Clinical and Physiologic Relationships in Mitral Valve Disease

By Philip Samet, M.D., Robert S. Litwak, M.D., William H. Bernstein, M.D., Eugene M. Fierer, M.D., and Leonard M. Silverman, M.D.

Physiologic data obtained during right and combined right and left heart catheterization are presented in a variety of subjects with mitral valve disease. These studies have led to a broader understanding of the pathophysiology of this disease. The clinical value of combined heart catheterization is illustrated.

Much has been written relative to the physiologic abnormalities produced by mitral stenosis and insufficiency. Most of the data and the concepts derived therefrom have been obtained by right heart catheterization.1-8 The introduction of left heart and combined heart catheterization9-19 has greatly enhanced the value of physiologic study in patients with rheumatic mitral valve disease and has permitted a reevaluation of the concepts previously developed.

The major purpose of the present report is to delineate and separate the varied types of rheumatic mitral valve disease and to illustrate the importance of combined simultaneous right and left heart catheterization. Evaluation of some of the clinical and physiologic effects of mitral commissurotomy are also presented.

Methods and Materials

Fifty-three subjects with varied types of mitral valve disease were studied. The physical characteristics and diagnoses are given in table 1.8 Multivalvular disease was present in 13 subjects. Fifty-one of the 53 patients had symptoms at the time of study. The complaints included dyspnea at rest or on exertion, orthopnea, weakness and easy fatigability, cough with or without hemoptysis, palpitation, and edema. Gross heart failure, left or right, was not present in any subject at the time of study. The majority had been digitalized prior to catheterization. Several were digitalized during or subsequent to the first study. There was no clinical evidence of active rheumatic fever or subacute bacterial endocarditis noted in any of these subjects.

Each subject had a complete history, physical examination, cardiac fluoroscopy, and electrocardiogram performed prior to physiologic study. Laboratory studies included prothrombin time, bleeding and clotting time, and platelet count in addition to the usual determinations. The hemotologic work-up was especially required prior to left heart catheterization. All subjects were hospitalized for a sufficient period of time prior to catheterization to permit attainment of the maximum possible cardiac compensation.

Right heart catheterization and arterial cannulation were performed via the same arm (whenever possible), in the usual manner in the basal postabsorptive state to permit cardiac output determination by the Fick principle. Multiple steady-state pressure and cardiac output determinations were made at rest and during exercise and recovery. When feasible, double-lumen or triple-lumen catheters were employed to permit simultaneous pressure recording from multiple sites in the pulmonary artery and right heart. With the right heart catheter and brachial artery needle in situ, the patient was then turned to the prone position. Repeat right heart pressures were obtained, followed by the intramuscular administration of 50 to 75 mg. of meperidine hydrochloride.

Left heart catheterization was carried out by a modification of the technic of posterior percutaneous puncture of Fisher,12 subsequent to fluoroscopic visualization of the left atrium in the prone position. Two 6 to 8 inch no. 17 thin-walled styletted needles were inserted in the left atrium. Polyethylene tubing was then passed through these
In the supine and prone positions, the selected reference level for right heart pressures was 5 cm. dorsal to the angle of Louis; the corresponding level for left heart pressures was 10 cm. dorsal to this angle.

Left atrial and left ventricular pressures were determined simultaneously in the operating room immediately prior to and subsequent to mitral commissurotomy. The zero level was 10 cm. posterior to the angle of Louis. The left-sided chamber pressures were recorded via a 1½-inch no. 20 gage needle, 48 inches of black polyvinyl tubing, and Statham P23AA strain gages.

**RESULTS**

The pressure data obtained in the course of these studies are given in table 2. The cardiac output data are outlined in table 3. These data permit evaluation of a number of relationships.

The pulmonary artery wedge pressure has been employed widely as a measure of left atrial pressure. The relation between these 2 pressure levels in 22 patients is illustrated in figure 2. The pulmonary artery wedge pressure was determined at the onset of right heart catheterization, supine. The left atrial pressure was determined during combined right and left heart catheterization after return to the supine position. A straight line drawn at an inclination of 45° represents the theoretical line of identity. Most points fall to the right of the 45° line. The average pulmonary artery wedge pressure is 14 mm. Hg; the average left atrial mean pressure is 17 mm. Hg. The average difference, regardless of the sign, is 3.5 mm. Hg. This would suggest that the mean pulmonary artery wedge pressure gives a fair approximation of mean left atrial pressure and, by inference, an approximation of the degree of narrowing of the mitral valve. In figure 3 the mean pulmonary artery wedge pressure is plotted on the ordinate. The corresponding left atrial-left ventricular mean diastolic gradients are plotted on the abscissa. The numbers at any one level of pulmonary artery wedge pressure refer to the prone and supine gradients in patients 1, 2, 3, etc. Figure 3 readily demonstrates the poor correlation between these 2 variables. If the upper limit of normal wedge

