with diabetic nephropathy and to demonstrate by needle biopsy studies the pathogenic relationship of these defects to the development of the renal lesions.

Cases of diabetic nephropathy showed hypoalbuminaemia, hyperglobulinaemia, hypercholesterolaemia in many instances, a rise in the protein-bound serum polysaccharides, hyponatraemia, and hyperkalaemia. The urine showed excessive amounts of 17-hydroxycorticosteroids and low values of 17-ketosteroids. Most patients with diabetic nephropathy could not retain the greater part of a test-dose of vitamin B₁₂ administered parenterally.

The following endocrine and metabolic disturbances are believed to be probably responsible for the development of the renal lesions: a disturbance in protein metabolism resulting in a rise in α_2 and β -globulins; a disturbance in lipid metabolism causing lipaemia and especially a rise in the smaller aggregates of the serum lipoproteins; a disturbance in carbohydrate metabolism leading to a rise in the serum polysaccharide; excessive glucocorticoid activity; and inability to retain vitamin B₁₂.

The high serum mucopolysaccharides are probably related to the development of the lesions of diffuse and nodular glomerulosclerosis. The disturbed lipoprotein metabolism, vitamin B₁₂ metabolism, and the excessive glucocorticoid activity are probably related to the development of the hyaline fibrinoid lesions.

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MITRAL VALVOTOMY AND RESTENOSIS

BY

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The occurrence of restenosis after an adequate mitral valvotomy has been questioned, but reports in the literature of well-documented cases imply that it does undoubtedly occur (Jordan and Hellemis, 1952; Keyes and Lam, 1954; Donzelot; *et al.*, 1953; Santy *et al.*, 1954; McKusick, 1955; Glenn and Dineen, 1956). However, the true incidence of restenosis is not known.

In many patients apparent restenosis has been attributed to inadequate initial valvotomy. Thus Harken and Black (1955) have declared that restenosis is most uncommon. Glover *et al.* (1955) have seen no case of restenosis following valvotomy in their series. From their experience in a review of 250 cases subjected to mitral valvotomy followed from one to six years, Turner and Fraser (1956) felt that refusion of the commissures must be very rare. Of their cases five had second valvotomies and three more were under consideration at the time of writing. It was the opinion of the surgeon that in no case had refusion occurred, but that the original split had been inadequate.

On the other hand, Belcher (1958) described 12 cases in which revalvotomies were undertaken, and drew a

distinction between "true" and "false" restenosis. True restenosis occurred after one or both commissures had been fully split. Four cases fell into this group. In false restenosis either an original split was not obtained or there was no split beyond the area of insertion of the papillary muscles: there were eight cases of this type. Baker *et al.* (1955) found that three years after mitral valvotomy 10% of patients had lost all improvement gained by the operation. However, these were all severe cases operated upon early in their series. Wood (1954) reported an incidence of restenosis of 5% during the first three-year follow-up period after mitral valvotomy. Likoff and Uricchio (1958), reviewing the clinical status of 200 patients five to eight years after operation, found restenosis in 5% also. In the analysis by Bailey *et al.* (1957) of 1,000 cases following mitral valvotomy, restenosis had occurred in 22. In six there was necropsy evidence to support this, and further operations in the other 16 showed that restenosis had occurred. Soulié *et al.* (1957) report six cases of restenosis verified at second valvotomies.

It is the purpose of this paper to report 15 cases in which there was a recurrence of symptoms following mitral valvotomy. In seven restenosis of the mitral valve occurred after a satisfactory valvotomy. In the other eight the initial valvotomy was inadequate. Twelve of these patients have had second valvotomies and the other three are awaiting operation.

In addition to these 15 patients one further case of restenosis seen at necropsy is recorded.

The Patients

In general the 15 patients followed a similar clinical course. At the time of the first valvotomy they all presented the signs of critical mitral stenosis. There was an initial period of improvement after operation, with subsequent deterioration. The average duration of improvement in those who had had an apparently satisfactory valvotomy was three years, whereas it was two and a half years for those in whom the initial valvotomy was poor (Fig. 1). Gradual deterioration ensued in all patients from one to five years after the initial valvotomy. At the time of the second operation, or at the time of assessment of those awaiting second valvotomy, the incapacity caused by exertional dyspnoea was more severe than it had been prior to the first operation, with two exceptions (Table I). Coinciding with the period of improvement in the seven patients who had better valvotomies there was a diminution in the signs of mitral stenosis, in that the mitral diastolic murmur became shorter or softer, or even inaudible. At the time of assessment prior to the second valvotomy all again presented the signs of critical mitral stenosis.

