Intracardiac Phonocardiography

Intracardiac Sound and Pressure in Man

CHARLES F. WOOLEY, M.D.

Background and Evolution

INTRACARDIAC PHONOCARDIOGRAPHY (ICP) is another step in the development of the scientific basis for auscultation, one of many that date from immediate auscultation and extend through echophonocardiography and nuclear cardiology. The 25 year history of intracardiac phonocardiography, relatively brief in duration, is quite diverse due to the interrelations with other investigative and diagnostic methods that were evolving during the same era. Classic auscultation, external phonocardiography, pressure manometer and recording device development were the evolutionary forerunners of intracardiac phonocardiography, while cardiac catheterization techniques were the vehicle for implementation.

ICP, an investigative and diagnostic method, has yielded a body of information which confirmed certain traditional concepts and upset others. Early enthusiastic investigators frequently overemphasized the role of ICP in diagnosis; this misplaced emphasis tended to obscure certain fundamental contributions. In a more conservative vein, Leatham¹ observed that "intracardiac phonocardiography has mainly served to confirm or consolidate facts which were already known, or have been ascertained in the last 20 years using multichannel external recording apparatus."

Yamakawa and associates² used the term intracardiac phonocardiography in a study in which a condenser microphone was adapted to a catheter, and vascular and cardiac sounds were recorded in 20 dogs and three humans; illustrated tracings from the animal studies were published. There were no published records of the patient studies, and apparently there were severe limitations inherent in the initial methodology.

Lewis et al.³ recorded heart sounds and murmurs in the lesser circulation with a barium titinate transducer and noted the technique was capable of localizing heart sounds and murmurs to an extent not previously possible. The frequency response of the catheter preamplifier system was linear over the range of heart sounds; however, since the response of the barium titinate dropped off sharply below 10 Hz it was not possible to record simultaneous intracardiac pressures. A double lumen catheter was used to record pressure with an external manometer. These and additional studies in acquired⁴ and congenital⁵ heart disease were the initial ICP studies in the United States. The instrumentation and usage gave the entire field a worldwide impetus.

Luisada and associates⁶,⁷ used a simplified method of transducing pressure obtained through standard catheter systems to isolate pressure frequencies in the sound range. The technique, fluid column transmission, accelerated access to recording sound in the left heart, and was adapted or modified in a number of laboratories. An important outgrowth of these studies was the proposal by Shah et al.⁸ for revision of the classic auscultatory areas. The auscultatory areas were renamed according to the chamber or vessel in which a given sound or murmur was best recognized by intracardiac phonocardiography. Murmurs were further described as originating in the inflow or outflow tracts of the left and right heart. Grant's⁹ earlier physiologic concepts of ventricular inflow and outflow tracts were coupled to this anatomic and auscultatory framework. It is possible to take the matter a step further; for example, Leatham's¹⁰ classification of murmurs is easily adapted to this approach. The lessons learned from intracardiac phonocardiography provide a logical basis for the practice and teaching of auscultation.

From the developmental point of view, ICP took on a new perspective with the development in France of the micro-
manometer of Allard and Laurens, originally described in 1954, and the imaginative usage and meticulous documentation of intracardiac sound and pressure profiles by Soulé and associates. This instrument set new standards for clinical manometry and established the importance of high fidelity pressure recordings without transmission delay, not only for sound-murmur-pressure-angiographic correlates, but also for externally derived pressure pulses and ultrasound. Micromanometer pressure pulse recordings were quite different from those depicted in standard reference sources and formed a new basis for timing systolic and diastolic intervals and cardiac acoustic events.

An inductance microtransducer for intravascular pressure was described by Gauer and Gienapp and its evaluation and application were presented in 1951. The Allard-Laurens variation consisted of a single coil with a central core suspended between two diaphragms; displacement altered the self-inductance of the coil. The natural frequency was in the neighborhood of 2.5 kHz, the transducer was linear over the physiologic pressure range. Frequencies above 40 Hz were utilized to produce a sound tracing recorded simultaneously with pressure measurement. Piemme discussed variable inductance microtransducers from the perspective of 1963. He noted that the principle of variable inductance was ideally suited to the design of catheter-mounted microtransducers, since tiny coils could be wound containing a magnetic core of very small mass, yielding superb dynamic response characteristics. The Allard-Laurens manometer was considered to possess the finest response characteristics of any of the physiologic pressure sensing devices of the era. The practical disadvantages included size and stiffness of the catheter mounted manometers, initial equipment costs, cost of individual catheters, the need for careful handling and limited mechanical durability.

The 1961 publication of the monograph Le Son Intracardiaque by Soulé et al. presented an extensive experience with simultaneously recorded intracardiac sound and pressure (ICSP) in acquired and congenital heart disease. Soulé re-emphasized the contribution of turbulence in the production of certain murmurs, and anticipated the flow-velocity measurements of the 1970s. He considered extracardiac auscultation over the thorax to be a resultant of complex and disjointed vibratory phenomena, the components of which had timing that was different from one cavity to the other. Murmurs recorded in a cardiac or vascular chamber were propagated in the direction of the jet or turbulent flow which produced them, and they tended to stay localized in the cavity of their origin. These ICSP observations and speculations reawakened interest in turbulence, velocity, Venturi effect and flow phenomena in cardiac acoustics. Soulé stated, somewhat expansively, "The recording of intracardiac sounds had confirmed without question, that which logic led us to believe."

Many of the early right heart studies were confirmed, extended or modified in articles published during the early and mid 1960s. Barritt and Davies confirmed the elimination of transmission delay and the damping effect of a long saline column on pressure tracings with the catheter manometer and noted the more confident assessment of the relation between pressure changes and heart sounds and murmurs. Segal, Novack and Kasparian while agreeing with previous studies in general, stressed the disadvantages and limitations of the manometer and emphasized certain of the problems associated with transmission of loud left heart murmurs to the right heart. Wennvold also recorded certain aortic stenosis murmurs in the right heart, and on occasion the murmur of aortic regurgitation in the right ventricle.

Several texts from this decade contain a great deal of information concerning techniques and original observations. Gunther presented his personal experiences with ICP, and included approximately 180 references in a universal sampling. Similarly, Ferugio compared the available methods of ICP recording, and presented innovative methodology and a comprehensive personal experience. Extensive right heart experience in children was reported by Dahl.

Double manometer studies with two separate Allard-Laurens manometers required modifications of equipment; although technically awkward, several double manometer studies were used to time pressure pulse events, pressure crossovers and heart sound relations that had a significant impact on the study of the genesis of heart sounds in intact man.

