A Clinical Study of 1,000 Consecutive Cases of Mitral Stenosis Two to Nine Years after Mitral Valvuloplasty

By Laurence B. Ellis, M.D., Dwight E. Harken, M.D., and Harrison Black, M.D.

A study is presented of 1,000 cases of predominant mitral stenosis operated by valvuloplasty between 1949 and 1956. It is shown that the survival of these patients is better than would have been expected under medical management. Sixty-nine per cent of the survivors of the operation in groups II and III improved, and 55 per cent in group IV. Factors influencing the late results are discussed. After substantial improvement lasting a year or more, 228 of this series deteriorated; the factors affecting this deterioration are discussed, of which mitral insufficiency, an inadequate valvuloplasty, and recurrent rheumatic fever are the most striking.

The present study is a report of the clinical results in 1,000 consecutive cases with a preoperative diagnosis of predominant mitral stenosis on whom mitral valvuloplasty was performed between the years 1949 and March 1956. Ninety-two per cent of the operations were performed by D.E.H. and the remainder by H.B. The follow-up of all of these patients has been carried out under the direction of the cardiologist, L.B.E., who has had the final word in the preoperative classification of the patients and in the estimate of the degree of improvement that they have had. In 150 (table 1) mitral insufficiency of some degree was suspected before operation; 121 showed evidence of aortic stenosis or insufficiency but this was not thought to be clinically important, and there were 6 who were believed to have tricuspid stenosis. No attempt was made to classify patients with tricuspid insufficiency, which was presumably due in most cases to functional dilatation of the annulus in patients with a failing right ventricle. Patients in whom the preoperative diagnosis of significant mitral stenosis was in doubt or who had very substantial amounts of associated valvular disease, in whom exploratory cardiotomies were carried out, are not included in the present series and will be the subject of a separate report. No patient has been dropped from the series, even if the operative findings did not confirm the preoperative diagnosis.

The technic of operation has been described elsewhere.1,2 The basic principles of the valvuloplasty procedure have remained unchanged throughout the series, although with increasing experience the correction of stenosis has undoubtedly been improved. An initial group of 11 patients operated on between the years of 1947 and 1949 by technics not strictly comparable to the present one have not been included.

The results in the first 500 patients in this series followed for a shorter period of time and a preliminary statement of some of the results of the entire group of 1,000 have been previously published.3-6

The classification employed1 roughly corresponds to the functional classification of the New York Heart Association, but it is designed to represent a more dynamic picture
of the course of the patient's illness. This series included no patients in group I, that is patients without significant symptoms. Nineteen were in group II; these were patients somewhat handicapped by symptoms from their disease but who were able to carry on a sedentary occupation successfully and in whom the condition was not progressive. In 4 of these patients who did not have severe symptoms of cardiac disability the primary indication for operation was one or more peripheral emboli. Group III included patients suffering mainly from pulmonary symptoms, which were usually progressive in nature, and were sufficiently handicapped, so that ordinary activities were significantly limited. If these patients had had overt congestive failure, it had been because of some unusual precipitating cause such as pregnancy or a serious infection and they had rapidly recovered from it. There were 711 in this group. Group IV comprised cardiac patients with more severe symptoms who were mostly cardiac invalids suffering from chronic congestive failure or who were maintained in a precarious state of compensation only by vigorous medical means.

There were 270 in this group.

In 58 of the patients included in this series, a second operation was performed by us for mitral stenosis and in 1 patient 3 operations were done. We originally operated on 49 of these patients, and in 10 the operation had been previously performed elsewhere. In these patients the clinical evidence prior to the second operation pointed toward significant mitral stenosis and the operation was performed with a view toward carrying out a mitral valvuloplasty. Five patients in this series have had a second operation for mitral stenosis performed by other surgeons. Five have been reoperated on by us for mitral insufficiency, and in 5 an exploratory cardiotomy has been performed. In 2 a second operation for the correction of aortic stenosis has been carried out. This series includes 17 patients who have been counted twice and 1 who was counted 3 times. Hence, the number 1,000 refers to the number of operations rather than the number of patients. In the remaining 41 who were reoperated on, only 1 operation is included in this series, the other being done either before or after this series of 1,000 or was carried out elsewhere.

Twenty-one patients were operated on while they were pregnant and there were 3 deaths among them. Although this represents a special group, in a consideration of operative mortality, pregnancy does not alter the late results. In the follow-up studies these patients have been included with the others. The place of mitral surgery during pregnancy has been discussed elsewhere.

Females outnumbered males in this series about 3 to 1. 78 per cent of the patients in group III being women and 74 per cent of the group IV patients. The average age of the patients in the series was 39.4 years (38.8 years for women and 40.5 years for men) (table 3).

Accuracy of the Preoperative Diagnosis of Mitral Stenosis and Mitral Insufficiency Judged by Findings at Operation

A preoperative diagnosis of mitral insufficiency complicating mitral stenosis was not made unless it was considered to be clinically significant. This would correspond to the finding of a moderate or marked mitral insufficiency by the surgeon at operation. We have, therefore, compared the preoperative diagnosis with the operative finding at operation. When the preoperative diagnosis was pure mitral stenosis the findings were confirmed at operation in the group III patients in 84 per cent of those in atrial fibrillation and 94 per cent of patients in normal sinus rhythm, and in group IV patients in 83 and 75 per cent respectively. However, if a preoperative diagnosis of mitral stenosis and insufficiency was made, in only 56 per cent of the patients in both groups was the diagnosis of moderate to severe insufficiency confirmed at operation. If the situation is considered from the opposite point of view, the findings are similar. When pure mitral stenosis was found at operation the lesion had been correctly diagnosed pre-
CLINICAL STUDY OF MITRAL STENOSIS

Table 1.—Preoperative Diagnosis

<table>
<thead>
<tr>
<th>Group II and III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart lesions</td>
<td></td>
</tr>
<tr>
<td>Without associated valvular disease</td>
<td></td>
</tr>
<tr>
<td>With tricuspid stenosis</td>
<td></td>
</tr>
<tr>
<td>With coronary disease</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td></td>
</tr>
</tbody>
</table>

operatively in 94 per cent of the group III patients and 84 per cent in the group IV patients, whereas when significant mitral insufficiency was found by the surgeon at operation a correct diagnosis had been made prior to operation in 42 per cent of group III and 52 per cent of group IV patients.

