

# Preserving Myocardium during Acute Myocardial Infarction

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**INTRODUCTION:** On February 18th, 2002, members of the International Gruentzig Society gathered in St. Lucia, West Indies, for an exciting meeting that brought together an eclectic group of cardiologists, radiologists and vascular surgeons with representatives from the pharmaceutical and device industries. The co-directors of the meeting, Kirk Garratt from the Mayo Clinic and Jim Zidar from Duke, put together an excellent group of topics that focused on difficult problems facing cardiovascular specialists. The topics included preserving myocardium during acute myocardial infarction, supporting patients in shock, preventing restenosis with drug-coated stents, intracranial interventions, the intractable angina patient, and identifying vulnerable plaque. A major goal of Drs. Garratt and Zidar was to encourage the participation of everyone present and tap the extensive experience of the experts in the field, followed by lengthy discussion sections that were moderated by a leader and panel of experts in the area. This format was extremely successful and generated many new ideas related to these challenging problems faced by cardiovascular specialists. A unique feature of this meeting was the interaction between physicians and representatives from industry. These discussions focused on pricing of drug-eluting stents, the interaction of cardiologists, neurologists, neuroradiologists and neurosurgeons in acute stroke intervention programs, collaborative efforts to identify populations of patients with vulnerable plaque and the multi-therapeutic approach to the “no-reflow” problem after acute myocardial infarction interventions. In addition, there was extensive discussion on the challenges in training physicians to manage the entire vasculature of the patient.

Over the next few months, the discussion sessions from this meeting will be published in the *Journal of Invasive Cardiology*. This issue of the *Journal* includes the transcript from the discussion session entitled “Preserving Myocardium During Acute Myocardial Infarction.” Dr. Howard Cohen moderated this session and the panel included Drs. Tom Linnemeier, Paul Overlie and Brian O’Murchu. I think that you will find this discussion both informative and provocative.

*Richard E. Shaw, PhD, FACC*

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**Moderator:** *Howard Cohen, MD*

**Panel Members:** *Tom J. Linnemeier, MD, Paul A. Overlie, MD, Brian O’Murchu, MD*

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**Howard Cohen:** What routine pharmacologic therapy are you currently using in your lab for patients with acute myocardial infarction? Do you use anything in a routine fashion, or do you restore blood flow and see what happens? Are you routinely using IIb/IIIa receptor antagonists or adenosine?

**Paul Overlie:** As you might imagine, I am not the one to ask about pharmacologic therapies. We handle a large number of acute myocardial infarction therapies every year and have long believed that minimal but rapid instrumentation of acute infarcts is the best way to treat them. I always worry about the correct sizing of the devices used when no-reflow occurs. Our routine strategy in a patient with acute myocardial infarction is to give heparin, aspirin, Beta-blockers, and sometimes Plavix if there is time. We then take the patient to the cath lab for cardiac catheterization to determine risk stratification, find the culprit artery, open it, and now stent it as well. Roughly a third of the time, IIb/IIIa inhibitors are used,

but otherwise just heparin. I don’t know how frequently no-reflow occurs — perhaps others can answer that question — but it is certainly extremely uncommon in our experience. In my opinion, the timeliness of the intervention is the most crucial factor in these cases.

**Howard Cohen:** That is very clear. Much of the data show that the earlier we can intervene, the better the outcome. Tom, what is your routine “cocktail”?

**Tom Linnemeier:** The problem I have with no-reflow is that the predictive value of which patients will have no-reflow is extremely low. I agree that if you look at the statistics, there is a higher incidence of no-reflow the longer you wait to take the patient to the cath lab. I also agree that adenosine is a nice cocktail that works sometimes, but not every time. I think the AngioJet, because of its size, can sometimes actually make distal embolization worse. However, in some of the trials, it has been shown to lessen distal embolization. The whole concept of no-reflow is a very interesting one. Although I treasure all the moments I had with Andreas Gruentzig, I think the only thing he was wrong about was in the area of clinical outcomes. That is, you don’t want to throw anything downstream when performing routine angioplasty, and yet I think we do just that all of the time. It is probably more apparent during acute myocardial infarction, less apparent in angina and somewhere in

between in the case of unstable angina. Of all the topics that Kirk Garratt and Jim Zidar put on the agenda for this meeting, this particular one has the most potential to be solved within the next three to five years. I think it will be solved with a combination of distal embolic protection devices and pharmacologic solutions such as IIb/IIIa inhibitors. A succession of trials have shown the superiority of acute angioplasty over medical therapy or thrombolytics, yet the biggest problem we currently face is that a large number of patients still don't ever get to the cath lab. The problem is primarily a logistical one in many instances, and the only way to solve it is to have more interventional cardiologists on shift work if possible. Many cardiologists resist the idea, however.