Millar developed catheter mounted pressure transducers constructed from a pair of matched, unbonded silicon elements, geometrically arranged to act respectively in compression and extension upon application of pressure. Improved intrinsic gauge sensitivity, thermal stability, drift characteristics, linearity and mechanical durability represented a significant technical advance in catheter-tip pressure transduction. Multisensor catheters, designed by Murgo and associates and constructed by Millar, yielded multipressure capability unique in cardiac catheterization. Transducer frequency response is flat to within 2 db to 12 kHz. With filtering and amplification, the manometer characteristics allowed for separation of physiological pressure signals (approximately 0–40 Hz) from intravascular sound (approximately 50–500 Hz). The impact of this instrumentation is just becoming apparent in ICSP recording. The extensive field of manometer development and characteristics has been reviewed in a recent text, Indwelling and Implantable Pressure Transducers, which contains specifications of commercial pressure transducers.

The problem of artefact production and recognition has existed throughout the history of ICSP recording, but has diminished with each technological development. Careful auscultation prior to study, correlation during study with external phonocardiography and echocardiography, amplification of ICP during the study, a careful search for reproducibility of recorded phenomena, and correlation of recordings with increasingly refined catheterization-angiographic and echophonocardiographic techniques have reduced the potential for artefact error.

Direct calibration of intracardiac cardiovascular sound was performed by Soulé et al. with a transducer calibrated in units of mm Hg. Allard presented the rationale, instrumentation and methodology for comparing ICP with external phonocardiography; little clinical use of this approach has been reported. Sabbah and Stein used a pressure calibrated transducer (dynes/cm²) and approached the measurement of sound intensity with formulae for determining sound energy density and acoustic power output; this approach merits critical appraisal since it may provide quantification and comparisons in a hitherto elusive area of cardiovascular sound measurement.
Heart Sounds

ICSP studies established 1) sequence — the timing of heart sounds with pressure pulses, their derivatives, and pressure crossovers and 2) localization of sound components to right or left heart chambers or great vessels.

A germinal paper was the study by Piemme et al. who compared intravascular sound with pressure and flow events in the cardiac cycle in anesthetized dogs. Induced pressure transients were observed in all cardiac chambers, the lower frequencies appearing on conventional pressure tracings and the higher frequencies as intracardiac sound. The authors emphasized acceleration and deceleration of blood flow as sufficient and necessary conditions for the origin of cardiovascular sound transients, and presented the concept that abrupt acceleration or deceleration of blood flow was associated with an energy source sufficient to displace the mass of the heart, and that the mass oscillated at a sum of frequencies that were a function of the chamber mass and restoring forces. This approach was in keeping with concepts expressed previously, and currently, by Rushmer, who classified vibrations or sounds due to acceleration or deceleration of blood as heart sounds, and vibrations or sounds due to turbulence in flowing blood as murmurs.

First Heart Sound

The development of thought concerning the first heart sound (S1) was succinctly reviewed by Waider and Craig. The ability to record and to separate sound events temporally related to mitral and tricuspid closure from sound events related in time to ejection into the aorta and pulmonary artery, coupled with the development of technical approaches to mitral valve flow and motion, contributed to clarification of some of the earlier controversy that surrounded S1. Specifically, newer techniques have allowed us to consider heart sound components in terms of sequences involving onset of ventricular contraction or relaxation, pressure development, valve motion, pressure crossover, coaptation of leaflets, and termination of opening or closing motion.

A classification and terminology that deals with heart sounds associated with right and left heart atrioventricular (A-V) valve closure as separate and distinct from heart sounds related to right and left heart ejection events will be used in this discussion.

Sounds Associated With and Temporally Related to A-V Valve Closure

Mitrail Component

Piemme and associates recorded the first major component of the first heart sound simultaneously with the onset of isometric ventricular contraction and the occurrence of the left atrial “c” wave (which was frequently biphasic, occasionally an even more complex wave form).

Faber in a study of the origin and conduction of the mitral sound in the dog heart, calculated that it would take the mitral valve about 22 msec to close after the equalization of left atrial and left ventricular pressures. Laniado et al. stressed the dynamic relationship between pressure and flow across the mitral valve, and measured 1) timing of valve closure with a synchronized cinefluorogram of the motion of the cusps after they were made radiopaque, and 2) flow with a supra-annular mitral valve electromagnetic flow probe. Mitral valve closure did not occur at the crossing point of atrial and ventricular pressure, but 20–40 msec later due to inertia of mitral flow. The first major component of the first sound coincided with two simultaneous events: the cessation of mitral flow and the closure of the mitral valve, and reached maximal intensity with the atrial “c” wave.

Lakier et al. recorded the first major component of the first heart sound (M1) after LV-LA pressure crossover at the same time as the peak of left atrial “c” wave in 41 patients, all but five of whom had mitral valve disease. Mills et al. showed that LV-LA pressure crossover preceded mitral closure by 50 msec.

Stept et al. evaluated the amplitude of the mitral component of the first heart sound in dogs with fixed-rate sequential A-V pacing, and noted that both the timing of atrial and ventricular systoles and the force of left ventricular contraction were major, independent determinants of M1 amplitude.

Mitrail Component and Q-S1 Interval of Mitral Stenosis

The delayed, accentuated mitral component of the first sound in mitral stenosis was the subject of double manometer studies at surgery and at catheterization with angiographic correlation with very close agreement between the two studies (fig. 1). The delayed mitral component occurred at the time of the left atrial “c” wave, after left ventricular-left atrial pressure crossover, when left ventricular pressure exceeded the elevated left atrial pressure by approximately 14–18 mm Hg, at the time of a change in the slope (rate of rise) of the left ventricular pressure pulse. Cineangiography showed that the left ventricle drove the mobile sleeve or dome formed by the fused mitral leaflets to the closed position, and the mitral component occurred at high pressure at the termination of this ascent or eversion. These findings were compatible with prior observations by Rich, Nixon and Ross et al.

The Q-S1 interval of mitral stenosis in sinus rhythm, more specifically the Q-M1 interval, consisted of two successive intervals. The first interval began with the electrocardiographic Q wave and extended through the initial LV pressure rise to the crossover of LV-LA pressures. The second interval extended from the pressure crossover to a point where LV pressure exceeded the “c” of the left atrial pressure pulse by an average of 14 mm Hg, a change in the slope of LV pressure rise occurred and the delayed, increased amplitude mitral component was recorded. Most of the delay in prolonged Q-S1 of mitral stenosis occurred during the interval from Q wave to the point of LV-LA pressure crossover.

