Analysis of Coronary Responses to Various Doses of Intracoronary Nitroglycerin

ROBERT L. FELDMAN, M.D., J. DANIE MARX, M.D., CARL J. PEPINE, M.D., AND C. RICHARD CONTI, M.D.

SUMMARY We studied the degree of coronary artery dilation resulting from increasing doses of intracoronary nitroglycerin (NTG). Heart rate, aortic pressure and coronary artery angiograms were recorded before and after 5-, 50-, 150- and 250-μg doses of NTG infused into the left main coronary artery. Coronary artery diameters were measured by a magnification angiographic technique. After intracoronary NTG, heart rate was unchanged 2 minutes after each dose. Mean aortic pressure was unchanged after 5 μg (NS), but declined 5 mm Hg (mean) after 50 μg, 9 mm Hg after 150 μg and 18 mm Hg after 250 μg (all p < 0.05) compared with before NTG. The maximal increase in diameter occurred after 150 μg, and no additional increase was seen after 250 μg. After 5- and 50-μg doses, 67% and 75% maximal dilation responses, respectively, were observed. Compared with coronary artery diameter before NTG, the 150-μg dose increased the diameter of left main coronary artery by 5%, proximal coronary artery segments by 9%, middle segments by 19%, distal segments by 34%, collateral-filled coronary arteries by 38%, coronary artery stenoses by 5%, and small coronary arteries (0.4-1.0 mm) by 54%. These data indicate that relatively small doses of intracoronary NTG produce potentially important coronary artery dilation without important changes in heart rate and aortic pressure. These observations should prove helpful in choosing dosage schedules for intracoronary NTG.

PARENTERAL nitroglycerin (NTG) has recently become available for clinical use. Intracoronary NTG is now an important aid during diagnostic and interventional coronary arteriography. It is used to diagnose and relieve coronary artery spasm, to prevent spasm during percutaneous transluminal coronary angioplasty and to exclude or reverse spasm in patients considered for thrombolytic therapy after acute myocardial infarction. An appropriate dose of intracoronary NTG should yield maximal coronary artery dilation without adverse systemic effects.

After sublingual NTG, dilation of epicardial coronary arteries is the usual response observed during coronary angiography.1-4 The response of proximal and distal coronary artery segments and smaller intramyocardial coronary arteries to sublingual NTG has been quantified in man.5 Dilation is usually greater in left coronary artery segments with the smaller diameters before administration of NTG.6 Other studies have shown a dose-response relationship between coronary artery dilation and the amount of sublingual NTG administered.2

In this investigation, we quantified angiographic changes of the left coronary artery and its branches after graded doses of intracoronary NTG in patients with and without coronary artery disease.

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Methods

Patient Selection

Twenty male patients, average age 57 years (range 48–66 years), undergoing cardiac catheterization for further evaluation of chest pain were studied after giving informed consent. Patients with symptoms or electrocardiographic findings suggestive of variant angina were excluded. All patients took sublingual NTG (0.4 mg) for chest pain believed to be caused by transient myocardial ischemia. Seventeen patients were taking long-acting nitrates (Nitrol paste, 4–15 inches/day, or isosorbide dinitrate, 30 to 240 mg/day, or both). Ten patients were taking propranolol (80–800 mg/day).

Cardiac Catheterization

Patients were catheterized without premedication. Those who underwent catheterization in the early morning (8 a.m.) did not eat after dinner the preceding evening. Those catheterized in the late morning (11 a.m.) received a liquid breakfast at 7 a.m. Nitrates were withheld for at least 6 hours before catheterization, but propranolol treatment was not interrupted. A #8F Sones catheter was advanced from the right brachial artery to the left ventricle. Pressures were measured, and the catheter was withdrawn to the aorta. Mean aortic pressure was obtained by electronic filtration.

