Reply to: Timothy A C Snow, Cara A Wasywich and Fiona M Stewart. A case of breathlessness during pregnancy: the difficulty in diagnosing heart failure *Obstet Med* om.2012.120031; published ahead of print 20 December 2012, doi:10.1258/om.2012.120031

To the Editor,

Reply to: Timothy A C Snow, Cara A Wasywich and Fiona M Stewart. A case of breathlessness during pregnancy: the difficulty in diagnosing heart failure *Obstet Med* om.2012.120031;

I wish to thank Drs Snow *et al.* for their fascinating case report of cardiogenic shock with dilated cardiomyopathy in pregnancy.

It raised several questions:

- (1) Could the subjects' use of clomipramine have been a factor in her dilated cardiomyopathy?

A case/non-case study in the French Pharmacovigilance database found a reporting odds ratio of 11.5 with exposure to clomipramine and occurrence of dilated cardiomyopathy.¹ More than 20 cases of dilated cardiomyopathy have been reported after exposure to imipraminic antidepressants, left ventricular dysfunction resolving following drug withdrawal. A positive re-challenge was described in one case report.²

- (2) Were other underlying aetiologies considered for the subjects' presentation?

Catastrophic antiphospholipid syndrome may be associated with cardiogenic shock, renal failure, digital infarction and intrauterine fetal demise. Pheochromocytoma, especially tumours secreting predominantly adrenaline, may also present with refractory shock with dilated cardiomyopathy. Severe cardiogenic shock was reported in a patient with pheochromocytoma provoked by the use of imipramine, known to block the postsynaptic reuptake of noradrenaline.³

- (3) Is there a place for aldosterone antagonists in the management of dilated cardiomyopathy during pregnancy?

Aldosterone antagonists have been shown to improve survival in both mild and severely symptomatic subjects with dilated cardiomyopathy, and with left ventricular dysfunction after myocardial infarction.⁴ It has been commonly stated that spironolactone is contraindicated in pregnancy since a study published in 1980 reported demasculinisation of the external genitalia in the male offspring of exposed rats.⁵ A similar study performed five years earlier,

however, found no evidence of an antiandrogenic effect in male rats whose mothers were exposed to the human equivalent of 400 mg spironolactone per day from day 14 of pregnancy until delivery.⁶ To the best of my knowledge, demasculinisation of male infants has not been reported in human pregnancies where the mother was exposed to spironolactone, despite the medication being widely used for hypertension, pre-eclampsia, liver disease and myasthenia gravis prior to 1980. More recently, a further four human pregnancies have been reported where maternal treatment with spironolactone in doses of 25–400 mg per day caused no adverse effect on male offspring.^{7–9}

The use of eplerenone has only been reported in two pregnancies to date, with no effect apparent on the fetus.^{10,11}

I again thank Snow *et al.* for their thought-provoking article.

Competing interests: None.

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DOI: 10.1177/1753495X13479116

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