Tricuspid Component

Lakier et al. showed a precise temporal relationship between the second major component (T1) of the first heart sound and the peak of the right atrial “c” wave, i.e., T1 had the same relation to the peak of the right atrial “c” as M1 had to the left atrial “c” wave. O'Toole et al. recorded right and left atrial ICSP and the external phonocardiogram. The initial external high frequency component of S1 coincided with the left atrial “c” wave and the simultaneous internal sound designated as M1; the second external high frequency component of S1 was synchronous
with the right atrial “c” wave and the simultaneous internal sound component that was defined as T1, M1 preceded T1 with two exceptions (chronic left bundle branch block and mitral stenosis). It was concluded that right and left atrial “c” waves recorded with manometers could serve as markers for externally recorded M1 and T1. The reason that T1 was not as widely transmitted internally as M1 was not satisfactorily explained by this study.

Mills et al.39 showed that RA/RV pressure crossover consistently preceded tricuspid valve closure by 35–60 msec, 50 msec being the most consistent interval. A 25 msec delay was observed between pressure crossover and the start of rapid closure of the tricuspid valve.

Echophonocardiography was used in a variety of clinical situations (normal subjects, patients with ASD, RBBB, Ebstein’s anomaly, mitral stenosis) in which the authors demonstrated the simultaneous occurrence of mitral valve closure with M1 and tricuspid valve closure with T1. Leatham and Leech42 recorded high frequency phonocardiograms with echograms from four valves. Mitral and tricuspid valves closed simultaneously in normal subjects with a single first heart sound. In normal subjects with two major first sound components, the first coincided with mitral closure and the second with tricuspid closure. In situations where mitral and tricuspid closures were grossly asynchronous, each valve closure had an associated sound.

Tricuspid Component and the Systolic Sound of the Ebstein Anomaly

Fontana and Wooley48 recorded a systolic sound in the right ventricle or atrialized right ventricle in three patients with Ebstein’s anomaly, just after the peak of the “c” wave in atrialized right ventricle, at the point where the initial slow delta portion of the right ventricular pressure pulse gave rise to a rapid upstroke. This systolic sound was considered to arise when the large, sail-like tricuspid leaflet reached the limit of its systolic excursion, was designated as the “sail-sound” and was considered to be the most specific auscultatory event in Ebstein’s anomaly. Wennevold and Hansen44 studied Ebstein’s disease and noted identical findings regarding this accentuated first sound component. These observations confirmed an earlier hypothesis by Pocock et al.42 Studies in Ebstein’s anomaly by Crews et al.46 showed that the only constant auscultatory abnormality was abnormally wide splitting of the first heart sound with accentuation of the delayed component. Echophonocardiography confirmed that tricuspid closure was greatly delayed and coincided exactly with the abnormal sound.

Thus, it seems reasonably well established that intracardiac pressure changes initiate valve movements, A-V closure follows atrial-ventricular pressure crossover, and high frequency components of the first sound are associated with termination of closure movements of mitral and tricuspid valves. These sounds have been recorded internally and externally, in health and disease, simultaneously with intracardiac manometer pressure pulse transients that we now know signal termination of valve closing motions, and with echocardiograms that demonstrate simultaneity of respective A-V valve closure.

Sounds Associated With Ejection

Ejection Sounds in the Aorta

Patients with an aortic ejection sound (AES) without aortic valve disease were studied by Whittaker et al.47 The onset of the AES, coincident with the onset of pressure rise in the aortic root, led the authors to conclude that the AES without aortic valve disease was an exaggerated ejection.
component of the normal first heart sound, an aortic root phenomenon related to forceful ejection of blood into the aorta, identical with the ejection component ("second major component of first heart sound") recorded from the central aorta by Pienme et al. This mechanism was used to explain the occurrence of aortic ejection sounds in clinical situations associated with forceful left ventricular ejection (thyrotoxicosis, anemia, high output states), or situations in which changes in aortic root compliance exist (sclerotic aortic root in elderly, hypertensive cardiovascular disease). Inotropic agents markedly increased the amplitude of the ejection sound in both the human and the animal studies.

Laniado and co-workers recorded the aortic valve echogram simultaneously with aortic flow, acceleration of flow, aortic and left ventricular pressures, and intracardiac phonocardiograms. Aortic sound vibrations, recorded in the aortic root, were classified as the aortic component of the first sound; this sound started after the mitral component which was recorded in the left ventricle, and before the onset of aortic valve opening and acceleration of flow. The intensity of the aortic component was closely associated with changes in acceleration of aortic flow. The authors stated that these observations supported previous suggestions that early acceleration of ejected blood was responsible for vibrations that originated in the aortic root.

Lack of a fixed temporal relationship between this sound and the time at which the aortic cusps achieved maximal amplitude of opening was viewed as confirmation of Waider and Craig's observations that in the normal aortic valve the cusps do not participate in the genesis of the first sound, and with Whittaker's conclusion that aortic ejection sounds heard in subjects without aortic valve disease were the exaggerated ejection component of the first sound. The limitations of the study by Laniado et al. were the open chest preparation and the lack of correlation with externally recorded sound.

There is evidence that ejection vibrations arise in, and may be recorded within, the aortic root in the absence of aortic valve disease. At times these sounds are audible, may be heard and recorded externally, and are of clinical significance. More precise definition should result from studies of the temporal relations of aortic valve opening, acceleration of blood flow and behavior of the aortic root during ejection, with appropriate clinical correlations.

Whittaker et al. recorded the aortic ejection sound (AES) in patients with valvular aortic stenosis. The aortic root pressure rise preceded the AES. The AES was coincident with the anacrotic notch on the upstroke of the central aortic pressure, and occurred when the domed aortic valve reached its maximal excursion on the timed cineangiogram. The authors concluded the AES in valvular aortic stenosis was valvular in origin. Waider and Craig showed in cases of aortic valve deformity that the aortic ejection sound occurred synchronously with the achievement by the valve of its fully open position. These observations confirmed the earlier angio-phonocardiographic findings of Ross and Criley and the clinical correlates established by Hancock. There is agreement, based on multiple methods of study, that termination of the opening movement of the mobile, stenotic aortic valve contributes to the production of the AES of valvular aortic stenosis. Figure 2 illustrates AES recorded in the left heart.

**Ejection Sounds in the Pulmonary Artery**

The ejection sound which occurs in the presence of pulmonary artery hypertension or dilatation was studied by Martin et al. The pulmonary ejection sound (PES) associated with pulmonary hypertension was recorded simultaneously with the onset of pulmonary artery pressure rise; this sound was considered to be the right heart equivalent of the aortic root ejection sound. The PES accompanying a dilated pulmonary artery with normal pressures was delayed by a variable interval after right ventricular pulmonary artery pressure crossover, and was discussed in terms of distensibility or compliance of the proximal pulmonary artery. Echophonocardiography studies showed that PES occurred "at the moment of maximal semilunar valve opening" or "precisely with the achievement of a fully open position by the pulmonic valve," whether associated with pulmonary stenosis or hypertension. Additional integrative studies of the temporal relations of pulmonary valve opening, acceleration of blood flow and behavior of the proximal pulmonary artery may be required before a unifying concept is available.

