LETTERS TO THE EDITOR

- The British Heart Journal welcomes letters commenting on papers that it has published within the past six months.
- All letters must be typed with double spacing and signed by all authors.
- No letter should be more than 600 words.
- In general, no letter should contain more than six references (also typed with double spacing).

β -Endorphin release in patients after spontaneous and provoked acute myocardial ischaemia

SIR,—Oldroyd *et al* (*British Heart Journal* 1992;67:230-5) claimed that there were no previously published data on the β -endorphin response to myocardial ischaemia or infarction and that they were first to show that β -endorphin is released to plasma during myocardial infarction. This is not correct. In our study published in 1987 we used a specific β -endorphin radioimmunoassay to show increased concentrations of β -endorphin during myocardial infarction but normal concentrations during unstable angina pectoris.¹ The highest β -endorphin concentrations were found in patients with cardiac failure and in those who died within 24 hours. Pain ratings by use of a visual analogue scale were no different in myocardial infarction and unstable angina pectoris. These results are beautifully replicated by Oldroyd *et al* in a similarly designed study.² It is disappointing that our similar previous study is not cited among their 46 references. It is also appropriate to mention a study that found no increase in plasma β -endorphin during myocardial infarction but an inverse relation between pain intensity and plasma β -endorphin.³

FLEMMING W BACH
Anesthesiology Research Laboratory
University of California San Diego
La Jolla, CA 92093, USA

- 1 Bach FW, Fahrenkrug J, Jensen K, Dahlström G, Ekman R. Plasma β -endorphin during clinical and experimental ischaemic pain. *Scand J Clin Lab Invest* 1987;47:751-8.
- 2 Oldroyd KG, Harvey K, Gray CE, Beastall GH, Cobbe SM. β -Endorphin release in patients after spontaneous and provoked acute myocardial ischaemia. *Br Heart J* 1992;67:230-5.
- 3 Stoupe E, Pinchas A, Gilad I, Laron Z, Agmon J. β -endorphin in acute myocardial infarction. *Clin Cardiol* 1986;9:409-12.

This letter was shown to the author who replies as follows:

SIR,—I apologise to Dr Bach and colleagues and Dr Stoupe and colleagues for failing to identify their important publications.^{1,2} It is reassuring to note that in many respects their preliminary observations were confirmed in our larger study population. I would like to make the following brief comments.

Despite using a similar assay system with a normal range that was comparable to that used by Bach *et al* we were unable to identify

any relation between pain scores and β -endorphin concentrations in patients with myocardial infarction. The statistically significant but biologically weak positive correlation reported by Bach *et al* was not obtained with visual analogue pain scores as stated but with a "four point verbal rating scale". A visual analogue scale was used to assess pain during induced forearm ischaemia and no correlation with β -endorphin concentrations was found.

In the study of Stoupe *et al* the absence of any difference in β -endorphin concentrations between healthy controls ($n = 7$) and patients with acute myocardial infarction ($n = 26$) is probably the result of the much longer delay from the onset of symptoms to the time of blood sampling in their study. This also explains the spurious negative correlation with pain intensity. Their results are consistent with our observations in showing that the highest β -endorphin concentrations were seen in patients with creatine kinase concentrations > 1500 IU/l.

KEITH G OLDROYD
The Toronto Hospital,
585 University Avenue,
Toronto, Ontario M5G 2C4 Canada

- 1 Bach FW, Fahrenkrug J, Jensen K, Dahlström G, Ekman R. Plasma β endorphin during clinical and experimental ischaemic pain. *Scand J Clin Lab Invest* 1987;47:751-8.
- 2 Stoupe E, Pinchas A, Gilad I, Laron Z, Agmon J. β endorphins in acute myocardial infarction. *Clin Cardiol* 1986;9:409-12.

