6 Heart Sounds

Contents

PRINCIPLES OF SOUND FORMATION IN THE HEART

In the past, many theories have been advanced to explain the origins of sounds during the cardiac cycle. These included simple concepts of sound originating from the actual contact of valve cusps upon closure. When it was realized that the strength of contraction of the left ventricle had a significant effect on the intensity of the first heart sound, the myocardial theory of the origin of the sound was postulated. Some even had suggested extracardiac origin of sounds such as the third heart sound. It is now, however, well established by several investigators and accepted that the formation of all sounds in the heart can be explained by a "*unified concept*" *(1–10)*.

It is a common experience to hear sound produced when a pipe half-filled with water is moved back and forth, splashing the water against the two palms of the hands held against the ends of the pipe. We have all heard banging sounds sometime produced in the water pipes of the plumbing systems of our homes when air is introduced into the plumbing. In both examples, the mechanism of sound production is the same. When the moving column of water in either case comes to sudden stop or marked deceleration, the energy of the column dissipates and in the process generates vibration of the pipes as well as the column of water. These vibrations, when they are in the audible range, are heard as sounds. The intensity of the sound will very much depend on the initial energy of the moving column of water. Of the two examples, the sounds in the second case are usually very loud and may be heard throughout the whole house. This is mainly because the water pressure in the system is approximately 40 lb/in^2.

Similarly, all heart sounds are formed when a moving column of blood comes to a sudden stop or decelerates significantly. The intensity of a heart sound will depend on the level of energy that the moving column of blood has attained. The sudden deceleration causes dissipation of energy, which results in the production of vibrations affecting the contiguous cardiohemic mass *(3)*. The factors affecting the acceleration and deceleration of columns of blood involved in the formation of the various heart sounds are different and may be many. These will have to be considered for each sound separately, taking into account the physiology and the pathophysiology of the phase of the cardiac cycle involved.

FIRST HEART SOUND (S1)

The first heart sound occurs at the onset of ventricular contraction. To better understand the physiology of the first heart sound, one needs to know the cardiac events that occur around the time of the first heart sound. At the end of diastole, the atrium contracts and gives an extra stretch and filling to the ventricle. This is immediately followed by the ventricular contraction. When the ventricular pressure rises and exceeds the atrial pressure, the mitral and the tricuspid valve leaflets become apposed and close. As the ventricular pressures continue to rise and exceed that of the aorta and the pulmonary artery, the semilunar valves open and the ejection phase begins. All these events occur in rapid succession over a short period of time and contribute to the production of the first heart sound. As a result, S1 is relatively wide and is made of many components, which overlap each other. These components are "atrial," "mitral," "tricuspid," and "aortic" *(2, 5,7,10–14)*.

Atrial Component

The energy of the column of blood pushed by the atrial contraction becomes dissipated as the column decelerates against the ventricular walls. This deceleration is gradual in most normal subjects because of good compliance and distensibility of the ventricles. Therefore, the sound generated by this has a very low frequency and is not audible. This will be discussed further in relation to the fourth heart sound. However, when the PR interval on the electrocardiogram is short, this component can occur very close to the onset of the ventricular contraction and actually be part of the first heart sound and contribute to its duration. Aside from this, it has no clinical significance *(11,14)*.

Mitral Component

This is the most important component of S1. It corresponds in timing to the closure of the mitral valve leaflets *(10,12)*. However, the mere apposition of the valve leaflets does not produce the sound. As the ventricle starts contracting, the pressure rises and imparts energy into the mass of blood within its cavity. When the pressure in the ventricle just exceeds that of the atrium, the column of blood is put into motion. Since the aortic pressure is much higher than the atrial pressure and the aortic valve remains closed at this time, the blood contained in the ventricle can only rush toward the atrium. Because of the anatomical construction of the mitral valve similar to that of a parachute, the leaflets are lifted by the moving blood into a closed position. The papillary muscles contracting and pulling on the chordae tendineae prevent leaflet eversion into the atrium. The closed leaflets held back by the papillary muscles, reaching the limits of their stretch, stop the column of blood from moving into the atrium. This sudden deceleration of the column of blood causes the mitral component, or M1 (Figs. 1 and 2A,B). The energy dissipation

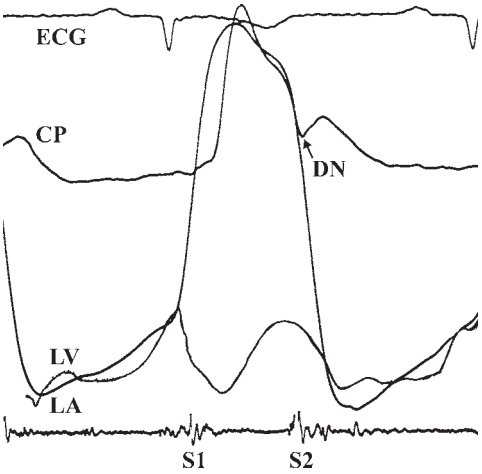

Fig. 1. Simultaneous recordings of electrocardiogram (ECG), carotid pulse (CP), left ventricular (LV), and left atrial (LA) pressures. When the rising LV pressure exceeds the LA pressure, the column of blood contained in the ventricle is put into motion because the aortic valve is still closed at this time. Because the LA pressure is relatively low, the column of blood will tend to rush toward the LA. The anatomical construction of the mitral valve is such that the leaflets close and are prevented from eversion by the contraction of the papillary muscles. The valve closure leads to sudden deceleration of the moving column of blood. The resulting dissipation of energy leads to the production of the mitral component of the S1. The rise of CP indirectly reflects aortic pressure rise. However, there is a transmission delay. DN, Dicrotic notch.

causes vibrations of the column of blood as well as the entire surrounding structures, i.e., the mitral valve structures and the ventricular wall *(15)*. The mechanism of sound formation of this M1 is very similar to the sound produced by the parachute filling with wind as it stretches and causes the deceleration of the moving mass of air or by the sail of a sailboat that snaps when filled with a gust of wind.

Tricuspid Component

This component is obviously similar in origin to the M1 for similar cardiac events occur involving the right-sided structures, namely, the tricuspid valve leaflets and the right ventricular wall. However, these events occur at much lower pressures and slightly delayed. The effects of the mechanical events of the right ventricle begin slightly later than that of the left ventricle. Therefore, the tricuspid component (T1) follows the M1 *(13)*. It must be noted that this component because of the lower pressures is usually low in frequency. The T1 in the normal adult subjects, although it may be recordable, may contribute to the duration of S1 but not be audible as a distinct component *(16,17)*.

Aortic Component

The aortic component (A1) is usually the second component of audibly split S1 in adults *(7,17)*. After mitral and tricuspid valve closures, the ventricular pressure continues to rise during the phase of isovolumic contraction. When the pressure exceeds the aortic and pulmonary diastolic pressures, the ejection phase begins as the semilunar valves open. The column of blood ejected into the aorta as it hits the aortic walls decelerates and when the deceleration is significant will result in an audible sound *(18)* (Fig. 2C).

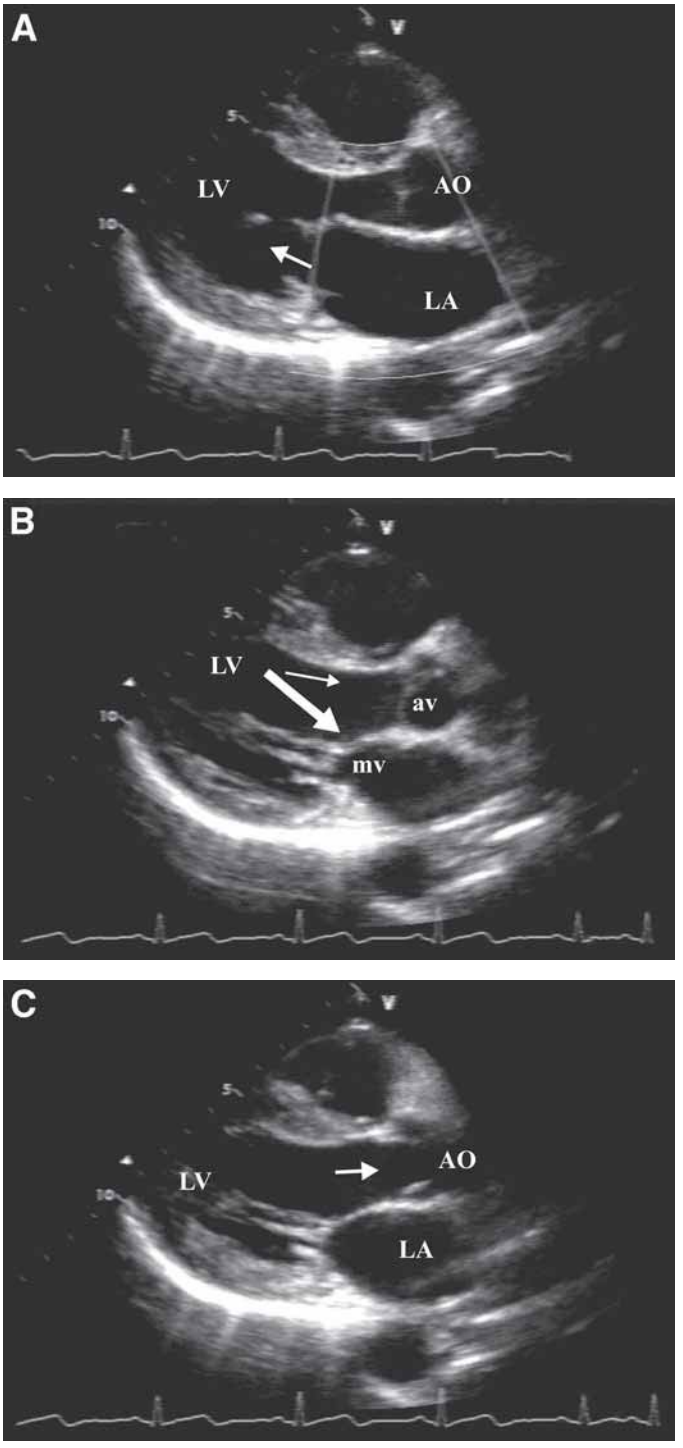

Fig. 2. Stop frames from the two-dimensional echocardiographic recordings taken in the parasternal long axis from a normal subject showing the left ventricle (LV), mitral valve (mv), left atrium (LA), aorta (AO), and aortic valve (av) at end-diastole **(A)**, onset systole **(B)**, and onset ejection **(C)**.

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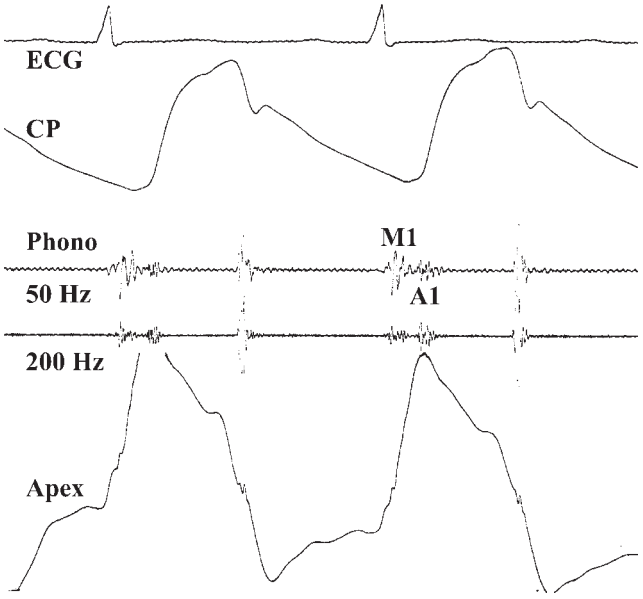

Fig. 3. Phonocardiogram (Phono) recorded at the lower left parasternal area close to the apex showing two distinct components of the normal S1, namely the mitral component M1 and the aortic component A1. The M1 precedes the onset of the carotid pulse, whereas the A1 occurs with it. Note the externally recorded carotid pulse tracing has a pulse transmission delay. Simultaneously recorded electrocardiogram (ECG), carotid pulse (CP), and apexcardiogram (Apex) are shown to indicate the timing.

Normal S1

Because the major and the most important component of S1 is M1, the S1 is usually heard loudest at the apex and the lower left sternal border around the fourth left intercostal space. The sound is usually low pitched and longer in duration compared to the sharper, shorter, and higher-frequency second heart sound (S2). It can be timed to occur at the onset of a carotid pulse or the apical impulse and is a useful way of distinguishing it from S2. It can be mimicked by the syllable "Lubbb" as opposed to the sharper S2, which sounds like "dub." It may be audibly split into two components in some patients when the separation exceeds at least 20 ms. When such a split is heard it could be because of M1-T1 in children and young adolescents and is usually due to M1-A1 in the adults (Fig. 3). The T1 component tends to be maximally heard over the sternum and the left sternal border and not usually over the apex, which is formed by the left ventricle in the

Fig. 2. *(Continued)* The heads of the arrows indicate the direction of movement of the column of blood in the left heart. At end-diastole, the diastolic filling of LV is nearly completed. With onset of systole, the rising LV pressure puts the column of blood into motion, with the main direction (thicker arrow) toward the low-pressure LA, where it is decelerated by the closure of the mv. This leads to production of the mitral component M1. When the rising LV pressure exceeds the aortic pressure with further contraction of the ventricle, the aortic valve opens and ejection phase begins. When the ejected column of blood hits the walls of the aorta, deceleration occurs again, leading to the production of the A1.

normal subjects. T1 also tends to get louder on inspiration because of greater volume and Starling effect during inspiratory phase of respiration on the right side. The A1, on the other hand, does not vary with respiration and is just as loud over the apex.

It must be pointed out that not all patients have a split S1 that is audible. This may be because of various factors involved in the production of the T1 and the A1. The normal T1 may not be loud enough to be audible. The A1, which occurs after the isovolumic contraction phase, may be too narrowly split to be heard as a separate distinct sound, especially when the isovolumic phase is short. The other reason may be that the orientation of the left ventricular axis in relation to the aortic axis may be such that the ejected blood easily flows out into the aorta without much deceleration at the walls. When the axial orientations form a less obtuse angle, the chances for greater deceleration and formation of audible A1 component increase. Such variations in the axial orientations can be observed in angiographic or two-dimensional echocardiographic studies in most patients.

Intensity of S1 (Loudness)

The intensity of S1 is obviously related to the intensity or loudness of the individual components, namely M1, T1, and A1. Since the major determinant of S1 intensity is M1, we shall consider this first.

M1 Intensity

Because the M1 component corresponds to the mitral valve closure and is produced by sudden deceleration and dissipation of energy of the moving column of blood in the left ventricle, its intensity will depend on the energy imparted to that column of blood by the contracting ventricle. The level of energy imparted will depend on the degree of acceleration achieved by the contracting myofibrils at the time of mitral valve closure. As the ventricle begins to contract, more and more myofibrils are recruited, which help in achieving faster rate of pressure rise (*dP/dt*) in the ventricle.

The mitral valve will close only when the pressure in the contracting left ventricle reaches and just surpasses the pressure in the left atrium. If the atrial pressure were high at the time of mitral valve closure, the ventricle would have achieved a high *dP/dt*. If the atrial pressure were low, on the other hand, at the time of mitral valve closure, the *dP/dt* achieved by the left ventricle would be similarly low. The energy in the moving column of blood in the left ventricle, which is dissipated upon closure of the valve, is dependent on the *dP/dt* achieved by the left ventricle at the time of closure. *The higher the* dP/dt *achieved by the contracting left ventricle at the time of mitral valve closure (the pressure crossover point), the louder will be the intensity of the M1 (6,12,19,20)*. The corollary of this implies that the lower the *dP/dt* is at the time of mitral closure, the softer will be the intensity of M1.

The *dP/dt* achieved at the time of mitral closure will depend on the contractility of the left ventricle and the left atrial pressure. The left atrial pressure at the time of mitral valve closure may be high for one of the following reasons:

1. Mitral stenosis or mitral obstruction
2. Incomplete atrial relaxation at the time of valve closure (short PR interval)
3. Short diastoles in atrial fibrillation
4. Heart failure
5. Mitral regurgitation

However, not all of the above are associated with a loud M1.

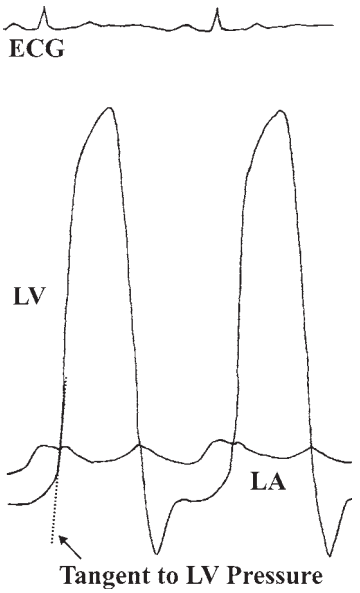

Fig. 4. Diagrammatic illustration of the left ventricular (LV) and left atrial (LA) pressure curves in a patient with mitral stenosis showing the diastolic pressure gradient between LA and the LV reflecting the mitral stenosis. When the rising LV pressure with onset of systole exceeds that of the LA, the mitral valve will close. Note that the tangent to LV pressure drawn at the point of the crossover of the two pressure curves during this phase of LV systolic pressure rise is steep, showing that the ventricle has achieved a faster rate of contraction and higher *dP/dt*.

M1 in Mitral Stenosis or Obstruction Secondary to Atrial Myxoma

It used to be thought that the loud S1 (M1) characteristic of severe mitral stenosis was caused by closure of the valve that was kept wide open by high left atrial pressure. Some even may have thought that calcification of the leaflets contributed to the intensity upon closure.

In mitral stenosis, S1 (M1) is loud because the valve closure occurs at a time when the *dP/dt* in the ventricle is high as a result of a higher pressure crossover point (Figs. 4 and 5). In some patients with very severe mitral stenosis, usually associated with heavily calcified valves, the M1 may not be loud. This probably stems from the fact that the left ventricles in such patients are grossly underfilled from the mitral obstruction and therefore are unable to achieve good contractility and *dP/dt*.

In left atrial myxoma, which causes mitral obstruction, the M1 will be loud for the same reason as in mitral stenosis.

M1 and PR Intervals

After left atrial contraction, if the left ventricle begins to contract before the left atrium has a chance to fully relax, the left atrial pressure will be high at the time of pressure crossover and mitral closure. This is likely to occur when the PR interval is short. This will result also in a louder M1 component (Fig. 6A). The corollary to this means that a long PR interval will result in a soft M1 (Fig. 6B). This is because of complete relaxation

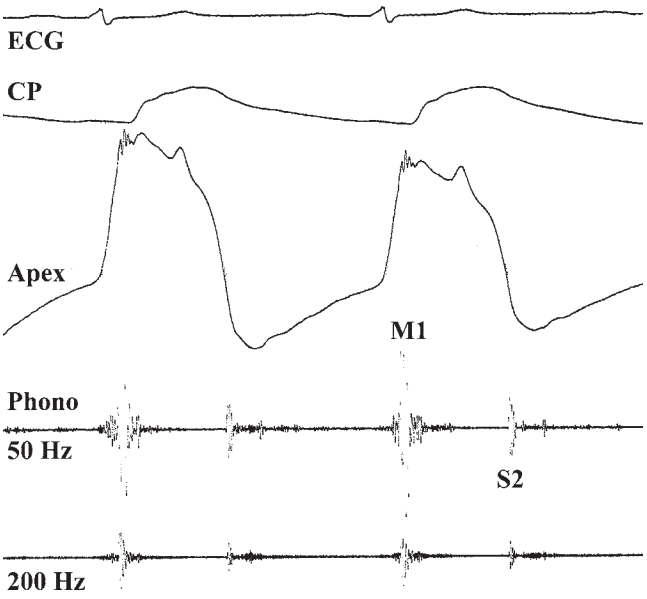

Fig. 5. Phonocardiographic (Phono) recording from a patient with mitral stenosis showing the loud intensity first heart sound caused by the loud mitral component M1.

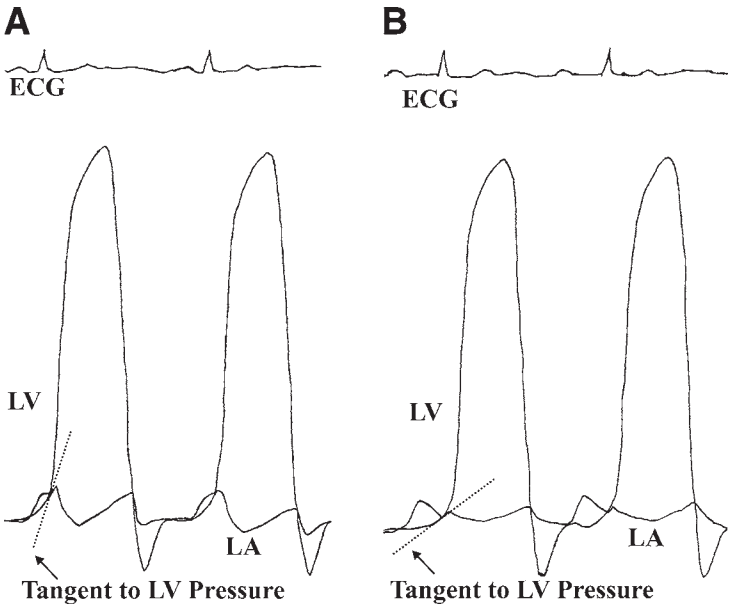

Fig. 6. Diagrammatic illustrations of the superimposed left ventricular (LV) and left atrial (LA) pressure curves to show the differences in the slope of the LV pressure rise at the point of the crossover of the two pressures with onset of systole caused by short PR interval **(A)** and long PR interval **(B)**. The slope is steeper when the PR is short, whereas it is flatter when the PR is long. This will result in M1 being loud when the PR is short, but soft when the PR is long.

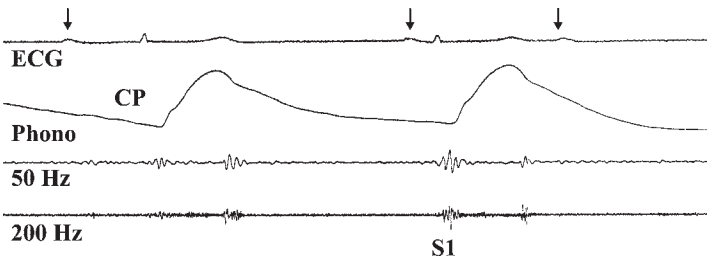

Fig. 7. Phonocardiographic (Phono) tracing from a patient with complete atrioventricular (A-V) block recorded from the apex area. Arrows show the nonconducted P waves in the electrocardiogram (ECG). The effect of the variations in the PR interval caused by the A-V block on the S1 intensity can be seen. The first beat with long PR has a poor-intensity S1, whereas the second beat with a shorter PR has much better S1 intensity.

of the left atrium before the left ventricular contraction and maximal fall in the left atrial pressure, resulting in a very low-pressure crossover point where the *dP/dt* achieved by the left ventricle will be low.

When the PR interval changes, as in atrioventricular (A-V) dissociation (e.g., complete A-V block) or type I second-degree A-V block (Wenckebach), the intensity of M1 will also vary according to the PR interval. It will be louder with shorter interval and softer with longer intervals (Fig. 7).