Associated Valve Lesions.—In these patients associated valve lesions or mitral incompetence were not considered to have contributed in any material way to the worsening of their symptoms and signs. In fact, in eight no other lesion was present. In five patients faint early diastolic murmurs were heard. There were no peripheral signs of aortic incompetence. In two slight mitral incompetence was produced at the first operation. Minimal left ventricular hypertrophy on the electrocardiogram was present in two.

Radiology.—Prior to the second operation there had been a deterioration in the radiological signs since the time of the first valvotomy in 11 patients. This was judged by an increase in heart size, the appearance of horizontal costophrenic lines, and an increase in the radiological signs of pulmonary arterial hypertension.

Electrocardiography.—In five patients the degree of right ventricular hypertrophy had increased between the two valvotomies. But in six patients a definite but transient diminution in the degree of right ventricular hypertrophy did occur after the first operation. The changes, however, were slight (Fig. 2).

Cardiac Catheterization.—Of the 15 patients, 11 were catheterized before the second operation. All pressures were measured from 5 cm. below the sternal angle. In nine the mean pulmonary capillary pressure was recorded. The readings obtained were within the range of 20 to 35 mm. Hg with the

FIG. 1.—Level of exercise intolerance in relation to each valvotomy. Cases 7 and 8 are excluded.

TABLE I.—Clinical Data

Case No.	Age at 1st Valvotomy	Exercise Intolerance*		Clinical Signs		Years of Improvement Following 1st Valvotomy
		Before 1st Valvotomy	Before 2nd Valvotomy	Before 1st Valvotomy	Before 2nd Valvotomy	
1	45	3	3	Pure M.S.	Pure tight M.S.	4
2	27	3	2B	Mobile valve	Mobile valve	3
3	38	3	4	Pure tight M.S.	" "	2
4	39	2A	2B	Severe P.H.T.	Severe P.H.T.	1
5	43	3	4	Mobile valve	Mobile valve	4
6	40	2A	2B	Pure tight M.S.	Pure tight M.S.	2
7	18	2A	1	Mobile valve	Tight M.S.	2
8	50	2B	2B	P.H.T.	Slight M.I.	1
9	32	3	4	Pure tight M.S.	Mobile valve	1
10	37	2A	2B	P.H.T.	P.H.T. + +	2
11	36	3	2B	Pure tight M.S.	Pure tight M.S.	4
12	40	2B	2B	Mobile valve	Mobile valve	4
13	46	2A	3	P.H.T.	P.H.T.	3
14	47	3	3	Pure tight M.S.	Pure tight M.S.	5
15	31	2B	2B	Mobile valve	Mobile valve	2

Restenosis patients, Cases 8-14.

* Exercise intolerance: grades 0-4 according to the classification of the American Heart Association. M.I.=Mitral incompetence. P.H.T.=Pulmonary hypertension. M.S.=Mitral stenosis. P.I.=Pulmonary incompetence.

exception of one which was 16 mm. Hg (Table II). The pulmonary wedge or left atrial pressure had been measured before the first operation in three, and in each case the pressure was higher at the later assessment. The pulmonary artery pressure was measured prior to the second operation in 11 cases. The pressure before the second operation was much higher than before the first in four of five patients in whom a reading immediately preceding the first operation had been obtained, and there was an increase in total pulmonary resistance during the interval period (Table II).

Findings at Valvotomy.—In two cases no actual fracture of a commissure was achieved at the first operation, and in another five, though the valve was split, the increase in size was small and the differences found at the second operation were not great. In the

other five patients who had a second operation the valves had been split reasonably well on the first occasion, the average size of the orifice produced being 3 cm. in diameter. The average orifice diameter found at the second operation was 1.1 cm. Likewise, in the three cases awaiting second valvotomies definite valve splits had previously been obtained. In one the split was poor, but in the other two 3-cm. and 3.5-cm. valves were produced (Table III).

Pathology.—Biopsies were taken from the left atrial appendage in 11 patients at the first operation. Aschoff bodies were present in three, and were considered by Professor C. V. Harrison to show evidence of active rheumatism. Two of these patients had good initial valvotomies.

