Nitroglycerin to Unmask Reversible Asynergy
Correlation with Post Coronary Bypass Ventriculography

By Richard H. Helfant, M.D., Rogelio Pine, M.D., Steven G. Meister, M.D., Michael S. Feldman, M.D., Robert G. Trout, M.D., and Vidya S. Banka, M.D.

SUMMARY
The value of nitroglycerin in determining the potential reversibility of asynergy was examined in 35 patients with coronary heart disease. Ventriculograms performed at rest and after sublingual nitroglycerin were analyzed for (1) location of asynergy relative to distribution of the 3 major coronary arteries and (2) severity of asynergy. Of the 41 hypokinetic zones, 30 (73%) improved following nitroglycerin. Of 28 akinetic zones, 16 (57%) improved (7 of the 16 segments becoming normal) following nitroglycerin. None of 7 dyskinetic zones showed change following nitroglycerin. Twelve patients were restudied following coronary bypass surgery. There was an excellent over-all correlation between the segments that responded to nitroglycerin and bypass surgery in those segments with open grafts. Eighteen segments which improved following nitroglycerin had patent postoperative grafts, and in 15 segments there was a corresponding improvement following bypass surgery. Two segments which were unresponsive to nitroglycerin preoperatively had patent postoperative bypass grafts. Neither segment improved despite graft patency. In summary, sublingual nitroglycerin is useful in unmasking residual contractile ability in asynergic zones. A positive response to nitroglycerin appears to be predictive of corresponding beneficial effect from a coronary bypass graft. The data strongly suggest that the use of nitroglycerin to determine residual contractile ability may be of considerable value in better defining the potential risks and benefits of coronary bypass surgery.

Additional Indexing Words:
Left ventricular function
Dyskinesis
Contractile ability

Hypokinesis
Akinesis

DIRECT MYOCARDIAL revascularization utilizing the technique of coronary bypass surgery is currently being widely used in the treatment of patients with angina pectoris. Several studies have described the surgical mortality,1, 2 graft patency,3 and effects on left ventricular performance.4-11 The surgical risk is determined in large part by the contractile state of the left ventricle.4 However, the effect of bypass surgery on ventricular performance has been controversial,5-11 and it has recently been pointed out that methods of evaluating residual contractile ability in asynergic areas are needed to determine both the risk and potential benefits of bypass surgery.12 The present study was undertaken to determine whether sublingual nitroglycerin, by pharmacologically improving the balance between oxygen supply and demand, unmask residual contractile ability of asynergic zones. In addition the effects of nitroglycerin were compared with the results of coronary bypass surgery on wall motion in the same left ventricular zones.

Methods
Studies were performed in 35 patients undergoing cardiac catheterization for evaluation of coronary heart disease. Criteria for admission to the study were: (1) asynergy on ventriculography (defined as a localized abnormality of left ventricular contraction), (2) significant (greater than 75%) obstruction of one or more of the three major coronary arteries, (left anterior descending, right and circumflex arteries), and (3) absence by catheterization of other etiologic heart disease. All patients were postabsorptive and premedicated intramuscularly with 50 mg nembutal, 50 mg demerol, and 0.4 mg atropine.

Right heart catheterization was performed via an antecubital vein cutdown and left heart catheterization either via a right brachial arteriotomy or percutaneously utilizing a femoral artery. Following recording of left ven-
tricular pressure (using Statham P23 Db transducers) and cardiac output (dyed-dilution method using indocyanine green), left ventriculography (control ventriculogram) was performed in the 45° right anterior oblique projection using 30 to 40 cc of Meglumine Diatrizoate (Renographin-76) injected into the left ventricle. In no case was this performed during or immediately after anginal symptoms. When asynergy was observed, nitroglycerin (gr. 1/150 sublingual) was administered 15-20 min following the initial ventriculogram. Following nitroglycerin administration, after a variable time period of one to four minutes, a progressive fall in systolic pressure and rise in heart rate took place over a period of one to three minutes at which time these parameters stabilized. After observation of the stability of the systolic pressure and heart rate for approximately 30 sec, the ventriculogram (TNG ventriculogram) was repeated in the same degree of obliquity and using the same amount of contrast material and tube to table top distance. Selective cine triculography (bypass ventriculogram) was then performed using either the Sones or Judkins technique. Cines were taken on 10 × 6 inch dual-field image intensifier (Siemans) at 64 frames/sec using 35mm Kodak Shellburst film. Hemodynamics were monitored and recorded on an Electronics for Medicine oscillographic recorder.

