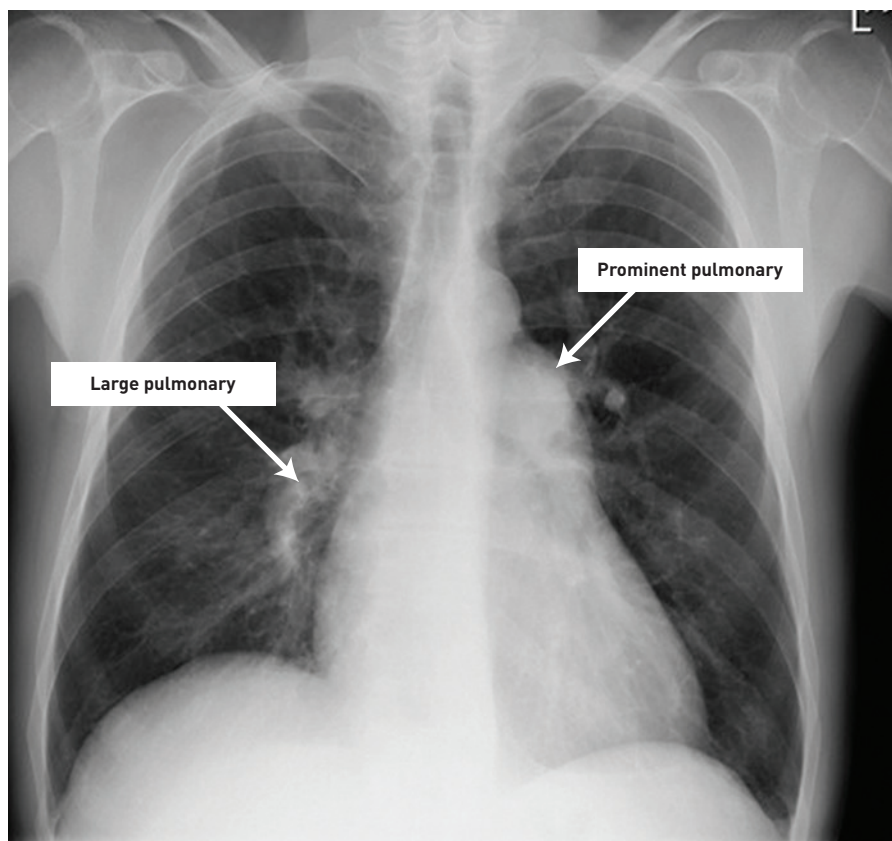


Figure 1. PA erect film demonstrating radiological features of pulmonary hypertension.

ventricle. Again, a normal chest X-ray does not exclude pulmonary hypertension. Further imaging such as CT can identify diseases of the lung parenchyma. V/Q scanning, CT pulmonary angiography, and eventually pulmonary angiography aid in the investigation of patients with CTEPH. Lung function testing is usually performed to demonstrate obstructive or restrictive defects in ventilation. A decreased diffusion capacity and mild obstruction in the distal airways is usually present. Blood tests help screen for associated conditions such as connective tissue disease or HIV. The most important serum markers for pulmonary hypertension are brain natriuretic peptide (BNP) and NT-proBNP; strongly elevated values may suggest right ventricular failure. The most important non-invasive diagnostic tool is echocardiography. Besides the evaluation of left cardiac causes of pulmonary hypertension, it permits the estimation of right ventricular and thus pulmonary arterial systolic pressure. Furthermore, indirect signs of pulmonary hypertension, such as dilatation and hypertrophy or impaired function of the right ventricle and atrium may be detected.

REFERRAL

Referral to one of the UK's specialist centres (Table 1) should normally be

made but if your patient's symptoms are worsening, referral should not be delayed. At a specialist centre, patients undergo right heart catheterisation (RHC) to provide a definitive diagnosis. During RHC a vasodilator test is performed, allowing the identification of 'responders', a small minority of PAH patients who may profit from therapy with high-dose calcium channel antagonists.