FIG. 2.—Case 3. Electrocardiogram in relation to valvotomies. The dominant R in lead V₁ disappeared after the first valvotomy and reappeared coinciding with a return of symptoms. It disappeared again after the second valvotomy.

TABLE II.—Catheter Data

Case No.	Prior to 1st Valvotomy					Between Valvotomies						
	Date of Catheter	Pressures mm./Hg		Cardiac Output (l./min.)	Total Pulmonary Resistance (Units)	Date of Operation	Date of Catheter	Pressures mm./Hg		Cardiac Output (l./min.)	Total Pulmonary Resistance (Units)	Date of Operation
		P.A. or R.V.	P.C.P.					P.A. or R.V.	P.C.P.			
1	1/1/51	67/2 (R.V.)		3.6		7/3/51	23/3/56	70/35	32	6.0	7.0	4/4/56
2	29/1/51	36/19		5.4	3.7	9/4/52	6.5/57	41/21	23	6.0	3.8	17/5/57
3	17/1/52	128/67				6/2/52	14/8/56	78/10 (R.V.)		2.7		18/8/56
4						13/1/54	28/5/58	40/17	16	4.6	4.0	30/5/58
5						10/2/52						5/9/58
6						6/5/52	15/10/56	45/15	26	4.6	3.9	6/11/58
7						20/1/54	18/1/57	65/45	25	6.0	5.8	10/4/57
8						4/8/54	15/3/57	79/48		1.7	31	18/10/57
9	27/10/50	78/18 (R.V.)		3.2		30/5/51	18/4/52	56/38		2.3	17	12/9/56
10	29/4/53	34/19		4.5	4.2	29/4/53	6/2/58	100/60	35	3.5	19	18/8/58
11						16/1/52						16/3/59
12	18/2/53	46/27		4.7	6	12/3/54	12/1/59	62/30	20	4.4	8.2	29/1/59
13	28/4/54	35/14		8.1	2	22/9/54	1/12/58	74/37	34	5	8.8	
14			16 at operation			10/9/52						
15	5/1/53	38/21	22	5.3	4	29/9/54	14/1/59	75/43	30	8.5	6.0	

Restenosis patients, Cases 8-14. P.A.=Pulmonary artery. R.V.=Right ventricle. P.C.P.=Pulmonary capillary pressure.

TABLE III.—Operation Data

Case No.	1st Valvotomy					2nd Valvotomy				
	Valve Size	Calcium	Mobility	Commissure(s) Split	Final Valve Size	Valve Size	Calcium	Mobility	Commissure(s) Split	Final Valve Size
1	1 cm.	0	Both cusps	0	2 cm.	1 cm.	0	Both cusps	Both	3 cm.
2	1 "	0	" "	0	2 "	1 "	0	" "	Lateral	3.5 "
3	0.8 "	0	Ant. cusp	Lateral	1.75 "	0.8 "	0	Ant. cusp	Both	4 "
4	1.2 "	0	" "	" "	2.5 "	1.8 "	0	" "	" "	3 "
5	1 "	0	Both cusps	" "	2.5 "	0.8 "	0	Both cusps	" "	4 "
6	1.5 "	0	" "	" "	3 "	1.5 "	0	Ant. cusp	" "	3.4 "
7	1 "	0	" "	" "	2 "	0.8 "	0	Both cusps	Aortic cusp torn	3 "
8	0.8 "	+	Ant. cusp	" "	2.5 "	1.5 "	++	Almost immobile	Both	4 "
9	1.2 "	0	Both cusps	" "	3 "	1 "	0	Both cusps	Lat. part of medial	3.5 "
10	0.9 "	+	Ant. cusp	" "	3 "	1 "	+	Ant. cusp	Both	3.5 "
11	0.7 "	0	Both cusps	Medial; $\frac{1}{2}$ lateral	3 "	1.25 "	0	Both cusps	" "	3.5 "
12	1.5 "	0	" "	Lateral	3 "	1 "	0	" "	Lateral	3 "
13	1.5 "	+	Partially mobile	" "	3.5 "					
14	0.8 "	+	Not stated	" "	3 "					
15	1.5 "	0	Fair	Partial, lateral	2.5 "					

Necropsy Material

In addition to the cases already presented there was one patient in whom necropsy showed restenosis present 12 months after a successful valvotomy in which both commissures were completely split.

