Reactivation of Rheumatic Fever Following Mitral Commissurotomy

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A febrile syndrome following mitral commissurotomy is described. This syndrome consists of the episodic recurrence of a combination of events first occurring after a variable latent phase following mitral commissurotomy and is uniformly characterized by precordial pain and fever, is commonly featured by the precipitation or intensification of pre-existing heart failure, is variably accompanied by migratory joint pains, arrhythmias, hemoptysis or psychosis and sometimes terminates in death. The syndrome was found to occur in 43 (24.0 per cent) of 179 consecutive individuals subjected to mitral commissurotomy. Because we have never encountered such a syndrome following any other type of nonrheumatic cardiac or pulmonary surgery and for other reasons we are compelled to regard it as a reactivation of rheumatic fever.

Mitral commissurotomy is a procedure that was designed to relieve obstruction at a mitral valve damaged by rheumatic fever. It is not intended to control the rheumatic state. On the contrary, a surgeon performing a mitral commissurotomy operates in a field that is potentially the seat of subclinical active infection. So long as there is no specific method of controlling rheumatic fever the possibility exists that such an operation may activate rheumatic infection to clinical recognition or spread rheumatic fever subclinically. This implicit fear forms the basis for the almost universal acceptance of clinically active rheumatic fever as a contraindication to mitral commissurotomy.

Yet, it is well known that progressive rheumatic cardiac deterioration may occur in individuals in whom rheumatic activity cannot otherwise be recognized on clinical grounds and who, at necropsy, have characteristic stigmata of active rheumatic carditis. Indeed, it is because of the frequency of such findings at necropsy in children or adolescents dead of cardiac failure due to rheumatic heart disease, that many students of rheumatic fever think that any rheumatic child or adolescent with progressive cardiac failure has active rheumatic carditis. One could anticipate, therefore, an occasional postoperative unmasking of obviously clinically active rheumatic fever in individuals who were preoperatively regarded as having inactive or doubtfully active rheumatic fever. We have seen such occurrences. Fortunately, in our experience, they are rare, perhaps because of the care used to exclude from operation individuals who have any manifestations that can be interpreted as possibly due to active rheumatic fever.

However, we have observed a distressingly high incidence of a combination of events that occurs after a variable latent period following mitral commissurotomy. As far as we know, this combination of events, which has as its common denominator pain and fever, does not occur following any other type of nonrheumatic cardiac or pulmonary surgery. The purpose of this report is to describe the incidence and
character of these events that we are compelled to regard as a reactivation of rheumatic fever.

**Material**

The records were examined of 183 consecutive individuals subjected to mitral commissurotomy. Four were excluded because of the immediate precipitation by operation of active rheumatic fever. None of the other 179 was regarded preoperatively as having active rheumatic fever even in retrospect. Of these 179, 67 (37.4 per cent) had pain of delayed onset after discharge from the hospital. Of these 67, 43 (24.0 per cent of the 179) were recognized to have pain and fever of delayed onset. The character of the delayed pain occurring in those with pain alone was similar to that occurring in those with pain and fever. Although we have some evidence to suggest that in those with pain of delayed onset without recognized fever, the presence of fever may have been overlooked or suppressed by medication, only those 43 individuals with pain and fever of delayed onset form the basis of this report. The follow-up period varies from 6 to 24 months.

**Characteristics of the Pain and of the Fever of Delayed Onset**

**Pain.** Pain of delayed onset is most easily recognized when it occurs in an individual whose incisural pain has subsided considerably in intensity. After the gradual subsidence of incisural pain over a period of 10 days to 4 weeks, the individual is often terrified by the abrupt onset of severe pain. When pain appears to be an intensification of incisural pain or insidiously replaces the incisural pain, its true nature may not be recognized until one is struck by its changing character or location or until fever is found to be present.

The pain is variously described as dull, aching or more commonly bone-crushing, excruciating, knife-like, vise-like, as severe tightness or as a sensation as if "an elephant stepped on one's chest." Pain is commonly localized to the precordial area, particularly to the lower left parasternal region. It may radiate to the back, particularly to the left infrascapular region, to the epigastrium, to the left shoulder, to the left side of the neck or even to the left side of the upper jaw. It may start in the upper jaw and mimic a tooth abscess, its true nature being recognized only later when radiation occurs and localization to the precordial area takes place. It may radiate to both shoulders or across the entire anterior chest wall. Pain is usually aggravated by change of body position, by deep breathing and by swallowing. Pain is modified but not completely relieved by ordinary analgesics. Pain with variation in intensity may last from 10 days to 4 weeks. After an interval of freedom from pain for two weeks to one month, pain may recur and follow more or less closely the temporal course of the bouts of fever that will be described next.