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pressure is taken as 12 mm. Hg, it appears that significant gradients are present in 5 subjects with normal wedge pressures. Dickens et al. have observed similar findings.24

The effect of position upon the left atrial-left ventricular gradient is worthy of comment. The average gradient prone in 25 patients (before and after operation) at rest prone was 10 mm. Hg. In these same subjects the mean gradient at rest supine equaled 7 mm. Hg. During exercise in the supine position, the gradient rose to 12 mm. Hg. Similar data were available in 15 preoperative studies. These latter gradients averaged 14 mm. Hg at rest prone, 10 mm. Hg at rest supine, and 18 mm. Hg during exercise supine.

Position, prone or supine, has also been found to have a definite effect on pulmonary artery pressure (fig. 4). The abscissa is the mean pulmonary artery pressure, supine, during right heart catheterization only. The corresponding pulmonary artery mean pressures prone (during right and during combined heart catheterization) and during combined heart catheterization supine, are shown on the ordinate. The numbers at any one level of pulmonary artery mean pressure, supine, right heart catheterization only, refer to the pulmonary artery mean pressures during combined heart catheterization (prone or supine) and during right heart catheterization, prone, in patients 1, 2, 3, etc. The great majority of the points fall above the 45° line of identity.

The relationship between cardiac index and the mean diastolic left atrial–left ventricular gradient at rest and exercise during combined heart catheterization is pictured in figure 5. The preoperative and postoperative cases are readily separated in this fashion, except for 2 patients, A. Gre. and W. Cur. The former is a 30-year-old asymptomatic white woman, the latter a 36-year-old white man in whom the myocardial factor was considered to be the primary cause of the patient's symptomatology. The gross increase in gradient induced by relatively small increases in flow (and potentiated by the concomitant tachy-
against the corresponding pressure prone, before and after insertion of the left heart needles, and against the pulmonary artery mean pressure, supine, during combined heart catheterization. The straight line is the 45° line of identity. Note that most points fall above the line. The small numbers at any one level of the abscissa refer to individual cases as in figure 3.

Cardiac output (i.e., the oxygen consumption values in the 2 states, i.e., before and after operation, reveals virtually identical figures, 119 and 122 ml./min./M.² respectively. The average difference in oxygen uptake, regardless of the sign of the deviation, is 8 ml./min./M.².

A comparison of the mean left atrial-left ventricular diastolic gradient obtained in the course of combined heart catheterization with those available at the operating table is provided in table 5. In the prone position the mean gradient for 13 patients was 13.5 mm. Hg. The corresponding figure for the preoperative operating room gradient was 14.7 mm. Hg. In the supine position, the gradient averaged 10 mm. Hg in 8 subjects, in whom these data were available. In these same 8 subjects, the gradient in the prone position was 12 mm. Hg; the operating room average gradient was 15 mm. Hg.

**DISCUSSION**

The development of left and combined heart catheterization has permitted a more comprehensive view of the hemodynamic abnormalities resulting from mitral valve disease and also a firmer basis upon which to evaluate the results of mitral commissurotomy. The physiologic hallmark of mitral stenosis is the existence of a significant mean diastolic left atrial-left ventricular gradient. Gradients of 8 mm. Hg at rest prone, 5 mm. Hg at rest supine, and 10 mm. Hg during exercise supine have, somewhat arbitrarily, been defined as the minimal gradients suggestive of physiologically and clinically significant mitral stenosis. These levels were chosen after due study of the postoperative gradients obtained in subjects with good to excellent symptomatic improvement after surgery.

