atenolol 50 mg daily and nifedipine 40 mg daily. Detailed enquiry revealed that he had had several episodes of palpitations, anxiety and headaches while taking this treatment. On examination the blood pressure was 180/80 mmHg. During the second day of admission an episode of chest pain occurred with T-wave inversion on the ECG. The blood pressure was 220/120 mmHg and a labetalol infusion was started. Five minutes after the start of the infusion the blood pressure rose to 230/130 mmHg and the patient had a grand mal fit. A phaeochromocytoma was suspected, the labetalol was stopped and a phenoxybenzamine infusion started. The blood pressure became well controlled and no further fits occurred. The 24-hour urinary free noradrenaline level was 36 300 nmol/l (normal <880 nmol/l) and a CT scan revealed a 6-cm left adrenal mass which later showed uptake with radiolabelled meta-iodobenzyl- guanidine. After further treatment with phenoxybenzamine and propranolol, the mass was resected and confirmed histologically to be a phaeochromocytoma. Two years after surgery he remains normotensive and requires no medication.

Catecholamines act at α- and β-adrenergic receptors. Activation of α-adrenoreceptors mediates vasoconstriction, while activity at β_1-adrenoreceptors may cause cardiac palpitations and arrhythmias, but β_2-receptors also vasodilate arterioles, especially in skeletal muscle. This vasodilatation may protect the patient. If this 'protective' β_2-action is blocked, unopposed activity at α-adrenoreceptors (including vasoconstriction) may lead to a phaeochromocytoma crisis. Case 1 illustrates the catastrophic effects of prolonged unopposed α-adrenergic activity after propranolol. The drug was continued for four days before correct treatment was started, and the intense vasoconstriction appeared to lead to severe end-organ damage and eventually death. In case 2, intravenous labetalol, which has only weak α-blocking activity, exacerbated the hypertension and this probably induced the fit. There have been several reports of worsening of hypertension in phaeochromocytoma patients treated with labetalol,[3-5] and alternative drugs are available.[6] Furthermore, labetalol may interfere with the measurement of urinary catecholamines.[7]

Several cases of hypertensive crisis or pulmonary oedema have been reported in phaeochromocytoma patients treated with propranolol prior to α-blockade,[8-10] sometimes with a fatal outcome if the correct diagnosis is not made quickly.[11]

While β-blockers do play a role in the management of phaeochromocytomas, they should only be used after full α-adrenoceptor blockade. Phaeochromocytomas are rare, and propranolol is a widely used, cheap and effective drug for treating essential hypertension.[12] Nevertheless, if any patient deteriorates after starting a β-adrenergic blocker, the drug should be stopped and the patient investigated as a matter of urgency. Finally, if a phaeochromocytoma is diagnosed, a β-blocking drug should only be given after full α-adrenoreceptor blockade.

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AIDS and dilated cardiomyopathy

Sir,

Acquired immunodeficiency syndrome (AIDS) is increasingly recognised as an important aetiological factor in dilated cardiomyopathy.[1] Echocardiographic features consistent with dilated cardiomyopathy have been reported in 30 to 40% of patients with AIDS. Moreover, with the increasing success in treating opportunistic infections many patients will now survive to develop human immune-deficiency virus (HIV) cardiomyopathy and succumb to congestive heart failure. The pathogenesis of HIV cardiomyopathy, and particularly its relation to myocarditis, has not been established, and there is only a loose correlation between myocarditis and the development of HIV-dilated cardiomyopathy. I suggest an important mechanism which may be, at least in part, responsible.

Several studies have shown increased serum levels of tumour necrosis factor-α (TNF) in AIDS patients, and that this increase is positively correlated with the severity of the disease. This cytokine has recently been shown to play an important role in the pathogenesis of AIDS and of many disorders associated with the latter.[2] Elevated levels of serum TNF may induce significant myocardial depression, directly by depressing myocyte shortening, and indirectly by the release of secondary mediators, such as nitric oxide (NO) and oxygen-free radicals.[3]

NO is released in response to TNF which induces the expression and synthesis of NO synthase in endothelial cells and other cells including macrophages and smooth muscle cells. It has recently been demonstrated that NO is also produced within the myocytes themselves. Two forms of NO synthase have been identified. The first is the constitutive calcium-dependent NO synthase (CNOS), which synthesizes the major component of endothelium-derived relaxing factor. The second is the inducible, calcium-independent enzyme (INOS), which is induced by endotoxin or cytokines, particularly TNF, and predominates in vascular smooth muscle. Synthesis of NO by this pathway in the vessel wall is involved in the vasodilatation and probably, the tissue damage of endotoxic shock.[3,4] It has been demonstrated that normal rat myocardium contains CNOS and expresses INOS during endotoxaemia, and that isolated rat myocytes express INOS only after stimulation with cytokines.[4] Furthermore, it has been shown recently that heart tissue from patients with dilated cardiomyopathy showed significant INOS activity, while CNOS activity was 10–11-fold lower or not detectable.[4] Several recent studies have shown that NO may induce myocardial depression, and that the negative inotropic effects of TNF on the heart may partly be mediated by NO.[3] Furthermore, it has also been demonstrated that inhibitors of NO and NO synthase can decrease significantly the depressed myocardial contractility induced both by NO itself and by TNF.[3]

TNF promotes local and systemic release of oxygen-free radicals, particularly from activated neutrophils. Several studies have demonstrated that oxygen-free radicals depress cardiac function and myocardial contractility, and that scavengers of oxygen-free radicals may protect the heart from their deleterious effects.[3]

The above data strongly suggest an important role for TNF in the development of myocardial dysfunction and dilated cardiomyopathy in AIDS patients. Indeed, it has been shown that chronic treatment with TNF may cause a permanent decrease in myocardial contractility and ultimately dilated cardiomyopathy.[5] Antagonists of TNF and of NO, and scavengers of oxygen-free radicals may therefore have important therapeutic benefits in preventing the development of HIV cardiomyopathy.

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Gross cholestatic dysfunction in giant cell arteritis

Sir,

Mild to moderate hepatic dysfunction is a common observation during the acute phase of temporal arteritis and polymyalgia rheumatica but gross cholestatic dysfunction is unusual.

A 75-year-old woman was admitted with sudden bilateral blindness over a period of five days. Over the previous few weeks she