Twelve patients were also restudied following aortocoronary saphenous vein bypass surgery. Ventriculography (bypass ventriculogram) was performed in an identical fashion to the preoperative study. In addition, selective opacification of the grafts was performed in at least two projections. If selective injection was not possible, graft patency or occlusion was ascertained by 50 cc contrast injection into the aorta just above the valve.

Ventriculograms were analyzed in both a qualitative and quantitative fashion. Qualitatively, ventricular contraction was assessed with respect to (1) location of myocardial segment perfused by each of the three major coronary arteries.

Thus, the "antero-descending segment" was taken as the anterior-apical portion, "right segment" as the remaining portion of the inferior wall, and "circumflex segment" as the inferior wall between the posterior papillary muscle and apex. (2) The severity of contraction abnormality of each segment. Thus, hypokinesis refers to diminished contraction, akinesis the total absence of contraction and dyskinesis to paradoxical systolic expansion.

A quantitative analysis was performed by superimposing tracings of end diastolic and end systolic frames using the cardiac apex to mid-aortic valve as fixed points. Hemixias were drawn which trisected the long axis at right angles to it. Each hemixias was measured and recorded as a percentage change from end diastole to ascertain the amount of regional contraction. Apical motion was calculated on the basis of percent change of the apex to base axis. Ventriculograms associated with more than occasional ectopic beats or exhibiting poor ventricular opacification were excluded from the study.

**Results**

**Responsiveness to Nitroglycerin**

Table 1 indicates the responses to nitroglycerin according to the functional severity of asynergy. Of 41 hypokinetic segments, 30 improved after nitroglycerin (73%). Sixteen of 28 akinetic segments responded to nitroglycerin (57%). Seven of the akinetic segments became normal following nitroglycerin while the remaining 9 segments became hypokinetic. In contrast, none of the 7 dyskinetic segments improved following nitroglycerin.

The quantitative data correlated with the qualitative analysis. In the responsive hypokinetic segments, there was a 24.6 ± 8.2% increase in corresponding hemiaxis shortening compared to a 4.8 ± 2.2% increase in unresponsive segments ($P < 0.001$). Similarly, in the akinetic segments, a 17.2 ± 7.7% increase in percent hemiaxis shortening occurred in the responsive segments as opposed to a 2.3 ± 1.2% change in the unresponsive zones ($P < 0.001$). The 7 unresponsive dyskinetic segments which did not exhibit a change on qualitative assessment also did not change quantitatively (table 1).

**Responsiveness to Bypass Surgery**

Table 2 demonstrates the segmental responses to patent bypass grafts as a function of the severity of asynergy. Ten of 11 hypokinetic segments improved, while 5 of 8 akinetic segments improved. One dyskinetic segment was unchanged (table 2). This was also borne out by the percent changes in hemiaxis shortening (table 2).

**Correlation of Nitroglycerin and Bypass Ventriculograms**

The data correlating the responses to nitroglycerin with that following coronary bypass surgery are indicated in table 3, and with respect to wall motion analysis in table 4. There was an excellent over-all correlation between the segments that responded to

<table>
<thead>
<tr>
<th>Table 1: Responsiveness to Nitroglycerin Relative to Severity of Asynergy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity of asynergy</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Hypokinesis</td>
</tr>
<tr>
<td>Akinasis</td>
</tr>
<tr>
<td>Dyskinesis</td>
</tr>
</tbody>
</table>

Abbreviation: TNG = nitroglycerin.

* = standard error of the mean.
nitroglycerin and improvement after bypass surgery in those segments with open grafts (table 5). Eighteen segments which improved following nitroglycerin also had patent postoperative bypass grafts demonstrated angiographically. In 15 of the 18 segments, there was a corresponding improvement following bypass surgery (table 5). Of the 11 hypokinetic segments responding to nitroglycerin, 10 also responded to the bypass graft (table 5). Of the 7 akinetic segments responding to nitroglycerin, 5 responded to bypass (table 5). Three segments (in 2 patients) worsened following bypass despite patent grafts. In both patients new pathologic Q waves appeared on the postoperative electrocardiogram in the corresponding zones. A cine illustration of the response to nitroglycerin and bypass surgery is illustrated in figure 1.

Two segments which were unresponsive to nitroglycerin preoperatively had bypass grafts which were found patent on angiography. Neither segment improved despite graft patency. Five segments that did not respond to nitroglycerin preoperatively had nonpatent grafts on postoperative study. Asynergy was unchanged in 2 and worsened in 3.

