Respiratory and circulatory effects of pentazocine

Review of analgesics used after myocardial infarction

R. E. Nagle and J. Pilcher
From Selly Oak Hospital, Birmingham, and the Royal Infirmary, Sheffield

The analgesic pentazocine has been studied in myocardial infarction. A dose of 30 mg given intravenously provokes significant respiratory depression (which may be potentiated by lignocaine). This dose caused a small, but not significant rise in systemic arterial pressure and heart rate when breathing air. Attempts to provoke postural hypotension failed. Changes in pulmonary arterial pressure and arteriovenous oxygen difference were small and not significant.

The published reports have been reviewed with a view to determining the most suitable intravenous analgesic for use after myocardial infarction. Pethidine and morphine appear to be unsatisfactory. Pentazocine is preferable to either, but less satisfactory than heroin in a normotensive patient. Dosage should be as small as practicable and injection slow. Oxygen should be given routinely; phenothiazines should not.

Blood gas tensions are altered by myocardial infarction (Mackenzie *et al.*, 1964) but are also influenced by analgesics required for the

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relief of pain. This paper describes the effect of pentazocine 30 mg intravenously upon blood gases and upon heart rate and mean

TABLE I Blood gases after pentazocine 30 mg IV

		PaO ₂		PaCO ₂		pH		Base deficit excess	
		Control	Comparison	Control	Comparison	Control	Comparison	Control	Comparison
(1) Air	Mean value	70.9	62.4	40.7	43.2	7.414	7.395	+ 1.6	+ 1.5
	SD	8.9	7.5	3.8	3.2	0.044	0.044	2.3	3.1
	Significance	< 0.01		< 0.01		< 0.05		NS (> 0.25)	
	No. of cases	10	10	10	10	10	10	10	10
	Mean value	67.0	62.1	40.6	42.7	7.417	7.401	+ 1.6	+ 1.5
	SD	12.6	10.8	4.4	5.2	0.048	0.043	2.7	2.9
30 minutes	Significance	< 0.01		< 0.01		NS		NS (> 0.25)	
	No. of cases	18	18	18	18	18	18	18	18
60 minutes	Mean value	71.2	67.4	41.0	43.4	7.407	7.392	+ 1.6	+ 1.3
	SD	9.4	8.9	3.9	4.5	0.046	0.045	2.5	2.8
	Significance	NS		< 0.05		< 0.05		NS (> 0.25)	
	No. of cases	9	9	9	9	9	9	9	9
(2) Oxygen	Mean value	262.5	245.0	44.0	44.7				
	SD	127.9	124.2	6.2	5.2				
	Significance	NS		NS					
30 minutes		No. of cases	6	6	6	6			

NS = not significant.

systemic and pulmonary artery pressures in such patients, and compares these effects with those published for other analgesics (morphine, heroin, and pethidine).

Subjects

There were 17 men and 3 women whose ages ranged from 43 to 82 (mean age 59.2, SD 11.4). A diagnosis of myocardial infarction was made when a typical history was accompanied by a rise in the serum aspartate aminotransferase and diagnostic changes in the electrocardiogram. These criteria were met by 18 out of 20 patients. The remaining 2 patients suffered ischaemic pain but without recent infarction. Seventeen patients were studied within 24 hours, and all within 48 hours, of the onset of symptoms.

Seven patients were in left ventricular failure and 2 were in a state of shock. One was drowsy as a side effect of an intravenous infusion of lignocaine (1.5 mg/min) required to control ventricular premature beats. The other 10 patients were free of complications apart from pain which was present in 8. One patient was being paced for a third degree heart block and one, already mentioned, had ventricular premature beats. The others were in sinus rhythm.

Methods

The patients were studied recumbent in bed before and after the administration of pentazocine 30 mg. The drug was injected into a previously set up intravenous infusion of dextrose-saline, and the patient was usually unaware that any medication had been given.

