APPENDIX TO GREEN FORM

Diet Drug Settlement With American Home Products Corporation

Settlement Matrix Compensation Benefits Guide for Physicians, Attorneys and Class Members

A. A Nationwide Class Action Settlement has been reached with American Home Products Corporation, which will resolve the claims of individuals who took the diet drugs Pondimin® and/or Redux™.

B. Under the Settlement, patients who took the diet drugs Pondimin® and/or Redux™ have a right to receive compensation if they have developed serious levels of valvular heart disease.

C. The amounts which individuals are entitled to recover under this Settlement depend on the person's age at diagnosis of valvular heart disease, the person's "Level of Severity" and additional criteria as set forth below. Payments will be made according to these "Matrices". The original Matrix payment amounts stated in the original Green Form have increased under Section IV.C.1 of the Settlement Agreement. The increases have been at an annual two percent amount. As of January 3, 2025, after applying the two percent annual increase in Matrix payment amounts under Section IV.C.1 of the Settlement Agreement for calendar year 2025, the Matrix payment amounts are the following (less the 6.3947% directed by the Court as fees to Class Counsel representing Class Members generally), and these amounts will continue to increase at two percent annually on January 3rd of each year thereafter:

Matrix A-1 ***Age at diagnosis/event***

Severity Level	≤ 24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-79
I	$182,663	$173,530	$164,854	$156,610	$148,780	$141,340	$134,273	$127,560	$121,182	$109,063	$54,532
II	$949,845	$902,353	$857,236	$814,374	$773,655	$734,972	$698,224	$663,314	$630,148	$567,134	$283,568
III	$1,388,236	$1,318,824	$1,252,882	$1,190,238	$1,130,726	$1,074,190	$1,020,481	$969,456	$920,984	$828,885	$414,443
IV	$1,972,756	$1,874,118	$1,780,412	$1,691,391	$1,606,821	$1,526,481	$1,450,156	$1,377,648	$1,308,766	$1,177,890	$588,946
V	$2,191,951	$2,082,353	$1,978,237	$1,879,324	$1,785,358	$1,696,090	$1,611,286	$1,530,721	$1,454,186	$1,308,767	$654,384

Matrix B-1 ***Age at Diagnosis/event***

Severity Level	≤ 24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-79
I	$36,533	$34,707	$32,971	$31,323	$29,756	$28,270	$26,855	$25,512	$24,237	$21,813	$10,907
II	$189,969	$180,471	$171,447	$162,875	$154,731	$146,995	$139,644	$132,662	$126,031	$113,426	$56,713
III	$277,647	$263,765	$250,576	$238,047	$226,144	$214,838	$204,095	$193,891	$184,198	$165,776	$82,888
IV	$394,551	$374,824	$356,082	$338,278	$321,364	$305,295	$290,030	$275,529	$261,753	$235,578	$117,790
V	$438,390	$416,471	$395,648	$375,866	$357,071	$339,218	$322,257	$306,144	$290,837	$261,753	$130,876

D. The circumstances which determine whether "Matrix A-1" or "Matrix B-1" is applicable are as follows:

1. **For Matrix A-1:** Diet Drug Recipients who ingested Pondimin® and/or Redux™ for 61 or more days, who were diagnosed as FDA Positive, whose conditions are eligible for matrix payments but who do not have any condition or circumstance which makes Matrix B-1 applicable, receive payments on Matrix A-1.

2. **For Matrix B-1:** Diet Drug Recipients who are eligible for matrix payments and to whom one or more of the following conditions apply, receive payments on Matrix B-1:

   - For claims as to the mitral valve, Diet Drug Recipients who were diagnosed as having Mild Mitral Regurgitation (regardless of the duration of ingestion of Pondimin® and/or Redux™).
   - Diet Drug Recipients who ingested Pondimin® and/or Redux™ for 60 days or less, who were diagnosed as FDA Positive.
   - Diet Drug Recipients who ingested Pondimin® and/or Redux™ for 61 or more days, who were diagnosed as FDA Positive with any of the following conditions:

   With respect to an aortic valve claim:

   - The following congenital aortic valve abnormalities: unicuspid, bicuspid or quadricuspid valves, ventricular septal defect associated with aortic regurgitation;
   - Aortic dissection involving the aortic root and/or aortic valve;
   - Aortic stenosis with an aortic valve area <1.0 square centimeter by the Continuity Equation;
   - Aortic sclerosis in people who are greater or equal to 60 years old as of the time they are first diagnosed as FDA Positive;
   - Aortic root dilation > 5.0cm.

   With respect to a mitral valve claim:

   - The following congenital mitral valve abnormalities: parachute valve, cleft of the mitral valve associated with atrial septal defect;
   - Mitral Valve Prolapse as determined by Echocardiogram. “Mitral Valve Prolapse” refers to a condition where (a) the echocardiogram video tape or disk includes the parasternal long axis view and (b) that echocardiographic view shows displacement of one or both mitral leaflets >2mm above the atrial-ventricular border during systole, and >5mm leaflet thickening during diastole, as determined by a Board-Certified Cardiologist;
   - Chordae tendineae rupture or papillary muscle rupture; or acute myocardial infarction associated with acute mitral regurgitation;
   - Mitral annular calcification;
   - M-Mode and 2-D Echocardiographic evidence of rheumatic mitral valves (doming of the anterior leaflet and/or anterior motion of the posterior leaflet and/or commissural fusion), except where there is no evidence of rheumatic valve disease upon pathological examination of mitral valve tissue.

   With respect to claims for the aortic and/or mitral valve(s):

   - Heart valve surgery prior to Pondimin® and/or Redux™ use on the valve that is the basis of

claim;

- Bacterial endocarditis prior to Pondimin® and/or Redux™ use;
- FDA Positive regurgitation (confirmed by Echocardiogram) prior to Pondimin® and/or Redux™ use for the valve that is the basis of claim;
- Systemic Lupus Erythematosus or Rheumatoid Arthritis[1] and valvular regurgitation and/or valvular abnormalities of a type associated with those conditions;[2]
- Carcinoid tumor of a type associated with aortic and/or mitral valve lesions;
- History of daily use of methysergide or ergotamines for a continuous period of longer than 120 days.

