Editorial:  
Regional Streptokinase in Myocardial Infarction 

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IN THIS ISSUE of Circulation, Mathey and co-workers report on a large group of patients who had transmural myocardial infarction with early coronary angiography and intracoronary streptokinase. The authors are to be complimented for their skill and for the effort required to maintain emergency angiographic teams and facilities.

This work adds evidence that intracoronary thrombosis is a part of the occlusive coronary process in the early hours of infarction. It confirms that lysis of this thrombus can reestablish angiographically obvious antegrade coronary flow. This work also supports the recent experience that intracoronary nitroglycerin given in large doses seldom reverses complete coronary occlusion, contrary to the report of Oliva and Breckinridge.

The size of a myocardial infarction must be determined by the size of the myocardial zone supplied by an occluded coronary artery and by the availability of collateral circulation. It must secondarily be determined by many other factors, delineated by Maroko et al. Clinical trials of pharmacologic agents for infarct reduction are concentrating on these secondary factors. Propranolol, hyaluronidase, steroids and glucose, insulin and potassium have been or are being studied. None of these agents has produced consistent and easily demonstrable myocardial salvage. Other interventions have been designed to reduce the coronary flow deficit. Nitroglycerin has produced mixed results. Calcium antagonists, which affect both coronary flow and myocardial oxygen demand, have not undergone conclusive trials in man. Even attempts to augment collateral flow with the intra-aortic balloon pump have not been uniformly successful.

Acute coronary occlusion with thrombosis produces a distal flow deficit of graded intensity, depending on immediately available collateral circulation. This problem is different from the chronic situation where the significance of collateral circulation has been both challenged and confirmed. The acute problem can be identified by early angiography of both coronary arteries. An angiographically avascular left ventricular myocardial zone will predictably undergo extensive necrosis. A collateralized myocardial segment has a less predictable outcome. Unfortunately, Mathey and co-workers do not report the acute angiographic results of both right and left coronary opacification. Pretreatment angiography was limited to visualization of the "coronary artery judged to be occluded." Thus, the collateral pathways available to their patients are unknown. The reader is also unsure of clinical changes in the patients between admission and streptokinase treatment and the course of ST elevation during this interval. ST-segment improvement between admission and therapy would correlate with collateral flow and would give some information about the urgency for this reflow procedure. This may be especially true for patients with inferior infarction (26 of the 41 patients presented), in whom collateral pathways may be more available and in whom rapid resolution of ST-segment elevation may occur without invasive therapy.

The authors also demonstrate a significant increase in ejection fraction in the weeks after admission in patients in whom reflow was successfully established (their figure 8). Four patients showed remarkable improvement, with ejection fractions rising from below 30%. However, the majority of reflowed patients showed an ejection fraction above 40% immediately after streptokinase. It is tempting to conclude that this preservation of ejection fraction is a consequence of clot lysis. However, the rate of return of ventricular function with reperfusion after prolonged ischemia may not be this rapid. If return of function is slow, another explanation is needed for the higher early ejection fractions in the reflowed group. Better function could be the result of undescribed collateral circulation or the result of smaller zones of injury, such as those produced by occlusion of a moderate-sized right coronary artery. A collateralized patient with a smaller infarction could show improvement in ejection fraction in the postinfarction period similar to some of the successfully treated streptokinase patients.

The reversal of shock in three patients was dramatic and indicates the power of the technique. Shock secondary to a large avascular necrotic zone carries a mortality, despite all therapy, of about 50%. The 0% mortality in this paper is a praiseworthy beginning to the elimination of this problem. One could conclude that this evidence for myocardial salvage is an indication for administration of streptokinase to all patients.

*MILIS (Multicenter Investigation of Limitation of Infarct Size).

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with myocardial infarction. This approach would be conceivable if the technique had no morbidity, produced a stable cessation of injury over the long term, and was the only method by which injury could be reduced, not to mention expense.

The morbidity of acute coronary angiography was 2.8% in the recent report from Spokane. Angiography produced ventricular fibrillation twice in the report of Mathey et al. Instrumentation of the coronary arteries with special catheters and guidewires carries the risk of coronary dissection that can produce more proximal occlusion and, in rare cases, perforation. Regional streptokinase administration in the heparinized patient may induce bleeding. Reperfusion can induce ventricular fibrillation, and distal coronary embolization of clot may induce other arrhythmias, such as complete atrioventricular block. Clot lysis often does not produce a stable cessation of injury because residual coronary stenosis is usually high-grade and reocclusion may occur. In some cases, an ischemic zone supplied by an unstable coronary artery may be more hazardous than unreversed coronary occlusion with more uniform necrosis. Therefore, some investigators have recommended coronary vein bypass surgery for patients who respond well to streptokinase in whom the infarction is small but in whom the zone of continued jeopardy is large.

Other methods do control myocardial injury in some patients. Rapid ST-segment resolution and preservation of R waves have been seen with several interventions and are occasionally the result of hospitalization and administration of morphine and oxygen. This experience emphasizes the importance of serial observations in individual patients rather than simply quantifying the degree of injury at the time of admission. Serial observations can be used to direct patients who are rapidly improving to more conventional therapy.

Patients who resist pharmacologic attempts to control injury have the greatest need for myocardial reperfusion. The major problem with this group is the short time from the onset of injury to irreversible necrosis. Mathey and co-workers reestablished flow 2–4 hours after the onset of acute myocardial infarction, which is remarkable considering the delays in many hospitals. Nevertheless, all but six of the 30 recanalized patients showed electrocardiographic evidence of some transmural infarction. We do not suggest that the treatment was too late for any beneficial effect; only that others who seek to duplicate this kind of salvage must move with comparable speed.

Regional streptokinase treatment requires specially trained teams and available catheter laboratories and may require surgical intervention before therapy is complete. It could prevent major myocardial infarctions, and therefore, shock. In patients who present very early, it may prevent infarction almost entirely. Investigations in this area may change the responsibilities of the angiographer from the recording of coronary events to a participatory role in their reversal. It will be fascinating to see this form of therapy take its place in the management of the acute coronary patient.

References

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