THE ISOLATED SYSTOLIC MURMUR

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Accuracy in the diagnosis of heart disease has increased considerably during the last decade, mainly as the result of new and improved techniques in cardiac catheterization, angiocardiography, electrocardiography and phonocardiography. Modern cardiac surgery has afforded the opportunity for confirmation or revision of the physician's diagnosis. The accuracy of physical examination of the heart has thus also advanced, and clinical auscultation remains of major importance in modern cardiology.

The assessment of an isolated systolic murmur is one of the most common and important problems confronting the physician and one which can almost always be solved by clinical examination alone. It is the purpose of this paper to discuss the recognition, causes and significance of the various systolic murmurs which may occur with minimal or no other evidence of heart disease.

As a result of experience in the examination of recruits during the First World War, Lewis[1] and MacKenzie[2] refuted the concept that a systolic murmur always indicated valvular damage or impaired cardiac function and stressed that the heart could be completely normal. However, they were unable to differentiate pathological from innocent systolic murmurs except by other evidence of heart disease. In 1933 Levine[3] introduced a classification of systolic murmurs based on intensity. He considered that, in the absence of increased blood flow, a murmur of more than slight intensity (grade 2) was usually indicative of organic valvular disease. It is now appreciated that assessment on loudness alone is of limited value and often very misleading. Leatham[4] in 1955 classified systolic murmurs into two main groups, viz. ejection and regurgitant. This concept, which is based on anatomical and haemodynamic considerations, has been widely adopted.

A. Ejection Systolic Murmur

An ejection systolic murmur results from forward flow of blood through the left or right ventricular outflow tracts and can theoretically occur in one or a combination of the

following circumstances: (1) Increased rate of ejection; (2) valvular, subvalvular or supravalvular stenosis; (3) valvular damage or anomaly without stenosis; and (4) dilatation of the vessel distal to the valve.

An aortic or pulmonary ejection murmur starts after the component of the first sound and ends before the component of the second sound of the side of the heart in which it arises. An ejection systolic murmur is crescendo-decrescendo in shape; it is longer and accentuates later when caused by obstruction to the ventricular outflow[5, 6] as opposed to the other mechanisms of production (Fig. 1).

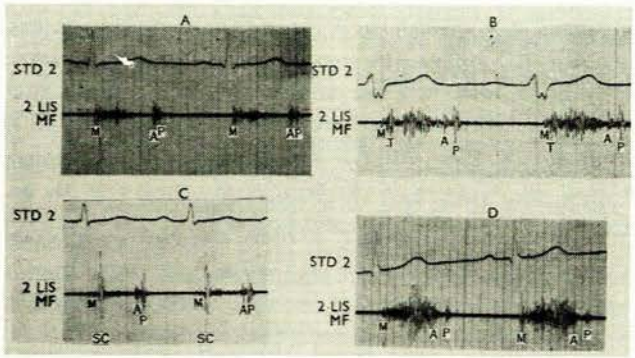

Fig. 1. Pulmonary ejection systolic murmurs. 2LIS = second left intercostal space, MF = medium frequency, M = mitral component of the first sound, T = tricuspid component of the first sound, A = aortic component of the second sound, P = pulmonary component of the second sound, SC = systolic click. Time interval between the heavy vertical lines is 0·2 seconds.

A. Normal heart. The murmur is short, accentuates early and the second sound is normal. The phonocardiogram is recorded during inspiration and the second sound is split 0·03—0·04 seconds.

B. Atrial septal defect. A similar short ejection murmur is present, but the second sound is split 0·06 seconds with accentuation of P2. Recorded during expiration.

C. Idiopathic dilatation of the pulmonary artery. The murmur is soft and short and an ejection click is present 0·10 seconds after Q of the electrocardiogram. The second sound is split 0·03 seconds and P2 accentuated. Recorded during expiration.

D. Pulmonary stenosis. The murmur accentuates in mid-systole and extends to A2. The second sound is split 0·06 seconds and P2 is soft. The gradient across the pulmonary valve was 55 mm.Hg. Recorded during expiration.

B. Regurgitant Systolic Murmur

Regurgitant systolic murmurs are caused by backflow of blood from a high pressure chamber to one at a lower pressure. A regurgitant murmur may therefore result from an incompetent atrio-ventricular valve or from a defect in the ventricular septum. As a pressure gradient is usually present throughout systole, regurgitant murmurs are frequently pansystolic. Thus, a typical murmur of mitral incompetence starts with the mitral component of the first sound and extends through the aortic closure sound.[7] However, the pansystolic nature of a regurgitant murmur may be modified by pressure or anatomical factors and these will be discussed in relation to the specific types of systolic murmur.

It is important to appreciate that irrespective of length or intensity, a regurgitant systolic murmur is always pathological.

GENERAL CONSIDERATIONS IN THE ASSESSMENT OF A SYSTOLIC MURMUR

1. *The Second Heart Sound*

In the assessment of any systolic murmur, the character of the second heart sound is of major importance. The intensity and timing of both the aortic (A2) and pulmonary (P2) components must therefore be elicited in every instance. During normal respiration there is variation in the splitting of the second sound. On inspiration the interval increases owing mainly to delay in P2,[8] although an earlier movement of A2[9-13] also contributes to the separation of the two valve closure sounds. A normal inspiratory increase, when measured phonocardiographically, is usually 0·02—0·04 seconds but, according to Aygen and Braunwald,[12] may be as much as 0·06 seconds. During expiration the second sound appears single in the majority of instances, but narrow splitting of 0·01 - 0·02 seconds occasionally persists. The aortic component is normally louder and is heard over the whole precordium whereas the softer P2 is seldom audible beyond the area of the second, third and fourth intercostal spaces just to the left of the sternum. The timing and intensity of the two components are best elicited during natural respiration, and voluntary deep breathing is seldom contributory.

It is outside the scope of this paper to discuss the many variations of the second sound which are encountered in heart disease, but some will be mentioned when specific types of systolic murmur are considered.

