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AN APPRECIATION OF MITRAL STENOSIS*

PART I. CLINICAL FEATURES

BY

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During the past three years mitral valve disease has been studied intensively at the Institute of Cardiology and at the Cardiac Department of the Brompton Hospital. It is the purpose of this paper to present a comprehensive review of the facts ascertained during this period. The work represents an elaboration of one of the papers opening the discussion on mitral stenosis at the European Congress of Cardiology held in London on September 9 to 12, 1952, and summarized in the Abstracts of Scientific Communications.

Material

The material comprises 150 cases submitted for operation, and another 150 which were considered unsuitable for surgical treatment. Amongst the surgical cases were four put up for repair of mitral incompetence; amongst the medical cases were 50 believed to have predominant mitral incompetence and another 32 in which mitral incompetence was thought to be as important as stenosis, if not more important. A further 50 patients have been studied, but are not included in the main series because they are awaiting either catheterization or valvotomy.

The material is analysed more fully in Table XXIII in the Summary, at the end of Part II. All cases were examined and assessed personally by the author, who was responsible for their medical care, including that before and after operation.

Method

These 300 cases were analysed in respect of 50 medical points, including those pertaining to radiography, fluoroscopy, and electrocardiography. Auscultation was often checked but rarely influenced by phonocardiography; and fluoroscopy was sometimes checked but never influenced by electrokymography. Where applicable, all cases were also analysed in respect of eight points relating to cardiac catheterization, 14 to valvotomy itself, and 20 to the subsequent course. Thus the great majority of those treated surgically were subjected to a 90-point analysis. All symptoms, measurements, and graphic patterns were graded from 0 (absent) to 4, the four positive grades representing the common English adjectives of degree—slight, moderate, considerable, and gross. If thought desirable, the moderate grade was divided into grades 2A and 2B, A being less severe than B.

Cardiac catheterization was carried out in 125 of the surgical cases, 42 of the medical, 17 of those with pure mitral incompetence, and in 23 awaiting valvotomy —that is, in a total of 207 cases. Pressures were recorded with reference to the sternal angle by means of a Sanborn electromanometer and polyviso, the oxygen consumption was measured by means of a Sanborn metabulator, and blood gas analysis using a Haldane type instrument. The left atrial pressure was obtained by wedging the catheter in a peripheral pulmonary artery as described by Lagerlöf and Werkö (1949). The tracing was accepted as an accurate record of the left atrial pressure if it was venous in form. This assumption has been proved valid in our laboratory at Brompton by Epps and Adler (1953). The data for calculating cardiac output and pulmonary resistance were obtained in quick succession, but not simultaneously. In one-third of the cases the left atrial and pulmonary artery pressures were also measured during and after standard exercise. The pulmonary vascular resistance was expressed in simple units obtained from dividing the mean pulmonary artery pressure minus the mean left atrial pressure (mm. Hg) by the pulmonary blood flow (l./min.), as explained in the section on resistance.

Nearly two-thirds of the surgical cases were operated on by Mr. R. C. Brock, who performed the first mitral valvotomy at Brompton on March 29, 1950. In the remainder, valvotomy was undertaken by Sir Clement Price-Thomas (5), Mr. Norman Barrett (14), Mr. Oswald Tubbs (3), Mr. W. P. Cleland (14), and Mr. Ian Hill (5) at the Brompton Hospital; by Professor R. Pilcher (13) at University College Hospital; and by Mr. Holmes Sellors (2) at the Middlesex Hospital.

The surgeons' observations with regard to the presence or absence of clot, mitral incompetence (before and after valvotomy), mitral calcification, mobility of the cusps, valve structure, and size of the mitral orifice before and after valvotomy were accepted without question. Direct pressures from the left atrium and pulmonary artery were recorded before and after valvotomy in about two-thirds of the cases. A biopsy from the left atrial appendage was obtained routinely, and from the lung in many cases. The post-operative physical signs and the general assessment of the situation and

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operative achievement were recorded as a routine before the surgeon's report was read. Follow-up notes were then made at intervals of three, six, or twelve months.

Incidence

In his Harveian oration of 1945, Sir John Parkinson produced statistical evidence indicating that in 1942 there were approximately 144,000 men between the ages of 18 and 44 with established heart disease in Great Britain, and that 80% of these—that is, 115,200—were rheumatic. Since the incidence of rheumatic heart disease is higher in women than in men, and since there are rather more women than men in the country, the total incidence of rheumatic heart disease in both sexes between the ages of 18 and 44 must be not fewer than 240,000. At least two-thirds of these, or 160,000, are predominantly mitral.

It is clear from the material comprising this paper that about one-half of all mitral cases—that is, 80,000 in the age group stated above—require valvotomy. At a conservative estimate, therefore, there should be approximately 3,000 valvotomies carried out in Great Britain per annum in order to cope with the situation.

Incidence of Individual Valve Involvement

It has never been quite clear what determines the relative frequency with which each particular valve is involved in rheumatism. According to Cabot (1926) the mitral valve is involved in 85%, the aortic in 44%, the tricuspid in 10 to 16%, and the pulmonary in 1 to 2%. These figures would not be seriously disputed at the present time. Various attempts have been made to correlate them with the frequency with which each valve was vascularized—for example, Gross and Kugel (1931). But Wearn *et al.* (1936), using indian ink instead of a barium gel, were unable to demonstrate any such correlation; they found blood vessels in 66% of the mitral valves studied, in 64% of the tricuspid valves, in 28% of the pulmonary, and in only 16% of the aortic. It has long seemed obvious to me that there might be a much simpler explanation for the phenomenon under discussion—that it depended on the degree of stress to which each valve was subjected. In a child of 10 the systemic blood pressure is about 100/60, the pulmonary about 15/6. Thus the load against which the mitral, aortic, tricuspid, and pulmonary valves have to work is in the proportion of 100, 60, 15, and 6 mm. Hg respectively. If the mitral valve was involved in 80% of cases the expected frequency of aortic, tricuspid, and pulmonary valve involvement would be 48, 12, and 5% respectively. This approximates very closely to Cabot's figures.

Age and Sex

The average age of patients in various groups and subgroups is presented in Table I. It was usually around 37.6 years, the average for the whole series. Surgical cases with simple mitral stenosis tended to be younger than their medical counterparts, although usually more severe; and patients with auricular fibrillation were usually considerably older than those with normal rhythm; but neither mitral incompetence nor an extreme pulmonary vascular resistance was related to age.

The sex incidence in the various types of mitral valve disease is presented in Table II. The figures confirm the well-known bias that mitral stenosis has for women and that mitral incompetence has for men. The extraordinarily high proportion of women in the group with a high pulmonary vascular resistance (*active* pulmonary hypertension in the table) may be due partly to the same sex factor that operates in primary pulmonary hypertension and partly to the fact that it is stenosis rather than incompetence which favours the development of a high resistance (see below).

TABLE I.—*Age Incidence*

	Groups			Total	M.S. Uncomplicated		M.S. M.I.		Extreme Resistance		Rhythm	
	Surg.	Med.	M.I.		Surg.	Med.	Surg.	Med.	Surg.	Med.	Normal	A.F.
Average age ..	36·8	37·5	37·2	37·6	35·4	41·5	37·6	38·8	37·6	38	33·6	41
Range ..	18–58	19–66	13–65	13–66								

TABLE II.—*Sex Incidence*

	Sex Ratio	
	Male	Female
M.S. with active pulmonary hypertension ..	1	7
„ uncomplicated	1	4
„ with trivial M.I.	1	3
„ „ serious M.I.	1	1
Mitral incompetence	3	2
All cases	1	2

History of Rheumatic Fever, Chorea, or Growing Pains

A previous history of the active rheumatic state was obtained in 68% of the whole series. In relatively pure mitral stenosis, with or without a high pulmonary vascular resistance, a history of previous rheumatism was obtained in 60%; when there was a serious degree of mitral incompetence with or without clinical stenosis, the incidence rose to 71.7%, and when more than one valve was causing trouble it was as high as 96%. Thus pure mitral stenosis would seem to be the least florid form of rheumatic heart disease.

Of those giving a previous history of the rheumatic state 45.7% had had a single attack of rheumatic fever, 31.5% recurrent attacks, 12.5% chorea alone, 4.8% both chorea and rheumatism, and 5.5% had had only subacute rheumatism or growing pains. Cases with significant mitral incompetence or multiple valve lesions were ten times more likely to have had recurrent rheumatic fever than isolated chorea; in relatively mild cases of pure mitral stenosis, on the other hand, a previous history of chorea alone was twice as common as recurrent rheumatic fever. This supports the conclusion drawn from the previous paragraph.

Life History

The chief landmarks in the life histories of all patients with symptoms are presented in Table III. The cases were divided into two groups according to whether mitral stenosis or incompetence was predominant. The figures for each grade were computed only from those cases which had completed their period in the grade under consideration by deteriorating sufficiently to enter the next grade. Thus the duration of grade IV symptoms could be assessed only from those who died from medical causes.

TABLE III.—*Life History*

	Latent period			Duration of Symptoms				From Onset Symptoms to Total Incapacity (Years)
	Age Initial Attack	Latent Period (Years)	Age Onset Symptoms	Grade 1 (Years)	Grade 2 (Years)	Grade 3 (Years)	Grade 4 (Years)	
Mitral stenosis	12	19	31	2·7 (0–17)	2·7 (0–18)	1·94 (0·5–11)	2 (0·5–4)	7·3
Mitral incompetence	12·5	20	32·5	2 (0–9)	1·1 (0–5)	2·25 (0–7)	>1 (0·3–3)	5·4

The rapid deterioration shown in the table suggests that there can be little point in delaying mitral valvotomy long in anatomically suitable cases once unmistakable symptoms of stenosis have developed; to do so is to invite complications such as embolism and to deprive patients of good physical health at a time of life when they have the right to expect it. Against operating too soon, however, are the surgical mortality of 6%, the 24% incidence of poor or indifferent results, and the possibility that stenosis may recur.