**Fever.** Fever, if recognized, usually appears synchronously with pain. At times, fever may precede or follow by a day or two the appearance of pain. Fever usually rises slowly to 100 to 102 F. Rarely, it rises abruptly to as high as 104 F. The temperature varies daily from 1 to 3 degrees. It may remain elevated for 10 days to 4 weeks. Most patients are extremely enervated and toxic. Some perspire so profusely that pajamas and bed linen have to be changed several times a day. In others, perspiration is not noteworthy. Fever can be lowered and occasionally brought to normal by salicylates. Adrenocorticotropic hormone tends to be antipyretic. In no instance was an unrelated illness uncovered to account for the fever.

The patient may have one such bout or, more commonly, after an interval of one to four weeks of freedom from fever, another similar cycle may be ushered in. About an equal number of patients have had two, three and four bouts, several have had five and seven bouts and one had 14 bouts.

The syndrome of pain and fever of delayed onset following mitral commissurotomy has been divided into eight groups according to the associated clinical findings.

1. **Bouts of Pain and Fever Uncomplicated by Other Clinical Phenomena**

This group consisted of six individuals. Aschoff bodies were found in two of the six biopsies of the left auricular appendage. Of the others, three showed hypertrophy and the remaining one a degenerative reaction. Fever and pain were the only clinical manifestations. There was no precipitation or exacerbation of heart failure. There were nonspecific labora-
tory signs of infection. The electrocardiogram showed T-wave changes. No additional cardiac medication was required. Two received adrenocorticotropic hormone and one of these two also received cortisone during another bout with subsequent improvement but not with complete relief of pain or fever.

The following case, characteristic of this group, also illustrates the recurrent episodic nature of this syndrome.

Case 1. M. E., a 41 year old white female, was first admitted to the Episcopal Hospital on Oct. 10, 1952 for mitral commissurotomy. She had known of a heart murmur since the age of 5 when she had had St. Vitus' dance. She suffered a left cerebrovascular embolus on Aug. 19, 1951. Following this event, shortness of breath developed slowly and progressively.

Physical and roentgenologic studies were typical for mitral stenosis. The electrocardiogram disclosed auricular flutter with a ventricular rate of 100 per minute. Venous pressure was 180 mm. (fluid). The ether time was six seconds and the Decholin time 55 seconds. Blood count and urinalysis were normal. The sedimentation rate was 10 mm. in one hour (Wintrobe).

The ventricular rate was slowed by digitalis and the auricular flutter changed to flutter-fibrillation.

A mitral commissurotomy was performed on Oct. 30, 1952. Biopsy of the left auricular appendage disclosed only a degenerative reaction. Postoperatively, the patient responded satisfactorily. She was discharged on Nov. 14, 1952, to continue convalescence at home.

Two weeks later, she began to experience chest pain. It was sharp and localized to the left precordial area and aggravated by swallowing, breathing or movement. There was usually constant aching, frequently with superimposed recurrent attacks of sharp pain, "like a visé pushing in front and back." Sweating was frequent and profuse. Because of increasing pain and lack of relief by salicylates, she was readmitted to the hospital on Dec. 3, 1952. She was in marked distress. Respirations were increased in rate but voluntarily reduced in depth because of pain. She was pallid but not cyanotic. The veins were not distended. The precordial area was tender. The cardiac impulse was palpable in the fifth intercostal space 2 cm. to the left of the midclavicular line. The rhythm of the heart was grossly irregular at an average ventricular rate of 100 per minute with a pulse deficit of 10 per minute. There was no friction rub. A diastolic rumbling murmur was audible at the apex. The second sound at the pulmonic area and the first sound at the apex were accentuated. There was no friction rub. The liver and spleen were not palpable. There was no edema.

The blood pressure was 110/80. The oral temperature was 100 F. Chest roentgenogram disclosed considerable cardiac enlargement. A few linear strands were seen in the right lower lobe. An electrocardiogram showed auricular fibrillation and ST-T changes. The S-T segment was depressed and the T wave was inverted in the left chest leads. The leukocyte count was 12,500 per cubic millimeter with 80 per cent neutrophils. The sedimentation rate was 42 mm. in one hour. Urinalysis was negative. Antistreptolysin titer was 1:48 and antihyaluronidase titer was less than 1:24. The venous pressure was 165 mm. (fluid). The ether time was 17 seconds and the Decholin time 22 seconds.