Coronary Angiographic Technique

Multiple views of the left coronary artery were obtained using a conventional 35-mm cineangiographic technique. Fluoroscopic images were simultaneously recorded on a video disk recorder (Videomatic, OM C7560B; General Electric). These recordings were reviewed, and an optimal right anterior oblique projection was chosen to minimize overlapping of proximal left coronary artery branches and maximize visualization of any proximal coronary stenosis. Projections ranged from 10% to 40% rotation, with various de-
degrees of sagittal plane angulation. The same optimal projection was used in any given patient in all study periods.

**Control Period**

The control period was defined as a symptom-free interval during which the left ventricular pressure and heart rate remained unchanged (± 10%) for 10–15 minutes. After ECG and pressure changes related to injection of selective coronary contrast material returned to baseline (about 5 minutes), a control 105-mm photospot selective coronary angiogram was filmed using 6 ml of Renografin-76. The filming technique and photographic equipment have been described.2, 3, 5, 6

**Nitroglycerin Period**

**Nitroglycerin Preparation**

Administration of parenteral NTG was approved by appropriate institutional committees. A solution containing 5 mg of NTG and 45 mg of propylene glycol dissolved in 70% ethanol (volume 1 ml) was mixed in a glass vial with 99 ml of normal saline. The NTG concentration of this solution was 50 µg/ml. This solution was also diluted to obtain a solution with a NTG concentration of 5 µg/ml.

**Nitroglycerin Administration**

After the angiogram was filmed and ECG and pressures returned to values before the angiogram, 5 µg of NTG were infused over 10–20 seconds directly into the left main coronary artery in 14 patients. Then, 3 ml of normal saline were flushed through the Sones catheter into the left coronary artery. Aortic pressure recordings (phasic and mean) were made 2 minutes later. A 105-mm photospot selective coronary angiogram was filmed 2–3 minutes after NTG administration. The same sequence of events was followed after additional NTG doses of 50 µg (cumulative, 55 µg) and 150 µg (cumulative, 205 µg) were administered. In three of these 14 patients, another NTG dose of 250 µg (cumulative, 455 µg) was given to determine whether additional dilation resulted. In three other patients, three 5-µg intracoronary NTG doses were infused to evaluate the cumulative effect of repeated small doses. Finally, in three patients, 4 ml of vehicle were infused to evaluate its effect on coronary artery diameters. The vehicle was made by mixing 45 µg of propylene glycol dissolved in 70% ethanol, volume 1 ml, and 99 ml of normal saline. Then, 200 µg of NTG were infused to determine whether additional dilation resulted.

**Coronary Artery Diameter Measurements**

Left coronary artery diameters were measured at preselected branch points at × 6 or × 10 magnification using photospot angiographic frames filmed at enddiastole and matched for position at each dose. The technique and locations at which coronary artery segments were measured have been described.2, 3, 5, 6 Unblinded measurements were made to the nearest 0.1 mm. Photospot frames were marked for NTG dose (fig. 1).

**Calculations and Statistical Analysis**

Actual coronary artery diameter (in millimeters) was calculated by reference to the Sones catheter tip diameter (1.7 mm). The percent change in diameter was used to quantify the magnitude of dilation and was calculated as ([coronary diameter after NTG - control coronary diameter]/control coronary) × 100%. The mean and standard deviation were calculated for measurements from control and NTG angiograms. Analysis of variance and appropriate multiple comparison procedures were used to compare the percent change after NTG for different NTG doses and for different coronary artery locations. A p value ≤ 0.05 was considered significant.

**Results**

**Coronary Angiography**

Before NTG, 18 of the 20 patients had coronary stenoses ≥ 50% diameter reduction involving one or more major branches of the left coronary artery. No patients had a stenosis of the left main coronary artery.