M1 and Short Diastoles in Atrial Fibrillation

Variable M1 intensity is also characteristic of atrial fibrillation. The mechanism, however, relates to the varying diastolic filling and its effect on contractility as well as varying levels of atrial pressure at the time of mitral closure. Following shorter diastoles, while the filling of the left ventricle may be poor leading to decreased Starling effect and contractility, the left atrial pressure does not have a chance to fall to lower levels. This results in a higher left atrial pressure. Since these two will have opposing effects on M1 intensity, usually the higher left atrial pressure effect dominates, causing louder M1 with shorter diastoles.

M1 in Heart Failure

Although the left atrial pressure in heart failure is invariably elevated, this does not always result in a loud S1. The marked decrease in contractility of the left ventricle results in a poor *dP/dt* development at the time of mitral closure. In these patients there is often a high sympathetic tone and high levels of catecholamines. These tend to compensate and attempt to improve the contractility of the myocardium. At times this may in fact succeed in improving the initial rise in left ventricular pressure, although the effect may not be sustained throughout systole. This may be sufficient to produce a reasonable intensity of S1. In very severely damaged hearts such compensation often does not result in any significant improvement in the *dP/dt*, and therefore the S1 (M1) is very soft and sometimes inaudible.

M1 in Mitral Regurgitation

Because the intensity of M1 is dependent on sudden deceleration of the moving column of blood in the left ventricle, the presence of significant mitral regurgitation

would preclude such sudden deceleration. This in effect may lead to a softer M1. On the other hand, the mitral regurgitation may raise the mean left atrial pressure and therefore the pressure crossover point. It also presents a volume overload effect for the left ventricle, thereby increasing its contractility through the Starling mechanism. These two effects will tend to increase the intensity of the M1. Therefore, the M1 intensity in mitral regurgitation in any given patient will depend on the severity of the mitral regurgitation, the acuteness of its onset, and the underlying left ventricular function. The opposing effects of these on the M1 may result in a normal M1 intensity.

In acute mitral regurgitation, the left atrial pressure usually rises much higher because of a relatively noncompliant left atrium. This in a patient with ruptured chordae with relatively normal left ventricular function may tend to favor production of a good intensity of M1 as long as the mitral regurgitation is not too severe. In severe mitral regurgitation, however, hardly any deceleration will be possible because of the valvular insufficiency. Similarly, in a patient with ruptured papillary muscle and acute myocardial infarction, the M1 will be inaudible. This is not only because of decreased myocardial contractility, but also mainly because of the wide-open nature of the mitral regurgitation and poor or no deceleration of the column of blood.

Lesions That Interfere With the Integrity of the Isovolumic Phase of Systole

The importance of the integrity of the isovolumic systole for the preservation of the intensity of the M1 has been pointed out by Shah *(12)*. This essentially pertains to the fact that for a good-intensity M1 to occur the column of blood needs to accelerate toward the mitral valve for it to be decelerated by the closure. The cited examples of lesions that interfere with the integrity of the isovolumic phase of contraction include significant mitral regurgitation, significant aortic regurgitation, large ventricular septal defect, and large ventricular aneurysm. In these entities, the moment the left ventricular pressure rises the ejection phase begins to transfer the blood out of the contracting left ventricle. The M1 in wide-open mitral regurgitation will be soft, as pointed out earlier. M1 in aortic regurgitation is of particular interest.

M1 in Aortic Regurgitation

Aortic regurgitation, being also a volume overload situation for the left ventricle, will lead to increased contractility and therefore would be expected to have a good amplitude of S1 (M1). In severe and acute types of aortic valve regurgitation, however, the left ventricular diastolic pressures often rise to very high levels to the point that the pressure in the left ventricle may equal the aortic diastolic pressure and exceed that in the left atrium before ventricular systole begins. This will essentially result in premature mitral valve closure. In some instances, the mitral leaflets could be incompletely closed with perhaps some diastolic bulging into the left atrium under the high left ventricular diastolic pressure, allowing some diastolic mitral regurgitation. However, with the onset of ventricular systole, the leaflets may be fully closed with papillary muscle contraction even before significant pressure rise, at a time when the developed dP/dt in the left ventricle will be still low. Because the left ventricular and aortic diastolic pressures are often equal, there will be very little or no isovolumic phase of contraction. The moment the ventricular pressure begins to rise faster, the ejection will occur with the column of blood essentially moving toward the aorta. Because the mitral valve is already closed,

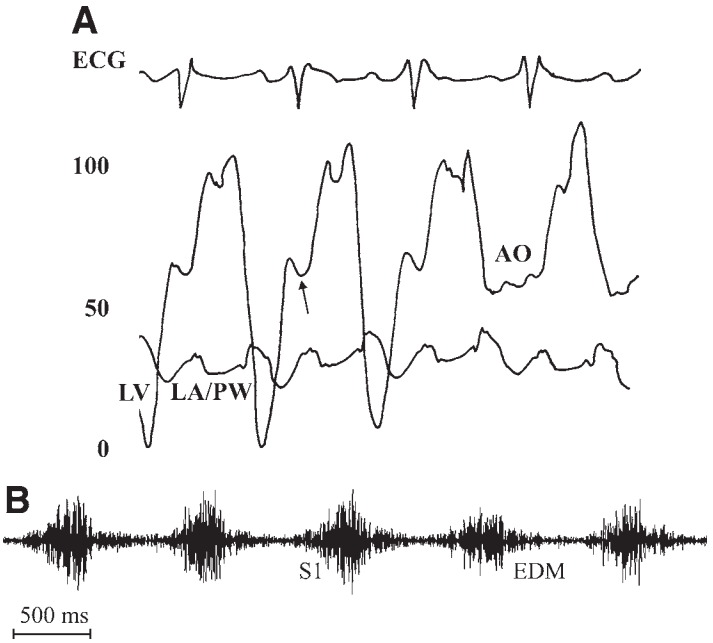

Fig. 8. **(A)** Simultaneous recordings of indirect left atrial (LA) pressure (the pulmonary capillary wedge [PW] pressure) and the left ventricular (LV) pressure from a patient with acute severe aortic regurgitation (shown in the first two beats). The recording catheter is withdrawn to the aorta to show the aortic (AO) pressure (fourth beat). The arrow points to the end-diastolic pressure in the LV, which is almost equal to the diastolic pressure in the AO. The diastolic pressure in the LV rises quite abruptly and in the middle of diastole exceeds the level of the LA pressure, thereby closing the mitral valve prematurely before the onset of systole. This will result in a poor intensity S1 (*see* Fig. 8B). **(B)** Digital display of the magnetic audio recording from a patient with severe aortic regurgitation recorded close to the apex area. Note the crescendo–decrescendo systolic ejection murmur followed by the early diastolic murmur (EDM) of the aortic regurgitation. The former is due to large stroke volume ejected from the left ventricle as a result of the volume overload. The S1 is soft and is poorly recorded.

there will be no acceleration of column of blood toward the left atrium and therefore no deceleration to cause a sound. This will lead to a very soft and inaudible M1 (S1) *(20–23)* (Figs. 8A,B).

T1 Intensity

The T1 intensity is usually soft in the normal adults and therefore not easily audible. However, its intensity may be increased under certain circumstances.

Increased Right Ventricular Contractility

T1 intensity may be increased when there is increased right ventricular contractility, as may be seen with right ventricular volume overload causing increased Starling effect (Fig. 9). These states most commonly include left-to-right shunt through an atrial septal defect. In tricuspid regurgitation, although the volume overload is present, the regurgitation does not allow adequate deceleration of the column of blood, therefore the T1 intensity is not

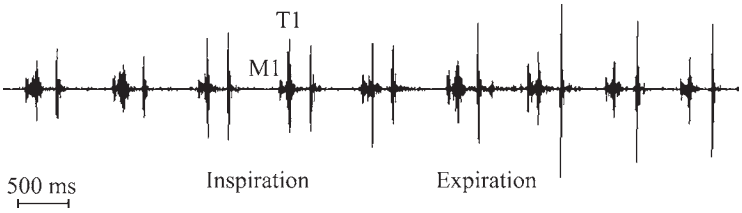

Fig. 9. Digital display of the magnetic audio recording from a 16-year-old man with a large and slightly redundant tricuspid valve taken at the lower left sternal border area. Two components (M1 and T1) of the S1 are seen, the second component of which is intensified on inspiration showing that it is the T1.

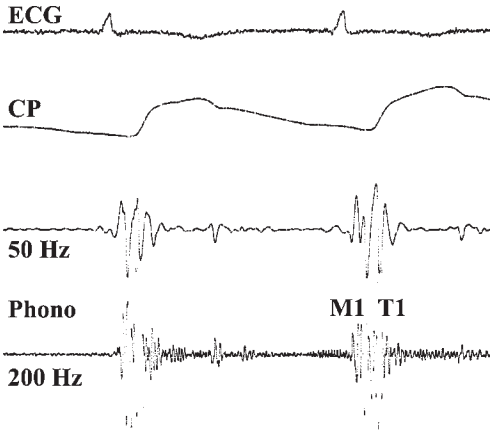

Fig. 10. Phonocardiogram (Phono) recording from a patient with Ebstein's anomaly of the tricuspid valve recorded from the lower left sternal area showing a delayed louder-intensity T1.

generally increased. In congenital pulmonary regurgitation with normal pulmonary pressures and normal right ventricular function, the T1 intensity will be increased. With iatrogenic pulmonary regurgitation, as may often occur following operative repair of tetralogy of Fallot, the T1 intensity may not be increased particularly if there is associated right ventricular damage. Similar consideration will apply also in patients with pulmonary regurgitation secondary to pulmonary hypertension.

Higher Right Atrial Pressure at the Time of Tricuspid Valve Closure

In tricuspid obstruction caused by either tricuspid stenosis (which is rare) or by tumors such as atrial myxoma, the right atrial pressure will be elevated and this will lead to a higher pressure crossover point on the right side. This will result in higher *dP/dt* achieved by the right ventricle at the time of tricuspid valve closure, resulting in loud T1.

When the tricuspid valve is abnormally large and redundant, as seen in some patients with *Ebstein's anomaly*, the actual deceleration of the column of blood may occur slightly later because of the redundancy. By this time the right ventricular *dP/dt* may have reached a steeper slope contributing to an increased intensity of T1 (Fig. 10). The *sail sound* described in some patients with Ebstein's anomaly represents the louder delayed T1 *(24)*.

A1 Intensity

The A1 may or may not be present depending on whether or not the ejected jet during onset of ejection decelerates sufficiently against the wall of the aortic root to cause a sound. This is perhaps purely determined by the anatomy. When present it usually is coincident with the onset of pressure rise in the central aorta. The only controlling factor determining its intensity will be the left ventricular contractility.

A1 may be increased in the presence of hyperdynamic states such as anemia, thyrotoxicosis, and Paget's disease.

Aortic Ejection Sound and Click

Certain conditions may lead to effective deceleration of the ejected jet at onset of systole, resulting in loud, sharp, and clicky sounds. These may either arise from the aortic root, as in normal A1, or from the aortic valve. Sometimes, however, the sound may not be as clicky. This may occur at the usual timing of normal A1 or slightly later. When it arises as a result of exaggeration of the normal A1, it will occur at the onset of aortic pressure rise. Strong inotropic agents (e.g., isoproterenol and norepinephrine) can be shown to increase the amplitude of the aortic root ejection sound. On the other hand, methoxamine, which lacks the inotropic effect, will decrease the amplitude *(18)*.

The most common causes of these aortic ejection sounds and/or clicks are:

1. *Bicuspid aortic valve* where the cusps are often unequal in size and the opening may be eccentric, resulting in an *eccentric jet*. The latter would therefore be expected to decelerate against the wall of the aorta. The direction of the jet may be almost perpendicular to the aortic wall, resulting in a sharper and louder sound. The timing of this is usually similar to the normal A1 or delayed only to a slight degree (Figs. 11A–C).
2. In *congenital aortic valvular stenosis*, the aortic valve is often domed. When the aortic valve is domed and stenosed and does not freely open, the deceleration may occur against the *doming valve* itself *(25)*. The sound in these instances will often be clicky. The aortic ejection clicks have been shown to correspond to the timing of the maximal doming. The click precedes the onset of the aortic stenosis murmur and occurs 20–30 ms after the onset of the aortic pressure rise. It occurs at the anacrotic shoulder of the aortic pressure pulse (Fig. 12). When the stenosis is severe and the valve is immobile and calcified, aortic ejection clicks are not heard. The presence of the ejection click in obstruction of the left ventricular outflow tract will suggest a valvular origin of the stenosis *(18,26)*.
3. In *aortic root aneurysm*, the column of ejected blood will make close to a 90° angle with the wall of the aorta because of distortion caused by the aneurysmal dilatation (Fig. 13). The aorta may also be noncompliant. This will result in more of a clicky sound, usually later than the normal A1 (Fig. 14).

Aortic ejection sounds and clicks, when present, are usually heard over the left sternal border and the apex. However, when caused by aortic root aneurysm they may be louder at the second and third right intercostal space at the sternal border.

Pulmonary Ejection Sound and Click

Because the normal pulmonary pressures are low, there is no audible or recordable normal pulmonary ejection sound. Therefore, when a pulmonary ejection sound or click is heard, it is always pathological.

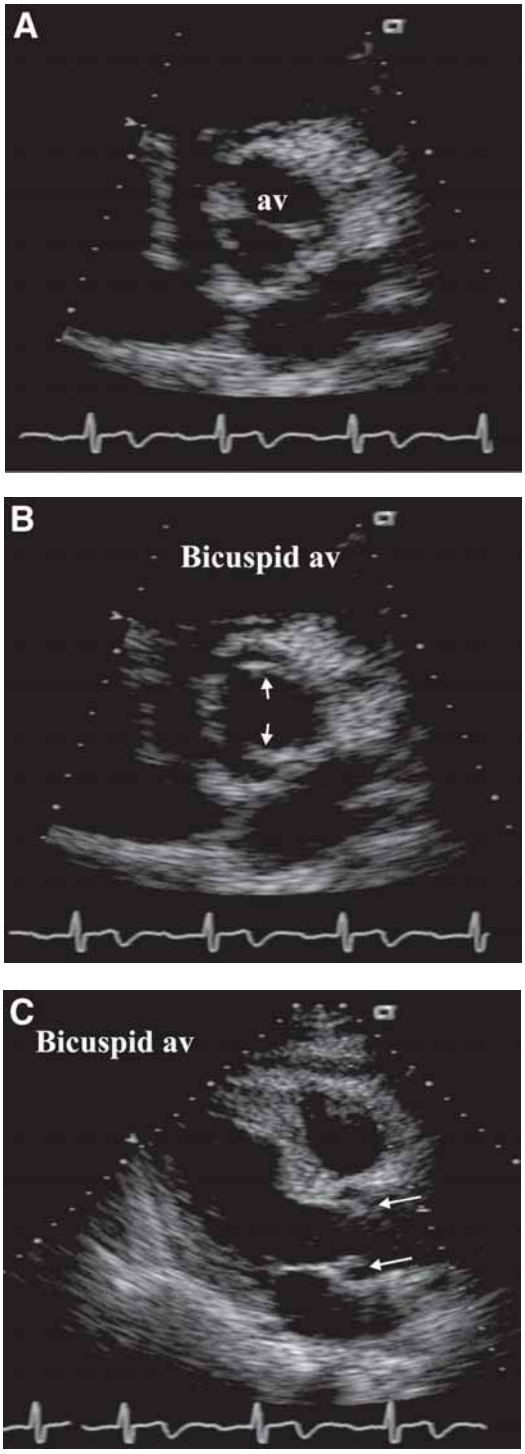

Fig.11. Stop frames from two-dimensional echocardiogram taken from a patient with a bicuspid aortic valve and aortic ejection click. The short axis shows the two cusps **(A)** in the closed position and **(B)** in the open position. The aortic valve cusps are seen to be slightly domed in systole (arrows) as observed in the parasternal long axis **(C)**.

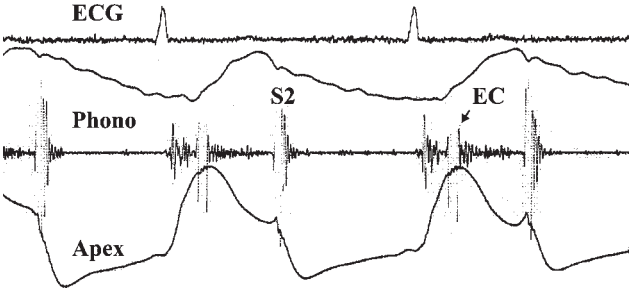

Fig. 12. Phonocardiogram (Phono) recording from a patient with congenital aortic valve stenosis with domed bicuspid aortic valve. Note that the aortic ejection click (EC) is slightly delayed and seen to correspond to the anacrotic hump on the carotid pulse (CP).

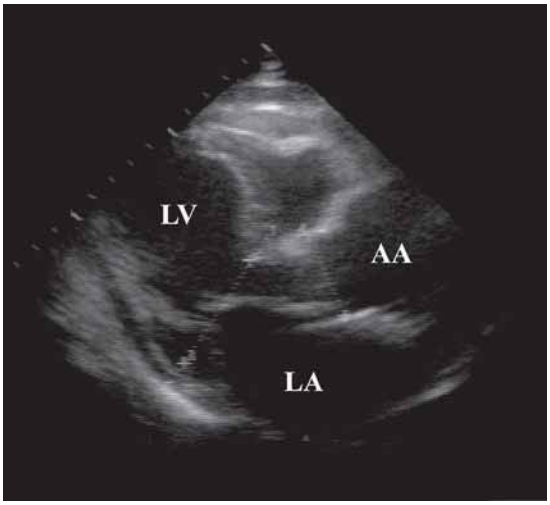

Fig. 13. Stop frame from two-dimensional echocardiogram from a patient taken in the parasternal long axis showing dilated aneurysmal ascending aorta (AA) just above the aortic valve. Note that the orientation of the AA is such that it is at a 90º angle to the longitudinal axis of the left ventricle (LV).

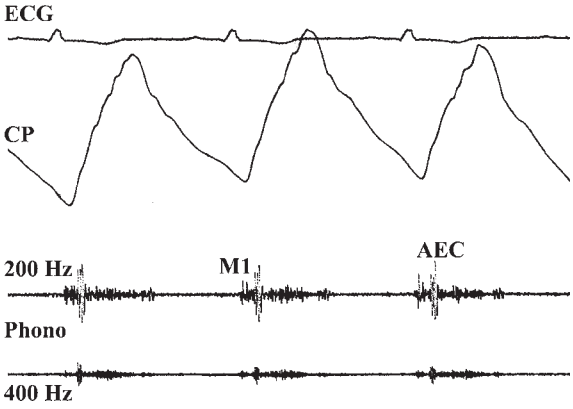

Fig. 14. Phonocardiogram (Phono) recording from a patient with hypertension and dilated aortic root taken at the lower left sternal border area showing an aortic ejection click (AEC).

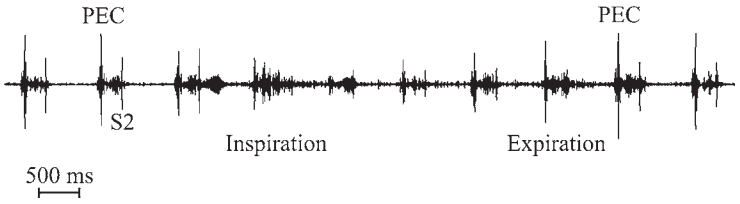

Fig. 15. Digital display of magnetic audio recording from a patient with congenital pulmonary valve stenosis taken from the lower left sternal area showing the pulmonary ejection click (PEC). Note that the sharp sound that begins the systolic murmur (PEC) is seen to become very soft and almost disappear on inspiration, becoming clicky and sharp on expiration.

There are usually two causes of pulmonary ejection clicks *(27)*:

1. Dilated pulmonary artery: The pulmonary artery may become dilated as a result of severe longstanding pulmonary hypertension or be of idiopathic origin with normal pulmonary pressures. The ejected column of blood because of distortion caused by dilatation of the root will be decelerating against the wall of the pulmonary artery causing a clicky sound. This click—as with all other right-sided events—will increase in intensity with inspiration.
2. Congenital pulmonary valvular stenosis: In congenital pulmonary valvular stenosis, the click occurs with the maximal doming of the valve. The deceleration of the column of blood is against the domed valve. The mechanism is similar to that observed in aortic valvular stenosis, except it is present invariably in all patients. The pulmonary valve is usually very pliable and never calcified. *This click, however, has a unique variation with respiration, which in fact helps to identify its origin. The click becomes softer or even inaudible on inspiration* (28) (Fig. 15). *This is the only exception to the rule that the right-sided events become exaggerated with inspiration.* In these patients the pulmonary artery pressure is usually very low. During inspiration the increased venous return into a hypertrophied and somewhat noncompliant right ventricle raises the right ventricular end-diastolic pressure during right atrial contraction. This may exceed the pulmonary artery diastolic pressure. This in effect would cause the doming of the pulmonary valve even before the ventricular contraction starts. Thus, with ventricular systole as the column of blood is set into motion, the valve being maximally domed, there is no sudden deceleration against the valve itself, and therefore no sound.

Pulmonary ejection clicks are maximally loud over the second and third left intercostal spaces at the left sternal border. However, when they are loud they can be heard over a wide area of the precordium, including the xiphoid region.

CLINICAL ASSESSMENT OF S1 AND COMPONENTS

When assessing the S1 at the bedside, one should assess the following:

1. Intensity or loudness
2. Variability of intensity (loudness)
3. Presence of more than one component (split S1)
4. Quality
5. Location of maximal loudness
6. Effect of respiration

Intensity or Loudness

Because loudness can vary due to noncardiac factors such as body shape or chest wall deformities or the presence of pulmonary disease, these should be taken into account in assessing the true loudness, which may be attenuated.

The loudness of the sound, however, can be graded using the system of grading murmurs. The system allows six categories of loudness. Grades I–III are not loud enough to be palpable, whereas grades IV–VI are loud and palpable. Grade I requires tuning in to mentally filter out room noise from the actual sound. The grade II sound is audible the moment the auscultation is begun even without having to concentrate and eliminate the room noise. This is the usual intensity heard by beginners. The grade III sound is the loudest sound audible, which, however, is not palpable. The grade IV sound, although palpable, requires full contact of the stethoscope against the chest wall for audibility. The grade V sound requires only the edge of the stethoscope to touch the chest wall to hear the sound. The grade VI sound, however, can be heard with the stethoscope slightly but completely off the chest wall.

When S1 intensity is graded using the above system, all grades IV–VI are abnormal. Even grade III may be significant in some patients. However, it is difficult to diagnose a true decrease in S1 intensity because of extracardiac factors, which attenuate the sound. Other methods to overcome part of this problem were discussed in Chapter 3 in relation to the blood pressure and the assessment of ventricular function.

When S1 is loud, it is important to locate the area of maximal loudness, which may be possible by palpation. If the apical impulse is left ventricular as defined by the presence of medial retraction and the maximal loudness of S1 is at the apex, then one can safely assume that the M1 is the loud component. But it is important to remember that the other components of S1 can at times be the loudest and may become palpable. Occasionally ejection clicks (both aortic and pulmonary) when very loud may also become palpable. These will have to be identified by other features on auscultation.

