Diastolic Murmurs in the Presence of
Starr-Edwards Mitral Prosthesis

With Emphasis on the Genesis of the Austin Flint Murmur

By Richard A. Schaefer, M.D., John H. McAnulty, M.D., Albert Starr, M.D.,
and Shahbudin H. Rahimtoola, M.B., F.R.C.P.

SUMMARY

Diastolic murmurs associated with the Starr-Edwards mitral prosthesis have not been described previously. In this report, five patients with mitral prostheses are described in whom apical mid-diastolic and presystolic murmurs resulted from two different causes. Three patients had clots obstructing the prosthetic orifice. The other two had normally functioning prostheses and moderately severe aortic insufficiency. The occurrence of mid-diastolic and presystolic murmurs in the presence of a normally functioning prosthetic mitral valve demonstrates that 1) the mid-diastolic Austin Flint murmur can occur in the absence of incomplete mitral valve opening, premature mitral valve closure, vibrating mitral leaflets, or relative mitral stenosis and 2) the presystolic Austin Flint murmur can occur in the absence of incomplete valve opening or presystolic mitral regurgitation. However, the presystolic murmur was associated with early closure movement of the prosthetic poppet.

Additional Indexing Words:
Mitral stenosis
Aortic regurgitation
Prosthetic valves

DIASTOLIC MURMURS associated with a Starr-Edwards mitral prosthesis have not been previously reported. We are describing five such patients: in three, the prosthetic orifice was obstructed, and in the other two, aortic regurgitation produced an Austin Flint murmur.

Clinical Material

Case 1

F. W., a 62-year-old woman, was admitted to the University of Oregon Medical School Hospital in September, 1968, with a ten year history of fatigue, dyspnea on exertion, and orthopnea which had progressed to functional Class III. Physical examination showed severe mitral stenosis and regurgitation and this was confirmed by cardiac catheterization. In January, 1969, a Starr-Edwards model 6500, size 3M, disc mitral prosthesis was implanted. The patient was functional Class II on sodium warfarin, digitalis, and diuretics until October, 1973, when she developed a sudden dense right hemiparesis and aphasia. In spite of several other embolic episodes, she refused cardiac catheterization and further cardiac surgery. The prothrombin time was 26% of control. Sulfinpyrazone 200 mg q.i.d. was added to her medications. In April, 1974, the patient consented to further cardiac evaluation. Examination revealed the absence of prosthetic opening and closing sounds. There was a grade II/VI high-pitched diastolic decrescendo murmur at the apex. The electrocardiogram showed atrial fibrillation and left ventricular hypertrophy. Chest X-ray showed cardiomegaly, increased pulmonary vascular markings, and Kerley B lines. Cardiac catheterization demonstrated severe prosthetic valve stenosis and moderate regurgitation (table 1). The excursion of the disc poppet was markedly limited. The coronary arteries were normal. On the morning she was scheduled for mitral prosthesis replacement, the patient became severely hypotensive and oliguric. Vaspressors were administered and she was taken to the operating room where her prosthesis was found fixed in a half-open position by laminated clot. The clotted prosthesis was removed and a Starr-Edwards model 6400, size 2M, ball valve prosthesis was implanted. Postoperatively, the diastolic murmur was absent and the patient became functional Class II. She remains so on sodium warfarin, digoxin, procaine amide, and hydrochlorothiazide.

Case 2

J. D., a 32-year-old man, was admitted to the University of Oregon Medical School Hospital in congestive heart failure. Clinical examination showed findings of severe mitral stenosis. The chest X-ray demonstrated a large left atrium and pulmonary venous congestion. The electrocardiogram showed left atrial enlargement, right axis deviation, and right ventricular hypertrophy. Cardiac catheterization and angiography demonstrated isolated severe mitral stenosis. A severely deformed rheumatic mitral valve was replaced with a model 6320 Starr-Edwards, size 2M, mitral...
Hemodynamic Data at the Time Murmurs Were Present Across Mitral Prosthesis