**Effects of the Vehicle on Hemodynamics and Coronary Diameter**

The vehicle in which the NTG was dissolved for intracoronary administration did not change heart rate (−2, 2 and 3 beats/min) or mean aortic pressure (−5, −7 and 2 mm Hg) in a consistent pattern. Paired angiograms performed before and after administration of the vehicle showed that only three of 25 diameters changed (range −0.1 to 0.1 mm). After 200 µg of NTG, 23 of the 25 segments were dilated compared with diameters after the vehicle alone.

**Hemodynamic Effects of Cumulative Doses of Intracoronary NTG**

No significant changes in heart rate occurred at any cumulative dosage of NTG studied. After intracoronary NTG, mean aortic pressure decreased 3 ± 6 mm Hg after 5 µg (NS), 5 ± 10 mm Hg after a cumulative dose of 55 µg (p < 0.05 vs control and 5 µg NTG) and 9 ± 8 mm Hg after a cumulative dose of 205 µg (p < 0.05 vs control, 5 µg and 55 µg NTG). In the three patients who received a cumulative dose of 455 µg, mean aortic pressure decreased an average of 18 and 10 mm Hg compared with control values and values after 205 µg NTG, respectively. No important change in heart rate or mean aortic pressure was found after each of the three 5-µg NTG doses.

The 14 patients who received increasing doses of intracoronary NTG (5, 50 and 150 µg) were subgrouped into those taking propranolol (seven patients) and those not taking propranolol (seven patients). Control heart rate was 65 ± 12 beats/min in patients taking propranolol and 76 ± 16 beats/min in patients not taking propranolol (0.05 < p < 0.10). Heart rate did not change in patients receiving propranolol after 5-,
50- or 150-μg NTG doses and increased only 1 beat/min in patients not receiving propranolol after the 50- and 150-μg doses (all NS). Mean aortic pressure was similar in patients whether or not they received propranolol (92 ± 15 and 91 ± 22 mm Hg, respectively). Mean aortic pressure decreased similarly in patients receiving and not receiving propranolol after the 5-, 50- and 150-μg doses (4, 6, and 9 and 2, 5, and 9 mm Hg, respectively).

**Effect of NTG (Cumulative Doses of 5–205 μg) on Diameter of Left Coronary Artery Segments**

In the 14 patients who received increasing doses of intracoronary NTG (5, 50 and 150 μg), there was an important increase in coronary artery diameter in most segments (table 1) after each dose. Concomitant propranolol therapy did not have an important effect on coronary artery dilation after any NTG dose or on coronary artery diameter before NTG. Therefore, left coronary artery responses were combined in the subsequent data analysis.

The left main coronary artery diameter increased after each dose (all \( p < 0.05 \) compared with diameter during control and with the next lower dose of NTG). Diameters of both proximal segments increased after each dose (all \( p < 0.05 \)). Diameters of proximal left anterior descending (LAD) and circumflex (Cx) coronary arteries were similar (NS) before and after each dose of NTG. The diameter of the middle LAD segment after each NTG dose was larger than the control diameter (all \( p < 0.05 \)). The diameter after cumulative doses of 5 and 55 μg did not change significantly, but was larger after the 205-μg dose (\( p < 0.05 \)). For both middle Cx segments (Cx1, obtuse marginal branch at
TABLE 1.  Left Coronary Artery Diameters (mm) After Intracoronary Nitroglycerin