Pregnancy

In the whole series there were 83 mothers who between them had had 140 pregnancies. Cardiac symptoms had developed or increased during pregnancy in 43, but not in the other 97. On account of these symptoms two cases had been terminated at three months, one had had a hysterotomy at five months, one had been medically delivered at eight months, and two had had caesarean section; the remainder had been delivered naturally at term.

Of the 43 patients who deteriorated during pregnancy, 19 subsequently regained their previous state of health and 24 did not. Thus 24 out of 140 pregnancies, or 17%, precipitated permanent disability. In those cases in which pregnancy caused no trouble, cardiac symptoms did not develop for an average period of 10.4 years afterwards (range 1 to 28).

Cardiac symptoms developing during pregnancy were always due to pulmonary venous congestion and consisted of cough, breathlessness, orthopnoea, paroxysmal cardiac dyspnoea, or pulmonary oedema; sudden haemoptysis (pulmonary apoplexy) occurred in 12 out of the 43 cases (28%). Auricular fibrillation, systemic embolism, and congestive failure were rare complications. There was no evidence that those patients who developed symptoms during pregnancy were more or less likely to present later with a high pulmonary vascular resistance (34%) than those who did not (28%).

SPECIAL SYMPTOMS

Dyspnoea and Grading

Effort intolerance commonly due to dyspnoea was graded according to its severity as mentioned in the introduction under "Method." Patients in grade 1 were able to lead normal lives, but could not keep up with their fellows physically, although they might not be deterred from attempting to do so. They became unduly breathless on hurrying, running, walking up hills, or playing games. Patients in grade 2 were unable to run or hurry and found walking up hills difficult; they could walk indefinitely on the level, and were not orthopnoeic. To clarify the situation further this grade was usually divided into 2a and 2b. In grade 3 patients could walk only a few hundred yards on the level, and shopping and housework were carried out only with difficulty. Walking up hill was almost impossible and stairs had to be negotiated slowly. Patients who were more or less totally incapacitated were placed in grade 4; they could hardly manage 100 yards on the level and had abandoned their shopping and housework; many of them were virtually confined to bed. The majority of patients with orthopnoea, paroxysmal cardiac dyspnoea, or pulmonary oedema were in grade 3 or 4; out of respect for custom, cases with indisputable congestive heart failure were arbitrarily placed in grade 4.

Of the 150 patients selected for surgical treatment 19% were in grade 2 (all but two in grade 2b), 41% in grade 3, and 39% in grade 4. One patient with no effort intolerance was operated on because of recurring systemic embolism.

There were many patients in the medical and mitral incompetent groups who were only slightly breathless on effort or not at all, and it may be observed here that when such patients were catheterized the left atrial pressure was usually well below 10 mm. Hg with reference to the sternal angle. In striking contrast is the fact that of all the patients treated surgically there was only one with a left atrial pressure in this range, and that was the individual with recurrent embolism just mentioned. The belief that breathlessness in mitral valve disease is closely associated with pulmonary venous congestion is thus strongly supported.

Orthopnoea and Paroxysmal Cardiac Dyspnoea

Orthopnoea occurred in 69% of the surgical patients, in 30% of the medical, and in 44% of those with mitral incompetence—that is, in 53% of the whole series. The respective figures for *paroxysmal cardiac dyspnoea* were 49%, 16%, 32%, and 35%. It should be remembered that there were a number of relatively mild cases in the two medical groups.

In attempting to find out what particular factors governed the incidence of the major pulmonary venous congestive symptoms, patients with paroxysmal cardiac dyspnoea were compared with those who had neither paroxysmal cardiac dyspnoea nor orthopnoea, only cases with well-marked disability (grade 2b to grade 4) being selected for study, so that the two groups were matched in this respect. There were over 50 cases in each group.

The most important results of the analysis are shown in Table IV. It will be seen that the degree of stenosis was certainly not responsible for the difference in functional behaviour between the two groups. The left atrial pressure and the cardiac output at rest were both a little higher, and the rhythm was more often normal in those with paroxysmal dyspnoea, but these differences were not great. The pulmonary vascular resistance, on the other hand, showed a remarkable difference, the level in cases of paroxysmal dyspnoea being exactly half what it was in the others. If the figures are examined more closely it will be noticed that the important difference is confined to the extreme grade of resistance which was found nine times more frequently in those without paroxysmal dyspnoea or orthopnoea. Resistance lower than 10 units did not protect the lungs adequately.

TABLE IV

	Normal Rhythm (%)	L.A.P. mm. Hg	C.O. l./min.	Unusually Tight or Extreme Stenosis (%)	Resistance Units				
					1–3·9 %	4–5·9 %	6–9·9 %	10–30 %	Average
Pulmonary oedema (history of) ..	76	23	4·6	36	66·5	33·5	—	—	2·9
Paroxysmal cardiac dyspnoea (history of) ..	59	23	4·0	50	50	26	20	4	4·6
Cases without P.C.D. or orthopnoea ..	42	22	3·5	46	21	26	15	38	9·2
Whole surgical series ..	59	22·5	3·8	43	38·4	26	23	12·6	6·0

It may be tempting to assume that in their natural life history all cases of tight mitral stenosis sooner or later develop orthopnoea and paroxysmal cardiac dyspnoea, and that they then either die from pulmonary oedema or are protected by developing a high pulmonary vascular resistance; by obstructing the circulation proximal to the pulmonary capillaries this prevents dangerous rises of pulmonary venous pressure, so that patients are saved from drowning at the expense of a low cardiac output, and symptoms of pulmonary venous congestion are replaced by fatigue and oedema. This attractive hypothesis, however, is not properly supported by the facts. In the whole series such a life history was encountered in only six instances, or in 22% of all those with a resistance of 10 units or more. On the contrary, 78% of patients with a really high pulmonary vascular resistance had never had orthopnoea or paroxysmal cardiac dyspnoea at any stage. One is forced to conclude that if an extreme resistance is going to develop in mitral stenosis it does so relatively early in the course of the disease.

Frank Pulmonary Oedema

Manifest pulmonary oedema occurred in 11% of the surgical cases, in 2% of the medical, and in 6.5% of those with mitral incompetence, or in 7.5% of the whole series. Nearly 80% of such cases had more or less pure mitral stenosis, 15% combined stenosis and incompetence, and only 5% pure incompetence. Amongst the cases with stenosis 94% were women; in the small group with incompetence 75% were men.

The series is analysed in Table IV. The patients were distinctly younger (average age 32) than those who had never had pulmonary oedema (average age 37), and normal rhythm was more frequent. At rest, when free from attacks, the left atrial pressure averaged 23 mm. Hg, which was no higher than in the other cases; but in two or three instances, when an attack was threatened during cardiac catheterization, it was between 30 and 35 mm. Hg. The average cardiac output was relatively high (4.6 litres/minute). The pulmonary vascular resistance was remarkably low, averaging only 2.9 units, and never exceeding 5.2 units. The mitral orifice at operation was a little less tight than in the surgical series as a whole, not more tight.

It is concluded that pulmonary oedema tends to occur in relatively young women with average stenosis, when the pulmonary vascular resistance is unusually low. Sudden surges of cardiac output are possible because the pulmonary blood flow is not damped by the pulmonary resistance, and this allows extremely high pressures to develop in the pulmonary venous system. Thus, although these cases are rightly given top surgical priority, they are not necessarily *advanced* cases of mitral stenosis—rather to the contrary.

Haemoptysis

There are five kinds of haemoptysis complicating mitral valve disease: (1) the sudden unexpected profuse haemorrhage (pulmonary apoplexy); (2) blood-stained sputum associated with attacks of dyspnoea due to acute pulmonary venous congestion; (3) blood-streaked sputum associated with attacks of winter bronchitis, presumably due to a combination of bronchial inflammation and pulmonary venous congestion; (4) pink frothy sputum accompanying acute pulmonary oedema; and (5) frank haemoptysis due to pulmonary infarction.

Pulmonary Apoplexy

This was never seen in truly mild cases of mitral valve disease. Its incidence is given in Table V. By "serious cases only" in that Table are meant all the surgical cases,

TABLE V.—*Percentage Incidence of Haemoptysis*

	Whole Series				Serious Cases Only			Resistance Units		
	Surg.	Med.	M.I.	Total	M.S.	M.S., M.I.	M.I.	1–5·9	6–9·9	10–30
Pulmonary apoplexy..	24	13	13	18·3	22	33	15	25	20	12·5
Congestive haemoptysis: All cases ..	24	9	9	16·5	30	19	8·3	20	30	21
Recent cases								16	10	4
Pulmonary apoplexy, congestive haemoptysis, or both ..	44	25	20	34						
Pulmonary infarction	6	11	2	8·5						

but only those of comparable severity in the two medical groups, so that the relative importance of stenosis and incompetence might be probed. This column does in fact reveal that persons with combined lesions are particularly prone to pulmonary apoplexy.

It has often been stated, though with little factual support, that haemoptysis (meaning pulmonary apoplexy) occurs especially in cases of mitral stenosis complicated by pulmonary hypertension (e.g., Logan and Turner, 1953). presumably with the idea that it is akin to cerebral haemorrhage in essential hypertension. This statement is incorrect. Pulmonary apoplexy is rare when the pulmonary arterial resistance is really high, for the haemorrhage is venous and the high resistance tends to protect the pulmonary venous system from developing too high a pressure. This is shown in the third major column of the Table. Moreover, when haemorrhage was recorded in a case with extremely high resistance it had always occurred several years previously, at a time when the resistance may well have been lower. There was no single instance of pulmonary apoplexy occurring within a period of three years previous to the actual measurement of the high resistance. In the cases that have come to be regarded as being only partly protected (pulmonary resistance 6 to 9 units) pulmonary apoplexy had ceased in two-thirds.