2. *Characteristics of the Systolic Murmur*

There are certain features which should be evaluated in the assessment of any systolic murmur:

(a) *Site and radiation.* The position of maximal intensity and radiation of a murmur are largely determined by its site of origin and the direction of blood flow. The murmur of aortic stenosis, for example, is loud in the second right interspace and is transmitted to the vessels of the neck.[14-16]

(b) *Intensity.* An increased velocity of blood flow and a decrease in blood viscosity will accentuate a murmur. The anatomy at the site of origin influences the intensity, and an abrupt protuberance produces a louder murmur than a smooth surface.[17] All heart sounds and murmurs are softer in the presence of a thick chest wall, pulmonary emphysema or a pericardial effusion. Very loud murmurs (grade 5 and 6) are invariably organic. Innocent ejection murmurs may be of grade 3 or even grade 4 intensity, whereas a regurgitant murmur, even if grade 1, always denotes a pathological heart. Furthermore, a loud murmur of organic origin does not necessarily signify a more severe lesion than a softer one. The ejection murmur of severe aortic stenosis in a patient with a failing myocardium may be only grade 2, whereas a very loud systolic murmur may occur in aortic sclerosis without a significant gradient. The murmur of severe mitral incompetence is usually loud but may occasionally be soft, and even silent mitral regurgitation has been claimed.[18]

(c) *Quality (pitch and tone).* The exact mode of production of heart murmurs and the factors which determine their vibration frequency are not fully understood. They can be recognized as having a 'harsh', 'blowing' or 'musical' quality. These are useful descriptive terms but do not of themselves provide much diagnostic information. For example, although the murmur of mitral regurgitation is frequently blowing, it may be rough or harsh and then resemble in quality that of aortic stenosis.[19-21] A notable exception is the 'vibratory' systolic murmur of childhood in which the low-pitched buzzing quality is characteristic.

A 'musical' murmur has been defined by McKusick[22] as 'the improved ability to represent the murmur by conventional musical notation'. He considered that some are produced outside the heart, but in our experience musical murmurs have invariably been accompanied by signs of heart disease and hence an intracardiac origin is probable. We have encountered musical murmurs (Fig. 2) arising at the mitral, aortic and tricuspid valves and, in one instance, a short musical murmur resulted from ejection through the narrow neck of a left ventricular aneurysm.[23] The factors which determine the musical intonation of a murmur are not always apparent, but there is

frequently a structure, such as an everted aortic cusp[22] or an aberrant chorda tendinea,[24] which is 'set into vibration in a specifically periodic, and therefore musical manner'.[22]

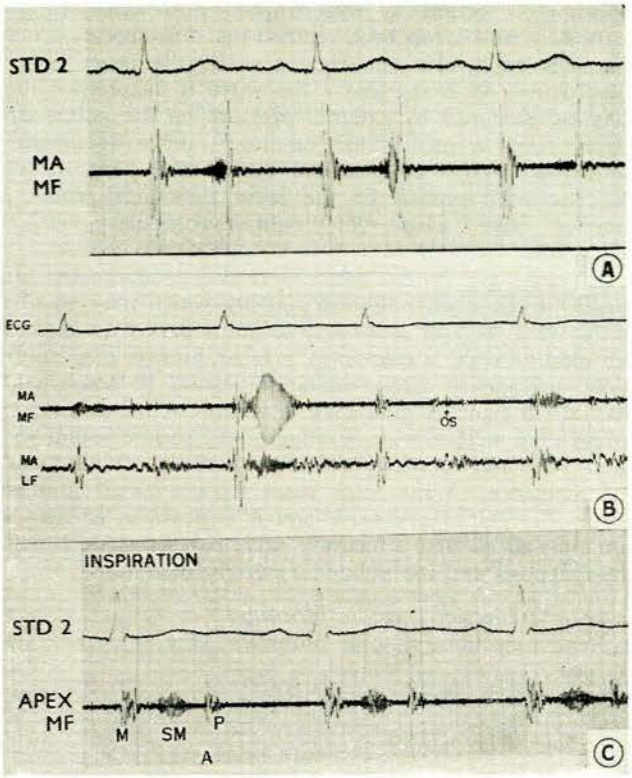

Fig. 2. Musical systolic murmurs. MA = mitral area, LF = low frequency, SM = systolic murmur, OS = opening snap.
A. Late systolic murmur of mitral incompetence. The murmur is loudest during inspiration. (By courtesy of the Editor and publishers of the *Journal of Chronic Diseases.*)
B. Mitral incompetence. The murmur shows marked variation in length and intensity, both increasing during inspiration. The patient has tight mitral stenosis, atrial fibrillation and the degree of mitral regurgitation is minimal. An opening snap and long mid-diastolic murmur are demonstrated.
C. Obstructive cardiomyopathy. Late onset murmur with regular high-frequency vibrations.

(d) *Length and timing.* The length of a systolic murmur is important and the distinction on this basis between ejection and regurgitant murmurs has been discussed. In addition, it has been mentioned that the length of ejection murmurs and their time of maximal intensity are related to the severity of outflow obstruction. In severe outflow obstruction the long ejection murmur will extend up to, or beyond, the normal semilunar valve closure sound of the unaffected side of the heart, but ends before its own delayed and soft second sound component (Fig. 3C). It should not, therefore, be confused with a pansystolic regurgitant murmur.

The time of onset of a murmur can provide useful information. Although most systolic murmurs start with or immediately after the first heart sound, there are several which are characterized by a delayed onset. These include the murmur of hypertrophic obstructive cardiomyopathy and the late systolic murmur of mild mitral regurgitation.

