

2. The premature stimulus should not (a) cause overdrive suppression of the sinus pacemaker; (b) change sinoatrial conduction time in the returning beat; or (c) shift the sinus pacemaker location.

3. The anterograde and retrograde sinoatrial conduction times should be equal.

Our studies in conscious animals and other *in vitro* studies<sup>1,2</sup> suggest that these criteria are seldom, if ever, fulfilled. Therefore we would be surprised if there were a good correlation between sinoatrial conduction time measured using the single premature stimulus technique and sinoatrial conduction time measured by direct recording of sinus potential.

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#### CHROMONAR AND CORONARY STEAL

Wartier and co-workers<sup>1</sup> reported that the intravenous administration of chromonar (Intensain®) induced coronary steal after acute occlusion of a peripheral branch of the left anterior descending coronary artery. This decreased collateral flow to the ischemic region and increased the extent of myocardial infarction. One wonders, however, whether the methods used were sufficient to prove these statements.

First, the dose used (8.0 mg/kg) is two to four times larger than the recommended dose for animal experiments<sup>2</sup> or human treatment<sup>3,4</sup> and should have had beneficial effects on oxygen supply to the heart and cardiac metabolism. Second, after intravenous administration, chromonar is hydrolyzed after 10 minutes to its metabolite, the corresponding acid, which has a plasma half-life of 1 hour in the dog.<sup>5</sup> Thus, chromonar could hardly evoke effects on the early ischemia because it was administered 10 minutes after the onset of ligation. Furthermore, about half of the drug's effects vanished 1 hour after administration during the 2 hour occlusion time. Third, the measured endocardial collateral flow (their Table I) of 1.18 ml/min per g (= 118 ml/min\*100 g) seems extremely high and cannot be explained either by the ventilatory or the preparatory conditions. However, total coronary flow ranged between 50 and 65 ml/min (their Fig. 2). The normal coronary collateral flow was reported to be an average of 12 ml/min\*100 g with a total coronary flow of about 55 ml/min under comparable experimental conditions.<sup>6</sup> Therefore, it seems doubtful that collateral flow was measured properly. Fourth, the reported decrease in collateral flow within the ischemic zones is not adequately explained. A decrease in collateral flow concomitant to a flow increase in the supplying epicardial artery (that is, the left circumflex artery) depends on (1) the resistance of the left circumflex artery, and (2) on the pressure

gradient over the collateral vessels; that is,  $PG = 1 - (AoP - PCP/AoP)(AoP = \text{aortic pressure; } PCP = \text{post-stenotic coronary arterial pressure})$ . Unfortunately, post-stenotic coronary arterial pressure was not measured in the study. Because no significant changes in blood pressure were reported by the authors, and the epicardial left circumflex arterial resistance is negligible under vasodilation, the collateral flow indeed should have been at a constant level when coronary flow in the left circumflex artery increased because of the lack of a sufficient pressure gradient. In addition, Schaper and co-workers<sup>7</sup> have shown that collateral flow is redistributed during the ensuing hours after coronary arterial occlusion: It decreases in the subendocardium and increases in the subepicardium. The total amount of necrosis is therefore a function of the amount of collateral flow and how it is distributed with time. It seems that the "chromonar-induced" shift in collateral flow after occlusion of the left anterior descending artery occurred as a naturally occurring pathophysiologic event independent of the drug's effect.

Finally, the measured infarct size (Table III) is too small in the control group. A recent paper<sup>8</sup> reported an infarct size of about 14 percent of the perfusion area of the small peripheral left anterior descending arterial side branch after 90 minutes of occlusion. Also, the authors did not express the area of necrosis relative to the area at risk of the occluded vessel so that the size of the artery significantly influenced the final infarct size. The number of animals seems to be too small to elucidate the naturally occurring anatomic variations in the left anterior descending perfusion area.

Besides these objections, the study suggests a general comment. The steal phenomenon after coronary occlusion is a condition that cannot be compared with clinical conditions where the term "steal" is used to explain anginal pain rather than the sequence of acute myocardial infarction. The measurement of "steal" in acute coronary occlusion is technically very difficult because the acute collateral flow is very low.<sup>8</sup> So far it remains unclear whether a pure flow-induced steal plays an important role in the development of acute coronary occlusion or what the clinical consequences may be.

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#### REPLY

In summary, our study demonstrated that maximal vasodilation of the coronary vasculature by chromonar (Intensain®)