Again, pulmonary apoplexy was a truly early symptom of mitral valve disease in 68% of the cases in which it occurred: it pre-dated the onset of grade 1 effort intolerance in 12.7%, initiated symptoms in 42.5%, and was an early symptom occurring within a year or so of the onset of effort breathlessness in 12.8%. It was a relatively late symptom in only one-third of the cases, occurring about half-way through the period of symptoms in 17% and being really late in 15%. The same truth was established in another way: the average duration of symptoms in all the cases with pulmonary apoplexy was 6.8 years; the average time of the onset of haemoptysis was one year after the onset of effort dyspnoea; and the average time at which haemorrhages ceased was three years before the patient was seen.

Pulmonary apoplexy was recurrent in 58% of the cases in which it occurred and was single in 42%; it was precipitated by pregnancy in 27%, and was sometimes provoked by physical effort.

This analysis suggests that sudden profuse haemoptysis in mitral stenosis is due to a venous haemorrhage occurring at a time when the pulmonary venous pressure has risen rather suddenly, and that such haemorrhages tend to cease when abrupt rises of pulmonary venous pressure are prevented by a high pulmonary vascular resistance, and also perhaps when the pulmonary veins and their anastomotic communications with the bronchial venous system have had time to hypertrophy in response to the raised pressure within them. It follows that pulmonary apoplexy is not a serious symptom, and this is borne out by the fact that it has never proved fatal in my experience. Indeed, this sort of haemorrhage may be regarded as a safety valve and is inevitably self-limiting, ceasing when the pulmonary venous pressure has fallen sufficiently. Whether the haemorrhage arises from rupture of a pulmonary vein or from rupture of a bronchial vein or broncho-pulmonary venous communication is beyond the scope of this paper (see Gilroy *et al.*, 1952).

Congestive Haemoptysis

This refers to blood-stained or blood-streaked sputum associated with attacks of severe dyspnoea. The haemoptysis is far less important than the dyspnoea. Its incidence is given in Table V. The second main column shows that, unlike pulmonary apoplexy, congestive haemoptysis favours mitral stenosis rather than combined lesions or pure mitral incompetence. In the third main column the lower set of figures refers only to cases with recent haemoptysis, and may correct a false impression that might be gained from the upper set, which refers also to blood-spitting many years ago.

It is worth noting that 44% of the surgical cases had either pulmonary apoplexy or congestive haemoptysis: one of the outstanding results of mitral valvotomy has been the abolition of these haemoptyses, which have occurred subsequently in only two cases. In one of these it was found impossible to perform a valvotomy, and in the other, which

was the first case operated on at Brompton Hospital, mitral stenosis has just recurred, the haemoptysis is very recent, and the patient has been advised to have a second operation.

Haemoptysis Associated with Winter Bronchitis

These cases were not separately analysed, because it was rarely possible to distinguish them from the congestive group. A few of them appear to have been included in Table V among the 25% with pulmonary apoplexy, congestive haemoptysis, or both, in the medical group.

Haemorrhage in Pulmonary Oedema

Whether acute pulmonary oedema is associated with *pink* frothy sputum or not is a matter of small moment, and such cases have not been specially studied.

Pulmonary Infarction

This was a less common cause of haemoptysis, as shown in Table V. It is invariably a late development, all such cases but two being totally incapacitated. Phlebothrombosis in the legs was nearly always responsible for the infarct; in only two was local thrombosis in a peripheral pulmonary artery or vein thought possible. In 58% of the cases with infarcts the pulmonary resistance was unduly high, usually extreme. Indeed, amongst the 100 medical cases there were eight deaths: seven of these were due to pulmonary embolism, and in six of them the pulmonary vascular resistance was over 10 units. Since this danger has been recognized, all high-resistance cases have been maintained on anticoagulants while awaiting valvotomy, and have been given high priority. The phlebothrombosis is attributed to the low cardiac output.

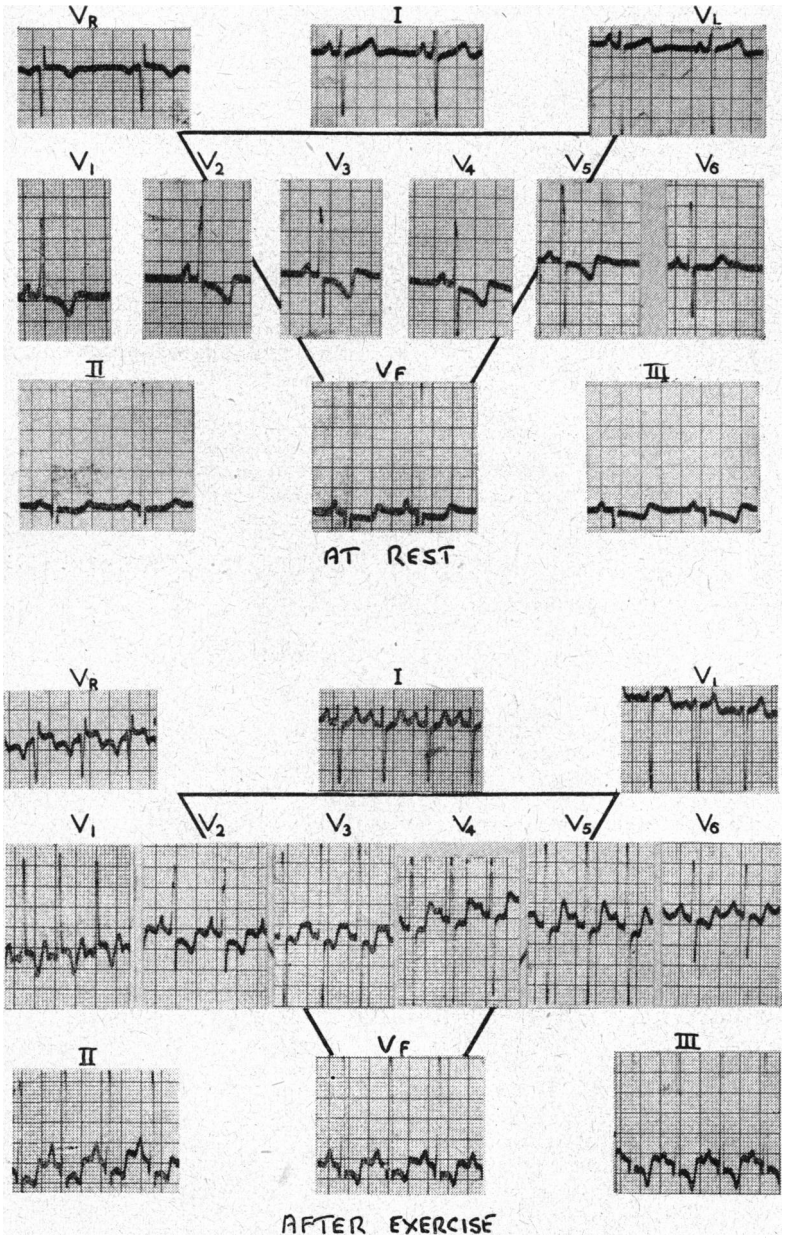

FIG. 1.—The electrocardiogram at rest and after exercise in a patient with angina pectoris complicating mitral stenosis with an extreme pulmonary vascular resistance. Note the changes in leads V_5 and V_6.

Angina Pectoris

Angina pectoris, indistinguishable in site, radiation, quality, duration of attacks, and relationship to effort from that encountered in occlusive coronary atherosclerosis, occurred in 12% of the surgical cases, 5% of the medical, and in 3% of those with almost pure mitral incompetence—that is, in 8.4% of the whole series; all of the medical cases also had serious incompetence. The average age of these patients was 36 years, or about the same as those without angina. The sex ratio was 5.5:1 in favour of women. One-third of the cases had auricular fibrillation. No significant coronary atherosclerosis was found in the four that came to necropsy. Angina disappeared in all those who had a technically successful valvotomy.

The pulmonary vascular resistance was extremely high, averaging 19.5 units, in just over a quarter of the cases, an incidence twice that in the surgical series as a whole. It is clear from Table VI, however, that angina was by no means confined to that group; a high resistance seemed to contribute to the development of angina, but was certainly not solely responsible for it.

There was some correlation between angina pectoris and the size of the mitral orifice. Thus about 40% of the cases with angina had extreme stenosis, an incidence twice as high as in the surgical series as a whole. Combined stenosis and incompetence was also twice as frequent as expected. Angina was rare in cases with virtually pure incompetence, and was not encountered at all in mild cases of any kind.

The resting electrocardiogram did not show ischaemic depression of the ST segment in any of the cases, but an ischaemic graph was sometimes obtained after effort, and the depression was then seen in left ventricular surface leads or their equivalents, even in cases with an extremely high pulmonary vascular resistance (Fig. 1).

It is believed that angina pectoris in mitral stenosis is due to functional insufficiency of the coronary blood flow resulting from strict limitation of the cardiac output, and that it is the left ventricle which suffers most. A high pulmonary resistance may encourage angina more by limiting the cardiac output than by increasing the work of the right ventricle.

TABLE VI.—*Angina Pectoris*

	Resistance Units					Size of Mitral Orifice (mm.)				
	Average	1–3·9 %	4–5·9 %	6–9·9 %	10–30 %	M.I. %	13×7 %	10×5 %	8×4 %	5×3 %
Angina pectoris ..	8	45	14	14	27	20	10	15	15	40
Whole surgical series ..	6	38	26	23	13	10	5	46	18	21
All groups (estimate)	4·2	60	20	12	8					

Systemic Embolism

A history of systemic embolism was obtained in 14% of the surgical cases, 11.5% of the medical, 9.7% of those with mitral incompetence, and in 13% of the whole series. The embolism was cerebral in 75%, peripheral in 33%, and visceral in 6%; 22% of the afflicted patients had both cerebral and peripheral emboli.

Auricular fibrillation was present in two-thirds of these cases, which is appreciably higher than in the rest of the series (Table VII). Just how often paroxysmal fibrillation was responsible for embolism in those who were regarded as having normal rhythm is unknown.