SIR,—Oldroyd *et al* (*British Heart Journal* 1992;67:230-5) conclude that β -endorphin release is a component of the neuro-endocrine activation associated with myocardial ischaemia/infarction.¹

This conclusion is imprecise. A component, almost by definition, is something which occurs in most, if not all, cases. And their sample of patients with "unstable angina" all had proven ischaemia but only 23% had raised β -endorphin.

It is more correct to conclude that "something occurring, perhaps incidentally, in three quarters of myocardial infarctions, half of angioplasties, and some episodes of ischaemia stimulates β -endorphin release".

Oldroyd *et al* suggest in their discussion that β -endorphin is released as a "pulse". An alternative explanation is that the stimulus could be one that is subject to rapid homeostasis, and therefore is short-lived.

To find out what the stimulus is, we must (bearing in mind it occurs also in endotoxic and cardiac shock and after exercise) look for something that might plausibly occur in 74% of infarctions, 42% of angioplasties, and 23% of cases of ischaemia. The task seems impossible, until one returns to cardiovascular physiology, and the dictum that "the vasomotor control centre includes so many inter-related neuron pools that almost any pattern of response may be obtained with certain stimuli".

Myocardial infarction is a case in point. In a study of patients seen within 30 minutes of proven infarction, 92% showed autonomic disturbance, of which 56% had vagal and 36% sympathetic preponderance.²

Secretion of β -endorphin (and α -

melanocyte stimulating hormone) from the intermediate lobe of the pituitary has been found to be under dual control by dopaminergic and β -adrenergic mechanisms.³

Interestingly, sympathetic reflexes to experimental coronary occlusion have long been described.⁴ Coronary occlusion is (3 times?) more likely to occur in infarction than ischaemia.

Consider the hypothesis that it is some pattern of autonomic tone that is the stimulus to β -endorphin release here. (Certainly, after exercise particular temporal patterns of sympathetic and vagal tone accompany endorphin release.) β -Endorphin release could be consequent on a pressure or occlusion phenomenon which sometimes accompanies infarction—rather than on infarction itself. Hence the importance of stating conclusions carefully.

Oldroyd *et al* mention that the beneficial effects of opiate antagonists in canine cardiac failure may be sympathetically mediated. If β -endorphin damps down the sympathetic response, yet is released by β -adrenergic stimulation, then perhaps some sort of double feedback loop is acting?

F ROMAN
Department of Medicine,
Chemical Sciences Building,
St James's University Hospital,
Leeds LS9 7TF

Address for correspondence: 65 Roebuck Road, Sheffield S6 6GQ

- 1 Oldroyd KG, Harvey K, Gray CE, Beastall GH, Cobbe SM. β endorphin release in patients after spontaneous and provoked myocardial ischaemia. *Br Heart J* 1992;67:230-5.
- 2 Webb SW, Adgey AAJ, Pantridge JF. Autonomic disturbance at onset of acute myocardial infarction. *Br Med J* 1972; iii:89-92.
- 3 Smelik PG, Berkenbosch F, Vermees I, Tilders FJH. The role of catecholamines in the control of the secretion of pro-opiomelanocortin-derived peptides from the anterior and intermediate lobes and implications in the response to stress. In: Bhatnagar AS. The anterior pituitary gland. New York: Raven Press, 1983;495-580.
- 4 Malliani A, Schwartz PJ, Zanchetti A. Sympathetic response to experimental coronary artery occlusion. *Am J Physiol* 1969; 217:703-7.

A model to simulate the effects of right heart pulsatile flow after modified Fontain procedure.

SIR,—Tamaki *et al* reported in vitro flow studies showing that in their apparatus active pulsation of a valveless chamber, designed to represent the right heart in a Fontan circulation, led to a measurable rise of flow in the tubing downstream.¹ They took this to indicate "that pulsatile pulmonary blood flow is likely to have a beneficial effect on the pulmonary circulation after the modified Fontan procedure".

They may be correct in suggesting that pulsatility has a beneficial effect in the living pulmonary vasculature, reducing the net resistance of a branching system of delicate, compliant vessels, but we believe they are wrong to deduce this from their experiment.