One of the patients who had been classed in group III preoperatively had a valve that appeared normal at operation. In all, 15 group III patients were found to have valves of 2.0 cm. or more, prior to valvuloplasty; of these 6 had some degree of mitral insufficiency. In 3 of these 15 the chief indication for surgery was a history of emboli. In 25 more the preoperative valve size was from 1.5 to 1.9 cm.; and 18 of these had mitral insufficiency.

Two patients in group IV had normal mitral valves; 1 had a large atrial thrombus overlying the valve, and in the other the heart failure was presumably due to coronary atherosclerosis. Two other patients in group IV had valve orifices of 2.0 cm. or more, and in 3 the preoperative valve size was from 1.5 to 1.9 cm. In all 5 of these patients substantial mitral insufficiency was present.

Operative Mortality

The over-all operative mortality for this group has been previously reported and is given in table 2. Because of the very small number of group-II patients in this series these have been included with group-III patients in the subsequent analyses, and whenever the expression "group III" is used, it denotes group II and III patients. There was 1 operative death in the group-II patients. For the purpose of this analysis "operative mortality" denotes death during the operation or during the period of the hospitalization when the operation was performed.

The operative mortality according to age is given in table 3, and it will be seen that there is no significant change in operative mortality depending upon age. It is a matter of interest that none of the 42 patients over 50 in group III died an operative death.

The operative mortality for males in group III was 2.5 per cent and for females it was 3.3 per cent. Among the group-IV patients the mortality was somewhat higher in the male group, being 29.6 per cent as compared to 21.6 in the females but this difference is not significant since the p value is between 0.05 and 0.10.* These figures are for the entire 1,000 cases. Actually, the operative mortality has fallen strikingly in the second 500 cases, particularly in group-III patients (table 2).

Peripheral Embolization

One hundred eighty-six of the 1,000 patients had had one or more well-documented attacks of peripheral embolization prior to surgery. The time of onset of these episodes varied from many years before surgery to a few days. The risk of developing an operative embolus in the last 500 patients operated upon was

*Unless otherwise noted, p values shown here and in the ensuing discussion are based on a contingency \( \chi^2 \) test.* Values of \( p \) less than .05 are significant.
2.1 per cent in group III and 8.0 per cent in group IV (table 4). The higher rate of operative embolization in the first 500 patients has been discussed elsewhere. The figures for the second 500 reflect more accurately our current experience. Only 1 of the 8 emboli in group III was fatal, but 8 of the 10 in group IV had a fatal outcome. Although the number of emboli occurring in fibrillating patients was higher than in patients with normal rhythm, the differences are not statistically significant. The frequency of embolization in patients with normal rhythm is of interest.

Of the entire group of 913 patients who survived operation 25 have developed one or more peripheral emboli after the operative period to July 1, 1958. Most of the patients who developed late peripheral emboli were fibrillating at the time of surgery and were presumably fibrillating at the time of embolization. A few who were in normal rhythm at the time of surgery were known to have developed fibrillation prior to the occurrence of their late emboli. No relationship, however, could be ascertained between the occurrence of late emboli and emboli occurring at operation or a history of embolization occurring prior to surgery. The average duration of time since operation in this group is almost exactly 4 years and this therefore represents an experience of about 3,600 patient years or an embolization rate of 0.7 per cent per year in this group. More than half of the surviving patients were in chronic atrial fibrillation. It is our opinion that valvuloplasty confers substantial protection against peripheral embolization in patients of this type.

**SURVIVAL**

In spite of the great number of studies that have been made over the years on the survival of patients with mitral stenosis it is extremely difficult to obtain data on medically treated patients that are comparable to this series. Many studies are statistically invalid or are made on groups that are not easily comparable, or consider only the survival period of those who ultimately were known to be dead. Most studies based on autopsy statistics are retrospective, so that it is almost impossible to determine when and to what degree the patients became symptomatic. A recent study has been reported by Wilson and Lim on the survival of patients followed into the third, fourth, and fifth decades of life from the onset of rheumatic fever in childhood. Although this is an important study, it is difficult to compare it with our own. Elsewhere we have commented on the studies made by Grant, Wilson and Greenwood, and Hamilton and Thompson. Vedoya, Nessi, and Mendelson have also reported the ominous prognosis of patients with symptomatic mitral stenosis. Recently, Rowe et al. found that 40 per cent of 250 patients with mitral stenosis followed 10 years were dead, and Donzelot et
al.\textsuperscript{15} have published results that have indicated that surgically treated patients have a better prognosis than those medically followed. So far as these studies are comparable to ours, they indicate that survival under medical therapy is less than for our surgically treated patients.

As we have previously indicated,\textsuperscript{8} the series most comparable to ours which has been medically treated and followed is that by Olesen,\textsuperscript{16} who studied a group of patients first observed between the years of 1933 and 1949 in Copenhagen. In this series 72 per cent of the patients were females as compared to 77 per cent in our group and the average age of his patients was 41.5 years as compared to 39.4 years in our series. He classified his patients according to the grouping of the American Heart Association and also subdivided the class-2 and class-3 patients into those who were fibrillating and those in normal sinus rhythm. Our group-III patients would most closely approximate his class-3 patients and class-2 patients with atrial fibrillation, and our group-IV patients are comparable to his class-4 patients. We have therefore utilized his data to compare our group-III patients with his male and female patients in class 3 and class 2 in atrial fibrillation. Figures 1 and 2 show the survival of our patients compared to Olesen’s groups. Patients who have been reoperated on and are counted twice in the series are counted only once in the calculation of the survival curves.\textsuperscript{*} It will be seen that, including an operative mortality of 3 per cent, 83 per cent of our group-III patients have survived over the period of observation up to 7 years, and 71 per cent to 9 years, although the numbers dealt with in the last 2 years are small. This survival is better than for the medically treated patients. In group IV 57 per cent have survived up to 9 years, which include an operative mortality of 24 per cent for the group as a whole. This survival is vastly better than for the medically treated patients of whom none was alive at 8 years.