<table>
<thead>
<tr>
<th>Segment</th>
<th>Control</th>
<th>Cumulative nitroglycerin dose (μg)</th>
<th>5</th>
<th>55</th>
<th>205</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main</td>
<td>4.35 ± 0.99</td>
<td>4.44 ± 0.95</td>
<td>4.49 ± 0.95</td>
<td>4.54 ± 0.95</td>
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<tr>
<td>Proximal LAD</td>
<td>3.31 ± 0.72</td>
<td>3.49 ± 0.75</td>
<td>3.57 ± 0.78</td>
<td>3.66 ± 0.81</td>
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</tr>
<tr>
<td>Proximal Cx</td>
<td>3.13 ± 0.58</td>
<td>3.27 ± 0.59</td>
<td>3.34 ± 0.57</td>
<td>3.39 ± 0.58</td>
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</tr>
<tr>
<td>Middle LAD</td>
<td>2.29 ± 0.44</td>
<td>2.55 ± 0.44</td>
<td>2.55 ± 0.48</td>
<td>2.66 ± 0.46</td>
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</tr>
<tr>
<td>Middle Cx&lt;sub&gt;1&lt;/sub&gt;</td>
<td>2.41 ± 0.63</td>
<td>2.71 ± 0.62</td>
<td>2.80 ± 0.63</td>
<td>2.87 ± 0.60</td>
<td></td>
</tr>
<tr>
<td>Middle Cx&lt;sub&gt;2&lt;/sub&gt;</td>
<td>2.31 ± 0.52</td>
<td>2.56 ± 0.43</td>
<td>2.71 ± 0.48</td>
<td>2.79 ± 0.49</td>
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<tr>
<td>Distal LAD</td>
<td>1.60 ± 0.38</td>
<td>1.87 ± 0.42</td>
<td>2.03 ± 0.44</td>
<td>2.13 ± 0.39</td>
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<tr>
<td>Distal Cx</td>
<td>1.50 ± 0.35</td>
<td>1.83 ± 0.24</td>
<td>1.93 ± 0.26</td>
<td>1.99 ± 0.29</td>
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<tr>
<td>Small CA</td>
<td>0.76 ± 0.17</td>
<td>0.99 ± 0.15</td>
<td>1.09 ± 0.14</td>
<td>1.16 ± 0.15</td>
<td></td>
</tr>
<tr>
<td>Vessels filled by collaterals</td>
<td>1.28 ± 0.33</td>
<td>1.54 ± 0.40</td>
<td>1.66 ± 0.36</td>
<td>1.74 ± 0.34</td>
<td></td>
</tr>
<tr>
<td>Coronary stenoses</td>
<td>1.79 ± 0.66</td>
<td>1.86 ± 0.65</td>
<td>1.87 ± 0.67</td>
<td>1.87 ± 0.67</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Abbreviations: LAD = left anterior descending coronary artery; Cx = circumflex coronary artery; Cx<sub>1</sub> = obtuse marginal branch at its origin; Cx<sub>2</sub> = atrioventricular groove just distal to the obtuse marginal branch; CA = coronary artery.

TABLE 2.  Average Percent Coronary Artery Dilation After Intracoronary Nitroglycerin

<table>
<thead>
<tr>
<th>Segment</th>
<th>Cumulative nitroglycerin dose (μg)</th>
<th>5</th>
<th>55</th>
<th>205</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Proximal (LAD, Cx)</td>
<td>5</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Middle (LAD, Cx)</td>
<td>13</td>
<td>17</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Distal (LAD, Cx)</td>
<td>22</td>
<td>30</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Small CA</td>
<td>31</td>
<td>46</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Coronary stenoses</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>CA filled by collaterals</td>
<td>20</td>
<td>31</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: See table 1.
μg) and third (cumulative dose, 15 μg) doses was usually greater than after the preceding dose, but less than that with 50- and 150-μg) doses.

**Discussion**

Coronary angiography showed dilation in all segments of the left coronary artery. Most of the dilation usually occurred after relatively small doses of intracoronary NTG. Approximately two-thirds of the total dilation was detected after 5 μg of NTG and three-fourths after the cumulative dose of 55 μg (fig. 1). In most patients, the largest cumulative dose was 205 μg. When a larger cumulative dose (455 μg) was given to some patients, large decreases in aortic pressure occurred and further dilation was usually not observed. Thus, it appears that 50–200 μg of NTG produces maximal coronary artery dilation without major changes in systemic pressure.