E. Diet Drug Recipients' spouses, children and "significant others" ("Derivative Claimants") may also be eligible for Matrix Payments under the law, and if so, they will be paid an amount set forth in one of "Derivative Matrices"- Matrix A-2 or Matrix B-2. As noted above, the Matrix payment amounts increase annually at the rate of two percent per year. As of January 3, 2025, after applying the two percent annual increase in Matrix payment amounts under Section IV.C.1 of the Settlement Agreement (less the 6.3947% directed by the Court as fees to Class Counsel representing Class Members generally), the Matrix payment amounts for Derivative Claimants are set forth in the tables below. Derivative Claimants will be paid at the same "Level of Severity" and age at diagnosis as the Diet Drug Recipient. Matrix A-2 will be used where the Diet Drug Recipient was eligible for Matrix A-1 payments and Matrix B-2 will be used where the Diet Drug Recipient was eligible for Matrix B-1 payments:

Matrix A-2 ***Age at diagnosis/event***

Severity Level	≤ 24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-79
I	$1,845	$1,752	$1,665	$1,582	$1,503	$1,427	$1,357	$1,289	$1,224	$1,091	$738
II	$9,594	$9,115	$8,659	$8,226	$7,814	$7,425	$7,053	$6,700	$6,365	$5,671	$2,836
III	$14,023	$13,321	$12,656	$12,023	$11,422	$10,851	$10,307	$9,792	$9,302	$8,290	$4,145
IV	$19,927	$18,930	$17,984	$17,085	$16,231	$15,419	$14,648	$13,916	$13,220	$11,779	$5,889
V	$22,141	$21,034	$19,981	$18,984	$18,035	$17,133	$16,275	$15,462	$14,688	$13,088	$6,543

Matrix B-2 ***Age at diagnosis/event***

Severity Level	≤ 24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-79
I	$738	$738	$738	$738	$738	$738	$738	$738	$738	$738	$738
II	$1,919	$1,823	$1,731	$1,646	$1,563	$1,485	$1,411	$1,340	$1,272	$1,134	$738
III	$2,805	$2,664	$2,531	$2,405	$2,285	$2,170	$2,062	$1,959	$1,860	$1,658	$830
IV	$3,985	$3,786	$3,597	$3,417	$3,246	$3,083	$2,930	$2,782	$2,644	$2,356	$1,178
V	$4,428	$4,207	$3,996	$3,796	$3,607	$3,426	$3,255	$3,092	$2,937	$2,617	$1,308

F. Under the matrices, the "Levels of Severity" which qualify Diet Drug Recipients for recovery on the Settlement matrices are as follows:

(1) **Matrix Level** I is severe left sided valvular heart disease without complicating factors, and is defined as one of the following:

(a) Severe aortic regurgitation (AR) > 49% jet height/left ventricular outflow tract height (JH/LVOTH)[3] and/or severe mitral regurgitation (MR) > 40% regurgitant jet area/left atrial area (RJA LAA)[4,5] and no complicating factors as defined below;

(b) FDA Positive valvular regurgitation[6] with bacterial endocarditis contracted after commencement of Pondimin® and/or Redux™ use.

(2) **Matrix Level** II is left sided valvular heart disease with complicating factors, and is defined as:

(a) Moderate AR (25%-49% JH/LVOTH)[7] or Severe AR (> 49% JH/LVOTH)[8] with one or more of the following:

i) Pulmonary hypertension secondary to **severe aortic regurgitation** with a peak systolic pulmonary artery pressure > 40 mm Hg measured by cardiac catheterization or with a peak systolic pulmonary artery pressure > 45 mm Hg[9] measured by Doppler Echocardiography, at rest, utilizing standard procedures[10],[11] assuming a right atrial pressure of 10 mm Hg;

ii) Abnormal left ventricular end-systolic dimension > 50 mm[12] by M-mode or 2-D Echocardiography or abnormal left ventricular end-diastolic dimension > 70 mm[13] as measured by M-mode or 2-D Echocardiography;

iii) Ejection fraction of< 50%[14]; and/or

(b) Moderate MR (20%-40% RJA/LAA)[15] or Severe MR(> 40% RJA/LAA)[16] with one or more of the following:

i) Pulmonary hypertension secondary to valvular heart disease with peak systolic pulmonary artery pressure > 40 mm Hg measured by cardiac catheterization or with a peak systolic pulmonary artery pressure > 45 mm Hg[17] measured by Doppler Echocardiography, at rest, utilizing the procedures described in Section F.2.(a)(i);

ii) Abnormal left atrial supero-inferior systolic dimension> 5.3 cm[18] (apical four chamber view) or abnormal left atrial antero-posterior systolic dimension > 4.0 cm (parasternal long axis view) measured by 2-D directed M-mode or 2-D echocardiography with normal sinus rhythm using sites of measurement recommended by the American Society of Echocardiography[19];

iii) Abnormal left ventricular end-systolic dimension $\geq$ 45 mm[20] by M-mode or 2-D Echocardiogram;

iv) Ejection fraction of $\leq$ 60%[21].

v) Arrhythmias, defined as chronic atrial fibrillation/flutter that cannot be converted to normal sinus rhythm, or atrial fibrillation/flutter requiring ongoing medical therapy, either of which are associated with left atrial enlargement; as defined in Section F.2.(b)(ii).

(3) **Matrix Level** III is left sided valvular heart disease requiring surgery or conditions of equal severity, and is defined as:

(a) Surgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin® and/or Redux™; or

(b) Severe regurgitation and the presence of ACC/AHA Class I indications for surgery to repair or replace the aortic[22] and/or mitral[23] valve(s) and a statement from the attending Board Certified Cardiothoracic Surgeon or Board Certified Cardiologist supported by medical records regarding the recommendations made to the patient concerning valvular surgery, with the reason why the surgery is not being performed; or

(c) Qualification for payment at Matrix Level I(b) (as described in Section F.1.b. above) or Matrix Level II and, in addition, a stroke due to bacterial endocarditis contracted after use of Pondimin® and/or Redux™ or as a consequence of chronic atrial fibrillation with left atrial enlargement as defined in Section F.2.(b)(ii) which results in a permanent condition which meets the criteria of AHA Stroke Outcome Classification[24] Functional Level II, determined six months after the event.