(e) *Effect of respiration and posture.* Many systolic murmurs vary in intensity during respiration, and the majority are loudest in expiration when the heart is nearer the chest wall. An important exception is the regurgitant systolic murmur of tricuspid incompetence which increases in intensity during inspiration as a result of the augmented venous return to the right side of the heart. Pulmonary ejection murmurs do not, however, show this inspiratory increase, and possibly positional factors here predominate. Musical systolic murmurs arising in the left side of the heart may also be louder during inspiration (Fig. 2A and B) and slight distortion at the site of origin of the murmur is the probable explanation rather than any haemodynamic change.[25]

The so-called 'cardio-respiratory' murmur was regarded by Lewis[26] as 'the commonest murmur heard in the region of the heart's impulse'. It has been described as a high-pitched short 'squeal'[27] which is loudest at the apex and characteristically varies with respiration. The murmur is possibly an abnormal breath sound produced by entry of air into overlying lung during ventricular systole.[22, 28] In the past, many murmurs

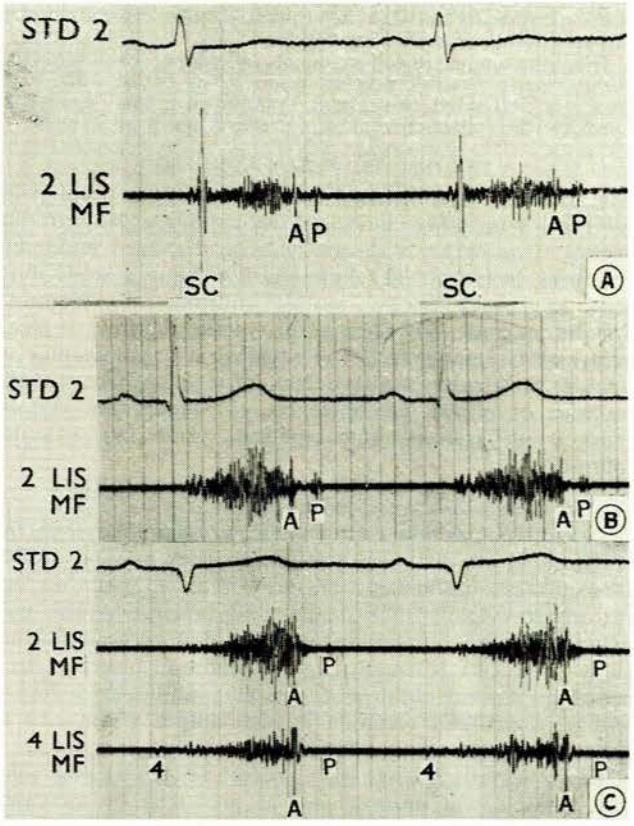

Fig. 3. Pulmonary stenosis. The pulmonary ejection murmur is longer and accentuates later in the more severe degrees of stenosis and P2 is correspondingly softer and more delayed. 4 = atrial sound.
A. Gradient of 45 mm.Hg. A2—P2 interval = 0·05 seconds.
B. Gradient 55 mm.Hg. A2—P2 interval = 0·06 seconds.
C. Gradient 150 mm.Hg. A2—P2 interval = 0.10 seconds.

showing respiratory variation were presumably called 'cardio-respiratory', and the example described by Castle and Craige[29] appears identical to the late systolic murmur of mild mitral regurgitation. Since the 'cardio-respiratory' murmur is not a distinct entity, we consider that the term should be abandoned.

The importance of the decrease in intensity of innocent systolic murmurs in the erect position has been exaggerated. Both innocent and organic murmurs become softer with this alteration in posture owing to reduction in venous return, and auscultation in the upright position is therefore seldom contributory. In the lateral position, however, the heart is brought closer to the chest wall and apical sounds or murmurs are consequently louder.

(f) *Effect of haemodynamic alterations.* Temporary alterations in arterial pressure, venous return or cardiac output modify the intensity and length of systolic murmurs and are useful in their assessment.

During the straining phase of a Valsalva manoeuvre, venous return to the heart is diminished and both left- and right-sided murmurs soften. After release of straining, right-sided murmurs regain their original intensity immediately, whereas the return of murmurs which arise in the left side is delayed by

the time taken for the blood to pass through the lungs.[30, 31]

The haemodynamic state can also be altered by drugs such as amyl nitrite,[32-37] phenylephrine,[25, 34, 37, 38] nor-epinephrine,[35] serotonin[35] and methoxamine.[35] Experience in this clinic has largely been confined to amyl nitrite inhalation and the intravenous administration of phenylephrine.

The inhalation of amyl nitrite causes marked vasodilatation and fall in systemic pressure, followed by tachycardia and increased venous return. Left-sided regurgitant systolic murmurs decrease in intensity during the phase of systemic hypotension, whereas in the slightly later phase of increased venous return, ejection murmurs and the regurgitant systolic murmur of tricuspid incompetence become louder.

The intravenous injection of phenylephrine causes a temporary rise in systemic pressure and a reflex bradycardia. Consequently, left-sided regurgitant systolic murmurs increase in intensity while ejection murmurs are essentially unchanged.

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The different systolic murmurs which may occur with minimal or no other clinical, electrocardiographic or radiological signs of heart disease will be discussed under the following headings: (1) Pulmonary ejection systolic murmur, (2) aortic ejection systolic murmur, (3) vibratory systolic murmur, (4) regurgitant systolic murmur of small ventricular septal defect, (5) atypical systolic murmur of minute ventricular septal defect, (6) regurgitant systolic murmur of mitral incompetence, (7) regurgitant systolic murmur of tricuspid incompetence, and (8) vascular murmurs.

1. *Pulmonary Ejection Systolic Murmur*

Pulmonary ejection systolic murmurs are loudest in the second or third left intercostal space. They may be audible in the neck, particularly on the left side,[39] but do not radiate specifically into the carotid arteries.[16] The pulmonary systolic murmur arising from flow across a normal valve (Fig. 1A) is usually high-pitched and blowing. It is heard in normal children and young adults,[13, 16, 27, 28, 40] and is particularly common in high output states such as anaemia, pregnancy and thyrotoxicosis.

