Reduction of Coronary Blood Flow during Coronary Artery Spasm Occurring Spontaneously and after Provocation by Ergonovine Maleate

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SUMMARY A 50-year-old man suffering from recurrent chest pain accompanied by transient ST-segment elevation developed spasm of the left anterior descending coronary artery after receiving ergonovine maleate. During spontaneous chest pain, thermodilution coronary sinus blood flow fell from 96 ml/min to 46 ml/min, while the coronary sinus arteriovenous oxygen difference widened from 9.82 volumes percent to 11.3 volumes percent. During spontaneous relief of pain, coincident with resolution of the ST-segment changes, coronary sinus blood flow gradually rose to 135 ml/min, while coronary sinus arteriovenous oxygen difference narrowed to 6.82 volumes percent.

CHEST PAIN occurs as a result of transient coronary artery spasm in some patients with variant angina pectoris. Reduction in myocardial perfusion, suggested by accompanying ST-segment elevation, recently has been documented by thallium-201 imaging. The magnitude of the reduced coronary artery blood flow that occurs as a consequence of coronary artery spasm has not been measured, however, This report demonstrates the alteration of coronary sinus blood flow, measured by the thermodilution technique, that accompanies spontaneous and ergonovine maleate-induced coronary artery spasm in a patient with variant angina pectoris.

Case Report

A 50-year-old male was admitted to the coronary care unit in December 1976 because of recurrent chest pain. Since 1973 he had experienced similar episodes of compressive, substernal discomfort radiating to the left elbow, occurring at rest, often in the early morning hours waking him from sleep, and resolving spontaneously or after sublingual nitroglycerin. Physical examination was normal. A resting electrocardiogram had T-wave inversions in the precordial leads. An electrocardiogram during pain showed ST-segment elevation in leads V₁ to V₄, after relief of pain by nitroglycerin, the ST segments returned to the baseline. Cardiac enzymes were normal, and no evolutionary changes of myocardial infarction occurred in the electrocardiogram. Repeated episodes of pain were accompanied by transient ST-segment elevation and all were relieved by nitroglycerin. The patient performed a graded exercise test on a bicycle ergometer, achieving a maximal workload of 900 kg/min for 3 min. The test was stopped because of fatigue, and the electrocardiogram showed no ischemic changes. Coronary arteriography performed on the third hospital day showed a mild (<50%) focal narrowing of the mid left anterior descending coronary artery (LAD). The remainder of the vessels were normal. Because coronary artery spasm did not occur spontaneously during the routine procedure, and because the organic lesions were unlikely to have produced the clinical presentation, ergonovine maleate 0.05 mg was administered intravenously in an attempt to provoke coronary artery spasm. Chest pain and ST-segment elevation in leads V₁-V₄ occurred 3 min after administration of the drug, and coronary arteriography showed occlusive spasm of the LAD in its entire length distal to the first diagonal (fig. 1). Nitroglycerin, 0.4 mg sublingually, provided prompt relief of pain and spasm.

To gain further insight into the pathophysiology of our patient's problem, we brought him to the cardiac catheterization laboratory the next day to measure coronary sinus blood flow and to administer thallium-201 intravenously during coronary artery spasm. The risks of the procedure were explained to the patient and he gave his informed consent in accordance with the Stanford University Medical Committee on the Use of Human Subjects in Research. A thermodilution catheter was inserted approximately 5 cm into the coronary sinus from the left antecubital vein and stabilized at the venous entry site to avoid migration of the catheter within the coronary sinus. The catheter tip was visualized frequently by fluoroscopy, with reference to bony landmarks, to confirm stability of catheter position. Coronary sinus blood flow was measured using the technique of Ganz et al. by constant infusion of room-temperature 5% dextrose in water at a rate of 54 ml/min. Blood pressure was monitored from a short...
catheter in the femoral artery, and the lead V₅ electrocardiogram was recorded.

Shortly after a baseline determination of coronary sinus blood flow was made, and arterial and coronary sinus blood samples were collected for measurement of oxygen content, the patient complained of chest pain, occurring spontaneously and accompanied by ST-segment elevation. Arterial and coronary sinus blood collection was quickly repeated and immediately thereafter a measurement made of the coronary sinus blood flow. Spontaneous reduction of pain occurred after about two minutes, during which time coronary sinus blood flow was continuously measured (fig. 2). Immediately after discontinuing the coronary sinus infusion, arterial and coronary sinus blood samples were obtained. Several minutes later, while the patient remained free from pain, and after coronary sinus blood flow measurements were repeated to confirm re-establishment of a new basal state, ergonovine maleate, 0.05 mg, was administered intravenously. Approximately three minutes later, the patient complained of chest pain, and ST-segment elevation occurred. Thallium-201, 2 mCi, was injected intravenously and the measurement of coronary sinus blood flow repeated. Phentolamine mesylate (Regitine) 10 mg was given intravenously and after relief of pain, a third successive blood flow measurement was made (fig. 3). Ten minutes later the myocardial distribution of thallium-201 was measured in anterior, 45° left anterior oblique, and lateral projections, using a portable Ohio Nuclear camera. Scintigraphy data were stored on magnetic tape, and after interpolative background subtraction the images were analyzed using a 14-level gray scale (fig. 4).⁹,¹⁰

Results and Discussion

Coronary sinus blood flow during spontaneous pain fell 52%, from a control of 96 ml/min to 46 ml/min, whereas

![Figure 1](image_url)  
**Figure 1.** Single frames from the cineangiogram taken during selective left coronary arteriography in the right anterior oblique projection. The inset of each frame contains the lead V₅ complex recorded immediately before the coronary injection. A) Control. The left anterior descending coronary artery (LAD) has a minor (< 50%) irregularity proximally (arrow) and is normal distally. B) During ergonovine maleate-induced chest pain. The LAD distal to the first diagonal is completely obliterated by spasm while lead V₅ shows ST-segment elevation. C) After relief of chest pain. LAD spasm has resolved, and lead V₅ has returned to the control pattern.

