We indicated in our report that we excluded patients with a provisional or previously confirmed diagnosis of autonomic failure, whether primary or secondary, which led to the relatively small proportion who had autonomic failure. We are not alone in believing that some with autonomic failure are suspected, autonomic investigation plays a key part in diagnosis and management.1,2

The diagnostic criteria for carotid sinus hypersensitivity vary in different centres, hence our providing a reference (to a review chapter) and stating the criteria we used. We were aware in certain reports of the high prevalence of carotid sinus syndrome in the elderly, and restricted comment to our own findings and possible explanation. We also clearly describe the overlap between carotid sinus hypersensitivity and orthostatic hypotension in the results section, and with vasovagal syncope in the discussion. We must add that the patients we studied were referred because of their clinical problems, and we can but share our experiences.

Disorders such as syncope have multiple causes, which are dependent on many factors. Prevalence is difficult to establish, especially in disorders for which diagnostic criteria are not clearly defined. The numbers and cause of syncope are expected to vary in primary care and between district and tertiary hospitals. Even in specialised units, differences in causes of syncope might vary depending on the age-mix of the feeder population. Thus, any one study is unlikely to be all-embracing and applicable in every clinical setting, as John Davison and colleagues ideally seek. Our studies emphasise the view that, because the diseases that can cause syncope span many specialties, collaboration with relevant specialists to devise an optimum assessment and management plan for each patient is prudent.1 This plan should ideally now include specialists with experience in autonomic disorders especially once cardiac, non-neurological, and metabolic causes have been excluded.


Mitochondrial toxic effects and ribavirin

Sir—Alain Lafeuillade and colleagues (Jan 27, p 280) report on 15 patients who developed raised lactate and pyruvate concentrations while taking ribavirin and highly active anti-retroviral therapy. Because ribavirin can potentially inhibit mitochondrial DNA polymerase, they conclude that ribavirin elicits mitochondrial toxic effects. However, there may be other explanations for their observations.

Two patients were being treated with didanosine and had been for several years when ribavirin was started. Ribavirin is a 5'-monophosphate dehydrogenase inhibitor that stimulates the activation of didanosine in vitro. Concentrations of the active anabole, 2',3'-dideoxyadenosine-triphosphate (ddATP), is around two-fold greater in cells exposed to didanosine with ribavirin than in those exposed to didanosine alone. The increase in ddATP formation is accompanied by an increase in anti-HIV activity.1 Drugs that can potentiate the anti-HIV activity of nucleoside analogues can also increase their toxic effects. Adverse effects related to didanosine, such as peripheral neuropathy,