Variability of Intensity

Variations in S1 intensity from cycle to cycle are usually a result of variations in M1. There are four basic causes for variations in M1 intensity.

1. A-V dissociation, where the P-R relationship may vary haphazardly from beat to beat. The shorter PR intervals will have louder M1, whereas the longer PR will have softer M1. This phenomenon can occur in complete A-V block, patients with electronic pacemakers, and also in ventricular rhythms.
2. In Mobitz type I second-degree A-V block, the S1 intensity may become progressively softer as the PR lengthens before the dropped beat and pause.
3. Atrial fibrillation, where the diastolic filling periods keep changing constantly, causing various degrees of Starling effect and variations in left atrial pressure at the time of mitral valve closure.
4. Pulsus alternans, where because of instability of intracellular calcium shifts, the contractility alternates between weak and strong beats. This usually occurs only in severe cardiomyopathies.

Components of S1 and Quality

One should on auscultation determine whether or not more than one component of S1 is audible (split S1). Then one should try to ascertain the origin of each component and compare their relative loudness. At the same time, any clicky quality of the components should also be noted. Such clicky quality to S1 or one of its components should alert one to the presence of aortic or pulmonary ejection click. Normal M1 is not clicky, although a mechanical mitral prosthetic ball valve usually would cause a clicky M1 at the time of its closure.

When one of the components of S1 is very loud it can have a masking effect on the other component, thereby appearing on auscultation to have only a single component. When the S1 is loud one should not always assume this to be because of loud M1. It is important to identify its features thereby identifying its origin. The M1 and the A1 will be maximally loud at the apex and will not change with respiration. The same rule applies to the aortic ejection click, although it may be equally loud at the second right intercostal space. The T1, on the other hand, is loudest at the lower left sternal border and over the xiphoid area and can be noted to increase in loudness on inspiration. Occasionally when the right ventricle is very large and forms the apex of the heart (lateral retraction present), the T1 may be loudest over the apex.

It is also important to note that a loud pulmonary ejection click, being very close in timing to the normal S1, may be mistaken for one of its components. However, this can be easily solved by the fact that it will get softer on inspiration and may sometimes be audible only on expiration. The maximal loudness of a pulmonary ejection click is usually over the second and third left intercostal space.

When A1 is clicky and/or loud enough to cause a good split S1, one can further confirm it to be M1 and A1 by observing the effect of standing. Standing by reducing the venous return will tend to lower the left atrial pressure and the left ventricular end-diastolic pressure. While there may be a slight rise in heart rate secondary to sympathetic stimulation, the decreased filling pressure will lead to a slower rate of pressure rise in the left ventricle. This will imply some lengthening of the isovolumic contraction phase. The A1, which comes at onset of ejection, therefore coming after the end of the isovolumic contraction phase, will be somewhat delayed from the M1, thereby making the split somewhat wider on standing.

(For additional examples review Phono Files 0–9 and Echo Phono File 1 under Heart Sounds on the Companion CD.)

SECOND HEART SOUND (S2)

The second heart sound occurs at the end of the ejection phase of systole. It is related to the closure of the semilunar valves. Since there are two semilunar valves, aortic and pulmonary, there are also two components for the S2, namely the aortic component (A2) and the pulmonary component (P2).

Mechanism of Formation of S2

As the blood is ejected into the aorta and the pulmonary artery during systole (stroke volume), the aortic and the pulmonary pressures rise and these two vessels become

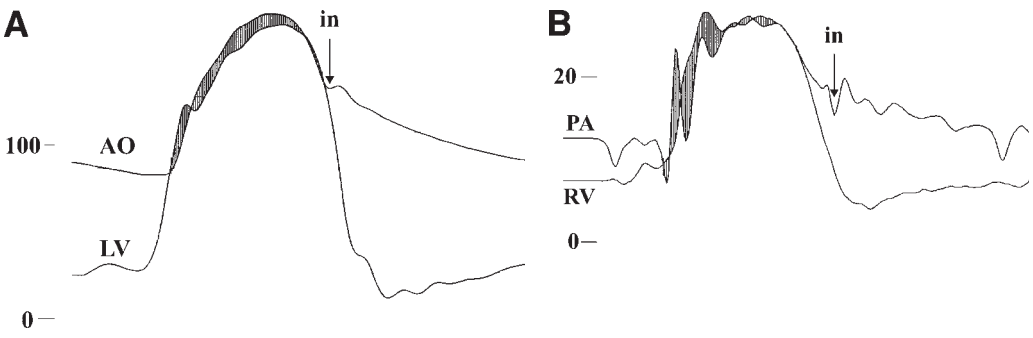

Fig. 16. Simultaneous left ventricular (LV) and aortic (AO) pressure and simultaneous right ventricular (RV) and pulmonary artery (PA) pressure are shown in **(A)** and **(B)**, respectively. The falling ventricular pressure at the end of systole leads to the development of a pressure gradient between the AO and the LV on the left side and between the PA and the RV on the right side. The aortic and the pulmonary components of the S2 occur at the time of the respective incisura (in) in the AO and PA pressures. *(Continued on next page)*

distended. At the end of systole, as the ventricular pressures begin to fall, the elastic components of the great vessels maintaining a higher pressure results in a pressure gradient, which drives the columns of blood back into the ventricles. The columns of blood in the great vessels preferably flow toward the ventricles at this time because of the lower resistance with the dropping ventricular pressures compared to the periphery. The reverse flow of the columns of blood in the aorta and the pulmonary artery parachutes the cusps of the aortic and the pulmonary valves, closing them. The sudden deceleration of the columns of blood against the closed semilunar valves causes dissipation of energy, resulting in the A2 and the P2 components of S2 (Figs. 16A–D).

NORMAL S2

The S2 is usually sharper, crisper, and shorter in duration compared to S1. This is because of the fact that the semilunar valve closures occur at much higher pressures than the A-V valves and the dissipated energy in the columns of blood is much greater. In normal young subjects one can often hear both components of S2 (A2 and P2). The S2 will therefore be heard as a split sound. The first of the two components is the A2. The higher impedance (i.e., resistance to forward flow) in the systemic circulation results in earlier acceleration of reverse flow in the aortic root, causing the aortic valve to close earlier *(29,30)*.

The pulmonary arterial bed is larger and offers markedly less resistance to forward flow. This will make the tendency to reverse flow occur later and slower compared to the left side. In addition, it is also possible that the lower pressures achieved by the right ventricle during systole may actually result in a slower rate of relaxation of the right ventricle compared to the left ventricle. For these reasons, the P2 component occurs later.

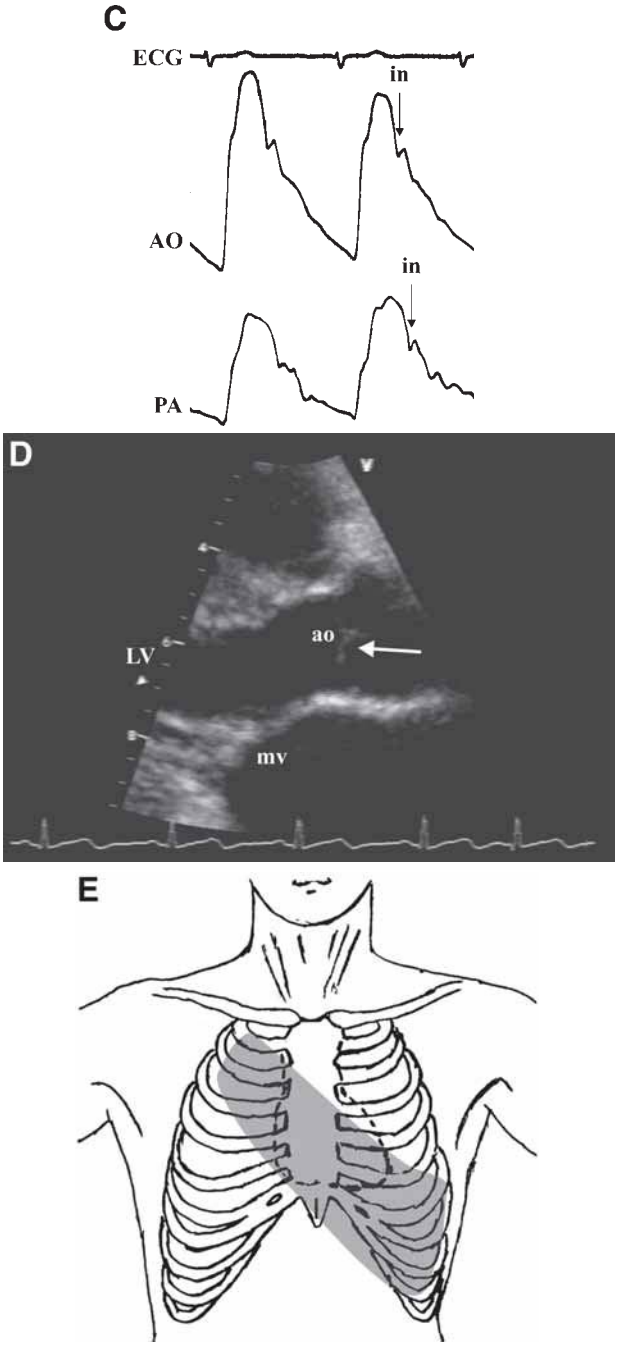

Fig. 16. *(Continued)* **(C)** Recording of the simultaneous aortic (AO) and pulmonary artery (PA) pressures show that the incisura (in) in the AO occurs earlier than in the PA. **(D)** Stop frame from a two-dimensional echocardiogram from a normal subject taken at the parasternal long axis showing the aortic valve in the closed position causing the deceleration of the column of blood, which is trying to enter the left ventricle from the aorta as a result of the pressure gradient at the end of systole between the AO and the LV. **(E)** Diagram of the chest showing the true aortic area, which is the sash area (shaded area) extending from the second right interspace to the apex.

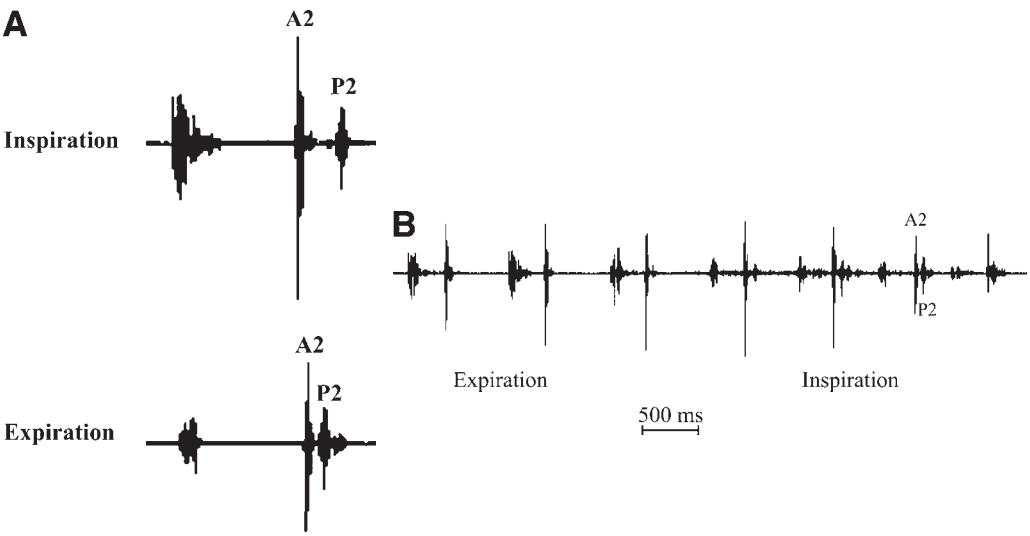

Fig. 17. **(A)** Diagram showing the two components of the S2 and their variation with respiration in normals. The normal sequence is that the aortic component (A2) occurs before the pulmonary component (P2). On inspiration, the A2 comes slightly earlier, but the P2 is significantly more delayed, widening the split. The reverse occurs on expiration, with the split becoming quite narrow. **(B)** Digital display of the magnetic audio recording from a normal young subject taken from the third left intercostal space at the left sternal border showing the normal S2 split on inspiration into A2 and P2 and essentially a single S2 on expiration.

The A2 component is normally heard over the true aortic area, which is the *sash area* (the area extending from the second right intercostal space at the sternal border to the apex) (Fig. 16E). P2, on the other hand, is heard over the second and the third left intercostal spaces near the sternal border. Therefore, the splitting of the normal S2 is best appreciated at the second and third left intercostal space. The relative loudness of the two components is such that in the normal, the A2 is always louder than the P2 mainly because the systemic arterial resistance is normally 10 times higher than the pulmonary arterial resistance *(4, 16,30)*.

Normal Respiratory Variations of A2-P2 Split

In normal subjects the splitting is often best recognized on inspiration because the two components tend to move away from each other, causing them to separate better. On expiration they tend to move closer to each other. This often results in them becoming single, or if they are still separated, the splitting is very narrow (Figs. 17A,B). During inspiration there is increased venous return to the right heart because of the fall in the intrathoracic pressures. There is also expansion of the lungs, resulting in decreased resistance in the pulmonary circulation. The expansion of the lungs also increases the pulmonary vascular capacity, leading to a slightly decreased left-sided filling. These changes affect both components of the S2 in terms of their timing, causing the A2 to come earlier and the P2 to be delayed. However, the A2 is affected to a very small degree because the systemic resistance is not affected by respiration. The P2, on the other hand,

is delayed on inspiration for two reasons: the increased volume on the right side and the fall in the pulmonary resistance on inspiration. The former will result in an increase in the right ventricular ejection time. The latter will allow easier forward flow, resulting in slower tendency for reversal. On expiration, with rise in the intrathoracic pressure, the venous return to the right heart decreases and the right ventricular ejection time will shorten. The lungs collapse, the pulmonary capacity will diminish, and the resistance will rise. These changes will result in P2 occurring early on expiration *(4,16,31,32)*.

The normal respiratory variation is not as prevalent in the elderly as it is in younger patients *(32)*. This may be because of decreased compliance of the chest wall and great vessels and the relatively increased impedances in both systemic and pulmonary circulations.

ABNORMAL S2

The abnormalities of S2 may occur as a result of changes in the intensity of the individual components or changes in their timing. The latter often may lead to abnormal respiratory variations.

Intensity of S2

The loudness or intensity of the S2 can be determined by the grading system previously alluded to in relation to S1. The sounds with loudness grades IV–VI would be abnormal and increased. When S2 is either inaudible or grade I in loudness, it could be considered decreased when S1 or other sounds are normal.

Intensity of A2

The A2 intensity is dependent on the amount of energy that the column of blood in the aortic root attains in its attempt to flow toward the ventricle (assuming the integrity of the aortic valve). This in turn is dependent on the stroke volume, aortic elasticity, and most importantly the peripheral resistance. When the stroke volume is either normal or increased, the peripheral resistance becomes the major determinant of the intensity. When there is increased peripheral resistance, the diastolic pressure in the aorta remains higher than normal. When the left ventricular pressure falls because of onset of ventricular relaxation in late systole, the maintained higher pressure in the aorta provides a greater pressure head to act on the column of blood in the aortic root. The higher pressure head trying to move the column of blood in the aortic root toward the left ventricle imparts greater energy. Thus, when it decelerates it causes a louder A2. Thus, in systemic hypertension, A2 becomes louder, may be palpable, and may become musical in quality because of maintained vibrations under high tension. The sound mimics the beating on a tambour.

In patients with severe heart failure and poor stroke volume, A2 can become soft and, rarely, inaudible despite high peripheral resistance. The poor stroke volume causes poor distension of the elastic components of the aortic root, and therefore the energy in the column of blood closing the valve is very low. These patients often have low pulse pressure and low-amplitude arterial pulse.

In severe aortic stenosis, the stroke volume is ejected slowly and over a longer period and also leads to poor distension of the aortic root, leading to often a lower intensity A2, and this may be inaudible.

A2 Intensity in Aortic Regurgitation

Aortic regurgitation can occur as a result of valvular disease or aortic root pathology. Aortic regurgitation leads to increased stroke volume. The peripheral resistance is usually low because of compensatory mechanisms. The large stroke volume causes greater distension of the aortic root and therefore would cause a greater amount of energy in the column of blood in the aortic root trying to close the valve. The degree of deceleration achieved by the reversing column of blood will depend on the anatomical cause and the severity of the regurgitation. Despite significant aortic regurgitation, because of increased energy in the column of blood, the A2 intensity is often well preserved. The lower peripheral resistance will have a tendency to reduce the intensity of A2. The two effects often may balance each other. However, in very severe (wide-open) regurgitation, A2 intensity may decrease significantly because of poor deceleration. When patients with aortic regurgitation develop left ventricular failure, their stroke volume will be reduced to normal levels and their A2 may become soft or inaudible.

Sometimes A2 may be louder than normal for anatomical reasons, namely, conditions that make the aorta anterior and closer to the chest wall. These include a thin chest, straight back syndrome with decreased antero-posterior diameter, transposition of the great vessels (congenitally corrected or uncorrected), and tetralogy of Fallot where, in addition, the P2 may be attenuated because of a deformed pulmonary valve.

Intensity of P2

P2 intensity, like A2 intensity, is dependent on the stroke volume, pulmonary artery elasticity, and the pulmonary arterial resistance. When the right ventricular stroke volume is significantly increased as in left-to-right shunts through an atrial septal defect, the P2 may become louder, but not reaching the level of palpability unless significant pulmonary hypertension is also present. Along with the increased size of the right ventricle, this may also contribute to the audibility of the P2 over a wider area of the precordium. The pulmonary artery remains elastic except in severe pulmonary hypertension. The major determinant of increased P2 intensity is, in fact, the pulmonary arterial resistance. In pulmonary hypertension, whether acute or chronic, the pulmonary arterial resistance is increased because of vasospasm (increased vascular tone). Also, when the pulmonary hypertension is chronic, structural changes occur in the arterial wall with medial hypertrophy and increased intimal thickening, which make the pulmonary arterial system stiff and less elastic. The increased resistance raises the pulmonary arterial systolic and diastolic pressures. The right ventricular relaxation may be impaired, taking a longer time for the right ventricular systolic pressure to fall. In addition, the increased pulmonary pressures provide a greater pressure head. The higher pressure head, together with increased resistance to forward flow, acts to impart greater energy and velocity to the column of blood in the pulmonary root in its attempt to flow toward the right ventricle. Therefore, when it decelerates it produces a louder-intensity P2. When the P2 becomes palpable (grades IV–VI), it invariably indicates severe pulmonary hypertension.

Because of low pressures on the right side, the P2 is often soft and occasionally not audible. In significant pulmonary stenosis, the stroke volume may be quite low, and this, together with very low pulmonary arterial pressures, may lead to a very low intensity P2 that may be inaudible.

Abnormal Timing of A2 and P2 Components

The time of occurrence of the individual components A2 and P2 may be delayed if the duration of systole is lengthened either because of electrical or mechanical delays or if the onset of flow reversal in the aortic root or the pulmonary artery is delayed because of changes in impedance to forward flow *(4,32–36)* .

Electrical Delay

When there is an electrical conduction defect such as a bundle branch block, the affected side will lengthen the electrical portion of the duration of the electromechanical systole. This in turn will result in the delayed occurrence of the individual A2 and P2 components. Left bundle branch block (LBBB) will cause A2 delay, and right bundle branch block (RBBB) will cause P2 delay (Figs. 18A,B). Similar conduction defect can also be produced artificially by pacing either ventricle, which will produce late activation of the nonpaced ventricle. In other words, right ventricular pacing will cause LBBB effect, and left ventricular pacing will cause RBBB effect. Transient bundle branch block effect can also occur during ventricular ectopic beats. The site of origin of the ectopics will determine which of the two ventricles will be delayed in excitation. Right ventricular ectopics will have LBBB and left ventricular ectopics will have RBBB morphology and effects, respectively.

Mechanical Delay

The mechanical portion of systole may be delayed when there is significant outflow obstruction. This would result in high intraventricular pressure, which is required to overcome the obstruction. The time taken for the pressures to fall below the level of the pressure in the great vessel (aorta or the pulmonary artery) would be lengthened. The reversal of flow at the aortic or the pulmonary root would start later because of the delay, and this in turn would delay the occurrence of the individual component of S2 on the affected side (Fig. 19).

Similar delay may also be caused in ischemic ventricular dysfunction where the ischemic muscle fibers may lag in onset of contraction and therefore maintain the developed intraventricular pressures for a longer period preventing its fall. Because ischemia often involves primarily the left ventricle, this type of delay is more likely to affect the A2.

The A2 and the P2 components usually coincide in timing with the incisural notch on the aortic and the pulmonary artery pressure curve, respectively (Figs. 16A,B). In general, the durations of the electromechanical systole on the left side and the right side are about equal under normal circumstances if the duration of the electromechanical systole is defined as the interval from the beginning of the electrical activation (QRS onset) to the respective time when the ventricular pressures fall below the level in the great vessels (aorta and the pulmonary artery).

Right ventricular myocardial dysfunction may develop with time in pulmonary hypertension when it is severe. The rate of rise of the right ventricular systolic pressure as well as its decline during relaxation may become slower. This may selectively increase the duration of systole on the right side relative to the left side, contributing to a delayed P2 *(30)*. Similar situation tends to develop more readily in acute pulmonary hypertension.

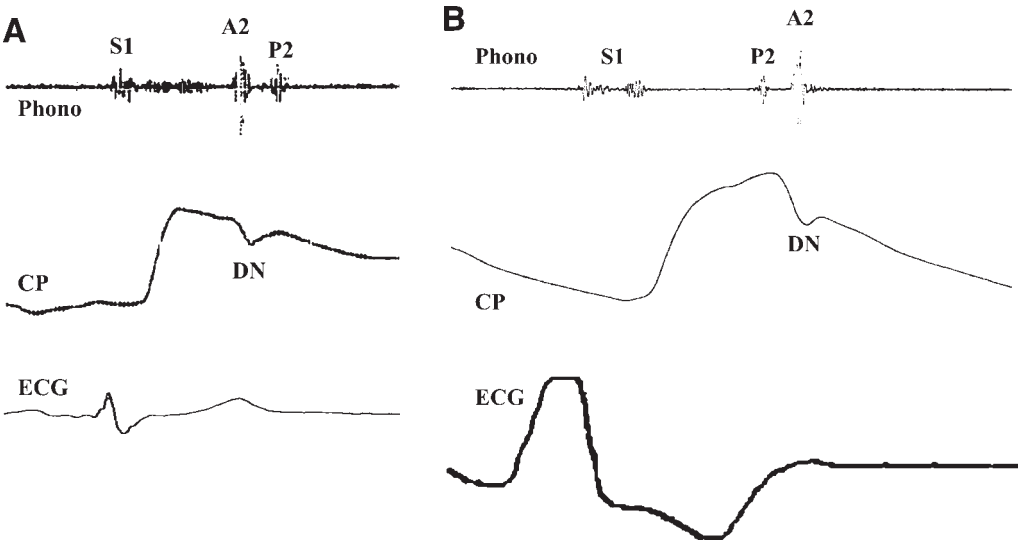

Fig. 18. **(A)** Diagram showing delayed P2 producing a wide split of the S2 in the right bundle branch block, which causes electrical delay of conduction to the right side. Note that the sequence is normal, with A2 occurring first, followed by P2. The component that is closest to the dicrotic notch (DN) on the CP is A2. The DN lags slightly behind because of the pulse transmission delay. **(B)** Diagram showing the abnormal sequence of the S2 components caused by the electrical delay because of left bundle branch block. P2 occurs before A2. The A2 is the component closest to the dicrotic notch (DN) on the CP.

