assessment of only non–Q-wave MIs, which dates from a period when the non–Q wave MI was assumed to be a valid subset with unique characteristics. It is to be hoped that this misconception has been permanently put to rest and, further, that investigations of outcome after MI will avoid the egregious error of combining random mixtures of first and subsequent infarcts.

Brendan P. Phibbs, MD
Chief of Cardiology
Kino Community Hospital
2800 East Ajo Way
Tucson, Arizona 85713

REFERENCE

Does Flow Reserve Match Contractility?
I have read with great interest the report by Barilla et al. (1). The data reported are intriguing because, to the best of my knowledge, this is the first report indicating that the restoration of regional contractility during low dose dobutamine administration may occur despite different perfusion patterns, depending on the presence or absence of collateral filling.

Let me raise an issue not addressed in the Discussion of Barilla’s article. I definitely agree with Bonow (2) that the increase in flow in patients with collateral filling is expected, because the drop of pressure beyond the fixed obstruction can increase the flow, despite the coronary driving pressure’s being unchanged. The no-measurable-flow response in patients without collateral channels can also be expected. In fact, why should the flow increase through a stenosis or an occlusion? Irrespective of flow regimen, the authors (1) noted an amelioration in contractility of dysfunctional myocardium—one that was still present at 2-methoxy-isobutyl-isonitrile (MIBI) administration and during the time allowed for it to distribute to the myocardium (i.e., up to 8 min), I presume, because no mention was ever made to subsequent deterioration of wall motion. This is an astonishingly long time, which would more appropriately define the response to low dose dobutamine of stunned myocardium (but this was not the case, as indicated by the low sestamibi uptake). It seems inconceivable that such a prolonged increase in contractility may occur in the absence of an adequate increase in blood flow, the situation being absolutely different from the postextrasystolic potentiation of contractility, when myocytes burn their energy stores all in one go. By contrast, the increase in contractility of ischemic but viable myocardium at low dose dobutamine is a short-lived phenomenon: it may begin at very low dosage (as low as 2.5 µg/kg body weight per min, in our experience) and usually fades away at 10 µg/kg per min, seldom at 20 µg/kg per min. In patients with very severe coronary stenosis or coronary occlusion without collateral blood filling, a biphasic response to dobutamine should be expected at a dosage even lower than that at which the authors injected technetium–99m sestamibi. Given this, as well as the notion of the ischemic cascade (3,4), I make the point that Barilla et al. (1) described an intermediate phase of the biphasic response phenomenon—that is, the time when the flow reserve is exhausted, but wall contractility has not yet deteriorated in response to forthcoming or ongoing ischemia, or both. I suggest that this possibility is whispered to the reader.

Giuseppe Barletta, MD, FESC
Viale Morgagni 85, Careggi Hospital
50134 Florence, Italy
E-mail: g.barletta@dfc.unifi.it

REFERENCES

REPLY
We are grateful to Dr. Barletta for his comments. Obviously, the findings we have reported constitute an intermediate step of a biphasic response phenomenon, as stated by Dr. Barletta. However, a 5-min step protocol for low dose dobutamine echocardiography is common (1,2), and a biphasic response (i.e., wall motion improvement followed by worsening) is rarely observed at low doses of 5 to 10 µg/kg body weight per min (3). Nevertheless, no change in wall motion and thickening occurred during the 3 min after tracer injection, even when we used 10 µg/kg per min of dobutamine.

We also wish to emphasize that our study was not intended to describe the behavior of inotropic contractile reserve during low dose dobutamine infusion, but it was aimed at investigating the pathophysiologic and clinical implications of the presumed mismatch between perfusion and contractility in areas with severely hypoperfused viable myocardium.

Francesco Barillà, MD
Second Section of Cardiology
University of Rome “La Sapienza”
Policlinico Umberto I
Viale del Policlinico, 155
00161 Rome, Italy

REFERENCES
2. Panza JA, Dilsizian V, Laurienzo JM, Curiel RV, Katsiyannis PT. Relation between thallium uptake and contractile response to dobutamine: implications regarding myocardial viability in patients with...

Preconditioning, Collateral Recruitment and Adenosine

We read with interest the recent article by Billinger et al. (1). It shows that the myocardial adaptation to repetitive ischemia during percutaneous transluminal coronary angioplasty (PTCA) is partially due to collateral recruitment, which accounted for 30% of the observed variation in intracoronary ST segment shifts and is mainly related to ischemic preconditioning. These findings are in agreement with several previous reports by our group (2–4) and others (5,6) using the PTCA model of ischemic preconditioning. However, it is surprising that, by contrast to extensive evidence supporting a prominent role for adenosine and its receptors in mediating the cardioprotective effects of preconditioning in both experimental (7–9) and clinical (10–12) studies, Billinger et al. (1) failed to show pharmacologic preconditioning with adenosine during PTCA. However, the authors measured ST segment shifts only 1 min after the beginning of balloon inflation, a period insufficient for the achievement of the full evolution of ST segment shift, as previously demonstrated (6). Furthermore, for the assessment of myocardial ischemia severity, Billinger et al. (1) adjusted ST segment amplitude with QRS amplitude. This adjusted index of myocardial ischemia remains to be validated in the experimental setting of repeated balloon inflations, especially because during PTCA there are changes in the QRS amplitude, which are variably correlated ($r^2 = 0.29$ to 0.81) with those of ST segment shifts (13).

Surprisingly, unadjusted ST segment changes, which have been experimentally validated (14,15), are not provided. Thus, it would be interesting to know whether the results obtained by Billinger et al. (1) regarding the effects of adenosine on preconditioning are confirmed when absolute ST segment changes measured after 2 min of balloon inflation are utilized. Similar considerations apply to the relation between changes of ST segment shift and those of collateral flow index. This would make it possible to compare their results with those of several previous published studies on this topic (2–6,10–12,16).

Fabrizio Tomai, MD, FACC, FESC
Filippo Crea, MD, FACC, FESC
Pier A. Gioffrè, MD, FESC
Divisione di Cardiochirurgia
Università di Roma Tor Vergata
European Hospital
Via Portuense 700
Rome, Italy

REFERENCES
15. Cohlen MV, Yang XM, Downey JM. Attenuation of S-T segment elevation during repetitive coronary occlusions truly reflects the protection of ischemic preconditioning and is not an epiphenomenon. Basic Res Cardiol 1997;92:426–34.

REPLY

We thank Tomai and colleagues for their comments on our recent investigation (1). Their reading of our report is different from the wording as well as from the intended meaning, which was that even in patients with only a few collateral channels, their recruitment, as an adaptive mechanism to repetitive ischemia does occur. Our study did not show that the development of ischemic tolerance “is mainly related to ischemic preconditioning.” If collateral recruitment was observed to account for 30% of the variation in electrocardiographic ST segment shifts, the quoted conclusion certainly cannot be drawn. It can only be suggested (as we did in our conclusion) that ischemic preconditioning may be a relevant factor in the development of tolerance to ischemia. It is correct that we could not reproduce recent data from the published reports on the effectiveness of adenosine as “preconditioner.” This was the case despite the fact that we used a study protocol and dosage of adenosine identical to that used by Leesar et al. in their investigation (2). To call the three cited studies in humans on the effect of adenosine “extensive evidence” appears slightly exaggerated to us.