(4) **Matrix Level** IV is defined as follows:

(a) Qualification for payment at Matrix Level I(b) (as described in Section F.1.b. above), II or III and, in addition, a stroke due to bacterial endocarditis contracted after use of Pondimin® and/or Redux™ or as a consequence of chronic atrial fibrillation with left atrial enlargement as defined in Section F.2.(b)(ii) which results in a permanent condition which meets the criteria of AHA Stroke Outcome Classification[25] Functional Level Ill, determined six months after the event; or

(b) Qualification for payment at Matrix Level I(b), II, or III and, in addition, a peripheral embolus due to Bacterial Endocarditis contracted after use of Pondimin® and/or Redux™ or as a consequence of atrial fibrillation with left atrial enlargement as defined in Section F.2.(b)(ii) which results in severe permanent impairment to the kidneys, abdominal organs, or extremities, where severe permanent impairment means:

i) for the kidneys, chronic severe renal failure requiring hemodialysis or Continuous Abdominal Peritoneal Dialysis for more than six months;

ii) for the abdominal organs, impairment requiring intra-abdominal surgery;

iii) for the extremities, impairment requiring amputation of a major limb; or

(c) The individual has the following:

i) Qualification for payment at Matrix Level III; and

ii) New York Heart Association Functional Class I or Class II symptoms as documented by the attending Board Certified Cardiothoracic Surgeon or Board-Certified Cardiologist; and

iii) Valvular repair and replacement surgery or ineligibility for surgery due to medical reasons as documented by the attending Board-Certified Cardiothoracic Surgeon or Board-Certified Cardiologist; and

iv) Significant damage to the heart muscle, defined as: (a) a left ventricular ejection fraction < 30% with aortic regurgitation or a left ventricular ejection fraction < 35% with mitral regurgitation in patients who have not had surgery and meet the criteria of Section F.3.(b) or a left ventricular ejection fraction < 40% six months after valvular repair or replacement surgery in patients who have had such surgery; or

(d) The individual has had valvular repair or replacement surgery and has one or more of the following complications which occur either during surgery, within 30 days after surgery, or during the same hospital stay as the surgery:

i) Renal failure, defined as chronic severe renal failure requiring regular hemodialysis or Continuous Abdominal Peritoneal Dialysis for greater than six months following aortic and/or mitral valve replacement surgery;

ii) Peripheral embolus following surgery resulting in severe permanent impairment to the kidneys, abdominal organs, or extremities;

iii) Quadriplegia or paraplegia resulting from cervical spine injury during valvular heart surgery; or

(e) A stroke caused by aortic and/or mitral valve surgery and the stroke has produced a permanent condition which meets the criteria of the AHA Stroke Outcome Functional Levels II or III determined six months after the event.[26]

(f) The individual has had valvular repair or replacement surgery and suffers from post operative endocarditis, mediastinitis or sternal osteomyelitis, either of which requires reopening the median sternotomy for treatment, or a post-operative serious infection defined as HIV or Hepatitis C within six months of surgery as a result of blood transfusion associated with the heart valve surgery.

(g) The individual has had valvular repair or replacement surgery and requires a second surgery through the sternum within 18 months of the initial surgery due to prosthetic valve malfunction, poor fit, or complications reasonably related to the initial surgery.

(5) **Matrix Level V** is defined as:

(a) Endocardial Fibrosis (A) diagnosed by (1) endomyocardial biopsy that demonstrates fibrosis and cardiac catheterization that demonstrates restrictive cardiomyopathy or (2) autopsy that demonstrates endocardial fibrosis and (B) other causes, including dilated cardiomyopathy, myocardial infarction, amyloid, Loeffler's endocarditis, endomyocardial fibrosis as defined in Braunwald (involving one or both ventricles, located in the inflow tracts of the ventricles, commonly involving the chordae tendineae, with partial obliteration of either ventricle commonly present)[27], focal fibrosis secondary to valvular regurgitation *(e.g.,* "jet lesions"), focal fibrosis secondary to catheter instrumentation, and hypertrophic cardiomyopathy with septal fibrosis, have been excluded; or

(b) Left sided valvular heart disease with severe complications, defined as Matrix Levels I(b) (as described in Section F.1.b. above), III or IV above with one or more of the following:

i) A severe stroke following aortic and/or mitral valve surgery or due to bacterial endocarditis contracted after use of Pondimin® and/or Redux™ or as a consequence of chronic atrial fibrillation with left atrial enlargement as defined in Section F.2.b.(ii) and the severe stroke has resulted in a permanent condition which meets the criteria of AHA Stroke Outcome Classification[28] Functional Levels IV or V, determined six months after the event; or

ii) The individual has the following:

a) Qualification for payment at Matrix Levels III or IV; and

b) New York Heart Association Functional Class III or Class IV symptoms as documented by the attending Board-Certified Cardiothoracic Surgeon or Board-Certified Cardiologist; and

c) Valvular repair or replacement surgery or ineligibility for surgery due to medical reasons as documented by the attending Board-Certified Cardiothoracic Surgeon or Board-Certified Cardiologist; and

d) Significant damage to the heart muscle, defined as: (i) a left ventricular ejection fraction < 30% with aortic regurgitation or a left ventricular ejection fraction < 35% with mitral regurgitation, in patients who have not had surgery and meet the criteria of Section F.3.b. or (ii) a left ventricular ejection fraction < 40% six months after valvular repair or replacement surgery in patients who have had such surgery; or

iii) Heart transplant;

iv) Irreversible pulmonary hypertension **(PH)** secondary to valvular heart disease defined as peak-systolic pulmonary artery pressure > 50 mm Hg[29] (by cardiac catheterization) at rest following repair or replacement surgery of the aortic and/or mitral valve(s);

v) Persistent non-cognitive state[30] caused by a complication of valvular heart disease *(e.g.,* cardiac arrest) or valvular repair/replacement surgery supported by a statement from the attending Board-Certified Cardiothoracic Surgeon or Board-Certified Cardiologist, supported by medical records; or

(b) Death resulting from a condition caused by valvular heart disease or valvular repair/replacement surgery which occurred post-Pondimin® and/or Redux™ use supported by a statement from the attending Board Certified Cardiothoracic Surgeon or Board Certified Cardiologist, supported by medical records; or

(c) The individual otherwise qualifies for payment at Matrix Level II, III, or IV and suffers from ventricular fibrillation or sustained ventricular tachycardia which results in hemodynamic compromise.