Case Report.—At the age of 37 the patient (M.Y.) had an attack of chest pain with cardiographic changes suggestive of antero-lateral ischaemia. A clinical diagnosis of coronary embolism and tight mitral stenosis was made. After an interval of six months a mitral valvotomy was performed and a 1-cm. mobile valve was found. Both commissures were split with the finger to the valve ring. There was no subvalvular stenosis. After the operation the mitral diastolic murmur, which had previously been full length, was noted to be short on several occasions. Twelve months after operation the patient died suddenly in bed at home. At necropsy a definite line of refusion of the cusps along the medial commissure could clearly be seen (Fig. 3). An old postero-lateral myocardial infarct was also present. The coronary vessels were healthy. A histological section taken at right angles to the line of refusion of the valve showed a mass of fibrous tissue joining the two cusps (Fig. 3c). There was no evidence of rheumatic activity either in the biopsy of the left atrial appendage taken at operation or in the sections taken post mortem.

In this case refusion occurred after a complete split of both commissures. The cause of death was not revealed by the necropsy. The evidence, however, of an old cardiac infarction due to coronary embolism suggests that it may have been due to arrhythmia.

Discussion

There is little doubt that in 7 of the 15 patients considerable restenosis occurred. In six of these a complete split of the lateral commissure was achieved at the first operation, and in the seventh the medial commissure was split to the valve ring and the lateral commissure was partially split also. In no case was subvalvular stenosis found. Symptomatic improvement followed in all. In each the mitral diastolic murmur became shorter or softer, and in three the degree of right ventricular hypertrophy seen on the electrocardiogram became temporarily less. In the five patients of this group who have had second valvotomies (Cases 8–12) definite proof of restenosis was provided by comparing the valve size found at the second operation with the orifice size known to have been produced at the first (Table III). Thus the average valve diameter produced at the first operation in this group was 3 cm., while the average size of the valve orifice found at the second operation was 1.1 cm. At the time of maximum

deterioration immediately preceding the second valvotomy the signs of critical mitral stenosis were again present. The electrocardiographic and radiological changes were as marked as they had previously been or were more severe (Table I), and the pulmonary artery pressure, where measured, had risen in all except one case.

Baden (1958) refers to restenosis occurring after only one commissure has been split as "false" restenosis and accepts as examples of "true" restenosis only those cases in which restenosis has occurred after a complete splitting of both commissures. However, it would seem that if one commissure is completely split and the chordae tendineae are freed and then refusion occurs, this is as "true" a restenosis as if both are split and then re-fuse. Also, even though the first valvotomies were poor in the other eight patients there is evidence that structural changes occurred in the valves between valvotomies to convert a partially relieved obstruction to a critical stenosis again (Table III). Hence some restenosis may fairly be said to have occurred.

Few well-authenticated cases have been reported in which restenosis has occurred in a mobile valve following a complete split of both commissures and separation of fused chordae, as in case M. Y. In neither this case nor that of Baden (1958) was there any evidence of rheumatic activity. In the case reported by Harken and Black (1955) thrombus had formed between the valve edges producing a recurrence of a part of the original stenosis. In two further cases they attribute restenosis to traumatic endocarditis produced by blunt dissection. In McKusick's (1955) case there was good evidence of continuing rheumatic activity.

Bailey *et al.* (1957) have suggested that restenosis is related to the mobility of the valve and that fibrin and platelet deposition on the valve as demonstrated by Magarey (1951) is more likely to occur if the valve leaflets are moving sluggishly. Brock (1952) implied a similar mechanism if the movement of the valve cusps is not restored by division and separation of the critical areas of tendon insertion. Nevertheless, he felt that if the lateral commissure only was completely split and the corresponding area of tendon insertion freed, mobility of the valve would be restored and recurrence was unlikely. Glover *et al.* (1955) and Harken and Black (1955) also expressed this view.