<table>
<thead>
<tr>
<th></th>
<th>Obstructed mitral prostheses</th>
<th>Nonobstructed mitral prostheses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Atrial Fibrillation</td>
<td>Sinus</td>
</tr>
<tr>
<td>Heart rate</td>
<td>73</td>
<td>72</td>
</tr>
<tr>
<td>Right atrial pressure a wave</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>v wave</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Right ventricular pressure</td>
<td>50/6</td>
<td>—</td>
</tr>
<tr>
<td>Pulmonary artery pressure</td>
<td>58/25 (38)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery wedge pressure a wave</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>v wave</td>
<td>28</td>
<td>—</td>
</tr>
<tr>
<td>Left atrial pressure a wave</td>
<td>30</td>
<td>—</td>
</tr>
<tr>
<td>v wave</td>
<td>22</td>
<td>112/13</td>
</tr>
<tr>
<td>Brachial artery pressure</td>
<td>137/65 (35)</td>
<td>115/72 (100)</td>
</tr>
<tr>
<td>Cardiac index (L/min/M²)</td>
<td>2.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Mean mitral gradient (mm Hg)</td>
<td>23.5</td>
<td>11</td>
</tr>
<tr>
<td>Mitral valve area (cm²)</td>
<td>0.65</td>
<td>1.6</td>
</tr>
<tr>
<td>Mitral valve area index (cm²/M²)</td>
<td>0.40</td>
<td>0.88</td>
</tr>
<tr>
<td>Left ventricular volumes (ml/M²)</td>
<td>End-diastolic</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>81</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.70</td>
<td>0.41</td>
</tr>
</tbody>
</table>

All pressures are in mm Hg. Mean pressures are in brackets.

prosthesis in February, 1972. The postoperative course was uncomplicated. In July, 1972, the patient developed congestive heart failure over a period of a few days. On examination, he had normal prosthetic valve sounds. A grade II/VI mid-systolic apical murmur and grade II/VI apical mid-diastolic and presystolic murmurs were heard for the first time since valve replacement. The chest X-ray showed pulmonary venous congestion with a right pleural effusion. The electrocardiogram was unchanged. His prothrombin time was 100% of control. He improved only minimally with digitalis and diuretics. Cardiac catheterization and angiography (table 1) demonstrated moderately severe stenosis of the prosthesis with no mitral or aortic regurgitation. At open heart surgery a large mural thrombus was found in the left atrium and the prosthetic orifice was narrowed by clot. The valve was replaced by a model 6320, size 3M, Starr-Edwards prosthesis. The postoperative course was complicated by atrial fibrillation requiring cardioversion following which the patient became and remains functional Class I in sinus rhythm on digitalis and sodium warfarin. He has no murmurs.

Case 3

H. W. was a 53-year-old woman who had had rheumatic fever in childhood. She had undergone mitral and aortic commissurotomies in 1953. In 1965, she underwent triple valve replacement receiving a Starr-Edwards model 1000, size 8A, aortic prosthesis and model 6000, size 2M, mitral and tricuspid prostheses. She had improved from severe functional Class III to Class II and was maintained on sodium warfarin, digoxin, and hydrochlorothiazide. There was a brief episode of right hemiparesis in 1968 and of left hemiparesis in 1970. She was admitted to the University of Oregon Medical School Hospital in January, 1974, with a two year history of gradually worsening congestive heart failure which accelerated prior to admission. Examination revealed crisp prosthetic sounds with a grade II/VI blowing diastolic murmur along the left sternal border and a grade II/VI apical decrescendo rumble, which was accentuated with amyl nitrate inhalation (fig. 1). There was a grade II/VI systolic ejection murmur. The electrocardiogram showed atrial fibrillation with a slow ventricular rate, left axis deviation, and left ventricular hypertrophy. The chest X-ray showed a pleural effusion, Kerley B lines, pulmonary venous engorgement and cardiomegaly. The prothrombin time was 46% of control.

Cardiac catheterization and angiography (table 1) demonstrated stenosis of the mitral prosthesis (fig. 2) without regurgitation and mild regurgitation of the aortic prosthesis. The coronary arteries were normal. At operation, the mitral prosthesis was removed and found to be severely obstructed by clot at both the primary and secondary orifices. The aortic valve showed only minimal evidence of silastic poppet degeneration and this poppet was replaced. The tricuspid prosthesis was not examined. The postoperative course was complicated by bleeding requiring reoperation, wound infection leading to sepsis, respiratory failure, and renal failure. A diastolic rumble was not noted following operation. The patient died and permission for autopsy was not granted.