The explanation that they offered for their finding was that pulsation decreased the resistance to flow through the non-elastic tubing downstream of their valveless pump chamber. This explanation is unlikely to be correct. Superimposition of pulsatility on continuous flow through non-elastic

tubing increases levels of turbulence in the fluid entering the tube and this results in a slight increase in resistance to flow.²

The true explanation for the net increase in forward flow during pulsation in Tamaki *et al*'s apparatus could be more complex, being dependent on a slight forward pump-like effect resulting from asymmetry of the arrangement of tubes and vessels on either side of the valveless pumping chamber.

Before explaining this hypothesis, however, a second point needs to be made regarding the apparatus of Tamaki *et al*. Flow through their system was sustained by a predetermined head of water in the inlet tank, maintained at a level approximating to the level of systemic venous pressure after Fontan operation. In the Fontan circulation, however, the power source for the circulation is the systemic ventricle, which sustains flow through the systemic resistance as well as the right heart and pulmonary resistance, all in series. Relatively subtle changes in conditions of flow through the right heart, therefore, have little influence on mean flow, but can significantly alter the level of pressure in the systemic veins. In Tamaki *et al*'s apparatus the predetermined inlet head and omission of an analogue of the systemic part of circulation mean that effects of right heart pulsatility on systemic venous pressure would not have been apparent, whereas any influence on mean forward flow would have been exaggerated by a factor of about four.

Returning now to the postulated valveless pump-like effect. It is an intriguing, rather counter-intuitive phenomenon that we explored before publication of our *in vitro* flow studies relating to the Fontan circulation. We had hoped to make use of the effect, looking for some modification of the Fontan right heart that could, without valves, work to enhance net forward flow.

This pump-like effect operates when a valveless, pulsatile chamber is connected in an asymmetrical arrangement of tubes, with tubes or vessels on either side of the chamber having differing mechanical properties. For example, if there is a length of non-compliant tubing on one side of the chamber and a capacitant vessel adjacent to the other side, a slight pump-like effect, capable of sustaining forward flow or a net pressure gain or both, is found to operate in the direction of the length of non-compliant tubing.

How does this work? It may be explained in terms of energy propagation: the pulsatile chamber imparts energy in both directions. If the "forward" direction is via a length of non-compliant tubing, a column of fluid in the tube is given forward momentum and the energy of this moving fluid is propagated forwards. If in the other direction, however, flow enters a freely capacitant vessel (this can either be an open chamber, as in Tamaki *et al*'s apparatus, or a thin walled, collapsible tube), the kinetic energy of the fluid impelled in this direction is rapidly dissipated in turbulence, with minimal propagation of energy further back upstream.

We suggest that the simplest way to test whether this explanation is relevant to the findings of Tamaki *et al* would be for them to reconstruct their apparatus with a symmetrical arrangement of tubes and vessels on either side of the pump chamber, and to see whether the observed effect on net forward flow is abolished.

The suggestion that a pump-like effect explains Tamaki *et al*'s findings leads to the question whether such an effect has relevance to the Fontan circulation.

One of our preliminary *in vitro* studies made use of a circuit incorporating lengths of fresh caval vein on the upstream side and pulmonary artery on the downstream side of a valveless, pulsatile "atrial" chamber. A positive, but very inefficient pump-like effect was achievable only if the caval wall remained collapsible—that is, with very low (normal) transmural pressure. The caval vein in this state is apparently well suited *not* to propagate energy back upstream, but we found that if the caval vein was distended by an internal pressure of 12 mm Hg or more, as is inevitable in the Fontan circulation, the forward pump-like effect ceased to work. The vein then behaved more as a rigid tube, transmitting atrial systolic work back upstream at least as effectively as the pulmonary artery sent it forwards. We failed to find a way of making the valveless pump work to advantage in the conditions of the Fontan setting, and in the process became aware of the adverse effects of turbulence generated by pulsation.