In the cases described in this paper in which restenosis occurred after a seemingly adequate valvotomy there is no good evidence that restenosis and lack of mobility of the valve leaflets ran parallel. The mobility of both

cusps was described as good in three cases at the time of the first valvotomy; only the anterior cusp moved in a further 3, and the mobility is not recorded in the other (Table III). In the necropsy case (M.Y.) both cusps were freely mobile. These findings correlated well with the clinical estimate of valve mobility based on the loudness of the first heart sound in the mitral area and the presence and intensity of the opening snap. In four of these seven patients some valve calcium was found; no macroscopic calcium was present in the necropsy case. Thus calcium was present in 50%, as compared with 33% in the series of 93 patients followed from five to seven years after valvotomy. The incidence, therefore, was slightly higher in the restenosis cases, but the numbers are small.

Persistent rheumatic activity did not appear to be a likely factor in the pathogenesis of restenosis in these patients. In no case was there a definite further attack of rheumatic fever. Aschoff bodies were found in the left

atrial biopsy in two patients at the first operation. In one of these (Case 11) gradual deterioration followed an attack of mild joint pains lasting several weeks. There was no clinical evidence of rheumatic activity as indicated by normal erythrocyte sedimentation rate, normal temperature, and anti-streptolysin titre, but despite these results the episode may have been a manifestation of further rheumatic activity. McKeown (1953) has shown that the pathology of the left atrial biopsy is representative of the changes in the myocardium of the ventricle, yet discrepancy between the biopsy and the clinical findings has been the general rule. No correlation was found between the atrial biopsy and the subsequent clinical course by Baker *et al.* (1955) or by Goodwin *et al.* (1955). The same percentage of positive biopsies was found in the patients in whom restenosis occurred as in the whole series in Likoff and Uricchio's (1958) cases.

It is difficult to see how lack of valve mobility in these patients could explain the much higher incidence of restenosis seen after a complete split of one commissure, with or without a partial split of the other, compared with the incidence after a complete split of both commissures. Under these conditions restenosis is rare after a similar follow-up period, according to the literature. It is tempting to conjecture that this difference is purely a matter of time and that with a longer period of follow-up many more cases of restenosis appearing after complete splits of both commissures will emerge. This would seem inevitable if Magarey's (1951) view is correct that fibrin and platelet deposition on the valve surface with subsequent organization occurs as the initial stage in the development of restenosis.

Incidence of Restenosis

Any attempt to establish the incidence of restenosis must relate it to the extent and nature of the valve split previously obtained. At times it may be difficult for the surgeon to be precise on this point, and so the incidence must remain approximate. The seven patients with restenosis after a successful valvotomy were among 70 patients who had a satisfactory commissural split to produce a valve size of at least 2.5 cm. in diameter and who have been followed for five to seven years. They were taken from 93 who had valvotomies and who have been followed for a similar time. Of these, 10 died during the follow-up period and 13 had poor valvotomies and have been excluded. Thus there is an incidence of restenosis of 10% after five to seven years in the patients who had a successful valvotomy. The valve splits in the 70 patients were as follows:

Lateral commissure only	35
" and partial split of the medial commissure	19
Medial commissure only	3
" and partial split of the lateral commissure	4
Both commissures	9

There has so far been no evidence of restenosis in the cases above in which both commissures were divided as was seen in case M.Y. The incidence after a split of one commissure, usually the lateral with or without a partial split of the other, is therefore 11% after five to seven years. This is higher than was found by Likoff and Uricchio (1958), but roughly the same as Wood's (1956) figure of 2% per annum. However, neither figure was correlated with the extent and nature of the commissural splits. The incidence after a partial split of a commissure of a dilatation only of a valve is very much higher again. Eight of the 13 patients

FIG. 3.—Case M.Y. A and B: Necropsy specimen of heart showing line of refusion of cusps along medial commissure. C: There is dense fibrous tissue joining the two cusps. (Haematoxylin and eosin. $\times 7,027$.)

who had poor valvotomies are described in this paper (Cases 1 to 7 and Case 15) and seven to date have had second valvotomies.

Method of Valvotomy

A dilator introduced through the wall of the left ventricle as described by Logan (1954, personal communication) was employed at the second valvotomy in 10 patients. In eight a splitting of both commissures was obtained and in one a split of the lateral commissure only. Unfortunately, in the other patient (Case 7) the aortic cusp was torn and gross mitral incompetence was produced. Nevertheless, it does seem that a more complete splitting of both commissures is possible with this instrument. In Table IV the valve splits obtained in the last 50 cases in which the transventricular dilator was employed are compared with those obtained in the last 61 cases in which the surgeon's finger was used with or without a valvotomy knife. These valvotomies were all performed later than December, 1954.