The murmur of atrial septal defect (Fig. 1B) resembles this physiological murmur and is produced by increased flow across a normal pulmonary valve. An atrial septal defect is recognized by the associated features of wide fixed splitting of the second sound,[12, 41] loud P2 and tricuspid component of the first sound,[41] and a tricuspid mid-diastolic murmur.[41, 42] A very small atrial septal defect (pulmonary to systemic flow ratio of less than 1·5:1·0) or an isolated anomalous pulmonary vein may be clinically indistinguishable from a normal heart with a physiological pulmonary ejection murmur and an unusually widely split second sound.[43] However, since such lesions are exceptionally rare[12, 44-46] this problem is seldom encountered.

Pulmonary stenosis (Fig. 1D and Fig. 3) is characterized by a harsher and longer systolic murmur with a delayed and soft P2.[5] The length of the murmur[5, 6] and the degree of delay and softness of P2[47] correlate with the severity of the outflow obstruction (Fig. 3). Obstruction may be above, below or at valve level. Pulmonary valve stenosis is almost invariably congenital, but acquired conditions such as carcinoid[48] or myxomatous tumour[49] of the valve may occasionally be the causative factor. Subvalvular obstruction is also usually congenital in origin and is most often at infundibular level. However, the recently described entity of double-chambered right ventricle,[50, 51] in which the site of obstruction is in the body of the ventricle, is a second congenital cause. Acquired right ventricular obstruction is found in hypertrophic obstructive cardiomyopathy, and it has been reputed that this condition may occasionally involve the right side of the heart only.[52] Obstruction occurring above the valve is uncommon, but may be produced by external pressure on the pulmonary artery from a mediastinal tumour,[53] aortic aneurysm,[54] pericardial cyst,[55] or localized constrictive pericarditis.[56] A congenital stenosis of the main pulmonary trunk is another rare cause of right ventricular outflow obstruction.[57]

A pulmonary systolic murmur is also produced by dilatation of the main pulmonary artery which may be idiopathic (Fig. 1C) or secondary to pulmonary hypertension. An ejection click is frequently present, and on this feature alone pulmonary artery dilatation should be suspected.[58] Associated signs of idiopathic dilatation of the pulmonary artery may include wide splitting of the second sound with loud P2[59] and an early diastolic murmur of pulmonary incompetence. Many such cases have a small gradient across the pulmonary valve and it is possible, at least in some instances, that a bicuspid valve is responsible for the mild stenosis and the pulmonary artery dilatation.

2. *Aortic Ejection Systolic Murmur*

Aortic ejection systolic murmurs (Fig. 4) are often

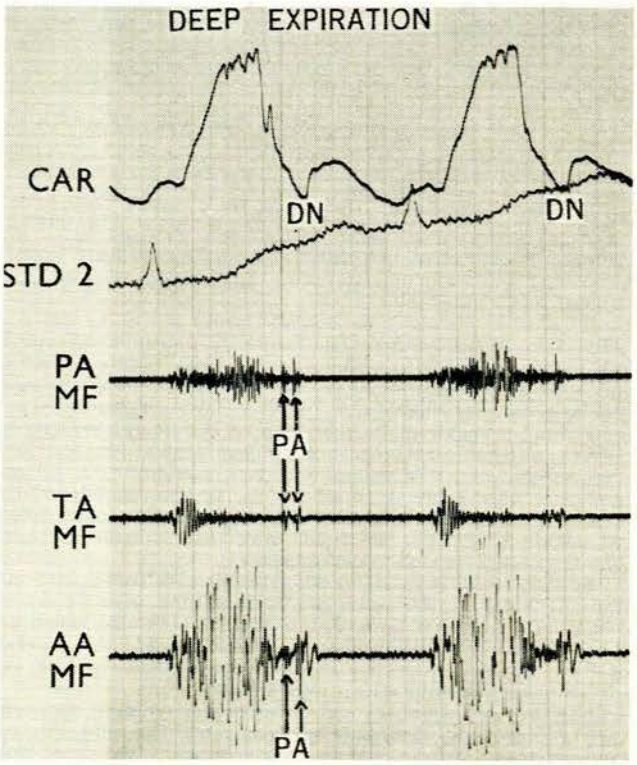

Fig. 4. Valvular aortic stenosis (gradient 130 mm.Hg). The ejection murmur is long and accentuates in mid-systole. The second heart sound is paradoxically split (see text). CAR=external carotid tracing, DN=dicrotic notch, PA = pulmonary area, TA = tricuspid area, AA = aortic area.

audible over the entire precordium and may be maximal at the apex, base or left sternal border.[60-62] They are louder in the second right intercostal space than the corresponding space on the left, and a characteristic feature is their specific radiation to the carotid arteries. They are therefore better heard over the carotids than over the adjacent tissues of the neck.[16] Aortic systolic murmurs are harsh and have the crescendo-decrescendo shape of all ejection murmurs. If there is significant stenosis, the murmur is longer and accentuates in mid- or late systole.

Unlike pulmonary murmurs, an aortic ejection systolic murmur does not occur in a normal heart.[16] However, cases of complete heart block with a large stroke volume often have prominent basal systolic murmurs,[63] and it is possible that some of these are partly of aortic origin. In the absence of dilatation of the aorta or organic valve disease, aortic ejection murmurs occur in systemic hypertension[62] and have been reported[64] in patients with a narrow antero-posterior diameter of the chest. In our experience, however, the basal murmurs caused by either a depressed sternum or the so-called straight-back syndrome are invariably of right-sided origin.