The survival rates have also been analyzed according to age, sex, and rhythm. Total survival curves for each of these classes are not shown in detail. The survival rates of patients at the end of 5 years are shown in table 5.

The survival of female patients is somewhat better than of males; those in normal rhythm do better than fibrillating patients; and younger patients in group III survive longer than do those who are older. The only one of the differences, however, which is statistically significant is the sex difference in group III ($p < .01$).

**Late Deaths**

Ninety-five patients have died since operation. The causes of the deaths are given in table 6. Eleven died of conditions clearly unrelated to their heart disease. Two of these, however, were patients in which death might be considered related to the operative procedure, including 1 death 2½ months following surgery from hepatitis, which might have been homologous serum jaundice acquired from a transfusion at the time of surgery, and

\textsuperscript{*}The survival curves were calculated according to the method of Berkson et al.\textsuperscript{17}
Sex had lowing of course have been due to the origin.

Follow-up Studies

Table 5.—Survival Rates of Patients at the End of Five Years in Relation to Age, Sex, and Rhythm

<table>
<thead>
<tr>
<th>Age by decades</th>
<th>Groups II and III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-19</td>
<td></td>
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<tr>
<td>20-29</td>
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<tr>
<td>30-39</td>
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<tr>
<td>40-49</td>
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<tr>
<td>50-59</td>
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<td></td>
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<tr>
<td>60-69</td>
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</tbody>
</table>

1 death from a reaction occurring during the course of an intercostal block for treatment of residual intercostal pain. There were 4 sudden deaths that have been assumed to be cardiac in origin. Patients developing cerebral vascular accidents, whether fatal or not, following surgery have been considered to have had these on the basis of emboli dislodged from the heart, though some of these may have been due to independent vascular disease of the brain. In the calculation of the survival curves all deaths have been included, whether or not they were of cardiac origin.

1. Ellis, Harken, and Black

Table 6.—Causes of Late Deaths

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primarily cardiac</td>
<td>76</td>
</tr>
<tr>
<td>Heart failure</td>
<td>60</td>
</tr>
<tr>
<td>Sudden</td>
<td>4</td>
</tr>
<tr>
<td>Peripheral emboli</td>
<td>9</td>
</tr>
<tr>
<td>Pulmonary infarcts</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia and heart failure</td>
<td>1</td>
</tr>
<tr>
<td>None cardiac</td>
<td>11</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>95</td>
</tr>
</tbody>
</table>

An additional group of the patients who have had a second cardiac operation have been dropped from the series as unimproved at that point and hence are technically "lost to follow-up." All of the remainder have been followed up to the latest anniversary of their operation. All patients have been followed by annual questionnaires so worded as to obtain not only the subjective opinion of the patient concerning his improvement but to provide evidence from which an estimate can be made as to whether the patient is capable of carrying on with in less disability than he had prior to operation. In addition all other obtainable data concerning these patients have been utilized. These include personal examinations of a large number of these patients, letters from doctors, hospital reports, and so forth. In a previously reported study a comparison has been made of the accuracy of method of follow-up with a follow-up examination made personally by one of us on a sample of 101 patients from this group. It was found that the grading of patients by the questionnaire method was stricter and somewhat lower than the grading of patients by personal examination. The final estimate of the degree of improvement of each of the patients has been made by one of us on the basis of all the information obtainable. Very often this is less than the subjective opinion of the patient himself. Some patients, of course, have proved to be difficult to evaluate, particularly when they have had other diseases or noncardiac
symptoms. This is especially true of many patients with neurotic symptoms, and of patients handicapped by the residua of vascular accidents occurring either before or during surgery. Patients who have been partially incapacitated by vascular accidents occurring at the time of surgery have been graded in accordance with the handicap they have suffered from the neurologic residua of their emboli irrespective of the cardiac status.

**Criteria of Improvement**

Patients have been classed as markedly improved, moderately improved, slightly improved, unchanged, and worse. *Markedly improved* patients are those who have gone up 2 grades in the American Heart Association classification or the few group-II patients who have lost all their symptoms. Thus patients who were originally in group III are considered markedly improved if they are now in class 1 of the American Heart Association classification, and for the group-IV patients an improvement into class 1 or 2 of the American Heart Association classification would justify a grading of markedly improved. *Moderately improved* patients are those who have improved 1 grade in the American Heart Association classification. For the sake of the analysis in the following discussion patients who are *moderately to markedly improved* have been classed together as "*significantly improved*" or as "*improved*"; those who are only *slightly improved, unchanged, worse, or dead* are considered as "*unimproved."*

**Cumulative Improvement**

Figure 3 shows the improvement of the patients at each year of follow-up. This improvement is calculated on the basis of the follow-up of each patient at each anniversary of his operation for the total period of follow-up. In a few patients where there has been a hiatus of more than 1 year between 2 follow-up reports, the state of improvement reported at the first follow-up has been considered to have been maintained to the year preceding the next time that information is available by a follow-up report, unless it is clear from the information on the last follow-up just when any change in status occurred.

The improvement in both groups III and IV has tended to drop somewhat with succeeding years of follow-up. To some extent this may be due to the obvious fact that those patients who have been followed for the longest time are also those who were operated on early in our experience with this operation, and the operative attack on the valve may have been less adequate at that time. While the quality of surgery undoubtedly improved progressively in this series no fundamental changes in technical principles were made until early in the second thousand operations. The tendency for the improvement to become less over the years represents at least in part the inevitable ravages of the disease process. Residual damage to the cardiac muscle, pulmonary vasculature, liver, and so forth may have persisted and left its effect, particularly in the group-IV patients. In addition, other factors which may be present are an operative fracture which was less than adequate; restenosis; mitral insufficiency; associated valvular disease, and recurrent rheumatic activity. A more detailed analysis will be made later in this report of the factors affecting the deterioration of patients who previously have been significantly improved.
In group IV significant differences due to age, sex, or rhythm are not apparent, although the same tendencies are observed as in group III.