**Howard Cohen:** Brian, in terms of pharmacology in the cath lab, what are you currently doing at Temple?

**Brian O'Murchu:** Our approach has been very similar to that of the other panel members here. That is, we try to get the patients to the cath lab quickly. There are a number of interesting possibilities related to the area of direct thrombin inhibitors which have not been looked at in this context. The free fatty-acid inhibitors also have some potential in terms of protecting from ischemia in myocardium, and I think it is worth investigating whether they might have an effect on microcirculation as well. We have not been innovating "outside of that box." Also, we should discuss the importance of regularly updating our "door-to-balloon" time because we think we do a good job and have all said that the door-to-balloon time is perhaps the most powerful agent we currently have. I wonder how well we are all doing in that regard.

**Howard Cohen:** Those are very good points, Brian. Let me ask the panel members, in regard to pharmacology, in what percentage of patients are you using a IIb/IIIa receptor antagonist and are you administering it I.V. or I.C.?

**Brian O'Murchu:** We administer it intravenously in the case of myocardial infarction in those patients who meet the typical ST-segment elevation criteria. We administer it in 90% of our patients.

**Howard Cohen:** Tom, how about your lab?

**Tom Linnemeier:** Yes. We administer it intravenously. There are data out there to support large molecule versus small molecule during acute myocardial infarction.

**Howard Cohen:** And Paul, how about your lab?

**Paul Overlie:** Somewhere between 30% and 50%, depending on whether the patient comes from well out in our region or from nearby.

**Howard Cohen:** Let me ask you another question. At our institution, we frequently receive calls from allied hospitals located some distance away. Thus, I would say that at least 50% of our intervention patients, or perhaps even 75%, are flown in by helicopter. Western Pennsylvania has a helicopter system established in which helicopters are available throughout the region, making it possible to transport patients fairly quickly to the hospital. However, there is still a time delay. At the very best, there is about a 30-minute delay from the time we receive the call until the patient arrives in our cath lab. That delay can be up to an hour or an hour and

a half if the patient is having a problem — or even two hours sometimes. If the patient is already in your hospital's emergency room and is coming directly to your cath lab, it is of course easy to keep the door-to-balloon time down. But if the patient is, say, an hour or more out, what do you think about the combination therapy of lytic and IIb/IIIa? Do you recommend that to the emergency room physician or do you tell him/her to just send you the patient for treatment?

**Tom Linnemeier:** Yes, that is the dilemma. When I was at Indiana Heart Institute, we actually got to the point where there were up to 88 cardiologists spread across the state. There were about 45 cardiologists at the mothership of St. Vincent Hospital and the remainder at various clinics in Lafayette, Kokomo, Anderson, etc. The cardiologists who are out in the field — let's say Lafayette — are located about a 45-minute drive from St. Vincent Hospital, which represents maybe about a 20-minute helicopter ride from the mothership hospital. These cardiologists absolutely must know what the patient is going to receive on the other end when he/she arrives at St. Vincent. And it is extremely difficult for those doctors to have a syringe full of t-PA or t-NK in their hand and realize that they can achieve a 60–70% reperfusion rate within the next hour to not give that drug unless he/she is absolutely positive that someone is on the other end waiting with an open cath lab — no matter when, 24 hours a day. It would depend, therefore, on the time of day. If the event occurs during the daytime, there would be an open cath lab between 7:00 am and 7:00 pm and most patients would be sent to the cath lab at St. Vincent Hospital where they are likely to receive a IIb/IIIa receptor blocker, aspirin, beta-blockers, etc. If, however, the event occurs at 2:00 am, the scenario is usually different. Typically, patients in the outlying areas would end up receiving the lytic — sometimes the IIb/IIIa — and then would be transported to St. Vincent. The patient often would stabilize, but if not, he/she would be sent to the cath lab. I am not saying that this is the best system, but that's the way it worked in Indiana. As I said earlier, we interventional cardiologists are an odd bunch because we pretend we are not working when we are on call, but we really are working. Some nights you get sleep, while others find you up answering calls. So I think we should just call it what it really is: work! And if you truly believe that PTCA for acute myocardial infarction is the best thing to be doing for patients, then you ought to be available to do it 24 hours a day, seven days a week, 365 days a year.

**Brian O'Murchu:** I have a quick question, Tom. Were the patients getting full-dose lytic therapy?

**Tom Linnemeier:** Yes.

**Howard Cohen:** We have six interventional cardiologists at our institution, so it depends on the interventionist and the time of day. If I know the patient is an hour or more away, I advise the physician to administer a half-dose of lytic and a IIb/IIIa inhibitor and then have the patient brought in for evaluation. If the patient is totally pain-free and the ST-segments have completely resolved, we may not study the patient that night, but bring the patient in the next morning. If, on the

other hand, there is any sign of an ongoing problem, we will study the patient at that time and intervene if necessary.