Isolated aortic systolic murmurs are not unusual in the older age group and have been shown by Bruns and Van der Hauwaert[17] to result from atherosclerotic thickening of the base of the cusp. In young subjects the commonest cause of an aortic ejection murmur is rheumatic disease, but an early diastolic murmur and evidence of associated mitral valve involvement is then often present. The reported incidence of congenital bicuspid aortic valves in the general population has varied from 0·14[65] to 1%.[66] Bicuspid valves are subject to early degenerative thickening and sclerosis[67, 68] and it is probable that this anomaly is a common cause of an isolated aortic systolic murmur.[16, 67, 69] They are particularly liable to develop subacute bacterial endocarditis,[68, 70-72] and an incidence as high as 25% has been given.[14] It is therefore important to realize that an isolated aortic systolic murmur may be the only sign of this congenital valve anomaly. Other causes of aortic valve pathology include rheumatoid arthritis,[73, 74] ankylosing spondylitis,[75, 76] Hunter's polydystrophy,[77, 78] lupus erythematosus,[79] Marfan's syndrome,[80] syphilis, hypercholesterolaemic xanthomatosis[81] and Ehlers-Danlos syndrome.[82]

In haemodynamically significant aortic stenosis there is delay and a decreased intensity of A2. The delayed aortic closure can be detected by paradoxical splitting[83] of the second sound which is therefore single in inspiration and reduplicated in expiration (Fig. 4). In less severe cases or where there is a large respiratory movement of P2, we have found that P2 will precede A2 in expiration but will follow it in inspiration. We have called this 'pseudoparadoxical' splitting. Valvular aortic stenosis may be congenital or the result of rheumatic endocarditis. Calcific aortic stenosis usually involves a valve which is bicuspid, and Edwards[84] considers that the majority of these bicuspid aortic valves have a congenital rather than a rheumatic background.

Subaortic stenosis has been classified into the discrete and diffuse varieties.[85] Discrete subaortic stenosis is produced by a congenital subvalvular membrane or fibromuscular band. Diffuse subaortic stenosis consists of an area of hypertrophied muscle which obstructs left ventricular outflow. Such hypertrophy is invariably part of the generalized cardiac muscle disorder known as functional hypertrophic subaortic stenosis[86] or idiopathic hypertrophic obstructive cardiomyopathy.[87] Glycogen storage disease[88] is another process which may cause diffuse myocardial involvement and secondary subaortic stenosis.

Stenosis above the valve is a rare site of obstruction to left ventricular outflow. Three forms[84] are recognized — the hour-glass, membranous and hypoplastic types. Associated features, such as hypercalcaemia,[89, 90] pulmonary artery stenosis,[91] and mental deficiency with a characteristic facies,[91, 92] may be found.

The clinical distinction of these forms of left ventricular outflow obstruction is difficult. However, the characteristics of the systolic murmur and the presence or absence of an ejection click and an early diastolic murmur are helpful. Supravalvular aortic stenosis has no ejection click or diastolic murmur, and the systolic murmur is usually maximal just below the right clavicle.[91] Ejection clicks are common in valvular stenosis but, according to Braunwald *et al.*,[85] also occur in about one-third of patients with discrete subvalvular stenosis. The incidence of aortic early diastolic murmurs in subaortic stenosis is high.[85, 93] The murmur of hypertrophic obstructive cardiomyopathy is characteristically late in onset (Fig. 2C and Fig. 5). It is

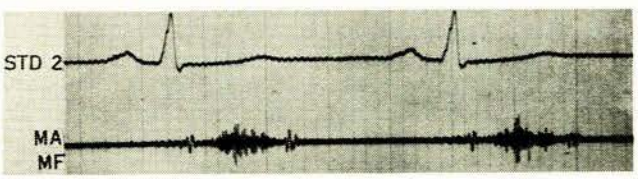

Fig. 5. Obstructive cardiomyopathy. The onset of the murmur is 0·08 seconds after the first heart sound and 0·15 seconds after the Q of the electrocardiogram.

loudest at the lower sternal border and does not radiate well to the carotids. Unlike any other systolic murmur of left-sided origin, this murmur decreases in intensity following phenylephrine[94, 95] and methoxamine[95] and is sometimes louder during the straining phase of a Valsalva manoeuvre.[46] In rare instances early diastolic murmurs[95, 96] and ejection clicks[95, 96] have also been observed.

3. *Vibratory Systolic Murmur*

This murmur was first described in 1909 by George Still[97] as a 'physiological bruit'. Common in childhood, the incidence decreases during adolescence, although the murmur may still occur in young adults.[16, 27, 29] It was present in 85% of 146 children with systolic murmurs studied by Fogel.[27] In another series,[16] a vibratory systolic murmur was heard in 67% of 200 normal children, 25% of 100 normal pregnant women and 10% of 100 normal young adults. The characteristic feature is the low-pitched buzzing quality which has resulted in a variety of descriptive terms such as 'musical',[22] 'twanging string',[98] 'fiddle string'[99] and 'vibratory'.[100] Fogel,[27] who prefers the title 'parasternal-precordial' murmur, mentions that 'squeaky', 'rasping', 'snorting', 'groaning', 'scraping' and 'grating' are other terms which have been employed.

The site of maximal intensity of the murmur is the lower sternal border or inside the apex, but it may be

heard over the entire precordium and the carotids.[16, 99] Usually grade 1—3 in intensity, it is sometimes as loud as grade 4.[22, 27, 46] The murmur is short, ending before or just after mid-systole, and is crescendo-decrescendo in shape. It increases in intensity with exercise[27, 29, 101] and amyl nitrite inhalation.[33, 101] A phonocardiogram (Fig. 6)

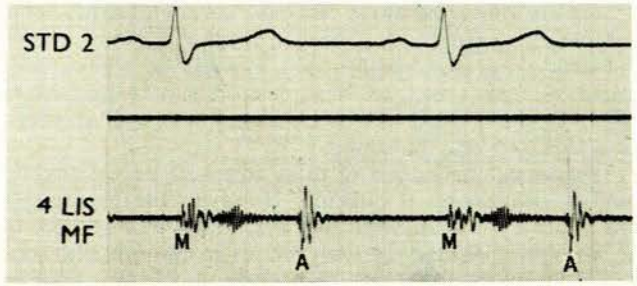

Fig. 6. Vibratory systolic murmur. The regular, low-frequency vibrations are well demonstrated.

shows typical uniform vibrations of low frequency, the onset of which are separated from the first heart sound by a short interval.[16, 27, 29, 100-103] The second heart sound is normal in all respects.