TABLE VII.—*Systemic Embolism. The Incidence of Auricular Fibrillation, Serious Mitral Incompetence, Left Atrial Dilatation, Left Atrial Thrombosis Found at Operation, and Operative Embolism in Cases Giving a History of Peripheral Embolism and in Cases Giving no such History*

	Aur. Fib. %	M.S. M.I. %	Left Atrial Dilatation. Grade		L.A. Clot at Operation %	Embolism at Operation %
			Surg. Group	All Cases		
History of embolism ..	66	44	1·74	1·86	21	10·5
No previous embolism	42	28	1·48	1·79	22·6	8

A significant degree of mitral incompetence was present more often than in cases without a history of embolism (Table VII). The influence of regurgitation on the size of the left atrium or left atrial appendage might seem to explain this; but less correlation than expected was found between the incidence of embolism and the estimated size of the left atrium (Table VII), although the figures for the surgical group may be significant.

No correlation was found between the incidence of embolism and the pulmonary vascular resistance, the cardiac output, or the size of the mitral orifice. In 12.5% of the embolic cases embolism was the first symptom, occurring at a time when there was no effort intolerance, and when the rest of the data indicated that the mitral lesion was not advanced.

At operation a clot was found in the left atrium or left atrial appendage in 21% of those who gave a history of embolism and in 23% of those who did not. Embolism was an immediate complication of mitral valvotomy in 10% of the surgical cases. A clot was detected in the left atrium in two-thirds of these. The incidence of embolism at operation was not significantly higher in those who gave a history of previous embolism than in those who did not (Table VII). Of those cases in which a clot was found in the left atrium at the time of operation one-fifth developed an embolism. This was either noticed then and there or was discovered when the patient regained consciousness in the ward. Embolism occurred only once during the post-operative course, on the third day, and has not been recorded so far at the follow-up clinic.

Several interesting conclusions can be drawn from this analysis: (1) The risk of embolism occurring at operation is almost as high as the risk of spontaneous embolism (10% compared with 13%). It is therefore unwise to advise mitral valvotomy in order to prevent future embolism in someone who has so far been free from this complication. (2) In advising mitral valvotomy to prevent a recurrence of spontaneous embolism there need be no special fear that the operation itself may cause a recurrence, the risk being no greater in those who have had previous emboli than in those who have not. (3) The infrequency of left atrial clots in patients who have given a history of embolism suggests that only fresh clots are thrown out into the circulation, and that once a clot is organized there is little danger of embolism from that source. Operative intervention alone is likely to dislodge a fragment of old thrombus.

Winter Bronchitis

Attacks of acute bronchitis, commonly in the winter, occurred in 28% of the surgical group. Its incidence was not dissimilar in medical cases of equal severity. No special correlation could be found between bronchitis and any of the other factors analysed, except that it was not a feature of mild cases. It was at first thought probable that the high incidence of bronchitis in advanced mitral valve disease depended on an excessive bronchial reaction to trivial upper respiratory tract infections because of the congested state of the bronchial mucosa. On this hypothesis the incidence of bronchitis was expected to be higher in patients with symptoms of pulmonary venous congestion than in those without. No special correlation, however, could be established. For example, the average left atrial pressure for the cases giving a history of bronchitis was 23 mm. Hg, which is practically the same as in the whole surgical group (Table VIII). Again, the incidence of bronchitis was not influenced by the pulmonary vascular resistance, although this is known to prevent excessive pulmonary venous congestion. Finally, auricular fibrillation was present rather more often in cases with bronchitis than in the controls, and it has already been shown that auricular fibrillation does not encourage pulmonary venous congestion. These negative findings do not entirely invalidate the hypothesis defined above, but seem to demand some other determinant.

TABLE VIII.—*Bronchitis*

	L.A.P. (Average) mm. Hg	Resistance Units			Aur. Fib. %	L.A. Size. Average Grade	Art. Oxygen Sat.			C.O. l./min.
		1–5·9 %	6–9·9 %	10–30 %			96–92 %	91–88 %	87–83 %	
Bronchitis (surgical group only)	23	61	23	16	50	1·6	46	38	16	3·6
Whole surgical group	22·5	64	23	13	41	1·6	52	34	14	3·8

It is well known that great dilatation of the left atrium may compress either main bronchus and cause collapse of the lung. It was thought possible that partial bronchial compression might encourage bronchitis. The size of the left atrium in the bronchitic group was therefore compared with that in the rest of the series, but no difference was found (Table VIII); nor was bronchitis more common in cases of mitral incompetence with grade 3 dilatation of the left atrium than in cases of pure mitral stenosis with relatively small left atria.

No serious effects of recurrent bronchitis on the pulmonary circulation were detected in the majority of patients. Figures for the arterial oxygen saturation, cardiac output, and pulmonary resistance are given in Table VIII, where they are compared with figures compiled from the surgical group as a whole; there was no significant difference. It is clear that cor pulmonale does not ordinarily develop from recurrent bronchitis and emphysema associated with mitral stenosis.

One of the remarkable results of technically successful mitral valvotomy is the disappearance of winter bronchitis. This certainly supports the view that the bronchitis depends on a state of chronic pulmonary venous congestion in the majority of cases.

Auricular Fibrillation

Persistent auricular fibrillation (Table IX) occurred in 41% of the surgical cases, 40% of the medical, 30% of those with pure mitral incompetence, and 39% of the whole series; the respective figures for paroxysmal fibrillation were 5%, 7%, 6%, and 6%. Although auricular fibrillation was rather

TABLE IX.—*Auricular Fibrillation*

	Age (Yrs.)	+ve Biopsy (%)	Atrial Dilatation		Resistance Units				C.O. l./min.	Stenosis	
			L.A. Grade	R.A. Grade	Average	1–5·9 (%)	6–9·9 (%)	10–30 (%)		Mild or Average (%)	Tight or Extreme (%)
Auricular fibrillation ..	41	13	1·78	1·78	7·0	52·5	35·5	12	3·6	66	34
Normal rhythm	33·6	24	1·45	1·04	5·9	72	18·5	9·5	4·1	50	50

less common in those with pure mitral incompetence, it was most common when a significant degree of mitral incompetence was associated with mitral stenosis, being present in 69% of such cases.

Patients with auricular fibrillation tended to be older than those with normal rhythm, the average age for the two groups being 41 and 33.6 respectively (surgical cases only).

The relationship of auricular fibrillation to systemic emboli has been described in a previous section. Something more should be said here, however, about *the relationship of auricular fibrillation to paroxysmal cardiac dyspnoea.* It was stated, when discussing that subject, that normal rhythm rather than auricular fibrillation favoured attacks of paroxysmal dyspnoea. There is, however, a rider to that: seven out of ten surgical cases with paroxysmal auricular fibrillation had paroxysmal cardiac dyspnoea, and in three of these cases paroxysmal auricular fibrillation was known to have precipitated the attack of dyspnoea. There is reason to believe that the sudden onset of auricular fibrillation may precipitate severe dyspnoea or right ventricular failure, according to the response of the cardiovascular system to the altered haemodynamics and to the type of case in which it occurs. When the pulmonary vascular resistance is relatively normal a sudden increase of heart rate may interfere with left ventricular diastolic filling and so increase the degree of pulmonary venous congestion (Gorlin *et al.*, 1951).

On the other hand, when the pulmonary vascular resistance is high the right ventricle is more likely to fail, particularly since it is denied the auricular support which it needs under these circumstances. Again, if the rate is too fast, even with a normal pulmonary vascular resistance, the right ventricular output may fall and so relieve pulmonary venous congestion, or a grossly irregular rhythm may have a similar effect. In short, the symptomatic pattern that results from the onset of auricular fibrillation depends on several factors which include the pulmonary vascular resistance, the rate of the heart, and the degree of irregularity of the rhythm. In cases of relatively mild mitral stenosis with attacks of dyspnoea due to paroxysmal auricular fibrillation, symptoms may be abolished by permanent digitalis therapy. This does not prevent the rhythm change, but by controlling the ventricular rate when attacks do occur it prevents the dyspnoea.

It is often stated that if auricular fibrillation occurs under the age of 20 rheumatic activity may be safely assumed. Whether this is so or not, it must not be concluded that rheumatic activity is in any way responsible for auricular fibrillation in established mitral stenosis. In the present series only 13% of cases with auricular fibrillation had positive biopsies (Aschoff nodes in the left atrial appendage), compared with 24% of those with normal rhythm. The difference is no doubt due to the age factor. Even so, the two youngest patients with auricular fibrillation (aged 18 and 23) both had negative biopsies.

It would naturally be expected that auricular fibrillation in mitral stenosis might be related to the size of the left atrium. In fact, the average size of the left atrium in the group with fibrillation was grade 1.78 compared with grade 1.45 in those with normal rhythm. This is a significant difference, but does not indicate whether the enlargement caused the fibrillation or vice versa. It should be noted, however, that the grade of right atrial enlargement was also 1.78 in the group with fibrillation and only 1.04 in the group with normal rhythm, an even greater difference. Since the right atrium is not ordinarily enlarged in mitral stenosis unless the pulmonary vascular resistance is high, it follows that atrial enlargement is more likely to be the result than the cause of auricular fibrillation, unless the latter can be shown to be closely related to pulmonary hypertension.

The pulmonary vascular resistance averaged 7.0 units in those with auricular fibrillation and 5.9 units in those with normal rhythm. Further details are given in Table IX. It may be seen that a high resistance (6 to 9 units) was nearly twice as frequent with auricular fibrillation as with normal rhythm, but the relationship did not embrace extreme resistances. The paradox may be explained by the rarity of mitral incompetence in cases with an extreme resistance. Although these figures do not deny that a dilated right atrium from pulmonary hypertension may precipitate auricular fibrillation, they are not convincing. There is no doubt that the left atrium is apt to be greatly distended in cases of combined mitral stenosis and incompetence, and auricular fibrillation is particularly common in this group. This certainly suggests that atrial dilatation can cause fibrillation. The same conclusion may be drawn from the fact that in pure mitral incompetence grade 3 or 4 left atrial dilatation occurred in 75% of those with auricular fibrillation, and in only 16.6% of those with normal rhythm.

The cardiac output tended to be lower in patients with auricular fibrillation than in those with normal rhythm, averaging 3.6 litres a minute in the former and 4.1 litres a minute in the latter (analysed from the surgical group only).