The qualitative data derived from hemiaxes calculations correlated with more qualitatively described analysis (table 4). An example of the quantitative responses to nitroglycerin and bypass is illustrated in figure 2.

At surgery, scar tissue was frequently, although not invariably observed in the unresponsive hypokinetic areas. This was more frequent in the akinetic zones which were unresponsive, and was invariably in the dyskinetic areas.

Nitroglycerin was given to three patients with normal resting ventriculograms. In all three nitroglycerin ventriculograms there was a uniform improvement (increase) in wall motion in all segments. Similar improvement was also regularly observed in the normal zones of ventriculograms exhibiting asynergic segments. Conversely, four patients have had repeat ventriculograms, without nitroglycerin administration, performed 15-20 minutes after the initial angiogram. At this time, the pressures and rate changes invariably had returned to baseline. The changes in the second ventriculogram were infrequent and minor. One previously normal zone became mildly hypokinetic and two mildly hypokinetic zones increased to more moderate hypokinesis. In no instance was improvement of an asynergic segment seen under these circumstances.

Although patients were restudied over a variable

Table 2

<table>
<thead>
<tr>
<th>Severity of asynergy</th>
<th>Total number of segments</th>
<th>Number of segments</th>
<th>% hemiaxis shortening</th>
<th>Number of segments</th>
<th>% hemiaxis shortening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypokinesis</td>
<td>11</td>
<td>10/11 (91%)</td>
<td>28.8 ± 5.6*</td>
<td>1/1 (9%)</td>
<td>3.0</td>
</tr>
<tr>
<td>Akinisis</td>
<td>8</td>
<td>5/8 (63%)</td>
<td>20.4 ± 7.1</td>
<td>3/3 (37%)</td>
<td>2.6 ± 1.4</td>
</tr>
<tr>
<td>Dyskinesis</td>
<td>1</td>
<td>0/1 (0%)</td>
<td>—</td>
<td>1/1 (100%)</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* = standard error of the mean.

Table 3

<table>
<thead>
<tr>
<th>Pt.</th>
<th>LAD segment</th>
<th>RCA segment</th>
<th>LCF segment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control TNG Bypass Graft</td>
<td>Control TNG Bypass Graft</td>
<td>Control TNG Bypass Graft</td>
</tr>
<tr>
<td>RC</td>
<td>Akin Wnl Wnl O</td>
<td>Hypo Wnl Wnl O</td>
<td>Akin Akin Akin No</td>
</tr>
<tr>
<td>JM</td>
<td>Hypo Wnl Wnl O</td>
<td>Hypo Wnl Wnl O</td>
<td>Wnl Wnl Wnl No</td>
</tr>
<tr>
<td>JM</td>
<td>Hypo Wnl Wnl O</td>
<td>Hypo Wnl Akin O</td>
<td>Hypo Wnl Wnl O</td>
</tr>
<tr>
<td>CB</td>
<td>Hypo Wnl Wnl O</td>
<td>Akin Akin Akin O</td>
<td>Wnl Wnl Wnl No</td>
</tr>
<tr>
<td>FG</td>
<td>Akin Wnl Wnl O</td>
<td>Wnl Wnl Akin O</td>
<td>Wnl Wnl Wnl O</td>
</tr>
<tr>
<td>EH</td>
<td>Hypo Wnl Hypo C</td>
<td>Hypo Wnl Hypo O</td>
<td>Hypo Wnl Hypo No</td>
</tr>
<tr>
<td>ES</td>
<td>Hypo Wnl Hypo C</td>
<td>Akin Hypo Hypo O</td>
<td>Hypo Wnl Hypo No</td>
</tr>
<tr>
<td>CT</td>
<td>Akin Hypo Hypo O</td>
<td>Hypo Wnl Hypo C</td>
<td>Hypo Wnl Hypo No</td>
</tr>
<tr>
<td>MM</td>
<td>Hypo Wnl Wnl O</td>
<td>Hypo Hypo Akin C</td>
<td>Hypo Hypo Hypo No</td>
</tr>
<tr>
<td>FB</td>
<td>Dys Dys Dys No</td>
<td>Hypo Wnl Wnl O</td>
<td>Wnl Wnl Wnl No</td>
</tr>
</tbody>
</table>

Abbreviations: Pt. = patient; LAD = left anterior descending; RCA = right coronary artery; LCF = circumflex; TNG = nitroglycerin; Wnl = normal; Hypo = hypokinesis; Akin = akinesis; Dys = dyskinesis; O = open; C = closed; No = no graft.
time period of 2 weeks to 4 months postoperatively, no differences were found in ventriculographic correlation as a function of elapsed time following bypass. Similarly, no statistically significant changes in myocardial oxygen requirement determinants were found postoperatively concerning heart rate, preload or afterload.