![Figure 2](image_url)  
**Figure 2.** Continuous recording of thermodilution coronary sinus blood flow, blood pressure and V₅ electrocardiogram during relief from spontaneous chest pain. The coronary sinus injection was begun (vertical arrow) immediately after collecting coronary sinus sample for determination of oxygen content at the peak of chest pain, accompanied by ST segment elevation (slanted arrow). Flow reached a nadir of 46 ml/min, and gradually rose to 135 ml/min as the pain eased and the ST-segment returned to the control state. The blood pressure remains constant at 145/80 mm Hg. The coronary sinus arteriovenous oxygen difference (A-VO₂) narrows as pain is relieved. A baseline measure of coronary sinus flow recorded moments before the onset of pain was 96 ml/min, and coronary sinus A-VO₂ was 9.82 volume percent.
during ergonovine maleate-induced pain, flow fell 40%, from 110 ml/min to 66 ml/min. No marked changes in heart rate or blood pressure preceded the onset of pain in either instance. As the pain eased, coronary sinus blood flow gradually rose to 135 ml/min, coincident with a return of the ST-segment to the pattern in the control state. After relief of ergonovine-induced pain, a similar overshoot above the control level of coronary sinus blood flow occurred, to 142 ml/min (figs. 2 and 3).

The thermodilution technique is especially suited to measure changes in coronary sinus blood flow, but does not allow quantitation of blood flow per unit weight of myocardial.
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...ium perfused. Previous studies to determine reproducibility in our laboratory, using an analysis of 26 duplicate determinations during the basal state or during stable atrial pacing in 18 patients, showed a mean change between measurements of 4.0% ± 1.7% (± SEM) (unpublished observations). Therefore, the flow measured during pain, in the absence of a change in catheter position, represents a significant reduction compared with control values. The coronary sinus drains approximately 90% of the inflow from the LAD as well as a portion of circumflex flow. Thus, major alterations of flow in the LAD are likely to be represented by similar changes in coronary sinus flow although the absolute values will vary depending upon individual anatomic variations and the presence of fixed obstructive disease.

Our results, therefore, indicate that blood flow in the LAD was critically reduced during both spontaneous and ergonovine-induced pain. The ST-segment elevations that developed during pain in both instances mirrored the electrocardiographic changes that occurred during angiographically-proved spasm of the LAD and, accordingly, are likely to be a result of coronary artery spasm. Thus, we conclude that spasm of the LAD produces a marked limitation in blood flow which is reflected by a reduction in coronary sinus flow.

The extensive ST-segment elevations that occurred in our patient during spasm are suggestive of transient transmural ischemia of the septal region and anterior left ventricular wall, a pattern compatible with a severe limitation of LAD flow. Further evidence for a marked reduction rests in the analysis of the arterial and coronary sinus oxygen content during coronary spasm and after relief of spasm. The coronary sinus arteriovenous oxygen difference (A-VO2) widened during spasm from 9.82 volumes percent to 11.3 volumes percent and narrowed to 6.82 volumes percent after release of spasm. In compensation for limitation of flow, myocardial extraction of oxygen increased, as represented by widening of the coronary sinus A-VO2. Although myocardial oxygen extraction is believed to be near maximal during the basal state and oxygen delivery to be flow-limited, it appears that during states of markedly reduced flow the myocardium retains the capacity, at least transiently, to extract a greater amount of oxygen from the blood. The thallium-201 study adds further evidence for regional hypoperfusion during spasm: a defect appears in the area supplied by the LAD that correlates with the electrocardiographic changes (fig. 4).

After relief of pain and resolution of ST changes, suggesting release of coronary spasm, the coronary sinus blood flow rose to 130% to 140% of the control flow, coincident with a marked narrowing of the coronary sinus A-VO2. These data are consistent with a hyperemic response of the coronary circulation after spasm-induced myocardial ischemia. The scintigram taken four hours after release of spasm showed reperfusion of the previously ischemic area (fig. 4), confirming transience of the flow deficit and supporting the other data demonstrating restitution of flow.

Our report supports the thesis that a limitation of coronary sinus blood flow is present with spasm of a large epicardial artery. We believe this is a primary pathophysiological correlate of this clinical syndrome. Spasm provoked by ergonovine maleate produces coronary hemodynamic effects similar to those accompanying spontaneously occurring spasm. Finally, our findings suggest that coronary spasm is accompanied by increased myocardial oxygen extraction and that a hyperemic response occurs after release of spasm.

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References

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