The PES of pulmonic valve stenosis recorded externally and internally occurred after the onset of pulmonary artery pressure rise at the time of a prominent anacrotic notch on the pulmonary artery pressure pulse, after right ventricular pressure crossover. These observations were in agreement with earlier right ventricular cineangiograms and simultaneous pressure measurements which showed coincidence of the pulmonary valve ejection sound with abrupt checking of the upward doming motion of the thickened valve after right ventricular-pulmonary artery pressure crossover, prior to distention of the pulmonary artery. Echophonocardiography was consistent with the explanation that vibrations resulting from the movement of the stenotic...
diaphragm-like valve with right ventricular systole and its halting were responsible for the ejection sound or click. The ICSP observations dealing with the PES of pulmonary valve stenosis substantiate or are in agreement with other methods of study.

Second Heart Sound

Pulmonic Closure and P2

The events of the cardiac cycle were recorded with high fidelity micromanometers. Aortic and pulmonic closure sounds were coincident with the incisurae of their respective arterial tracings; the durations of left and right ventricular electromechanical systole were nearly equal. The greater delay of the pulmonary incisura compared with the aortic incisura was associated with a larger interval separating the pulmonary incisura from the right ventricular pressure compared with the same left-sided interval. The duration of this interval was considered to be a reflection of the impedance of the vascular bed into which the ventricle was ejecting (fig. 3). A reappraisal of the dynamics of second heart sound production, with additional insights into the mechanisms of second heart sound splitting incorporated the concept of impedance characteristics of the pulmonary bed, and represents a blending of thought arising from traditional auscultation, classical phonocardiography and ICSP analysis.

Aortic Closure and A2

The precise relationship between the aortic closure sound (A2) and aortic valve closure has been questioned. Piemme et al. concluded that the second heart sound began significantly before aortic valve closure, while forward flow was still going on, and was proportional to the magnitude of deceleration of blood flow. Anastassiades et al. analyzed the temporal relationship between aortic valve closure and onset of aortic component of the second heart sound (A2) in three subjects. A2 coincided with the incisura of the central aortic pressure; coaptation of aortic cusps occurred either simultaneously with, or up to 10 msec prior to, A2. The authors suggested that A2 did not originate from the coaptation of aortic valve cusps, but was related to events that occurred at the time of or slightly after coaptation.

Sabbah and Stein studied human subjects with no apparent valvular disease, dogs, and an in vitro model system. Simultaneous high speed motion pictures were used with the model system. The aortic closure sound was of higher amplitude in the ventricle than in the aorta in all three parts of this study. The direction of inscription of the main components of intra-articular sound was opposite in direction to the components of intraventricular sound, consistent with expansion and compression wave registration. The amplitude of the closure sound varied with diastolic pressure, but remained unchanged with augmentation of forward and retrograde aortic flow. Cine studies in the model system showed that the second sound began after complete valvular closure. The authors concluded that the semilunar valves, when closed, acted as an elastic membrane, which, when set in motion, generated compression and expansion of blood, and produced transient pressure changes indicative of sound; the magnitude of the initial stretch was related to the differential pressure between the arterial and ventricular chambers. That the second sound began coincident with the rapid deceleration of aortic flow was in agreement with Piemme et al., however, the cine studies showed that the valves were fully closed at this time, contrary to the thought expressed by Piemme that A2 began before the valve closed.

Laniado et al. recorded the aortic valve echogram in open chest dogs simultaneously with aortic flow, acceleration of flow, aortic and left ventricular pressures and intracardiac phonocardiograms. The echogram showed close temporal relation between aortic valve closure, the dicrotic notch of the aortic pressure and the “large amplitude vibrations” of the second sound. There was a short time lag in the range of 4–10 msec between the point of the initial cusp apposition and the beginning of the major sound component and the dicrotic notch. Interestingly, in view of Sabbah and Stein’s work, some records demonstrated a rapidly vibrating motion of the sealed cusps which started immediately following closure and occurred simultaneously with the major sound component. The authors considered that the assumption by Piemme et al. that the onset of the second sound occurred 25 msec before valve closure was apparently incorrect. The intensity of the second aortic sound did not correlate with the maximal amplitude of cusp opening, but was closely associated with the rate of flow deceleration and the aortic pressure at the time of valve closure. The authors suggested that the second sound originated in the aortic valve, not at the time of initial closure and cusp apposition but shortly after when sealed cusps tense and vibrate under the action of a rapidly applied force.

Hirschfeld and associates studied sixteen patients, aged 3–20 years with simultaneous aortic valve echogram, aortic root pressure tracings and intracardiac phonocardiograms. Echographic coaptation of aortic valve leaflets coincided with the trough of the aortic pressure incisura and the onset of intracardiac A2. The authors concluded that closure of the
aortic valve initiated A2, and suggested that the higher frequency components of A2 were the results of tensing of the closed semilunar valve. Craigie64 noted that "our own observations [echophonocardiography] disclose an unvarying simultaneity of aortic valve closure and the initial high frequency vibrations of A2."

If one reviews the ICSP records noted above, it becomes apparent that there is a real problem in interpretation of the exact timing of the onset and duration of A2. As recorded in the aortic root, A2 is composed of multiple vibrations, leading to variations in interpretation of the point of initial deflection from baseline, the onset of initial high frequency deflection, major deflection, etc. Signal processing and resultant timing may account for certain inconsistencies in the interpretation or comparison of the results of these studies. These inconsistencies remain to be clarified. There would appear to be room for consideration of a sequence involving the near-simultaneous occurrence of 1) leaflet coaptation, 2) valve closure, 3) the incisural trough of aortic pressure pulse and 4) the initial high frequency vibrations of A2; followed by 5) the rise of the aortic pressure pulse following the incisura (as a reflection of the closed valve generating a compression-expansion phenomenon) with 6) the production of the latter part of the sound.

The Opening Snap of Mitral Stenosis. ICSP studies35, 36 showed that the opening snap in patients with noncalcific mitral stenosis and sinus rhythm occurred at a significant interval 1) after the left atrial "v" wave peak, and 2) after left ventricular-left atrial pressure crossover, simultaneously with an abrupt change or interruption in the left atrial "y" descent (the opening snap notch), at a time when left atrial pressure exceeded left ventricular pressure by an average of 14 mm Hg (fig. 1). The sound and left atrial pressure pulse relations were in agreement with earlier catheter and external phonocardiographic observations by Rich37 and by Nixon.38 The timed cineangiograms and external phonocardiograms of Ross and Criley41 showed the mitral opening snap occurred at the moment of maximum descent of the mitral valve, that the mitral opening snap was related temporally to the tensing of mitral valve tissue at the end of its downward movement and that the event also corresponded to a sudden change in the velocity of the bolus of blood moving downward from the atrium into the ventricle.