The percent dilation of individual epicardial and small intramycardial coronary arteries varied, but some group responses differed. These differences in response to intracoronary NTG appear related to size of the coronary artery before NTG and location of the segment relative to the left coronary artery os: The smaller the segment, the larger the percent dilation. This finding was similar to results after sublingual NTG. The actual magnitude of dilation, however (diameter after NTG minus control diameter), was greater or similar for large coronary arteries compared with smaller ones. The mechanism of apparent NTG-induced differential dilation was unclear.

Although the number of patients to whom we have administered similar doses of sublingual and intracoronary NTG is small, a comparison of coronary diameter and systemic responses seems appropriate. After sublingual NTG doses of 75 and 150 μg, no significant change in heart rate or aortic pressure occurred, and 450 μg decreased aortic pressure 10 mm Hg and increased heart rate approximately 5 beats/min. After intracoronary NTG, aortic pressure decreased slightly with cumulative doses as low as 55 μg, and further decreases occurred with higher cumulative doses. At the highest cumulative dose (455 μg), a larger decrease in aortic pressure occurred (18 mm Hg) than was seen after a similar NTG dose administered sublingually. No significant change in heart rate accompanied the decline in aortic pressure after intracoronary NTG, whereas heart rate was increased after sublingual NTG. This lack of reflex tachycardia after intracoronary NTG was surprising, and was present whether or not the patient was taking propranolol. The absence of reflex tachycardia suggests that intracoronary NTG may increase vagal efferent activity, producing a Bezold-Jarish-like response. This response may be mediated through release of prostacyclin by coronary vessels to the high local NTG concentrations achieved after intracoronary administration. Additionally, the maximal percent dilation of various left coronary artery segments differed for some segments when the two routes of administration were compared. After intracoronary NTG, the percent dilation of segments nearest the left coronary artery os was similar to or slightly less than that after sublingual NTG. In contrast, the percent dilation of distal segments and small intramyocardial branches was greater after intracoronary NTG. The mechanism of these different responses is unknown. With intracoronary administration, if mixing was adequate, larger NTG concentrations should be available for interaction with coronary artery smooth muscle receptors. At the same time, perfusion pressure was lowered only slightly more and diastolic filling time was longer. Therefore, we expected at least as much dilation in all segments after intracoronary NTG as after sublingual NTG. These differences might be related, at least in part, to the amount of NTG to which a coronary artery segment was exposed. Sublingual NTG would expose the full length of the left coronary artery to the same NTG concentration over a long period of time. After intracoronary NTG, there was an initial brief exposure to a high NTG concentration, and later, after recirculation, equal exposure of the full length of the left coronary artery to much lower concentrations. Because of streaming, intracoronary NTG could produce "poor contact" of the injectate with more proximal segments. In more distal segments, one would expect better mixing and better contact with the vessel wall. More observations in patients receiving intracoronary NTG are necessary to further explain and measure the different hemodynamic and angiographic responses after sublingual and intracoronary NTG.

The magnitude of dilation of coronary arteries filled by collaterals was similar to that of coronary arteries of comparable location and initial size. We could not determine whether this dilation was indirectly related to NTG-induced alterations in regional flow, collateral perfusion pressure and left ventricular wall stress, or was directly related to NTG action on coronary artery smooth muscle. Many coronary stenoses also dilated after intracoronary NTG. The percent dilation and number of stenoses that appear to dilate (approximately half) seemed similar after either intracoronary or sublingual NTG. We also considered the effect of intracoronary NTG on segments located beyond these stenoses. The effect of NTG on coronary artery diameter was a consequence of changes in smooth muscle tone, external compressive forces and blood pressure in the lumen. After intracoronary NTG, there should be considerable dilation of the downstream "arteriolar" bed and in segments located beyond some stenoses, this could result in decreased distal pressure. Thus, as has been described for several experimental models, coronary artery segment diameter could decrease during arteriolar dilation. We did not observe a decrease in any coronary artery diameter after any intracoronary NTG dose. Therefore, our findings suggest that after intracoronary NTG, decreases in smooth muscle tone were the predominant physiologic effect. However, 2–3 minutes after a bolus of intracoronary NTG at the time we performed angiography, "arteriolar" dilation may no longer have been present. Angiograms taken within 1 minute of intracoro-
nary NTG administration, when arteriolar dilation would be more pronounced, might yield different findings.