G. In defining the "Levels of Severity" which qualify Class Members for Matrix Compensation Benefits, the Settlement requires the application of a standardized methodology or protocol. Endnotes have been used in the description of levels of valvular heart disease to indicate reference to a standardized methodology or protocol. The referenced methodologies or protocols, together with the corresponding endnote, are as follows:

ENDNOTES

[1] *See Harrison's Principles of Internal Medicine,* 1878, 1885 (14th ed. 1998).

[2] *See C. Otto, The Practice of Clinical Echocardiography,* 589-91, 592-93 (1997): Mitral regurgitation can be associated with rheumatoid arthritis. The mitral valve may have the following echocardiographic features: rheumatoid nodules present-usually <0.5 cm in diameter; may occur at any location on leaflet, homogeneous soft tissue reflectance and irregular body border; usually rounded shape. The following echocardiographic features of valvular abnormalities associated with Systemic Lupus Erythematosus include: diffuse valvular thickening-aortic and mitral valves, decreased leaflet mobility, and presence of Libman-Sacks vegetations, usually < 1cm in diameter.

[3] *See* J.P. Singh, et al., "Prevalence and Clinical Determinants of Mitral, Tricuspid and Aortic Regurgitation (The Framingham Heart Study)," *American J. Cardiology,* 83:897-902 (1999):

TABLE I Definitions of Grades of Regurgitation

GRADES	MR	AR
Absent	--	--
Trace	w/in 1 cm of valve	JH/LVOH < 10%
Mild	RJA/LAA < 19%	10%-24%
Moderate	20%-40%	25%-49%
Severe	>41%	>50%

Valvular regurgitation was assessed qualitatively using these semiquantitative categories as guidelines.
JH= jet height; LAA= left atrial area; LVOH= left ventricular outflow height; RAA= right atrial area; RJA= regurgitant jet area; w/in= within.

Conventional pulsed Doppler echocardiograph was performed routinely in apical 4 and 5 chamber views by selective placement of the sample volume on the color Doppler echocardiographic regurgitation signals when present. Valvular regurgitation was diagnosed using color-coded Doppler imaging proximal to the valve plane during its closure and extended into the chamber proximal to the valve. For color Doppler studies, gain settings were adjusted to eliminate background speckling and to maximize the extent of intracavity velocity coding. MR was sought from the parasternal long axis, apical 4- and 2-chamber, apical long-axis, and subcostal views. AR was sought using the parasternal long-axis, parasternal short-axis, apical 5-chamber, and apical long-axis views.

MR was considered to be present if blue, green, or mosaic signals were seen originating from the mitral valve and spreading into the left atrium during systole. AR was considered to be present if red, yellow, or mosaic signals (blue in the parasternal long axis) were seen originating from the aortic valve and spreading into the left ventricle during diastole. Valvular regurgitation was assessed qualitatively using semiquantitative guidelines and graded none, trace, mild, moderate, or severe (Table I).

[4] *Id.*

[5] Helmcke, F., Nanda, N.C., Hsiung, M.C., Soto, B., Adey, C.K., Goyal, R.G., Gatewood, R.P., Jr., "Color Doppler Assessment of Mitral Regurgitation with Orthogonal Planes," *Circulation,* 75(1):175-83 (1987):

Three two-dimensional echocardiographic planes (parasternal long and short axis, apical four-chamber view) were used to analyze variables of the mitral regurgitant jet signals in the left atrium. The best correlation with angiography was obtained when the regurgitantjet area **(**RJA**)** (maximum or average from three planes) expressed as a percentage of the left atrial area (LAA) obtained in the same plane as the maximum regurgitant area was considered. The maximum RJA/LAA was under 20% in 34 of 36 patients with angiographic grade I mitral regurgitation, between 20% and 40% in 17 of 18 patients with grade II mitral regurgitation, and over 40% in 26 of 28 patients with severe mitral regurgitation.

[6] *See* Centers for Disease Control and Prevention, "Cardiac Valvulopathy Associated with Exposure to Fenfluramine or Dexfenfluramine: US Department of Health and Human Services Interim Public Health Recommendations," *MMWR Morb. And Mortal. Wkly Rep.,* 46:1061-66 (1997):

Minimal degrees of regurgitation (i.e., trace or mild mitral regurgitation [MR] or trace aortic regurgitation [AR]) are relatively common in the general population and are not generally considered abnormal. Therefore, in this analysis, a case of fenfluramine- or dexfenfluramine-associated cardiac valvulopathy was defined as documented AR of mild or greater severity and/or MR of moderate or greater severity after exposure to these drugs.

[7] *See* Singh, *supra,* note 3.

[8] *Id.*

[9] E. Braunwald, *Heart Disease. A Textbook of Cardiovascular Medicine* 796-98 (1997):

Although pulmonary hypertension is widely recognized as developing in patients with left atrial hypertension due to mitral stenosis, it can also occur in patients with pure mitral regurgitation. In one series, nearly half of a cohort of 41 patients with severe mitral regurgitation had pulmonary artery systolic pressures in excess of 50 mm Hg (citation omitted).

Left ventricular diastolic failure may result from hypertension; aortic stenosis; ischemic heart disease; hypertrophic restrictive and congestive cardiomyopathies; and constrictive pericarditis. Because chronic increases in mean left ventricular filling pressure exceeding 25mm Hg are uncommon, the resulting pulmonary arterial hypertension is only moderate unless reactive pulmonary hypertension also occurs. In the absence of the latter, a normal pulmonary artery mean pressure of 15 mm Hg may arise to approximately 30 mm Hg as a result of left ventricular diastolic dysfunction. Because cardiac output is usually reduced in such patients, the mean pulmonary artery pressure would be considerably less than 30 mm Hg if pulmonary vascular resistance remains unchanged. However, many patients with left ventricular diastolic dysfunction exhibit increased pulmonary vascular resistance and moderately severe pulmonary hypertension.

[10] H. Feigenbaum, *Echocardiography* 201-03 (5th ed. 1994):

The principle technique for determining pulmonary artery pressure involves the use of the tricuspid regurgitant jet

and the Bernoulli equation. By determining the right ventricular systolic pressure and ruling out the existence of any obstruction in the right ventricular outflow tract, one can determine the pulmonary artery systolic pressure. This technique is probably the most accurate for quantitating pulmonary artery pressure (citation omitted).