Let me ask the panel this question: In patients with acute myocardial infarction, what percentage of them will be treated with a distal protection device when it becomes readily available?

**Paul Overlie:** I am going to skip the question right now about distal protection devices because I want to comment on our institution's long history with acute infarct therapies. Two-thirds of our patients come from outside our county. A network of active air transportation with a variety of aircraft are available. Throughout the years, my colleagues and I have watched the thrombolytic trials in progress and have been involved in most of the acute infarct trials. We have also been in discussion with Steve Ellis and colleagues at the Cleveland Clinic about the value of rescue angioplasty and agree that it is a very valuable therapy, but we are often accused of the "in our hands" issue that comes with a lot of the investigations. That is, you have a small group of skilled operators who are used to doing the procedure. For many years, we took virtually every patient to the cath lab. Listening to this discussion today, we have also lapsed into that too. We can transmit 12 leads from helicopters, from the ground, anywhere. I can look at the situation from my home, and if I can see the 12 leads come through, the ST-segments are no longer elevated and the patient is pain-free, I won't necessarily have the patient brought immediately to the cath lab. But for those patients with ST-segment elevation infarcts, we find that it's crucial to get them to the cath lab early, minimally invade them and get their arteries open.

**Howard Cohen:** To what extent do you think primary angioplasty should be performed in outside hospitals with skilled operators where there is no surgical back-up? As you know, in certain states such as Massachusetts, an ongoing program called Special Project looks at primary angioplasty in small hospitals performed by physicians who are skilled but have no surgical back-up. In Minnesota, I believe, a similar type of program exists. Let's move ahead now and we can perhaps revisit that topic later.

I would like to return to the question about the percentage of interventions for acute myocardial infarctions where there is thrombus burden for which distal protection devices will be used: 50%, 100%?

**Brian O'Murchu:** I think our institution does this extremely well. Because of the technical ease of the procedure we perform, I would say that roughly 5–10% of the patients we treat receive distal protection devices, and these are patients in whom we visually detect a large mass of thrombus.

**Howard Cohen:** Tom, what do you think?

**Tom Linnemeier:** I agree that you don't get into trouble very often with PTCA in acute MI, but when you do, you do. With a good embolic protection device, that is to say, one that can catch something, there would be no reason not to use it every single time. And I would bet that in the acute MI situation, you would end up catching a lot of stuff in the basket or filter each time. The problem, I believe, is that dur-

ing an acute MI, the device currently available is somewhat cumbersome to use. Some of the devices that Gary Roubin showed in his presentation, however, have the potential to "catch crap" as I call it. And I don't think that having "crap" downstream is a very good thing for anyone. So if there was a good "crap catcher," I would use it.

**Howard Cohen:** A small device that is easily deployed would be useful. The other point is that we don't always do as good a job as we think we do with the flow we appear to achieve — and the beauty is always in the eye of the beholder, especially at 4:00 am! We often say, "That's good; we've got the artery open." But the flow is actually not very good. In support of that, the size of the infarcts we see and the size of the infarcts seen by nuclear studies, even in patients who achieve good epicardial blood flow, are usually fairly sizable. The extent to which the wall motion and the regional and global ejection fraction improve is often rather minimal, even though the vessel has been opened. I think we can do better with other mechanisms to improve blood flow. So I would agree with Tom; if we had a device that was well designed and easy to deploy, I can't see why we wouldn't use it 100% of the time. This assumes, of course, that the cost of such a device would be reasonable.

**Jeff Werner:** We have performed a fair amount of acute angioplasties as well, and I am interested in the fact that it is rather uncommon, it seems to me, to find a lot of large, distal thrombus. Perhaps occasionally there is a small cut-off vessel if you start with thrombus, particularly if you are administering an agent such as IIb/IIIa. We've seen in post-procedure studies some cases in which something like a small PDA cut off at the end is gone the following day, with flow resumed. Along with your comments on microvascular problems, what troubles me most has been to have the artery open and know that there is either very little capillary flow or you just can't do anything. You try vasodilators and do all kinds of things, but basically, there is not good flow. I think that speaks to microvascular problems being far more important in the majority of cases. I don't think those filters are very easy to use. I agree with Tom that the filter currently available is rather cumbersome to use. I would not use it very often in acute MI cases. If microvascular problems are really what we are talking about, are these filters going to help us that much? And if not, are they worth it?

**Howard Cohen:** It is also interesting that studies have shown that it is not only in the vessel you're working in where microvascular flow is reduced, but it is actually systemic in nature. If you are working in the LAD, for instance, it can be in the circumflex, in the right. Thus there are vasoactive substances released locally that have a systemic effect. I also believe that we can do a better job. Cooling, for example, is another mechanism that has been suggested. At least in the experimental model, cooling markedly reduces the size of the infarct when used in animals.