The figures for improvement by age, sex, and rhythm at the end of 1 year of follow-up show the same tendencies that were observed at 5 years, although differences become more striking at the 5-year period.

Of interest are the results in relation to the findings at the time of operation. These include the degree of mitral stenosis, the presence and amount of mitral insufficiency, and the adequacy of the valvuloplasty as estimated by the surgeon at the time of operation. There are a number of factors that affect the operative results, some of which are within the control of the surgeon, depending on his skill and experience, and others are inherent in the state of a valve as it is found at operation. These include the degree of calcification and its location, the rigidity of the leaflets, and the extent of fusion and shortening of the chordae tendineae. The quality of the valvuloplasty is of the greatest importance in long-term results.

With an increasing degree of mitral insufficiency, the results at the end of 5 years are progressively worse (table 8). The degree of insufficiency was that amount which was estimated to be present by the surgeon after completion of the valvuloplasty. In group III 78 per cent of patients with pure mitral stenosis were improved as compared to only 48 per cent of those showing 2-plus or greater regurgitation at the time of surgery. In group IV the improvement rate dropped from 69 to 36 per cent. These differences are all significant ($p$ less than 0.01) except for the comparison of patients with no versus 1-plus insufficiency in group III, and between 1 plus versus 2 to 3-plus insufficiency in group IV.

If the same correlations are made at the end of 1 year instead of 5, then the difference in the degree of improvement between those with no insufficiency and those with increasing degrees of insufficiency is much less apparent.
It would appear, therefore, that the damaging effect of mitral insufficiency takes time to appear.

When patients are studied in respect to their improvement in relation to the preoperative valve size, it is apparent that the patients who had tight mitral stenosis, that is an estimated valve area of 1 cm.², or less, did better at the end of 5 years than did patients whose valve area was larger. This is true in both group III and group IV. Again this difference was observed in patients when they were studied at the end of 1 year in group IV but was not apparent in group III.

The effects of increasing degrees of mitral insufficiency and of a larger preoperative valve size in mitigating against a successful outcome were additive, as demonstrated by the adjusted rates.

The majority of these patients had only anterior fusion bridge fracture or valvulotome incision. More recently a technic has been developed for the adequate fracture of the posterior fusion bridge as well. The effect of this "more adequate" (certainly more extensive) operation on sustained improvement, refusion, or indeed deterioration from subsequent mitral insufficiency will be discussed in another communication. The technic of this operation is discussed elsewhere.²

The presence of associated valve disease had no statistically significant effect on the results at the end of 5 years in either group III or group IV.

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### Table 8.—Status at the End of One and of Five Years

<table>
<thead>
<tr>
<th>Sex</th>
<th>Groups II and III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One year</td>
<td>Five years</td>
</tr>
<tr>
<td></td>
<td>No. of patients</td>
<td>Per cent of patients improved</td>
</tr>
<tr>
<td>Mule</td>
<td>151</td>
<td>83</td>
</tr>
<tr>
<td>Female</td>
<td>554</td>
<td>85</td>
</tr>
<tr>
<td>Rhythm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal sinus</td>
<td>408</td>
<td>88</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>297</td>
<td>80</td>
</tr>
<tr>
<td>Age by decades</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-19</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>20-29</td>
<td>116</td>
<td>91</td>
</tr>
<tr>
<td>30-39</td>
<td>277</td>
<td>89</td>
</tr>
<tr>
<td>40-49</td>
<td>262</td>
<td>76</td>
</tr>
<tr>
<td>50-59</td>
<td>40</td>
<td>73</td>
</tr>
<tr>
<td>60-69</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Mitral insufficiency†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>401</td>
<td>88</td>
</tr>
<tr>
<td>+</td>
<td>174</td>
<td>86</td>
</tr>
<tr>
<td>++ &amp; ++++</td>
<td>103</td>
<td>79</td>
</tr>
<tr>
<td>Preoperative valve size†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0 cm.² or less</td>
<td>438</td>
<td>86</td>
</tr>
<tr>
<td>1.1 cm.² or more</td>
<td>240</td>
<td>84</td>
</tr>
</tbody>
</table>

*Adjusted rates calculated by indirect method.
†In a few patients clinical information regarding valve size or mitral insufficiency was lacking and these have been omitted from consideration.
IMPROVEMENT IN RELATION TO POSTOPERATIVE COMPLICATION

Following surgery many of the patients complained in varying degrees of symptoms not directly related to the status of their cardiac compensation. Some of these symptoms comprise a syndrome that has been reported under the term of "postoperative" or "post-commissurotomy syndrome," and is characterized chiefly by exacerbation of pain in the chest of varying types, with fever. There may be evidence of pericarditis, pleuritis, and pneumonitis in varying degrees. In our experience this situation has been benign and self-limited, lasting a week or 2 and has not appeared to be affected particularly by the type of therapy given, such as acetylsalicylic acid, penicillin, or adrenal steroids. The syndrome is considered by some to be an activation of rheumatic infection. In our experience, however, clear-cut evidence of rheumatic fever occurs in only a minority of patients. The syndrome tends to be recurrent and may appear for the first time several years after surgery and recurrences may occur over several years. The relation, therefore, to the surgical procedure is obscure. It has been pointed out by Ito, Engle, and Goldberg\(^1\) that this syndrome also occurs in patients with nonrheumatic heart disease who have had intracardiac surgery involving opening of the pericardium and it is their opinion that this may represent recurring nonspecific pericarditis. We have no evidence bearing on this point, except that we have no patients with pericardial effusions in the postoperative period or later.