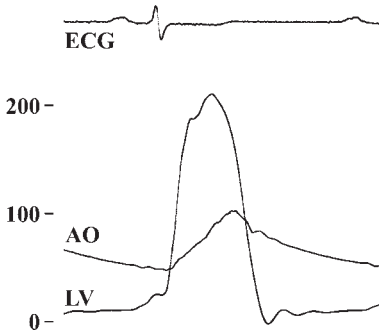

Fig. 19. Simultaneous left ventricular (LV) and aortic (AO) pressures from a patient with severe aortic valve stenosis. Note that the severe mechanical obstruction leads to high intraventricular pressure, which will take longer to fall to the level of the AO pressure, thereby delaying the A2.

Delay Secondary to Effects of Impedance

Impedance refers to resistance to forward flow of blood in the great vessels. If the impedance to forward flow is low, as the ventricular pressures begin to fall below that of the great vessels, the tendency for reversal of flow at the aortic or pulmonary root will be delayed. Therefore, the occurrence of the A2 or the P2 will be delayed depending on which circuit is affected. If the impedance is high, then the reversal tendency will be earlier, causing earlier occurrence of the affected component. This can be understood

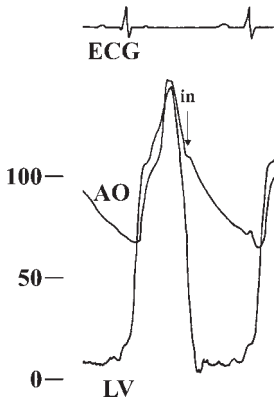

Fig. 20. Simultaneous left ventricular (LV) and aortic (AO) pressures from a patient with chronic aortic regurgitation. The A2 will occur simultaneously with the incisural notch (in) in the aortic pressure. Note the slight delay between the ventricular pressure at the leve l of the incisura (in) on the AO recording and the actual occurrence of the incisura (A2 timing). This delay has been termed by some as the *hang-out* interval, which reflects the impedance of the circuit. The hang-out interval on the pulmonary side will be greater because the pulmonary impedance is normally very low.

easily by the analogy of an automobile in motion and how far it is likely to travel after the application of the brakes. This will not only depend on the momentum of the vehicle but also on the character of the road surface: whether wet, slippery, or rough, whether there is a slope, and, if so, whether the grade is down or up as well as the resistance offered by the wind velocity and direction. The combined effects of these factors constitute the impedance to the moving automobile and will determine how far the vehicle will travel and how long before it will eventually halt. The impedance to forward flow in the great vessels is provided by the combined effects of various factors. These include the vascular capacity and how filled the system is, the vasomotor tone of the vessels (the systemic or the pulmonary vascular resistance), and the viscosity of the blood. In normal adults, the aortic or systemic impedance is approximately 10 times higher than the pulmonary impedance. This is a major factor that contributes to the earlier occurrence of A2 compared to P2. This is because the pulmonary vascular capacity is large; the pulmonary vascular resistance is low compared to that of the systemic side *(30)*.

When the ventricular pressure in late systole begins to fall below that in the aorta or the pulmonary artery, it leads to the development of a pressure gradient between the great vessel and the ventricle. The lower ventricular pressure provides a lower pressure route for the column of blood to take in the aorta or the pulmonary artery. However, the flow may still continue forward if the impedance is low. This will be reflected by the delay in the incisural notch of the aortic or the pulmonary pressure curve as measured from the point in time when the falling intraventricular pressure reaches the level of the incisural pressure (the pressure at which the aortic and the pulmonary valves close, respectively). This delay in the incisural notch has been termed by some investigators as the "*hang-out*" *interval (29)* (Figs. 16A,B and 20). This interval is quite small on the aortic side, averaging 15 ms, whereas it is usually considerably longer (between 30 and 80 ms) on the pulmonary side, almost completely accounting for the normal A2-P2 separation.

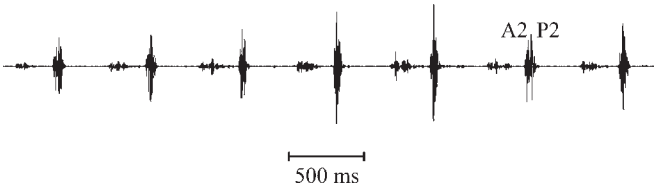

Fig. 21. Digital display of a magnetic audio recording from a patient with significant pulmonary hypertension with compensated right ventricular function, taken from the third left intercostal space at the sternal edge. P2 occurs much earlier because of high pulmonary impedance, causing a very narrow split of S2.

Because the systemic impedance is high at basal state, change in impedance must be significant to cause an appreciable effect on the A2 timing. On the other hand, small changes of the pulmonary impedance, which is usually low, may have an effect on the P2 timing because the percentage change will tend to be higher. Thus, with normal inspiration, the expansion of lungs will increase the pulmonary vascular capacity, thereby lowering the pulmonary impedance considerably in terms of percentage change. This is one of the more important contributing factors for the normal inspiratory delay of P2.

In pulmonary hypertension, the increased pulmonary impedance has the effect of shortening the delay of the incisural notch, making the P2 occur earlier because of course to the earlier occurrence of the flow reversal at the pulmonary root. This will be expected to cause a narrower split of S2 (Fig. 21).

In patients with left-to-right shunts through a ventricular septal defect who eventually develop severe pulmonary hypertension secondary to the occurrence of pulmonary vascular disease, the shunt becomes reversed, leading to cyanosis. In these patients, who are termed to have the *Eisenmenger's syndrome*, the systemic and the pulmonary impedance are about equal and would result in a single S2 *(37)*.

Effect of Delayed Occurrence of the S2 Components on the Respiratory Variation of S2 Splitting

When the A2 is delayed, however the delay is caused, if the delay is long enough then the sequence becomes altered, namely, a P2-A2 sequence is produced instead of the normal A2-P2 sequence. On inspiration when there is more volume on the right side as well as a significant drop in pulmonary impedance, the P2 will be delayed. This delayed P2 will come closer to the already delayed A2 and may actually fuse and may become a single S2. On expiration, the reverse will occur, with the P2 now coming earlier because of decreased volume being ejected by the right ventricle and a rise in the pulmonary impedance because of decreasing pulmonary vascular capacity secondary to collapsing lungs. This will then result in a split S2 on expiration *persistent or audible expiratory splitting*) *(33)*. Because the two components tend to come together on inspiration and separate from each other, causing a split S2 on expiration, it is termed *paradoxical or reversed splitting of S2 (36)* (Fig. 22A,B).

If the P2 is delayed, on the other hand, the sequence will still be normal: A2 followed by P2 *(35)*. However, the P2 will tend to be separated from A2 all the time. The separation will be greater on inspiration when the P2 is normally delayed and the separation may

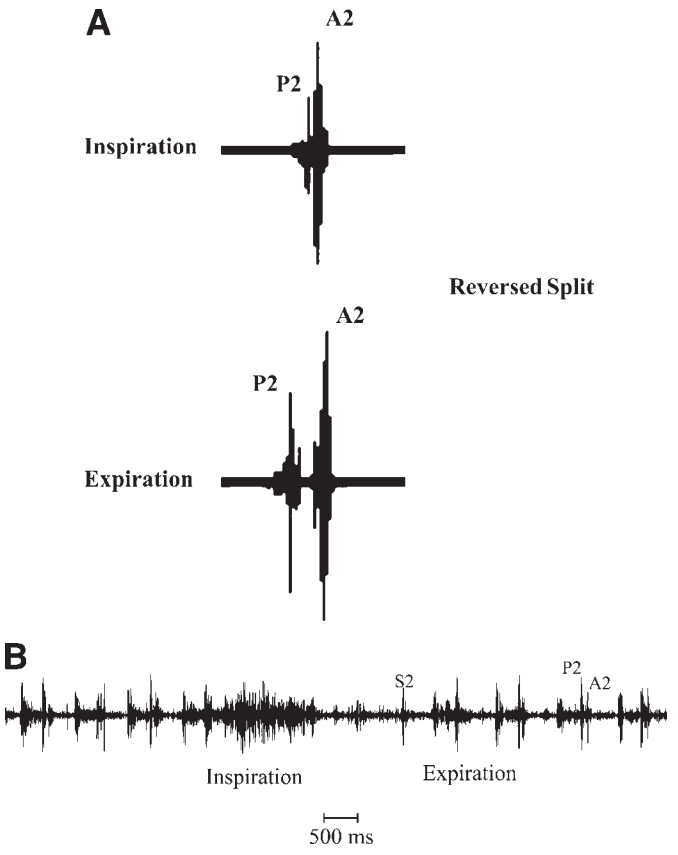

Fig. 22. **(A)** Diagram showing a reversed sequence of the S2 components caused by delayed A2, producing a paradoxical split with respiration. The normal inspiratory delay of the P2 makes the two components come together on inspiration with very little or no obvious split. On expiration the opposite occurs, with P2 coming earlier so as to make an audible split. **(B)** Digital display of a magnetic audio recording from a young patient with significant left-to-right shunt through a persistent ductus arteriosus taken from the third left interspace showing a paradoxical split of S2 caused by very low systemic impedance making a delayed A2 component. The noise in the baseline is exaggerated because of inspiration. The S2 becomes single for at least two beats after the end of inspiration. On expiration there is, on the other hand, a clear split of S2.

be narrower but maintained even on expiration. In other words, there will be a persistent expiratory split of S2 with normal physiological widening of S2 split expected because of inspiration. This can also be termed as a *wide physiological splitting of S2*.

Delayed A2

The causes of a delayed A2 component can be considered under the three general categories.

Left Bundle Branch Block

When there is LBBB, the mechanical onset of contraction will be delayed because of the delay in electrical activation. The depolarization wave will have to reach the left ventricle through the "working-class" myocardial cells, which is a slow process as

opposed to conduction through the normal His-Purkinje fibers. If the disease process in the left bundle system is focal and very proximal at its origin, then the electrical wave front may latch on to the normal Purkinje fibers of the distal divisions of the left bundle, and this may speed up the process of activation. The resulting electromechanical delay may not be severely prolonged. However, when the disease process in the left bundle branch is more extensive and involves the distal divisions, then the delay can be significant. Thus, varying degrees of electromechanical coupling may occur in different regions of the left ventricular myocardium. This will lead to delayed onset of contraction in the affected segments of the left ventricular myocardium. The QRS duration may therefore show varying degrees of prolongation of 0.12 s or more. If electromechanical coupling is variably delayed, then the rise in ventricular pressure during isovolumic phase will not be smooth and orderly. This will lead to lengthening of isovolumic contraction and a slower rate of rise of pressure. This may occur independent of the underlying myocardial function. In fact, in the majority of such patients with more extensive disease, the measurement of the individual components of the duration of the electromechanical systole will show not only lengthening of the Q-S1 interval (electrical delay), but also lengthening of the isovolumic contraction phase (the interval between S1 and the onset of ejection as assessed by aortic pressure recording) *(33,34)*.

Mechanical Delay

Aortic Valvular Stenosis

When the obstruction is significant and fixed, as in severe aortic valvular stenosis, the left ventricular pressure often rises to very high levels in systole. It is necessary to overcome the obstruction for the ejection to occur. The high intraventricular systolic pressure takes a longer time to fall below that of the aorta, and the ejection continues slowly and is maintained for a longer period. This prolongation in ejection contributes to the delayed occurrence of the A2. The sequence will be reversed. The P2 may actually be buried in the end portion of the systolic ejection murmur, which is often long in significant aortic stenosis. The A2 may be soft and may be the only audible component of S2. The reversed splitting and the reversed sequence, which can be theoretically expected, may not be noticeable clinically.

Hypertrophic Obstructive Cardiomyopathy

In this disorder the interventricular septum is markedly hypertrophied. The ejection is often rapid at onset. The rapid ejection of blood has a Venturi effect on the anterior mitral leaflet, which together with the interventricular septum forms the left ventricular outflow tract. This in effect pulls the anterior mitral leaflet from its initial closed position to an open anterior position moving toward the septum (*systolic anterior motion*). This systolic anterior motion actually leads the anterior leaflet to come in contact with the interventricular septum in midsystole. This results in the outflow obstruction. This leads to near cessation of ejection and development of mitral regurgitation because of the open mitral orifice and lower left atrial pressure. The obstruction thus developed in midsystole is maintained until the later part of systole when the Venturi effect wears off and the anterior leaflet moves back to its closed posterior position. The ejection resumes during this late phase. Thus, the ejection is prolonged, causing delayed A2. The reverse sequence and the reversed splitting of S2 may in fact be clinically appreciated in this disorder when the obstruction is severe *(36)*.

Severe Hypertension

In severe hypertension, the left ventricle often has to eject blood, overcoming significant rise in peripheral resistance. Very high levels of intraventricular systolic pressure may take a longer time to fall to the level of pressure of aortic valve closure. In addition, there may often be impairment in both the onset of relaxation as well as in the rate of relaxation, resulting in slower rate of fall in the intraventricular pressure. Also, there may be coexisting ischemia aggravated by high pressures, increasing the myocardial oxygen demand. Ischemia will further aggravate the poor relaxation in addition to prolonging the mechanical systole (*see* next section). For all these reasons, the occurrence of A2 may be delayed significantly. The sequence may be reversed resulting in reversed splitting of S2. This usually requires a relatively well-preserved overall left ventricular systolic function because significant decrease in systolic function would mean decreased ejection fraction and diminished stroke volume. This will tend to shorten the duration of the mechanical systole and not lengthen it.

Ischemia

Ischemic myocardial dysfunction often involves predominantly the left ventricle. The ischemic portion of the myocardium may have delayed electrical activation and/or delayed onset of mechanical contraction contributing to prolongation of mechanical systole delaying the A2. In the presence of ischemic left ventricular dysfunction, segmental or regional variations may also come into play because coronary lesions are often nonuniform. The nonischemic areas will begin the contractile process, raising the ventricular pressure. The delayed contraction of the ischemic areas occurring after the normal segments have contracted will help to maintain the ventricular pressure preventing its fall, although the peak pressure attained may in fact be lower. This in turn will prolong the duration of mechanical systole, causing delayed A2. The same is, however, not expected in the case of completed infarction. In this instance, the infarcted area will not contract at all, causing no prolongation of the duration of mechanical systole. Therefore, in patients with acute myocardial infarction, the presence of a reversed splitting of S2 should indicate significant co-existing ischemia. Transient paradoxical splitting may occur during angina pectoris in some patients, reflecting the ischemic left ventricular dysfunction *(33)*.

Decreased Systemic Impedance

The systemic impedance is normally high, and therefore in order for the A2 to be delayed on account of impedance change, the aortic impedance must become very low. Such situations are not common. Reversed splitting of S2 is occasionally encountered in patients with large left-to-right shunts at the aortic level through a persistent ductus arteriosus *(36,38)* (Fig. 22B). This is explainable by the fact that the aortic outflow impedance is considerably reduced in such patients because of the communication to the pulmonary artery and its branches. Decreased impedance has been considered to play a part for the delayed A2 seen in some patients with aortic stenosis and significant poststenotic dilatation as well as in some patients with chronic severe aortic regurgitation *(36)*.

Delayed P2

The causes of a delayed P2 component can also be approached using the same three categories as mentioned for delayed A2.

Right Bundle Branch Block

The right bundle branch is a long thin fascicle running under the endocardium on the right ventricular side of the interventricular septum. It crosses the right ventricular cavity through the muscle bundle called the moderator band and arborizes as a Purkinje network at the base of the anterior right ventricular papillary muscle. The conduction through the right bundle can be interrupted very easily even by some mechanical pressure as applied through a catheter placed in the right heart. The lesions causing RBBB need not, therefore, be extensive. The delayed electrical activation of the right ventricle in complete RBBB with QRS width of 0.12 s by itself can cause the delay in the P2. Rarely, delayed mechanical contraction with prolongation of the isovolumic contraction on the right side may also play a part.

Left ventricular pacing and left ventricular ectopics can also be associated with delayed P2 by producing late activation of the right ventricle.

Mechanical Delay

Right Ventricular Outflow Obstruction

In pulmonary stenosis (infundibular or valvular), the elevated right ventricular systolic pressure will take a longer time to fall to the level of the pulmonary artery, prolonging the duration of the mechanical systole on the right side. This would result in a delayed P2. The mechanism is very similar to that described with reference to aortic stenosis. The delay, however, may vary with severity.

Pulmonary Hypertension

The effects of increased pulmonary impedance in significant pulmonary hypertension will be expected to cause an early occurrence of P2, which should result in a narrowly split S2 (Fig. 21). This is what happens in general in the early stages of chronic pulmonary hypertension. At this stage the right ventricular myocardial performance is still normal despite the high pulmonary pressures.

The mechanical effects of chronic pulmonary hypertension on the right ventricular myocardial performance may vary not only with the severity but also with the duration of the pulmonary hypertension and the development and adequacy of compensation. Right ventricular hypertrophy developing over a long period when the process is chronic may be adequate to maintain normal systolic function. However, before actual systolic dysfunction develops leading to right ventricular failure, the diastolic function will become impaired, very similar to what one finds in left ventricular dysfunction and failure. The right ventricle will manifest the diastolic dysfunction by the slower rate of relaxation in a later part of systole and during the isovolumic relaxation phase. The systolic dysfunction may also be reflected in a slower rate of rise of the systolic pressure during the isovolumic phase of contraction. The slower rate of rise and decline of right ventricular systolic pressure would lead to the prolongation of right ventricular mechanical systole relative to the left side. This often can be observed to be associated with the development of abnormal contours in the jugular venous pulsations where jugular descents show less prominence of the *x′ descent* and more dominance of the *y descent* compared to the usually dominant *x′ descent*. In other words, the jugular contour will show $x' = y$, $x' < y$, or *single y descent* as opposed to single x' or $x' > y$ *descent* contour, which is normally seen with the preserved right ventricular function. These changes indicate the development of right ventricular dysfunction *(39)*. In such instances, the

relative lengthening of duration of right ventricular systole compared to that of the left side would result in a delayed P2. This is not uncommon when decompensation develops in chronic pulmonary hypertension *(30,40,41)*. The net effect will of course lead to a widely split S2. Rarely, the splitting may be relatively fixed as well. The latter has been attributed to the inability of the right ventricle to increase the stroke volume on inspiration *(42)*.

The right ventricle is not an efficient chamber in handling sudden rise in pulmonary artery pressures and resistance, as seen in acute pulmonary embolism. Similar myocardial dysfunction may develop in some patients with acute pulmonary embolism causing a delayed P2 *(43)*, and the effects of the delayed P2 may persist for several days and may be observed to improve and become more normal when full clinical recovery occurs.

Decreased Pulmonary Impedance

Pulmonary impedance is generally low even in the normal, as discussed earlier (*see* p. 166). However, in some instances the impedance becomes considerably lower because of increased pulmonary vascular capacity. This is the case with atrial septal defect with large pulmonary arteries and branches because of the longstanding high pulmonary flow due to the left-to-right shunt.

Persistent wide splitting of S2 in patients who have had their atrial septal defect corrected is also probably a reflection of their increased pulmonary vascular capacity with decreased pulmonary impedance. An increased pulmonary vascular capacitance can occasionally be the cause of a wider split S2, which fails to close on expiration in some normal adults *(35)*.

Idiopathic and Poststenotic Dilatation of the Pulmonary Artery

In idiopathic dilatation of the pulmonary artery as well as in poststenotic dilatation of pulmonary artery accompanying mild to moderate pulmonary valvular stenosis, there is probably some deficiency of the elastic tissue in the pulmonary artery, which may be responsible for the excessive dilatation. This may result in slower elastic recoil of the pulmonary artery, partly accounting for the delayed P2. In addition, the increased capacitance may have a lowering effect on the impedance *(30,33,44)*.

Early A2

In severe mitral regurgitation, the A2 may occur early. Mitral regurgitation offers an extra outlet for the left ventricle to empty during systole, reducing considerably the resistance to ejection. Mitral regurgitation presents a volume overload on the left ventricle because the left ventricle has to accept the regurgitant volume as well as the normal pulmonary venous return during diastole. The increased volume would increase the left ventricular contractility by its Starling effect. This, together with an extra outlet for the left ventricle, would cause more rapid and faster ejection. This will have the effect of making A2 occur early.

The effect of an early A2 is to make a relatively wide separation of A2 and P2. The splitting of S2 may be recognizable as a persistent expiratory split of S2. This often tends to occur only when the mitral regurgitation is severe and either acute or subacute, as seen, for instance, with ruptured chordae tendineae *(33)*. The clinical conditions that may result in such mitral regurgitation are usually nonrheumatic in origin.

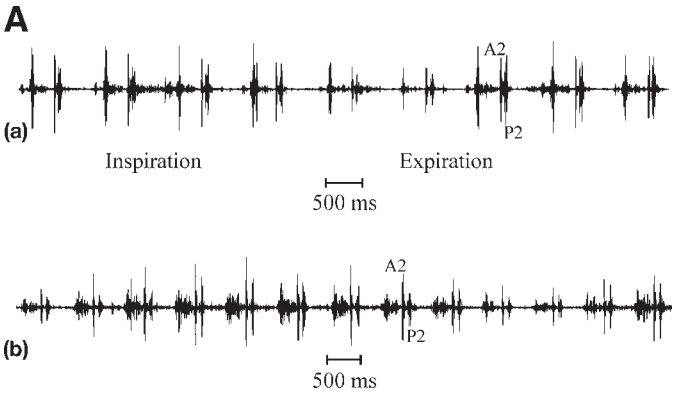

Fig. 23. **(A)** Digital display of magnetic audio recordings from two different patients with secundum atrial septal defect taken from the lower left sternal border region. Both show a relatively fixed split of S2. In **(a)** the split is somewhat narrower, whereas in **(b)** it is wider.

(Continued on next page)

Early P2

The effect of high pulmonary impedance in significant pulmonary hypertension causes the P2 to occur earlier than normal. However, this effect cannot make P2 come earlier than A2. The result of an earlier-than-normal timing of P2 will be to make a narrower split of S2 on inspiration, which will close on expiration and become a single S2.

Abnormal Respiratory Variations of A2-P2 Split

The normal respiratory variation of S2 split with A2 coming earlier and P2 occurring later on inspiration, and the reverse on expiration, depends on the inspiratory increase in venous return increasing the right ventricular volume, as well as an expanding lung increasing the pulmonary vascular capacity. The former would increase the right ventricular ejection time, and the latter would decrease the pulmonary impedance. Such a normal separation of the A2 from the P2 during inspiration is usually not noticeable in the normal adult particularly in the elderly. Even in the young adult, A2-P2 split will usually disappear and be replaced by a single S2 on expiration when the patient is examined in the standing position. If the A2-P2 split persists on expiration in the standing position but narrower than is observed on inspiration, then one has a relatively wide physiological splitting of S2. While this could be a normal variant in some, in most individuals one needs to consider the causes of a delayed P2 to account for the wide physiological splitting. Both the normal split and the relatively wide split of S2 require a normal A2-P2 sequence.