The S2-opening snap (O.S.) interval, specifically the A2-O.S. interval, long regarded as a potential indicator of the severity of mitral stenosis, was shown to consist of two discrete time intervals.35, 36 The first interval began with the near-simultaneous onset of the aortic closure sound and the left atrial "v" wave peak, and extended through the time when left atrial and left ventricular pressure fell simultaneously until the pressure crossover point. The second interval began with the pressure crossover and extended to the opening snap; during this interval left ventricular pressure fell approximately 14 mm Hg below left atrial pressure, to the point of the abrupt interruption of the left atrial "y" descent (the opening snap notch), which was simultaneous with the recording of the mitral opening snap. Kalmanson et al.42 recorded blood flow velocity through the mitral valve orifice in patients with mitral stenosis, and timed the mitral opening snap with external phonocardiograms. Their findings supported the concept of sudden tensing of the valve at the time of maximum excursion of the leaflets and the opening snap. The A2-O.S. interval was composed of two successive intervals, the first from A2 to the onset (on the flow velocity curve) of the ascending limb of the initial diastolic filling wave of the left ventricle; this interval was considered synchronous with the isovolumic relaxation period. The second interval was the time from this point to the opening snap (considered as excursion time of valve cusps).

When the A2-O.S. interval is dissected and analyzed by these different methods and techniques, there are some differences in interpretation. However, it seems clear that multiple factors affect these A2-O.S. intervals. Many conflicting statements in the literature about the diagnostic reliability of the A2-O.S. interval and its derivatives are oversimplifications that ignore the complexity and multiplicity of factors determining the A2-O.S. interval.

Reciprocal Sounds

The Q-S2 (mitral component), A2-mitral opening snap, time and pressure relations led us to propose35 that the mitral opening snap should be considered as the reciprocal of the mitral component of S1 in mitral stenosis. Since the verb reciprocate means to move alternately backward and forward, a fused valve unit, moving alternately backward and forward or up and down, and contributing to sound production at the termination of these motions, would contribute to production of reciprocal sounds, i.e., a sound for which there is a counterpart or an equivalent in another part of the cardiac cycle. The tricuspid component of S1 and tricuspid opening snap of tricuspid stenosis, the AES and intact A2 of mobile valvular aortic stenosis (fig. 2), or the PES and pulmonary closure sound of valvular pulmonic stenosis are other examples of reciprocal sounds.

Third and Fourth Heart Sounds

Crevasse et al.42 studied the mechanism of generation of third and fourth heart sounds. Audible third and fourth heart sounds had a common origin in the ventricles. The third heart sound occurred during early rapid diastolic filling when the A-V pressure relationship indicated that the A-V valves were open, and was attributed to ventricular muscular vibrations. The audible fourth sound followed atrial contraction, was recorded in the ventricle and on the ventricular muscular wall, and was related to sudden augmentation of late diastolic ventricular filling with resultant audible ventricular muscular vibrations. These sounds, which were generated within either ventricle, were considered to have essentially the same temporal and hemodynamic relationship regardless of etiology.

No definitive or detailed ICSP studies dealing with third and fourth sounds following this study are in the literature, although a number of articles mention recording third and fourth sounds as part of broader studies. Craigie64 commented that the third sound occurs in a variety of circumstances where the common denominator physiologically is rapid ventricular filling (the normal youthful subject, mitral regurgitation, heart failure). In echophonocardiographic records, the third sound occurred during the E-F or closing slope of the mitral valve in early diastole. No distinctive role of the mitral valve in the production of the third sound was delineated by this technique. The fourth sound occurred after the mitral valve had reopened in late diastole.
in response to atrial contraction. The fourth sound occurred during the A-C period in echocardiographic records, while the valve was in the act of closing, and no significant alteration in valve motion was detected at the time of sound production. Although the pathogenesis of the fourth sound was incompletely understood, its significance was considered as an indicator of an alteration in ventricular compliance, occurring when atrial systole produced a disproportionate rise in pressure in the ventricle in late diastole.

Heart Murmurs

Heart murmurs have been localized to specific cardiac chambers, right and left heart inflow and outflow tracts by ICSP studies. The definition of external auscultatory areas that have a sound anatomic basis provides the framework for clinical auscultation; regional considerations of murmur production and transmission fit this framework in most clinical situations. Awareness of the intensity of intracardiac murmurs reawakened interest in detection and quantification of turbulence, as well as the relations between disordered flow, murmur production and intensity of audible murmurs. The timing and definition of valve opening and closing by echophonocardiography have clarified the mechanisms of certain inflow tract diastolic murmurs. Lastly, the discovery that certain patients may have four, five or six murmurs which cannot always be separated or distinguished on the chest wall has been a unique contribution of ICP.

Murmurs Recorded in the Right Heart

The Right Atrium

Systolic murmurs were recorded in the right atrium with tricuspid regurgitation (fig. 4) and with left ventricular-right atrial communications. Lewis et al. recorded the murmur of tricuspid regurgitation (TR) in the right atrium in situations where the contour of the right atrial pressure curve did not suggest TR, and also confirmed the inspiratory increase in intensity of the TR murmur within the right atrium which was initially described by Rivero Carvallo with external recordings. The sensitivity of ICSP techniques in the detection of TR led to a new appreciation of the frequency of TR in a variety of clinical settings, and to a proposal that the classic "functional versus organic" TR classification be discarded and replaced by a categorical approach to the broad spectrum of TR based on disorders of function of the tricuspid valve complex.

