mechanisms remains to be fully elucidated, but its widespread distribution, numerous effects, and subtle interrelations with other physiological control systems, particularly in controlling oxygen balance, suggest that it may be a most important homoeostatic metabolite.

ANDREW H WATT
Clinical research officer

PHILIP A ROUTLEDGE
Senior lecturer

Department of Pharmacology and Therapeutics,
University of Wales College of Medicine,
Cardiff CF4 4XN

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Primary pulmonary hypertension

Pulmonary hypertension is usually secondary to cardiac or pulmonary disease, and only rarely is it "primary" or "unexplained." At sea level for a cardiac output of 5-6 litres systolic pulmonary arterial pressure is about 20 mm Hg and diastolic about 12 mm Hg. In pulmonary hypertension the mean arterial pressure is above 19-20 mm Hg. Although rare,[1] primary pulmonary hypertension is important because it affects young people and has a 10 year survival of only 25%.[2]

The diagnosis is often delayed[3] as the signs of raised pulmonary vascular resistance without a cardiac cause, respiratory insufficiency, or collagen vascular disease may be missed. The diagnosis must be considered in breathless patients, particularly when associated with syncope and angina.[2 4] Right heart failure develops late,[4] but a loud pulmonary second heart sound is often heard.[2 4] Signs of raised pulmonary vascular resistance on chest radiograph and electrocardiogram are found in 95% of cases.[2] Spirometric values are normal, but gas transfer for carbon monoxide may be low.[5] Doppler M mode echocardiography shows characteristic signs and allows an assessment of pulmonary artery pressure and exclusion of a left to right shunt.[6-8] Ventilation and perfusion lung scintigraphy can exclude proximal vessel thromboemboli.[9]

Right heart catheterisation confirms the diagnosis and provides prognostic information: the lower the cardiac output the worse the prognosis.[2 4] The most discriminating test is the mixed venous oxygen saturation: when it is less than 63% survival at five years is 17%, whereas when it is greater than 63% survival is as high as 55%.[2] "Spontaneous" recovery may occur in those with high cardiac output.[4 10]

Surgical endarterectomy can improve the haemodynamic measurements and symptoms in patients with longstanding proximal pulmonary artery obstruction from thromboembolism.[11 12] Diagnosis is with ventilation and perfusion lung scintigraphy and preoperative assessment requires pulmonary angiography.[9]

In patients without proximal vessel obstruction the haemodynamic disturbance is a result of a "restriction" of the peripheral pulmonary vasculature, in contrast to the "vasoconstriction" of hypoxia.[13] Idiopathic pulmonary hypertension is associated with a generalised loss in the precapillary non-muscular vessels,[13 14] whereas in patients with primary pulmonary hypertension and peripheral thrombosis muscular and non-muscular arteries are obstructed in a patchy distribution.[13] Adaptive dilatational lesions

and smooth muscle hypertrophy with intimal fibrosis are seen in vessels upstream from these restrictions.[15-17]

Treatment is aimed at reducing the consequences of the low cardiac output. By preventing secondary thromboembolism anticoagulants improve survival in both idiopathic and peripheral thrombotic forms.[2] By raising cardiac output, and therefore oxygen tissue delivery, vasodilators relieve the symptoms.[18] A trial of vasodilators during catheterisation identifies responders.[19] A titrated dose of intravenous prostacyclin is the most effective acute vasodilator[20] and because of its short half life[21] avoids the dangers of a sustained fall in systemic arterial pressure.[22] Successful vasodilatation is shown by a greater than 30% rise in cardiac output[23] without an increase in pulmonary artery pressure and a less than 20% fall in systemic arterial pressure.

Patients with clear ventilation and perfusion scans and a mixed venous oxygen saturation greater than 63% should be given anticoagulants and an oral vasodilator (hydralazine,[24] captopril,[25] or diltiazem[26]) if they have responded to prostacyclin at catheterisation. If the mixed venous oxygen saturation is less than 63% and prostacyclin was successful at catheterisation a long term infusion of prostacyclin, though expensive, can improve the quality of life.[18 27] As prostacyclin inhibits platelet aggregation[28] anticoagulants are theoretically not needed. The optimal long term dose of vasodilators can be calculated from monitoring systemic arterial pressure and by measuring maximum rate of oxygen consumption during exercise testing.[29] When the mixed venous oxygen saturation is less than 63% and there is no response to vasodilators at catheterisation heart-lung transplantation may be the treatment.[30] The 5-10% of patients with primary pulmonary hypertension and veno-occlusive disease can probably be managed according to the same system.

More effective treatments will come only when we learn more of the homoeostatic mechanisms governing the interface between the blood and endothelium. Acute experimental injury of pulmonary endothelium may lead to obliteration of the precapillary arteries.[31 32] Clinical conditions associated with thrombosis—for example, with lupus anticoagulant—may cause primary pulmonary hypertension.[33] This protein (an IgM or IgG) may act by interfering with prostacyclin formation.[34 35] Other inherited thrombotic disorders—for example, deficiencies of antithrombin III[36] or heparin cofactor II[37]—may account for some familial cases of primary pulmonary hypertension[38] and for some people developing the disease after taking aminorex fumarate[39] or fenfluramine.[40]

TIM HIGENBOTTAM

Consultant Physician and Director,
Regional Pulmonary Function Laboratory,
Papworth Hospital,
Cambridge CB3 8RE

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Long live health promotion

Health promotion is an intensely political issue. Twenty years ago people naively imagined that a whiff of advertising and a few leaflets would be enough to solve the smoking problem. Now most people—although the minister currently responsible for prevention would seem to be an exception—recognise that exhorting people to eat better, pull themselves together, "get on their bikes," or "just say no" is not enough. Information is certainly needed (and it must be carefully composed), but in addition those who want to improve the health of the people will have to do battle with the immensely powerful organisations that have a vested interest in, for example, keeping people smoking, drinking large quantities of alcohol, and eating unhealthy food. As Peter Taylor clearly described in *Smoke Ring: the Politics of Tobacco*[1] and as the television programme *Yes, Prime Minister*[2] has so humorously but so chillingly illustrated, those campaigners are also likely