Treatment was symptomatic. Temperature returned to normal in four days. Pain gradually subsided over a period of 10 days. Repeated electrocardiograms were similar except for a change of the ventricular rate to slower levels. She was discharged on Dec. 19, 1952. Digitalis dosage was maintained.

Again she remained at bed rest at home. She felt tired. In one week precordial pain, similar in character to that experienced previously, reappeared. Sweating was profuse. She was readmitted to the hospital on Jan. 3, 1953. Examination revealed pallor but no dyspnea. The heart was enlarged to the left. Presystolic and systolic murmurs were audible at the apex. Fever was present. Chest roentgenogram disclosed no further increase in heart size. An electrocardiogram showed increased negativity of the T waves in the left chest leads. The venous pressure was 130 mm. (fluid). The ether time was 15 seconds and the Decholin time 17 seconds. The leukocyte count was 9300 per cubic millimeter with 73 per cent neutrophils. The sedimentation rate was 38 mm. in one hour. Blood cultures were sterile. Antistreptolysin titer was 1:32 and antihyaluronidase titer was less than 1:24. Temperature remained elevated, reaching 104 F. rectally. Pain was severe. Penicillin and salicylates were ineffectual. Adrenocorticotropic hormone (5 mg. in 1000 cc. of 5 per cent glucose in water) was administered intravenously on Jan. 9, 1952, and resulted in moderate relief of pain. Thereafter, symptoms gradually subsided and she was discharged on Jan. 14, 1953.

One week later, pain reappeared. At first, it was aching in character. Temperature was occasionally elevated to 100 F. In the following week, pain increased in severity. The patient was readmitted to the hospital on Jan. 29, 1953. Examination revealed the cardiac impulse to be in the fifth intercostal space slightly to the left of the midclavicular line. The rhythm was grossly irregular at an average ventricular rate of 100 per minute with a pulse deficit of 5 per minute. A diastolic rumble with accentuation of the first sound and a slight systolic murmur were heard at the apex. The lungs were clear. There was no evidence of failure. Chest
roentgenogram revealed no significant changes. An electrocardiogram was similar to the one taken previously. The leukocyte count was 2750 per cubic millimeter with 75 per cent neutrophils. There was a mild anemia. The sedimentation rate was 40 mm. in one hour. Blood cultures were sterile. No "L. E." cells were found. Antistreptolysin titer was 1:32 and antihyaluronidase titer 1:24. Temperature remained elevated for three days. Salicylates were without effect upon the pain. Cortisone was administered for a few days with moderate amelioration of the pain. Repeated chest roentgenograms and electrocardiograms were similar to those taken previously. Chest pain gradually subsided during hospitalization. The sedimentation rate gradually decreased and on February 17 was 5 mm. in one hour. Body weight remained essentially unchanged. She was discharged on Feb. 19, 1953, to continue convalescence at home.

Since discharge, she has remained afebrile and has gradually increased her activities. For a few weeks, she continued to experience a dull aching sensation in the precordial region and occasionally required salicylates for relief. At present, she has no pain or fever and states that she has not felt as well in years.

A graphic presentation of the temperature record and of other pertinent findings is shown in figure 1.

2. Bouts of Pain, Fever and Psychoses

This group consisted of four individuals. Aschoff bodies were found in one of the two biopsies of the left auricular appendage. Three requiring digitalis preoperatively required an identical amount after operation. Neurologic findings suggestive of a focal cerebral lesion were not present. We cannot elaborate on the nature or significance of the psychoses. We do not know whether it was a depressive reaction to the operation, a manifestation of rheumatic brain disease, unrecognized cerebral emboli, or whether, as suggested by one of the cases, the psychosis was an accentuation of one not recognized preoperatively.

3. Bouts of Pain, Fever and Heart Failure

This group consisted of eleven individuals. Aschoff bodies were found in two of nine biopsies of the left auricular appendage. The others showed hypertrophy and, in addition, in one a thrombus. During the bouts, these individuals not only had pain and fever but heart failure as well. In all instances, heart failure was of the combined right and left type. Left heart failure was partly masked by pain. The objective signs were almost invariably predominantly those of right heart failure. Indeed, these findings were so striking in some instances that the possibility of cardiac
tamponade due to rheumatic pericarditis with effusion was considered, at least, as a contributory factor. However, the cardiac size, although larger than that present preoperatively, was not increased to the extent that one could seriously entertain, on the basis of roentgen findings, the presence of sufficient fluid in the pericardial sac to embarrass the circulation. In some individuals, residual distension of the neck veins and hepatomegaly persisted. In such individuals, we are strongly suspicious of the surgical production of an increase in mitral regurgitation. We believe so because in three instances, not included in this series, in which an immediate significant mitral regurgitation was produced, not only was dyspnea increased, but a large liver and bulging neck veins appeared. In these individuals, dyspnea was partly controlled by medication but the signs of right heart failure were constant.