A "new" murmur of tricuspid valve origin, the late systolic murmur of tricuspid valve prolapse, was initially defined by cineangio and external phonocardiograms by Gooch and associates and recorded within the right ventricular inflow tract in our laboratories. Diastolic murmurs in the right atrium included flow murmurs at the site of the defect in patients with atrial septal defects. Sakamoto et al. and Kambe et al. summarized earlier observations and their own considerable experience. Three types of flow murmurs were recorded in the right atrium at the defect area: 1) the crescendo-decrescendo,

![Figure 4](https://example.com/figure4.png)

**Figure 4.** Tricuspid regurgitation. A patient with chronic calcific constrictive pericardial disease and a lower left sternal border systolic murmur which was augmented with inspiration. Left panel, top to bottom: respirometer signal (inspiration); external phonocardiogram, lower left sternal border; intracardiac phonocardiogram; right ventricular pressure pulse; electrocardiogram. Right panel, top to bottom: respirometer signal (expiration); external phonocardiogram, lower left sternal border; intracardiac phonocardiogram; right atrial pressure pulse; electrocardiogram. The manometer pressure pulses are those of constrictive pericardial disease. The systolic murmur was localized to the tricuspid valve; vibrations also appear on the C-V wave of the right atrial pressure pulse. Time lines 40 msec. Paper speed 100 mm/sec.
late systolic-early diastolic murmur closely related to the atrial “v” wave was recorded in 32 of 48 patients with secundum defects; 2) an atriostylyotic murmur, closely related to the atrial “a” wave, was recorded in 17 of 48 patients with secundum defects; 3) a mid-diastolic murmur was found at the defect in four of the 48 patients. Catheter tip directional Doppler velocity studies showed the ASD shunting pattern occurred from left to right throughout late systole and diastole; a typical pattern consisted of three distinct waves of acceleration, a late systolic wave prolonged into early diastole, a mid-diastolic wave, and a late diastolic wave during atrial contraction. Thus the location and timing of the right atrial diastolic shunt murmurs have correlates with phasic flow velocity patterns of the shunt as determined by directional Doppler ultrasound, as well as with fiberoptics, interatrial pressure gradients and biplane cineangiograms.

The Right Ventricle

Systolic murmurs have been recorded 1) at various levels in the right ventricle with ventricular septal defects, and 2) in the presence of right ventricular intraventricular pressure gradients in patients with congenital infundibular pulmonic stenosis, and 3) with hypertrophic obstructive cardiomyopathy.

Ventricular septal defects vary in anatomic location in the septum with flow characteristics which differ sufficiently to affect the site of murmur production, transmission and detection. In general, the intracardiac point of maximum murmur intensity in the right ventricle coincides with the precordial point of maximum murmur intensity. The jet of the subpulmonic defect enters the right ventricle high in the outflow tract; the murmur is recorded in the main pulmonary artery or right ventricular outflow tract, or both; a palpable precordial thrill is common, and the maximum intensity of the external pansystolic murmur is in the second left intercostal space. The murmur of a septal defect under the septal leaflet of the tricuspid valve may only be recorded with the transducer resting on the tricuspid septal leaflet; the septal leaflet buffers the jet which may not strike the free wall of the right ventricle. As a result, the location of the murmur is lower on the chest wall and a palpable thrill may be absent.

"New" systolic murmurs of right ventricular origin documented by ICSP studies included the murmur caused by the septal hypertrophy of obstructive cardiomyopathy (IHSS). The precordial murmur of biventricular obstruction to outflow represents the summation of two murmurs.

Diastolic murmurs recorded in the right ventricular inflow tract (RVIT) include the murmur of tricuspid valvular stenosis, which frequently follows a tricuspid opening snap and is augmented by inspiration. The atrial systolic murmur of tricuspid stenosis is discrete, tends to be presystolic in time if the relationship of atrial systole to ventricular systole is physiologic, is crescendo-decrescendo in contour following the contour of the tricuspid A-V pressure gradient, and exhibits inspiratory augmentation (fig. 5).

Ventricular filling murmurs recorded in the RVIT are associated with increased tricuspid flow, are of short duration, confined to the rapid filling phase, are usually augmented with inspiration and have been recorded in the presence of left-to-right shunts at the atrial level, and with tricuspid regurgitation. Echophonocardiography has furthered the understanding of the mechanisms of these murmurs with the observation that the tricuspid valve is closing in the presence of continuing, excessive antegrade flow across the tricuspid valve.

Green et al. recorded a mid-diastolic murmur and a presystolic murmur in the RVIT in a man with multiple congenital defects, a pandiastolic murmur of pulmonary regurgitation in the right ventricular outflow tract (RVOT) and diastolic fluttering of a tricuspid leaflet. Echophonocardiograms showed that the mid-diastolic murmur occurred when the tricuspid valve leaflet was moving posteriorly in early diastole, and the presystolic murmur occurred when the tricuspid leaflet was moving posteriorly to a closed position following atrial systole. The authors considered this murmur to be the right-sided equivalent of the Austin-Flint murmur.

Diastolic murmurs recorded in the RVOT (fig. 6) included
the murmur of pulmonary regurgitation accompanying pulmo-
nary artery hypertension, and the murmur of pulmonary valvular regurgitation due to deformities of the pulmonary
valve or to congenital absence of the pulmonary valve.

Levin et al. related the delayed onset, relatively brief crescendo-decrescendo murmur of organic pulmonary regurgitation to the delayed onset, rapidly diminishing diastolic pressure gradient between the main pulmonary artery and RVOT.

An interesting early observation by Lewis et al. was their inability to record the Graham-Steel murmur in patients with mitral stenosis, recording the murmur of aortic regurgitation instead. This observation stimulated a number of studies re-evaluating the frequency of the Graham-Steel murmur. ICSP studies remain the most sensitive and reliable methods of detecting pulmonary valvular regurgitation.

The Pulmonary Artery

Multiple mechanisms (increased flow or rate of ejection, pulmonary valve or RVOT obstruction, pulmonary valve abnormality, pulmonary artery dilatation, or combinations) may contribute to the production of systolic murmurs recorded in the main pulmonary artery (MPA). The murmurs of valvular pulmonary stenosis, idiopathic dilatation of the main pulmonary artery, high cardiac output states and atrial septal defects were consistently recorded in the MPA. Modifying factors such as the frequency, timing and duration of the murmur, the presence or absence of a pulmonary ejection sound, and the behavior of the second heart sound components helped to define individual auscultatory complexes, which for the most part fit precisely within the established tenets of external phonocardiography.

Leatham, in his classification of ejection murmurs, considered a subgroup of murmurs related to physiological ejec-
tion. Wennemol, in a study of the origin of innocent heart murmurs, investigated pulmonary ejection murmurs (soft, low frequency, second left intercostal space). Fifty-four patients had the murmur recorded in the MPA or main branches of the pulmonary artery; in 11 of these subjects it was only recorded in the pulmonary artery branches. However, in 15 subjects with a systolic "vibratory" murmur (low pitched, musical quality, widespread, maximum intensity within the apex or at the lower left sternal border), the murmur was not found in the right side of the heart with one exception, where it was thought to be transmitted from the aortic or subaortic area. The latter observations were a natural forerunner to a later study dealing with the aortic origin of innocent murmurs.

Stein and Sabbah measured intra-arterial sound just dis-
tal to the aortic and pulmonary valves of 10 subjects with no apparent valve disease. The intensity of intra-arterially recorded ejection murmurs during control measurements in all patients was significantly greater in the region of the aor-
tic valve than in the region of the pulmonary valve. Four patients with audible innocent murmurs (grade 1–2, short systolic murmurs, left sternal border) had murmurs of greater intensity in the aorta than in the pulmonary artery; two of these patients had no murmur within the pulmonary artery. These observations suggest that certain innocent murmurs are produced at the aortic rather than the pulmonary valve.