The exact cause and site of origin remain uncertain. Vibration of part of the heart muscle,[103] an extracardiac origin[22] and 'trigonoidation' of the pulmonary cusps[22] or another mechanism operating at this site,[104] are some of the theories that have been put forward. Stuckey[105] postulated that it is produced by a disproportion between the size of the normal aortic valve orifice and the ascending aorta. On the response of the murmur to a Valsalva manoeuvre, Barlow and Bosman[106] confirmed a left-sided origin and suggested that it is produced in the left ventricular outflow tract. Whatever the exact site of origin, there is little doubt that the murmur is innocent and this is supported by a recent 20-year follow-up of 96 cases.[107]

4. *The Regurgitant Systolic Murmur of Small Ventricular Septal Defect*

Defects of the ventricular septum may be single or multiple. Usually congenital, they are situated high in the membranous or low in the muscular part of the septum. Less commonly the defect is acquired and may be secondary to rupture of a myocardial infarction[108, 109] or a congenital aneurysm[110] involving the septum. Traumatic perforation of the septum[111] or septal rupture following closed chest injury[112] are other rare causes of acquired ventricular septal defect.

The typical murmur of ventricular septal defect is pansystolic,[42, 113, 114] often accompanied by a thrill, and is usually loudest in the third or fourth intercostal space. It is crescendo-decrescendo in shape with maximal accentuation in mid-systole (Fig. 7A). Late systolic accentuation (Fig. 7B) is sometimes seen in small defects.[46, 115] The murmur is often harsh but may have a high-pitched blowing quality. In small left-to-right shunts the second heart sound is usually normal, although some authors[113, 116] consider that wide splitting is common. An apical mid-diastolic flow murmur is seldom present if the shunt is less than 2:1.[46, 113]

If the second heart sound is normal and a pulmonary ejection click absent, the murmur of mild pulmonary stenosis may be confused with that of a ventricular septal defect. The distinction should then be made by the re-

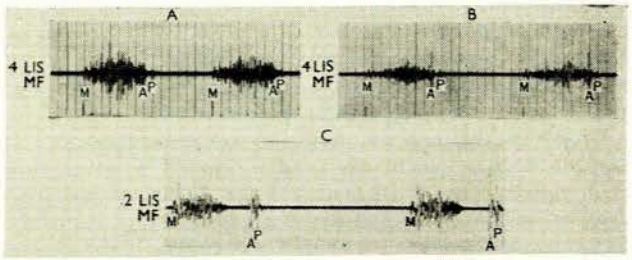

Fig. 7. Ventricular septal defect.

A. Pansystolic crescendo-decrescendo murmur with mid-systolic accentuation.

B. Pansystolic crescendo-decrescendo murmur with maximal accentuation later in systole.

C. Short 'atypical' murmur.

sponse to vasoactive drugs and the Valsalva manoeuvre. However, these methods are not contributory in the differentiation of mild mitral incompetence from ventricular septal defect, since in both the regurgitant murmur is left-sided and the response thus identical. A murmur of mitral regurgitation is usually loudest at the apex and radiates to the axilla, but difficulty may arise in children where the precordial area is small. Furthermore, the quality of both murmurs is similar, and although late systolic accentuation is common in mitral incompetence, this can occur in small ventricular defects. We have found, however, that the presence of an apical mid-diastolic murmur and a careful assessment of the second sound are invaluable in differentiating mild mitral regurgitation from a small ventricular septal defect. Whereas a normal second sound and a short mid-diastolic murmur are common in mild mitral incompetence, a mid-diastolic murmur is not present in a ventricular septal defect unless the shunt is significant. In such cases the second sound is widely split, P2 increased in intensity, and clinical evidence of some right ventricular hypertrophy apparent. Thus a left-sided regurgitant systolic murmur with a mid-diastolic murmur and normal second sound favour mild mitral incompetence, whereas in the absence of a mid-diastolic murmur, the diagnosis is likely to be that of a small ventricular septal defect. Differentiation from a regurgitant systolic murmur of tricuspid incompetence is seldom a problem in view of the rarity of this condition as an isolated entity. Should difficulty arise, the effects of vasoactive drugs are again of value.

5. *Atypical Systolic Murmur of Minute Ventricular Septal Defect*

Very small defects of the ventricular septum cause a crescendo-decrescendo murmur which ends well before the second heart sound (Fig. 7C) and therefore resembles an ejection murmur.[42, 116, 117] This 'atypical' murmur is usually maximal at the fourth left intercostal space or lower sternal area and often has a high-pitched blowing quality. It is easily recognized but, should difficulty arise,

a decreased intensity after amyl nitrite inhalation and increased intensity after phenylephrine injection (Fig. 8) will distinguish it from any isolated ejection murmur.

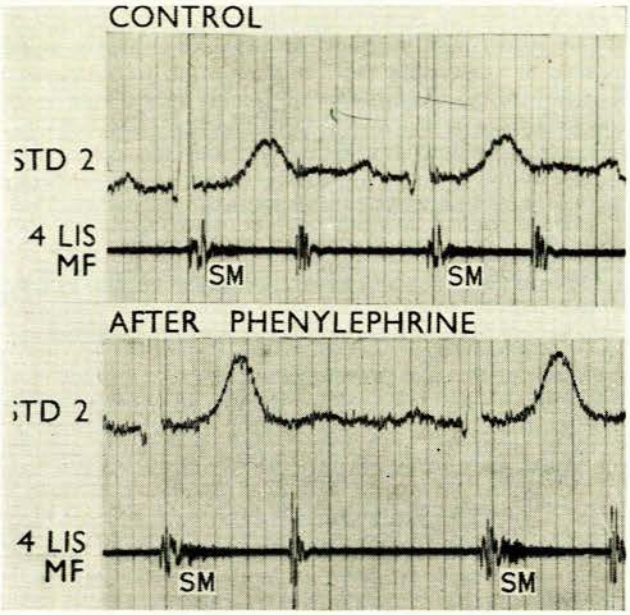

Fig. 8. Atypical murmur of small ventricular septal defect. Phonocardiograms before and after the injection of phenylephrine showing the increase in intensity of the regurgitant murmur during the period of hypertension.