**Tim Fischell:** I have a couple of quick comments about no-reflow. I think the pathophysiology of no-reflow is extremely complicated. If you enter into this problem thinking it's one thing, you will be fooled and get burned. This is

not just a mechanical athero-embolic problem; this is not just a clot problem; and this is not just a vaso-constricting problem. It is a complex interaction between all of these things. What people tend to underestimate is the microvascular vasospastic component of this problem. This is particularly true in the vein graft setting, and probably a little less true in the acute MI setting, where there is likely more of an embolic component — true embolic stimulus and obstruction. The idea that no-reflow is due to mechanical athero- and clot emboli that are occluding so much of the microvascular bed causing high resistance and slow flow is too simple an explanation. There is a tremendous vaso-constricting stimulus to the microvasculature that is made worse by ischemia. The endothelial cells that have been subjected to ischemia for 90 minutes or more start swelling and probably don't make much EDRF, and they begin making more EDCF. Endothelial production is likely increased. Thus, you get a real pro-vaso-constricting milieu in the microvasculature. The endothelial cells are swollen, therefore they don't accommodate debris very well. Each patient is a little different: some throw more debris; others throw less; some have clot; others have cholesterol; and some don't throw much debris, but have sympathetic and clot- and platelet-mediated vasoconstriction. Thus the pathophysiology is very complex and that is why just putting a filter in probably won't be enough to stop it.

We will have to come up with a very slick process whereby we inhibit the clot with IIb/IIIa agents, stop the embolic debris from knocking off sidebranches, and give very potent vasodilators — looking at multiple arms of the vasodilating pathways, not just a single drug. Adenosine is a great drug, but we also should think about multi-drug cocktails. At our lab, we tend to use nicardipine, which has been shown with Doppler in some studies to have the most potent microvascular vasodilating effects and the most prolonged effect: three to five minutes of effect with a single bolus of nicardipine is twice as potent as Cardizem or Verapamil. Nicardipine could thus be combined with adenosine, which is also a good drug but is short-acting. These two drugs could then perhaps be combined with nitroprusside — a third arm of a vasodilating mechanism in the microvasculature. We should move toward the use of cocktails comprised of nifedipine, calcium blockers and adenosine; we should move toward stopping big debris if there is a simple, routine way to do it; and we should give very potent systemic antiplatelet drugs because platelets are the ones releasing much of the vaso-constricting agents. Attacking all arms of the problem will be the only effective way to solve it.

**Jim Zidar:** I agree with Tim's comments. Our approach at Duke in the past year has evolved. We finally standardized our practice whereby if a patient arrives in our emergency room and is not on a protocol and has ST-segment elevation or ST-segment depression, he/she is taken to the cath lab no matter the time of day. In just the last six months, we initiated a protocol with abciximab given in the emergency room up front. The data from the ADMIRAL trial from France

were very impressive compared to the large CADILLAC trial where abciximab is not administered until the time of intervention and the patients were actually eligible to be randomized. The difference between these two was very striking: there is almost a doubling in the patency rates. I very much agree with Paul's comments about time being the issue. The quicker the patient gets to the lab and the artery is open, the less chance there will be for edema and reflow problems. Also, we have noted that using the 12-lead ambulance EKG to make a decision about whether to take a patient to the lab prior to the emergency room EKG has advanced the process for us by about 45 minutes — because the ambulance EKG is actually the most revealing one. Perhaps you have this information from helicopters. North Carolina is a fairly rural state, other than the Charlotte, Raleigh-Durham and Greensboro areas. David Cox and his team in Charlotte have addressed this by placing an interventionist on the night shift. They are also doing this in Tyler, Texas. It may be a difference in the way we practice medicine — meaning we must get patients to the cath lab quickly and open the vessels. Chris Granger at Duke, the CCU director, has initiated a regional acute MI program where we are working with ambulance technicians to identify ST-segment elevation, ST-segment depression, or patients in shock, to determine who among these patients needs to come to the lab immediately. The CCU doctor at Duke receives the EKG and, if needed, sends out a global page to the cath lab staff to come in.