[11] K.L. Chan, et al., "Comparison of Three Doppler Ultrasound Methods in the Prediction of Pulmonary Artery Pressure," *JACC* 9:549-54 (1987):

Pulmonary artery pressure was noninvasively estimated by three Doppler echocardiographic methods in 50 consecutive patients undergoing cardiac catheterization. First, a systolic transtricuspid gradient was calculated from Doppler-detected triscuspid regurgitation; clinical jugular venous pressure or a fixed value of 14 mm Hg was added to yield systolic pulmonary artery pressure. Second, acceleration time from pulmonary flow analysis was used in a regression equation to derive mean pulmonary artery pressure. Third, right ventricular isovolumic relaxation time was calculated from Doppler-determined pulmonary valve closure and tricuspid valve opening; systolic pulmonary artery pressure was then derived from a nomogram.

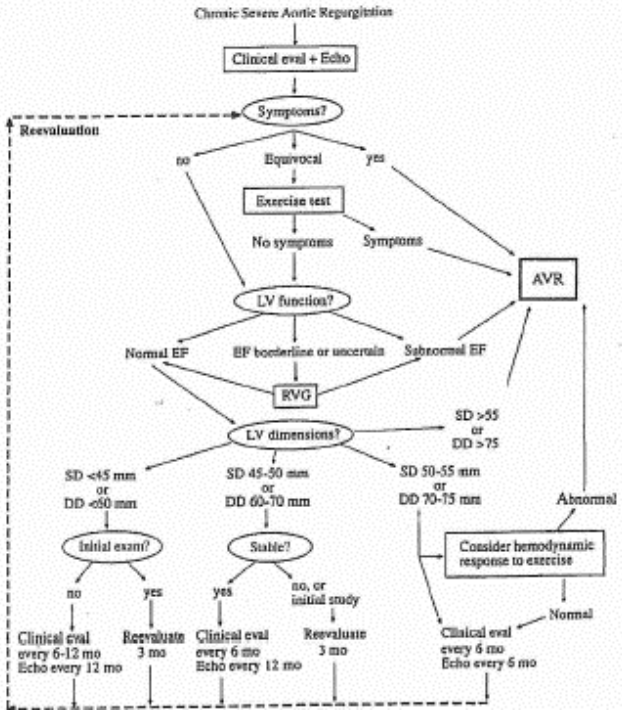
In 48 patients (96%) at least one of the methods could be employed. A tricuspid pressure gradient, obtained in 36 patients (72%), provided reliable prediction of systolic pulmonary artery pressure. The prediction was superior when 14 mm Hg rather than estimated jugular venous pressure was used to account for right atrial pressure. In 44 patients (88%), pulmonary artery flow was analyzed. Prediction of mean pulmonary artery pressure was unsatisfactory (r= 0.65) but improved (r= 0.85) when only patients with a heart rate between 60 and 100 beats/min were considered. The effect of correcting pulmonary flow indexes for heart rate was examined by correlating different flow indexes before and after correction for heart rate. There was a good correlation between corrected acceleration time and either systolic (r= -0.85) or mean (r= -0.83) pulmonary artery pressure. Because of a high incidence of arrhythmia, right ventricular relaxation time could be determined in only 11 patients (22%).

Noninvasive prediction of pulmonary artery pressure is feasible in most patients. Among the three methods, tricuspid gradient measurement seems to be the most useful and practical. Heart rate correction may improve the accuracy of using acceleration time in predicting pulmonary artery pressure; Doppler-determined right ventricular relaxation time seems to be of limited usefulness.

Doppler recordings were obtained from apical, parasternal and subcostal positions. The tricuspid regurgitation signal moved away from the transducer and consisted of a relatively dense high velocity spectral representation. Systematic search for the Doppler signal of tricuspid regurgitation was performed to achieve optimal recording, which consisted of highest maximal velocity with a distinct envelope on the spectral display. No correction was used to compensate for any presumed angle between the ultrasound beam and the direction of maximal velocity flow. The modified Bernoulli equation was employed to derive a systolic transtricuspid gradient that equals 4 v^2, in which v is the maximal regurgitant velocity in meters per second.

There is no systematic difference in systolic pulmonary artery pressure between the Doppler-derived and manometric measurements. In individual patients, considerable difference may occur. This may be related to the variability of the angle between the ultrasound beam and the blood flow. The SEE was similar to that reported in other series (citations omitted). With an estimated pressure of 50 mm Hg, the 95% limits were 34 and 66 mm Hg. Such an estimate is probably within the bounds of clinical usefulness, because pulmonary artery pressure is a dynamic measurement and can vary by more than 30% within a 24 hour period (citation omitted).

[12] *See* R.O. Bonow, et al., “Guidelines for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines”(Committee on Manaement of Patients with Valvular Heart Disease), *JACC* 32:1510-14 (1998):



Description of Figure. Management strategy for patients with chronic severe aortic regurgitation. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is discordance between clinical findings and echocardiography. In some centers, serial follow-up may be performed with RVG or MRI rather than echocardiography to assess LV volume and systolic function.
Abbreviations:
DD= end-diastolic dimension,
RVG= radionuclide ventriculography,
SD= end-systolic dimension.

Asymptomatic patients with normal systolic function but severe AR and significant LV dilatation (end-diastolic dimension > 60mm) require more frequent and careful reevaluation, with a history and physical examination every 6 months and echocardiography every 6 to 12 months, depending on the severity of dilatation and stability of measurements. If stable, echocardiographic measurements are not required more frequently than every 12 months. In patients with more advanced LV dilatation (end-diastolic dimension >70 mm or end-systolic dimension >50 mm), for whom the risk of developing symptoms or LV dysfunction ranges between 10% and 20% per year (citations omitted), it is reasonable to perform serial echocardiograms as frequently as every 4 to 6 months. Serial chest x-rays and ECGs have less value but are helpful in selected patients.

Repeat echocardiograms are also recommended when the patient has onset of symptoms, there is an equivocal history of changing symptoms or exercise tolerance, or there are clinical findings suggesting worsening regurgitation or progressive LV dilatation. Patients with echocardiographic evidence of progressive ventricular dilatation or declining systolic function have a greater likelihood of developing symptoms or LV dysfunction (citation omitted) and should have more frequent follow-up examinations (every 6 months) than those with stable LV function.

Indications for Aortic Valve Replacement. In patients with pure, chronic AR, AVR should be considered only if AR is severe. Patients with only mild AR are not candidates for valve replacement, and if such patients have symptoms or LV dysfunction, other etiologies should be considered, such as CAD, hypertension, or cardiomyopathic processes. If the severity of AR is uncertain after a review of clinical and echocardiographic data, additional information may be needed, such as invasive hemodynamic and angiographic data. The following discussion applies only to those patients with pure, severe AR.