Circulation, Volume 51, March 1975
stenosis and aortic insufficiency. The electrocardiogram showed atrial fibrillation with a ventricular rate of 85 beats/min and nonspecific ST-T wave abnormalities. Cardiac catheterization and angiocardiography demonstrated severe mitral stenosis, mild mitral regurgitation, and moderate aortic insufficiency. The mitral valve was replaced with a model 6400, size 3M, Starr-Edwards prosthesis. The aortic valve was reported to be normal to palpation and was not replaced. Several days after surgery cardioversion resulted in sinus rhythm with first degree atrioventricular block. Following discharge, while on diuretics, the patient was in functional NYHA Class III with mild congestive heart failure. She was readmitted because of this in October, 1973, at which time the blood pressure was 150/80 and the pulse was 80 and regular. There were scattered rales in both lung bases. The prosthetic valve sounds were normal. There was a coarse grade 1/VI systolic ejection murmur along the left sternal border radiating to the carotids. There was a grade III/VI immediate diastolic decrescendo blowing murmur along the left sternal border and a grade III/VI mid-diastolic rumble with presystolic accentuation at the apex. Phonocardiography confirmed the mid-diastolic and presystolic murmurs. Inhalation of amyl nitrate decreased the blood pressure from 137/65 to 110/50 and diminished the intensity of the mid-diastolic and presystolic murmurs both by auscultation and by phonocardiography. The electrocardiogram showed a P-R interval of 0.24 sec, changes compatible with left atrial enlargement, and nonspecific ST-T abnormalities. The chest X-ray showed cardiomegaly without pulmonary venous congestion. Cardiac catheterization and angiography demonstrated a normally functioning mitral prosthesis (table 1 and fig. 3) and moderately severe aortic insufficiency. Left ventricular angiography showed no mitral regurgitation. Poppet movement was assessed by

**Figure 1**

Patient 4. Simultaneous recording of the pulmonary artery wedge (PA wedge) and left ventricular (LV) pressures with the electrocardiogram (ECG). The small pressure gradient becomes even smaller when the time lag due to the delay in the PA wedge recording was taken into account. This small gradient is similar to that found with normally functioning mitral valve prostheses.

**Figure 2**

Patient 3. Simultaneous left atrial (LA), left ventricular (LV), and electrocardiographic (ECG) tracings. The diastolic pressure gradient is shown by the stippled area.
simultaneous electrocardiogram and cinefluorography (fig. 4) with the beginning of poppet closure occurring 33 msec prior to the upstroke of the R wave. At surgery the 6400 mitral prosthesis was well-healed. The absence of mitral regurgitation was confirmed and the poppet was noted to move freely in the cage. The aortic valve was replaced with a model 2400, size 11A, Starr-Edwards valve. Postoperatively, the patient remained in sinus rhythm with a P-R interval of 0.24 sec and the mid-diastolic and presystolic murmurs were absent. Poppet movement (fig. 5) appeared normal and differed from the preoperative study in that closure began 50 msec after the R wave upstroke. This indicated that, preoperatively, the onset of mitral poppet closure movement was "premature."