Pulmonary artery wedge pressure (upper level of normal 12 mm. Hg) has been utilized as a measure of mean left atrial pressure and also as a measure of the presence or absence of physiologically significant mitral valve block. The data in the present study raise serious doubt as to the validity of such an approach. Not only may wide variations occur in individual cases in the level of mean pul-
monary artery wedge and mean left atrial pressure (fig. 2), but even more fundamental is the fact that significant left atrioventricular diastolic gradients may coexist with normal pulmonary artery wedge pressures (fig. 3). The existence of tight mitral stenosis has been surgically verified in 3 of these subjects with normal pulmonary artery wedge pressures, E. Coo. and W. McB. in table 2, and a third subject not listed in tables 1 to 3. Furthermore, an elevated pulmonary artery wedge pressure was found 10 months postoperatively in D. Dix.; left atrial mean pressure was normal at this time and the gradients at rest were 2 and 1 mm. Hg prone and supine respectively. Substitution of pulmonary artery wedge mean pressure for left atrial mean pressure, as is still being done, is thus fraught with considerable potential error.

The finding that mean pulmonary artery wedge pressure may be recorded as lower than mean left atrial pressure (fig. 2) requires comment. At first thought, this observation is difficult to understand. The fact that the zero baseline for the pulmonary artery wedge pressure is taken as 5 cm. dorsal to the angle of Louis while that for the left atrial pressure supine is taken as 10 cm. dorsal to this point does not explain the difference in pressures. Actually, pulmonary artery wedge pressure is recorded in an "unsteady state" at the onset of right heart catheterization in this laboratory. A large L-shaped lead shield (to protect the operator from stray x-ray radiation) is still in situ on the fluoroscopic table at this time. The patient's arm rests in the angle of this shield. The room lights have just been turned on after positioning the catheter in the wedge position. The wedge pressure is recorded as rapidly as possible and the catheter tip withdrawn to the right or left pulmonary artery to prevent any complications from the wedging procedure. Simultaneously recorded pulmonary artery pressures and ventricular rates are usually significantly higher at this point than the corresponding values obtained later in the study when the tip is withdrawn to the pulmonary artery and a steady state is achieved. These findings suggest that the true steady-state pulmonary artery wedge pressures would be lower than those in figure 2, and that the differences between steady-state wedge pressures and steady-state left atrial pressures su-

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before operation</th>
<th>After operation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiac index (Lx. / min./M.²)</td>
<td>O₂ consumption (ml./ min./M.²)</td>
</tr>
<tr>
<td>S. Bri.</td>
<td>2.50</td>
<td>111</td>
</tr>
<tr>
<td>J. Van.</td>
<td>2.50</td>
<td>125</td>
</tr>
<tr>
<td>D. Dix.</td>
<td>1.92</td>
<td>127</td>
</tr>
<tr>
<td>R. Ros.</td>
<td>3.17</td>
<td>120</td>
</tr>
<tr>
<td>S. Wor.</td>
<td>1.92</td>
<td>128</td>
</tr>
<tr>
<td>L. Kar.</td>
<td>2.33</td>
<td>118</td>
</tr>
<tr>
<td>S. Jon.</td>
<td>2.32</td>
<td>136</td>
</tr>
<tr>
<td>E. Ros.</td>
<td>1.99</td>
<td>107</td>
</tr>
<tr>
<td>S. Tal.</td>
<td>1.91</td>
<td>102</td>
</tr>
<tr>
<td>G. Doy.</td>
<td>2.37</td>
<td>107</td>
</tr>
<tr>
<td>M. Mul.</td>
<td>1.91</td>
<td>111</td>
</tr>
<tr>
<td>R. Rie.</td>
<td>2.54</td>
<td>129</td>
</tr>
</tbody>
</table>

Average difference (excluding S. Bri.)
Average difference (excluding S. Bri.)
Cardiac index: 0.24 Lx./min./M.²
O₂ consumption: 8 ml./min./M.²

Table 5.—Comparison of Preoperative Catheterization and Operating Room Mean Diastolic Atrioventricular Gradients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Preoperative</th>
<th>Prone</th>
<th>Supine</th>
<th>In operating room</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. Ros.</td>
<td>10</td>
<td>6</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>E. Coo.</td>
<td>9</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>A. Dan.</td>
<td>8</td>
<td>—</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>D. Dix.</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>R. Ros.</td>
<td>18</td>
<td>16</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>S. Wor.</td>
<td>24</td>
<td>—</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>L. Kar.</td>
<td>7</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>W. McB.</td>
<td>10</td>
<td>8</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>F. Lip.</td>
<td>14</td>
<td>7</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>J. Gay.</td>
<td>15</td>
<td>—</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>G. Doy.</td>
<td>20</td>
<td>12</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>R. Vog.</td>
<td>13</td>
<td>—</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>R. Cos.</td>
<td>17</td>
<td>—</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