TABLE IV

	Using Transventricular Dilator	Using Finger and Valvotomy Knife
Lateral commissure only	11	31
and partial split		
of the medial commissure	9	6
Medial commissure only	2	4
and partial split		
of the lateral commissure	4	1
Both commissures	22	7
Partial split of both commissures	2	0
Poor or no split	0	12
Total	50	61

The efficacy of this method in obtaining a maximum valve split is apparent. Complete splits of both commissures were obtained in 44% with the transventricular dilator as compared with 11.4% using the finger and valvotomy knife, and 9.4% in the five to seven-year follow-up cases operated upon before December, 1954. The dilator produced torrential mitral incompetence in one patient (Case 7). If the incidence of severe mitral incompetence is shown not to be higher after this technique than after other methods it may well become the method of choice when it is not possible to split the valve satisfactorily with the finger alone.

Conclusions

Recurrence of symptoms following mitral valvotomy is often due to restenosis. It is probable that restenosis is much more common than hitherto supposed. The incidence of restenosis in the group in which one commissure only is split (usually the lateral), with or without a partial split of the other, is of the order of 11% after five to seven years. The incidence in the group in whom both commissures are split cannot be determined, but the literature suggests that it is rare after a similar follow-up period. The incidence after a partial split of one commissure or a dilatation only of a valve is very high—8 out of 13 cases. There is no evidence to suggest that there is any fundamental difference between the processes of "true" and "false" restenosis and there seems no reason to use these terms. If the valvotomy is poor there is a considerable chance of further obstruction developing. If the valvotomy is moderate then the chance of refusion occurring is less, whereas if it is excellent the chances are very slight for this follow-up period. It is unlikely that continuing or

renewed rheumatic activity is commonly responsible for restenosis. Progressive organization of fibrin and platelet deposit on the opposing surfaces of the valve leaflets is the theory of the pathogenesis of restenosis which best fits the known facts. Restenosis may occur whether the valve is mobile or not.

It seems certain that in the near future a much greater number of second valvotomies will be performed. There are two reasons for this. First, many of the earlier valvotomies were inadequate and not even a complete split of one commissure was obtained. Second, the period of five to seven years has now elapsed since operations producing a complete split of one commissure were performed, and it can be expected that approximately 11% of those will restenose. Furthermore, even with the more modern techniques and greater experience it seems very probable that there will always be a number of patients in whom it is technically impossible to split completely more than one commissure at operation. The transventricular dilator provides a method by which a very satisfactory valve split can usually be obtained, although the long-term results following its use have yet to be evaluated.

The appreciable incidence of restenosis suggests that mitral valvotomy should not usually be advised until the patient's symptoms warrant it.

Summary

The incidence of restenosis following mitral valvotomy is higher than is generally believed. It is currently believed that an adequate valvotomy is performed if one commissure, usually the lateral commissure, is split completely to the valve ring with freeing of the chordae tendineae with or without a partial split of the other commissure. Evidence is presented to show that approximately 11% of these patients restenose after five to seven years. Seven cases illustrating this are described. It is rare for restenosis to occur in patients in whom there has been a complete split of both commissures to the valve ring during a similar follow-up period. One such case seen at necropsy 12 months after valvotomy is reported. Deterioration after a period of improvement following mitral valvotomy very often follows an inadequate initial valvotomy. Eight cases of this type are described. The incidence of restenosis is related to the degree and nature of the valve split obtained at operation. There is no evidence of any fundamental difference in the pathogenesis of "true" and "false" restenosis. The theories relating to restenosis are discussed and the literature is reviewed.

Second valvotomies have been performed on 12 patients. A transventricular dilator was employed in 10 of these. The valve splits obtained by the transventricular dilator in 50 cases are described and compared with the splits obtained with the finger and valvotomy knife.

The possibility of restenosis is emphasized and should be considered before advising early valvotomy.

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[ADDENDUM.—Since submitting this paper the three patients awaiting second valvotomy have had their operations and in each case the valve was tightly stenosed.]

