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Reply:

I thank Drs. Geier et al. for their interest in the recently published Images in Anesthesia feature.[1] Dr. Geier is correct in detailing the etiology and pathophysiology of hypertrophic cardiomyopathy (HCM). The case report however, does not in any way imply that the cause for the left ventricular outflow tract (LVOT) obstruction was the presence of the long standing hypertension. It rather highlighted the positive findings of the clinical history and physical exam, with the main emphasis being on the echocardiography images. As mentioned, most patients with HCM are asymptomatic.[2] However, dynamic LVOT obstruction can occur in patients with normal ventricles,[3] as well as in patients with hypertensive heart disease. In context of an Images in Anesthesia feature, the main purpose was to demonstrate the echocardiographic images of LVOT obstruction, and to highlight the importance of the intraoperative echocardiography as a monitor in confirming the diagnosis.

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Methylene blue is a potent monoamine oxidase inhibitor

To the Editor:

I was pleased to read Dr. Ng's case report, for which he sought my expertise and assistance, but sorry he did not avail himself of our results, that have established the monoamine oxidase inhibitors (MAOI) potency of methylene blue, published in September 2007.[1]

It is therefore worthwhile adding the 'final chapter' to this interesting story for your readers, and rectifying some particulars that are unclear or inexact in his discussion. My initial report in 2006[2] postulated that the severity of the serotonin toxicity symptoms in these cases was such as to indicate methylene blue *must* be acting as an MAOI. I stated '… further corroboration and quantification of methylene blue's potency (as an MAOI) is in progress.' That paper has confirmed the prediction by demonstrating experimentally, that it is a potent tight binding MAO-A inhibitor at nanomolar concentrations: i.e., it is ~ 100 times more potent than moclobemide.[1] There can now be no doubt about the cause effect relationship of drugs [methylene blue + selective serotonin reuptake inhibitors (SSRIs)] to symptoms (serotonin toxicity).

Furthermore, serotonin toxicity is predictable because the spectrum concept explains it as a continuum of increasing effects, not an idiosyncratic reaction like neuroleptic malignant syndrome (this is why it is clearer to stick to the term serotonin toxicity, and avoid serotonin syndrome). This, and other aspects of serotonin toxicity, are covered in reviews.[3,4] Different classes of drugs exhibit distinct degrees to which they can elevate serotonin.[5] Thus, over-doses of SSRIs produce only mild to moderate degrees of serotonin toxicity, whereas combinations of monoamine oxidase inhibitors, (including reversible inhibitors of monoamine oxidase-A like moclobemide) with any serotonin reuptake inhibitor, *predictably and frequently* precipitate severe serotonergic side effects that can progress to frank serotonin toxicity (depending on dose).

I do endorse Dr. Ng's point 'This illustrates the importance of a high level of clinical suspicion and an appropriately focussed assessment.' But it is also crucial to link that idea to the spectrum concept, and to appreciate that increasing serotonergic side effects and serotonin toxicity is likely, not just possible, with

therapeutic doses of this drug combination (MAOI + SRI). If such drugs have been used, the clinician needs to have a low threshold for suspecting a serotinergically-mediated adverse drug reaction, and to act even if the full gamut of typical symptoms are not yet present. Thus, if an overdose of moclobemide plus an SSRI has been ingested, one should not wait for symptoms to emerge, one should prepare to act as if they are likely to manifest soon and severely. One should also note anesthetics, benzodiazepines and muscle relaxants will substantially alter the picture by suppressing and masking symptoms. Indeed they constitute 'treatment', and withdrawing them may precipitate an exacerbation.

It is only drugs with SRI properties that need to be avoided preoperatively for a few days (depending on half-life: fluoxetine may need a 30-day washout): drugs with other mechanisms of serotonergic action will not be dangerous. Further detailed information, references and discussion is available through my web site www.psychotropical.com

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Reply:

We appreciate Dr. Gillman's comments and recent assistance in providing some of his references. The publication of methylene blue's experimental properties as a monoamine oxidase inhibitor was subsequent to our submission. We are pleased that it has been highlighted.[1]

Based on two published cases, it was hypothesized that serotonin syndrome could be the result of a drug interaction between methylene blue and selective serotonin reuptake inhibitors.[2] *Our review suggests that this combination may be responsible for the majority of reported cases, but one case had methylene blue alone causing delirium.*[3] *Serotonin reuptake inhibitors are frequently prescribed, and it must be presumed that many patients receiving these medications have been exposed to methylene blue without any obvious ill effect. There are currently no data to suggest this is a predictable, or frequent reaction.*

There is a need to act early in the context of a suspected reaction, but there is no definitive cure or treatment for serotonin syndrome. We advocate prevention through a multidisciplinary approach, with cooperation between anesthesia, psychiatry and surgery. Anesthesiologists and surgeons need to be vigilant for potential interactions during preoperative assessments, and discuss with psychiatric colleagues the option of discontinuing medications or delaying surgery. However, in complex clinical scenarios, such solutions may be neither pragmatic nor convenient, and surgeons should consider alternative techniques to localize the parathyroid glands.

Until further data become available, we disagree that this is the final chapter to an unusual and challenging clinical problem.

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Problems with laryngeal mask airway cuff pressure

To the Editor:
Regarding the recently-published article by Lardner *et al.*[1], one concern of any supraglottic inflatable airway