When the A2-P2 separation occurs on expiration and the S2 becomes single on inspiration, then a delayed A2 mechanism is in place, causing an abnormal sequence of P2-A2. This of course is termed the reversed or paradoxical splitting of S2.

When the A2-P2 separation remains relatively fixed and does not appreciably change with respiration, then one has a *fixed splitting of S2*, which usually occurs in atrial septal defect (Figs. 23A–C). The communication between the two atria and the flow through the defect compensates for changing venous return on both inspiration and expiration.

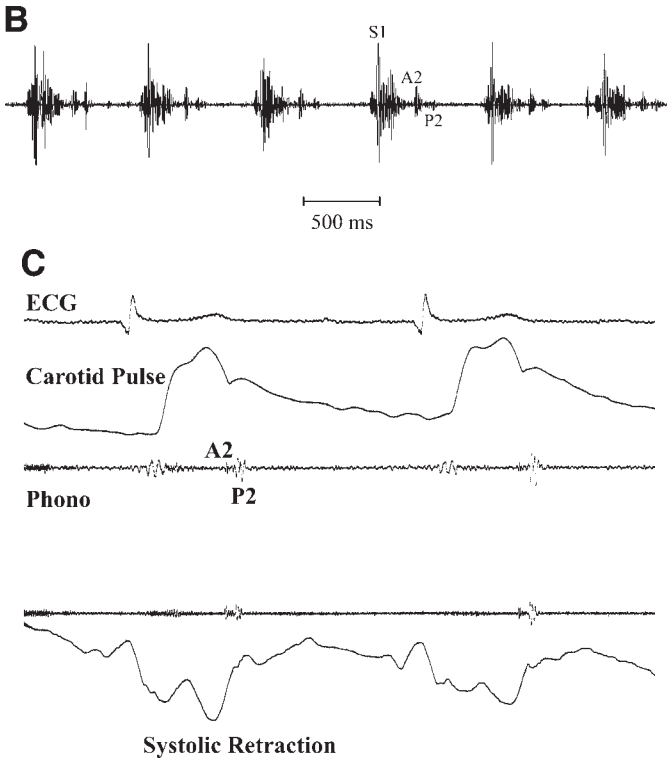

Fig. 23. *(Continued)* **(B)** Digital display of a magnetic audio recording from a patient with a secundum atrial septal defect showing a split S2 at the apex. The S1 has high amplitude because of a loud T1 component. It is followed by an ejection systolic murmur. This patient had a large right ventricle, which formed the apex beat. **(C)** Phonocardiogram (Phono) recording from a patient with atrial septal defect taken at the apex area showing a split S2. Systolic retraction is seen on the simultaneous apex recording. This area of retraction was lateral to the apical impulse caused by the enlarged right ventricle.

The inspiratory increase in right ventricular volume is associated with a decrease in the amount of shunt into the right atrium from the left side. On expiration, the venous return diminishes; this is associated with an increase in the shunt flow through the atrial septum. In other words, the right ventricular volume is more or less the same on both inspiration and expiration. Thus, the right ventricular ejection time remains the same on both inspiration and expiration, accounting for the relatively fixed S2 split. The A2-P2 sequence remains normal in atrial septal defect *(45,46)*.

CLINICAL ASSESSMENT OF S2

S2 is a sharper, crisper sound and can be mimicked by the syllable "dub." It marks the end of systole and beginning of diastole. With normal heart rates, diastole is of course longer than systole. If the jugular contour is normal and visible in

the patient, then the S2 can be noted to coincide with the systolic descent or the *x′ descent* of the jugular pulse. The *x′ descent* is noted to fall onto the S2. Because the *x′ descent* can also be timed independently with the radial arterial pulse with which it coincides, it can be used to focus one's attention on the S2 at the time of auscultation. This may help the beginner, providing a visual marker for the S2 timing and appreciation of its components.

When assessing the S2, one needs to pay attention to the intensity as well as to define the nature of the individual components and their variation with respiration. Trying to pose a series of questions and answer them in a systematic manner is a useful bedside method to adapt:

1. Is the S2 single or split?
2. If split sometimes and single at other times, is the patient breathing in or out during split?
3. If split all the time, is it wider sometimes and narrower at other times or does it remain about the same all the time?
4. If wider sometimes and narrower at other times, is the patient breathing in or out when the wider split is heard?
5. If components are more or less equally separated all the time and no variation is appreciated, is it the same or does it close with patient in standing position to maximize the respiratory variation in volume on the right side?
6. When the S2 is split, over how wide an area of the precordium is the split S2 heard?
7. Is the split heard over the lower left sternal border region? Does it extend over the xiphoid area?
8. Is the split heard over the apex area?
9. If heard over the apex area, is the apical impulse palpable and, if so, is the apical impulse left or right ventricular in origin?
10. What is the grade of loudness of the S2?
11. Which is the area of maximum loudness?
12. Is it palpable?
13. Where is it best palpated?
14. If split, which component is louder, A2 or P2?
15. If split and the respiratory variation cannot be assigned clearly, is it possible to detect the sequence, whether A2-P2 or P2-A2?

Split S2

The normal A2 is heard over a sash area extending from the second right intercostal space to the apex area. The normal P2 is heard over the second and third left intercostal space. Thus, a normal split of the S2 is best heard over the second or third left intercostal space, where both components are audible. Asking the patient to take a breath in may bring in too much noise caused by the breath sounds. This may actually interfere with the assessment of the split, whether present or not, and, if present, to further assess the variation and their relationship to the phase of the respiration. Thus, it may be easier to listen to the S2 and identify its components, whether split or not, and then merely observe the relationship to normal breathing. Occasionally one may be able to direct the patient to breathe with medium effort without making too much respiratory noise. But this may be more difficult than watching the effect of the normal respirations.

The A2 is equally loud at the left ventricular apex as it is in the second right intercostal space, and it may occasionally be loudest at the apex. A2 is never palpably loud unless significant systemic hypertension is present. The intensity of the A2 does not vary with respiration.

P2, on the other hand, is never heard normally beyond the second and third left interspace, and when heard over the lower sternal border region and/or to the xiphoid region would indicate either a louder intensity P2 as in pulmonary hypertension or that the right ventricle is enlarged because of a volume-overload state such as in atrial septal defect or tricuspid or pulmonary regurgitation. For the same reason, the P2 is not usually audible at the normal apex area, which is usually formed by the left ventricle and identified as such by the presence of a medial area of retraction. On the other hand, if the apex is formed by an enlarged right ventricle, as identified by the presence of a lateral area of retraction, then the normal P2 could be audible over the apex area.

P2 often can be noted to increase in intensity with inspiration. The increased volume in the right side presumably provides a greater right ventricular stroke volume, distending the pulmonary root to a greater degree.

A palpable P2 in the second left intercostal space usually indicates pulmonary hypertension. This often correlates to a pulmonary systolic pressure of at least 75 mmHg. Grade III A2 and grade III P2 fusing on expiration may occasionally become palpable. If this happens, the S2 palpability will be restricted to expiration. But if S2 were palpable throughout inspiration and expiration in the second left intercostal space, it would definitely indicate pulmonary hypertension even if there were coexistent systemic hypertension. This stems from the fact that a palpable A2 is not felt maximally at the second left intercostal space. On the other hand, the location of maximal loudness of P2 is second left intercostal space. The exception, when an A2 may be actually palpable at the second left interspace, is transposition of the great vessels (whether congenitally corrected or not) where the aortic root is anterior, superior, and leftward.

In young, thin adults, adolescents, and children, because of the thinner chest wall the P2 may be normally audible over a larger area than in the normal adult. These patients will tend to have an easily audible split of the S2, which is sometimes wide. When examined in the erect position, the respiratory variations become maximal and can often be seen to become closer on expiration, if not actually becoming single. In patients older than 60 yr it is unusual to hear a good split of S2 because of poor chest wall compliance as well as age-related increases in the pulmonary impedance. Therefore, split S2 in the elderly is often abnormal and deserves clarification.

Sequence Identification

In the normal, A2 precedes P2. While A2 is heard over the apex, P2 is usually not heard at the normal apex, which is formed by the left ventricle. If one auscultates over the second or third left intercostal space and hears a split S2 and then quickly changes over to apex with the rhythm of the split S2 in mind, one may be able to detect which of the two components is dropped or not heard at the apex. If the first of the two components is dropped at the apex, then the sequence will have to be P2-

A2. If the second component of the split is dropped, then the sequence will be A2-P2. These conclusions stem from the fact that the normal P2 is the one that is not heard at the apex. This technique can occasionally work much more easily, particularly with practice. Sometimes it may be easier than trying to assess the relationship to respiratory phases. It is particularly useful when the split is very wide and does not close on expiration and the patient is being examined in situations where it is not possible to adapt an erect or standing position, such as in critically ill patients.

Rule of the S2 Split at the Apex

In view of the above observations, one can easily state that a split S2 at the apex is abnormal (Figs. 23B,C) and should make one consider the following possibilities:

1. P2 is loud and may indicate the presence of pulmonary hypertension.
2. If the P2 is not loud and there is no evidence of pulmonary hypertension, the right ventricle may be enlarged, as in volume overload, and one should consider lesions such as an atrial septal defect.
3. P2 is normal and probably audible at apex because of a thin chest, as in children.
4. The split S2 effect is mimicked by a normal single A2, followed by another sound such as an opening snap (OS) or S3.

Persistent or Audible Expiratory Split of S2

A split S2 that is audible on expiration is often a clue to some abnormality of the timing of the individual A2 and P2 components (Fig. 23A). It may indicate one of three possibilities:

1. Relatively wide physiological split of S2 with normal sequence and one must consider the causes of a delayed P2.
2. Reverse or paradoxical split of S2 and abnormal P2-A2 sequence and one must consider the causes of a delayed A2.
3. Relatively fixed split of S2 as in atrial septal defect.

In the normal adult, the S2 split can be made to close on expiration, particularly if assessed in the erect position with the patient either sitting or standing. This allows for maximum variation of right ventricular volume changes with inspiration and expiration. Thus, in most normal adults it would be abnormal to get a persistent S2 split on expiration when examined in this position. Therefore, one should never diagnose abnormal persistent expiratory split of S2 unless the patient has been examined in the erect and preferably standing position.

Often, applying the technique of sequence detection, particularly if the split is not heard at the apex area, one may be able to narrow down the possibilities. Even if the split is heard at the apex and the apex is formed by the left ventricle, then the concept that the P2 must be softer at the apex than at the second or third left intercostal space can be applied to detect the component that gets softer as one approaches the apex, listening and inching the stethoscope from the base to the lower left sternal border region and then to the apex. A reverse sequence is detected if the first of the two components get softer at the apex. Then causes of the A2 delay must be considered. A normal sequence is detected if the second of the two components gets softer at the apex. Then causes of delayed P2 must be considered.

These deductions are made on the basis that the apex in the given patient is left ventricular in origin.

In atrial septal defect, the persistent expiratory split may or may not be associated with a wide splitting of S2. Splitting can be fixed and yet narrow in atrial septal defect, particularly if the pulmonary flow is markedly increased and the pulmonary bed is relatively overfilled and behaves like a system with high impedance. This will tend to bring the P2 forward, causing a narrower split. The development of some degree of pulmonary hypertension may also contribute to increased impedance and a narrower split. Nevertheless, it will be relatively fixed and will not appreciably change with respiration. One must carefully assess the patient with the patient in the erect or standing position before reaching a conclusion about a fixed split. Occasionally the pulmonary systolic murmur, because of flow, may not be impressive, and often the diagnosis of atrial septal defect hinges on diagnosing a fixed split S2.

Partial anomalous pulmonary venous drainage into the right atrium may also cause a wide and sometimes relatively fixed split of S2. This lesion often coexists with an atrial septal defect and may rarely be an isolated anomaly. The clinical features often resemble atrial septal defect *(42)*. When it occurs with an intact atrial septum, fixed splitting does not occur *(47,48)*.

Patients with primary pulmonary hypertension developing some degree of decompensation may have a wide persistent split of the S2, and the variation with respiration may be minimal and therefore may mimic a relatively fixed splitting of atrial septal defect. Sometimes the effect of a *post-Valsalva strain* may help to distinguish the two. During the strain phase of the *Valsalva maneuver*, the patient attempts to breathe against a closed glottis. This leads to increased abdominal and intrathoracic pressure, which prevents normal venous return, which would lead to considerable decrease in the right heart volume. Following the release of the Valsalva strain, there is a sudden drop in intrathoracic and abdominal pressure, which leads to sudden increase in the venous return. This would markedly increase the right heart volume for a few beats, diminishing again afterwards. In the normal, the splitting may increase over 20 ms immediately following the release of strain. A few seconds later, the S2 splitting may become narrower or single *(46)*. In atrial septal defect, the flow through the septal defect from the left atrium to the right side will compensate for the changes in the venous return, more or less keeping the right ventricular volume the same. Therefore, the S2 split will remain relatively the same *(46)*. On the other hand, in primary pulmonary hypertension, the S2 split will be much wider immediately after release because of an increase in the duration of right ventricular systole due to the abnormal behavior of the right ventricle in handling the volume load, and the split will become narrower after a few beats when the venous return decreases. Exercise may also help to distinguish pulmonary hypertension from atrial septal defect. Exercise will widen the split in right ventricular failure from pulmonary hypertension and will not do so in atrial septal defect *(16)*.

(For additional examples review Phono Files 10–27 under Heart Sounds on the Companion CD.)

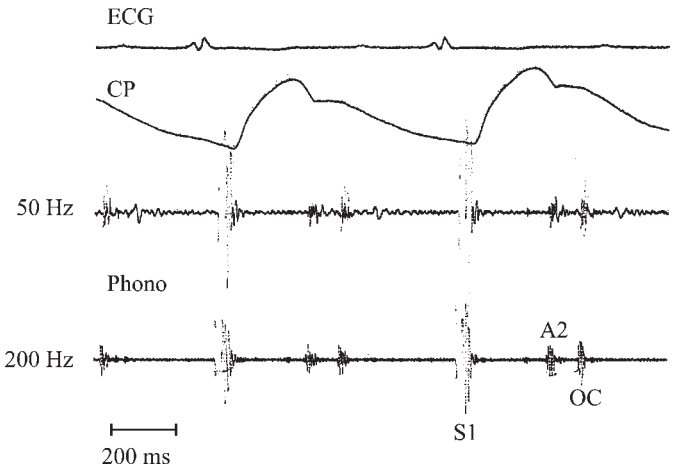

Fig. 24. Phonocardiogram (Phono) recording from a patient with a mechanical mitral valve prosthesis taken from the lower left parasternal area showing clicky sharp sounds associated with opening and closure of the mechanical valve. The closing of the valve causes a clicky sharp S1 and when it opens it produces a sharp opening click (OC) after the S2.

OPENING SNAP (OS)

After the closure of the semilunar valves, which is associated with the occurrence of the S2, the ventricles continue to relax and the ventricular pressures continue to fall. When the ventricular pressure falls below that of the atrium, the isovolumic phase of relaxation comes to an end and the A-V valves open to begin the phase of diastolic filling. If an artificial mechanical prosthetic valve has been used to replace the native valve, say the mitral valve, then one can often hear an opening click at this time of the cardiac cycle, which will follow the S2. Because such an artificial prosthetic mitral valve will also make a sharp closing click corresponding to the timing of S1 (Fig. 24), one will actually hear a cadence or rhythm made by the clicky S1 followed by S2 and an opening click. The rhythm is *Click.....Two...Click....*

Unlike the artificial mechanical prosthetic valve, when the normal mitral and tricuspid valves open, there is usually no formation of sounds. This is mainly because the valve opening causes the individual leaflets to move away from each other more or less symmetrically, resulting in no real deceleration of the moving column of blood from the atria against the leaflets themselves in their attempt to enter the ventricles. However, when the valves are stiffened and fused at the commissures, resulting in some degree of stenosis, as seen in rheumatic mitral stenosis, then one may hear a sound associated with the opening of the mitral valve. The sound is often snapping and sharp in quality and hence termed the *opening snap (49–51)*. As discussed previously in relation to S1, the M1 in mitral stenosis is loud and snapping. The OS can be considered the reverse of the closing snap, which is the loud M1 in mitral stenosis (Figs. 25A,B). The presence of a loud M1 followed by a normal S2 and a sharp OS gives rise to a recognizable cadence:

One.....Two….O..... Lubb.....Pa...Ta.....

A similar sound can occur in rheumatic tricuspid stenosis, but the latter is very rare and therefore need not be discussed further.

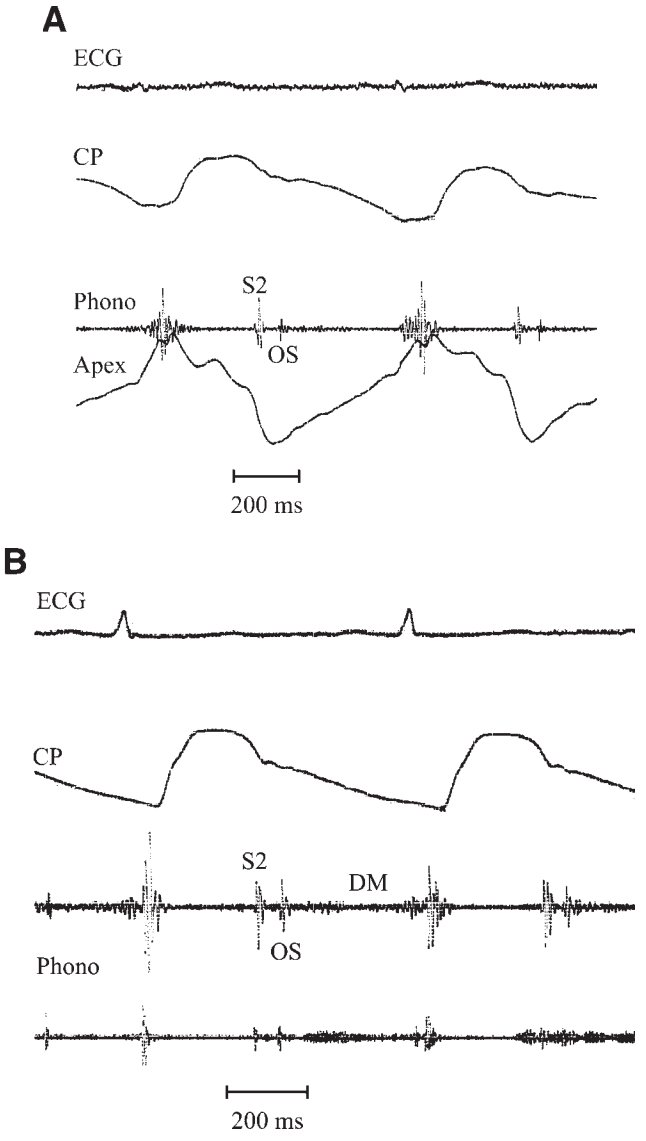

Fig. 25. **(A)** Phonocardiogram (Phono) recording taken at the apex area from a patient with rheumatic mitral stenosis who had a previous mitral valve commissurotomy for relief of the obstruction. The S1 is relatively loud. Note a sharp sound following the S2, which is the opening snap (OS). The OS occurs almost simultaneously with the most nadir point of the apex tracing, which is termed the O point. **(B)** Phonocardiogram (Phono) recording from another patient with mitral stenosis taken close to the apex area showing the loud S1 followed by the S2 and the opening snap (OS). Also seen is the diastolic murmur (DM) of the mitral stenosis.

The Mechanism of Formation of the Opening Snap

In mitral stenosis, the commissural fusion results in anatomical distortion of the mitral valve, and the valve behaves like a stiffened funnel. The tethering of the leaflets at the commissures does not allow free opening of the leaflets. Both the anterior and the pos-

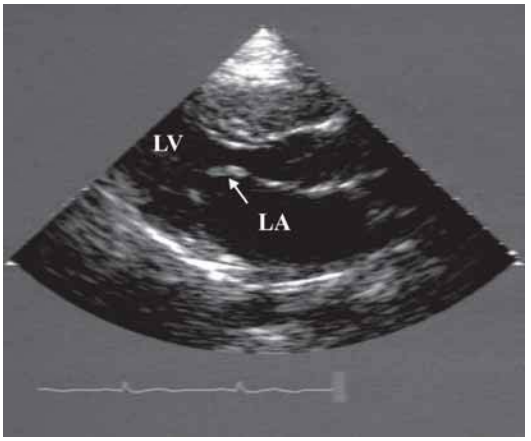

Fig. 26. Stop frame of a two-dimensional echocardiogram from a patient with mitral stenosis in the parasternal long axis at onset of diastole showing the typical bowing of the anterior mitral leaflet (arrow). Note that the leaflet tip is pointing posteriorly because of tethering caused by the stenosis making a funnel-like opening. Part of the column of blood trying to enter the left ventricle (LV) from the left atrium (LA) during diastole is oriented toward the belly of the leaflet. When the leaflet excursion reaches its anatomical limits caused by the tethering, this column of blood is suddenly decelerated. This leads to the production of the opening snap (OS).

terior leaflets tend to move together in the same direction anteriorly. If there is no excessive calcification of the main body of the anterior leaflet, it will be seen to actually bow anteriorly toward the ventricular septum with the opening motion of the valve at onset of diastole (Fig. 26). During systole, when it closes it will have a shape almost like a hockey stick, particularly when seen on a two-dimensional echocardiogram. The column of blood from the left atrium begins to enter the left ventricle when the pressure in the ventricle falls below that of the *v wave* peak in left atrial pressure, which will lead to opening of the valve. Because of the distorted orifice and incomplete separation of the leaflets, part of the column of blood will actually be oriented against the body of the anterior leaflet instead of being oriented toward the orifice. When the leaflet excursion comes to its anatomical limits because of its commissural tethering, this part of the column of blood will be decelerated suddenly, along with the leaflet. The dissipated energy at this time can be expected to produce the sound. Because in mitral stenosis the left atrial pressure is often elevated, the column of blood moving from the left atrium is under a higher pressure gradient than normal. Therefore, there is relatively greater energy in the moving column contributing to a louder sound. Characteristically, when the valve is relatively mobile, it leads to the production of the sharp snapping OS *(51–53)*.

Opening Snap in the Absence of Mitral stenosis

Rarely, excessive flow across the mitral valve in certain clinical conditions can be associated with the presence of an OS associated with the opening of the mitral valve in the absence of mitral stenosis. These include pure mitral regurgitation, ventricular septal defect, persistent ductus arteriosus, tricuspid atresia with large atrial septal defect, and thyrotoxicosis *(54–56)*. In atrial septal defect, the torrential flow across the tricuspid valve may be associated with a tricuspid OS *(56)*.