The left-to-right shunt is too small to be detected by oxygen saturations, and shunts of less than 10% have been demonstrated with dye dilution techniques.[117] The murmur is an example of a regurgitant murmur being *non-pansystolic* owing to an anatomical factor. A large ventricular septal defect with increased pulmonary resistance will also result in a non-pansystolic regurgitant murmur, but this is readily distinguished from that of a minute defect by the accompanying signs of pulmonary hypertension.

6. *The Regurgitant Systolic Murmur of Mitral Incompetence*

Mitral incompetence is produced by abnormalities of the valve leaflets, annulus, chordae tendineae or papillary muscles. The many causes include rheumatic and bacterial endocarditis, atherosclerosis, systemic lupus erythematosus,[79] rheumatoid arthritis,[74] Marfan's syndrome,[80, 118, 119] Hunter's polydystrophy,[77, 78] left atrial myxoma,[120-122] Ehlers-Danlos syndrome,[82] endomyocardial fibrosis,[123] subvalvular left ventricular aneurysms,[124, 125] ruptured chordae tendineae,[19-21] rupture[126] or dysfunction[127, 128] of a papillary muscle, hypertrophic obstructive cardiomyopathy,[86, 87, 95, 96] congenital cleft leaflet,[129, 130] aneurysmal protrusion of the posterior leaflet,[131] and ostium primum defects.

The systolic murmur of mitral regurgitation is loudest at the apex and usually radiates to the axilla. It may be audible over the whole precordium and over the back.[132] Prominent medial radiation is a feature of posterior leaflet incompetence.[133] The murmur is commonly blowing but can be harsh or even musical (Fig. 2A and B).

Although an apical systolic murmur may provide the only evidence of mild mitral incompetence, more significant regurgitation has other auscultatory features. The mitral component of the first sound is soft except where the pathology is mainly confined to the posterior leaflet. Owing to shortened left ventricular ejection, A2 occurs early and is of decreased intensity. The second sound is therefore widely reduplicated although the degree of splitting still varies during respiration. A short loud starting mid-diastolic murmur is invariably heard at the apex.

The typical murmur of mitral regurgitation is pansystolic[7, 132] in that it starts with the mitral closure sound and extends up to, or just beyond, the aortic component of the second sound. However, it has recently been demonstrated that the murmur may occupy part of systole only.[25, 37, 134, 135] If the length and shape of the murmur were determined solely by the pressure gradient between the left ventricle and left atrium, it would always be pansystolic with maximal accentuation in mid-systole, at the time of the largest gradient. However, such configuration is seen only where there is gross incompetence (Fig. 9B)

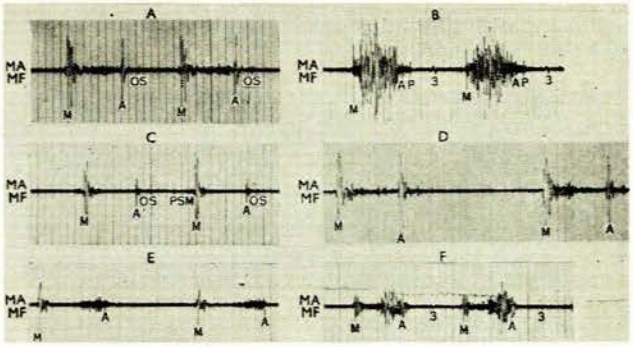

Fig. 9. Phonocardiograms of 6 types of regurgitant murmurs of mitral incompetence — for explanation and full description, see text. A = pansystolic plateau-shaped, B = crescendo-decrescendo, C = decrescendo, non-pansystolic, D = decrescendo pansystolic, E = late systolic, F = pansystolic with late accentuation. (3 = 3rd heart sound, PSM = pre-systolic murmur)

and is well exemplified by the pansystolic crescendo-decrescendo murmur of ruptured chordae tendineae. The configuration, time of onset and length of other systolic murmurs of mitral regurgitation must therefore depend on another factor.

The functional anatomy of the mitral valve is complex,[129] and Barlow[25] postulated that functional anatomical factors during ventricular contraction control the degree of regurgitation in early, mid-, or late systole, and consequently the length and shape of the systolic murmur. Decrescendo (Fig. 9D) and late accentuating (Fig. 9F) pansystolic murmurs imply maximal regurgitation during early and late systole respectively, whereas a constant degree of reflux results in a plateau-shaped (Fig. 9A) pansystolic murmur. The same mechanism would explain a *non-pansystolic* murmur of mitral regurgitation in which the valve is incompetent during part of systole only, thus resulting in an early descrescendo murmur (Fig. 9C) or one confined to late systole (Fig. 9E).

The murmur confined to late systole has, in fact, provoked some interest and warrants discussion as a separate entity. Whereas it has generally been accepted that an apical late accentuating pansystolic murmur results from mitral regurgitation,[3] the murmur which has no early systolic vibrations on a phonocardiogram has been regarded as innocent[40, 103, 132, 136] and probably extracardiac in origin.[22, 23, 137-141] Mid-late (non-ejection) systolic clicks are often associated with late systolic murmurs, and these have also been thought to arise outside the heart.[137, 142-146] By cine-angiocardiography and other means it has now been conclusively demonstrated that an apical late systolic murmur denotes mild mitral regurgitation.[25, 37, 118, 125, 131, 134, 135, 147] On the available evidence, it is very probable that the frequently associated non-ejection systolic clicks are intracardiac in origin and are produced by abnormality of the chordae tendineae.[25, 37, 131, 148, 149] A few soft vibrations occurring immediately before or after a non-ejection systolic click can occasionally be heard and demonstrated phonocardiographically (Fig. 10) as an extremely short scratchy 'murmur'. Humphries and McKusick[140] postulated a pericardial origin for this 'circumscribed' murmur, but in our opinion it is produced by a vibratory movement of abnormal chordae tendineae.