Arterial blood samples were obtained from indwelling catheters, inserted by the Seldinger technique, in 11 patients and by direct arterial puncture in 9. These 9 were little disturbed by arterial puncture. Samples were collected in heparinized glass syringes and analysed in duplicate, using standard Radiometer microelectrode equipment, for pH, PO_2 , and PCO_2 . Samples from patients breathing oxygen were analysed within 10 minutes and those from patients breathing air within 60 minutes, the samples being kept meanwhile on ice. Duplicate readings were accepted if they agreed to within 0.01 units of pH, 1 mmHg of CO_2 , and 10 mmHg of O_2 in the 0–1200 range or 2 mmHg in the 0–125 range. The pH and PCO_2 electrodes were calibrated according to the maker's instructions and the PO_2 electrode with saturated gases analysed by a Haldane apparatus.

Systemic arterial blood pressure was measured by direct intra-arterial recordings in 9 patients. Readings were begun when the patient was in a steady state as indicated by heart rate and blood pressure. Forty-five minutes after pentazocine had been given, the bed-head was abruptly raised (with prior zero correction) so that the patient made an angle of 30 degrees to the horizontal. Pulmonary artery pressures and central venous samples were obtained in 5 of these patients via the floating catheter technique described by Bradley (1964).

The effect of pentazocine on the response to oxygen was separately studied in 6 patients. Readings were taken breathing air and again at least 15 minutes after the patient had breathed oxygen from nasal spectacles in 3 cases and from a mask and reservoir in the other 3. The readings were then repeated 30 minutes after pentazocine had been given.

Base excess and per cent oxygen saturation were calculated from PO_2 , pH, PCO_2 , and haemoglobin levels, while paired *t* tests have been used to assess statistical significances.

Results—pentazocine

Though this study was not designed to assess the analgesic effectiveness of pentazocine, it was noted that a dose of 30 mg relieved the pain of myocardial infarction when it was moderate or slight but only partially when it was severe. Transient vertigo was the only harmful side effect while a beneficial sedative action was seen in 5 patients.

Arterial blood gases and acid-base balance (room air) (Table 1) (1) PaO_2 . In none of 10 patients at 10 minutes after injection was PaO_2 at or above control levels. Thereafter there was a tendency for PaO_2 to approximate towards control levels (2 of 18 patients at 30 minutes and 3 of 9 at 60 minutes). Depression of PaO_2 at 10 and 30 minutes achieves significance ($P < 0.01$). There was no correlation between the extent of the

% saturation		AV O_2 difference	
Control	Comparison	Control	Comparison
93.8	90.7	{ Arterial saturation minus central venous saturation	
2.6	3.5		
10	10	—	—
91.8	90.0	29.6	27.1
6.5	6.3	9.1	7.0
18	18	5	5
91.5	90.3	—	—
2.7	4.6	—	—
9	9	—	—

change and the clinical condition of the patients or between the extent of change and control values. One patient, already drowsy from a lignocaine infusion, developed a striking fall in P_{aO_2} from a control value of 60 mmHg to levels of 48 mm at 10 and 30 minutes. She did not achieve the control value even after 2 hours.

(2) P_{aCO_2} . Changes in P_{aO_2} were roughly mirrored by those affecting P_{aCO_2} . Thus, at 10 minutes only 1 of 10 patients had a level at or below the control value, while by 30 minutes this had become 2 of 18 patients and by 60 minutes 2 of 9. This rise in P_{aCO_2} is significant ($P < 0.01$ at 10 and 30 minutes; $P < 0.05$ at 60 minutes).

(3) pH and base-deficit or excess. There were significant falls in pH after pentazocine, but the total lack of change in base deficit or excess indicates that these pH changes were due solely to the rise of P_{aCO_2} described above.

Oxygen saturation—room air (Table 1)

There were significant falls in arterial oxygen saturation after pentazocine, these being greatest 10 minutes after the drug ($P < 0.01$). By 60 minutes differences between control and observed values were slight and not significant. Though mean arterial oxygen saturations did not fall below 90 per cent, in 2 patients, whose clinical condition was judged to be good, levels did fall from above 94 per cent to 89 and 89.5 per cent, respectively. Maximal depression was observed in the patient receiving a lignocaine infusion, levels falling from 92 per cent to 84 per cent 10 minutes after injection.