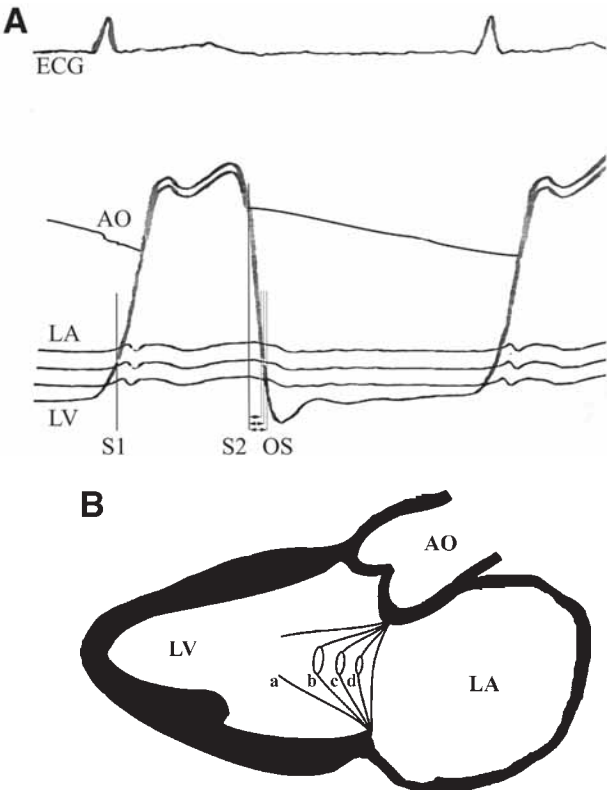

Fig. 27. **(A)** Diagram showing simultaneous left ventricular (LV) and left atrial (LA) pressures in mild, moderate, and severe degrees of mitral stenosis. The more severe the stenosis, the higher will be the left atrial pressure. The opening snap (OS) occurs at the end of the isovolumic relaxation phase of the left ventricle when the left ventricular pressure falls just below the left atrial pressure. The OS will therefore tend to occur earlier with higher LA pressure and later with lower LA pressure. Thus, the S2-OS interval is short with severe mitral stenosis and long with mild mitral stenosis. **(B)** Visual representation of the excursion of the mitral leaflets in mitral stenosis of different degrees of severity: a, normal; b, mild; c, moderate; d, severe. With milder stenosis the column of blood has to travel further before deceleration against the valve, thereby making a late OS.

Congenital mitral stenosis is not usually associated with OS because these valves are abnormal and not pliable.

Timing of the OS and the S2-OS Interval

The OS will be expected to occur at the end of the isovolumic phase of relaxation. The latter has an average duration of at least 60 ms. The S2-OS interval then must be expected to be at least 50 ms or longer. In general the OS may occur anywhere between 50 and 110 ms after S2. The OS has been reported to follow A2 by a delay ranging from 30 to 150 ms *(56)*. The interval will depend on the level of the aortic pressure, the rate of isovolumic relaxation, and the left atrial *v wave* pressure peak. Of these three, the most important determinant is the level of the peak left atrial pressure. Thus, if the left atrial *v wave* is higher, then the OS will occur earlier than when the left atrial *v wave* is lower (Fig. 27A).

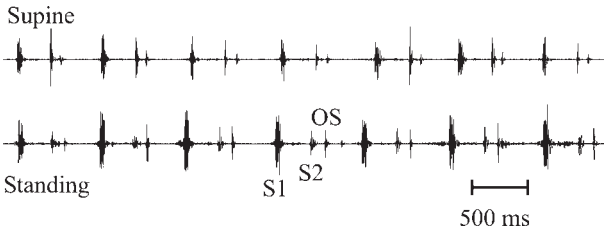

Fig. 28. Digital display of a magnetic audio recording from a patient with mitral stenosis taken at the lower left parasternal region showing the variation in the S2-OS interval between supine and standing position. The S2-OS interval is slightly longer on standing than when supine. The fall in the left atrial pressure caused by the upright posture makes the OS come later after S2. The A2-P2 split, however, will either narrow considerably or become a single S2 on assuming an upright position.

Because the height of the left atrial pressure is indirectly related to the severity of the mitral stenosis, the more severe the stenosis, the higher will be the left atrial pressure and the earlier the OS will occur after the S2 (Fig. 27A). The S2-OS interval can be either short, close to 60–70 ms; medium, close to 80–100 ms; or long, 100–120 ms.

A short S2-OS interval can be simulated by the syllables, *Lubbb...pa..da* when said as fast as one can. It can be medium and may simulate the syllables, *Lubbb...pa....ta* when said as fast as one can. When it is late it will be mimicked by *Lubbb...pa.....pa*, again said as rapidly as possible.

It can also be easily visualized that the extent of the excursion of the leaflet before its sudden tensing because of the tethering will vary according to the severity of the mitral stenosis. The more severe the stenosis, the less will be the extent of the excursion and therefore the earlier will be the OS (Fig. 27B).

Because besides the left atrial pressure, the aortic pressure and the rate of isovolumic relaxation control the S2-OS interval, this interval may not always accurately predict the severity of mitral stenosis, especially in elderly patients and in the presence of hypertension. This interval will vary in atrial fibrillation because of the varying diastolic lengths. The longer cycles will be followed by lower left atrial pressure because of longer time for left atrial emptying, and the next systole will also be more likely to have a lower left atrial pressure. Thus, following long diastoles the S2-OS interval will be longer. In the presence of low cardiac output and a very large left atrium, one may have a long S2-OS interval even with significant mitral stenosis. In view of these confounding factors, a short S2–OS interval may be more helpful than a wide S2-OS interval in predicting the degree of mitral stenosis.

Maneuvers that make the left atrial pressures fall, such as making the patient stand up from a supine position, will make the OS come later (Fig. 28). The reason for this is the decreased venous return that occurs with assuming the erect posture, which will lower the left atrial pressure.

Following supine exercise, the S2-OS interval shortens because of rising left atrial pressure. Postexercise S2-OS interval of less than 60 ms will be suggestive of significant mitral stenosis *(56)*.

The Intensity of OS

In general, the presence of a good-intensity OS requires a fairly mobile valve. When the stenosis is relieved by surgical mitral valve commissurotomy, the OS will not always be abolished because there may be still enough tethering of the leaflets at the commissures with all the anatomical prerequisites for the OS production. When it is excessively restricted because of heavy calcification, the OS is unlikely to occur.

When there is severe mitral stenosis with very low cardiac output and decreased stroke volume, the OS intensity may be diminished because of the low flow. When there is significant pulmonary hypertension associated with severe mitral stenosis, the accompanying large right ventricle and low flow because of obstruction at the pulmonary arterioles will also tend to make the OS soft. When there is co-existing aortic valve disease with aortic regurgitation, the regurgitant stream is often directed toward the anterior mitral leaflet. In these patients the energy of the sudden deceleration of the mitral inflow against the anterior mitral leaflet is somewhat cushioned by the regurgitant stream and the resulting sound is often soft and may be even absent.

Clinical Assessment of the OS

The OS is generally maximally loud somewhere between the lower left sternal border and the apex. When it is very loud it can be heard over a wide area, including the base. At the apex, it coincides with the onset of the diastolic murmur of the mitral stenosis. The presence of OS following the S2 almost always simulates a widely split S2. In addition, a good-intensity OS tends to be associated with a loud S1. Thus, when one hears a loud S1 and what sounds like a widely split S2, one should always suspect an OS, and attempts should be made to confirm or rule out its presence. This essentially consists in looking for the following specific features of the OS:

1. It is maximally loud between the left sternal border and the apex.
2. It is sharp and generally high in frequency
3. Its intensity may vary slightly, with respiration becoming slightly softer on inspiration because of less blood flowing through the left side and slightly louder on expiration because of increase in flow through the left heart. It behaves similar to A2 in this regard. It is different from P2, which will become louder on inspiration.
4. The S2-OS interval tends to remain relatively the same with inspiration and expiration. Sometimes the P2 coming earlier on expiration may give one the impression that the S2-OS interval is widening. A wide paradoxical split of LBBB may sometimes be confused with S2-OS. In the absence of LBBB, however, if the second component of a wide split should increase in loudness at the apex or the split should become wider on expiration, it is unlikely to be a delayed P2, and an OS should then be suspected as the cause of the split.
5. When the patient's posture is changed from supine to sitting with feet dangling or, better still, to a standing position, the OS will be found to come later. In other words, the fall in the left atrial pressure that accompanies the erect position because of the decreased venous return will make the OS occur later, and this will make the split wider than when supine. The A2-P2 split will do the opposite because any decrease in venous return will make the P2 come earlier. This simple observation will often help in distinguishing between the two. Occasionally, however, the OS may become

too soft altogether on standing because of a significant drop in output and flow across the mitral valve, particularly in severe mitral stenosis.

6. The most definite way of recognizing the presence of OS is the ability to appreciate all three components on inspiration, namely, A2, P2, and the OS. This tends to happen in most patients when it is specifically looked for. The effect of such a triple sound on auscultation is unique, and once heard anyone can appreciate it. The tripling or trilling on inspiration with a simple split on expiration can be picked up over the second to fourth left sternal border area, depending on the width of the area where the P2 is audible in a given patient (Fig. 29). The *trill* usually sounds like beating on a snare drum. It can also be mimicked by triple-clicking on the commonly used mouse attachment on any modern computer.

A late OS, when soft, may mimic an early S3. The distinctions will be discussed under S3.

(For additional examples review Phono Files 28–34 under Heart Sounds on the Companion CD.)

THIRD HEART SOUND (S3)

After the opening of the mitral and the tricuspid valves, blood flows into the ventricles from the atria during diastole. Diastolic filling of the ventricle is divisible into three phases, an early rapid filling phase followed by a slow filling phase or diastasis and at the end by the atrial contraction phase. The early phase of the ventricular filling is characterized by sudden vigorous expansion associated with rapid inflow of blood. The peak of this filling period may be accompanied by a sound, which is termed the third heart sound, or S3.

Diastolic Function

The rapid filling phase of diastole is a very dynamic process, which begins with the active ventricular relaxation. Henderson wrote in 1923, "in the heart, diastolic relaxation is a vital factor and not merely a mechanical stretching like that of a rubber bag" *(57)*. It begins at the later half of systole and involves the isovolumic relaxation phase and the early rapid filling phase. It involves actin–myosin cross-bridge dissociation by the reuptake of Ca^{2+}. Relaxation is an active process because it is energy dependent and requires ATP and phosphorylation of phospholamban (one of the proteins involved in the modification of sarcoplasmic calcium ATPase function) for uptake of calcium into the sarcoplasmic reticulum. Metabolic control of this complex process is through coronary perfusion and neurohumoral and cardiac endothelial activation. For instance, cyclical release of nitric oxide has been noted to be most marked subendocardially, peaking at the time of relaxation and diastolic filling. In addition, the intrinsic viscoelastic properties of the myocardium are also important. Fibrosis that accompanies hypertrophy probably plays a role in the impairment of relaxation *(58–60)*.

Just as force of contraction is alterable because of variation in filling or preload and afterload (the systolic load that the left ventricle has to face after it starts to contract), mechanical factors can also alter the rate of relaxation *(61)*. Five types of loading affecting relaxation are recognized. One slows the rate of relaxation, and four tend to increase the rate of relaxation *(62–64)* (Fig. 30).

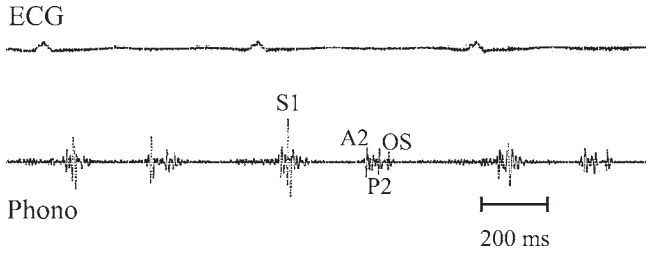

Fig. 29. Phonocardiogram (Phono) recording from a patient with mitral stenosis taken from the third left interspace showing the split S2 with A2 and P2 as well as the opening snap (OS) making a triple sound (trill), which is easily recognized.

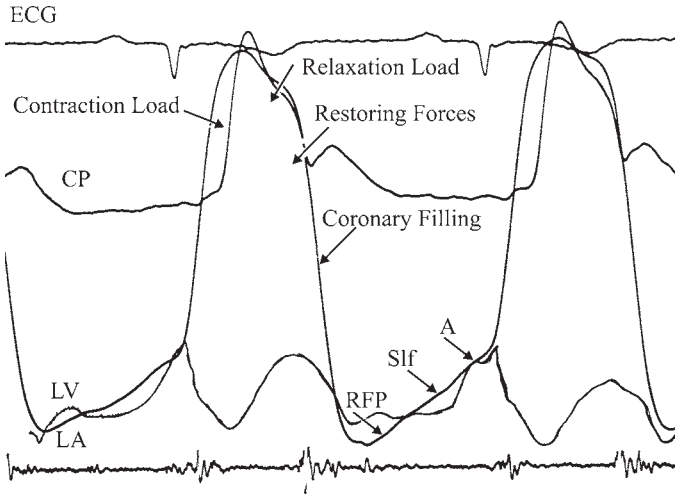

Fig. 30. Diagram of simultaneous left ventricular (LV) and left atrial (LA) pressures and the carotid pulse (CP), indicating the various mechanical forces affecting the relaxation of the left ventricle operating at different phases of the cardiac cycle. While an increase in volume or pressure in early systole (contraction load) slows relaxation, the same in later systole (relaxation load) hastens it. Restoring force resulting from the deformation of contraction and the coronary filling during isovolumic relaxation improves relaxation. When the LV pressure falls below that of the LA, diastolic filling begins. Diastole consists of three phases: the early rapid filling phase (RFP), followed by the slow filling phase (Slf), and finally the atrial contraction (A) phase. Active expansion during RFP is favored by increasing wall stress (*see* the text).

1. Increase in volume or pressure in the early phase of systole tends to slow relaxation.
2. Increase in volume or pressure in late systole hasten relaxation.
3. The deformation caused by contraction itself provides a stored potential energy, which contributes to the restoring forces.
4. During the period of isovolumic phase of relaxation, coronary filling begins and acts to improve relaxation.
5. The prevailing wall stress affects the rate of relaxation during the early rapid filling phase of diastole.

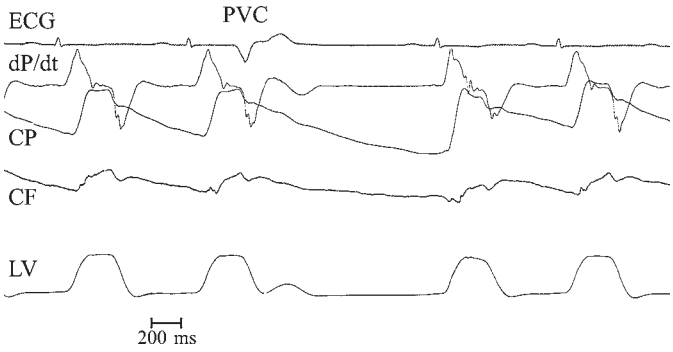

Fig. 31. Simultaneous left ventricular (LV) pressure and its first derivative (*dP/dt*) shown along with the carotid pulse (CP) and electrocardiogram (ECG). Note that the first beat following the premature ventricular beat (PVC) has a significant decrease in the rate of relaxation, as shown by the depth of the negative *dP/dt*.

The load effect on the rate of relaxation has been studied in isolated muscle-clamp experiments as well as in canine hearts studied with microcomputer-assisted pumps. In these studies volume increments in specific portions of systole have demonstrated the same phenomenon *(63,65)*. The potential energy gained by contraction is thought to act through cytoskeletal proteins, such as titin, which are compressed. During diastole they expand like springs, expending this stored energy, and provide a recoiling force for the myocardial filament to regain its length *(59)*.

Three clinical examples will be considered.

Hypertrophic Cardiomyopathy With Obstruction

The nature of this condition is such that it is accompanied by impairment of relaxation. The fibrosis that accompanies the hypertrophy may be expected to contribute to this *(60)*. One can expect some load-dependent alteration in relaxation as well. In hypertrophic cardiomyopathy with obstruction, the midsystolic obstruction will lead to increased pressure in the left ventricle, which will act as an increased "contraction-phase" load. In addition, these patients have a very high ejection fraction and low end-systolic volume. This leads to poor late systolic relaxation load. Both of these factors could also contribute to poor relaxation.

Postextrasystolic Beat

It is common knowledge that the beat following an extrasystole is strong and forceful, but it is usually not recognized that this postectopic beat has slower relaxation. If one records the rate of ventricular pressure rise and fall (*dP/dt*), it will be seen that the peak negative *dP/dt* reflecting the rate of relaxation is smaller in the postectopic beat compared to the normal beat (Fig. 31). The reasons for this are probably twofold. An excess of calcium is made available to the myocardial cells from the extrasystole, and the cells are somewhat calcium overloaded, which would be expected to slow relaxation. The second reason is the poor relaxation phase load in the postectopic beat because of near-complete ejection.

Mild Left Ventricular Dysfunction

In a study of left ventricular function using characteristics of the apical impulse as measured by apexcardiography *(66)*, we observed that the rate of isovolumic relaxation slope was slower in patients with mild left ventricular systolic dysfunction, whereas this slope was not abnormally slow when the ventricular systolic function was moderately or severely depressed. In the presence of significant systolic dysfunction, the ejection fraction is reduced. This leads to an increased end-systolic volume. It is conceivable that this may act as a "relaxation-phase" load, which could indirectly help in improving relaxation. It is known that the rate of left ventricular relaxation as measured by peak negative *dP/dt* is impaired in patients with ischemic heart disease and known systolic dysfunction and decreased ejection fraction *(67)*. The diastolic time intervals, like the isovolumic relaxation time and other noninvasive measurements, however, are affected by many factors, and they do not consistently gauge left ventricular relaxation *(68)*. This may be the reason that this noninvasive measurement by apexcardiography failed to pick up the abnormality in the presence of significant left ventricular dysfunction.

Finally, both the process of calcium inactivation and the load effects on the rate of relaxation could be variable and not uniform through the entire myocardium, depending on the pathological process *(62)*. This is best exemplified by ischemic heart disease, which is often segmental.

Early Rapid-Filling Phase

The *rapid filling phase* of diastole is part of this active phase of relaxation. The S3, when present, occurs at the end of this period. The rate of expansion of the ventricle during this phase is conditioned by the prevailing load or wall stress, increasing with the increasing wall stress. The latter can be defined by Lamé's modification of the *Laplace relationship*, where the wall stress or the wall tension is directly proportional to the pressure and the dimension or the radius and inversely related to the wall thickness. This phase begins at the onset of mitral and tricuspid valve opening. The peak pressure head driving the filling of the ventricle is the peak *v wave* pressure in the atrium because the ventricular pressure is close to zero at the beginning of this phase. During this phase of filling, the ventricle receives volume and expands, and its walls continue to thin. This means that there is an increasing wall stress from the beginning of this phase (at the mitral opening) to the end of this period. Thus, this period of filling accelerates under increasing rate of active expansion favored by the increasing wall stress, which characterizes this period. If the *v wave* height is increased for any reason, then this will add to the wall stress achieved, further hastening relaxation and expansion *(62)* (Fig. 30).

Slow Filling Phase and Atrial Contraction Phase

As opposed to the early rapid filling phase of diastole, the period of *slow filling or diastasis* and the *atrial contraction phase* are influenced by compliance, which is mainly secondary to the passive elastic properties of the myocardium (Fig. 30). Compliance can be expressed for the whole ventricle in terms of volume–pressure relationship (*dV/dP*) or the converse, expressing it as unit pressure change for unit increase in volume (*dP/dV*). The latter is termed *chamber stiffness*. When the same is expressed for an individual muscle fiber, it is called *muscle stiffness* (measured by stress–strain relationship, force per unit area/fractional change in dimension) *(69–73)*.

Factors that affect the compliance of the ventricle are:

1. *Completeness of relaxation*
2. *Chamber size*
3. *Thickness of the wall*
4. *Composition of the wall (inflammation, infiltrate, ischemia or infarction, scars, etc.)*
5. *Pericardium*
6. *Right ventricular volume/pressure and effects on the left ventricular compliance*

The ventricle can become stiff and offer more resistance to expansion when the overall size is small, as in children. It also is stiffer when the process of relaxation is impaired for any of the reasons mentioned previously (e.g., hypertrophic cardiomyopathy with obstruction, ischemic heart disease because of ischemia). The degree of decrease in compliance when there is hypertrophy of the myocardium depends on the cause of hypertrophy. When there is physiological hypertrophy, as seen in athletes, the decrease in compliance is slight. When the hypertrophy is a result of pressure load, as in significant hypertension or outflow obstruction (e.g., aortic stenosis), the decrease in compliance is more marked. Profound decrease in compliance tends to occur in hypertrophic cardiomyopathy. In addition, any pathological process (ischemia, scars, inflammation, infiltrative process, etc.) that affects the myocardium can alter the compliance of the ventricle by making the affected segments stiff. Ischemia is particularly of interest. It makes the ischemic segments relax poorly. The segments become stiff because of incomplete relaxation *(74)*. This affects the overall distensibility of the ventricle when the ischemia is significant. The decreased compliance leads to increased diastolic filling pressure when the ventricle fills during diastole. The increased diastolic pressure is transmitted to the atrium because the mitral valve is open during diastole and the increased left atrial pressure is in turn transmitted to the pulmonary capillary bed. This increased pulmonary alveolar capillary pressure leads to the production of symptoms of dyspnea during an episode of angina. The increased diastolic pressure in the ventricle, however, causes greater stretch of the nonschemic segments and increases their contractility, thereby preserving the forward cardiac output.

If for any reason the ventricle becomes stiff or less compliant, then the expansion during the slow filling period becomes difficult and slower. The compensation for this inadequate ventricular filling is provided by a stronger-than-normal contraction of the atrium during the atrial contraction phase, assuming that the atrium is healthy.

Mechanism of Formation of S3

S3 occurs at the end of the rapid filling phase of diastole *(75,76)*. The column of blood entering the ventricle during this phase is under the pressure head provided by the *v wave* pressure in the atrium. This phase of diastolic expansion is generally rapid and vigorous for reasons discussed earlier. But in almost all hearts this rapid expansion suddenly changes to a period of slower expansion. Thus, there is a tendency almost in all hearts for the moving column of blood entering the ventricle during the rapid-filling phase to decelerate somewhat toward the end of this period (Fig. 32). When the transition becomes more abrupt, this will be expected to affect the moving column of blood, causing it to decelerate more abruptly. The factors that are likely to make the transition more abrupt in general are those that decrease the compliance of the ventricle *(77–80)*.

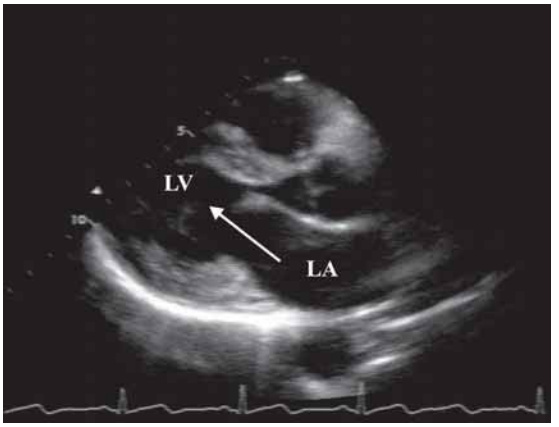

Fig. 32. Stop frame of a two-dimensional echocardiogram taken from a normal subject in the parasternal long axis at the end of the rapid filling phase of diastole when the moving column of blood (arrow) entering the left ventricle (LV) from the left atrium (LA) is suddenly decelerated because of the fact that the rapid expansion suddenly changes to a period of slower expansion. Factors that make the transition more abrupt tend to produce an S3 (*see* the text).

