LETTERS TO THE EDITOR

Scope

Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation

Letters should be:

- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors

They may contain short tables or a small figures. **Please send a copy of your letter on disk.** Full instructions to authors appear in the January 1998 issue of *Heart* (page 106).

Transient hypertension in male adolescents when measured by a woman

SIR,—It is known that transient elevations in blood pressure are not solely attributable to internal factors; the person who takes the blood pressure measurement may also induce an increase in blood pressure.¹ An example of this phenomenon is white coat hypertension.² The present study compared the difference between blood pressure readings in male Japanese adolescents when measured by men and women.

We studied 373 consecutive male college freshmen (aged 18–20 years) during an annual check up programme. None of them

had any evidence of clinically significant disease such as hypertension (≥ 140 mm Hg), heart valve disease, arrhythmia, hypercholesterolaemia, renal impairment, or liver disease. In March 1997, blood pressures and pulse rates of these subjects were measured using a semiautomatic sphygmomanometer (Parama Co, Tokyo, Japan). All subjects were in a relaxed sitting position for a minimum of 15 minutes. After checking the pulsation of the brachial artery, the measurer placed the cuff over the subject's bare right arm. A total of 231 subjects were monitored by men (M group) and 142 subjects were monitored by women (W group). There were six measurers, two women and four men, aged 22–24 years. All were fifth year medical students at the University of Tokyo. When the systolic blood pressure level was ≥ 150 mm Hg, the same measurer repeated the measurements after engaging the subject in relaxed conversation for approximately five minutes and instructing him to take several deep breaths.

The distribution of the systolic and diastolic blood pressures in the W group was shifted to the right compared with that in the M group (fig 1). There was a highly significant difference (two sample *t* test) in the systolic and diastolic blood pressures between the two groups (mean (SEM) systolic, 135.7 (0.9) *v* 130.7 (0.9) mm Hg, *p* = 0.0012; diastolic 74.4 (0.9) *v* 69.7 (0.8) mm Hg, *p* < 0.0001). In addition, 10.6% (15 of 142) of the readings obtained by the women showed a raised systolic blood pressure (≥ 150 mm Hg) *v* 3.9% (9 of 231) of the M group (*p* = 0.0198, χ^2). All of these subjects were shown to be normotensive (< 140 mm Hg) on repeated measurements. The pulse rate of the same subjects also showed a highly significant transient rise (13.5 (2.1) beats/min) above the repeat pulse measurements (paired two sample *t* test, *p* < 0.0001). The latter was weakly, but significantly, correlated with the increase in systolic blood pressure (*r* = 0.329, *p* = 0.0328). The subjects with transient

hypertension had no demonstrable abnormalities on the electrocardiogram. Their total cholesterol concentrations and family history of hypertension did not differ from those of the consistently normotensive subjects.

The presence of a physician can cause an increase in blood pressure related to the patient's nervousness (white coat hypertension).² The rightward shift of blood pressure distributions presented in this study may be attributed to a different mechanism—that is, the men's physical response to a woman taking the blood pressure. Interestingly, when blood pressure was assessed in the female freshman students (*n* = 113, aged 18–20 years), the sex of the six observers did not affect the distribution of blood pressures or pulse rates (data not shown).

We therefore propose the concept of "white skirt" hypertension to describe reactive hypertension in a young man whose blood pressure is measured by a woman. Follow up studies are needed to verify this phenomenon.

The authors reported this study on behalf of the colleagues who were in charge of the health screening programme: K Andoh, H Chang, Y Uehara, W S Shin, S Uwatoko, M Fujisawa, Z Honda, and T Okuda. This work was supported by a grant-in-aid for scientific research from the Ministry of Education, Science, Sports and Culture, Japan.

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1 Rose GA, Holland WW, Crowley EA. A sphygmomanometer for epidemiologists. *Lancet* 1964;i:296–300.

2 Mancia G, Bertinieri G, Grassi G, Parati G, Pomidossi G, Ferrari A, *et al.* Effects of blood-pressure measurement by the doctor on patient's blood pressure and heart rate. *Lancet* 1983;ii:695–8.