Murmurs of peripheral pulmonary artery origin, usually systolic (only occasionally continuous), have been recorded within the pulmonary arteries in patients with stenosis of the pulmonary artery and its branches. The systolic murmurs must be differentiated from peripheral pulmonary murmurs associated with large shunts, or loud cardiac murmurs from coexisting malformations.

Continuous Murmurs

Continuous murmurs, usually due to unidirectional flow through an arterial-venous communication or fistula, have been precisely localized within cardiac chambers or great vessels, to the site at which the fistula or communication terminated or emptied. Although not usually considered or classified as right heart murmurs, ICSP studies have shown that most continuous murmurs involving the heart and the great vessels in the thorax are of maximum intensity in the right heart structures which serve as the receiving chamber or vessel for the fistulous tract or communication (fig. 7). Huffman et al. recorded continuous murmurs in acyanotic adults with shunts, and developed a classification of con-
tinuous murmurs with an anatomic basis. Continuous murmurs were classified as to location in a specific chamber or vessel, and to the auscultatory area of that chamber or vessel on the chest wall. This is a reasonably logical classification and is of value in bedside auscultation.

The differential between unidirectional-flow, continuous murmurs and to-and-fro murmurs (due to bidirectional flow across a valve that combines obstruction to outflow with regurgitation, or to increased forward stroke volume with valvular regurgitation) has been further defined by ICSP study. A continuous murmur is usually recorded in its totality at the site of communication or emptying, while a to-and-fro murmur is recorded as two distinct murmurs, the out-
flow ejection murmur recorded in the respective great vessel and the regurgitant murmur in the respective ventricle.

**Murmurs Recorded in the Left Heart**

**The Left Ventricular Inflow Tract**

ICP studies in the left heart discovered clicks, whoops, rumbles and snaps, the genesis of which were incompletely understood until the era of catheter-angio graphic, ICSP and echophonocardiographic techniques. ICP access to the left heart via the technique of Luisada has been mentioned; Forman et al. and Beuren and Apitz developed transeptal techniques using the Allard-Laurens and barium titanate transducers. More recent use of the Millar manometers in the left heart has extended the exploratory process.

Reid's suggestion that mid-systolic clicks and late systolic murmurs originated within the heart and were probably of atrioventricular valve origin was quickly followed by Barlow's description of the clinical, auscultatory and electrocardiographic findings in the systolic click-late systolic murmur syndrome (billowing mitral leaflet syndrome, mitral valve prolapse syndrome). Left heart ICSP studies by Ronan et al., Leighton and associates and Leon and associates confirmed the mitral valve origin of the systolic clicks, late systolic murmur and systolic whoops. Correlation of cineangiograms with intracardiac and external phonocardiograms by Criley et al. provided the functional basis for the auscultatory findings, since the systolic click coincided with the time of maximal valve prolapse and the late onset systolic murmur reflected valvular regurgitation as mitral valve prolapse occurred. The complementary overlap of multiple clinical observations by investigators in all parts of the world clarified the origins of these sounds and murmurs (traditionally considered to be of extracardiac origin) in a brief interval, with effects that have been far reaching.

Gunther and Munster studied patients with "pure" mitral regurgitation confirmed by cineangiography and recorded the systolic murmur in the left atrium (which was of different shape and contour than the chest wall recording), as well as mitral opening sounds and protodiastolic vibrations in the left ventricle.

Auscultatory and ICSP findings in acute mitral regurgitation were correlated with hemodynamics, angiography and surgical findings by Littler et al. The systolic murmur was of greatest intensity in the left atrium immediately above the mitral valve; the configuration of the murmur was similar to that of the external phonocardiogram. The left ventricular third sound (LV-S3) was recorded in the left ventricle, the vibrations most marked immediately below the mitral valve, and was associated with a short mid-diastolic murmur. A left ventricular fourth heart sound (LV-S4) was also recorded in the left ventricle in four patients, all of whom had an external fourth heart sound. Although the systolic murmur showed a number of different configurations, the predominant pattern was a pansystolic murmur with a crescendo in mid-systole and a late systolic decrease in murmur intensity; the systolic pressure gradient between left ventricle and left atrium showed a mid-systolic peak coinciding with the peak of the systolic murmur. The tail left atrial "v" wave in late systole was associated with a simultaneous, marked reduction in the gradient with a corresponding decrease in both the amount of regurgitation and the intensity of the systolic murmur. The propagation of the murmur appeared to depend on the direction of the jet of mitral regurgitation, i.e., medial and forward jet direction toward the atrial septum and aortic root resulted in propagation of the systolic murmur toward the base of the

---

**Figure 7.** Patent ductus arteriosus. Continuous murmur recorded in the pulmonary artery at the main pulmonary-left pulmonary artery junction. Top to bottom: external phonocardiogram, second left intercostal space; external phonocardiogram, fifth left intercostal space; intracardiac phonocardiogram; pulmonary artery pressure pulse; electrocardiogram. Time lines 40 msec. Paper speed 100 mm/sec. (Reproduced by permission from American Journal of Medicine.)
heart and up into the neck; posterior and lateral jet direction produced a murmur conducted toward the axilla and spine. This study, and the mitral valve prolapse studies noted above, show ICSP observations to the best advantage, performed and interpreted in a hemodynamic environment, correlated with external phonocardiography, cineangiographic or surgical observations and contributing to the basic understanding of auscultatory observations as indicators of specific clinical entities.

The diastolic murmur of mitral stenosis was recorded in the left ventricular inflow tract immediately following the mitral opening snap, and the relations of the murmur to catheter manometer left atrial-left ventricular pressure pulses were defined (fig. 1). The mechanism for the crescendo presystolic murmur was defined by the ultrasound studies of Edler, and timed cineangiographic and phonocardiographic techniques and echophonocardiography. In essence, these investigators concluded that the crescendo presystolic murmur resulted from a closing motion of the mitral valve in the face of an atrioventricular pressure gradient with a resultant increase in velocity of flow across the mitral valve. A complete review of the mechanical and acoustical events in mitral stenosis has been published recently. The observations were extended by Fortuin and Craigie to include other conditions in which antegrade flow persists as the mitral valve is closing rapidly and a murmur with low frequency characteristics is produced (i.e., the Austin-Flint murmur, mitral regurgitation or left-to-right shunt with a mid-diastolic murmur). A combined ICSP-echo study of the Austin-Flint murmur was performed by Reddy et al. The murmur was recorded in the left ventricular inflow tract and was not present in the left atrium; murmur onset occurred after a significant silent interval following A2, and there was usually presystolic accentuation. Diastolic mitral regurgitation was not related to the genesis of the Austin-Flint murmur, nor was there any correlation between presystolic murmurs and end-diastolic LV to LA pressure gradients.