The following recent case not included in our tables illustrates the type of heart failure seen in this group.

Case 2. A. F., a 46 year old white woman, was first seen by one of us (L.A.S.) on June 11, 1946, because of pain in the substernal and left infrascapular regions, palpitation and dyspnea while climbing steps.

Physical and roentgenologic studies (fig. 2) were typical of a mitral stenosis. The electrocardiogram disclosed many premature auricular beats and deformed P waves. On March 25, 1947, she developed permanent auricular fibrillation. Over the succeeding years her symptoms waxed and waned until Sept. 1, 1952 when she developed progressive dyspnea that terminated in an attack of pulmonary edema during the first week in October.

Mitral commissurotomy was performed on Oct. 23, 1952. The patient had an uneventful postopera-

**Fig. 2. Case 2. (A. F.) Preoperative chest roentgenogram, P-A view.** There is slight cardiac enlargement, prominence of the pulmonic segment, increased hilar markings, left auricular enlargement and calcification in the region of the mitral valve.

**Fig. 3. Case 2. (A. F.) Chest roentgenogram, P-A view, two months postoperatively.** There is an overall increase in the size of the cardiac silhouette.

tive course except for the usual incisural pain and left the hospital in 10 days.

Two weeks after discharge, she was seized with severe pain in the left lower parasternal region which radiated up into the left side of the neck. Pain also shot across the entire anterior chest wall to the right shoulder.

Physical examination revealed that she had gained 10 pounds since discharge from the hospital. The neck veins bulged. The cardiac impulse was in the fifth intercostal space slightly to the left of the midclavicular line. The rhythm was grossly irregular at a ventricular rate of 100 per minute with a slight pulse deficit. A precordial systolic murmur was present and loudest (grade 2) at the apex where a presystolic murmur was also heard. The first sound at the apex and the second sound at the pulmonic area
were accentuated. Subcrepitant rales were present at the lung bases. The liver was enlarged and tender and when pressed resulted in increased distention of the neck veins. The legs appeared full, the skin being tight and shiny, but pitting edema could not be demonstrated. Her temperature was 101 F. The antihyaluronidase titer was 1:96 and antistreptolysin titer was 1:48.

She was placed upon a strict salt-poor diet, acetylsalicylic acid and codeine. Acetylsalicylic acid lowered the temperature by 1 to 2 degrees. Fever persisted for 10 days. Several times the patient thought her temperature was normal and stopped taking acetylsalicylic acid only to find it rise in the next few hours to above normal. After a two-week interval of freedom of fever, fever recurred and was present off and on until the first week of January, 1953.

Roentgenographic study on Dec. 21, 1952, showed an overall increase in size of the cardiac silhouette and possibly even of the left auricle (fig. 3).

The patient, in addition to digitalis and a salt-poor diet, requires mercurial injections about once in 10 days. The neck veins are still abnormally distended and the liver is palpable. She had less dyspnea and was otherwise comfortable except for tightness across the upper half of her abdomen and increasing dyspnea about every eight or nine days after a mercurial injection. On May 27, 1953, at 2 a.m. she developed an attack of pulmonary edema that, she states, was similar in every way to the attack she developed before operation.

4. Bouts of Pain, Fever, Heart Failure and Arrhythmia

This group of 12 individuals had the highest incidence of biopsies positive for the presence of Aschoff bodies, 7 of 11 left auricular appendages examined. Of the other four, one showed hypertrophy, two were reported as normal and one was the seat of hemorrhage. The arrhythmias noted were rapid ventricular rate uncontrollable with digitalis in one, multiple ventricular ectopic beats in another, recurrent paroxysmal auricular tachycardia in two, auricular fibrillation in seven and auricular flutter followed by auricular fibrillation in one. This last patient required massive doses of digitalis to control the ventricular rate. Quinidine sulfate converted auricular fibrillation in one individual back to sinus rhythm. All arrhythmias were associated with a precipitation or intensification of heart failure. The one who did not require digitalis before operation required it during the bouts and still does. All required additional cardiac medication.

It is noteworthy that 10 of these 12 individuals had a sinus rhythm before operation. A change in rhythm from a sinus mechanism to auricular fibrillation is frequently easily recognized by both the physician and the patient. On the other hand, changes from auricular fibrillation to a different arrhythmia or additional arrhythmias such as multiple ectopic beats are difficult to recognize without electrocardiographic evidence or unless the rate becomes exceptionally fast. It is possible, therefore, that changes in rhythm in this syndrome are commoner than we report.