Auricular fibrillation could not be correlated directly with *the size of the mitral orifice.* Cases complicated by serious mitral incompetence were excluded from this analysis, for these are particularly prone to fibrillate and would therefore load the figures in favour of auricular fibrillation being associated with a relatively large orifice. Despite this precaution, however, cases with auricular fibrillation had unusually tight or extreme stenosis less often than cases with normal rhythm (Table IX).

The chief conclusions from these observations are that auricular fibrillation in mitral valve disease tends to be provoked by age and distension of the left atrium especially as a result of mitral incompetence, but that it also causes dilatation of both atria; it is not related to rheumatic activity or to the degree of stenosis itself. Uncontrolled auricular fibrillation may cause intense dyspnoea or congestive heart failure in cases which would not otherwise develop serious symptoms at the time.

Essential Hypertension

Only 3% of the present series had a blood pressure of 160/100 or above, and only 1% had a diastolic pressure as high as 120 mm. Hg. This figure is in harmony with Bechgaard's (1946) converse finding that only 1% of cases of essential hypertension have mitral stenosis.

PHYSICAL SIGNS

Mitral Facies

Peripheral cyanosis in the face and hands was common, and has been attributed to peripheral vasoconstriction secondary to a low cardiac output. In order to test this hypothesis, patients with the characteristic mitral facies of at least moderate degree were compared with cases in which there was no cyanosis of either face or hands. The

TABLE X.—*Mitral Facies*

	Pul. Vasc. Resistance Units	C.O. l./min.	Grade 4 Eff. Intol. (C.F.) (%)	Aur. Fib. (%)	Reduced Art. O_2 Sat. 83–89% (%)
Mitral facies ..	11·7	3·3	73	68	52·4
No peripheral vasoconstriction ..	4·1	4·25	9·3	25	20

results are shown in Table X, and strongly confirm the hypothesis. An extreme pulmonary vascular resistance tends to keep the output low and fixed. Grade 4 effort intolerance or complete incapacity usually means congestive heart failure proper (low output type), and auricular fibrillation also tends to keep the output low. The only other factor which seemed to contribute to the mitral facies was an arterial oxygen saturation of less than 90%.

In three cases with an extremely high pulmonary vascular resistance a bright palmar flush and hot hands were observed instead of peripheral cyanosis. This unexpected finding was attributed to hepatic dysfunction.

Peripheral Pulse

The quality of the brachial pulse was noted carefully and recorded as a routine in all cases. Quality should not be confused with amplitude (quantity). The latter was small in the great majority of all groups, being considered normal in only 11.5% of the whole series. A water-hammer quality (abrupt and collapsing) was detected in 26% of the whole series; but, whereas it was present in only 8% of the surgical cases, it was found in 29% of the medical and 84% of those with pure mitral incompetence. Again, a water-hammer pulse was recognized in only 5% of the surgical cases which were proved at operation to have no significant incompetence, whereas it was recorded in 71% of all cases with a serious degree of incompetence. It is concluded that a small water-hammer pulse is an important sign of mitral incompetence. Cases complicated by aortic incompetence were excluded from this analysis.

A careful study of routine arterial pressure tracings in many cases of mitral valve disease has confirmed this clinical observation. In cases of more or less pure stenosis the arterial tracing was blunt: the upstroke was rarely abrupt and took at least 0.08 second to reach the beginning of the summit; the summit itself was rounded and occupied about 0.07 second. The down-stroke proper was not unduly steep and rarely began before 0.15 second after the onset (Fig. 2). In mitral incompetence, on the other hand, the upstroke was often abrupt and the beginning of the summit was usually reached within 0.07 second; the peak itself was sharper, and occupied only about 0.05 second; the down-stroke proper was earlier, usually within 0.12 second after the onset and was more precipitous (Fig. 3).

The characteristic pulse of mitral incompetence may be attributed to a combination of overfilling of the left ventricle, a systolic leak into the left atrium, and a low cardiac output. Left ventricular systole is hyperdynamic and imparts an abrupt wave front to the pulse; the low resistance at the mitral orifice causes systolic collapse; the poor cardiac output results in peripheral vasoconstriction, which diminishes the amplitude of the pulse.

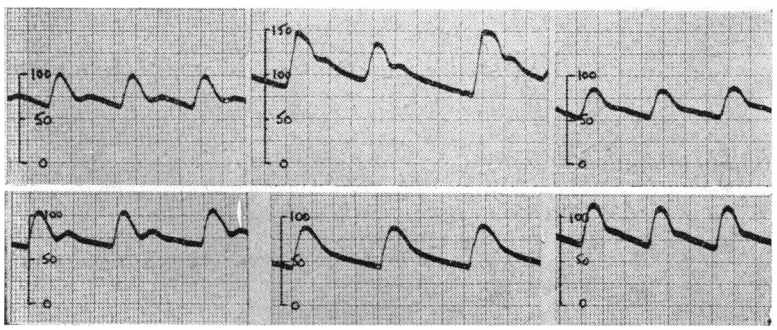

FIG. 2.—Intra-arterial pressure tracings from six unselected cases of mitral stenosis.

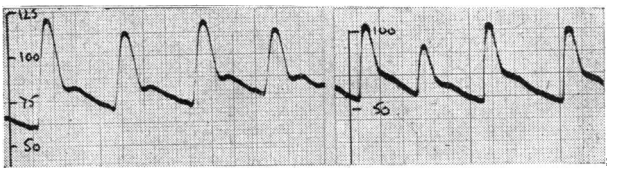

FIG. 3.—Intra-arterial pressure tracings from two cases of serious mitral incompetence. Neither had aortic incompetence.

Jugular Venous Pressure and Pulse

The jugular venous pressure was raised in 25% of the whole series. This means that the top of the oscillating venous column in the neck was at least 5 cm. of saline above the sternal angle when the patient was propped up at 30 degrees.

A giant a *wave* (Wood, 1950, 1952; Abrahams and Wood, 1951) was seen in 12 cases (4%) and always denoted an extremely high pulmonary vascular resistance (9 cases) or tricuspid stenosis (3 cases).

A combined va *wave* followed by an *x* descent, necessarily associated with sinus tachycardia, was recorded as such in five cases. None of these had a high resistance, and it is doubted if any of them were in true heart failure.

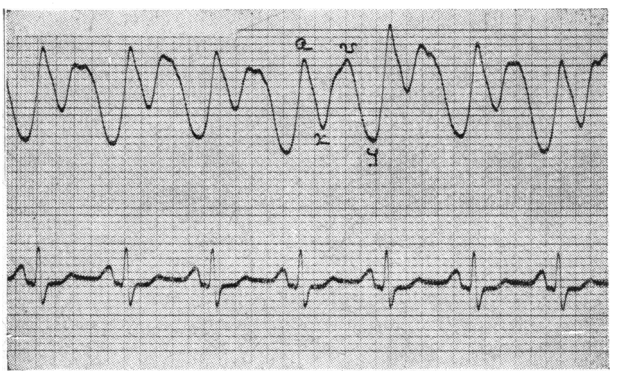

FIG. 4.—Jugular phlebogram illustrating the steep *y* descent in a patient with heart failure secondary to mitral stenosis with an extreme pulmonary vascular resistance.

This sort of venous pulse was seen in cases of severe mitral stenosis with intense pulmonary venous congestion and passive pulmonary hypertension.

a *and* v *waves of equal amplitude* were found in nine cases (3%). When the venous pressure level was around 5 cm. above the sternal angle these cases did not differ from those in the previous paragraph. When the pressure was higher, however, around 10 cm. of saline, the *v* wave was followed by a *steep y descent* which was seen only in congestive heart failure proper (Fig. 4). An extremely high pulmonary vascular resistance was responsible for the failure in the few cases of relatively pure mitral stenosis that showed this type of venous pulse; four others, however, had dominant or pure mitral incompetence, and in these the pulmonary vascular resistance was not unduly high. It is believed that some other factor operates in mitral incompetence which causes congestive heart failure with a low cardiac output in the absence of extreme pulmonary hypertension.

Mackenzie's *ventricular form of the venous pulse*, which is characterized by a single systolic wave, was recorded in

right atrial pressure tracings in all cases of auricular fibrillation and was associated with a raised venous pressure, as previously defined, in 10% of the whole series: the pulmonary vascular resistance then averaged 9 units in those with mitral stenosis; the lowest resistance was 6.4 units.

In the same group there were eight cases with a serious degree of mitral incompetence and only one of these had a high pulmonary resistance. There were also two cases with tricuspid stenosis and one with coronary embolism; the resistance was relatively normal in each of these.

Tricuspid incompetence was diagnosed when the amplitude of the *v* wave was very much greater than that ordinarily seen in normal rhythm or auricular fibrillation,

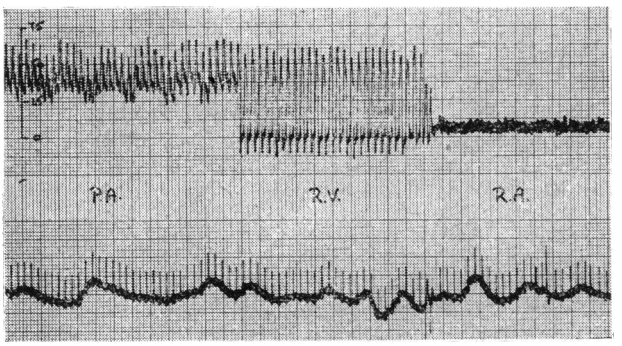

FIG. 5.—Case of tricuspid stenosis showing a diastolic pressure gradient across the tricuspid valve.

and as a rule the top of the oscillating venous column was exceptionally high. A venous pulse of this kind was seen in 6% of the whole series. Tricuspid stenosis was excluded by means of cardiac catheterization (see below). The average pulmonary vascular resistance for this group was 14.5 units, being extreme in all but three of the 18 cases and between 6 and 9 units in the exceptions. Functional tricuspid incompetence associated with mitral valve disease clearly results from right ventricular stress of a high order.