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CALCIFIC MITRAL STENOSIS AND MITRAL VALVOTOMY

BY

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Approximately one-third of all patients submitted to surgery for the relief of mitral stenosis have calcium deposits on the valve leaflets (Sellers *et al.*, 1953; Wood, 1954; Goodwin *et al.*, 1955; Turner and Fraser, 1956; Bailey and Morse, 1957). Most authors stress the hazards of mitral valvotomy in the presence of heavy valve calcification. Calcific emboli may occur (Bailey, 1955; Turner and Fraser, 1956; Black and Harken, 1957), and valvotomy may be incomplete (Bailey, 1955; Turner and Fraser, 1956; Windsor, 1956). Wood (1954) concluded that heavy calcification is a serious drawback to surgery, not only because it suggests an appreciable degree of associated incompetence, but because it is also likely to favour the production of incompetence at operation. Black and Harken (1957) take a more optimistic view, stating that some of their best results were in patients with valvular calcification.

Calcification of the mitral-valve leaflets is a consequence of a previous rheumatic infection, is commoner after middle age, and occurs more often in males than females (Epstein, 1940; Turner and Fraser, 1956). Extension of calcium to the annulus in rheumatic cases is relatively uncommon and usually occurs after the age of 40 (Epstein, 1940). The mitral annulus alone can be involved in the absence of a previous rheumatic infection. It may be found in otherwise normal hearts after middle age, and in contrast to rheumatic calcifica-

tion is slightly commoner in women. Simon and Liu (1954) found annular calcification in 10% of unselected hearts examined at necropsy. Such calcification is functionally not significant; its importance is that it may be misinterpreted radiographically as being due to infiltration of the valve leaflets.

Calcium on the mitral-valve leaflets in a case of mitral stenosis is often suspected at the bedside, the associated valve rigidity modifying the characteristic auscultatory signs. The loud first sound tends to become normal or muffled, the opening snap disappears (Vaquez, 1894; Wolferth and Margolies, 1937; Wynn, 1953), and a systolic murmur is often present (Wynn, 1953).

The raised left atrial pressure in mitral stenosis causes the valve orifice to remain open until the onset of ventricular systole, when its sudden closure is audible as an accentuated first sound. With calcification and rigidity of the valve orifice, the edges are unable to snap together, so the first sound is characteristically normal or muffled. However, the first sound may be accentuated despite calcification (Wynn, 1953; Davies and Bucky, 1959). In Wynn's series of 60 patients with heavy mitral-valve calcification, the first sound was accentuated in 55%. In many patients with valve calcium a muffled first sound may become accentuated with tachycardia (Wynn, 1953).

The opening snap of the mitral valve occurs at the end of the period of isometric relaxation of the left ventricle, when the atrio-ventricular gradient is reversed. It may be due to sudden billowing of the aortic cusp into the left ventricular cavity (Sansom, 1881, 1892; Vaquez, 1894; Margolies and Wolferth, 1932), or to movement of the stenotic valve diaphragm deep into the left ventricle (Leatham, 1958). The latter is possibly the correct explanation, because rigidity and calcification of the valves does not always result in loss of the opening snap. Wynn found it to be present in 48%. The opening snap is absent in pure mitral incompetence (Brigden and Leatham, 1953).

The first sound may also be damped by associated mitral incompetence or a high pulmonary vascular resistance (Wood, 1954; Goodwin *et al.*, 1955). In addition to the above two factors, the opening snap may disappear in the presence of associated aortic incompetence, perhaps because the reflux into the left ventricle interferes with the sudden billowing of the aortic cusp of the mitral valve (Wood, 1954).

Calcium deposition on or around the valve orifice may also prevent effective closure during ventricular systole, hence some incompetence is often present despite otherwise severe stenosis. Wynn (1953) observed a systolic murmur in 80% of patients with heavy calcification. Goodwin *et al.* (1955) found that 10 of their 28 patients with mitral-valve calcification submitted to valvotomy had some incompetence. However, calcification is uncommon with pure incompetence (Goodwin *et al.*, 1955; Wood, 1956; Linko and Sysimetsä, 1958).

Radiology

Valvular calcification, if extreme, may be recorded on a telerradiogram. It is seen comparatively commonly in cases of calcification of the aortic valve, but rarely in the mitral. Klason (1921) was one of the first radiologists to report seeing mitral-valve calcium at fluoroscopy, after which fluoroscopy has remained the standard method of demonstrating intracardiac calcification. However, since Hohenner (1940) published a

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