Since most of these patients have returned to their homes and have been observed by their local doctors, and only occasionally personally by us, the reported incidence of this syndrome cannot be accurate, and may include some cases of pneumonia or other respiratory infections as well as pulmonary infarctions.

The incidence of the postoperative syndrome occurring in these patients was 30.8 per cent (30.4 per cent for group III and 32.2 per cent for group IV). This is comparable to that previously reported for the first 500 patients of this series followed for a shorter time,\(^3\) as well as reports of others. It is of interest, however, that the over-all improvement of patients suffering from the postoperative syndrome is essentially the same as for the groups as a whole (68 per cent in group III and 51 per cent in group IV).

Many patients complain also of vague joint pains. Whether the incidence of such joint pains is any higher in this group of patients than it would be in any other carefully followed group of middle-aged people with chronic disease is uncertain. We have divided our patients into those who have suffered from arthralgias only, and those who had a clear-cut arthritis, sometimes of the rheumatoid type, but with no clear evidence of rheumatic fever. A history of arthralgia or of arthritis did not affect the results strikingly, but in both groups III and IV the patients in whom rheumatic fever was diagnosed did poorly. This will be discussed in a later section.

IMPROVEMENT IN RELATION TO THE PRESENCE OF ASCHOFF BODIES IN THE BIOPSY OF THE LEFT ATRIAL APPENDAGE

In a previous study\(^20,\)\(^21\) the relationship of the presence of Aschoff bodies in biopsies of the left atrial appendages to the clinical findings was reported. The present study confirms the previous one. The biopsy reports utilized in the present study were routine reports received from the pathologic laboratories of the several hospitals concerned. No attempt was made to have the microscopic findings reviewed by a single pathologist as was the case in the earlier study. A total of 632 biopsy reports are available from this series of 1,000 cases. In the group-III patients 43 per cent were positive. In group IV the incidence of positive biopsies was 20 per cent. Table 9 shows that the incidence of positive biopsies is greatest in the younger age groups and falls progressively with increasing age but is still 21 per cent in the 50 to 59 decade group in group III and 18 per cent in group IV. The
positive biopsies are much more likely to be found in any age group in the patients with normal sinus rhythm than in patients with atrial fibrillation. Both of these findings confirm our previous report. When patients are compared by age groups, the percentage improvement of those with positive biopsies was the same as of those with negative biopsies.

When the incidence of positive biopsies is correlated with the occurrence of the various postoperative complications, no relation is evident. The percentage of positive biopsies in patients later developing the postoperative syndrome was nearly the same as for the group as a whole (40 per cent in group III, 15 per cent in group IV). Patients who subsequently developed definite rheumatic fever tended to have a slightly but not impressively higher incidence of positive biopsies (56 per cent).

**Factors Involved in the Deterioration of Patients Who Have Improved Following Mitral Valvuloplasty**

Two hundred twenty-eight of the patients in this study have become worse after having been significantly improved, that is "markedly" or "moderately," for at least 1 year after valvuloplasty. For the sake of this analysis, the definition of "deterioration" is that they have slipped by at least 1 class, according to the American Heart Association classification. Sixty-two of these patients slipped only from "markedly" to "moderately" improved, and hence would still be classed in the "improved" category. The remaining 166 deteriorated from either being originally "markedly" or "moderately" improved into the "unimproved" classification; that is, they are now either only "slightly" improved, their condition is unchanged as compared to the preoperative state, they are worse, or dead. Of these patients, 48 have died since operation, and 45 have been reoperated on for mitral valvular disease. These patients were not all personally observed by the authors at the time of their deterioration; evidence for their deterioration was obtained in some from their answers to annual questionnaires or from letters from their physicians.

There are a number of factors that may have been of importance in these 228 patients in producing the deterioration of these patients. Many of these occurred in combination. In 56 mitral insufficiency was present, either alone or in combination with other fac-
ELLIS, HARKEN, BLACK

Table 10.—Influence of Significant Mitral Insufficiency Found or Produced at Operation*

<table>
<thead>
<tr>
<th>Status of patients</th>
<th>Patients followed five years</th>
<th>All patients at latest follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Per cent with mitral insufficiency</td>
</tr>
<tr>
<td>Patients who deteriorated after substantial improvement</td>
<td>89</td>
<td>30</td>
</tr>
<tr>
<td>Patients who maintained improvement</td>
<td>196</td>
<td>12</td>
</tr>
<tr>
<td>Patients who failed to improve</td>
<td>43</td>
<td>28</td>
</tr>
</tbody>
</table>

*Patients in whom there were no adequate records of the presence or absence of mitral insufficiency have been omitted from consideration.

Table 11.—Influence of an Unsatisfactory Correction of Mitral Stenosis*

<table>
<thead>
<tr>
<th>Status of patients</th>
<th>Patients followed five years</th>
<th>All patients at latest follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Per cent with unsatisfactory correction</td>
</tr>
<tr>
<td>Patients who deteriorated after substantial improvement</td>
<td>93</td>
<td>23*</td>
</tr>
<tr>
<td>Patients who maintained improvement</td>
<td>193</td>
<td>9</td>
</tr>
<tr>
<td>Patients who failed to improve</td>
<td>73</td>
<td>15*</td>
</tr>
</tbody>
</table>

*Patients in whom it was impossible to assess adequately the quality of the operative procedure have been omitted from consideration.

ditors, at the time of surgery. This mitral insufficiency was of moderate to marked extent, and was either present prior to fracture of the valve or was produced at the time of surgery. From this particular study, it is, of course, impossible to say to what extent mitral insufficiency may have developed or increased both in patients in whom it had been previously recognized and in those in whom it had not been suspected.

In table 10 there is shown a comparison of 3 groups of patients all of whom have been followed for 5 years and thus can be compared on a statistical basis. It will be seen that patients from the present group who deteriorated after substantial improvement as well as patients who failed to improve at all exhibited mitral insufficiency at the time of operation much more often than did patients who showed a maintained improvement (p less than 0.01). There is no significant difference between the patients who deteriorated and those who failed to improve.