Mean central venous oxygen saturation in the 5 patients measured was 63.5 per cent (range 51.5% to 72.0%). Changes in arterio-venous oxygen difference after pentazocine were small and variable, 4 patients showing a small decrease and 1 a rather larger increase. These changes are not significant.

Arterial blood gases (oxygen) (Table 1)

In general terms the results are similar whether the patients were breathing air or oxygen—that is P_{aO_2} tended to fall and P_{aCO_2} to rise after the drug. Of the 6 patients tested, 5 were considered to be in good clinical condition and P_{aO_2} rose in none. One patient was in left ventricular failure when studied. His clinical condition improved after the drug and P_{aO_2} rose from 235 mmHg to 280 mm despite a fall in P_{iO_2} from 665 mm to 510 mm.

Heart rate and systemic and pulmonary arterial pressures (air) (Table 2) After pentazocine heart rate rose slightly in 4 patients, remained unchanged in 1, and fell slightly in 3. When these patients were tilted head up the rate remained unchanged in 6 patients and rose slightly in 2.

Mean systemic arterial pressure tended to rise—rising in 6 patients, remaining unchanged in 2, and falling slightly in 1 at 10 minutes after the drug. By 30 minutes pressure remained raised in 4 patients and approximated control values in the remainder. None of these changes achieves significance. When patients were tilted pressures rose slightly in 3 patients, fell slightly in 1, and were unchanged in the remainder. No patient became hypotensive.

Mean pulmonary artery pressures rose in 2 patients and fell in 3 after pentazocine. In general terms changes were small and not significant.

Heart rate and systemic arterial pressure (oxygen) (Table 2)

Alterations in heart rate when changed from air to oxygen breathing were small and insignificant. They were not affected by pentazocine. However, arterial pressure rose in all 6 patients when changed from air to oxygen and this increase is significant ($P < 0.01$). After pentazocine pressure then fell in 4 patients and rose yet again in 2 (one of these being in left ventricular failure). These changes are not significant.

Discussion

The ideal analgesic for use after myocardial infarction would relieve pain and allay anxiety without any cardiorespiratory or other action whatever. No such drug exists. Commonly used strong analgesics are morphine, heroin, pethidine, and pentazocine. Various studies have been undertaken on these drugs in myocardial infarction, namely morphine (Thomas *et al.*, 1965a; Hoel and Refsum, 1969; Grendahl and Hansteen, 1969), heroin (McDonald *et al.*, 1967), pethidine (Rees *et al.*, 1967), pentazocine (Lal, Savidge, and Chhabra, 1969; Jewitt, Maurer, and Hubner, 1970; this study), while Scott and Orr (1969) compared morphine, heroin, and pentazocine. It therefore seems apposite to review these studies with a view to determining the most suitable analgesic for use in myocardial infarction.

Analgesic action and relief of anxiety

All four drugs are effective analgesics in myo-

TABLE 2 Blood pressures and rate after pentazocine 30 mg IV

		Heart rate		Mean brachial artery pressure		Mean pulmonary artery pressure		
		Control	Comparison	Control	Comparison	Control	Comparison	
Air	mean value	78.8	79.4	92.7	99.0	20.4	20.0	Air
10 minutes	SD	17.3	12.4	17.4	18.8	7.1	5.7	
	Significance	NS		NS		NS		
	No. of cases	8	8	9	9	5	5	
Air	mean value	78.8	82.5	92.7	96.6	20.4	17.8	Air
30 minutes	SD	17.3	16.5	17.4	16.6	7.1	3.7	
	Significance	NS		NS		NS		
	No. of cases	8	8	9	9	5	5	
Air Tilt	mean value	82.5	83.4	96.6	96.8	—	—	Air
45 minutes	SD	16.5	16.7	16.6	16.6	—	—	
	Significance	NS		NS				
	No. of cases	8	8	9	9			
Air	Mean value	78.8	81.6	92.7	96.4	—	—	Air
60 minutes	SD	17.3	16.7	17.4	14.5	—	—	
	Significance	NS		NS				
	No. of cases	8	8	9	9			
		Heart rate		Mean brachial artery pressure				
		I Control	II O ₂	III O ₂	I Control	II O ₂	III O ₂	
		Air		Pentazocine	Air		Pentazocine	
Oxygen	Mean value	76.7	75.2	78.2	93.3	106.8	94.7	
15 minutes	SD	17.5	19.0	19.3	14.0	23.0	11.5	
between I and II	Significance	NS	NS		<0.01	NS		
30 minutes	No. of cases	6	6	6	6	6	6	

