Origin of the Third Heart Sound
I. Studies in Dogs

YUKIO OZAWA, M.D., DAMON SMITH, B.M.E., AND ERNEST CRAIGE, M.D.

SUMMARY We studied 13 anesthetized dogs in which a third heart sound (S₃) was repeatedly induced by hypoxemia plus fluid overload. A miniature accelerometer with a mass of about 1.1 g was applied at three levels — intact chest wall over cardiac apex, on the pericardium and on the epicardium — to record motion of the structures under observation as well as sound. Intraventricular pressure and sound were monitored using a Millar catheter. Application of two accelerometers simultaneously over the epicardium permitted observation of the chronologic sequence of ventricular wall dynamics in early diastole. The S₃ at each level occurred simultaneously with the sudden onset of reduced acceleration, or negative jerk. These dynamic phenomena were maximal at or near the cardiac apex. We conclude that the event that triggers the S₃ is a sudden intrinsic limitation of longitudinal expansion of the left ventricular wall.

THE THIRD HEART SOUND (S₃) is an important physical sign which, when found in a patient with a failing heart, is regarded empirically as a poor prognostic sign. Early diastolic sounds are regularly found in normal children as well as in diastolic overload conditions and constrictive pericarditis.

The physiologic basis of the S₃ remains controversial. The sound is most widely attributed to a termination of rapid filling at the moment that the elastic limit of the ventricular chamber is reached.¹ ² Two other theories attribute the sound to a valvular event⁶ or to extracardiac factors — the impact of the heart against the chest wall.⁷

The ventricular distention theory has been challenged by the observation of Prewitt et al.,⁸ who, using digitized measurements of the transverse diameter of the left ventricle as perceived by M-mode echocardiography, could not find any aspect of filling that could reproducibly and consistently be related to the appearance of an S₃.

Our studies⁹ using cineangiography have shown that in diastolic overload conditions, the achievement of maximum velocity and deceleration occurred later in the long axis than in the transverse or short axis, which was the only dimension that had been available to Prewitt et al.⁸ using M-mode echocardiography. Our cineangiographic studies indicate that in diastolic overload, long-axis filling movement may be paramount in genesis of the S₃.

The importance of valvular events in the genesis of the S₃ is controversial. Some authors have reported disappearance of the sound when the mitral valve is replaced by a prosthesis¹⁰,¹¹ and others have noted persistence of the sound following this operation in cases where valvular incompetence has occurred.¹²,¹³ The chest wall impact or tapping theory recently proposed by Reddy et al.⁷ is based on their observation that the intensity of the sound at the chest wall is much greater than any pressure vibration elicited from within the ventricular cavity.

We report a controlled canine experiment in which an S₃ was produced by a combination of hypoxemia and fluid overload. The sound was tracked from its manifestation on the chest wall through several layers to its source, which we believe is the wall of the left ventricle.

Materials and Methods

Thirteen mongrel dogs that weighed 23–35 kg were anesthetized with i.v. sodium pentobarbital. Respiration was controlled with a ventilator with intermittent positive pressure after endotracheal intubation. The
dogs were in the supine position. Initial observations to be described below were made with the chest closed. Subsequently, the chest was opened through a median sternotomy and observations were repeated through the intact pericardium. Finally, the pericardium was opened longitudinally and its free margins attached to the chest wall, leaving the heart exposed and supported by the suspended pericardium.

Ventricular dysfunction, manifest by cyanosis and dilatation, was precipitated by hypoxemia resulting from interrupting the ventilator followed by the rapid i.v. injection of a fluid overload consisting of 60–120 ml of 0.9% saline solution. The right vagus nerve in the neck was exposed and electrodes were attached. Intermittently, heart rate was slowed by electrical vagus stimulation to facilitate the observation of diastolic phenomena. During the course of the experiment phonocardiograms, surface acceleration (SAA) and surface velocity (SVA) were monitored, as were the ECGs.