Average (all 13) 13.5
Average (8) 12 10 15

Average 14.7

Average 15
pine would be even greater than those noted in figure 2. It is our belief that the recording of pulmonary artery wedge pressure is subject to considerable actual and potential error and that the best explanation for the differences in figure 2 is to be found in consideration of these errors. This problem will be discussed more fully elsewhere.\(^{33}\) The fact that cardiac output at rest and exercise, during combined heart catheterization supine, agreed closely with those during right heart catheterization alone\(^{31}\) suggests that the clinical condition of the patient had not deteriorated at the time of combined heart catheterization and that the difference between left atrial and pulmonary artery mean wedge pressures could not be ascribed to such deterioration.

Since different laboratories perform left heart catheterization in varying positions (supine in the bronchoscopic, direct left ventricular, and suprasternal approaches, and prone in the percutaneous transthoracic technic of Fisher), analysis of the effect of a change in position upon the mean diastolic left atrial-left ventricular gradient and upon pulmonary artery pressure is of considerable interest. The gradient is 3 mm. Hg larger in the prone than in the supine position for all cases (before and after operation) and 4 mm. Hg greater in the preoperative cases. Change in position, i.e., prone or supine, also results in a change in pulmonary artery pressure. The effects of left heart catheterization per se and of change in position from supine to prone and back again to supine are shown in figure 4. In 31 subjects mean pulmonary artery pressure was measured in the supine position and again in the prone position before insertion of the left atrial needles. The average pressure supine was 26 mm. Hg, the average pressure prone, 35 mm. Hg. The difference is significant, \(p<.001\). The 95 per cent confidence interval is 6 to 12 mm. Hg. In 13 patients, the mean pulmonary artery pressure in the prone position before insertion of the left heart needles averaged 41 mm. Hg; after insertion of the needles the mean pressure rose only to 44 mm. Hg; this difference is not statistically significant, \(3>p>2\). The 95 per cent confidence interval is \(-3\) to +8 mm. Hg. Left heart catheterization per se caused an insignificant rise in pulmonary artery pressure. In 20 studies mean pulmonary artery supine was 30 mm. Hg. Rotation into the prone position and insertion of the left heart needles resulted in a rise of 15 mm. Hg to 45 mm. Hg, \(p<.001\). The 95 per cent confidence interval is 10 to 20 mm. Hg. In 11 subjects mean pulmonary artery pressure prone after insertion of the left heart needles was 39 mm. Hg. This pres-

\[\text{Fig. 5 Left. The relation between atrioventricular gradient and cardiac index at rest and during exercise (supine) in the course of combined heart catheterization. The preoperative and postoperative cases are clearly separated except for A. Gre. and W. Cur.}\]

\[\text{Fig. 6 Right. Relationship between atrioventricular gradient and oxygen consumption at rest and during exercise. Data obtained during combined heart catheterization.}\]
sure level fell to 30 mm. Hg after rotation back into the supine position. The 95 per cent confidence interval is 4 to 15 mm. Hg. This again demonstrates the tendency of the prone position to cause a rise in pulmonary artery pressure. In 26 patients mean pulmonary artery pressure supine (during right heart catheterization alone) was 25 mm. Hg; after rotation into the prone position, insertion of the left heart needles, and rotation back to the supine position, the same pressure averaged 30 mm. Hg, p<.001. The 95 per cent confidence limit is 3 to 7 mm. Hg. This represents a rise of only 5 mm. Hg, compared to a rise of 15 mm. Hg in the group of 20 subjects referred to above.

At least part of the increase in pulmonary artery pressure and in left atrial-left ventricular mean diastolic gradient in the prone as opposed to the supine position may be ascribed to the increased ventricular rate in the prone position. The pernicious effect of tachycardia in patients with mitral stenosis is well known. The diastolic period of atrioventricular filling is shortened during tachycardia. This necessitates an increased rate of flow across the mitral valve in the shortened diastolic period if cardiac output is to be maintained. An increased rate of flow in turn necessitates a greater diastolic pressure gradient across the valve. Such an increase leads to further left atrial, pulmonary venous, and pulmonary artery hypertension. This effect is especially noted in patients with atrial fibrillation. The gradient is larger following a short R-R electrocardiographic interval, and progressively falls in the diastolic period between a prolonged R-R interval. In addition to a rise in left atrioventricular diastolic gradient and rise in pulmonary artery pressure (often with a rise in right ventricular end-diastolic pressure), the prone position was associated with the development of a cyanotic suffusion of the face, neck, and upper chest. This physical sign was noted only in the patients with mitral valve block, but was not invariably found in these patients. Attempts to reproduce this sign in bed on the ward proved unsuccessful, however.