(1) SYMPTOMATIC PATIENTS WITH NORMAL LV SYSTOLIC FUNCTION. AVR is indicate in patients with normal systolic function (defined as ejection fraction $\geq$ 0.50 at rest) who have NYHA functional Class III or IV symptoms

New onset of mild dyspnea has different implications in severe AR, especially in patients with increasing LV chamber size or evidence of declining LV systolic function into the low normal range.

(2) SYMPTOMATIC PATIENTS WITH LV DYSFUCTION. Patients with NYHA-functional Class II, III, or IV symptoms and with mild to moderate LV systolic dysfunction (ejection fraction 0.25 to 0.49) should undergo AVR. Patients with functional Class IV symptoms have worse postoperative survival rates and lower likelihood of recovery of systolic function compared with patients with less severe symptoms, but AVR will improve ventricular loading conditions and expedite subsequent management of LV dysfunction. Symptomatic patients with advanced LV dysfunction (ejection fraction <0.25 and/or end-systolic dimension >60mm) present difficult

management issues. Some patients will manifest meaningful recovery of LV function after operation, but many will have developed irreversible myocardial changes. The mortality associated with valve replacement approaches 10%, and postoperative mortality over the subsequent few years is high. Valve replacement should be considered more strongly in patients with NYHA functional Class II and III symptoms, especially if (1) symptoms and evidence of LV dysfunction are of recent onset and (2) intensive short-term therapy with vasodilators, diuretics, and/or intravenous positive inotropic agents results in substantial improvement in hemodynamics or systolic function. However, even in patients with NYHA functional Class IV symptoms and ejection fraction <0.25, the high risks associated with AVR and subsequent medical management of LV dysfunction are usually a better alternative than the higher risks of long-term medical management alone (citations omitted).

(3) ASYMPTOMATIC PATIENTS. AVR in asymptomatic patients remains a controversial topic, but it is generally agreed that valve replacement is indicated in patients with LV systolic dysfunction LV systolic dysfunction is defined as an ejection fraction below normal at rest. The lower limit of normal will be assumed to be 0.50, realizing that this lower limit is technique dependent and may vary among institutions (citation omitted).

It is recommended that 2 consecutive measurements be obtained before proceeding with a decision to recommend surgery in the asymptomatic patient. These consecutive measurements could be obtained with the same test repeated in a short time period (for example, a second echocardiogram after an initial echocardiogram) or with a separate independent test (for example, a radionuclide ventriculogram or a contrast left ventriculogram after an initial echocardiogram). Valve replacement is also recommended in patients with severe LV dilatation (end-diastolic dimension >75mm or end-systolic dimension >55mm), even if ejection fraction is normal.

Patients with severe AR in whom the degree of dilatation has not reached but is approaching these threshold values (for example, LV end-diastolic dimension of ·70 to 75 mm or end-systolic dimension of 50 to 55 mm) should be followed carefully with frequent echocardiograms every 4 to 6 months. In addition, it is reasonable to recommend AVR in such patients if there is evidence of declining exercise tolerance or abnormal hemodynamic responses to exercise, for example, an increase in pulmonary artery wedge pressure 2: 25 mm Hg with exercise.

A decrease in ejection fraction during exercise should not be used as an indication for AVR in asymptomatic patients with normal systolic function at rest, because the exercise ejection fraction response is multifactorial and the strength of the evidence is limited. The ejection fraction response to exercise has not proved to have independent prognostic value in patients undergoing surgery (citation omitted).

Valve replacement should also not be recommended in asymptomatic patients with normal systolic function merely because of evidence of LV dilation as long as the dilation is not severe (end-diastolic dimension <75 mm or end-systolic dimension <55 mm). Patients who demonstrate progression of LV dilatation or progressive decline in ejection fraction on serial studies represent a higher-risk group who require careful monitoring (citation omitted), but such patients often reach a new steady state and may do well for extended periods of time. Hence, valve replacement is not recommended until the threshold values noted above are reached or symptoms or LV systolic dysfunction develop.

Recommendations for Aortic Valve Replacement in Chronic Severe Aortic Regurgitation

INDICATION	CLASS
1. Patients with NYHA Functional Class III or IV symptoms and preserved LV systolic function, defined as normal ejection fraction at rest (ejection fraction $\geq$ 0.50).	I
2. Patients with NYHA Functional Class II symptoms and preserved LV systolic function (ejection fraction $\geq$ 0.50 at rest) but with progressive LV dilatation or declining ejection fraction at rest on serial studies or declining effort tolerance on exercise testing.	I
3. Patients with Canadian Heart Association Functional Class II or greater angina with or without CAD.	I

4. Asymptomatic or symptomatic patients with mild to moderate LV dysfunction at rest (ejection fraction 0.25 to 0.49).	I
5. Patients undergoing coronary artery bypass surgery or surgery on the aorta or other heart valves.	I

[13] *See Id.*

[14] *See Id.*

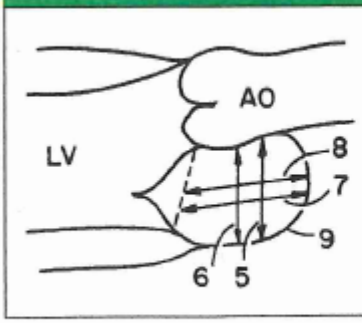
[15] *See* Singh, *supra* note 3.

[16] *See Id.*

[17] *See* Braunwald, *supra* note 9.

[18] *See* A.E. Weyman, *Principles and Practice of Echocardiography* 1290-92 (1994).

Normal Cross-Sectional Valves*



Parasternal Long Axis View	N	Mean ± SD*	Range
Left Atrium (end-systole):			
Antero-posterior dimension†			
5. Maximal	62	3.0 ± 0.3	2.3-3.8
6. Mid-cavity	62	3.0 ± 0.3	2.3-3.8

* All linear dimensions are in cm, and areas are in cm²
† Indicates the preferable view for obtaining a particular measurement.