The transducers used for monitoring sound and motion phenomena from the surface of the chest wall, pericardium and epicardium were miniature accelerometers (Entran Devices Model EGA 125R-30D). These are cylindrical, 3.43 mm in diameter and 6.75 mm long. The mass of the accelerometer is 0.5 g. The accelerometer is mounted to a 1-mm-thick rectangular plastic base approximately 13 by 17 mm in size. With this base and the wiring, the mass of the device becomes approximately 1.1 g. This plastic base is attached by ethyl cyanoacrylate glue to the surface under investigation. The transducer uses an inertial reference frame and is extremely sensitive to the rate of change of velocity, i.e., acceleration. The signals from the accelerometers were recorded with a frequency response that was essentially flat from 1 to 200 Hz and were equally sensitive to within 1.5 db over this range of frequencies. The accelerometer was oriented such that its sensitive axis was perpendicular to the surface to which it was attached. The sensitivity of the accelerometer to accelerations in a direction at right angles to the sensitive axis was no more than 3%. Since no quantification of the signal is attempted, the baseline or zero level of the SAA signal is not recorded on the tracings. This can be estimated, however, by the level of the signal in late diastole, when the acceleration signal is almost zero at moderate heart rates. An upward movement of the SAA signal above the baseline correlates with an outward acceleration of the surface under study. The SAA can be modified by integration to provide a measure of velocity, or filtered to show the graphic analog of audible sound. Thus, through headphones, the laboratory team could listen to the heart sounds — first and second sound, and when present, the third sound — with clarity and quality comparable to that provided by a stethoscope, without the potential artifact resulting from the application of the handheld endpiece on the surface under study. When, as was usually the case, two accelerometers were used simultaneously, their equisensitivity was established before the experiment. Intraventricular dP/dt and sound were obtained by a micromanometer-tipped catheter.* In using the catheter, we were concerned with potential artifact caused by contact with the mitral valve apparatus as it moves in early diastole. We therefore inserted the catheter directly through the left ventricular wall near the apex so that the catheter tip was approximately 2 cm deep into the ventricular chamber. We also verified that the catheter did not alter the SAA signal recorded at the apex by recording the signal with and without its presence. Tracings were made on a multichannel physiologic recorder (Electronics for Medicine Model VR-12) at paper speeds of 100 and 250 mm/sec with instant developer.

The S<sub>3</sub> was observed at three levels:

At the chest wall. In eight dogs, skin surface acceleration was determined at the cardiac apex, with velocity and phonocardiogram electrically derived from the signal as described above as well as an ECG. After a control period, an S<sub>3</sub> was induced by a combination of hypoxemia and fluid overload. Observations were repeated during the period of ventricular dysfunction (usually 2–5 minutes) and during the subsequent recovery period, when respiration was resumed.

On the pericardium. In 10 dogs, two accelerometers were applied simultaneously. They were attached to the pericardium by cyanoacrylate adhesive. One was placed near the apex in all 10 dogs, whereas the second one was placed over the anterolateral left ventricular free wall in six dogs and over the left ventricular anterior wall close to the interventricular septum in four. Recordings were made as at the chest wall — during a control period, during S<sub>3</sub> production and during recovery.

On the exposed heart (epicardium). With the pericardium open and the heart exposed and suspended in the pericardial cradle as described above, the two accelerometer transducers were applied as follows: at the epicardium at the apex in all 13 dogs, with the second transducer at the anterolateral free wall of the left ventricle in 10 dogs; at the left ventricular anterior wall close to interventricular septum in six; and at the right ventricular anterior wall in four (fig. 1). In five dogs of this group, intraventricular phonocardiograms, pressure and dP/dt were determined using a Millar catheter placed in the left ventricular cavity close to the apex through the left ventricular wall.

Recordings were again made during a control period, during an induced S<sub>3</sub> and during the recovery phase.

*Millar Instruments, Inc. The dP/dt signal was obtained by a single-pole, high-pass RC circuit with a time constant of 1.5 msec. The phonocardiogram was derived from this by high-pass filtering with corner frequency of 33 Hz, rolloff of 12 dB/octave. Comparison with filters used with other equipment such as the accelerometer or air-coupled microphones is inappropriate because of the differences in frequency response of the transducers themselves.
conventional stethoscope with funnel endpiece placed on the layer (skin, pericardium or epicardium) under observation.

**Results**

**At the Three Anatomic Layers**

**Chest Wall**

During the control period, the closed-chest dogs had no audible S₃. With hypoxemia, produced by interrupting the respirator, an S₃ became audible at the apex position on the chest wall (fig. 2). It was noted both with the headphones and by a conventional acoustic stethoscope. The addition of fluid volume overload augmented the intensity of the S₃, although fluid overload alone did not produce it. With resumption of respiration, the audible and graphic manifestations of the S₃ returned to control levels.