The importance of interrelations between heart rate, cardiac output, and diastolic atrioventricular gradient has been emphasized by many investigators. The graphic relation between mitral valve flow and mean diastolic gradient is illustrated in figure 5. There is a clear delineation between the preoperative and postoperative cases except for the asymptomatic, A. Gre. and for W. Cur. Mitral valve block results in a sharp rise in gradient for relatively small increases in blood flow.

The details of multiple hemodynamic studies in 2 patients (J. Van. and D. Dix.) are outlined in figures 7 and 8. Each was catheterized prior and subsequent to a successful mitral commissurotomy. The progressive fall in pulmonary artery pressure postoperatively is probably secondary to progressive regression of pulmonary vascular disease. In J. Van. the result was a completely normal pulmonary artery pressure at rest and exercise 1 year after surgery. In D. Dix., 5 weeks after surgery, moderately severe pulmonary hypertension persisted at rest and during exercise. Without simultaneous left heart catheterization, the persistent pulmonary hypertension could have been attributed to inadequate mitral commissurotomy. However, the small left atrial-left ventricular diastolic gradients at rest and exercise obtained at this time render such an explanation invalid. The all but complete abolition of the left atrial-left ventricular gradient after surgery, both at rest and during exercise, in both patients, is worthy of note.

The effect of mitral commissurotomy upon cardiac output has been extensively discussed in the literature. Two recent papers illustrate the problem of interpretation of output changes. Donald and co-workers determined cardiac outputs in 28 patients before and after mitral commissurotomy. In 26 these data were available prior to and after surgery. The average index preoperatively was 2.87 L./min./M.² (a rather surprisingly normal level). The postoperative average was 2.24 L./min./M.². This fall occurred despite pronounced clinical improvement postoperatively in 24 of the 28 subjects. Inspection of
FIG. 7. Preoperative and postoperative data in J. Van. (b and c under prone) refer to data in the prone position prior to and after insertion of the left heart needles.

the oxygen consumption figures, however, provides at least a partial explanation for the fall in output after commissurotomy. The average oxygen consumption preoperatively was 154 ml./min./M.²; the corresponding postoperative figure was 130. The average change (disregarding the sign of the change) is 26 ml./min./M.² In view of this large fall in oxygen consumption, comparison of preoperative cardiac indices is difficult. On the other hand, Dickens and co-investigators²⁵ noted an average cardiac index of 2.17 L./min./M.² in 13 patients prior to surgery. The output rose to 3.00 L./min./M.² after surgery. The preoperative oxygen consumption was 171 ml./min./M.²; the corresponding postoperative figure was 184 ml./min./M.² The average change was 25 ml./min./M.² At least part of the output rise after surgery must be attributed to an increase in oxygen consumption. Other workers have noted variable increases in flow after surgery.

Eleven output studies before and after operation are available in the present paper. In half, a significant increase in cardiac index occurred; in the other half the output was unchanged. The average increase in flow was about 10 per cent (table 4). The average oxygen uptake prior to surgery was 119 ml./min./M.²; postoperatively the oxygen consumption was 122. The average change, regardless of the sign of the change, was 8 ml./min./M.² The series is too small, however, to permit definite conclusions.

In view of the acknowledged importance of flow and heart rate in interpretation of a
diastolic atrioventricular gradient, the fairly close agreement between the catheterization and operating room gradients (table 5) is somewhat surprising. The scatter in agreement is wide, but the average gradient prone during catheterization of the left heart is of the same order of magnitude as that during surgery. The smaller gradients obtained in the supine position during catheterization again indicate that a more basal state is achieved in this position than in the prone position.