[19] *See* W.L. Henry et al., "Report of the American Society of Echocardiography Committee on Nomenclature and Standards in Two-dimensional Echocardiography," *Circulation,* 62:212-17 (1980):

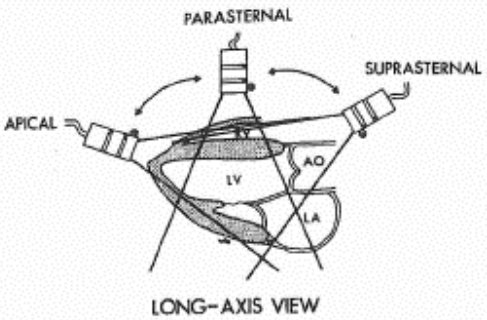
The Committee recommends that when the transducer is placed in the suprasternal notch that it be referred to as in the *suprasternal* location. When the transducer is located near the midline of the body and beneath the lowest ribs, the transducer should be referred to as in the *subcostal* location. When the transducer is located over the apex impulse, the Committee recommends that this be referred to as the *apical* location. If the term *apical* is used alone, it will be assumed that this refers to a *left-sided apical* position. The area bounded superiorly by the left clavicle, medially by the sternum and inferiorly by the apical region will be referred to as the *parasternal* location. If the term *parasternal* is used alone, it will be assumed to be the left parasternal location. In those unusual situations in which the apex impulse is palpated on the right chest, a transducer placed over the right- sided apex impulse will be referred to as in the *right apical* location. The region bounded superiorly by the right clavicle, medially by the sternum and inferiorly by the right apical region will be referred to as the *right parasternal* location.

Imaging Planes

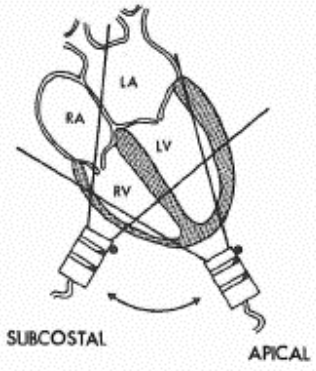
Three orthogonal planes will be used to describe the imaging planes used to visualize the heart with two-dimensional echocardiography. The imagining plane that transects the heart perpendicular to the dorsal and ventral surfaces of the body and parallel to the long axis of the heart will be referred to as the *long-axis* plane. The plane that transects the heart approximately parallel to the dorsal and ventral surfaces of the body will be referred to as the *four-chamber* plane.

Identification of Two-dimensional Images

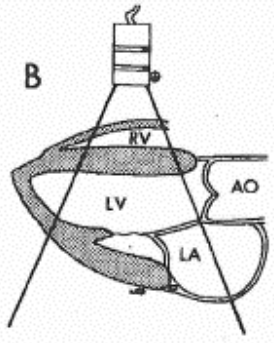
The Committee recommends that two-dimensional images be identified by referring to the transducer location and the imagining plane. For example, if the transducer is placed in the parasternal location and oriented so that the imaging plane transects the heart parallel to the long-axis of the heart, the Committee recommends that the resulting image be referred to as a *parasternal long-axis* view. As another example, if the transducer is placed in the apical location and oriented so that the four-chamber imaging plane is used, the Committee recommends that the resultant image be referred to as an *apical four-chamber* view.



Long-Axis View
Description of figure. Diagram of the transducer orientation used to obtain the long axis view of the heart. Note that the transducer index mark is always pointed either in the direction of the patient's head or the patient's left side.



Four-Chamber View
Description of figure. Diagram of the transducer orientation used to obtain the four-chamber view of the heart.



Parasternal Long-Axis
Description of figure. Illustration of the long-axis, two-dimensional images that result when the transducer is used to visualize the parasternal long-axis view.

[20] *See* R.O. Bonow, *supra* note 12 at 1533-35.

Timing of Surgery for Symptomatic Patients With Normal Left Ventricular Function. Patients with symptoms of congestive heart failure despite normal LV function on echocardiography (ejection fraction >0.60 and end- systolic dimension <45 mm) require surgery. Surgery should be performed in patients with mild symptoms and severe MR (Figure 6), especially if it appears that mitral valve repair rather than replacement can be performed. The feasibility of repair is dependent on several factors, including valve anatomy and surgical expertise. Successful surgical repair improves symptoms, preserves LV function, and avoids the problems of a prosthetic valve. When repair is not feasible, MVR with chordal preservation should relieve symptoms and maintain LV function.

Timing of Surgery for Asymptomatic or Symptomatic Patients with Left Ventricular Dysfunction. Preoperative variables that are predictive of postoperative survival, symptomatic improvement, and postoperative LV function are summarized in Table 20, page 1534 of this reference.

The timing of surgery for asymptomatic patients was controversial, but most would now agree that mitral valve surgery is indicated with the appearance of echocardiographic indicators of LV dysfunction. These include LV ejection fraction $\leq$0.60 and/or LV end-systolic dimension $\geq$45mm (See figure in footnote 20 on previous page). Surgery performed at this time will likely prevent further deterioration in LV function and improve longevity. This is true whether repair or replacement is performed, although repair is clearly preferred. Although some recommend a slightly lower threshold ejection fraction (0.55), it must be emphasized that, unlike timing of AVR for AR, LV ejection fraction should not be allowed to fall into the lower limit of the normal range in patients with chronic MR (citations omitted).

Mitral valve surgery should also be recommended for symptomatic patients with evidence of LV systolic dysfunction (ejection fraction $\leq$0.60 end-systolic dimension $\geq$45 mm). Determining the surgical candidacy of the

symptomatic patient with MR and far-advanced LV dysfunction is a common clinical dilemma. The question that often arises is whether the patient with MR has such advanced LV dysfunction that he or she is no longer a candidate for surgery. Often such cases present difficulty in distinguishing primary cardiomyopathy with secondary MR from primary MR with secondary myocardial dysfunction. In the latter case, if mitral valve repair appears likely, surgery should still be contemplated, provided ejection fraction is $\geq$0.30 (See figure in footnote 20 on previous page).

Asymptomatic Patients With Normal Left Ventricular Function. Repair of a severely regurgitant valve may be contemplated in an asymptomatic patient with normal LV function in order to preserve LV size and function and prevent the sequelae of chronic MR.

This approach is often recommended in hemodynamically stable patients with newly acquired severe MR**,** such as might occur with ruptured chordae. Surgery is also recommended in an asymptomatic patient with chronic MR with recent onset of episodic or chronic atrial fibrillation in whom there is a likelihood of successful valve repair.