Case 5
E. D., a 44-year-old woman, had had acute rheumatic fever at age 11. In 1967, she developed progressive dyspnea on exertion, orthopnea, and edema. A mitral commissurotomy was performed in 1970 and she was improved to functional Class I. With reappearance of her symptoms the patient was admitted to the University of Oregon Medical School Hospital in October, 1972. Cardiac catheterization and angiography showed moderate mitral stenosis and regurgitation and mild aortic insufficiency. In November, 1972, a Starr-Edwards model 6400, size 2M, mitral prosthesis was implanted. The aortic valve was palpated at operation and minimal disease was reported. Postoperatively, normal prosthetic sounds, a grade II/VI blowing decrescendo diastolic murmur and a grade II/VI systolic ejection murmur were present along the left sternal border. The patient improved to early Class II and was maintained on warfarin, digoxin, and quinidine. Fatigue, dyspnea on exertion, and orthopnea gradually reappeared and furosemide was added to her medications. In June, 1974, she was readmitted to the hospital in functional Class III. Examination showed a blood pressure of 120/50 and a bounding, bifid carotid pulse. The lungs were clear. The prosthetic valve sounds were normal. There was a grade III/VI rumbling apical mid-diastolic murmur with presystolic accentuation, a grade I/VI coarse systolic ejection murmur along the mid-left sternal border and a grade IV/VI high-pitched diastolic regurgitant murmur along the left sternal border. Inhalation of amyl nitrate decreased the
blood pressure to 105/30 and abolished the rumbling diastolic murmur (fig. 6). There was no peripheral edema. The electrocardiogram showed sinus rhythm, changes compatible with left atrial enlargement, and nonspecific ST-T abnormalities. The chest X-ray showed mild cardiomegaly, a large left atrium, and clear lung fields. Cardiac catheterization (table 1 and fig. 7) included simultaneous electrocardiographic tracings, left ventricular tracings, and cinefluorography of the mitral prosthesis (fig. 8). The poppet began to drift toward closure in diastole prior to atrial contraction. Though this is a normal movement for normal mitral valves, it is not seen by fluoroscopy in normally functioning ball valve prostheses. With atrial contraction, the poppet returned to the fully open position and then began to close 33 msec prior to the upstroke of the electrocardiographic R wave. Cineangiography revealed moderate aortic regurgitation and no mitral regurgitation. The gradient across the mitral valve prosthesis was 2.3 mm Hg. In July, 1974, the patient underwent aortic valve replacement with a Starr-Edwards, model 1200, size 8A, aortic prosthesis. The mitral prosthesis was well-healed and appeared normal. Postoperatively, the mid-diastolic and presystolic murmurs were absent. Cinefluorography of the valve postoperatively (fig. 9) revealed no poppet closure until 33 msec prior to the R wave upstroke. This closure time was equal to that of the final closure of the poppet prior to surgery. The patient was discharged from the hospital, doing well, on sodium salicylates, digoxin, and quinidine.

![Figure 7](image1)

**Figure 7**

*Patient 5. Simultaneous left atrial (LA), left ventricular (LV), and electrocardiographic (ECG) tracings in this patient with a normal mitral prosthesis and aortic insufficiency. The small gradient is consistent with the gradient present in patients with normally functioning mitral prostheses.*

![Figure 8](image2)

**Figure 8**

*Patient 5. Cinefluorographic study at 60 frames/sec of the mitral prosthesis before aortic valve replacement (with the poppet position labeled in relation to the completely closed (closed) or completely opened (open) positions). Selected frames marked by numbers 1 to 6 document the position of the poppet during the cardiac cycle. Simultaneous brachial artery (BA), left ventricular (LV), and left atrial (LA) pressure recordings as well as electrocardiographic (ECG) tracings are shown. The cine frame marker produces artifacts on the pressure and ECG tracings. The poppet starts to close well before atrial contraction (2) opens with this contraction (3) and then begins to close 33 msec prior to the R wave upstroke.*
MITRAL PROSTHETIC DIASTOLIC MURMUR

Figure 9
Patient 5. Cinefluorographic study of the mitral prosthesis after aortic valve replacement. The simultaneous electrocardiographic tracing is shown. The closure that occurred before atrial contraction prior to aortic valve replacement (fig. 5) has disappeared and poppet closure begins 33 msec before the onset of the R wave.