The incidence of mitral insufficiency in these 3 groups has also been compared among all of the patients at the time of their latest follow-up and a trend similar to that shown in the 5-year group is apparent. The relatively lower incidence of mitral insufficiency in the deteriorated group may possibly be due to the fact that mitral insufficiency takes time to produce its ravaging effect and the follow-up figures for the entire group include many patients followed less than 5 years.

At the time of operation, the surgeon was frequently unable to accomplish a fully satisfactory correction of the stenosis. This failure may have been due to conditions beyond his control, such as marked rigidity of the valve cusps, or widespread calcification or extreme shortening and fusion of the chordae tendineae. It is to be expected that with increasing experience a surgeon will become more skillful in effecting the maximum amount of correction while avoiding the production of insufficiency. There were 38 patients in the group of 228 who deteriorated, in whom an adequate correction of mitral stenosis was not effected at the time of operation, and 66 more in whom the correction was less than satisfactory. In table 11 a comparison is made of groups of patients followed for 5 years. Both the patients who deteriorated after substantial improvement and those who failed to improve at all were found to have an unsatisfactory correction of their stenosis in a much higher per-
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centage than did those who have shown maintained improvement (p less than .01 for both). The percentage of unsatisfactory corrections was somewhat higher in those who deteriorated than in those who failed to improve at all, but the difference is not significant (p between .30 and .20). However it is suggestive that if the operations consisted chiefly of dilatation of the valve or temporary mobilization of the cusps, the patient may do well for a while.

This table also shows the results at the latest follow-up of all patients. Although the same trends are evident, the percentage figures are lower in all categories. This is due to the fact that the over-all follow-up also includes patients operated on in the last half of the series, who have been followed less than 5 years. The number of unsatisfactory operations performed in these recently operated patients was lower than in the earlier half of the series. Indeed the number of unsatisfactory operations in the earlier group is higher than it appears, for the surgeon must have at times failed to recognize an unsatisfactory valvuloplasty. With greater experience the surgeon becomes more exacting in his acceptance of "an adequate operation."

The role of rheumatic fever in causing deterioration in patients is even more striking. There were 38 patients in the group of 228 who had rheumatic fever sometime after surgery. Of those followed for 5 years, 19 per cent deteriorated after substantial improvement (table 12). In contrast, only 1.5 per cent of the patients showing maintained improvement and 9 per cent of those who failed to improve at all gave evidence of rheumatic fever. The differences between patients showing maintained improvement and the other 2 groups are significant (p less than 0.01) but the difference between deteriorated patients and those who failed to improve is not statistically significant (p 0.10 to 0.05).

It is of course often difficult to make a clear-cut diagnosis of rheumatic fever in adults, and most of these patients were not personally seen by us. A diagnosis of rheumatic fever was only accepted in these pa-

\[\text{TABLE 12.—Influence of Rheumatic Fever Occurring Since Operation} \]

<table>
<thead>
<tr>
<th>Status of patients</th>
<th>No. of patients</th>
<th>Per cent with rheumatic fever</th>
<th>No. of patients</th>
<th>Per cent with rheumatic fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who deteriorated after substantial improvement</td>
<td>95</td>
<td>19</td>
<td>228</td>
<td>17</td>
</tr>
<tr>
<td>Patients who maintained improvement</td>
<td>193</td>
<td>1.5</td>
<td>541</td>
<td>2.2</td>
</tr>
<tr>
<td>Patients who failed to improve</td>
<td>73</td>
<td>9</td>
<td>142</td>
<td>14</td>
</tr>
</tbody>
</table>

patients, however, if they had reasonably convincing evidence of it. Patients who suffered from one or more attacks of the postoperative syndrome, and those who complained merely of vague joint pains did not show any unusual tendency to deteriorate.

Associated aortic valve disease occurred in the group of 228 patients who did poorly after initial improvement in 10 per cent, which is about the same percentage as in the series as a whole (12 per cent). Other causes possibly involved in the deterioration were peripheral emboli resulting in death or disability in 8 patients and subacute bacterial endocarditis in 3. In 62, there were no obvious factors explaining their deterioration. In some of these cases, the deterioration was unquestionably related to noncardiac causes, such as emotional states sometimes associated with the menopause, or other neurotic factors.

What does this study of patients who deteriorated reveal? Firstly, it shows that recurrent rheumatic fever often leads to deterioration of the cardiac status in these patients just as it does in rheumatic cardiac patients in general.

Secondly, it shows that mitral insufficiency is an important cause of relapse and that in many cases this incompetence may be produced or increased by the operative procedure. In another study we observed that mitral in-
sufficiency which was thought to be minimal or even not to exist at all at a first operation had become a major factor at the time of re-operation. If this is true also in regard to the entire group of 228 who deteriorated, it is evident that mitral insufficiency may well play an even more important role than was indicated by the 22 per cent incidence found in this group at surgery. The implication of this finding in connection with patients who are being considered for re-operation for mitral stenosis is obvious, as well as for surgery in mitral stenosis in general. It is evident that significant mitral insufficiency may be produced by the surgeon at operation and this may constitute a warning against too extensive or poorly directed fracture of valves in an effort to produce a complete relief of the stenosis. This also means that patients who have deteriorated and are being considered for re-operation must be scrutinized very carefully for the presence of mitral insufficiency before a second operation for mitral stenosis, since the major problem may really be mitral incompetence rather than stenosis and the conventional operation will not suffice.

Thirdly, this study shows how important is the quality of the technical performance. Not only must the production of mitral insufficiency be avoided but inadequate surgery for the relief of stenosis must also be avoided since the patients with unsatisfactorily performed mitral valvuloplasties deteriorate in a much higher percentage than do those in whom a good job was done.

Fourthly, the factor of predominant myocardial failure may well exist in many of these patients.