Many patients were receiving propranolol during this study. Because many potential candidates for intracoronary NTG therapy may also be receiving propranolol, we examined in detail the effect of intracoronary NTG in this subgroup. Propranolol increases coronary vascular resistance, presumably through blockade of the β1 receptor while α-mediated effects on coronary tone persist.13 Specific effects of propranolol on large-vessel coronary artery diameter in humans are not known. Patients who were receiving propranolol had a slightly lower resting heart rate. Aortic pressure and initial coronary artery diameters were similar in both groups. Propranolol therapy did not seem to affect coronary artery responses to intracoronary NTG.

The finding that coronary arteries 1 mm in diameter and smaller dilate relatively more than more proximal coronary arteries after intracoronary NTG agrees with our previous analysis of coronary responses after sublingual NTG,1 but differs from some previous findings in experimental animals.14,15 In isolated large (diameter > 1 mm) and small (< 0.50 mm) coronary arteries, the response of small coronary arteries to nitrates was usually different and less than that of large coronary arteries. Other groups have reported that isolated small and large coronary arteries often responded similarly to other stimuli.16,17 Why different responses of small and large coronary arteries have been observed by different investigators using isolated preparations is not clear; nor is it clear whether findings from isolated nonhuman coronary arteries are applicable to the in vivo responses of human coronary arteries. This has been discussed in detail previously.18

Our study had several limitations. First, the effect of repeated angiograms and repeated NTG doses could be important. Some of the dilation after cumulative intracoronary doses of 55 and 205 μg was secondary to repeated dosage and not necessarily caused by the larger dose. In three patients given repeated doses of 5 μg of intracoronary NTG, coronary artery diameter usually increased after each dose, but the percent dilation was less than that with larger doses. Repeated administration of intracoronary contrast material has either minimal or no detectable effects on large coronary artery diameters.19,20 Thus, it is unlikely that repeated injections of contrast material made an important contribution to the change in coronary artery diameter; nor did the vehicle used to deliver intracoronary NTG have an important effect on heart rate, pressure or coronary artery diameter. The second limitation concerns the accuracy and reproducibility of the measurements of coronary artery diameter. We used quantitative coronary angiographic techniques that have been described in detail.2,3,5,6 Intrareader and interreader reproducibility has been small, and the measuring technique should not be an important variable in considering these data. Third, all of these patients used nitrates. Systemic and coronary effects of NTG could differ in patients depending on whether they have been receiving nitrates.

In conclusion, these data indicate that coronary artery dilation occurs with as little as 5 μg of intracoronary NTG. With this small dose, more than half maximal dilation can be achieved. Moderate doses (50–200 μg) produce maximal or nearly maximal dilation without clinically important systemic effects. Larger doses (450 μg), similar to those usually administered when NTG is given sublingually, resulted in no additional detectable dilation but produced important systemic effects. Also, different degrees of dilation can be expected within different segments of the left coronary artery. When NTG was infused directly into the left main coronary artery, relatively less dilation occurred in proximal segments nearest the left main coronary artery than in the more distal segments. These data should be clinically useful when determining the dose of NTG for intracoronary administration. For maximal or nearly maximal coronary dilation during diagnostic coronary angiography, intracoronary NTG doses of 50–200 μg should be sufficient. Intracoronary doses of NTG in this range have usually been effective in relieving coronary spasm.19

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References

13. Schang SJ, Pepine CJ: Effects of propranolol on hemodynamic and metabolic responses to tachycardia stress in patients with and with-
Platelet Release and Thromboxane Synthesis in Symptomatic Coronary Artery Disease

Auke C. de Boer, M.D., Alexander G. G. Turpie, M.B., Rodney W. Butt, R.T., Raymond V. Johnston, M.B., and Edward Genton, M.D.