I have been a big proponent of administering a high dose of adenosine. I put the wire down and take a 2.0 mm or 2.5 mm balloon, dotter the lesion one time, pull it back and see how much thrombus is there. I like to give fairly high doses of adenosine in the setting of acute MI just to give me some idea of what is going on. I agree with the comments about the PercuSurge balloon being somewhat cumbersome. The new filters are better than AngioGuard, and the AccuNet used in the carotids has a much lower profile, first-generation, easy-to-cross system. Filters may have some benefit, but I think that pharmacology and timing are more important in the vast majority of patients. We have had about five cases in the last six months where there were huge amounts of thrombus. Instead of putting the PercuSurge balloon down, we just took the recovery catheter and sucked right on the lesion with 20 to 30 ccs several times and then went ahead and performed the intervention. Whether that makes a big difference, I'm not certain. The patients we have the most difficulty treating are those needing rescue angioplasty who have received thrombolytics in the field, have failed to reperfuse, and are between four to eight hours out. We open the vessel and find poor flow. Although we've done a nice job at the target site, we're disappointed with what we see downstream. In that case, we try to give the patient IIb/IIIa inhibitors and perhaps a prolonged one- or two-week course of subcutaneous Lovenox, hoping that the thrombus will fully dissolve and reabsorb. That has been our strategy at Duke.

**Mike Cowley:** Primary angioplasty, when feasible, is probably a superior way of handling this problem. However,

we are facing a manpower shortage in interventional cardiology. One of the downsides to primary angioplasty is that it is shortening the practical working life of interventionists because burnout frequently occurs. In addition, training programs have been cut significantly and manpower projections show that there is a growing need for interventionists despite the smaller numbers completing training programs. Thus, the pharmacologic strategies and alternative approaches will be important. Regionalization will help, but to get the patients treated early, we need to concentrate on combinations of lytics and potent antithrombotics because primary intervention is not going to be available for the bulk of these patients. Currently, approximately 20–25% of ST-elevation infarct patients receive acute intervention or are transferred for acute intervention, and the remainder are being treated in these other ways. I don't know what the solution is to the manpower shortage, but I think it will become increasingly serious — and we will all be up working more and more nights.

**Gary Roubin:** I would like to expand on something Tim Fischell said which is very important. There are actually two groups of patients we need to address here: 1) The patient who arrives quickly but who has a lot of clot and perhaps a lot of cholesterol in the plaque. We intervene quickly on this patient and do fine until we send all this debris downstream which unleashes the pathophysiological process Tim very thoroughly described; 2) The patient who is seen at the outlying hospital and who is treated with lytics and even IIb/IIIa inhibitors, perhaps settles, but maybe doesn't recanalize. Then at around 8, 12 or 24 hours, we receive the call and bring the patient in because he/she is not doing well. The patient still has ST-segment changes, sometimes elevation. We now open the vessel to essentially dead myocardium or a lot of very badly damaged myocardium with a large zone of tissue that can perhaps be saved. This is another problem because we routinely see poor distal perfusion in these cases. We need to address this group of patients; they overlap a lot because we often send a good amount of this material downstream and there is now a very badly damaged distal bed.

I also have a quick comment about using the PercuSurge device. We have performed 200–300 of these PercuSurge procedures in vein grafts and in carotids. We are therefore very familiar with this device and tend to use it frequently. We have had some remarkable results using the PercuSurge device for acute myocardial infarction. I believe we can get every single particle — we can actually wash the vessel and suck these particles out. I am convinced that a total occlusion approach and good retrieval of all the material is likely to be beneficial if it is made user-friendly. There have been cases in our lab where we have tried to get the PercuSurge — which is not very trackable — down, and ended up sending the material downstream. “The horse was out of the barn” at that point and it was too late. We tried Possis, Angiojet, and everything else possible, but nothing worked.

We haven't yet discussed the value of nitroprusside. We have talked about adenosine, but nitroprusside, in our hands,

has turned out to be very valuable as well.

**Philip Walker:** I am a peripheral vascular surgeon and find it very interesting to listen to this discussion. We see this problem in the periphery with acute limb ischemia. Often after using Fogarty catheters to actually mechanically clear the major axial vessels, we perform an angiogram and see the same situation you describe: there is no flow into the capillary beds or the muscles. A technique we employ to solve this is to administer a high dose of urokinase on the table selectively into those vessels. We let it sit there for 20 minutes, then do another angiogram and the improvement is phenomenal. I think it's interesting that no one is talking about using a lytic locally while you've got a catheter there. I would like to ask the panel to discuss this.

**Howard Cohen:** For one thing, we don't have urokinase available anymore, but we do have other lytic drugs. Is anyone using intracoronary lytic therapy?

**Tom Linnemeier:** Actually, there were some studies conducted in early PTCA for acute MI. These were the early PAMI studies in which the acute MI patients were found to do worse with a local application than they did with a systemic application of a lytic agent. Thus, most interventional cardiologists avoid that type of treatment.

**Howard Cohen:** Also, the pathology of what you see in peripheral vessels is often quite different than what you see in the intracoronary vessels.

**Kirk Garratt:** I have a question for you, Howard, and for the panel. First, though, I'd like to make a quick comment about urokinase: Patrick Whitlow summarized the field of intracoronary lytic administration very nicely when he said it was slow, painful and ineffective — other than that, it was almost a perfect therapy!