The case reported in group 6 also illustrates this type.

5. Bouts of Pain, Fever, Heart Failure and Arthritis

This group included three individuals. Biopsy of the left auricular appendage revealed Aschoff bodies in one, enlarged blood vessels in another, and dense collagenous material in the third. The arthritis was typically migratory. The joints were painful and tender but not red, hot or markedly swollen. In these individuals, the heart rhythm was not changed during the febrile bouts. The rheumatic nature of this affection may be recognized by the patient because of its similarity to a previous naturally occurring attack of rheumatic fever with joint manifestations. One of these three experienced bouts monthly for 14 months.

The following case illustrates the features of this group.

Case 3. F. K., a white female, 42 years old, was first seen by one of us (L.A.S.) on Jan. 25, 1945. She had rheumatic fever at the age of 11 years. In 1938, she was digitalized because of severe dyspnea. In the ensuing years, her symptoms waxed and waned but increased for the last three months before operation, so that mercurial injections were used once and, at times, twice a week. Clinical and roentgenologic studies were typical for mitral stenosis. Electrocardiogram revealed auricular fibrillation. Other laboratory studies were normal.

On April 17, 1952 a mitral commissurotomy was done. Biopsy of the left auricular appendage showed dense collagenous material but no Aschoff bodies. The postoperative course was uneventful. An elec-
trocardiogram showed increased depression of the S-T segment and inverted T waves in the left chest leads. She was discharged on April 30, 1952.

On May 8, 1952, pain in the chest appeared. Pain was substernal in location and occasionally severe but usually more of a sensation of tightness. Occasionally, she experienced mild aching of the joints. Fever was present and varied from 99 to 102 F. On July 9, 1952, the temperature was 102 F. and severe migratory joint pains affecting the shoulders, elbows, hips and knees were present. She volunteered that "it felt like my childhood rheumatic fever." She was extremely tired and had an almost constant sensation of near collapse. The leukocyte count was 8800 per cubic millimeter and the hemoglobin 11 Gm, per 100 cc. She was seen frequently in the following months. Joint pains accompanied by fever were almost constantly present. The neck veins were distended and hepatomegaly and edema were present. During the first week in October, all joint pain disappeared and the temperature returned to normal.

She is on a maintenance dose of digitalis and is almost entirely free of symptoms. She volunteered the information that she was able to walk even in cold weather against a mild wind without dyspnea for the first time in years. She has required no mercurial injection since recovery from the febrile syndrome.

6. Bouts of Pain, Fever, Heart Failure, Arrhythmia and Arthritis

This group consisted of two individuals. Biopsy of the left auricular appendage showed Aschoff bodies in one and endocardial thickening and a slight increase in cellularity in the other. Both individuals were on maintenance doses of digitalis and had a sinus rhythm preoperatively and postoperatively. During the febrile bouts, irregular heart action and overt heart failure occurred. An electrocardiographic study was done in one of these and revealed auricular fibrillation. The arrhythmias in these two individuals were transient. Sinus rhythm reappeared spontaneously after subsidence of the febrile episode. The joint pains were severe and protracted.

The following case shows the features of this group.

Case 4. S. N., a 36 year old white female, was first seen by one of us (L.A.S.) on March 8, 1951. She had been told eight years previously that she had rheumatic heart disease but was free of symptoms until July 1950 when she developed dyspnea on effort. Clinical and roentgenologic studies (fig. 4) were typical of mitral stenosis. During March and April, 1952 dyspnea became progressively worse.

She elected surgery, and mitral commissurotomy was done on May 15, 1952. Biopsy of the left auricular appendage failed to reveal Aschoff bodies. Postoperatively, a friction rub was heard in the left parasternal region. Otherwise, the postoperative course was uneventful. Chest roentgenogram on May 27 showed a slight increase in the over-all size of the heart, haziness of the left base and a strand-like density in the right lung field. Electrocardiogram on May 26 (fig. 5) showed a prolonged P-R interval of 0.27 second. In leads III and aV_{3}, J was slightly elevated, the S-T segment was convex upward and the T wave was sharply inverted. She was discharged on May 27, 1952, to continue her convalescence at home.

Two days later she developed pain in the left side of the neck and face, centering in the left upper gum. The next day, she developed a fever of 102 F.