Figure 1 Percentage distributions of systolic (A) and diastolic (B) blood pressure values measured by men (*n* = 231) or women (*n* = 142).

Malignant vasovagal syncope: a randomised trial of metoprolol and clonidine

SIR,—In a recent article, Biffi *et al* concluded that treatment guided by head up tilting is a reliable method of treating severely symptomatic and high risk patients with malignant vasovagal syndrome.¹ They also found metoprolol to be superior to clonidine treatment according to their protocol. Their “pharmacological test” comprised isoprenaline infusion in five progressive steps, from 1–5 µg/min at 80° head up tilt. The specificity of isoprenaline challenge with steep angles of head up testing has been questioned. Natale *et al* investigated the effects of both differing degrees of head up tilt and progressive rates of isoprenaline infusion in normal volunteers with no history of syncope or presyncope.² Testing at a 70° angle with a low dose isoprenaline infusion provided an adequate specificity of 88%, this fell to 60% during 80° head up testing. Limiting test duration at 80° to 10 minutes would have reduced the false positive rate to 16%. Furthermore, increasing the dose of isoprenaline to 3 and 5 µg/min at 70° head up tilt resulted in positive tests in 28% and 56%, respectively, of normal volunteers at a mean time of 8.2 to 9.7 minutes. Kapoor and Brant reported a similar experience (65% positive tests) in two control groups, each of 20 people, with a protocol using 80° head up tilt for a maximum of 15 minutes and mean isoprenaline doses of 1.7 and 1.9 µg/min, respectively.³

My understanding of the reported results by Biffi *et al* is that at least 14 of the 19 “failures” during tilt testing on clonidine occurred during isoprenaline infusion. I appreciate that their duration of head up tilt was limited to 10 minutes during testing. However, the apparently better results reported in the metoprolol group (average dose 280 mg) might partially or completely represent protection from the false positive effects of isoprenaline, rather than an intrinsic advantage of β blockade.

The use of the term “malignant vasovagal syncope” also merits comment. The original description emphasised a prolonged asystolic response during head up tilt.⁴ The term has now been broadened to denote clinical characteristics (frequent syncope without warning and/or traumatic outcome). As a following article in the same issue reports,⁵ the term malignant may be more emotive than scientifically accurate and consensus on its appropriateness is overdue.

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1 Biffi M, Boriani G, Sabbatani P, Bronzetti G, Frabetti L, Zannoli R, *et al*. Malignant vasovagal syncope: a randomised trial of metoprolol and clonidine *Heart* 1997;77:268–72.

2 Natale A, Masood A, Jazayeri M, Dhala A, Blanck Z, Deshpande S, *et al*. Provocation of hypotension during head-up tilt testing in subjects with no history of syncope or presyncope. *Circulation* 1995;92:54–8.

- 3 Wishwa N, Brant N. Evaluation of syncope by upright tilt testing with isoproterenol *Ann Intern Med* 1992;116:358–63.
- 4 Maloney J, Jeager F, Fouad-Tarazi F, Morris H. Malignant vasovagal syndrome: prolonged asystole provoked by head-up tilt. *Clev Clin J Med* 1988;55:542–8.
- 5 Pentousis D, Cooper JP, Cobbe SM. Prolonged asystole induced by head up tilt test. Report of four cases and brief review of the prognostic significance and medical management. *Heart* 1997;77:273–5.

This letter was shown to the authors, who reply as follows:

The question about the sensitivity and specificity of pharmacological testing with isoproterenol in patients with neurocardiogenic syncope is old and debated. Although false positive results have been reported in two studies,^{1,2} several observations have confirmed the high specificity and reproducibility of isoproterenol testing.^{3–6} Moreover, the average isoproterenol infusion rate at syncope was 1.6 µg/kg/min in our study,⁷ which is well within the limit of “specificity” obtained by Natale *et al*,² moreover, no patient in our study developed syncope at infusion rates greater than 3 µg/kg/min either during baseline head up tilting or during the two treatment phases. Once again, this is clearly within the limits of specificity claimed in the paper by Natale *et al*.² With respect to the second point, the occurrence of failures during clonidine treatment at isoproterenol infusion rates comparable to those at baseline head up tilting rules out any false positivity and confirms the intrinsic advantage of β blockade.