**Pericardium**

After thoracotomy and exposure of the pericardium, a low-frequency, low-intensity S₃ near the cardiac apex could be heard and was recorded in four of 10 dogs. No audible vibration had been noted earlier with the chest still closed in these dogs. In the other six dogs, a low-intensity, inaudible diastolic vibration was recorded from the same site. Left ventricular dysfunction, manifest by cyanosis and dilatation produced by global hypoxia, resulted in an S₃ of large amplitude in all dogs. Comparison of the signal intensity over the pericardium from two equisensitive transducers showed that the SAA and phonocardiographic vibration signals, at the time of S₃, were more intense over the cardiac apex than over the left ventricular anterolateral free wall (fig. 3). Similarly, the S₃ vibration was more intense over the cardiac apex than over the anterior wall close to the interventricular septum. A slight asynchrony of the SAA signals was noted, with apical acceleration peaking later than anterolateral (fig. 3). The development of an S₃ with hypoxemia was associ-

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**Figure 1.** Positions of the transducer.

In the course of each of the procedures described above, comparisons were made of the sounds as heard with head phones via the filtered signal from the accelerometer and the auscultatory findings heard through a conventional stethoscope with funnel endpiece placed on the layer (skin, pericardium or epicardium) under observation.

**Figure 2.** Phonocardiograms and chest wall dynamics with thorax intact. (Left) No third heart sound (S₃) is visible or audible. (right) The S₃ is recorded by phonocardiography at the apex, as the dog is subjected to increased hypoxia. The interrupted vertical line indicates the temporal relationship between the S₃ and a negative jerk, or abrupt downward excursion of the accelerometer signal (SAA) and an analogous point in the velocity curve (SVA). The other principal vibrations represent S₁ and S₂. Heart rate is slowed by electrical vagus stimulation.
ated with augmentation of the rapid filling component of the velocity signal at the apex (SVA in fig. 3).

On the Exposed Heart (Epicardium)

After controlled respiration was reinstituted, and with the pericardium open and heart exposed, seven of 13 dogs demonstrated an audible and recordable S₁ near the cardiac apex before the heart was subjected to additional hypoxemia and fluid overload. Under the adverse influence of oxygen deprivation and fluid, however, cyanosis and dilatation ensued and were accompanied by an audible S₃ that was recorded as a vibration of larger magnitude and higher frequency than in the control state. The S₃ was more intense at or near the apex than in the other areas sampled, such as the anterior wall or anterior wall near interventricular septum (fig. 4). An S₁ noted over the epicardium of the right ventricle appeared later in the cardiac cycle than the left-sided S₁. It was more easily induced by volume overload than by hypoxemia, in contrast to the left-sided S₁. In the dogs in which observations were made of intracardiac vs epicardial phonocardiograms, the S₁/S₃ ratio during hypoxemia was larger on the epicardium than within the left ventricle (fig. 5).

Correlation of Sound and Acceleration

The phonocardiographic S₁ vibrations were consistently associated with a distinct negative inflection or jerk in the surface acceleration signal (figs. 2–5). (Jerk is the time derivative of acceleration). This was true whether the surface under study was chest wall, pericardium or epicardium. When the S₁ was exaggerated in intensity, the magnitude of the negative jerk similarly increased.

Reproducibility of the S₃

In every dog, an S₃ could be produced by stopping the respirator. This was true with the chest closed or with exposure of the pericardium or the epicardium. Restarting the respirator resulted in disappearance or attenuation of the sound. Thus, we could make repeated observations in the same animal. Volume overload in combination with hypoxemia had a magnifying effect, but was inadequate alone to produce an S₃. While the hypoxemia insults appear to be reversible, the possibility of a cumulative deleterious effect throughout the course of the experiment cannot be excluded. Thus, a comparison of the control state at one anatomic layer with another cannot be made.

Discussion

The characteristics of gallop sounds and associated chest wall movements were first investigated by Potain in the latter part of the nineteenth century.¹ He attributed the S₁ to sudden cessation of distention of the ventricle in early diastole. Nixon¹⁴ noted a sudden reduction in the rate of outward movement of the left ventricular apex at the time of the S₁, an observation consistent with the classic theory of Potain.¹ Sakamoto et al.¹⁵ reported M-mode echocardiographic studies showing a checkpoint near the apex of the left ventricle, occurring coincident with the S₁. Arevalo et al.¹⁶ showed by intracardiac phonocardiography that the S₁ could be recorded maximally near the apex. In 1942, Boyer¹⁷
reported that an S₃ could be recorded directly from the surface of a dog’s heart. His pioneer study, however, had technical limitations, which prevented his pursuing further the origin of the sound.