The energy achieved by the moving column of blood during the active rapid filling phase of diastole is related to the rate of relaxation, the velocity, and the volume of blood entering the ventricle and the pressure head provided by the *v wave* peak in the atrium. When the momentum achieved by the moving column of blood is significant and the transition from the early rapid filling phase to the slow filling phase more abrupt because of decreased ventricular compliance, however brought about, then the deceleration will occur more suddenly and the dissipation of energy will result in the production of an audible sound within the ventricle. The sound will obviously occur at the peak of the rapid filling wave, which is the S3. Intraventricular pressure and transmitral flow studies in dogs have demonstrated a small but consistent reverse transmitral gradient to always accompany this deceleration *(81)*. In addition, the sounds accompanying the flow deceleration could be recorded inside the ventricles as well as over the epicardial surface of the exposed ventricles, ruling out the external origin theory of S3 *(82)*. The whole hemic mass, including the blood, as well as the ventricular wall and the papillary muscles probably participate in the vibration.

Physiological S3

This occurs in children and in pregnant women and in other conditions associated with rapid circulation such as anemia and thyrotoxicosis. In children, the rapid inflow and the small size of their hearts together contribute to the development of S3 (Fig. 33). The small size offers increased resistance to expansion initially, like when one tries to blow up a balloon. Once expanded, there is not much resistance to further filling. Physiological S3, however, is rare after the age of 35. In pregnant women, the blood volume is increased and there is a relatively rapid circulation and increased sympathetic tone. The compliance need not be decreased. In the presence of a rapidly moving large volume of inflow, the transition from the rapid expansion to slow expansion may be sufficient to cause enough deceleration to produce the S3.

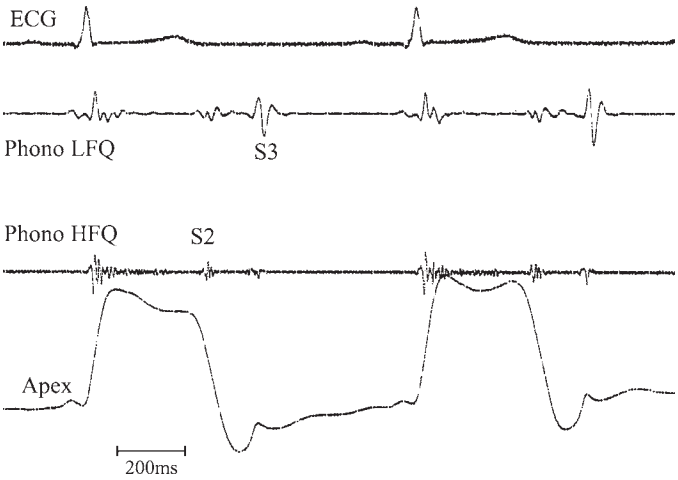

Fig. 33. Phonocardiogram (Phono) recording from a young subject taken at the apex area along with an apexcardiogram (Apex) showing a physiological S3. The S3 is well seen in the low-frequency (LFQ) range of 25–50 Hz. It is not as prominent in the high-frequency (HFQ) range of 200 Hz. The S3 is seen to coincide with the peak of the rapid filling wave (arrow) in diastole.

S3 in Ventricular Volume Overload

In volume overload states such as mitral and tricuspid regurgitations, the inflow volume during diastole into the ventricle is larger because the regurgitant blood into the atrium as well as the usual venous (systemic or pulmonary) return will enter the ventricle during diastole. The ventricle is also hyperdynamic in its contraction in these states because of the Starling effect caused by the large volume of diastolic filling. The relaxation following such stronger contraction will also be expected to be very rapid because of better restoring forces. In addition, the *v wave* peak pressure in the atrium will be higher because of the regurgitation (through the mitral and the tricuspid valves). For these reasons, the inflow into the ventricle not only will be large in volume but will also move with greater velocity, achieving greater energy. In fact, an apexcardiogram obtained in patients with volume-overloaded left ventricle will often show an exaggerated large rapid filling wave with an overshoot (Figs. 34A,B). The response of the ventricles to chronic volume overload is to dilate and enlarge. This is accompanied by increased compliance. Therefore, the deceleration is mainly brought about from the rapid expansion to slow expansion alone. The S3 in these states may in fact have enough duration and sound like a short murmur. In late stages when the ventricles have developed secondary hypertrophy and focal fibrosis, particularly in the subendocardial regions, the resulting decrease in compliance will also play a part in the production of the S3. Similar situations are also likely to occur and result in left-sided S3 in large left-to-right shunts through persistent ductus arteriosus and ventricular septal defects. In these conditions, the increased pulmonary flow received through the communication has to exit through the pulmonary veins into the left atrium.

In atrial septal defect with large shunts, the increased flow from the left atrium into the right atrium causes a right ventricular volume overload. Similar considerations apply.

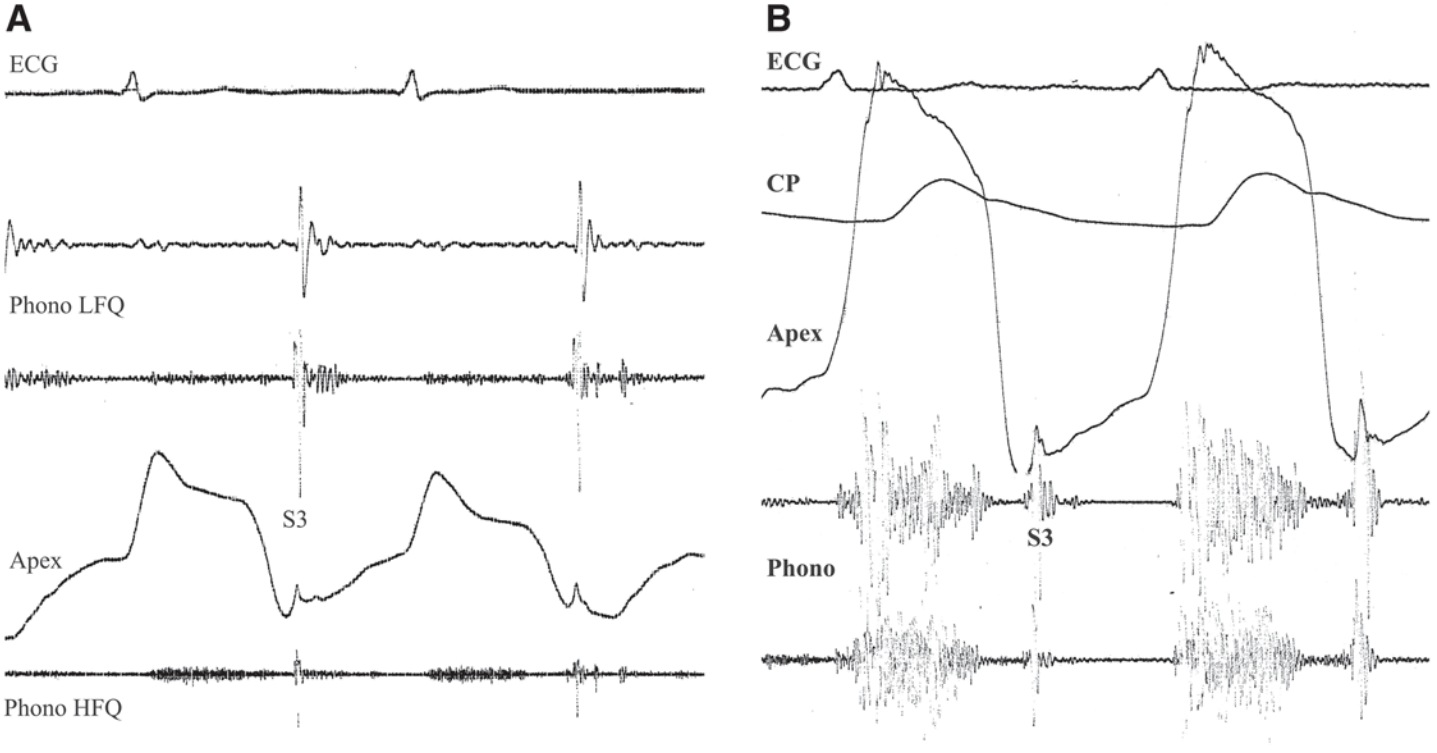

Fig. 34. Phonocardiogram (Phono) recordings taken from the apex area along with apexcardiogram (Apex) from two patients, both with significant mitral regurgitation causing left ventricular volume overloads. In both, overshoot of the rapid filling phase can be seen on the Apex coinciding with the S3 on the Phono.

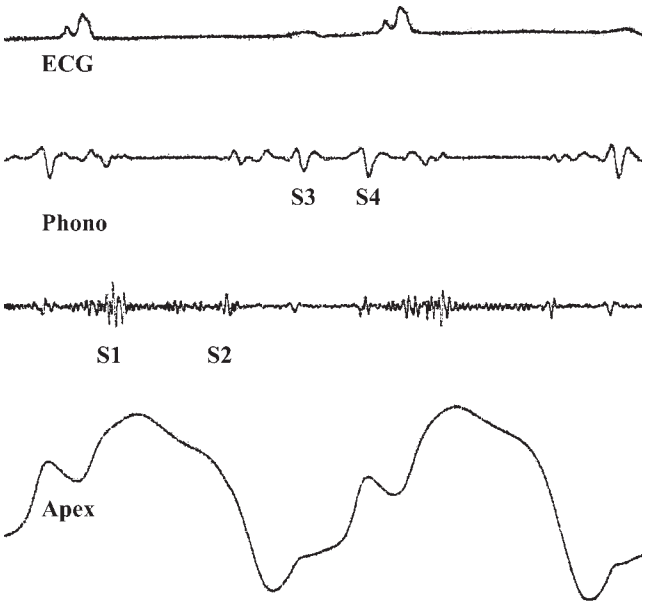

Fig. 35. Phonocardiogram (Phono) recording from a patient with severe aortic stenosis and left ventricular failure taken from the apex area along with the recoding of the apexcardiogram (Apex). The Phono shows both the fourth (S4) and third heart (S3) sounds.

However, because the right ventricle is more compliant than the left ventricle, increased flow through the tricuspid valve alone will not be sufficient to produce a right-sided S3. One can expect to hear a tricuspid inflow murmur in diastole instead *(83)*.

S3 in Ventricular Dysfunction

In patients with significant left ventricular dysfunction of whatever etiology, the left ventricular diastolic pressure will rise because of decreased ventricular compliance. Because during diastole the mitral valve is open, the rise in the left ventricular *pre-a wave* pressure will raise the baseline left atrial pressure. This will indirectly raise the level of both the *a* and *v waves* in the left atrium. The increased left atrial *v wave* pressure (in heart failure, cardiomyopathy, or in the postmyocardial infarction state) will aid in the development of greater energy acquired by the moving column of blood during the rapid filling phase. The ventricular compliance is generally decreased in these conditions because of the pathological processes involving the myocardium. Thus, the setup is there for the production of S3 in these states (Fig. 35). When the symptoms and signs of heart failure improve with therapy, there will be an associated fall in the left ventricular diastolic and the left atrial pressures. Often at this time the S3 will become soft or inaudible. If S3 remains relatively loud after the symptoms of dyspnea and edema have improved with associated radiological clearance of signs of failure, it indicates marked decrease in left ventricular compliance. This is usually not a good prognostic sign.

S3 in acute myocardial infarction usually occurs when there is a large infarct associated with left ventricular failure. If improvement in symptoms and signs of failure is accompanied by the disappearance of S3, it usually is a good prognostic sign. A loud persistent S3 in the postinfarction state may result either from significant mitral regurgitation or a marked decrease in compliance because of extensive myocardial damage. Occasionally both of these may play a role.

In patients with ventricular aneurysm, S3 is not usually seen in the absence of heart failure. Also, S3 is uncommon in acute ischemia unless it is severe enough to produce hemodynamic deterioration with or without mitral regurgitation secondary to papillary muscle dysfunction *(76)*.

In significant pulmonary hypertension when the right ventricle begins to fail, a right-sided S3 is likely to develop. The mechanism involves essentially the same principles as discussed for left ventricular dysfunction. The rise in right ventricular *pre-a wave* pressure leads to raised baseline pressure in the right atrium. This will add to the *v wave* pressure in the right atrium. With right ventricular dilatation, the tricuspid ring will eventually be stretched, leading to the development of tricuspid regurgitation. This adds further to the *v wave* pressure height in the right atrium. This is slightly different from the left side, where the mitral valve does not become fully stretched by left ventricular dilatation because only the posterior annulus, which is attached to the ventricle, becomes stretched. Anteriorly the mitral valve is attached to the aortic root. The latter does not stretch with left ventricular dilatation. Thus, mitral regurgitation does not usually arise from left ventricular dilatation alone. The increased right atrial *v wave* pressure head, together with significant decrease in compliance of the right ventricle brought about by the hypertrophy caused by the pulmonary hypertension, provides the setup for the right-sided S3. Right-sided S3 in general requires not only increased flow across the tricuspid valve, but also significant elevation of right atrial pressure, usually seen in the context of pulmonary hypertension during the stage of decompensation.

The right ventricle does not tolerate acute rises in pulmonary artery pressure, however. Thus, in acute pulmonary thromboembolism, the right ventricle will dilate acutely, and this may not only produce tricuspid regurgitation but also cause steep rises in the systolic and the diastolic pressures in the right ventricle. The latter, by raising the right atrial pressure, will provide the necessary conditions for the right-sided S3.

S3 in Constrictive Pericarditis (Pericardial Knock)

In chronic constrictive pericarditis, the thickened and fibrosed, sometimes even calcified pericardium surrounds the ventricles like steel armor, not allowing their full expansion. The ventricles generally are able to expand only during the phase of rapid inflow. Once the peak of this expansion is reached, further expansion is often impossible because of the thickened and unyielding pericardium. The diastolic pressure in the ventricles will abruptly rise to high levels and plateau thereafter until the end of diastole, giving the classic *square-root sign* to the ventricular pressure curves. In classic constrictive pericarditis, both the left and right ventricular diastolic pressures will in fact be equal under resting conditions (Fig. 36). The raised diastolic ventricular pressures will be transmitted to the respective atria. This, of course, is the reason for the raised *v wave* pressure head for the rapid filling period. The rapid inflows will be abruptly decelerated by the decreased compliance of the ventricles caused by the abnormal pericardium producing the S3 *(84)*.

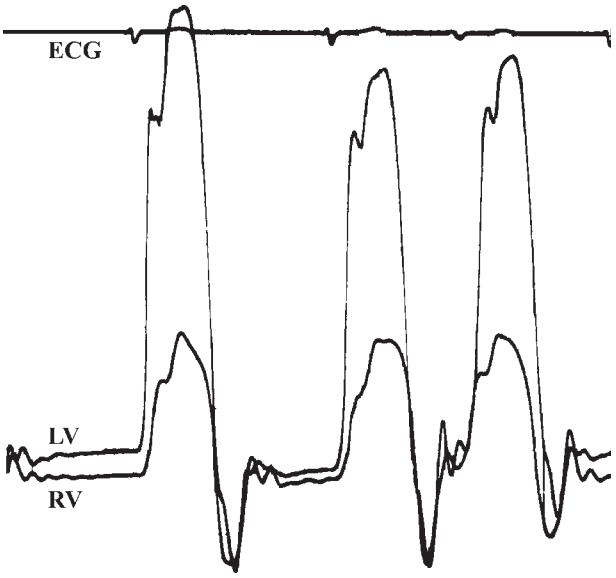

Fig. 36. Simultaneous recording of left ventricular (LV) and right ventricular (RV) pressures from a patient with severe chronic constrictive pericarditis showing the raised diastolic pressures with equalization between the two sides along with the typical dip and plateau pattern (the square-root sign).

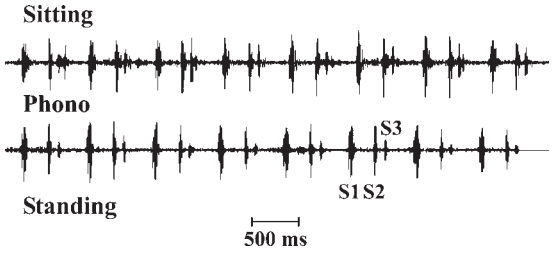

Fig. 37. Digital display of a magnetic audio recording from a patient with chronic constrictive pericarditis taken from the left lower parasternal area showing an early S3, which persists even in the erect position (standing) because of high atrial pressures.

The degree of cardiac compression may vary slightly in different patients. The rapid-filling phase may also be slightly shortened. The S3, therefore, may occur slightly earlier than usual. The sound may also be somewhat sharper *(84)* (Fig. 37). It is sometimes called a *pericardial knock*. However, in the majority the S3 is quite similar in character to the usual S3, most likely because the constriction does not shorten the rapid filling phase and begins to impede filling only at the end of the rapid filling phase.

S3 in Atrial Myxoma (Tumor Plop Sound)

In atrial myxoma, one may hear an S3-like sound termed the *tumor plop*. The sound is actually produced when the tumor plops into the ventricle in diastole. The tumor is usually attached by a stalk to the interatrial septum. For instance, in the case of a left atrial myxoma, the tumor may in fact protrude and get in the way of the mitral inflow, causing

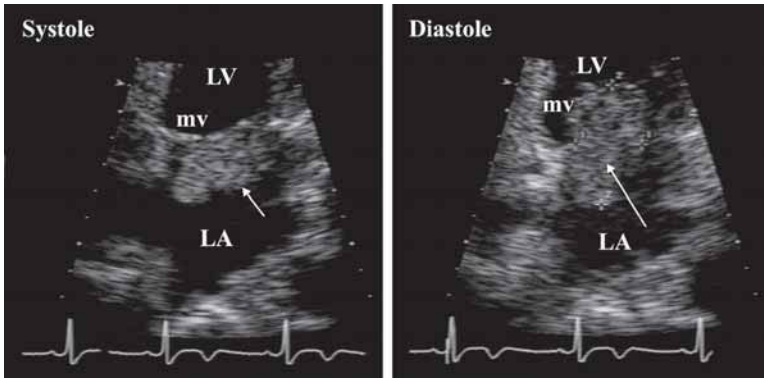

Fig. 38. Stop frames from two-dimensional echocardiogram taken from a patient with left atrial myxoma. During systole the dense echogenic mass representing the tumor in the left atrium (LA) is seen just at the edge of the closed mitral valve (mv). The tumor mass is seen to protrude into the left ventricle (LV) in diastole when the mv opens.

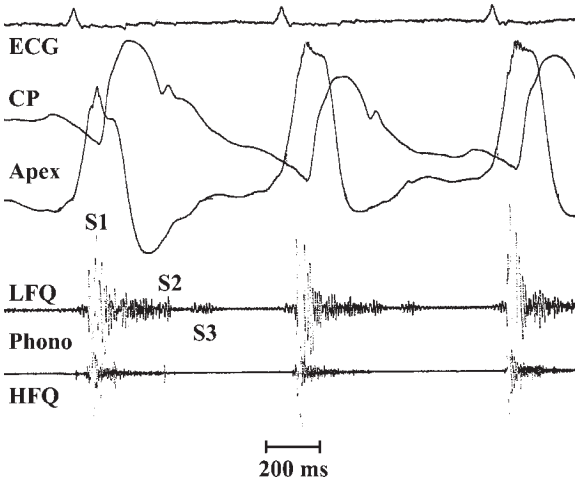

Fig. 39. Phonocardiogram (Phono) recording taken at the lower left sternal border area from a patient with left atrial myxoma along with the apexcardiogram (Apex) and carotid pulse (CP) recordings. The tumor plop sound (S3) is seen in the low-frequency (LFQ) range. Also seen in the Phono are the loud S1 and the systolic mitral regurgitation murmur.

mitral orifice obstruction. This, of course, also leads to elevation of the left atrial pressure, as in mitral stenosis. The elevated left atrial *v wave* pressure initiates a vigorous expansion during the rapid filling phase. When the opening of the mitral valve occurs, the tumor tends to move along with the anterior mitral leaflet and enters the left ventricle. When it reaches its maximum excursion, its further movement is suddenly stopped. This results in a sound that has characteristics similar to the S3 *(85)* (Fig. 38). The sound tends to occur slightly after the rapid filling wave peak. It often is followed by a low- to medium-frequency diastolic murmur because of the mitral obstruction. In addition, the elevated left atrial pressure produces a loud banging M1, which may be palpable (Fig. 39). Also, one will be able to note the presence of a systolic murmur of mitral regurgitation.

Summation Gallop

When the atrial contraction happens to occur during the rapid filling phase for any reason, then the energy acquired by the moving column of blood becomes augmented. In such situations, the deceleration that follows, because of the normal transition from the period of rapid expansion to the slow expansion, may be sufficient to generate an S3. This requires a normal atrial contraction and abnormal timing of the atrial depolarization in relationship to the ventricular depolarization. This can occur in the presence of mild sinus tachycardia with shortening of diastole, resulting in atrial contraction at the time of the rapid filling phase. This can also occur when the PR interval is long enough (first-degree A-V block) that the atrial contraction occurs early in diastole. It can also occur if the atrial contraction and the ventricular contraction are dissociated, as in A-V dissociation caused, for instance, by complete A-V block, or in patients whose ventricles are paced by an electronic pacemaker and who have an underlying undisturbed regular atrial rhythm. The augmentation can occur only when the atrial contraction occurs during the rapid filling phase. Therefore, in A-V dissociation this is likely to occur only intermittently.

When an S3 is made louder by the fortuitous occurrence of atrial contraction at the time of the rapid filling phase, it is termed a *summation sound or gallop*. When this occurs in the presence of mild sinus tachycardia, application of carotid sinus pressure by slowing the sinus rate may be able to prevent the atrial contraction from occurring at the rapid filling phase, thereby abolishing the summation effect.

Summation gallop itself may not signify a pathological state, particularly if seen only during mild sinus tachycardia. The significance of the summation gallop sound will depend on the clinical circumstance under which it develops *(76)*.

If either the S3 or S4 is pathological and the sound is made louder by the timing of the atrial contraction at the time of the rapid filling phase, the resulting sound is sometimes termed "*augmented gallops" (86)*.

Clinical Features of S3

S3 is a sound that occurs at the end of the rapid filling phase of diastole at pressures that are generally low. Therefore, the S3 is a low-frequency sound or a thud similar to the sound caused by a small lead ball falling on a cushioned floor. It occurs at the peak of the rapid filling phase and is therefore separated from the S2 by the combined duration of the isovolumic relaxation and the period of rapid inflow. The former is approximately between 60 and 100 ms. The latter lasts an average of 100 ms. The S3 occurs, therefore, a fair distance after S2. This creates a cadence:

Lubb .....dup....bum.

The left-sided S3 is obviously best audible over the apex area, which is usually formed by the left ventricle. It is best elicited by auscultation with the bell, which picks up the low frequencies. S3 is also somewhat affected by proximity. Often S3 may be best heard only when the patient is turned to the left lateral position and auscultated over the area of the apical impulse. It is usually uncommon to have S3 when the apex beat is not palpable. Rarely it may be audible in the absence of a palpable apex beat, e.g., in acute myocardial infarction, in severe cardiomyopathy with severe reduction in the left ventricular ejection fraction, and in constrictive pericarditis.