NS = not significant.

cardial infarction. Scott and Orr found intravenous morphine 10 mg, heroin 5 mg, and pentazocine 30 mg to be about equally effective, but that heroin produced pain relief quicker than did morphine or pentazocine, while the relief of pain from pentazocine was less long-lasting than that with the other two drugs. This is what would be expected from their actions in normal man (their respective durations of action being morphine 4 to 5 hours, heroin 3 to 4 hours, pentazocine 1 to 2 hours, and pethidine 2 to 4 hours (Goodman and Gilman, 1970)).

Dundee, Clarke, and Loan (1965, 1967) also found that heroin produced analgesia sooner than did morphine in normal man — and that in equianalgesic dosage it was more sedative than either morphine or pethidine. A sedative action is beneficial in myocardial

infarction in which anxiety is often a prominent feature. Scott and Orr state that morphine, heroin, and pentazocine all allayed this anxiety satisfactorily but that there was no significant degree of difference between them.

Respiratory depression Goodman and Gilman (1970) suggest that equianalgesic doses of morphine (10 mg), heroin (3 mg), and pethidine (100 mg) depress respiration to a similar extent in normal man. The equianalgesic dose suggested for pentazocine is 30–50 mg and the equidepressant dose 20 mg. The relevant doses used in these studies were heroin 5 mg, pethidine 100 mg, pentazocine 30 mg (this study) and 60 mg (Lal *et al.*, 1969). All were given intravenously. Hoel and Refsum (1969) gave 10 mg of morphine

intramuscularly. Owing to the obvious differences between these studies, it is not possible to determine with certainty whether one of these drugs has a greater depressant action in myocardial infarction than another. Maximal depression from control values after intravenous injection varied from -12 per cent P_{aO_2} (pentazocine 30 mg, 10 minutes) to -6.5 per cent P_{aO_2} (pethidine, 5 and 10 minutes) and +17.5 per cent P_{aCO_2} (heroin, 10 minutes) to +6 per cent P_{aCO_2} (pentazocine 30 mg, 10 minutes). Pentazocine 60 mg was only studied at 30 minutes. It is probable that greater depression would have been observed had studies of this dose been made earlier, since values of P_{aO_2} and P_{aCO_2} for pentazocine 30 mg, pethidine, and heroin suggest that depression is maximal between 10 and 30 minutes after intravenous injection and waning thereafter.

It is unfortunate that values for P_{aO_2} and P_{aCO_2} after intravenous morphine in myocardial infarction are too few and too scattered among authors to be of value. Keats and Telford (1964), in studies on normal man, found depression to be more prolonged by morphine than by pentazocine. This is presumably related to the shorter duration of action of pentazocine. Superficially the study of Hoel and Refsum suggests a lesser degree of depression after intramuscular injection of morphine than after intravenous injection of any of the other 3 drugs. However, they did not study their patients beyond one hour from injection (at which time depression was maximal) and it is probable that the actual degree of depression produced after morphine is similar whether the drug be given intramuscularly or intravenously (Dripps and Comroe, 1945).

Such respiratory depression is not of clinical significance in patients in whom initial P_{aO_2} values are high. However, P_{aO_2} is commonly depressed by the ventilation-perfusion abnormalities occurring after myocardial infarction. At an approximate level of 60 mmHg (dependent upon pH) the danger level of P_{aO_2} is reached from which small falls in P_{aO_2} cause disproportionately large falls in oxygen saturation below 90 per cent. Such levels are not uncommon after infarction and any further small fall provoked by analgesia is therefore dangerous.