What I am hearing today is the following: there is universal enthusiasm for early intervention to treat acute myocardial infarctions. Opinions seem to vary regarding how we might go about better addressing infarcts other than treating them earlier. Howard, you listed four areas we should pursue to improve outcomes: hemodynamic, metabolic, mechanical and pharmacologic. However, I have not heard a uniform sense of enthusiasm for any one of those areas. When we talk about facilitated angioplasty, it sounds like there is solid support for reducing the dose of lytics and applying IIb/IIIa agents, although my understanding of the literature is that, so far, the data are far from compelling in this area. There are some data that look fairly promising, but there are at least two large, randomized international trials now that have “skirted” around the issue and have produced data that are not terribly compelling.

With regard to early intervention, you have to wonder about a strategy that would withhold therapy from a patient for an hour, 90 minutes or two hours while he/she is being moved from an outlying hospital to your facility. This would happen if a patient was enrolled in a facilitated angioplasty trial and was unlucky enough to be randomized into the placebo arm of the study. It would seem unethical to conduct a trial like that. Another opportunity we have to treat

those patients more expediently would be to bring angioplasty to the patient rather than bringing the patient to angioplasty. Tom Wharton and colleagues from the New England area, and certainly the Duke group, have made tremendous strides in that regard. William O'Neill has been enthusiastically looking at some methods to bring angioplasty into the community hospitals that have not previously had it available. At Mayo Clinic, we are doing the same thing. In some hospitals that have interventionist talent on-site but that don't have on-site cardiac surgeons, Mayo is offering the opportunity for those people to perform urgent and elective angioplasty with an electronic system that basically brings their laboratory into ours. We don't supervise or police them in any way, but we provide them with a collegial support system just like they would enjoy if they were in the lab next door. In a two-year period, approximately 250 elective angioplasties and roughly 150 acute infarcts have been performed under this system. The results have been outstanding, with a very low mortality rate of less than 2% and no patient has needed to be urgently rushed from one medical center to another to manage a complication requiring a cardiac surgeon.

The question I have for the panel is this: Given what we've discussed here and given that we all admit there's room for improvement, and keeping in mind the four areas we need to pursue in order to improve things (hemodynamic, metabolic, mechanical and pharmacologic), if you were given the task of designing a research protocol that you were going to complete in the next couple of years, what would it look like?

**Howard Cohen:** I am very interested in looking further into hemodynamic support to see the size of the infarct as it would be affected by a ventricular assist device. A recently published paper in *Circulation* showed that in the animal model and in patients with cardiogenic shock, the ventricular assist device was effective, with a mortality rate of 55% rather than 80%. I think there is considerable potential to affect the size of the infarct using that device. Also, I believe that we don't do as good a job as we think we do in a lot of these patients and there is fairly compelling evidence showing that routine use of adenosine is very beneficial. We should also probably use more IIb/IIIa receptor antagonists.

The issue of cooling is a very exciting avenue to pursue, in my opinion. Though cooling appears to have potential, it is not very easy to institute in the way that hemodynamic support is. From my perspective, more hemodynamic intervention, more routine use of pharmacological therapy, and possibly cooling, are three areas we need to delve into. We tend to focus on the lesion: we see that it has been improved, TIMI 3 flow is achieved. But what we think is TIMI 3 flow angiographically is frequently not very good flow if you look at it in a more objective manner — with myocardial contrast echocardiography or Doppler, for example.

**Tom Linnemeier:** We haven't even discussed myocardial blush scores, which I think are very important. The approach I prefer presently corresponds to what Jim Zidar just present-

ed. I put a great deal of faith in Jim and the ADMIRAL trial which aims to "sock it to" the patient early with a IIb/IIIa inhibitor and get the patient immediately to the cath lab.

Looking down the road, as I mentioned in my opening statement, I believe this problem can be solved with both embolic protection devices and with pharmacologic agents. I think we will solve this problem. The biggest issue we still face is that only 20–25% of patients who are eligible for acute MI angioplasty are undergoing the procedure. That means that another 70–80% of the patients are not getting to the cath lab. I would also say, Kirk, that I don't think every single thing we do requires a prospective, randomized trial. We're up to TIMI 32, or whatever, in trials. Some common sense needs to be applied and I think that's exactly what Jim Zidar was talking about. Finally, I want to comment on local angioplasty without surgical back-up. I have completely turned around my view on that, influenced by the New England group and by an article in *The Journal of Invasive Cardiology* for which I wrote an editorial a couple of years ago. The authors listed 200–300 consecutive patients who had outstanding results. There was a means of follow-up with these patients who could be sent off for emergency bypass if there was a complication.