Although sudden deceleration of filling has been implicated in the genesis of the S₃, Prewitt et al. more recently showed a lack of a consistent relationship between S₃ and any feature of left ventricular filling movement as seen by M-mode echocardiography. They reported that the S₃ begins 51 ± 40 msec after the peak rate of filling of the transverse axis of the ventricle. Our recent investigation of patients with an S₃ included a group with diastolic overload abnormalities studied by cineangiography and another group observed noninvasively with phonocardiography and SAA. Our cineangiographic studies showed that the long-axis filling movement (which was inaccessible to Prewitt et al. by M-mode echocardiography) reaches maximum deceleration an average of 48 ± 21 msec later than the maximum velocity of the transverse axis. This delay is similar in magnitude to the interval between peak rate of filling in the transverse axis and appearance of S₃ noted by Prewitt et al.

The valvular theory should be mentioned in view of the obvious role of valvular events in the genesis of S₀, S₂, ejection sounds and opening snaps. However, Kuo et al. and Crevasse et al. showed that at the time of production of the sound, left atrial pressure exceeded that of the left ventricle, an observation that would not be compatible with a closing movement of the mitral valve. More recently, echophonocardiographic observations have shown no significant landmark on the mitral valve echo at the time of S₃, and the sound has been noted to persist after mitral valve replacement.

The tapping theory of Reddy et al. deserves more serious consideration, because it diverts our attention from an intrinsic limitation of filling movement, attributing S₃ genesis instead to the impact of the heart against the chest wall. They found that the S₃ vibration was of greater intensity on the skin surface than within

**Figure 4.** Transducers are attached to the exposed epicardium. With progressive hypoxia (panels 2 and 3), the third heart sound (S₃) appears and becomes more exaggerated at the apex on the phonocardiogram (PCG apex) and is again associated with negative jerk in accelerometer signal (SAA) tracing, as shown by dotted line and arrow. Heart rate is slowed by electrical vagus stimulation.

**Figure 5.** Combined intracardiac pressure and sound with heart surface records of heart sounds and acceleration in a dog with severe left ventricular (LV) dysfunction due to hypoxia. The third heart sound (S₃) on the intracardiac phonocardiogram (IVPCG) is minuscule compared with the S₁, while the S₃ in the PCG apex on the epicardium is very large and is coincident with a distinct negative jerk on the accelerometer signal (SAA) apex on the epicardium (arrow). The heart rate is slowed by electrical vagus stimulation.
the left ventricular chamber. To the extent that the $S_1$ vibration obtained by the Millar catheter and by the accelerometer sensors can be used as a reference, our findings are consistent with the observation of Reddy et al., since the $S_1/S_3$ ratio was greater on the epicardium than by intracardiac phonocardiogram. Indeed, no $S_3$ vibration was recordable from within the ventricular chamber except in the terminal stages of hypoxia, although $S_3$ vibrations of large amplitude could be detected on the heart’s surface. We agree with Reddy et al. that intracardiac pressure fluctuations are inadequate to explain the origin of the $S_3$. Our results, however, show that the audible $S_3$ is present on each of the underlying surfaces — pericardium and epicardium, even when the chest wall has been entirely excluded. During our experiments, we took pains to prevent tapping of the heart against the diaphragm, pericardium and posterior mediastinum. Nevertheless, we recognized an audible $S_3$ in all cases and furthermore the audible vibration was more intense at the apex than in any other position.

Tapping with the finger against the canine chest wall from the interior produced a clear positive initial deflection in the wave form of SAA — a positive jerk — of the skin surface. In the closed-chest canine experiments, however, the $S_3$ was related to a negative jerk of the skin surface (fig. 2). These findings are supported by our investigations in patients. The SAA signal obtained on the skin surface in the supine position showed results similar to those seen in the present canine experiments. The beginning of the $S_3$ vibration was coincident with a distinct negative jerk, the magnitude of which was directly related to the intensity of the sound. We believe that these observations make it highly unlikely that the tapping theory explains the genesis of $S_3$.

We had thought that the apical location may not apply in situations where this region has been rendered hypokinetic by ischemic injury. Recent observations in our laboratory by Ishimitsu and Smith have shown, however, that after ligation of the left anterior descending coronary artery with attendant cyanosis, bulging and hypokinesis of the apex, this region continues to manifest exaggerated negative jerk and to be the site of the $S_3$ genesis when global anoxia is added to regional ischemia (Ishimitsu T, Smith D — personal communication).

We conclude, as advocated by Potain nearly a century ago, that the event that triggers the $S_3$ is a sudden intrinsic limitation of longitudinal expansion of the left ventricular wall — an event manifest by the onset of reduced acceleration, or negative jerk in the region of the cardiac apex — as perceived in the accelerometer signal.

References

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