In 2 subjects acute digitalis studies were performed during the first catheterization. In 5 subjects the initial cardiac catheterization was performed in the undigitalized state and repeated within 1 to 2 weeks after continued digitalization. The results are of interest with regard to the possible role of the myocardial factor in the production of the abnormal hemodynamic findings in mitral stenosis. Acute digitalization (during the catheterization study) in A. Dan. (cath. no. 9) resulted in a distinct fall in pulmonary artery pressure, from 73/43,55 mm. Hg to 69/28,43, and a 12 per cent increase in cardiac index despite an 8 per cent fall in oxygen consumption (tables 2 and 3). The arteriovenous oxygen difference fell from 7.6 to 6.2 volumes per cent. Digitalis was continued for more than 1 week, and catheterization was repeated. A further fall in pulmonary artery pressure to 54/27,35 mm. Hg was noted. On left heart catheterization the left atrioventri-
The hemodynamic data in A. Dan., and F. Lip. noted above demonstrate that mitral valve block and myocardial weakness may at least coexist despite an improvement in physiologic data after acute or chronic digitalization. Such changes do not necessarily indicate the primacy of the myocardial factor in the production of symptomatology and cardiac enlargement. Both patients have had surgically proved mitral stenosis and an excellent response to mitral commissurotomy. Combined right and left heart catheterization was of great value in differentiating the causes of pulmonary hypertension in these patients. This has been discussed more fully elsewhere.27

A intensive search has been made for patients illustrative of the myocardial factor. To date only 1 and possibly 2 examples have been found. In theory, the absence of a significant left atrial - left ventricular mean diastolic gradient both at rest and during exercise is a necessary prerequisite for the diagnosis of the primacy of the myocardial factor. Previous definitions based on the absence of significant pulmonary hypertension at rest or exercise during right heart catheterization alone6,26 are inadequate, since significant diastolic atrioventricular gradients have been found in patients (E. Coo., L. Kar., and S. Ber.) with only minimal pulmonary hypertension at rest or exercise during right heart catheterization alone. In E. Coo. and L. Kar. surgical confirmation of the diagnosis has been obtained. The physiologic data in W. Cur. point to the importance of the myocardial factor. The mean diastolic left atrial - left ventricular gradient was 4 mm. Hg prone, 3 mm. Hg supine at rest, and 5 mm. Hg during exercise. The patient’s main complaints were weakness, easy fatigability, and exertional dyspnea. On physical examination a mitral opening snap and apical diastolic rumble with presystolic accentuation were audible. The electrocardiogram was atypical in that left bundle-branch block was found. The patient has been subsequently followed for 15 months and has been in clinical failure on several occasions. This patient has therefore been classified in the group wherein the myocardial factor rather than mitral valve block is responsible for the clinical, physical, and laboratory abnormalities. Surgical confirmation has, of course, not been obtained.

V. Whi. was a 37-year-old white woman who possibly, but not certainly, fell into this same category of the myocardial factor. The left atrial - left ventricular gradient was minimal at rest prone (during normal sinus rhythm) during left heart catheterization on 2 separate studies. During the second left heart study, nodal tachycardia developed with a rate about 140; the gradient thereupon rose to 10 mm. Hg prone, and 13 mm. Hg supine. Significant pulmonary hypertension was absent during both rest and exercise on 2 occasions during right heart catheterization. It is difficult to be certain just how to classify this patient. No other examples of the myocardial factor have been observed in this laboratory.

The studies available in J. Gla., a 34-year-old white man, illustrate the problem of recurrent mitral stenosis after commissurotomy.28 In 1950 he was catheterized elsewhere2 before and subsequent to mitral valve surgery. The pulmonary artery pressure was 74/49, 54 mm. Hg, preoperatively. The postoperative mean pulmonary artery pressure was 31 mm. Hg at rest. The preoperative

*In the laboratory of Dr. L. Dexter, in Boston, Mass.
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Table 6.—Comparison of Cardiac Output Data during Right Heart Catheterization Alone with Those Subsequent to Removal of the Bronchoscope (PB)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cardiac index (L./min./M.²)</th>
<th>A-V diff. (vol. %)</th>
<th>Oxygen consumption (ml./min./M.²)</th>
<th>Respiratory quotient (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rt.</td>
<td>PB</td>
<td>Rt.</td>
<td>PB</td>
</tr>
<tr>
<td>J. Gay.</td>
<td>2.50</td>
<td>2.45</td>
<td>6.0</td>
<td>6.2</td>
</tr>
<tr>
<td>N. Ber.</td>
<td>1.76</td>
<td>1.56</td>
<td>7.1</td>
<td>8.7</td>
</tr>
<tr>
<td>B. Wei.</td>
<td>2.53</td>
<td>3.30</td>
<td>4.9</td>
<td>4.4</td>
</tr>
<tr>
<td>E. Gec.</td>
<td>2.19</td>
<td>2.51</td>
<td>5.3</td>
<td>4.6</td>
</tr>
<tr>
<td>F. Eul.</td>
<td>2.53</td>
<td>2.99</td>
<td>5.2</td>
<td>5.1</td>
</tr>
<tr>
<td>Average</td>
<td>2.30</td>
<td>2.56</td>
<td>5.7</td>
<td>5.8</td>
</tr>
<tr>
<td>Average difference</td>
<td>.36</td>
<td>.6</td>
<td>11</td>
<td>.16</td>
</tr>
</tbody>
</table>