The maximal degree of respiratory depression (both in depth and in time) observed in this study occurred in the one patient receiving a lignocaine infusion (P_{aO_2} 20% fall, P_{aCO_2} 12% rise at 10 and at 30 minutes). Whether this apparent potentiation of respiratory depression by lignocaine affects analgesic

drugs other than pentazocine is not known but seems likely.

These facts argue strongly for the concomitant administration of oxygen to all patients sustaining a myocardial infarction. In this respect it is interesting that the figures of this study suggest that respiratory depression after pentazocine is less if the patient is breathing oxygen than if he is breathing air (mean P_{aCO_2} rise 5.2% on air, 1.6% on oxygen at 30 minutes). Figures after morphine (Thomas *et al.*, 1965a) also support this suggestion. These results may be caused by the administration of oxygen modifying the response of the respiratory centre to analgesia since oxygen has been shown to depress its sensitivity (Lambertsen *et al.*, 1963).

Lal *et al.* (1969) found the alveolar-arterial oxygen tension difference ($A-aDO_2$) was reduced (i.e. improved) after a 60 mg dose of pentazocine in 10 patients who had sustained a myocardial infarction. Conversely, it was increased in 2 similar patients after morphine 10 mg. Since they considered that an increase in $A-aDO_2$ was associated with a bad prognosis they concluded that 'in the relief of pain after myocardial infarction pentazocine would seem to be preferable to morphine'.

No one would deny that a rising $A-aDO_2$ is a bad prognostic sign. Unfortunately, Lal *et al.* do not state the clinical condition of their patients studied. Pulmonary function is unstable in myocardial infarction by nature of the illness, and clinical or subclinical degrees of left ventricular failure are common. These may improve or deteriorate independent of therapy given and with consequent alterations of $A-aDO_2$. It has also been suggested that $A-aDO_2$ should only be used for the evaluation of changes in alveolar-arterial gas exchange when alveolar ventilation remains unchanged (Kim and Refsum, 1963). Alveolar ventilation is of course diminished by the hypoventilation of respiratory depression. These facts make the validity of the conclusion that $A-aDO_2$ is improved by pentazocine and worsened by morphine open to doubt. Unfortunately no other investigators have measured R (the respiratory quotient - necessary for determination of $A-aDO_2$) and consequently no direct comparisons are possible. However, if the problem is greatly oversimplified, by assuming that R is unchanged by analgesia and by ignoring hypoventilation and changes due to infarction itself, it can be stated that a disproportionately greater fall in P_{aO_2} than rise in P_{aCO_2} , after the drug, will be reflected as a worsening

of A-aDO₂ and vice versa. The studies mentioned on intramuscular morphine, intravenous heroin, and pethidine after myocardial infarction then indicate either little change or some improvement in A-aDO₂, while the results of this study actually show worsening 10 minutes after pentazocine 30 mg. If these various patients are broken down into whether or not they were suffering from left ventricular failure it becomes apparent that changes in A-aDO₂ were variable and usually slight if failure were not present, and tended to improve should it be so, irrespective of the drug given. This of course is in agreement with the well-known clinical fact that left ventricular failure is improved by strong analgesics.

Cardiovascular effects

A. Morphine and heroin

Neither of these drugs had any consistent action upon heart rate after myocardial infarction and mean changes were small. Nevertheless, morphine is known to produce occasional profound and unpredictable bradycardia such as was observed and discussed by Thomas *et al.* (1965a). These authors also encountered severe postural hypotension as a side effect of morphine – noting that such hypotension was usually accompanied by the bradycardia, but could precede it. Such postural hypotension is well known to occur after morphine but surprisingly not so after heroin – since both drugs decrease the capacity of the cardiovascular system to respond to the stress of gravitational shifts. Apart from postural hypotension both drugs produce a small but definite fall in systemic arterial pressure – maximal shortly after injection and approaching control values by thirty minutes. They are probably of comparable magnitude for each drug.