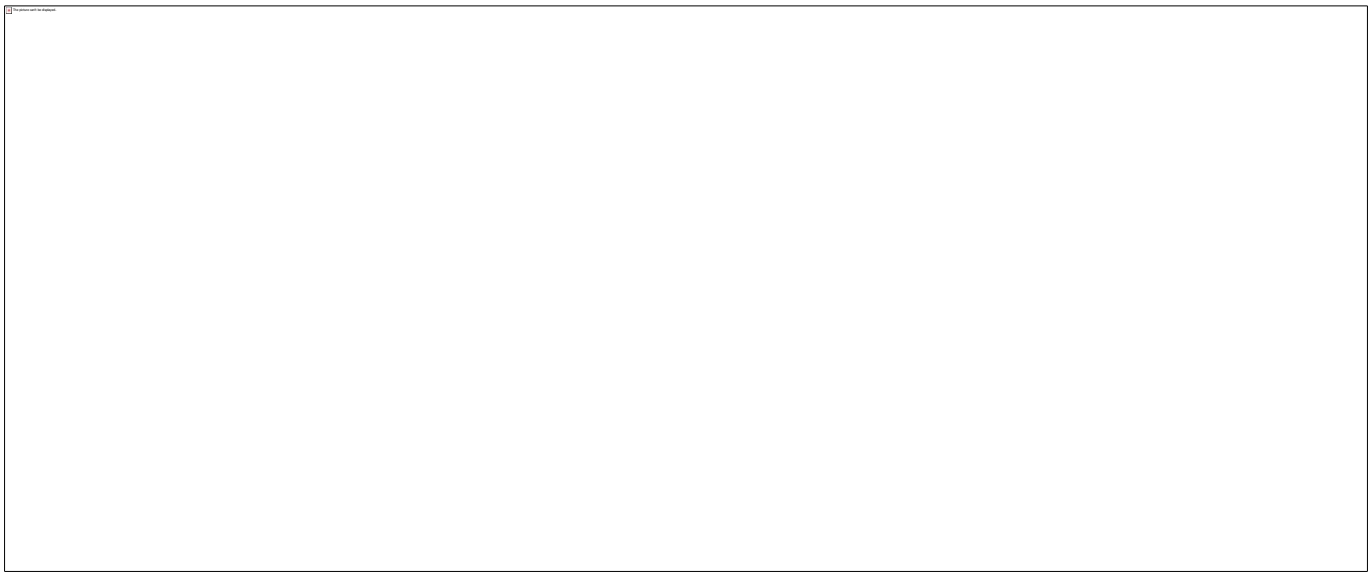
[21] *See Id.*

[22] *See Id.*

[23] *See Id.*

[24] *See* The American Heart Association Stroke Outcome Classification, approved by the American Heart Association Science Advisory and Coordinating Committee, Stroke 29: 1274-80 (1998):

The AHA Stroke Outcome Classification (AHA.SOC) score classifies the severity and extent of neurological impairments that are the basis for disability. The classification also identifies the level of independence of stroke patients according to basic and more complex activities of daily living both at home and in the community. The classification score is meant to describe the limitations resulting from the current stroke. It is not an evaluation of disabilities caused by other neurological events. Furthermore, it is a summary score.



Function

Level

I Independent in Basic Activities of Daily Living (BADL) and Instrumental Activities of Daily Living (IADL) activities and tasks required of roles patient had before the stroke. Patient is able to live alone, maintain a household, and access the community for leisure and/or productive activities such as shopping, employment, or volunteer work.

II Independent in BADL but partially dependent in routine IADL. Patient is able to live alone but requires assistance/supervision to access the community for shopping and leisure act1vities. Patient may require occasional assistance with meal preparation, household tasks, and taking medications.

III Partially dependent in BADL (<3 areas) and IADL. Patient is able to live alone with substantial daily help from family or community resources for more difficult BADL tasks such as dressing lower extremities, bathing, or climbing stairs. Patient requires assistance with such IADL tasks as meal preparation, home maintenance, community access, shopping, handling finances, and/or taking medications.

IV Partially dependent in BADL (≥3 areas). Patient is unable to live alone safely and requires assistance with IADL except for simple tasks such as answering the telephone.

V Completely dependent in BADL (≥5 areas) and IADL. Patient is unable to live alone safely and requires full-time care.

[25] *See Id.*

[26] *See Id.*

[27] E. Braunwald, supra note 9 at 1433-34:

Endomyocardial Fibrosis. EMF occurs most commonly in tropical and subtropical Africa, particularly Uganda and Nigeria. It is typified by fibrous endocardial lesions of the inflow portion of the right or left ventricle or both and often involves the AV valves, resulting in regurgitation (citation omitted).

Pathology. A pericardial effusion, which may be quite large, may be present. The heart is normal in size or slightly enlarged, but massive cardiomegaly does not occur. The right atrium is often dilated, and in patients with severe right ventricular involvement there may be massive enlargement of this chamber. Indentation of the right border of the heart above the apex as a result of apical scarring may occur (citation omitted). Combined right and left ventricular disease occurs in about half the cases, with pure left ventricular involvement occurring in 40 per cent and pure right ventricular involvement in the remaining 10 per cent of patients who are examined post m01tem (citation omitted).

Left ventricular involvement is similar, with fibrosis extending from the apex up the inflow portion of the left ventricle to the posterior mitral valve leaflet. The anterior leaflet of the mitral valve and the outflow portion of the left ventricle are usually spared. Thrombi often overlie the endocardial lesions, and widely distributed endocardial calcific deposits may occur. The coronary arteries are uninvolved, as is the remainder of the body (citation omitted).

Left Ventricular EMF. With predominant *left-sided* involvement, the endomyocardial fibrosis invades the apex of the ventricle and usually the chordae tendineae or the posterior mitral valve leaflet as well, leading to mitral valve regurgitation. The murmur may be confined to late systole, as is characteristic of the papillary muscle dysfunction type of murmur, or it may be pansystolic. Findings of pulmonary hypertension may be prominent. A protodiastolic gallop is commonly heard (citation omitted).

[28] *See American Heart Association Stroke Outcome Classification, supra* note 24.

[29] Braunwald *supra* note 9, at 796-98.

[30] *See* G. Adelman, *Encyclopedia of Neuroscience,* 268 (1987):

The vegetative state is the condition wherein arousal (i.e., sleep-wake cycles) returns or remains but appropriate testing measures elicit no evidence of the person's cognitive awareness of self or environment.