Because of persistence of pain and fever, she was readmitted to the Episcopal Hospital on June 2, 1952. Examination of the mouth, teeth and face was negative. There were rales at both bases of the lungs. The heart was slightly enlarged. The second pulmonary sound was accentuated. An apical systolic murmur was present. On admission, the leukocyte
count was 20,000 per cubic millimeter with 75 per cent neutrophils. Urinalysis was negative. Temperature varied from 99 to 101 F. for nine days. She perspired frequently. Pain, which at first was located in the left side of the face, now appeared to be radiating to this region from the retrosternal area and was described as a severe pressure sensation. Chest roentgenogram on June 12, Chest roentgenograms on June 14 revealed no significant change. She was discharged on June 17, 1952.

She returned to the office on July 3, 1952, complaining of pain in all the joints with stiffness of the adjacent areas, fatigue, profuse perspirations and a sensation of recurrent "jumping" heart beats. Temperature was 100 F. The heart rate was regular at 100 per minute. A friction rub was audible in the apical area. She was advised to rest in bed and to take acetosalicylic acid and codeine sulfate.

Because fever, pain and sweating increased, she was readmitted on July 7, 1952. An electrocardiogram on the day of admission, (fig. 5), showed the presence of auricular fibrillation at an average ventricular rate of 150 per minute with occasional ectopic ventricular beats. The leukocyte count was 8300 per cubic millimeter with 73 per cent neutrophils. Hemoglobin was 11.8 Gm. per 100 cc.; erythrocytes numbered 3.81 million per cubic millimeter, and hematocrit was 40 per cent. Blood culture was sterile. A chest roentgenogram on July 7, (fig. 6), showed an increase in size of the cardiac silhouette. Penicillin and salicylates were administered. Additional digitalis was necessary for control of the ventricular rate. Quinidine sulfate was given daily (0.2 Gm. every three hours for five doses) on July 14 and July 15. An electrocardiogram on July 16 (fig. 5) showed a sinus rhythm. The P-R interval was prolonged to 0.27 second. Temperature
was 98 to 101 F for two days and then was usually normal. She was discharged on her usual maintenance dose of digitalis on July 16, 1952.

On August 7, 1952, she returned to the office complaining of pain in the ankles and knees. Milder pain was present in the wrists upon motion. There was fatigue on effort and shortness of breath on lifting light objects. Temperature was 99.2 F. Recurrent mild joint pains and severe chest pain with fever persisted until September 16. At this time, she was afebrile and completely free of joint pains and able to walk five city blocks without discomfort. An electrocardiogram on October 6 (fig. 5) showed a sinus rhythm. The P-R interval was 0.24 second. The S-T segment was now isoelectric in leads III and aVF. The T waves were now positive in the left chest leads.

On Sept. 10, 1952, she became free of symptoms. She improved functionally and was able to dance on two different occasions. On October 16, digitalis was discontinued. She remained well until December 12, when joint pains and fever recurred. She became more tired and dyspneic. Fever and joint pains disappeared on Feb. 3, 1953, but dyspnea and fatigue continued to be present. She was redigitalized but states that she feels no better than she did before operation.

7. Bouts of Pain, Fever, Heart Failure and Hemoptysis

This group included two individuals. Biopsy of the left auricular appendage in one showed hypertrophy. One had three episodes of hemoptysis and the other had only one. Other than the hemoptysis, the findings were similar to those observed in group 3.

8. Bouts of Pain, Fever and Heart Failure Terminating in Death

This group included three individuals. Biopsy of the left auricular appendage in all three revealed only hypertrophy. Each individual had a delayed onset of pain and fever with progressive and intractable heart failure terminating in death. Necropsy was performed in one of these and revealed active rheumatic carditis.

A summary of these reactions and their incidence is shown in table 1.

**Laboratory Findings**

Neither we, nor the referring physicians, were successful in our search for causes of this reaction other than the operative procedure. None gave a history of a preceding sore throat, upper respiratory infection or any unrelated infection. Laboratory data on five individuals who consented to repeated hospitalization during the reactions failed to produce illuminating data. The leukocyte count varied from normal to 20,000 per cubic millimeter, with an average of 11,000 per cubic millimeter. The erythrocyte sedimentation rate (Wintrobe) was moderately increased to an average of 23 mm. in one hour. Cultures of the blood, throat, sputum and urine were all negative.

**Table 1.—Postcommissurotomy Febrile Syndrome of Delayed Onset—Incidence, 24.0%*; Summary of 43 Cases**

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<tr>
<th>Syndrome</th>
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<tr>
<td>Fever Only</td>
<td>6</td>
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<tr>
<td>Fever and Psychosis</td>
<td>4</td>
</tr>
<tr>
<td>Fever and Heart Failure</td>
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<td>Fever, Hemoptysis and Heart Failure</td>
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<tr>
<td>Fever, Heart Failure and Death</td>
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* 67 of 179 persons subjected to mitral commissurotomy had recurrent chest pain after discharge from the hospital. In 43 of these, the febrile syndrome occurred.