To substantiate our observation, we report here follow up data with respect to baseline head up tilting. According to Dr Smith's view, one would expect a higher recurrence of symptoms in patient who fainted during isoproterenol testing compared with those who fainted under basal conditions. In our experience, among the 19 patients who responded to drugs, four had recurrent symptoms: two of 11 who fainted under basal conditions and two of nine who fainted during isoproterenol testing at baseline head up tilting (NS); the former had four near syncopes and the latter three near syncopes at follow up (NS). Thus, the response to isoproterenol testing may not be considered a false positive, nor may it represent a predisposing factor to the positive effect of β blockers.

No consensus has been achieved regarding the term malignant vasovagal syncope. Prolonged asystole has been reported by many authors, and in our series we observed sinus arrest up to 39 seconds. Although this may indeed raise emotive reactions, it is rarely a marker of serious outcome or poor prognosis as in the paper by Pentousis *et al*,⁵ nor is it reproducible as demonstrated by Dhala *et al*.⁹ On the contrary, severe injuries due to sudden hypotension without prodromes occurred in eight of our patients in the absence of significant bradycardia. We believe therefore that, in the absence of universally

accepted definitions, the interpretation of malignancy based on syncope outcome is far less emotive than the mere observation of some degree of asystole.

- 1 Kapoor W, Brant N. Evaluation of syncope by upright tilt testing with isoproterenol. *Ann Intern Med* 1992;116:358–63.
- 2 Natale A, Akhtar M, Jazayeri M, *et al*. Provocation of hypotension during head-up tilt testing in subjects with no history of syncope or presyncope. *Circulation* 1995;92:54–8.
- 3 Sheldon R, Spalwinski J, Killman S. Reproducibility of isoproterenol tilt table test results in patients with syncope. *Am J Cardiol* 1992;69:1300–5.
- 4 Grubb BP, Wolfe D, Temesy-Armos P, *et al*. Reproducibility of head-upright tilt table results in patients with syncope. *PACE* 1992;15:1477–81.
- 5 Sheldon R, Rose S, Flanagan P, *et al*. Risk factors for syncope recurrence after a positive tilt-table test in patients with syncope. *Circulation* 1996;93:973–81.
- 6 Grubb BP, Temesy-Armos P, Moore J, *et al*. Head-upright tilt-table testing in evaluation and management of the malignant vasovagal syndrome. *Am J Cardiol* 1992;69:904–8.
- 7 Biffi M, Boriani G, Sabbatani P, *et al*. Malignant vasovagal syncope: a randomised trial of metoprolol and clonidine. *Heart* 1997;77:268–72.
- 8 Pentousis D, Cooper JP, Cobbe SM. Prolonged asystole induced by head up tilt test. Report of four cases and brief review of the prognostic significance and medical management. *Heart* 1997;77:273–5.
- 9 Dhala A, Natale A, Sra J, *et al*. Relevance of asystole during head-up tilt testing. *Am J Cardiol* 1995;75:251–4.

NOTICE

International Albrecht Fleckenstein Award 1998

This DM50 000 award, supported by Bayer AG, is presented every other year for work done on calcium antagonism and calcium channel modulation in experimental and/or clinical medicine. The award is open to researchers of all nationalities no older than 45 years.

Papers must be submitted in English and already have been published or accepted for publication in a peer review journal within the past two years. Deadline for submissions is 31 January 1998.

Seven copies of the paper, a curriculum vitae including a list of publications, a statement from the head of department confirming originality of the work, and one from the applicant documenting the major role played in the creation of the work should be submitted to: Dr David J Triggie, Dean of the Graduate School, University of Buffalo, State University of New York, 410 Capen Hall, Buffalo, NY 14260-1608, USA.