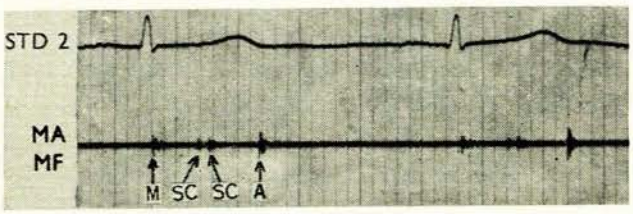

Fig. 10. Phonocardiogram of a symptomless 15-year-old girl. Two non-ejection clicks are demonstrated. A few vibrations follow the second click which gave the clinical impression of a short scratchy murmur.

Burch and co-workers[127, 128] consider that a specific type of non-pansystolic regurgitant murmur is produced by papillary muscle dysfunction. This murmur has a delayed onset, is crescendo-decrescendo in shape and reaches peak intensity in late systole. These authors postulated that the delayed onset and configuration of the murmur depended on functional anatomical factors. While agreeing with this postulate, in our experience the murmur of papillary muscle dysfunction does not differ essentially from any other late accentuating murmur of mitral regurgitation and, depending on the severity of the lesion, can vary from a pansystolic murmur to one confined to late systole.

7. *The Regurgitant Systolic Murmur of Tricuspid Incompetence*

Functional tricuspid incompetence is considerably more common than organic lesions of this valve and follows right ventricular dilatation from any cause.[42, 150] The signs of the underlying disease are then readily apparent.

Lone organic tricuspid incompetence is extremely rare. The commonest cause of organic tricuspid regurgitation is rheumatic disease, but there is then invariably associated mitral valve involvement.[151, 152] The carcinoid syndrome[48] and a right atrial myxoma[153, 154] are rare causes of tricuspid regurgitation. Congenital tricuspid incompetence may occur in association with endocardial cushion defects. Soft tricuspid systolic and mid-diastolic murmurs have been observed in several patients with pectus excavatum,[46] and these are possibly due to distortion of the valve ring.

The regurgitant murmur of organic tricuspid incompetence is pansystolic and characteristically increases in intensity during inspiration. It is best heard high in the epigastrium or at the lower sternal border. The immediate return after a Valsalva manoeuvre and the increased intensity following amyl nitrite inhalation would distinguish this murmur from that of a ventricular septal defect.[33]

8. *Vascular Murmurs*

Extracardiac murmurs arising in vessels of the neck and thorax require consideration since they may either mimic intracardiac murmurs or be misleading in their assessment.

(a) *Innocent Vascular Murmurs*

1. *Venous hum.* Over 75% of children and young adults,[141] and approximately 50% of older patients[141] are reputed to have a venous hum. This bruit is particularly common in high output states, and though characteristically a continuous murmur,[155] in the supine position it is frequently confined to systole.[156] Inspiration, the upright posture or rotation of the neck to the opposite side will increase the intensity of the murmur. Audible on one or both sides of the neck, a venous hum may radiate as far down as the third intercostal space.[141] Differentiation from an intracardiac murmur is made by its disappearance with pressure on the jugular veins.[155]

2. *Arterial bruit.* Innocent cervical arterial bruits are also common in children and young adults[141, 157] and possibly arise at the aortic arch[158] or the bifurcation of the innominate artery.[29] They are distinguished from an intracardiac ejection murmur, with which they may be coincidentally associated, by their short duration, greater intensity above the clavicles, delayed onset, and different quality.

3. *Mammary souffle.* In some pregnant women blood flow through dilated mammary vessels produces a murmur known as a mammary souffle.[159] This bruit is either continuous or confined to systole. It is abolished by firm pressure with the end-piece of a stethoscope and thus easily distinguished from all intracardiac murmurs.

(b) *Pathological Vascular Murmurs*

Murmurs produced by a communication between the systemic and pulmonary circulations, such as a patent ductus arteriosus, are continuous unless the diastolic component is abolished by a raised pulmonary vascular resistance. The systolic murmur is then, however, accompanied by signs of severe pulmonary hypertension.

A murmur can be regarded as continuous when vibrations extend through the second sound into diastole. Murmurs produced by reduction in the internal diameter of an artery are continuous or systolic in timing, depending on the degree of narrowing and the distance of the site of origin from the heart. Thus a tight constriction will result in a high pressure gradient in both systole and diastole, and the murmur may then be heard throughout the cardiac cycle. Even with a milder narrowing, however, the distance from the heart of the site of origin of a murmur produced only in systole, may result in its extending past the second heart sound.

The murmur of coarctation of the aorta[160] is heard at the apex, second left intercostal space, and back. The onset of the murmur is delayed and it may be confined to systole or flow over into diastole. A similar late onset systolic or continuous murmur is found in pulmonary artery

stenosis.[161, 162] Although this condition is generally associated with other congenital cardiac anomalies, such as ventricular septal defect, pulmonary stenosis, or supravalvular aortic stenosis, it is occasionally an isolated lesion.[56, 163] The murmur may be loudest on either side of the sternum, the lateral chest wall, or even posteriorly.[57, 162]

SUMMARY

1. The problem of the assessment of an isolated systolic murmur is one of the commonest which is encountered by a physician. It can almost invariably be solved by clinical examination alone, without resort to complicated diagnostic procedures.

2. The concept, based on haemodynamic considerations, of ejection and regurgitant systolic murmurs is discussed.

3. Consideration of the intensity and width of splitting of the aortic and pulmonary components of the second heart sound is essential to the correct interpretation of every systolic murmur.

4. Systolic murmurs should be assessed in terms of the site of maximal intensity, radiation, quality, length and timing, and the influence of respiration and posture. The effect of haemodynamic alterations produced by vasoactive drugs and the Valsalva manoeuvre provides additional diagnostic information.

5. The characteristics, causes and significance of the following isolated systolic murmurs are discussed: Pulmonary and aortic ejection, vibratory, regurgitant murmurs of small and minute ventricular septal defect and regurgitant murmurs of mitral and tricuspid incompetence. Vascular murmurs, which may cause difficulty in the assessment of intracardiac murmurs, are briefly mentioned.

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