In all instances where roentgenologic studies were available, the cardiac silhouette appeared to be slightly larger during the syndrome and subsequent to it than it was before operation. The silhouette was increased in all its diameters except, at times, along the left border in the region where presumably the left auricular appendage was before amputation. During the febrile stage, the individual chambers may not be so clearly demarcated from one another as they were previously or subsequent to the reaction.

The electrocardiographic changes noted during the febrile syndrome were (1) occasional prolongation of the auriculoventricular conduction time, (2) S-T segment changes which are suggestive of pericarditis or appear to be by comparison with previous tracings, (3) S-T segment changes suggestive of increased myocardial derangement, (4) lowering of the voltage of T or greater negativity of T and prolongation of Q-Tc, suggestive also of
increased myocardial derangement, (5) transient or permanent auricular fibrillation, (6) increased ventricular rate, and (7) auricular or ventricular ectopic beats or both.

DISCUSSION

Unfortunately, there is no specific test for rheumatic activity. We realize full well the difficult differential diagnosis of rheumatic fever, greatly enhanced by the effects of an operation upon the heart. The diagnostic problems arising in the immediate postoperative period are particularly difficult and will be the subject of a subsequent report. It is, however, inconceivable to us that the delayed phenomena we have described are simply manifestations of surgical trauma. Rather, we look upon the surgical operation as a trigger mechanism that sets in motion a series of events that in time rise to clinical manifestations. The pathogenesis of this mechanism at this time is purely speculative. We can think of several possibilities:

1. Operation in some manner permits the spread of endogenous streptococi that, after a variable latent period, causes the appearance of the delayed syndrome. This hypothesis was suggested to us by Dr. T. N. Harris.

2. Operation makes the individual more susceptible to mild and subclinical streptococcal infections.

Hypotheses 1 and 2 are now being tested by Dr. Harris by immunologic studies of individuals before and following mitral commissurotomy.

3. Surgical incision of inflammatory tissue directly spreads inflammatory agents that multiply and, after a latent period, give rise to clinical symptoms.

4. Surgical incision permits the escape of abnormal protein material to which the body responds after a variable time by the production of immune bodies with clinical manifestations.

Both 3 and 4 appear unlikely to us because the reaction is not a single one but frequently is of a cyclic or repetitive type.

5. This syndrome is another example of the hypersusceptibility of the rheumatic individual to nonspecific stimuli.

Almost from the beginning of the recognition of rheumatic fever, there have been sporadic reports of the relationship of trauma to not only rheumatic activity but its initial site. Drewitt, Bland and Jones, Swift, and Massell, Mote and Jones have commented upon this relationship. The last observers have produced in subjects with rheumatic fever subcutaneous nodules, clinically indistinguishable and histopathologically similar to spontaneous ones, by the injection of autologous blood into the subcutaneous and deep tissues in the region of the olecranon process followed by the application of frictional pressure. The more active the rheumatic fever, the larger the induced nodule and the longer its duration.

We have seen masses of red blood cells in the mitral valve beneath the commissurotomy wound in the few individuals we have had who died within two weeks of operation (fig. 7).
Frictional effects are exerted by the motion of the heart valve and other portions of the heart. It is quite possible that this mechanism described by Massell, Mote and Jones may be operative following mitral commissurotomy but that the reaction is more intense because the irritant is not at a distance from but directly upon abnormal rheumatic tissue.

We have seen in an individual dead 10 days after mitral commissurotomy, in whom biopsy of the left auricular appendage showed nonspecific inflammatory cells (fig. 8), Aschoff bodies in the papillary muscles (fig. 9) and nonspecific inflammatory cells in the parietal pericardium (fig. 10) along the line of suture that were as suspicious of rheumatic activity as were those seen in the left auricular appendage. We have seen a similar pericardial reaction in another individual, dead two weeks after operation, whose biopsy of the left auricular appendage was positive for Aschoff bodies. The greater incidence and greater severity of pain in this syndrome than that in naturally occurring clinical activation may be related to the greater involvement of the parietal pericardium.

We have not been able to correlate the

Fig. 8. Biopsy of the left auricular appendage showing nonspecific chronic inflammatory changes (200 X).