SPECIFIC AND SUPPORTIVE TREATMENT OF PULMONARY HYPERTENSION

Survival at 1, 3, and 5 years stands at 68, 48, and 34% respectively.⁵ Disease-specific therapy improves symptoms and prognosis (1, 3, and 5 year survival of PAH patients with modern medical treatment is 91, 74, 65% respectively⁵) but does not afford a cure.⁶ For group 1 PAH patients three groups of specific drugs are used in the expert centres: prostanoids; endothelin receptor antagonists; and phosphodiesterase-5 inhibitors. Although in severe cases an upfront combination therapy may be considered, generally a monotherapy is initiated first and eventually expanded to a sequential combination of drugs. Prostanoids appear to be the most effective drug treatment and are indicated in advanced disease. They may be administered intravenously, subcutaneously, or via inhalation. Side effects include systemic hypotension, flushing, headache, pain at the site of infusion, or catheter-associated infections.

Patients receiving endothelin receptor antagonists should undergo monthly liver function testing for rises in AST or ALT. Peripheral oedema is a common side effect of endothelin receptor antagonists.

Side effects of phosphodiesterase-5 inhibitors include epistaxis, headache, and heartburn. Patients on long-term nitrate therapy should not receive phosphodiesterase-5 inhibitors.

Besides specific therapy options, depending on the clinical picture, PAH patients may need supportive treatment with diuretics, antiarrhythmic treatment, and anticoagulation, as well as oxygen if clinically indicated. In end-stage disease, surgical options such as atrial septostomy and lung transplantation may be considered. Promising emerging therapies for PAH may include the tyrosine kinase inhibitor imatinib and the guanylate cyclase stimulator riociguat.

Patients from groups 2 and 3 generally should not be treated with specific PAH therapies. Here the goal is the treatment of the underlying cardiac or pulmonary

Table 1. Specialist centres for the diagnosis and management of pulmonary hypertension

Location	Hospital	Specialism (where applicable)	Contact details
London	Royal Free Hospital, Pond Street, NW3 2QG	Connective tissue disease	GP advice: 020 7794 0500 ext 38648; Pulmonary hypertension clinical fellow: 020 7794 0500, bleep 1404 Fax: 020 7443 5219 rfh.royalfreepah@nhs.net
London	Royal Brompton Hospital, Sydney Street, SW3 6NP	Chronic heart and lung disease	Tel: 020 7351 8362 Fax: 020 7351 8629 rbh-tr.nphs@nhs.net
London	Hammersmith Hospital, Du Carne Road, W12 0HS		Tel: 020 3313 2330 Fax: 020 3313 2331 nphs@imperial.nhs.uk
London	Great Ormond Street Hospital, Great Ormond Street, WC1N 3JH	Children	Tel: 020 7405 9200 Fax: 020 7829 8643
Cambridge	Papworth Hospital, Papworth Everard, Cambridgeshire, CB23 8RE	UK's only pulmonary endarterectomy service for chronic thromboembolic PH	Tel: 01480 830541 Fax: 01480 364267
Sheffield	Royal Hallamshire Hospital, Glossop Road, Sheffield, S10 2JF	Pulmonary arterial hypertension	Tel: 0114 271 2590 Fax: 0114 271 1718 spvdu@sth.nhs.uk
Newcastle	Freeman Hospital, Freeman Road, High Heaton, Newcastle upon Tyne, NE7 7DN		Tel: 0191 213 7742
Glasgow	Golden Jubilee National Hospital, Beardmore Street, Clydebank, West Dunbartonshire, G81 4HX		Tel: 0141 951 5497/5000 Fax: 0141 951 5442 SPVUnit@gjnh.scot.nhs.uk

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disease. Group 4 patients with CTEPH should be given warfarin and evaluated for pulmonary endarterectomy, which confers an outstanding prognosis (Table 1).

GENERAL MEASURES FOR THE GP TO CONSIDER

Patients with PAH or inoperable CTEPH must adapt to the uncertainty of living with a chronic, debilitating disease. Support groups are available,⁷ and patients should be encouraged to join these. Patients should be advised to take regular exercise at a pace which can be performed for at least 30 minutes without dyspnoea. More strenuous exercise increases PAP and should be avoided. Pregnancy is associated with a high mortality in PAH patients and should strongly be advised against. Some PAH drugs may decrease the effects of oral

contraceptives, necessitating combined methods. The oral contraceptive pill is not known to place women at an increased risk of developing PAH. Patients with pulmonary hypertension are at increased risk of chest infections, and should be offered the flu and pneumococcal vaccines. Anaemia will be less well tolerated and should be corrected.

Provenance

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