cardiac index was 2.1 L./min./M.² (oxygen consumption 153 ml./min./M.²); this rose to 3.2 L./min./M.² (oxygen consumption 139 ml./min./M.²) shortly after surgery. Six and one half years later pulmonary artery pressure had risen to 61/35, 42 mm. Hg. Cardiac index had fallen to 1.52 L./min./M.². Left atrial mean pressure prone was 32 mm. Hg at this time, and the diastolic atrioventricular gradient was 22 mm. Hg. Restenosis had evidently developed in the period between 1950 and 1956. A second commissurotomy was refused by the patient. His course was progressively downhill. At postmortem examination 5 months later, tight mitral stenosis was found.

Hemodynamic studies are available in 2 asymptomatic subjects with mitral stenosis. Both had typical physical findings of mitral stenosis. The left atrium was enlarged in both patients. The electrocardiogram exhibited P-wave abnormalities in both subjects, but no evidence of right or left ventricular hypertrophy. In the first patient, R. Sch., the pulmonary artery pressures were normal at rest, but slight pulmonary hypertension appeared during exercise. Cardiac index was normal at rest with an increase on exercise which was at the lower limits of normal. A. Gre., the other asymptomatic patient with mitral stenosis, was catheterized twice in the undigitalized state. The first was a combined right and left catheterization, the second a right heart catheterization. Mild pulmonary hypertension developed during exercise in both studies. The maximum mean diastolic left atrial-left ventricular gradient during exercise was 6 mm. Hg. Cardiac index was slightly depressed during the first study but was normal on the second occasion. There is little doubt that abnormal hemodynamic data may be found in at least some asymptomatic subjects with mitral stenosis.

As has recently been reemphasized by Brachfeld and co-workers, left heart catheterization may be of prime importance in the diagnosis of occult mitral stenosis. T. Rob., a 42-year-old white man, was severely disabled with exertional dyspnea and peripheral edema. Despite signs of right ventricular hypertrophy and probable pulmonary hypertension on physical examination, a mitral diastolic rumble was not present, although a soft diastolic blow was noted at the base. The electrocardiogram suggested atrial hypertrophy with marked right ventricular hypertrophy. The resting pulmonary artery pressure was 104/42, 65 mm. Hg. Left heart catheterization demonstrated atrial hypertension and a large atrioventricular gradient, 26 mm. Hg at rest. The diagnosis of very tight mitral stenosis was subsequently verified at surgery. Similar cases have been reported by others.

Left heart catheterization was performed by the bronchoscopic technic in 5 patients in whom cardiac output data were available prior to and subsequent to insertion and removal of the bronchoscope. At least 30 minutes elapsed between removal of the bronchoscope, and the postbronchoscopic outputs. The results are given in table 6. Gross differences in cardiac index and associated data are pres-
TABLE 7.—Comparison of Cardiac Output Data during Right Heart Catheterization Alone with Those during Combined Heart Catheterization by the Posterior Percutaneous Technic (24 Cases)

<table>
<thead>
<tr>
<th></th>
<th>Cardiac index (L./min./M.²)</th>
<th>A-V diff. (vol. %)</th>
<th>Oxygen consumption (ml./min./M.²)</th>
<th>Respiratory quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right Combined</td>
<td>Right Combined</td>
<td>Right Combined</td>
<td>Right Combined</td>
</tr>
<tr>
<td>Average</td>
<td>2.48 2.45</td>
<td>5.2 5.3</td>
<td>123 124</td>
<td>.80 .82</td>
</tr>
<tr>
<td>Average difference</td>
<td>.17 .4</td>
<td>8</td>
<td>.05</td>
<td></td>
</tr>
</tbody>
</table>

ent in 4 of the 5 patients. The averaged values vary considerably and the averaged differences are large. The corresponding data from output comparison (in 24 patients) of right and combined heart catheterization by the posterior percutaneous puncture technic is shown in table 7. In this laboratory the steady state is more readily achieved after left heart catheterization by the posterior percutaneous technic than by the bronchoscopic technic. In the only other comparison of cardiac output during right heart catheterization alone and during left or combined heart catheterization available in the literature to date, Morrow and co-workers noted a cardiac index of 3.05 and 2.26 L./min./M.² during right and during left heart catheterization respectively. The average difference in output in their 8 subjects was 0.86 L./min./M.² This variation is considerably larger than in the series of 24 patients referred to above.