When *tricuspid stenosis* was associated with normal rhythm, a giant *a* wave was seen in the venous pulse as described above; when auricular fibrillation was present, however, there was no clinical means of recognizing tricuspid stenosis from the character of the venous pulse, but it was suspected when there were no clinical, electrocardiographic, or radiological signs of a high pulmonary vascular resistance despite a really high venous pressure; in seven such cases the presence of tricuspid stenosis was subsequently established by means of cardiac catheterization, a diastolic pressure gradient across the tricuspid valve being demonstrated when the catheter was withdrawn from the right ventricle to the right atrium (Figs. 5 and 6).

The most important conclusions to be drawn from these observations are that (1) a giant *a* wave means extreme pulmonary hypertension if the clinical signs are in harmony, or tricuspid stenosis if they are not; (2) mitral stenosis does not ordinarily cause congestive failure in the absence of a high pulmonary vascular resistance—that is, passive pulmonary hypertension does not cause congestive failure; (3) tricuspid incompetence implies a pulmonary vascular resistance in the extreme grade; (4) a high venous pressure in the absence of signs of pulmonary hypertension may well mean tricuspid stenosis; and (5) some other mechanism seems to be involved in cases of congestive heart failure associated with mitral incompetence. As a corollary to all this is the very important fact that in mitral stenosis neither congestive heart failure nor tricuspid incompetence was ever seen as the result of myocarditis itself. In other words, the so-called myocardial factor was conspicuous by its absence. In isolated or other forms of myocarditis proper, including gross rheumatic myocarditis in children, congestive heart failure is associated with a high venous pressure, a low cardiac output, and a relatively normal pulmonary vascular resistance. The only type of case in the present series in which a dominant myocardial factor has not been excluded as a cause of right ventricular failure is that with a serious degree of mitral incompetence. No further comment can be made about this possibility as yet.

Cardiac Impulse

A left ventricular thrust at the apex beat was recorded in 12% of the surgical cases, 38% of the medical, and 86% of those with pure mitral incompetence. Of the 18 cases in the surgical group, eight had a significant degree of mitral incompetence, and two had aortic stenosis. The sign was recorded erroneously in three cases in which a huge right ventricle occupied the apex of the heart; this error was suspected in view of the physical signs, but was not finally laid by the heels until the electrocardiogram was inspected. Thus there were only five cases (3.3%) in which a thrusting left ventricular impulse was unexplained. No further light was thrown on these cases as the result of valvotomy, but an enlarged left ventricle was confirmed by direct inspection of the heart. It is suspected that previous mitral incompetence may have been responsible.

Of the medical cases with this type of cardiac impulse three-fifths had a serious degree of mitral incompetence, and one-quarter had significant aortic valve disease. One patient had cardiac infarction from coronary embolism, and one had essential hypertension. There were only two cases (2%) in which the thrusting left ventricle was unexplained.

Little need be said about the 50 cases with relatively pure mitral incompetence, since 86% showed this sign. When all these cases of significant mitral incompetence in the whole series were reviewed it was found that 70% had a hyperdynamic left ventricular thrust. The importance of this sign cannot be overestimated.

There was close correlation between a left ventricular cardiac impulse and left ventricular preponderance in the electrocardiogram. Thus the electrocardiogram showed left ventricular preponderance in 48% of these cases and normal left ventricular dominance in 40%; in other words, it was left-sided in 88%. A right-sided electrocardiogram was found in 11% (only once in a case of pure mitral incompetence), and the electrocardiogram showed cardiac infarction in the case with coronary embolism.

A lift over the right ventricle, usually maximum in the third and fourth intercostal space in the left parasternal line, was appreciated in 79% of the surgical cases, in 45% of the medical, and in 36% of those with pure mitral in-

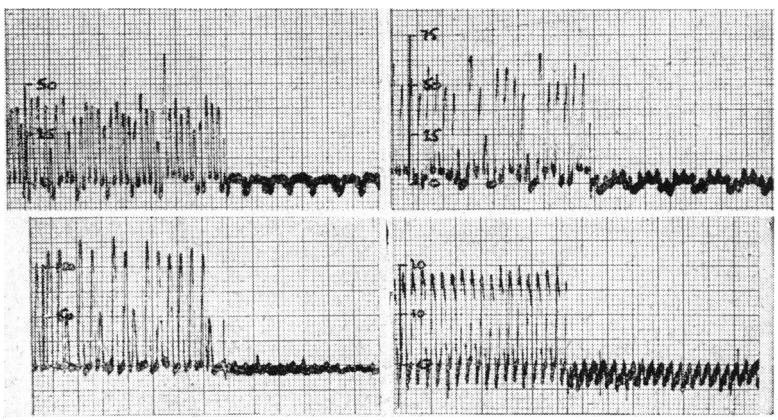

FIG. 6.—Four controls showing identical diastolic pressures in the right atrium and right ventricle.

competence, or in 61% of all cases. Since there has been a little uncertainty about the value and meaning of this sign, it was subjected to a searching cross analysis. Since the left atrium tends to be larger in cases with significant mitral incompetence than in those with pure stenosis, the figures themselves indicate that it is not the left atrium behind which is responsible for the parasternal lift in front. It was decided, therefore, to restrict the analysis to the surgical group, in which the evidence was more complete. The degree of right ventricular lift was recorded as a routine, and for the purpose of this particular analysis four groups were segregated, according to whether the lift was absent or grade 1, 2, or 3 in degree. There were 25 cases (chosen consecutively) in each group. In this way the degree of right ventricular lift was correlated with the degree of right ventricular preponderance in the electrocardiogram; the degree of dilatation of the left atrium, pulmonary artery, and right side of the heart as seen radiologically; the pulmonary vascular resistance; tricuspid incompetence; and congestive heart failure.

TABLE XI.—*Right Ventricular Lift*

R.V. Lift	R.V. Dominance (E.C.G.) Grade	Left Atrium Grade	Pulmonary Artery Grade	R. Atrium R. Ventricle Grade	Units of Resistance	T.I. %	C.F. %
0 ..	0·35	1·5	1·0	0·6	2·6	0	0
Grade 1	0·8	1·4	1·5	1·1	4·4	12	12
„ 2	1·8	1·6	2·1	1·6	6·8	12	28
„ 3 (or 4)	2·5	1·5	2·9	2·2	12·0	32	48

T.I. = Tricuspid incompetence. C.F. = Congestive heart failure.

The results are set out in Table XI. Each figure represents the average grade of the factor analysed as defined in the introduction. For example, the figure 2.9, at the bottom of the third column, represents the average grade of pulmonary artery dilatation in the 25 cases having a grade 3 (considerable) right ventricular lift. The table shows clearly that the right ventricular lift bears no relationship to the size of the left atrium, but is correlated closely with the degree of right ventricular preponderance in the electrocardiogram, with the degree of dilatation of the pulmonary artery and right side of the heart, and especially with the pulmonary vascular resistance; it was also related to the frequency of tricuspid incompetence and congestive heart failure. There can be no serious doubt that the fundamental factor which determines the degree of right ventricular thrust is the pulmonary vascular resistance.

AUSCULTATION

Presystolic Murmur

A presystolic murmur was heard in all but two of the surgical cases with normal rhythm, and there was a serious degree of mitral incompetence in the two exceptions. It was only just heard in one case in which there was an extremely high pulmonary vascular resistance. It was absent in one-third of the medical cases with normal rhythm; all but two of these had a serious degree of mitral incompetence, one had an extremely high pulmonary vascular resistance, and one was the mildest case of mitral valve disease in the whole series. It was absent in all cases classed as pure mitral incompetence. It is obvious from these figures that a presystolic murmur is excellent evidence against significant mitral incompetence. This conclusion was checked by analysing all cases of combined stenosis and incompetence in the surgical and medical groups. There were only 12 with normal rhythm, and of these only three had a presystolic murmur.

A presystolic murmur was heard in all of the six cases of mitral stenosis in which cardiac catheterization proved that the left atrial pressure (P.C.V.P.) did not exceed 10 mm. Hg with reference to the sternal angle; it was also present in all but one of the eight most trivial cases of mitral stenosis in the medical group, the exception having already been referred to above. It follows that a presystolic murmur is a sign of mitral *stenosis*, but not of its degree.

Considerable interest is attached to the effect of mitral valvotomy on the presystolic murmur. When a presystolic murmur was present before operation it was still heard afterwards in 42% of the cases, but could not be heard in 58%. One-third of the cases in which the murmur was still present were classed as excellent results, whereas two-thirds of those in which the murmur disappeared were so classed. When those cases which lost their presystolic murmur as a result of a serious degree of mitral incompetence caused by the operation were excluded from this latter group as many as 90% were classed as excellent. The significance of this will be especially appreciated in the light of the previous finding that a presystolic murmur may occur with only a trivial degree of stenosis.

First Heart Sound

The first heart sound was loud (grade 3 or 4) in 90% of cases of uncomplicated pure mitral stenosis with normal rhythm in the surgical group (Table XII). Of the exceptions, only one case had but slight accentuation and this was the mildest in the series, the left atrial pressure measuring only 10 mm. Hg and the mitral orifice measuring 1.5 cm. in length at operation. In the medical group there were 26 cases classed as mild mitral stenosis with normal rhythm; the first heart sound was markedly accentuated in 15 of them, moderately so in 6, and only slightly so in 5. In this group there were nine instances in which a loud first sound was associated with a left atrial pressure proved to be less than 10 mm. Hg.

TABLE XII

	First Heart Sound		
	Normal	Accentuated	
		Grade 1–2	Grade 3–4
M.S. mild, L.A.P. < 10 mm. ..	0	42	58
„ operated cases	0	10	90
„ *M.I.*	14	86	0
Pure M.I.	73	27	0

In the surgical group *auricular fibrillation* was present in only 14.5% of those with grade 3 accentuation of the first heart sound, but in 50% of those with grade 2 accentuation, indicating that auricular fibrillation tends to damp the intensity of the sound. In the majority of cases of auricular fibrillation the first heart sound was loud following a short diastolic period and soft after a pause, as described by Ravin and Bershof (1951). This is attributed to a tendency for the valve to close towards the end of diastole, when there is time for the ventricle to be properly filled. The absence of auricular systole favours such behaviour. In a limited number of cases, however, paradoxical accentuation of the first heart sound was noted—that is, it was softer after a short diastole and louder after a pause. No explanation for this phenomenon can yet be offered. In combined stenosis and incompetence there was usually little variation in the intensity of the first sound.