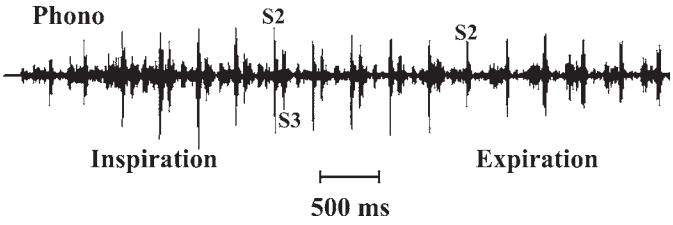

Fig. 40. Digital display of a magnetic audio recording taken at the xiphoid area of the sternum from a patient with severe pulmonary hypertension secondary to scleroderma with right ventricular decompensation. During inspiration (identified by the noise in the baseline) an S3 is seen clearly, which is not seen during expiration, confirming the right-sided origin of the sound.

If the apex beat were to hide behind the ribs during a certain phase of respiration, the S3 may also become soft or inaudible at that time. It may become audible only when the apex beat becomes palpable between the ribs, namely in the intercostal space. The phase of respiration during which this may happen may vary from patient to patient. Although the left ventricular filling becomes relatively greater on expiration, the usual left-sided S3 does not always increase on expiration. If the proximity effect is better on inspiration, it may become more audible only on inspiration. When loud, S3 may be audible even at the base. S3 generally will tend to disappear or become softer in the standing position because of decreased venous return.

Right-sided S3 generally is best heard over the xiphoid area and over the lower sternal region. It usually will increase in intensity or loudness on inspiration (Fig. 40).

Physiological S3 and pathological S3 are very similar in all respects with regard to the auscultatory features. Therefore, the distinction is only made by the associated features. Generally, S1 intensity is good in physiological S3, and the apical impulse will be normal and not sustained on palpation.

CLINICAL ASSESSMENT OF S3

S3 should be looked for in situations where it is expected to be heard, such as in children, pregnant women, rapid circulatory states, patients in whom the apical impulse is felt to be abnormal and sustained or hyperdynamic as in ventricular volume overload, or patients with signs and symptoms of peripheral or systemic congestion with elevated jugular venous pressure. Because it is a low-frequency sound, it must be searched for with the bell of the stethoscope. The patient should be turned to the left lateral position and the apical impulse located, and the area of the palpable apex beat must be auscultated. The presence of S3 is identified by its typical cadence, namely:

One…two…..bum

Lubb……dup…..bum.

In mitral regurgitation and other similar ventricular volume overload states, if S3 is heard it will often have some duration and sound more like a short low- to

medium-frequency murmur. The presence of S3 in these conditions often indicates that the lesion causing the volume overload is significant. In mitral regurgitation, for instance, the presence of S3 would only be heard when the degree of regurgitation is moderately severe or severe. If the degree of regurgitation is not significant and a definite S3 is present, then it must mean coexisting left ventricular dysfunction. If tricuspid regurgitation is considered, either on the basis of an elevated venous pressure with jugular contour showing a large prominently rising *v wave* with a *y descent* or by detecting the murmur, then a right-sided S3 should be looked for. A right-sided S3 is classically heard maximally over the xiphoid and the lower sternal area and increases typically on inspiration.

S3 Persisting on Standing

S3 generally disappears or becomes softer on standing. Most physiological S3, S3 associated with ventricular volume overload, and even the usual heart failure S3 generally follow this rule. However, if it persists and continues to be well heard, it must indicate an unusual situation in which a high *v wave* pressure in the atrium is associated with significant decrease in compliance. This may occur, for instance, in constrictive pericarditis and/or severe cardiomyopathy (Fig. 37).

S2-S3 Vs Wide-Split S2

1. S3 is separated far enough from the S2; therefore, it is unusual for it to be mistaken for a wide-split S2. In addition, when the S2 is widely split, both components of S2 are sharper and of higher frequencies. They also tend to be similar to each other. This is unlike the S3, which has a much lower frequency and is often better heard with the bell.
2. The maximum loudness of left-sided S3 is over the area of a palpable left ventricular apex beat. Split S2 when wide is often better heard over the second, third, and sometimes fourth left intercostal space at the left sternal border.
3. S3 tends to get softer and usually tends to disappear on standing.

S3 Differentiation From OS

A late-occurring OS may sometimes be mistaken for an S3. Distinguishing features are:

1. S3 is of low frequency and heard best over the apex, whereas the OS is of high frequency and often best heard between the apex and the lower left sternal border.
2. The S1 is often loud and may be palpable in the presence of a good OS. It is unusual to have a palpable S1 with an S3.
3. If a clear-cut "triple sound" or "trill" is identified, then the presence of OS is confirmed.
4. On standing, S3 will become softer or often disappear, whereas the OS, if still audible, will be found to come later.
5. If the sound in question is audible on standing and does not change much in timing, consider unusual S3 such as a pericardial knock or that caused by a severe cardiomyopathy.

Very rarely, one may encounter the presence of both an S3 and an OS. This may occur in the presence of significant mitral regurgitation in rheumatic mitral disease,

which is characterized by a shortened and severely restricted posterior mitral leaflet together with a freely mobile anterior leaflet. The severe mitral regurgitation may bring out the S3, and the freely mobile anterior leaflet may be part of the causation of the OS *(87)*.

S3 Differentiation From Tumor Plop

Tumor plop sounds like an S3. However, it is associated with a loud banging M1, which may be palpable. In addition, there often will be low- to medium-frequency diastolic murmur following the sound because of the mitral obstruction.

Intermittent S3

When heard, S3 is often intermittent and occasionally varies with different phases of respiration. The most common cause for this is proximity. The location of the apex beat and whether it hides intermittently behind the ribs may determine when it may be heard best.

When there is A-V dissociation as in complete A-V block or a patient with a permanent ventricular demand single-chamber electronic pacemaker, one may hear an S3 whenever the dissociated atrial contraction occurs during the rapid-filling phase of diastole. Such A-V dissociation will also be expected to affect the intensity of S1 and will produce variable softer and louder intensity of M1. If atrial contraction were to occur in the rapid filling phase and produce an S3 effect, the S1 immediately following the S3 would be soft. This unique situation with varying S1 intensity and intermittent S3 is likely to occur only with the presence of A-V dissociation.

(For additional examples review Phono Files 35–44 under Heart Sounds on the Companion CD.)

FOURTH HEART SOUND (S4)

Mechanism of Formation of S4

The atrium normally contracts at the end of diastole and gives an extra stretch to the ventricles. When the ventricular compliance is significantly reduced because of factors such as hypertrophy, ischemia, infarction, fibrosis, or infiltrates, then this evokes a more vigorous contraction from the atrium. This augments ventricular filling at the end of diastole and helps in its expansion *(88)*. The increased force of atrial contraction also raises the atrial *a wave* pressure peak. This augmented pressure head tends to accelerate the diastolic inflow at the end of diastole. Because the ventricular compliance is reduced, the accelerated inflow at this phase of diastole is decelerated fairly rapidly. This will depend, of course, on the extent of reduction in the compliance. This sudden deceleration of the column of blood entering the ventricle at end-diastole leads to dissipation of energy, which results in the production of the sound (Fig. 41). The sound forms inside the ventricle, and the entire hemic mass, the papillary muscles, and the underlying ventricular myocardium probably participate in its production. The sound is sometimes referred to as *atrial gallop* and can be simply called S4. The sound, being generated at

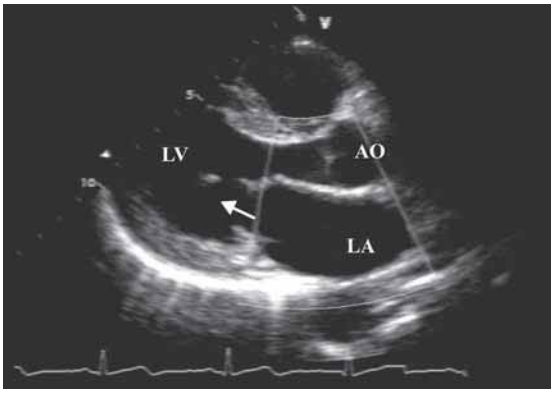

Fig. 41. Stop frame during end diastole from a two-dimensional echocardiogram of a patient taken in the parasternal long axis. The moving column of blood (arrow) from the left atrium (LA) into the left ventricle (LV) is shown. Strong atrial contraction during this phase augments the ventricular filling, which could be decelerated abruptly if the ventricular compliance is reduced for any reason, producing an S4.

low pressures of diastole, has a low frequency very similar to the S3. However, the timing is different; it is closer to S1.

The cadence therefore is different:

S4..S1…..S2……..Ha..ha…..tu……..

The prerequisites for S4 formation are:

1. *Reduced ventricular compliance*
2. *Healthy atrium*
3. *Regular sinus rhythm*
4. *Absence of A-V valve obstruction*

The causes of reduced compliance have been discussed in relation to S3. These are completeness of relaxation, chamber size, thickness of the wall, composition of the wall (inflammation, infiltrate, ischemia or infarction, scars, etc.), pericardium, and right ventricular volume/pressure in the case of the left ventricle.

While the small size of the ventricle in children offers resistance to rapid inflow in early diastole, once the ventricle has begun to expand because of the onrushing flow, by the end of diastole the size may no longer be restrictive to filling. This explains the usual absence of S4 in children. This is best appreciated by the analogy of blowing into a balloon to expand it. The resistance is maximal when the size is smallest, namely, when one first begins to blow. Once the balloon is partially expanded it is easier to inflate it further.

On the other hand, with increasing age, the ventricle does become more stiff because of various factors, including age-related hypertrophy as well as acquired diseases including ischemic heart disease, even if asymptomatic. Thus, S4 is often heard in older subjects (>60 yr) even in the absence of clear clinical heart disease *(89)*. Hypertension is the most common cause of hypertrophy in the elderly. However, there could also be atrial disease as well as sinus node dysfunction with development of atrial arrhythmias, such as atrial fibrillation. Therefore, S4 may not be always present in everyone in this age group. Calcific aortic stenosis is more common in people over the age of 65, and yet

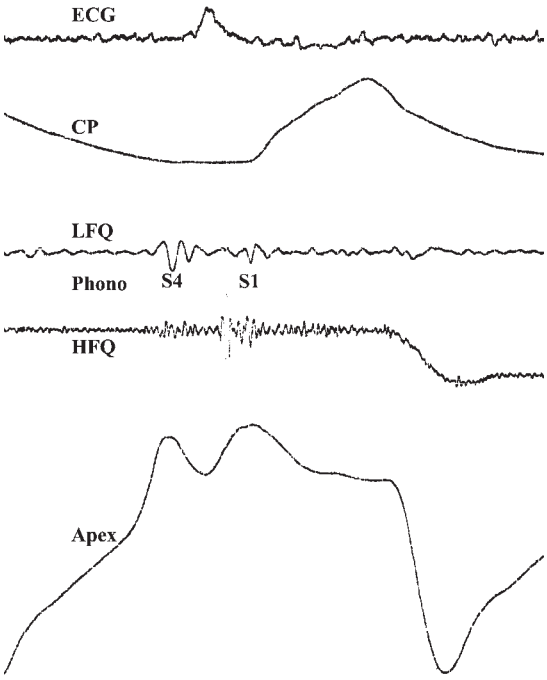

Fig. 42. Phonocardiogram (Phono) recording from a patient with significant aortic valvular stenosis taken from the apex area along with the apexcardiogram (Apex) and carotid pulse (CP) tracings. The Phono shows a low-frequency sound (S4) at the time of the augmented A wave in the Apex recording.

not everyone with significant stenosis (outflow gradient >74 mmHg) with resultant marked hypertrophy will have a definite S4.

Significant aortic stenosis in the younger age group, on the other hand, will have a loud S4 because the hypertrophy associated with such outflow obstruction not only will result in marked decrease in compliance of the ventricle, but also the left atrium is more than likely to be healthy and normal enough to help generate a strong contraction. When a vigorous left atrial contraction occurs in such a situation, the expansion of the ventricle at that time will raise its wall tension enough to become palpable at the apex. The palpable expansion of the apical impulse resulting from such a strong atrial contraction is referred to as the *atrial kick (88)* (Fig. 42). It must be understood that the sound itself never becomes loud enough to be palpable. The atrial kick has the same significance as the S4.

The presence of S4 in a hypertrophic ventricle with outflow tract obstruction usually indicates significant stenosis or obstruction whether right-sided or left-sided (pulmonary or aortic stenosis) *(90)*. S4 in the presence of systemic hypertension would imply a significant decrease in compliance because of hypertensive heart disease. The associated pathological changes may be significant hypertrophy, focal fibrosis, and/or associated coronary heart disease. In the absence of significant left ventricular outflow obstruction, such as aortic stenosis or significant hypertension, a loud S4 at the left ventricular apex area may be indicative of a cardiomyopathy (e.g., hypertrophic cardiomyopathy *[91]*, occasionally other myocardial diseases) or ischemic heart disease *(66,92–94)* (Figs. 43 and 44).

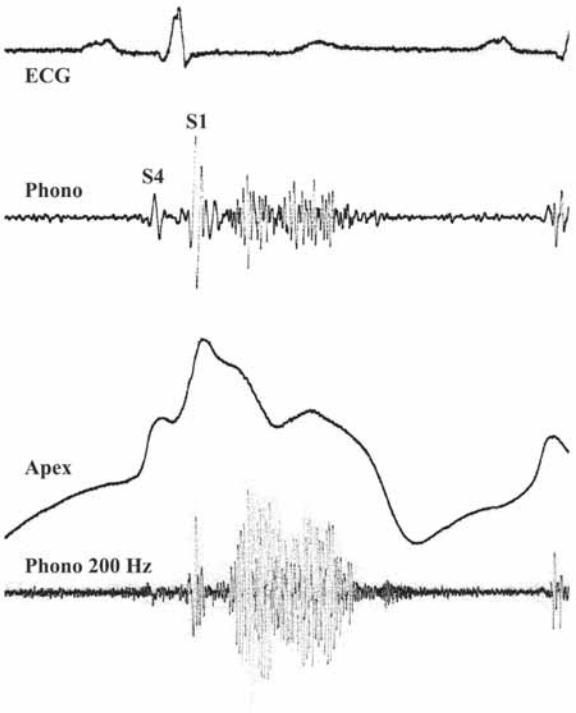

Fig. 43. Phonocardiogram recording from a patient with hypertrophic cardiomyopathy with significant left ventricular outflow tract obstruction taken from the apex area along with the apexcardiogram (Apex) tracing. The Phono shows a low-frequency sound (S4) at the time of the atrial kick in the Apex recording. Note also the systolic ejection murmur of the subaortic stenosis.

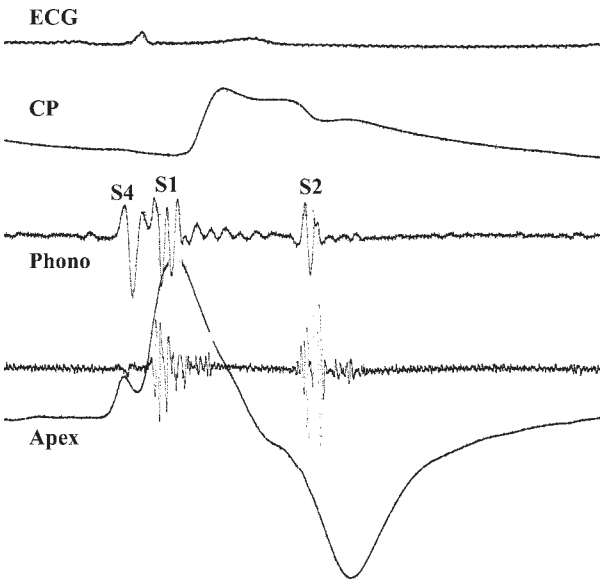

Fig. 44. Phonocardiogram (Phono) recording from a patient with ischemic heart disease taken from the apex area along with the apexcardiogram (Apex) and carotid pulse (CP) tracings. The Phono shows a low-frequency sound (S4) at the time of the augmented A wave in the Apex recording.

Ventricular volume overload usually causes dilatation of the ventricle and therefore is accompanied by better ventricular compliance. Thus, S4 is not a feature of volume-overload states such as mitral regurgitation. Acute mitral regurgitation because of ruptured chordae tendineae, either spontaneous or secondary to infective endocarditis, is, however, an exception in which an S4 may be heard *(95)*. In acute mitral regurgitation both the left atrium and the left ventricle are often presented with significant volume because of the regurgitation, and yet they have not had time to develop secondary dilatation. The lack of significant dilatation of the left ventricle means relatively decreased left ventricular compliance and raised left ventricular diastolic pressures. Sometimes the levels of the left ventricular diastolic pressures and the left atrial pressures are very high and may produce pulmonary edema. When left atrial pressure is elevated but not to the degree of causing pulmonary edema, then the extra stretch provided by the volume may evoke a powerful Starling effect from the left atrium. This in the presence of a relatively less compliant left ventricle produces an S4.

Constrictive pericarditis does not allow expansion of the ventricle beyond the early rapid filling phase, and therefore S4 is not a feature of this condition.

CLINICAL ASSESSMENT OF S4

Left-sided S4 is best audible close to the left ventricular apex area. Often when the S4 is loud, it may be heard over a wide area of the precordium. Right-sided S4 is best audible over the xiphoid area and the lower sternal region. It is detected by an increase in intensity on inspiration or audibility only on inspiration. The jugular contour is also likely to show a prominent rise before the usual systolic *x′ descent*. Left-sided S4 may also be somewhat better heard with the patient in the left lateral decubitus position, although when loud enough it does become audible in the usual supine position and medial to the apex. Occasionally, left-sided S4 may be accompanied by a palpable atrial kick of the apical impulse *(93)*. Rarely, with significant right ventricular hypertrophy, as in pulmonary hypertension, the right-sided S4 may be accompanied by similar right atrial kick, which may be palpated by the subxiphoid palpation of the right ventricle on deep inspiration.

S4, being a low frequency sound, is best elicited by listening with the bell of the stethoscope with just enough pressure to make an air seal. Firm pressure with the chest piece of the stethoscope may sometimes eliminate the transmission of such low frequencies by tightening the skin, thus making the S4 soft or altogether disappear. S4 is also affected by venous return and atrial filling. Thus, on standing, when the venous return falls and the atrial filling diminishes, S4 will either become soft or disappear. The increased sympathetic activity associated with diminished venous return may speed up the heart rate and shorten the PR interval and thus may also make the S4 come closer to S1 and actually merge with the latter.

In hypertrophic cardiomyopathy, the compliance is markedly decreased, and this often evokes a loud S4 *(91)*. When there is significant associated left ventricular outflow obstruction in this disorder, the strong atrial contraction may also generate a palpable atrial kick. These patients are generally younger and often have hypertrophied but otherwise healthy left atria early in the course of their disease process.

S4 also is usually sensitive to changes in venous return and filling of the heart. Maneuvers that reduce venous return, such as standing posture, will tend to decrease the intensity or abolish the S4 all together. Rapid volume expansion, cold pressor test, and isometric hand grip will accentuate the S4 *(93)*. Isometric hand grip tends to raise heart rate, cardiac output, and the blood pressure *(96,97)*. It can also raise the peripheral resistance.

If S4 does not disappear on standing, one must consider the presence of significant decrease in compliance as seen in patients with markedly hypertrophied hearts. The S4-S1 interval is not only determined by the PR interval but also to a certain extent by the degree of decrease in compliance or the severity of the underlying disease. When the decreased compliance is significant, as in markedly hypertrophied ventricle, the resultant S4 tends to be well separated from S1 *(93,98)*. Thus, in patients with significant decrease in compliance, S4 may still be heard on standing.

S4 Differentiation from Split S1

S4 sounds different from the M1 component that follows it because it contains more lower-frequency ranges and therefore is heard better with the bell. This is unlike the M1-A1 split, where both components are more or less similar in frequency and more often in the higher ranges. Thus, the split S1 is heard just as well with the diaphragm.

The lower-frequency S4 may be abolished or made softer by firm pressure with the chest piece (the bell), whereas the split S1 is not likely to be affected by such pressure.

Decreasing venous return by standing the patient will only lengthen the isovolumic contraction phase that separates the M1 from A1 by decreasing the rate of rise of ventricular pressure that will accompany reduced ventricular filling. Thus, the split is usually better separated on standing. On the other hand, the decreased atrial filling because of reduced venous return and the slight shortening of PR associated with increase in heart rate secondary to sympathetic stimulation will make the S4 softer and make it come closer to M1, making the separation less distinct.

(For additional examples review Phono Files 45–51 under Heart Sounds on the Companion CD.)

Gallop Rhythm

In the presence of tachycardia, diastole is somewhat shortened, and when an S3 is heard, it is often called the *protodiastolic gallop*, the *S3 gallop* or sometimes the *ventricular diastolic gallop*. The cadence or the rhythm of the S1 and S2 followed by S3 simulates the sounds of a galloping horse:

one ….tu…..bum…..one ….tu….bum….one….tu….bum

This is usually heard in patients with significant heart failure and decreased cardiac output. Occasionally in some patients with left ventricular dysfunction, the pathophysiological changes may provide the prerequisites for both an S3 and an S4. If the heart rate is fast, then both sounds may in fact merge with each other, causing a summation or

summation gallop. It will be difficult to distinguish this as such at these fast heart rates and may be simply detected as a gallop rhythm. However, when the heart rate is only mildly fast and both sounds are easily audible in diastole, this is called the *double gallop or the quadruple rhythm or gallop*. This will have a cadence of both S4 and S3 together, namely:

ha…ha …..tu……bum…ha…ha…..tu……bum.

Treatment of the heart failure and clearance of the symptoms and signs of failure may be accompanied by an S3 becoming either softer or totally inaudible. This usually indicates falling left atrial pressure as well as improvement in left ventricular function. At this time an S4 may become audible even if it was not present initially. This means that the left atrium is no longer overstretched or dilated, but the left ventricular compliance is still abnormal, thereby evoking a good atrial contraction. Such a sequence usually indicates good prognosis.

S3 and S4 and Left Ventricular Dysfunction

One recent study evaluating the sensitivity and the specificity of the presence of phonocardiographically detected S3 and/or S4 for detecting left ventricular dysfunction as measured by left ventricular diastolic pressures, left ventricular ejection fraction, and the B-type natriuretic peptide concluded, as expected, that the phonocardiographic S3 and S4 are not sensitive markers of left ventricular dysfunction and that the phonocardiographic S3 was more specific for left ventricular dysfunction than the phonocardiographic S4 *(99)*. Over the years, significant clinical experience has been accumulated as to the significance of these sounds when they are audible. When one takes proper account of the mechanisms behind the production of these sounds, it becomes obvious what their significance is when they are detected at the bedside. Thus, S4, when clinically audible, is relatable only to a strong atrial contraction of a healthy atrium in the presence of decreased left ventricular compliance. The latter could result from a variety of pathological processes, not all of which would necessarily entail left ventricular systolic dysfunction. Thus, it is not expected to be very specific for left ventricular systolic dysfunction. Because an S3 can be physiological as well as pathological, the clinical group of patients being evaluated is another important determinant of whether it is going to correlate clinically to significant left ventricular dysfunction. Therefore, the presence or otherwise of these sounds on auscultation will become relevant only when taken in conjunction with the clinical context. Finally, it is important to realize that studies based merely on phonocardiographic recordings of low-frequency vibrations could lead to misleading information, because they may not be audible.

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