Finally, it can be said that although re-stenosis of the mitral valve does occur, it is only one of several factors that are of importance in the deterioration of patients and significant re-stenosis requiring re-operation does not commonly occur if the original operation was adequately done. It is impossible, on the basis of these studies to give accurate figures as to the rate of occurrence of re-stenosis. There are too many variable factors.

**Discussion**

A great many papers have appeared concerning the clinical results in patients operated on for mitral stenosis. Although for the most part the degree of improvement reported in these various articles is in general agreement with our findings, in the majority of reports the length of follow-up has been relatively short. However, the reports by Likoff and Uricchio\(^{22}\) have dealt with patients followed for periods up to 8 years, and Glover et al.\(^{23}\) reported a series of 50 patients followed 5 or more years. It has now been well demonstrated that patients with mitral stenosis can be operated upon with an acceptable operative mortality and that they are improved in the vast majority of instances. It is becoming apparent what factors are affecting this improvement, both immediately and over a long period of time. As we have pointed out previously, this is still a palliative operation although it is often life-saving and may be followed by extraordinary improvement that may persist for a long time. However, factors remain which lead in a substantial number of the patients to a gradual recurrence of difficulty in many of those who have improved, and militate against improvement in others. To some extent this has to do with the state of the valve itself. Even under the best of circumstances the valve remains in a scarred condition which may be conducive to recurrence of stenosis or to fixation of the leaflets, so that mitral incompetence results. The patient still remains a rheumatic subject, one in whom recurrence of rheumatic activity is ever possible. Studies such as ours have been of relatively negative value so far as elucidating the knotty problem of persistent or recurrent rheumatic activity in adults with chronic rheumatic heart disease. It is apparent that for the most part the criteria for rheumatic activity are not clear-cut and only in a minority of instances can a definite diagnosis be made. When undoubtedly rheumatic fever does take place after operation, however, the likelihood of cardiac deterioration is greatly enhanced.
The role of mitral insufficiency, either present prior to surgery or developing at the time of or subsequent to the operation, as an important factor leading to deterioration is becoming ever more apparent. Although true re-stenosis of the mitral valve may occur in some patients, this is not common in our experience nor in that of most observers. Bailey and his group\textsuperscript{24} noted the increasing frequency of re-stenosis in the patients they are following over prolonged periods of time. It is apparent that symptoms of cardiac disability not infrequently recur in patients in whom the original operation was not fully satisfactory, either due to inexperience on the part of the surgeon or to other conditions. In any consideration of the problem of "re-stenosis," it is important to distinguish such recurrences after unsatisfactorily performed valvuloplasties from true re-fusion of the commissures after a completely satisfactory mobilization of the leaflets.

Myocardial failure is undoubtedly an important element in the poor results of some of the patients or in the deterioration of others. This has been pointed out by us and has been emphasized by Harvey and associates.\textsuperscript{25} Whether myocardial failure follows from prolonged mechanical strain on the heart due to valvular defects or whether it is the result of the residual damaging effect of previous rheumatic myocarditis, or even of persistent rheumatic activity has not been satisfactorily elucidated, nor is it possible at times to make a definite distinction between myocardial failure and the mechanical factors resulting from valvular defects. Even with the aid of catheterization findings obtained by experienced investigators a definite diagnosis may not be made. Hemodynamic formulae have their limitations, not the least being the fact that the application of such formulae must be with data obtained only on isolated occasions and under the most abnormal circumstances, namely the situation of cardiac catheterization itself. We have observed on a number of occasions patients who, from catheterization findings, have what one would call physiologic left ventricular failure although the patients had no symptoms or signs of clinical heart failure. Conversely, it is often possible for a patient to have manifestations of congestion without exhibiting hemodynamic manifestations of what one calls heart failure, namely an elevated left or right ventricular diastolic pressure.

It has been suggested\textsuperscript{25, 26} that hemodynamic studies made before and after the administration of a parenteral digitalis or strophanthin preparation may help to distinguish the myocardial failure from the mechanical effects of the mitral block. Such tests are difficult to carry out and only valid in the hands of the most experienced investigators and hence could never have wide applications, even for such limited value as they may have. Most important of all, the quantitative evaluation of the relative degrees of stenosis versus regurgitation at a valve has as yet been accomplished only very imperfectly by catheterization or any other technics. A careful clinical evaluation is still as reliable as any of the special laboratory technics.

**SUMMARY**

A report has been made of the clinical results in 1,000 consecutive cases with a preoperative diagnosis of mitral stenosis that underwent valvuloplasty between 1949 and 1956. All but 2 of the 913 survivors of the operation have been followed at least 1 year and most of them up to the latest anniversary of their operation from 2 to 8 years ago.

When the preoperative clinical diagnosis was pure mitral stenosis, the surgeon confirmed the diagnosis at operation in about 90 per cent of cases, but when mitral stenosis and insufficiency was diagnosed preoperatively, operation revealed significant insufficiency in only about one half of the cases.

The incidence of operative embolization in the second 500 of this series has been 2.1 per cent in group III and 8.0 per cent in group IV. In only 25 have peripheral emboli occurred since operation.
Including operative mortality, 83 per cent of group-III patients and 57 per cent of group-IV patients have survived 7 years. These figures are much higher than reported survival rates of medically treated patients. The effects of sex, rhythm, and age on survival have been discussed.

The over-all percentage of patients significantly improved by operation has been 69 per cent in group III and 55 per cent in group IV. The percentage improved has tended to drop somewhat with succeeding years of follow-up.

In group III, fibrillating patients and those over 40 years of age did less well than those in normal rhythm or under 40; there was, however, no difference due to sex. In group IV significant differences due to rhythm, age, or sex were not apparent.

With increasing degrees of mitral insufficiency the results were progressively poorer and the differences were more striking at the end of 5 years than at the end of 1 year. Patients with preoperative tight mitral stenosis (1.0 cm.² or less) did better than those whose stenosis was less severe. The presence of associated valve disease (usually aortic) of mild degree did not affect the ultimate outcome.