A high pulmonary vascular resistance also tended to damp the intensity of the first heart sound. Thus high or extremely high resistances were found in 25% of those with greatly accentuated first sounds, and in 41% of those with moderately accentuated first sounds. Nevertheless, extreme resistances never caused normal or soft first sounds.

Mitral incompetence was by far the most important factor modifying the first heart sound. Thus, of the surgical cases in which the degree of mitral incompetence was checked at operation, no case of significant incompetence had grade 3 accentuation of the first heart sound, 20% had grade 2 accentuation, and 66% grade 1. Again,

no case of significant mitral incompetence in the whole series had considerable accentuation of the first heart sound, 27% had grade 1 or 2 accentuation, and 73% had a normal or soft first sound. These figures were taken only from the cases without obvious calcification of the valve so that they would not be influenced by that factor. There were only three examples of marked calcification of the mitral valve without incompetence, and each of these had slight accentuation of the first heart sound. It follows that, although calcium alone may diminish the intensity of the sound, the soft first sound of mitral incompetence does not depend on its presence. As expected, there was a positive correlation between the intensity of the first heart sound and the presence and intensity of the opening snap.

It is believed that the first heart sound is loud in mitral stenosis because there is a sufficient pressure gradient across the mitral valve to billow the cusps deeply into the left ventricle right up to the moment when that chamber contracts. When there is no stenosis the left ventricle fills rapidly, so that towards the end of diastole, even when quite short, the mitral cusps tend to float into apposition, and therefore shut more quietly when the ventricle contracts (Dock, 1933). Normal rhythm favours accentuation of the first sound by increasing the pressure gradient across the valve at the end of ventricular diastole; a high pulmonary vascular resistance may damp the sound a little by encouraging the right ventricle to form the apex beat of the heart; mitral incompetence results in quicker left ventricular filling, and the rapid equalization of left atrial and left ventricular diastolic pressures may float mobile cusps into apposition before the ventricle contracts; moreover, mitral incompetence is often associated with rigid cusps, particularly in the presence of heavy calcification, and in these cases there may be little movement.

The effect of valvotomy on the intensity of the first heart sound was studied (Table XIII). When the first

TABLE XIII.—*Post-operative First Heart Sound*

First Heart Sound	Incidence	Functional Result		
		Excellent	Good	Fair or Poor
Intensity diminished by 2 or 3 grades. Now grade 1 or normal	30%	81·5%	18·5%	—
Intensity slightly diminished. Now grade 1 or 2	25%	30%	61%	9%
Unchanged	22%	20%	50%	30%
Now soft or normal due to mitral incompetence	23%	—	33·3%	66·6%

sound was greatly diminished after the operation 81.5% did excellently, whereas when it was unchanged or only slightly diminished only 20 to 30% did as well. When the first heart sound became soft as the result of mitral incompetence caused or increased by the valvotomy the result was poor or only fair in as many as two-thirds, and it was excellent in none. When it is remembered that the first heart sound is usually loud in trivial degrees of mitral stenosis the return to normal or near normal in about one-third of all cases operated on is remarkable.

It is concluded that a loud first heart sound is excellent evidence of mitral stenosis, but gives little indication of its degree; its presence is a talisman against serious mitral incompetence.

Mitral Systolic Murmur

A loud mitral systolic murmur (grade 3 or 4) was heard in all the cases of pure mitral incompetence except two in which the murmur was only moderate in degree; a thrill accompanied the murmur in 43%. A similar loud murmur was also heard in all the cases of combined mitral stenosis and incompetence in the medical group except two in which it was also only moderate in degree; a thrill accompanied this murmur in 14%. No case of significant mitral incompetence without a systolic murmur of at least moderate degree was encountered in the whole series. In the surgical group there were naturally far fewer cases of significant mitral incompetence: here a loud mitral systolic murmur was heard in 11.4%, a moderate murmur in 9.3%, a faint murmur in 8.6%, and no mitral systolic murmur at all in 66.4%; in 4.3% of cases a tricuspid systolic murmur extending far out to the left was mistaken for a mitral murmur by some observers.

When the surgical cases were analysed in respect of the mitral systolic murmur there was close correlation between the incidence and grading of the murmur and the presence and degree of mitral incompetence recognized by the surgeon by direct palpation of the valve (Table XIV). For

TABLE XIV.—*Mitral Systolic Murmur (Surgical Cases Only)*

Mitral Systolic Murmur	Grade of Mitral Incompetence			
	0	1	2	3
Absent	98%	2%	—	—
Grade 1	42%	42%	16%	—
„ 2	15%	70%	15%	—
„ 3 or 4	12%	18%	12%	58%

example, when there was no mitral systolic murmur there was no incompetence at all in 98% of cases; on the other hand, when the murmur was loud mitral incompetence was found in 88%, considerable in 58%, and mild or moderate in 30%. It can no longer be seriously maintained that a mitral systolic murmur is of little value in determining the presence or absence of mitral incompetence.

The effect of valvotomy on the mitral systolic murmur was recorded in all the surgical cases and has been correlated with the functional results (Table XV). As would

TABLE XV.—*Post-operative Mitral Systolic Murmur*

Mitral Systolic Murmur	Incidence	Functional Result			
		Excellent	Good	Fair	Poor
Grade 3 or 4 before and after	9%	—	10%	30%	60%
Increased to Grade 3 or 4	22%	4%	29%	38%	29%
Increased slightly to Grade 1 or 2	21%	53%	39%	4%	4%
No change Grade 0 to 2	41%	46·5%	38%	11%	4·5%
Diminished slightly	3·5%	50%	37·5%	12·5%	—
„ greatly	3·5%				

be expected, the development of a loud mitral systolic murmur (grade 3 or 4) was associated with an important degree of mitral incompetence in the great majority of cases in which it occurred (84%). The functional result was relatively poor in this group. Those cases with a loud systolic murmur before the operation nearly always had a loud murmur afterwards and did not do well, 90% of them being classed as fair or poor and none as excellent. Apart from these two groups the functional result was much the same whether a grade 1 or grade 2 mitral systolic murmur developed, whether such a murmur present before the operation diminished or even disappeared (which was rare), whether a grade 1 or grade 2 systolic murmur remained unchanged, or whether there was no murmur before or afterwards. As many as 41% of the whole surgical group had no mitral systolic murmur before or after the operation, and 55% of those without a pre-operative murmur did not develop one afterwards; since the functional result was excellent or good in 85% of such cases it is clear that mitral valvotomy is capable of restoring excellent valve function. Relatively few (14%) of those without a mitral systolic murmur before the operation developed a grade 3 or 4 murmur afterwards, and all but two of them then had other evidence of serious mitral incompetence.

The Pulmonary Second Sound

By the pulmonary second sound is meant the second or pulmonary element of the second heart sound; it is rarely heard beyond the pulmonary area. When the second sound seems single, splitting can nearly always be recognized

during rather deep inspiration. It was necessary to appreciate the split before the pulmonary element could be properly analysed. Table XVI shows the relationship between the intensity of this pulmonary second sound and the pulmonary vascular resistance. The correlation is not as close as might be expected, but cannot be ignored: thus

TABLE XVI.—*Pulmonary Element of Second Sound*

Pulmonary 2nd Sound	Resistance		
	<6 Units	6–10 Units	>10 Units
Normal	91%	8%	1%
Accentuated Grade 1	76%	16%	8%
,, ,, 2	42%	31%	26%
,, ,, 3 or 4 ..	33%	33%	33%

when the pulmonary second sound was normal the resistance was relatively normal in 81%; on the other hand, when the pulmonary element was markedly accentuated (grade 3 or 4) the pulmonary vascular resistance was high in 66%. Further details may be studied in the table. Closer correlation might well have been obtained if the second sound had been auscultated while the pulmonary artery pressure was being recorded, but this was impracticable.

It is concluded that the pulmonary element of the second heart sound is an important but not infallible guide to the degree of pulmonary hypertension present in mitral stenosis.

Pulmonary incompetence was recognized in 10% of the surgical cases, but in only 1% of the medical and in none of the cases of pure mitral incompetence. It was associated with an extremely high pulmonary vascular resistance in 55%, and with a high resistance (6 to 9 units) in the other 45%; it was never encountered when the resistance was under six units. The pulmonary artery was conspicuously dilated in nearly all these cases, the average degree of enlargement working out at just over grade 3.

The Mitral Opening Snap

This occurred in none of the group with pure mitral incompetence, but this only means that if a snap was present pure mitral incompetence was never diagnosed. There was, however, ample collateral evidence supporting this attitude.

Of the surgical cases 16.5% did not have an opening snap, excluding four cases which were put up for surgical repair of mitral incompetence. The absence of a snap was attributed to the following factors: (1) associated significant mitral incompetence without calcification (four cases); (2) associated significant mitral incompetence with heavy calcification (9 cases); (3) heavy calcification with trivial mitral incompetence (4 cases); (4) an extremely high pulmonary vascular resistance over 10 units (5 cases); (5) massive left atrial thrombosis (1 case); and (6) moderate aortic valve disease (1 case).

It is uncertain whether the explanation in these last two instances is correct. Since the opening snap is certainly due to the abrupt backward billowing of the mitral cusps, particularly the aortic, when the pressure within the left ventricle sinks rapidly below that in the left atrium at the end of the period of isometric relaxation, it is suggested that aortic reflux may prevent the snap by interfering with the backward movement of the aortic cusp.