There was no clinical evidence of congestive heart failure in the nitroglycerin responders. Although there frequently was hemodynamic evidence of heart failure, this did not correlate with nitroglycerin responses.

**Discussion**

Coronary bypass surgery is being employed increasingly as a therapeutic procedure for coronary heart disease despite continuing controversy regarding its efficacy. One of the major controversies concerns the effect of the procedure on left ventricular performance. Several groups have found significant improvement in left ventricular function after bypass, while other investigators have found no beneficial effects. Patent grafts were found variably to improve, not change or worsen segmental contraction in additional studies. The present data indicate that patent grafts improved contraction in 15 of 20 segments (table 2). Thus improvement was frequent but not variable.

It is apparent that a preoperative differentiation of potentially reversible from irreversible asynergy should enhance the predictability of a possible corresponding benefit from a bypass graft. The present study indicates that the administration of sublingual nitroglycerin is of considerable value in this regard (table 1). Although nitroglycerin has been used for more than a century to relieve the symptoms of ischemia, considerable uncertainty exists about its mechanism of action. Whether this agent acts primarily by inducing vasodilatation, by redistributing flow to ischemic areas or by reducing left ventricular oxygen consumption is unclear despite the general acceptance of its prompt and efficacious relief of ischemic symptoms.

Recent studies have demonstrated that atrial pacing and isometric handgrip exercise can precipitate asynergy, presumably by deleteriously affecting the relationship of myocardial oxygen supply and demand. The mechanism by which nitroglycerin is capable of improving contraction in some asynergic areas is presumably by favorably affecting this relationship. The responsiveness to nitroglycerin was, as might be expected, related to the severity of asynergy (table 1). Thus, while the majority of hypokinetic zones improved following nitroglycerin, none of the dyskinetic zones changed. The akinetic segments were intermediate (table 1). A recent preliminary report has indicated that epinephrine infusion may also be of value in determining residual contractile ability, presumably acting in a manner converse to propranolol.

One of the limitations of the right anterior oblique ventriculogram is the difficulty in completely defining

---

**Table 4**

<table>
<thead>
<tr>
<th></th>
<th>LAD segment</th>
<th></th>
<th>RCA segment</th>
<th></th>
<th>LCF segment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pt.</td>
<td>Control</td>
<td>TNG</td>
<td>Bypass</td>
<td>Graft</td>
<td>Control</td>
</tr>
<tr>
<td>RC</td>
<td>4</td>
<td>28</td>
<td>30</td>
<td>O</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>JM</td>
<td>14</td>
<td>56</td>
<td>54</td>
<td>O</td>
<td>22</td>
<td>52</td>
</tr>
<tr>
<td>JMcG</td>
<td>17</td>
<td>46</td>
<td>42</td>
<td>O</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>CB</td>
<td>10</td>
<td>38</td>
<td>42</td>
<td>O</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>JG</td>
<td>5</td>
<td>32</td>
<td>35</td>
<td>O</td>
<td>40</td>
<td>46</td>
</tr>
<tr>
<td>WH</td>
<td>6</td>
<td>36</td>
<td>34</td>
<td>O</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td>EH</td>
<td>-4</td>
<td>-4</td>
<td>-2</td>
<td>No</td>
<td>28</td>
<td>31</td>
</tr>
<tr>
<td>ES</td>
<td>18</td>
<td>32</td>
<td>16</td>
<td>C</td>
<td>16</td>
<td>38</td>
</tr>
<tr>
<td>JL</td>
<td>14</td>
<td>28</td>
<td>30</td>
<td>O</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>CT</td>
<td>4</td>
<td>18</td>
<td>18</td>
<td>O</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>MM</td>
<td>15</td>
<td>38</td>
<td>40</td>
<td>O</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>FB</td>
<td>-6</td>
<td>-4</td>
<td>-4</td>
<td>O</td>
<td>12</td>
<td>42</td>
</tr>
</tbody>
</table>

*Numbers indicate % hemi-axis shortening.