SUMMARY The incidence and significance of platelet activation in myocardial ischemia was evaluated by serial measurement of plasma thromboxane B\(_2\) (\(\text{TXB}_2\)) and \(\beta\) thromboglobulin (\(\beta\)TG) in plasma and urine in 98 patients admitted to a coronary care unit with chest pain. All measurements were normal in the 26 patients with noncardiac chest pain. Mean plasma \(\text{TXB}_2\) and \(\beta\)TG concentration, but not urine \(\beta\)TG, were elevated in the 25 patients with myocardial infarction and the 47 patients with angina. The \(\beta\)TG levels remained normal in 61% of the patients with angina or infarction. The \(\text{TXB}_2\) levels were significantly higher in patients with recurrent episodes of angina at rest than in those without ischemic episodes after admission. There was a weak correlation between plasma \(\text{TXB}_2\) and plasma \(\beta\)TG (\(r = 0.20, p < 0.01\)) and between plasma and urine \(\beta\)TG (\(r = 0.31, p < 0.01\)). Results indicate that platelets are frequently activated with myocardial ischemia or infarction. However, the measurement of \(\beta\)TG and \(\text{TXB}_2\) is of limited value in detecting or differentiating myocardial ischemia from infarction and therefore lacks clinical value in the management of patients with ischemic heart disease.

PLATELETS play an important role in the thrombotic and microembolic complications of coronary atherosclerosis.\(^1\) However, the role of platelets in myocardial ischemic events is uncertain. Numerous tests of platelet reactivity have been evaluated in patients with coronary artery disease (CAD) not only to establish the role of platelets in the pathogenesis and progression of the condition, but also to determine the effect of various therapeutic regimens directed at inhibition of platelet activation. However, most platelet tests provide only crude and indirect estimates of platelet activation in vivo and yield inconsistent results in CAD patients. Recently, highly specific, sensitive and reproducible radioimmunoassays of platelet release and prostaglandin synthesis were developed, including assays of \(\beta\) thromboglobulin (\(\beta\)TG), platelet factor 4 (PF4) and thromboxane B\(_2\) (\(\text{TXB}_2\)).\(^2,3\) Both \(\beta\)TG and PF4 are platelet-specific proteins liberated from platelets into plasma during the release reaction and partially excreted through the kidneys. Increased levels of these proteins in plasma and urine may reflect in vivo platelet activation.\(^4\)

Thromboxane A\(_2\) (\(\text{TXA}_2\)), an end product of prostaglandin synthesis from arachidonic acid by platelets and other cells including leukocytes, is a potent proaggregating and vasoconstrictor agent.\(^5\) \(\text{TXA}_2\) is rapidly and spontaneously degraded into the stable substance thromboxane B\(_2\) (\(\text{TXB}_2\)), which has no effect on platelet aggregation and can be measured by radioimmunoassay in plasma.\(^6\) Both \(\text{TXB}_2\) and the platelet-specific proteins have been studied in patients with CAD.\(^7-20\) The results of these studies have been variable. This study was carried out to clarify the relationship of platelet release and thromboxane synthesis in reversible myocardial ischemia and myocardial necrosis by serial measurements of \(\beta\)TG in plasma and urine and plasma \(\text{TXB}_2\) in a group of well-defined patients admitted to the coronary care unit with chest pain suggestive of myocardial ischemia.

Patients and Methods

Ninety-eight patients who presented with chest pain and were admitted to the coronary care unit with suspected ischemic heart disease were studied. All patients had a serial ECG, cardiac enzyme determinations and routine blood counts. Three diagnostic groups were defined: (1) Patients with acute myocardi-
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