These clinical and physiologic experiences in patients with mitral valve disease have led to a classification of mitral stenosis based upon the presence or absence of a left atrioventricular gradient. In the asymptomatic patient with mitral stenosis, demonstration by left heart catheterization of an absent or small gradient at rest or exercise certainly indicates that the degree of block is of little clinical or physiologic import at the moment. The demonstration of a significant gradient (as defined early in this paper) at rest or during exercise in the asymptomatic subject may in the future by a clear-cut indication for mitral commissurotomy. At present, the question of surgical intervention in such a patient remains a moot point, which may be decided by the ancillary electrocardiographic and fluoroscopic findings. It should be noted, however, that many patients realize the magnitude of their preoperative disability only after relief thereof by surgery.

In a similar fashion, symptomatic patients with pure mitral stenosis can be divided into 2 groups. Those with significant gradients during left heart catheterization obviously require commissurotomy in the absence of a clear-cut contraindication. The symptomatic patient with a small or absent gradient at rest or exercise probably falls into the category of the myocardial factor and should not be subjected to surgery. These patients can be detected only with left heart catheterization.

The complications of left heart catheterization deserve discussion. To date 120 combined right and left heart catheterizations have been performed in this laboratory. Three major complications occurred in the first 60 studies. The first was a cerebral embolus, which developed immediately after the removal of the left heart catheters in a 49-year-old white woman who had had previous systemic emboli. The second complication was the onset of ventricular fibrillation in a 41-year-old white man. This arrhythmia developed prior to removal of the left heart catheters. Sinus rhythm was restored by cardiac massage and electric defibrillation. Both subjects had performed exercise during combined right and left heart catheterization. The complications developed approximately 15 minutes after completion of the exercise. Both patients (with mitral valve disease) died, the first 36 hours and the second 18 hours after catheterization. The third complication was in a 36-year-old white woman with aortic stenosis. An unrecognized right hemothorax developed after the study. The patient died 8 hours later.
RELATIONSHIPS IN MITRAL VALVE DISEASE

Because of these complications, the procedure of combined heart catheterization in this laboratory was shortened. Exercise studies are no longer planned unless the resting mitral or aortic gradient alone is of questionable significance. The only significant complication in the last 60 studies has been 1 case of hemotorax, readily treated by thoracentesis alone. In the first 60 cases, the needles employed for left atrial puncture were deliberately blunted. The needles employed in the more recent procedures have had sharp edges. Left atrial puncture has been greatly facilitated by this change in technic.

SUMMARY

Left and combined right and left heart catheterization have greatly extended understanding of the pathophysiology of mitral valve disease. Previous concepts developed with right heart catheterization alone have proved to be limited in scope and viewpoint. The data of individual cases have been presented and discussed to elucidate some of these concepts. A classification of patients with pure mitral stenosis has been outlined, especially in relation to surgical intervention.

ACKNOWLEDGMENT

We are indebted to Stanley Dzwonkowski, B.A., and William Oliver, B.A., for technical aid, to Miss Hazel Stowe, L.P.N., for nursing aid, and to Miss Iris Kiem, M.S., M.P.H., for analysis of the statistical data.

SUMARIO IN INTERLINGUA

Catheterismo cardiac sinistre e dextero-sinistre in combination ha grandemente estendite nostre comprension del patho-physiologia de morbo del valvula mitral. Conceptiones disveloppate in le passato super le base de catheterismo dextero-cardiac sol se ha reve-late como restringite in applicabilitate e perspectiva. Es presentate datos ab casos individual, con discussiones visante a elucidar certes de ille conceptiones. Es delineate un classification de patientes con pur stenosis mitral, specialmente con respecto al problema del intervention chirurgie.

REFERENCES

13. Wood E., Sutterer, W., Swan, H. J. C., and Helmholtz, H. F.: The technique and special instrumentation problems associated with catheterization of the left side...