---

**Table 5**

**Correlation of Positive TNG Responses with Patent Grafts**

<table>
<thead>
<tr>
<th></th>
<th>LAD segment</th>
<th>RCA segment</th>
<th>LCF segment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TNG</td>
<td>By-pass</td>
<td>TNG</td>
<td>By-pass</td>
</tr>
<tr>
<td>Hypokinesis</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Akinesis</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

TNG = nitroglycerin.
The method of anatomic segmental analysis used in the present study has been utilized by other laboratories, the circumflex segment may not be completely identified without another oblique projection since only a portion of this artery's distribution is visualized in this plane. In the absence of a biplane angiographic facility, this would require four ventriculograms to accurately delineate the lateral and true posterior areas. In most laboratories this would not be practical for routine clinical usage, although it may be useful in some individual cases. The difficulties in assessing the circumflex segment in the right anterior oblique ventriculogram should therefore be kept in mind in interpreting these data in the clinical laboratory.

The most valuable use for the responsiveness of an asynergic segment to nitroglycerin is the degree to which it is predictive of a correspondingly beneficial effect of a coronary bypass graft. The findings of the present study indicate a very good correlation between the response to nitroglycerin and a patent bypass graft (table 5). Thus of a total of 18 segments which responded to nitroglycerin and had patent grafts, 15 also demonstrated postoperative improvement (table 5). Only two segments which were unresponsive to nitroglycerin had patent grafts and the bypass procedure did not improve either of these segments. Thus, although a positive response to nitroglycerin indicates the strong likelihood of a positive response to a patent bypass graft, the data are too fragmentary to draw conclusions on negative responses. The data do however strongly suggest that...
the use of nitroglycerin to determine residual contractile ability in asynergic left ventricular segments may
be of considerable value in better defining both the potential risks and benefits of coronary bypass surgery.

Acknowledgment

The authors wish to thank Mrs. Daryl Heyer, Mrs. Jeanne Frye and Miss Janice Phillips for their technical assistance, and Jeanne Harrison, Andrea Nybrick Karkella and Claudia Lee Gary for aid in preparing this manuscript.

References

   Circulation 48 (suppl III): 11-146, 1973
2. Collins JJ, Cohn LH, Sonnenblick EH, Herman MV, Cohn PF, Gorlin R: Determinants of survival after coronary
   Circulation 48 (suppl III): 113-184, 1973
4. Chatterjee K, Swan HC, Parmley WW, Sustaia H, Marcus H, Matloff J: Depression of left ventricular function due to
   acute myocardial ischemia and its reversal after aortocoronary saphenous-vein bypass. N Engl J Med 256: 1117,
   1972
   48: 487, 1973
7. Spencer FC, Green GE, Tice DA, Wallsh E, Mills WL, Glassman E: Coronary artery bypass grafts for congestive
8. Hamilton GW, Stewart DK, Gould KL, Kennedy JW: Left ventricular function following successful aortocoronary vein
   bypass. (abstr) Am J Cardiol 29: 268, 1972
9. Alderman EL, Sandler H, Marquis S, Harrison DC: Segmental analysis of left ventricular wall motion following
   aortocoronary bypass surgery. (abstr) Circulation 45 (suppl II): 11-68, 1972
    1154, 1972
13. Herman MV, Heinle RA, Kliin MD, Gorlin R: Localized disorders in myocardial contraction: Asynergy and its role
    Am J Cardiol 24: 154, 1969
    1972
17. Parker JD, West RO, DiGeorge S: The effect of nitroglycerin on coronary blood flow and the hemodynamic response to
    exercise in coronary artery disease. Am J Cardiol 26: 59, 1971
18. Pasternac A, Haft JI, Hampton JR, Gorlin R: Effect of ischemia induced by atrial pacing on left ventricular contraction
    patients with coronary heart disease. (abstr) Circulation 46 (suppl II): 11-106, 1973
20. Horn HR, Teichholtz LE, Cohn PF, Herman MV, Gorlin R: Augmentation of left ventricular contraction pattern in
    coronary artery disease by an inotropic catecholamine: The epinephrine ventriculogram. (abstr) Circulation 46
    (suppl II): 11-22, 1972
21. Helfant RH, Herman MV, Gorlin R: Abnormalities of left ventricular contraction induced by beta adrenergic
Nitroglycerin to Unmask Reversible Asynergy Correlation with Post Coronary Bypass Ventriculography

RICHARD H. HELFANT, ROGELIO PINE, STEVEN G. MEISTER, MICHAEL S. FELDMAN, ROBERT G. TROUT and VIDYA S. BANKA

Circulation. 1974;50:108-113
doi: 10.1161/01.CIR.50.1.108

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1974 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/50/1/108

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at: http://circ.ahajournals.org//subscriptions/