Aggravation and provocation of ventricular arrhythmias by antiarrhythmic drugs. *Circulation* 1982; 65: 886-94.

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

Sir,

Our citing of Simon and Berman¹ in a context that sotalol "may be arrhythmogenic" was a typographical error for which we apologise. We contend that our paper contains no other "errors of fact and interpretation."

The statement by the manufacturers, based on a "worldwide survey", that "the incidence of syncope or torsade de pointes with sotalol and Sotazide was 0.002% (25 incidents/1 202 000 prescriptions)" does not impress us, and we question their sources of information. We also remind them that side effects of many drugs have been missed for years until a first observation is made or a careful investigation is undertaken. The detection of the deleterious effects of practolol and of thalidomide exemplify this.

Because sotalol has a class III antiarrhythmic action surely it is readily understandable that it will also have arrhythmogenic effects in some instances? Although we emphasised that the presence of hypokalaemia or the concurrent use of other drugs which prolong the QT interval were highly important factors in the development of polymorphous ventricular tachycardia and syncope in most of our patients taking sotalol, Kuck *et al* have now reported the case of a 40 year old woman taking sotalol 320 mg daily who developed torsade de pointes but in whom no electrolyte disturbances were detected.² After our paper was

accepted for publication, we encountered two more patients, both hypokalaemic, who developed syncope during sotalol treatment.

It is not a "major conclusion" of ours that "other beta blockers do not confer any arrhythmogenic risk." We did not discuss that aspect. Our principal conclusions relate to the recognition that sotalol has unique antiarrhythmic, and therefore also arrhythmogenic, properties. We suggest that sotalol is superior to other beta receptor blocking agents in the treatment of conditions in which the class III effect is relevant. We assert that the combination of sotalol with a thiazide diuretic should be avoided in the long term treatment of a condition such as hypertension, in which hypokalaemia commonly ensues.

Our message is a simple one, and we consider that it is in the interest of many patients that the manufacturers of sotalol accept it.

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References

- 1 Simon A, Berman E. Long-term sotalol therapy in patients with arrhythmias. *J Clin Pharmacol* 1979; 19: 547-56.
- 2 Kuck KH, Kunze KP, Roewer N, Bleifeld W. Sotalol-induced torsade de pointes. *Am Heart J* 1984; 107: 179-80.

Ketanserin treatment in essential hypertension

Sir,

Fagard *et al*'s paper (1984; 51: 149-56) on ketanserin treatment in mildly hypertensive patients includes some haemorrheological aspects which might be noteworthy. The authors found a fall in pulmonary and systemic arterial resistance during treatment which they attribute exclusively to vasodilatation. Peripheral resistance, however, is composed of two components: vascular tone and the viscous hindrance of blood flow (for example, blood viscosity).¹ Blood viscosity is increased in essential hypertension¹ and can be decreased by ketanserin² and other alpha₁ antagonists.¹ This might be a contributory factor in the changes observed by Fagard *et al*. In fact a closer look at their results seems to confirm this. Haemo-

globin concentrations decrease and plasma volume is thought to increase with ketanserin, both of which would tend to lower blood viscosity³ and partly explain the findings.

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References

- 1 Letcher RL, Chien S, Laragh JH. Changes in blood viscosity accompanying the response to prazosin in patients with essential hypertension. *J Cardiovasc Pharmacol* 1979; 1 (suppl): S8-20.
- 2 De Clerck F, Jageneau A, Dom J. Haemorheological effects of ketanserin, a selective 5-HT₂ receptor antagonist, in aged, spontaneously hypertensive dogs. *Arch Int Pharmacodyn Ther* 1982; 258: 110-15.
- 3 Chien S. Biophysical behaviour of red cells in suspensions. In: Surgenor DM, ed. *The red blood cell*. 2nd ed. New York: Academic Press, 1975:1031-121.

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

Sir,

Calculated systemic vascular resistance is determined by the degree of narrowing of blood vessels, by active arteriolar constriction, and by the viscosity of the blood. Changes in systemic vascular resistance may therefore be caused by changes in any of these factors alone or in combination, but it must be admitted that the viscosity factor is usually neglected in the clinical pharmacology of antihypertensive drugs. In our study we did not measure whole blood viscosity, but the reduction in blood haemoglobin concentration suggests a lower blood viscosity during ketanserin treatment. Thirty minutes after intravenous administration of ketanserin in old hypertensive dogs De Clerck

*et al*¹ observed a mean reduction in whole blood viscosity and in blood haemoglobin concentration of 17%, which was, however, not dose dependent; their data did suggest a close relation between haematological findings and blood viscosity. In our study in hypertensive patients, in whom ketanserin was given orally in three doses of 40 mg daily for six weeks, blood haemoglobin concentration was reduced from 1% to 3% in the various experimental conditions. It cannot be excluded that a reduction in blood viscosity contributed to the reduced systemic vascular resistance observed in our study, but it is unlikely to explain the 14% reduction in vascular resistance.

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Reference

- 1 De Clerck F, Jageneau A, Dom J. Haemorheological effects of ketanserin, a selective 5-HT₂ receptor antagonist, in aged, spontaneously hypertensive dogs. *Arch Int Pharmacodyn Ther* 1982; 258: 100-15.

Notices

Research and the practice of cardiology

The fifth British Heart Foundation European symposium on the impact of research on the practice of cardiology will be held from 3 to 6 June 1985. Further details may be obtained from: Conference Office, British Heart Foundation, 102 Gloucester Place, London W1H 4DH.

British Cardiac Society

The Autumn Meeting will be held at the Wembley Conference Centre, London on 3 and 4 December 1984, and the closing date for receipt of abstracts was 15 August 1984.

The Annual General Meeting for 1985 will take place in Birmingham on 17 and 18 April 1985, and the closing date for receipt of abstracts will be 8 January 1985.