The "postoperative" or "postcommissurotomy" syndrome occurred in an estimated 30.8 per cent of patients, but its presence did not have any bearing on the results.

Aschoff bodies were described in the biopsies of atrial appendages in 43 per cent of group-III patients and in 20 per cent of group-IV patients. They were present in a higher percentage of patients in normal rhythm than those in fibrillation, and the incidence decreased progressively with age. The presence of a positive biopsy had no relation to the ultimate results or to the occurrence of the postoperative syndrome.

A group of 228 patients who deteriorated after substantial improvement persisting at least 1 year were analyzed. Factors that were found in a significantly higher percentage than in patients who maintained their improvement were mitral insufficiency, an unsatisfactorily performed valvuloplasty, and clear-cut rheumatic fever occurring since operation.

**Summario in Interlingua**

Es reportate le resultatos clinic in 1.000 casos consecutive in que le diagnose preoperatori de stenosis mitral eseva sequite per valvuloplastia, effectuate inter 1946 e 1956. Con 2 exceptiones, omne le 913 superviventes del operation eseva tenite sub observation durante al minus un anno. In le majoritate del casos, le observation eseva extendite usque al plus recente anniversario del operation effectuate inter 2 e 8 annos retro.

Quando le diagnose clinic preoperatori eseva pur stenosis mitral, le chirurgo confirmava le diagnose al operation in circa 90 pro cento del casos, sed inter le casos in que stenosis e insufficiencia mitral eseva diagnosticate ante le operation, le incidentia de insufficiencia significative constatate per le chirurgo eseva solmente circa 50 pro cento.

Le incidentia de embolisation operatori inter le secunde 500 casos del serie eseva 2,1 pro cento in gruppo III e 8,0 pro cento in gruppo IV. Embolos peripheric ha occurrite deposit le operation in solmente 25 casos.

Prendente in consideration le mortalitate operatori, 83 pro cento de patientes de gruppo III e 57 pro cento de patientes de gruppo IV ha supervivite 7 annos. Iste cifras es multo plus alte que illos reportate pro le supervivenitia de patientes tractate per mesuras medical. Le effectos de sexo, rhythmo, e etate super le prognose es discutite.

Le procentage total del patientes significativamente meliorate per le operation eseva 69 pro cento in gruppo III e 55 pro cento in gruppo IV. Iste procentages monstrava un tendentia descendente in le curso del annos postoperatori.

In gruppo III, patientes con fibrillation e patientes de plus que 40 annos de etate habeva un prognose minus favorable que patientes con rhythmo normal e patientes de minus que 40 annos de etate. Tamen, nulle differentia eseva constata secoundo le sexo. In gruppo IV, nulle significative differentias eseva notate secoundo rhythm o etate o sexo.

Parallel al augmento del grado de insufficientia mitral, le resultatos se pejorava progressivemente. Le differentias eseva plus frap-
pante al fin de 5 años que al fin de 1 año. Patientes con tense stenosis mitral ante le operation (1 cm² o minus) reageva melio que pacientes in qui le stenosis essea minus sever. Le associate presentia de morbo valvular (usualmente aortic), si illo essea de leve grados, non aficie le resultato final.

Le syndrome "postoperatori" o "postcommmissurotomic" occurreva estimatamente in 30,8 pro cento del patientes, sed su presentia o absentia no influentiava le resultato final.

Corpos de Aschoff essea describite in le biopsias de appendages atrial in 43 pro cento del patientes de gruppo III e in 20 pro cento del patientes de gruppo IV. Illos essea present in plus alte procentages in patientes con rhythm normal que in patientes con fibrillation. Lor incidentia descendeava progressive-mente con le avantiamento del etate. Le presentia de un biopsia positive habeva nulle relation con le resultato final o con le occur- rentia o non-ocurrentia del syndrome post-operatori.

Essea analyseate le casos de un gruppo de 228 patientes in qui marcate grados de deteri-oration se declarava post un melioration sub-stantial de un duration de al minus 1 año. Factores que se trovava in iste casos in pro-centages significativamente plus alte que in casos in que le melioration se manteniva in-clude insufficientia mitral, un valvuloplastia non effectue satisfactorimente, e le occur- rentia de clar episodios de febre rheumatic deposit le operation.

ACKNOWLEDGMENT

We are greatly indebted to Dr. Mindel Sheps of the Department of Preventive Medicine, Harvard Medical School, for her valuable advice and assistance in the statistical evaluation of the results. The collection of follow-up information and compilation of statistics were largely performed by Mrs. Georgiana, Mr. Arthur Spiro, and Mrs. Eleanor Angelokas.

REFERENCES


Medical Eponyms

By Robert W. Buck, M.D.

Babinski's Phenomenon. Joseph Francois Felix Babinski (1857-1932) described this sign in the Comptes rendus hebdomadaires des Séances et Mémoires de la Société de Biologie 48: 207-208 (Feb. 22) 1896. The title of the article from which the following quotation is taken is "A Plantar Cutaneous Reflex in Certain Organic Affections of the Central Nervous System" (Sur le Réflexe Cutané Plantaire dans Certaines Affections Organiques du Système Nerveux Central):

"I have observed in a certain number of cases of hemiplegia or monoplegia involving the leg which were associated with an organic affection of the central nervous system, a disturbance in the plantar reflex of which I here present a short description: On the healthy side, pricking of the sole of the foot causes a flexion of the thigh on the pelvis, the leg on the thigh, the foot on the leg, and the great toe on the metatarsus. This occurs similarly in normal patients. On the paralyzed side, a similar stimulus also gives rise to a flexion of the thigh on the pelvis, the leg on the thigh, the foot on the leg, but the great toe, instead of being flexed, is extended on the metatarsus."
A Clinical Study of 1,000 Consecutive Cases of Mitral Stenosis Two to Nine Years after Mitral Valvuloplasty
LAURENCE B. ELLIS, DWIGHT E. HARKEN and HARRISON BLACK

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