**Richard Myler:** I wanted to offer a quick perspective on how much has changed and how much has not changed in the past 5 years since I was actively practicing. There is a lot of heterogeneity in the problem itself, and it seems we are all touching on certain aspects of it. Perhaps my final point is how valuable humility is in addressing this huge problem and how little time we spend trying to prevent the problem from occurring in the first place — which is an entirely different sociologic, political and economic issue.

**Brian O'Murchu:** I would like to address Kirk Garratt's question. I am impressed with the half-dose thrombolytic therapy and the IIb/IIIa inhibitor data. In the absence of better data, I think that is what we need to do. If I were to set up a study, it would have to be done between the time of the recognition of the problem and the time the balloon crosses the lesion. Also, I think there are pharmacologic therapies, including the fatty acid inhibitors I mentioned earlier — nicorandil, for example — that can be given from the time the patient arrives in the emergency room. Distal protection devices, once their design is less cumbersome, will also be useful.

Perhaps Raoul Bonan could address this question from the intravascular ultrasound standpoint: Would it make sense to dotter the lesion with an ultrasound? Let's find out whether we can dichotomize patients who are going to develop no-reflow by looking at the intravascular ultrasound data on the presence or absence of the characteristics of the lesion at the time. It seems inconceivable that we would stop to perform an intravascular ultrasound before inflating the balloon, but if it was something we could accomplish very quickly and it gave us important information, perhaps it would be worth trying.

**Raoul Bonan:** I think the idea of IVUS is very interesting. The problem with IVUS is probably the size of the character again. We need to come up with a device on a wire that

looks very accurately at the lesion. The first commitment with such a device would be to cross the lesion so you can capture the image from inside. We talk about IVUS today, but tomorrow we could talk about MRI with an antenna. I think MRI will be an interesting possibility in the next five to ten years. Actually, for patients arriving in the emergency room with chest pain, we should be able to manage within 20 minutes to diagnose the problem and ascertain the functionality of the myocardium and its viability. I think MRI is something to be further developed. I am afraid that if you reduce the size of the catheter, we will never have the diagnostic quality we need, but MRI can offer such quality.

**Chris Cates:** I wanted to make a point and query the audience and the panel on a certain issue involving the socio-economic impact of what we have been discussing. Everyone realizes that direct angioplasty is a good therapy in the case of acute myocardial infarction, but we are suffering from a low penetration of that technique in our environment for many reasons, some of which we have already discussed today. Much of this seems to be hiding behind the shield of so-called surgical back-up. I have observed over the past several years — and I wonder if my colleagues would corroborate this — that it is probably a myth of surgical back-up, because a function of our success in developing technology has been that we have quite honestly had very few of those events occur in the current environment. We have observed in Atlanta, at least, both in my private practice at a very busy hospital and at Emory University, where a lot of this was propagated early on, that surgeons are, in fact, very reluctant to take acute patients from the cath lab because they are obviously considered too sick. The surgeons want to medically stabilize these patients for a few days to see whether they are surgical candidates. On occasion, we have actually had several patients die after catheterization where they were found to have tight left mains which occluded in the cath lab. And in a virgin case, surgeons would not take the patients from the cath lab because they were too sick. This is in direct contrast to the early days of angioplasty when we would frequently go down performing CPR on patients all the way to the cath lab. What has changed? I suspect that our surgeons feel more comfortable with our abilities in the lab and thus there is less experience taking these very sick patients from the cath lab to the O.R. I would guess that this occurs less than once a year at Emory, if even that often. Although we may have a handful of very sick patients, they are very often refused by the surgeons. My argument is that perhaps we ought to be more enthusiastically pushing the idea of providing angioplasty at the point of care where the patient presents, allowing skilled interventionists to act on-site despite the absence of a surgical back-up “shield.” I believe we would be doing patients a greater service by promoting the local angioplasty practice. I just wonder if I am the only one here who has observed this at his facility. Could the panel comment on this and could we give a show of hands as to how many have had a failed angioplasty resulting in a catastrophe in their cath lab and where the surgeon has refused to take the patient?

**Tom Linnemeier:** The answer is “yes.” (*laughter*)

**Paul Overlie:** When an acute infarct patient arrived, we used to at least inform the surgeons. As time has passed, however, we don’t even call the surgeon unless the patient is in cardiogenic shock when he/she comes to the cath lab. And in a frequent number of those patients, the surgeons will sometimes drop by and say, “You’re doing pretty well with those stents, son. Keep working.” (*laughter*) I have had refusals by the surgeons, however. So, from my experience, the answer is also “yes.”