Discussion
Prosthetic Stenosis Murmurs

Apical mid-diastolic and presystolic murmurs have been described as being associated with increased flow across a normal mitral valve, normal flow across an obstructed mitral valve into a dilated left ventricle, or with obstruction of the mitral orifice.1 One might, therefore, expect that obstruction of a prosthetic mitral valve would also produce an apical rumbling murmur as heard in patients 1, 2, and 3. Surprisingly, a review of several large published series of mitral valve replacements2-5 fails to document a diastolic murmur generated across either a normal or a stenotic Starr-Edwards mitral prosthesis. A normally functioning mitral prosthesis typically exhibits a 3 to 8 mm Hg transvalvular gradient,2-6 which may be due in part to impedance and in part to the prosthetic orifice being smaller than the natural orifice. The absence of diastolic murmurs across a mitral prosthesis cannot be attributed to a small gradient or to a low cardiac output since many of the patients with obstruction in the series cited above had large gradients and normal outputs. The apparent rarity of such murmurs suggests that such factors as orifice architecture and the characteristics of contiguous structures may be important to the generation of turbulence audible as a murmur.

Austin Flint Murmur

Patients 4 and 5 are the first reported examples of rumbling apical mid-diastolic and presystolic murmurs resulting from aortic insufficiency in the presence of a normally functioning mitral prosthetic valve. There is ample evidence that the mitral prostheses were functioning normally and that the patients had moderately severe aortic regurgitation. The transvalvular gradients of 3.7 and 2.3 mm Hg are well within the normal range for a Starr-Edwards mitral prosthesis.2,6 The poppet movements were free and brisk, as shown by cineangiography and cinefluorography (figs. 4 and 8).7 At the time of reoperation, the mitral prostheses were well-healed and without evidence of obstruction. Clinical examination suggested significant aortic insufficiency and this was confirmed by supravalvular cineangiography in both cases. Amyl nitrate inhalation decreased the intensities of the diastolic rumble in both patients, suggesting they resulted from aortic insufficiency.6 The apical mid-diastolic and presystolic murmurs disappeared following aortic valve replacement and the mitral prostheses were not altered during reoperation. Therefore, the evidence shows that the mid-diastolic and presystolic murmurs were related to the aortic insufficiency and that these two patients had Austin Flint murmurs.

The occurrence of an Austin Flint murmur in the presence of a mitral prosthesis has important implications with regard to the genesis of the murmur. Flint, in his original description of the murmur, was primarily concerned with the presystolic component: “Experiments show that when the ventricles are filled with liquid, the valvular curtains are floated away from the ventricular sides, approximating to each other and tending to closure of the auricular orifice. ... The distension of the ventricle is such in aortic insufficiency that the mitral curtains are brought into coaptation, and when auricular contraction takes place, the mitral direct current passing between the curtains throws them into vibration and gives rise to the characteristic blubbery murmur.”9 Thus, Flint believed that the murmur to which his name has been given was due to premature mitral valve closure induced by an increased diastolic volume. Subsequently, it has been shown that the murmur may also occur in mid-diastole or may be localized to mid-diastole.10-12 A number of other mechanisms for the Flint murmur have subsequently been postulated. The proven or postulated mechanisms are listed in table 2. It can be seen that most of these mechanisms were not present in our patients. The mid-diastolic and presystolic components of the Austin Flint murmur should be considered separately.

The mechanism of the mid-diastolic component of the murmur observed in patients 4 and 5 is unclear. None of the conditions listed in table 2 appear to have been present in our patients. Since early movement of

Circulation, Volume 51, March 1975
the poppet toward closure occurred after the onset of the mid-diastolic murmur in patient 5, and as this movement did not occur at all in patient 4, premature closure of the valve cannot explain the mid-diastolic component of the murmur. Rushmer and Morgan have suggested that cardiac murmurs are most likely generated by eddy currents on the boundaries of turbulent jets, by periodic fluctuating waves and by vortex shedding.19 In aortic insufficiency, the regurgitant blood forms an expanding turbulent jet in the left ventricle.14 Eddies form at the interface of this rapidly moving jet and the surrounding slowly moving stream. Thus, in some patients the mid-diastolic portion of the Austin Flint murmur may be the result of turbulence generated by the intersection of two blood streams: an expanding turbulent jet flowing retrograde through the aortic valve and a more slowly moving stream flowing antegrade across the mitral valve. Such a mechanism for the Austin Flint murmur was first postulated by DeRenzi16 and by Potain18 nearly 100 years ago. Since the shape of the expanding jet and the distribution of turbulence is related to blood flow velocities and to orifice and chamber architecture, the murmur may not be present in all patients. In our patients, the presence of a prosthesis in the left ventricle may have contributed to the generation of turbulence.