Changes in pulmonary arterial pressure after morphine in myocardial infarction have not been recorded, while those after heroin were small and inconsistent. Changes in cardiac output after morphine in normal man are small and inconsistent (Goodman and Gilman, 1970) and the findings after 15 mg intramuscularly in myocardial infarction (Grendahl and Hansteen, 1969) are in agreement with this. After 10 mg intravenously, Thomas *et al.* (1965a) found output to rise in 8 instances and remain unchanged in 7. This increase in output was certainly, in part at least, attributable to vomiting. Changes in output after heroin were variable but overall tended to fall slightly.

B. Pethidine

Rees *et al.* (1967) suggest that pethidine may have a dual action on the circulation in patients with myocardial infarction. They found an initial stimulatory phase lasting some 10 to 15 minutes from intravenous injection during which both heart rate and systemic arterial pressure was significantly increased. This was followed by a return of heart rate to control values but also by a greater and more significant fall of arterial pressure to values below the control, persistent up to 45 minutes from injection. These findings compare with an action in normal man in whom, after intravenous injection, there is an increase in peripheral blood flow and a decrease in peripheral arterial and venous resistance, sometimes accompanied by an increase in heart rate that may be alarming (Goodman and Gilman, 1970). Postural hypotension is not reported to be a side effect of pethidine in therapeutic dosage. Changes in pulmonary arterial pressure and cardiac output after the drug in myocardial infarction were small – output tending to fall and pressure to rise. Neither of these changes achieved significance.

C. Pentazocine

The cardiovascular actions of pentazocine are of considerable interest. All 4 studies of the drug indicate a rise in both heart rate and systemic arterial pressure after its use in myocardial infarction – though such rises in general only achieve significance after a 60 mg dose. This increase in systemic arterial pressure was assumed to be caused by changes in peripheral resistance. However, Levitsky *et al.* (1971), in experiments on dogs, have shown the drug to have a positive inotropic effect (as shown by changes in left ventricular dp/dt) and that this effect is blocked by propranolol. They found a very transient fall in peripheral vascular resistance but this had returned to control values before the inotropic effect was evident. They postulate that the drug has a β -stimulating effect and that this is occurring at myocardial receptor sites and is not due to suprarrenal release of catecholamines. Coronary blood flow was not affected.

Studies by Jewitt *et al.* (1970) on cardiac output after pentazocine in 15 patients with myocardial infarction showed no significant changes after a 30 mg dose. This is in agreement with the arteriovenous oxygen differences of this study. However, after a 60 mg dose output showed a significant fall at 5 minutes from the drug rising to or above

control values by 20 minutes. The same authors also studied pulmonary arterial pressure after the drug. They found this pressure to be consistently raised after both 30 mg and 60 mg and that it remained significantly raised at 30 minutes after the larger dose. Though these observations were not confirmed by the 30 mg dose of this study, they are important. Jewitt *et al.* comment that such rises in pulmonary artery pressure may be due either to worsened left ventricular function or to a direct increase in pulmonary vascular resistance. They did not measure left ventricular pressures in these patients but state that, in similar studies made on patients with angina pectoris, raised aortic and pulmonary arterial pressures were associated with an increase in left ventricular end-diastolic pressures. These results certainly suggest that a raised pulmonary arterial pressure after the drug is due to worsened left ventricular function.

These different findings provide a nice paradox. In an experimental situation the drug appears to have a beneficial effect upon the heart, while in a clinical situation the effects are potentially deleterious. However, unlike the findings of the experimental study – pentazocine provoked a significant rise in peripheral resistance after the 60 mg dose given after myocardial infarction. That an increase in peripheral resistance was not the sole factor operative in causing a rise in systemic pressure was shown by there also being a significant rise in systemic pressure 5 minutes after the 30 mg dose without change in peripheral resistance. General physiological principles associate a rise in peripheral resistance with a fall in heart rate which does not occur after the drug. Accordingly, in human myocardial infarction the rise of pressure is probably caused both by a rise in peripheral resistance and by a local β -stimulating effect on the heart.