**Richard Myler:** I was with Denton Cooley about two weeks ago. He reminded me about my first talk at Texas Heart nearly 25 years ago. Our surgeon was one of his students. He asked me — and this was during the second or third year of angioplasty: “What do you charge for angioplasty?” I replied, “Dr. Cooley, this is an experimental procedure as far as I’m concerned, so we don’t submit a charge for the procedure, only for the catheterization and angiogram components.” Then he said, “What about your surgeon? What does he submit for standby?” Now in those days, it was rather expensive, about \$1,000. Dr. Cooley said something which I loved: “Richard, when I retire (he’s 82 years old now and has yet to retire!), I’m going to come to San Francisco so that I can stand by for not doing surgery. Besides, we’re familiar with the concept in Texas where people are paid for not growing crops.” (*laughter*)

**Paul Overlie:** The most pressing issue I see is that we are still not treating enough patients. You realize that we are only taking 20–25% of all infarct patients to the cath lab. We have a 6–7% death rate after thrombolytic therapy, and in between, there is a huge number of patients who are not treated at all — which is a horrible problem.

In regard to what Gary Roubin was saying about distal protection devices, if we had a simple, extremely low-profile system to use during acute infarcts, we could use it as a guide wire and put it across the lesion. As soon as you get it across, you take a little injection and see how much junk is in there, then blow it up. It wouldn’t even add any time to the angioplasty procedure. Even though you aren’t taking on any of the vasospastic or clot problems, you could be getting rid of most of the no-reflow problems. As for hemodynamic support — we’ve done the cool MI patients. It amounts to a good deal of work and requires a lot of instrumentation. We are about to embark on the MI “hot” program to perfuse oxygenated blood down the coronary arteries. The goal is to get more oxygenation to the tissue so there will be less LV dysfunction. This requires heavy instrumentation and a significant time commitment, so I don’t know how widespread its use will be.

**Jeffrey Werner:** I am rather concerned when I hear people talk about performing acute angioplasty in small hospitals where there is no surgical standby — not because we use standby very often, but because some of those local physicians have not done a very large number of angioplasty procedures. I think the reason we have improved is (a) because we are performing a very large number of angioplasties; and

(b) because we are using stents. There was a major change if nothing else in acute angioplasty once we began using stents which have saved an enormous number of lives. We have essentially sent the surgeons back to bed thanks to stent use. But you have to choose the right artery; there are patients who get very sick during the procedure. I find Kirk's idea to be very interesting, but I imagine it would be quite expensive.

I just arrived in Northwest Arkansas where I am aware of a number of small hospitals that are equipped with cath labs and where physicians might be performing only 25 angioplasties a year on average. This is not unique and occurs in increasing frequency particularly rural areas and is not uncommon in parts of California as well. I wouldn't want to undergo acute angioplasty at one of those low-volume labs. I have seen the wrong vessel dilated at several facilities, and other vessels ignored.

**Howard Cohen:** I think it has to be done in a somewhat controlled fashion by experienced operators. In Minnesota, they have experienced operators working in a good system where they can beam into their cath lab electronically. In Massachusetts, the interventionists are not just performing angioplasties in local hospitals, they are actually working in larger university hospitals. They are taking their diagnostic patients who need angioplasty to Boston, Massachusetts General, Boston University, Beth Israel, and so on. Also, they are on-call at night for their local hospital. Thus, they have performed a good number of procedures and are fairly experienced, well-trained interventionists. If you perform acute infarct angioplasty, you will inevitably run into problems; it happens to everybody. But from what I have observed, these guys do a pretty good job and provide a valuable service to their local patients.

**Brian O'Murchu:** I have a quick anecdote and a comment to make. I would also like to pay a compliment to Richard Myler. In the five years after my fellowship at the San Francisco Heart Institute with Richard Myler and Dick Shaw, there was one particular patient on whom I was intervening. This patient had been referred in and all of a sudden (we've all had these types of patients), the patient became asystolic and was in the process of dying. In all the rush, I couldn't work out what had happened. I saw no error: the left main was intact; we were intervening on the second obtuse marginal; the patient had normal LV function — yet it was a catastrophe of enormous proportions. The cath lab staff had trained with Richard Myler and were fabulous in terms of their technical experience and understanding of the days when we didn't have the support systems we now enjoy. These staff members calmly and efficiently prepared the patient for the surgeon, who was Alex Zapolanski at the time. Next, I saw something I never had before. The patient was being rolled on a gurney down the corridor with one of the cath lab technologists, John Ryan, astride the patient, a knee on either side of the patient's chest, doing compressions. The patient survived despite tremendous difficulty and went home with normal mental function and is alive to this day. I think that as we become better at what we do, there will likely be a paradoxical loss of the edge we have in saving patients who actually do become critically ill on the table. I just wonder how we will maintain that fluency that I saw expressed so fabulously in Richard Myler's lab.

**Richard Myler:** Well I didn't train the staff...they trained me!