Clearly caution is needed when we attempt to draw conclusions from simplified *in vitro* models. The question of the effects of Fontan right atrial contraction, both detrimental and beneficial (that is, back into systemic veins as well as forward into pulmonary arteries), has still to be satisfactorily answered.

PHILIP KILNER
Magnetic Resonance Unit
Royal Brompton National Heart
and Lung Hospitals,
Sydney Street, London SW3 6HP

MARC DE LEVAL
Cardiothoracic Unit,
The Hospital for Sick Children,
Great Ormond Street,
London WC1N 3JH

- 1 Tamaki S, Kawazoe K, Yagihara T, Abe T. A model to simulate the haemodynamic effect of right heart pulsatile flow after modified Fontan procedure. *Br Heart J* 1992;67:177-9.
- 2 de Leval MR, Kilner PJ, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. *J Thorac Cardiovasc Surg* 1988;96:682-95.

A posteroseptal accessory pathway located in a coronary sinus aneurysm: diagnosis and radiofrequency catheter ablation.

SIR,—I congratulate Pedersen *et al* (*British Heart Journal* 1992;68:414-6) on their description and successful ablation of an accessory pathway located at the mouth of a coronary sinus diverticulum, which resembles a case described by us in 1991¹ and to which they refer.

I was, however, concerned that they made the point in their final sentence that they regarded radiofrequency current as less hazardous than low energy shocks in the thin-walled aneurysm. I wonder what evidence they have for this statement? I would contend quite the opposite. Low energy shocks have been used, particularly in our institution, for seven years, and have never resulted in rupture of any cardiac structure, including the coronary sinus (both proximal and distal) and the diverticulum referred to in our report. This is because the short duration shock through a special catheter

produces no explosion or shock wave, and thus damages only local tissue through electrical effects. Though we do not now advocate low energy shocks (or indeed any form of energy delivery) within the coronary sinus, there have been no hazards observed with this practice in the past.

In contrast, it has been shown that a critical factor for the success of radiofrequency ablation is contact pressure, and this leads to the concern that prolonged (30 seconds) application of radiofrequency energy in a thin-walled aneurysm could lead to progressive tissue damage, with the catheter advancing through the damaged tissue and eventually rupturing the structure. Exactly this complication has been reported by Dr W Jackman as one of the very few complications in his large series (First Augustus Waller Lecture. Royal Society of Medicine, December 1991).

I think it should be stressed that only on the basis of our case and the case of Pedersen *et al*, one should not be didactic about the general safety or otherwise of either technique in such cases.

A D CUNNINGHAM
Royal Brompton National Heart
and Lung Hospital,
Sydney Street, London SW3 6NP

- 1 Conelly DT, Rowland E, Ahsan AJ, Cunningham D. Low energy catheter ablation of a posteroseptal accessory pathway associated with a diverticulum of the coronary sinus. *PACE* 1991;14:1217-21.

BOOK REVIEW

The titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the UK and for members of the British Forces Overseas, but overseas customers should add £2 per item for postage and packing. Payment can be made by cheque in sterling drawn on a UK bank, or by credit card (MasterCard, VISA, or American Express) stating card number, expiry date, and your full name.

Percutaneous balloon valvuloplasty. Edited by Tsung O Cheng. (Pp 556; £107.) London: Williams and Wilkins, 1992. ISBN 0-8964-0216-9.

The past few years have seen rapid changes in both indications and techniques in balloon dilatation of valves but the dust is at least settling. With the widespread adoption of the Inoue method, balloon dilatation of the mitral valve is now poised to replace valvotomy. Balloon dilatation of the aortic valve has not lived up to its early promise and is now reserved for the exceptional cases when surgical risks are unacceptably high. With an internationally renowned list of contributors this book fulfils admirably the task of a reference text that will be relevant for some years to come.

With only minor lapses Dr Cheng shows excellent editorial control over such a large panel. There is minimal duplication of material and no tendency towards a half-hearted rework of previous publications. The topic is comprehensively covered with a cohesive sense of purpose. I strongly recommend the chapter on valve anatomy and