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Response

We agree entirely that HIV infection is an important secondary cause of immune thrombocytopenic purpura, and list it as a cause in Table 1 and refer to HIV testing as a baseline investigation under 'Clinical evaluation of the cytopenic patient'. Thank you for highlighting the NICE guidance further. ■

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Established endocrine practice

Editor – Pre-operative preparation with alpha receptor antagonists before phaeochromocytoma resection is established endocrine practice.¹ We therefore read with great interest the report by Faloon *et al*² detailing circumstances which precluded this. We congratulate them on the successful outcome of the case and for highlighting the ongoing absence of parenteral preparations of alpha blockers in the UK. This has significant implications for the management of a phaeochromocytoma crisis given the uniformity with which these agents are recommended in society guidelines.^{1,3}

The established mantra of alpha followed by beta blockade, whilst correct and widely held, is not achievable in the situation described. A range of alternative intravenous anti-hypertensive agents have been used in the management of phaeochromocytoma. Indeed, some units do not use alpha blockers even when available, but utilise the dihydropyridine calcium-channel blocker nicardipine⁴ which acts by preventing catecholamine-stimulated calcium influx into arterial smooth muscle. The combined α_1 and β antagonist labetalol has also been used⁵ and has the advantages of familiarity with acute care physicians and accessibility in the emergency department. However, like all beta blockers, concerns exist regarding the risk of paradoxical hypertension in spite of its α_1 activity and adverse events have been reported.⁶ Other drugs that also have a role are magnesium,⁷ sodium nitroprusside and glyceryl trinitrate.

Use of these agents may be limited by profound hypotension as they were in this case and this serves as an important reminder that patients with phaeochromocytoma are severely volume contracted due to alpha-mediated vasoconstriction. Volume expansion is therefore a key component to acute management and significant hypotension may follow successful tumour (and therefore catecholamine) removal.

We would like to remind readers that alternative parenteral treatment agents for this rare but life-threatening clinical situation are available in the UK. ■

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Mechanical circulatory support such as extracorporeal membrane oxygenation is indicated in phaeochromocytoma crisis with sustained hypotension

Editor – Faloon and colleagues describe a 26-year-old man who developed phaeochromocytoma crisis following blunt abdominal trauma and attempted embolisation.¹ The patient had a phase of sustained hypotension giving rise to multi-organ dysfunction. Ischaemia of the colon was treated with emergency laparotomy without alpha blockade. Emergency adrenalectomy was performed intraoperatively for a ruptured phaeochromocytoma and retroperitoneal haemorrhage. It is to the credit of the team that this patient survived the episode despite the high mortality associated with this condition.²

We suggest that there are two additional learning points from this case.

Firstly, phaeochromocytoma crisis with sustained hypotension is notoriously difficult to manage and there is normally a significant component of myocardial dysfunction due to catecholamine toxicity. An effective treatment (along with aggressive volume replacement) is some form of mechanical circulatory support such as cardiopulmonary bypass or veno-arterial extracorporeal membrane oxygenation.^{3,4} The use of this type of circulatory support is strongly associated with improved survival in hypotensive phaeochromocytoma crisis.² If required, urgent surgery can be performed whilst on mechanical support.⁵

Secondly, the authors correctly point out that intravenous alpha blockade (phentolamine and phenoxybenzamine) is currently difficult to access in UK. In preference to using no alpha blocking agents, clinicians who find themselves in these circumstances should consider using intravenous magnesium for medical stabilisation.^{2,6} There is an evidence base for intravenous magnesium^{7,8} as an alternative to alpha blockade and importantly the drug is familiar to many intensivists due to its critical role in eclampsia treatment. ■

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Response

We thank O'Toole, Brown and Drake for their informative response to our article.¹ We agree that it is important to highlight alternative parenteral regimens to alpha-blockers. In addition, volume expansion and careful management of fluid status is central to

successful management as in our case. We also thank Whitelaw, Prague and Mustafa for their insights into the use of mechanical circulatory support as rescue therapy. We acknowledge the association with myocardial dysfunction associated with catecholamine toxicity. In collaboration with colleagues in Oxford and London, we previously reported on the high prevalence of cardiac involvement in newly diagnosed phaeochromocytomas along with persistence of some parameters on cardiac magnetic resonance following successful surgery. We would advocate for the use of multi-centre registries for such rare conditions to improve treatment outcomes. ■

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CYP24A1 mutations and hypervitaminosis D

Editor – We read with interest the case report entitled 'Risks of the 'Sunshine pill' – a case of hypervitaminosis D'.¹ We wish to congratulate the authors on reporting this remarkable case, and hoped to make some additional contributions.

While noting that hypervitaminosis D is rare and can occur with excessively high doses of supplementation, they omit from their differential diagnoses the possibility of CYP24A1 mutations, a well-described alternate cause of the phenotype described in their patient. Loss of function mutations in CYP24A1 result in reduced action of 1,25-hydroxyvitamin-D₃-24-hydroxylase, which usually inactivates active vitamin D. As well as a neonatal presentation, patients with CYP24A1 mutations can present with adult-onset hypercalcaemia, together with low parathyroid hormone levels and high urinary calcium.^{2,3} If this genetic condition is present, even modest vitamin D supplementation can lead to significant hypercalcaemia. Indeed, high levels of active vitamin D metabolites are found in some CYP24A1-deficient individuals even without supplementation.³

We acknowledge that in the case described by Ellis *et al* supplemental doses were truly high,¹ but the possibility of vitamin D unmasking CYP24A1 mutations should have been considered. The identification of patients with CYP24A1 mutations is