The presystolic component of the Austin Flint murmur in patients 4 and 5 was associated with an early movement of the poppet toward the closed position. This association, however, does not necessarily mean there is a cause and effect relationship especially as, in one of the patients, this early movement persisted postoperatively, after aortic valve replacement, when the presystolic murmur had disappeared.

The generation of turbulence and thus a murmur from the mitral prosthesis would depend on the gradient and the cross-sectional areas across the prosthesis, the velocity of flow, and the architecture of structures encountered by that flow. Previous studies in patients with mitral stenosis and a presystolic murmur had shown that the gradient decreased toward end-diastole, and in fact, for 18 msec prior to mitral valve closure, there was a negative gradient across the valve.17 In calves with normal mitral valves and in those with prosthetic tricuspid valves, flow has been shown to decrease during this period of a decreasing gradient and to reverse transiently during the

The timing of murmurs was classified into two periods: a presystolic period and a mid-diastolic period. The timing of murmurs has been classified into two periods:

### Table 2

Postulated Mechanisms for the Generation of the Austin Flint Murmur

<table>
<thead>
<tr>
<th>Timing of murmur</th>
<th>Previously postulated mechanisms for murmur</th>
<th>References</th>
<th>Observations in our patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b. Incomplete opening of mitral valve because of regurgitant jet striking anterior mitral leaflet</td>
<td>24</td>
<td>b. Valve fully open throughout diastole. Valve gradient normal.</td>
</tr>
<tr>
<td></td>
<td>c. Premature closure of mitral valve: 1) decreased LV compliance 2) increased LV end-diastolic volume or pressure</td>
<td>21, 25, 26</td>
<td>c. In one patient no mid-diastolic closure. In the other patient, transient mid-diastolic valve closure followed the onset of murmur.</td>
</tr>
<tr>
<td></td>
<td>d. Relative stenosis of normal mitral valve because of large left ventricle</td>
<td>27</td>
<td>d. Normal transvalvular prosthetic gradient. Murmur found in such a setting usually short and faint.18</td>
</tr>
<tr>
<td></td>
<td>e. Transmission of low frequency components of aortic insufficiency murmur to apex</td>
<td>29</td>
<td>e. Would not explain presystolic accentuation.</td>
</tr>
<tr>
<td></td>
<td>c. Presystolic mitral regurgitation</td>
<td>12, 30-33</td>
<td>c. Absent angiographically. No reversal of pressure gradient if time delay of wedge pressure tracing taken into account24 in patient 4 and absent in patient 5.</td>
</tr>
</tbody>
</table>
Mitrail Prosthetic Diastolic Murmur

isovolumic contraction period.\textsuperscript{18, 19} A decrease in both the gradient and blood flow across a heart valve might be expected to decrease the murmur rather than to cause presystolic accentuation. Therefore, it has been proposed that partial closure of the mitral valve leaflets accentuates the presystolic murmur by increasing the velocity of flow and, thus, the turbulence.\textsuperscript{20, 21} In our patients, the presystolic accentuation of the murmur started at about the time of the beginning of valve closure. However, in one of our patients (4) the time of closure did not change after aortic valve replacement while the murmur had disappeared, making early poppet movement toward closure an unlikely sole cause of the murmur. As the diastolic movement of the poppets differed in our two patients with Austin Flint murmurs, a single explanation for the development of the presystolic component cannot be obtained from our findings. Until instantaneous changes in gradient, cross-sectional area, and velocity of flow across the valve can be measured simultaneously, the causes of the presystolic murmur must remain conjectural.

Apical mid-diastolic and presystolic murmurs are uncommon in patients with a Starr-Edwards mitral prosthesis. These murmurs occur with obstruction of the mitral prostheses and also with significant aortic insufficiency in the presence of a normal prosthesis.

References

Diastolic murmurs in the presence of Starr-Edwards mitral prosthesis.
R A Schaffer, J H McAnulty, A Starr and S H Rahimtooila

Circulation. 1975;51:402-409
doi: 10.1161/01.CIR.51.3.402

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/51/3/402

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/