

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

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- 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 Stoupele 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 Stoupele 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 Stoupele *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.

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- 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 Stoupele 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 neuroendocrine 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?

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- 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, Vermes 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 Fontan 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