Fig. 9. Biopsy of the papillary muscle of the same heart from which the biopsy of the left auricular appendage seen in figure 8 was obtained. Note the Aschoff body (200 X).
febrile syndrome following mitral commissurotomy with any event in the patient's history related to rheumatic fever or to the operative findings or to the biopsy report of the left auricular appendage. There were 15 biopsies of the left auricular appendage positive for Aschoff bodies out of a total of 37 (40.5 per cent). This percentage is practically identical with that of biopsies positive for Aschoff bodies in those who did not develop the postcommissurotomy syndrome. We, of course, were not surprised that the febrile syndrome occurred in some individuals with biopsies negative for Aschoff bodies because the tiny sample examined is but a small fraction of the entire heart. We have just illustrated a biopsy of the left auricular appendage negative for Aschoff bodies in a heart which contained Aschoff bodies within its papillary muscles. From these studies, we are inclined to agree with those who state that an individual with rheumatic heart disease has active rheumatic carditis through the rest of his life in the sense that a steady state of health or disease lasts as long as there is a balance between the disease-producing rheumatic agent and a healing tendency of the host. This balance can be readily upset and one method of doing so is apparently operative trauma. Perhaps, in the future, a more careful history with particular reference to the effect of all nonspecific insults on the immediate subsequent course of rheumatic heart disease may help to differentiate those individuals who will from those who will not develop the syndrome.

A discussion of the prognosis of the febrile syndrome involves a comparison with the prognosis of mitral commissurotomy in those individuals who did not develop the syndrome. The term "mitral commissurotomy" implies a uniform operative accomplishment. Unfortunately, not only is the operative accomplishment not uniform but also the operative findings before commissurotomy and a host of other factors are not uniform. We are in the process of attempting to analyze all of these factors in an attempt to evaluate the so-called functional results. For these reasons, we prefer to report our results in the following fashion that we admit is not entirely satisfactory. Of the 43 who developed the postcommissurotomy febrile syndrome, three died, four are psychotic, two developed hemiplegia and five developed permanent auricular fibrillation. Of the remaining 29, four required less medication than before operation and stated that they felt much better and were able to do much more. Eight required the same amount of medication as that required before operation and 17 required either intermittently or constantly more medication than before operation. Even in the group who required more cardiac medication following the postcommissurotomy syndrome, several stated that they felt better and were able to do more.
Finally, we believe that the incidence of this syndrome is greater than we have reported and may be closer to that of the incidence of pain that we have found. We believe this is so because (1) the incidence in those patients we have had the opportunity of following personally is higher, (2) we have seen in consultation several patients in whom fever was not recognized either because the temperature was not taken, the pain being regarded as of incisural origin, or taken incorrectly because lips were not sealed continuously while the oral temperature was taken, and (3) because several of our referring physicians are using large amounts of salicylates routinely after hospitalization, a practice that we heartily approve.

**Summary and Conclusions**

1. A febrile syndrome following mitral commissurotomy is described.

2. Excluding four individuals who developed an immediate precipitation of rheumatic fever, the syndrome occurred in 43 (24.0 per cent) of 179 consecutive individuals subjected to mitral commissurotomy.

3. This syndrome is characterized by the appearance of an episodic recurrence of a combination of events first occurring after a variable latent period following mitral commissurotomy and is uniformly characterized by precordial pain and fever, is frequently associated with the precipitation or intensification of heart failure and is at times accompanied by migratory joint pains, arrhythmias, hemoptysis or psychosis and sometimes terminates in death.

4. Because of the frequency of this syndrome following mitral commissurotomy and its absence following any other nonrheumatic cardiac or pulmonary surgery and because of the frequent cardiac involvement, the syndrome is regarded as a reactivation of rheumatic fever.

5. Reasons are given for believing that the incidence of this syndrome is even greater than herein reported.

**Sumario Español**

Un síndrome febril subsiguiente a la comisurotomía mitral se describe. El síndrome consiste de una repetición episódica de una combinación de sucesos que ocurren primariamente luego de una fase latente variable consiguiente a la comisurotomía mitral y uniformemente se caracteriza por dolor precordial y fiebre, comúnmente caracterizado por la precipitación o intensificación de decompensación cardiaca previamente existente y variablemente acompañado de dolores migratorios en las coyunturas, arritmias, hemotisis o psicosis y algunas veces terminando en desenlace fatal. El síndrome se encontró ocurrir en 43 (24 por ciento) de 179 sujetos consecutivos sometidos a una comisurotomía mitral. Porque nunca hemos observado este síndrome subsiguiente a ningún otro tipo de cirugía no reumática o cirugía pulmonar y por otras razones nos vemos compulsados a considerar esto como una reactivación de la fiebre reumática.

**Referencias**


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