Mitral incompetence of sufficient degree prevents the snap because in these cases there is far more destruction and rigidity of the mitral cusps than in pure stenosis, so that the rigging is disorganized and, if one thinks of the cusps as sails, they are too matted down to flap back as the pressure gradient is reversed. It may also be true that with sufficient incompetence the lack of obstruction at the mitral orifice itself prevents the snap by allowing free filling of the ventricle as in normal hearts.

It has been suggested that mitral calcification may be responsible for the absence of a snap (Wynn, 1953), and the findings here confirm this view. Conspicuous calcification is rare in the absence of incompetence, but it has occurred, and in addition to the four cases mentioned above two others have been seen recently both without a snap. Extreme rigidity of the cusps is assumed to be responsible. Of 13 additional surgical cases in which calcification was slight and in which there was no mitral incompetence, all had an opening snap.

An extremely high pulmonary vascular resistance obscured the snap in one-quarter of all such cases. Since the left atrial pressure was at a level which would certainly have been associated with a snap in uncomplicated cases of mitral stenosis, its relative lowering cannot be held responsible for the absence of the sign; moreover, the sign was in fact present in three-quarters of such cases, and was sometimes very loud. It is suggested that the snap may be masked by the very large pulmonary artery overlying the root of the aorta, so that sounds produced by the aortic cusp of the mitral valve are not readily heard at the base; also by a grossly distended right ventricle forming the apex of the heart, so that sounds transmitted through the left ventricle may be difficult to hear at the "mitral area." In one or two instances of extreme pulmonary hypertension the snap was recorded phonocardiographically when it could not be heard clinically; this was never so when a snap could not be heard in cases of mitral incompetence.

Amongst the 150 surgical cases there were only two instances of simple stenosis in which a snap was not recorded clinically. One of these had the largest mitral orifice in the series; in the other an error was suspected. Mitral valvotomy resulted in loss of the snap in 32% of the cases: half of these were associated with excellent results, the other half with the development of serious mitral incompetence.

In the medical cases an opening snap was not heard in 38%. The explanations were much as described for the surgical group, in that 16 had serious mitral incompetence without calcium, 10 had serious mitral incompetence with conspicuous calcification, one had conspicuous calcification without mitral incompetence, three had an extreme pulmonary vascular resistance, and one had moderate aortic valve disease. In addition, however, there were five cases in which the absence of a snap was attributed to the mildness of the lesion; in fact, 38% of really mild cases had no snap. It must be understood that in these the degree of stenosis approached the trivial. In relatively mild cases, in the sense that they were not severe enough to warrant valvotomy although otherwise quite well developed, a snap was always present. In the medical group also there was one case with predominant tricuspid stenosis in which a mitral opening snap could not be heard, and there was one instance in which failure to record a snap was believed to be a clinical error.

It is concluded that the opening snap is one of the most important signs of dominant mitral stenosis, and, like a loud first heart sound, is an excellent talisman against the presence of serious mitral incompetence. Although it signifies properly developed stenosis, being absent in many trivial cases, it does not necessarily mean that the stenosis is severe enough to warrant valvotomy.

The Third Heart Sound

This was never heard in cases of pure stenosis as noted by Brigden and Leatham (1953). It was present in 85% of the cases of well-developed mitral incompetence (grades 2 to 4) and in 25% of cases of mild mitral incompetence. It was present in 74% of the medical cases in which a serious degree of incompetence complicated mitral stenosis, but in only 25% of the surgical cases of similar kind, probably because there was relatively more stenosis in this small group. Of the surgical cases with a third heart sound not one did excellently or even well; indeed, three-quarters of them died. A third sound was never heard when a trivial degree of incompetence complicated mitral stenosis.

The sound was closely correlated with a hyperdynamic left ventricle. Thus 78% of all cases having such a left ventricular action without aortic incompetence had a third heart sound; conversely, 95% of cases with a third heart sound had a hyperdynamic left ventricle. This could be recognized both clinically and radiologically. The third heart sound, of course, is attributed to rapid filling of the left ventricle. The third sound was very closely correlated with the presence of a loud mitral systolic murmur; indeed, it was never heard without such a murmur. In fact, it was closely correlated with all the other signs of mitral incompetence as discussed elsewhere.

The difference between an opening snap and a third sound is usually obvious when both are classical, the opening snap being closer to the second sound, shorter, sharper, and higher-pitched in quality, and being very well heard at the left sternal edge; whereas a third heart sound is later, longer in duration, dull, relatively low-pitched, and best heard over the left ventricle at the apex of the heart. Again, the snap is well heard on expiration, whereas the third heart sound usually comes out better on inspiration. Unfortunately, the character of the third sound may become much more like an opening snap in advanced mitral incompetence in the sense that it may be less delayed and much sharper and higher pitched in quality than usual. The classical description of the third sound is based on its occurrence in normal individuals, usually children, and in association with heart failure (left ventricular diastolic gallop). In mitral incompetence the left ventricle fills more rapidly than in these conditions, and this is probably responsible for the modification of the sound.

When present before the operation, the third sound never disappeared afterwards; on the contrary, it was always louder. In the cases with combined stenosis and incompetence without a third sound pre-operatively, 85% developed the sound after valvotomy. In other words, relief of stenosis accentuated the signs of incompetence. In cases operated on for mitral stenosis with a trivial degree of incompetence, as many as 60% developed a third heart sound after valvotomy, although these patients often did very well functionally, the incompetence being only of moderate degree. A third sound associated with mitral incompetence also developed after valvotomy in 7.5% of cases without previous incompetence at all.

It is concluded that the presence of a third heart sound is excellent evidence of at least moderate mitral incompetence. Its presence offers a strong reason for not recommending valvotomy even in those rare instances in which a clinical opening snap is heard in addition to the third sound.

Mitral Diastolic Murmur

Particular attention was paid to the length as well as to the intensity of a mitral diastolic murmur, and whether or not it was accompanied by a thrill; both length and intensity were graded. By grade 4 length is meant that no gap could be detected between the murmur and the first heart sound, or between a diastolic murmur and presystolic accentuation; a grade 3 murmur means that a gap could just be recognized; a grade 2 murmur was of moderate length, and grade 1 very short. When there was tachycardia the heart was slowed by means of carotid sinus compression in order to grade the length of a murmur. When there was auricular fibrillation the length of the bruit was gauged during the longer pauses; sometimes these had to be induced by carotid sinus pressure.

The mitral diastolic murmur was long (grade 3 or 4 in equal proportion) in 85% of the surgical cases. In 15% only was it relatively short; one-third of these had an extremely high pulmonary vascular resistance (abolishing the murmur altogether in one instance); one-third had significant mitral incompetence; no explanation could be found in the remainder (5% of the whole series). An extremely high pulmonary vascular resistance also abolished the murmur in one of the medical cases.

In the group with almost pure mitral incompetence the murmur was very short in 48% and only moderate in length (grade 2) in 24%. It was never long, and was absent altogether in 28%. Moreover, when a diastolic murmur was present in mitral incompetence a third heart sound could nearly always be heard.

A mitral diastolic thrill was appreciated in 38% of the surgical group, in 29% of the medical, and in 20% of the cases with mitral incompetence. An attempt was made to find some factor which might favour the development of a thrill, but with little success. In the cases with a thrill valve calcification was present in 29%, against 28% in the group as a whole; the left atrial pressure averaged 21.4 mm. Hg, the cardiac output 3.95 litres a minute, and the pulmonary vascular resistance 5.1 units, against respective control figures of 22.5, 3.8, and 6.5; the mitral orifice was less stenosed than usual in 22%, average in 46%, tighter than usual in 22%, and extremely stenosed in 10%, against control figures of 9%, 48%, 17%, and 26% respectively, omitting cases with significant mitral incompetence. As a rule, the cusps were mobile in cases with a thrill; a tough fibrous orifice was present in 27%: these anatomical findings were much the same in the series as a whole.

It will be discerned that the only points of difference between cases with a diastolic thrill and the surgical group as a whole were that the pulmonary vascular resistance was a little lower, and that the incidence of cases with extreme and relatively mild stenosis was reversed. On looking into the resistance more closely it was found that an extreme resistance was present less than half as frequently in those with thrills as in those without. This was confirmed by an analysis of the medical group, in which none of the few with an extreme resistance had a thrill. This damping effect probably explained the relatively few cases of an extremely stenosed orifice amongst the cases with thrill referred to above.

The intensity of the mitral diastolic murmur has not been analysed separately, for the loudest murmurs were usually associated with a thrill, soft murmurs never.

[*Part II, with a list of references, will appear in our next issue.*]

Scientific Film Review for March, 1954, includes descriptions of eight new medical films. "Analysis of the Effect of Vasoactive Substances on the Blood Vessels in the Mesorchium of the Rat" (Ciba Laboratories) is described as a superb example of cinemicrography. Although intended for pharmacologists and physiologists, it is also suitable for medical societies. "The Children's Vocabulary of the New Sign Language" (Department of Phonetics, University College, London) demonstrates some 330 moving signs in Sir Richard Paget's new sign language. It is intended for teachers of the deaf and otologists. "Cold Agglutination of Human Blood" (Ciba Laboratories), partly in colour, is for haematologists and physiologists. "The Cyto-diagnosis of Uterine Cancer" (Ciba) is a useful colour film dealing with the recovery of vaginal contents, the technique of Papanicolaou's staining procedure, and the appearance of cancerous cells. The first part is primarily of value to gynaecologists and the remainder to pathologists and laboratory technicians. "Lymph Vessel Movement Studies in the Mesentery of the Rat" (Ciba) is meant for pharmacologists and physiologists. "Nalorphine" (Wellcome Film Unit) demonstrates the antagonistic action of this drug to morphine, methadone, and thiambutene. "A New Approach to the Surgery of Peptic Ulcer" (Allen and Hanbury) is a demonstration in colour of the difference between Billroth partial gastrectomies and the jejunal replacement technique, with particular emphasis on the latter. It is likely to be of special interest to gastric surgeons and surgical societies. "Nydrazid in the Treatment of Tuberculosis" (E. R. Squibb and Sons) is a coloured film intended for chest physicians, tuberculosis officers, etc.