However, excess catecholamine release is a known feature of myocardial infarction. The actual amount released correlates with the severity of the infarction (Rosenbaum and Doyle, 1970). Accordingly, the more severe the infarction the greater the endogenous β stimulation of the heart and the less will myocardial β receptors be responsive to exogenous stimulation. Any rise in peripheral resistance caused by pentazocine will cause simply an increased after-load, badly tolerated by a heart severely stressed by myocardial infarction – hence, a rise in left ventricular end-diastolic and pulmonary artery pressures.

Nausea and vomiting These side effects are particularly unwelcome since bradycardia

and hypotension may be caused by nausea, while the act of vomiting causes a considerable increase in cardiac work (via rises in systemic arterial pressure, cardiac output, and heart rate – Saprú, 1966). Both nausea and vomiting are seen sufficiently frequently after myocardial infarction, without prior analgesia, to be regarded as manifestations of the disorder. Unfortunately all four drugs may also cause these symptoms independently. In any study of these drugs in myocardial infarction it is difficult to determine how much the nausea or vomiting observed is due to the disorder and how much due to the drug. Scott and Orr (1969) in their study on heroin 5 mg, morphine 10 mg, and pentazocine 30 mg after myocardial infarction did not find any obvious difference between these drugs. They were obviously surprised at this and indeed these findings run counter to studies undertaken on normal man.

Morphine is usually regarded as the yardstick by which other drugs are measured – morphine itself being considered to show a 40 per cent incidence of nausea and a 16 per cent incidence of vomiting after a 15 mg dose (Goodman and Gilman, 1970). Heroin is certainly considered to be less emetic than is morphine (Douthwaite, 1953; Dundee *et al.*, 1967). Opinions are divided over pentazocine but their consensus appears to be that vomiting is less common (Goodman and Gilman, 1970). All 3 drugs can additionally produce dizziness after intravenous injection and this is more common after pentazocine than after morphine or heroin. This dizziness is also a side effect of intravenous pethidine. Popular belief thinks pethidine to be less emetic than morphine. This is not supported by fact – indeed, Dundee *et al.* (1965) actually found nausea and vomiting to be more common than after morphine.

The incidence of nausea and vomiting after analgesia is undoubtedly dose related. Dundee *et al.* (1967) found its incidence to rise sharply when doses of 10 mg morphine or 5 mg heroin were exceeded. It also seems likely that the route of administration may be important, but information is scant. Rapid intravenous injection should certainly be avoided.

It is common practice to administer phenothiazines concurrently with the opiates in order to avoid vomiting and enhance sedation. Since the phenothiazines not only augment opiate induced respiratory depression but also greatly increase the risk of hypotension (Goodman and Gilman, 1970), this practice is not to be recommended.

Summarizing the intravenous actions of the four drugs, it seems that neither pethidine

nor morphine are suitable for pain relief after myocardial infarction. The sedative action of pethidine is less and the incidence of complications – particularly cardiovascular – probably higher than with the other drugs. Morphine has a high incidence of emetic side effects and may cause profound and unpredictable hypotension. The choice therefore appears to lie between pentazocine and heroin. Pentazocine may be less emetic and has what appears to be an attractive side effect – the ability to raise systemic blood pressure. Unfortunately this rise in blood pressure after myocardial infarction is almost certainly due little to a positive inotropic action and largely to a rise in peripheral resistance. There are those who believe a rise in blood pressure to be entirely beneficial, stating that in severe myocardial ischaemia the coronary arteries are maximally dilated and therefore myocardial blood flow is entirely pressure dependent (Brachfeld and Gorlin, 1960). While this viewpoint has much to recommend it, it is absurd to raise the blood pressure further in a patient whose blood pressure is already adequate – the more particularly since oxygen, which should be given to all patients, has just this action (Thomas, Malmcrona, and Shillingford, 1965b). The sedative effect of heroin is probably better, its cardiovascular effects small, and its duration of action long. In most cases it seems preferable to pentazocine. J. P. was in receipt of a Sheldon Research Fellowship from the Birmingham Regional Hospital Board.

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Requests for reprints to Dr. J. Pilcher, Clinical Research Institute, Royal Infirmary, Sheffield, S6 3DA.