The Left Ventricle

The systolic murmur of hypertrophic obstructive cardiomyopathy was recorded within the left ventricle by Soulié et al., occasionally accompanied by a diastolic murmur; the frequent occurrence of co-existing mitral regurgitation was documented with left atrial ICSP recordings. Similar ICSP findings were noted by Gunther and Nishimura et al. Echocardiography of the mitral valve has subsequently shown an abnormal pattern of movement, with a sharp re-opening of the mitral valve during systole, to account for the mitral regurgitation in certain patients.

Stein and associates used ICSP in the evaluation of 10 patients with three types of subaortic obstruction, seven with hypertrophic subaortic stenosis, two with a subvalvular membrane and one with a subvalvular tunnel. The systolic murmur was recorded within the left ventricle in all, just distal to the obstruction, and was of lower amplitude distal to the aortic valve. In contrast, the murmur of valvular aortic stenosis was of greatest intensity distal to the valve.

Diastolic murmurs have been recorded in the left ventricular outflow tract (LVOT) in patients with valvular aortic regurgitation, and with aortic regurgitation associated with ventricular septal defects. With regard to the LVOT diastolic murmur of valvular aortic regurgitation, Lewis et al. noted that patients with mitral valve pathology, in whom they suspected the presence of a Graham-Steell murmur, had negative right heart studies for valvular pulmonary regurgitation, and an aortic diastolic murmur was demonstrated instead. This led to the suggestion that the true incidence of the Graham-Steell murmur required re-evaluation. Runco and Levin reviewed the subject and their earlier experiences. ICSP and angiographic studies in patients with rheumatic heart disease and basal diastolic murmurs demonstrated that aortic regurgitation was almost invariably the source of the murmur regardless of the clinical criteria favoring a Graham-Steell murmur. Hibi et al. discussed the differential diagnosis between pulmonary valvular and aortic valvular regurgitation. They used ICSP in 33 patients with 2nd to 4th left sternal border diastolic murmurs in various types of organic heart disease. Aortic valvular regurgitation was found in 25 patients, pulmonary regurgitation in eight. ICSP studies performed in conjunction with careful angiographic assessment have been of value in the differential diagnosis between aortic and pulmonary regurgitation, and have stimulated a reassessment of the relative frequency of the Graham-Steell murmur and established ICSP as a highly sensitive detector of pulmonary regurgitation.

The syndrome of acute aortic regurgitation was analyzed with ICSP by Reddy et al. The early diastolic murmur of acute aortic regurgitation was 1) of relatively short duration when compared to that of chronic aortic regurgitation, since the high LVEDP approximated aortic pressure resulting in abbreviation of the murmur, and 2) the murmur became softer with increasing severity of regurgitation. Additional findings included a soft or absent first heart sound, an aortic ejection sound following by a short ejection systolic murmur, and a left ventricular diastolic gallop followed by mid-diastolic and presystolic components of the Austin-Flint murmur. These observations complemented earlier hemodynamic and angiographic studies by Wigle and Labrosse and Rees et al.

The Effects of Respiration on Cardiac Murmurs

ICSP studies were used to evaluate the effect of respiration on cardiac murmurs. These have been qualitative studies, subject to the problems inherent in catheter-manometer movement during respiration. There has also been a lack of agreement as to whether phasic respiration, or post-inspiration, post-expiration apnea was the modality to be tested.

Levin et al. noted the effect of deeply held inspiration and expiration on the intensity of right heart murmurs in 15 patients with organic heart disease; the behavior of the precordial murmur during deep breathing was, in most patients, a poor reflection of the behavior of the murmur within the heart.

Leon et al. studied the effect of continuous accentuated respiration on the intracardiac murmurs of mitral regurgitation and tricuspid regurgitation with biastral ICSP. 11 patients with mitral regurgitation had no alteration in the intensity of the intracardiac (left atrial) murmur with respiration; in eight patients with mitral and tricuspid regurgitation, inspiratory augmentation of the tricuspid regurgitation
murmur was recorded in the right atrium. This study has great clinical applicability, and is a logical extension and adaptation of observations made by Rivero-Carvallo. It should be recalled, however, that the original studies by Rivero-Carvallo dealt with observations made during post-inspiratory and post-expiratory apnea.

Gunther and Bohm studied the effect of deep inspiration on right and left heart murmurs in 20 patients; although right heart murmurs and occasional left heart murmurs increased with deep inspiration, some intracardiac murmurs were not changed. Lack of specificity and constancy between intracardiac and external sound phenomena during this type of respiratory maneuver were consistent in certain respects with the observations by Levin et al.

The effects of respiration on cardiovascular sound production and transmission will undoubtedly be the subject of future studies using multisensor catheters with pressure-sound-flow velocity signals in a manner similar to the elegant studies by Murgo et al. of the beat-to-beat hemodynamic changes during the Valsalva maneuver.

**Sound Transmission**

Feruglio reviewed the available techniques for detecting intracardiac acoustics and introduced the vibrocatheter (a catheter with lateral opening near the tip covered with a thin latex cuff connected to the tubing of binaural stethoscope for direct auscultation, or to a piezoelectric microphone to record the intracardiac phonocardiogram). Observations in valvular and congenital heart disease with this system were similar to those obtained with the methods described earlier in this paper. The innovative use of the system consisted of delivery of sounds of known frequency content or intensity into the heart; the vibrocatheter was connected to a magnetodynamic unit of an acoustically insulated loud speaker connected to a variable-frequency oscillator or tape recorder. The artificial sounds delivered into the heart were then recorded from chest surface sites in order to study the modifying effects of sound transmission from cardiac chambers to chest wall. The attenuation of cardiovascular sound depended on the site of intrathoracic production, the frequency components of the sounds, and the characteristics of the conducting tissues. The greatest attenuation occurred when sound originated in the right and left pulmonary arteries; attenuation was less when sound arose in the right atrium and main pulmonary artery; sound was well conducted to the chest wall from the right ventricle. The distance from sound source to chest wall and the interposition of poorly conducting tissues were considered to be the reasons for the different degrees of attenuation. Frequencies below 100 Hz and above 350 Hz were greatly attenuated; frequencies of about 200 Hz were conducted with little attenuation (presumably because these frequencies were in the same general range as the natural frequency of the thorax). Although the vibrocatheter approach was considered to be a promising means for calibrating cardiovascular sound, additional studies dealing with this potential have not been published.

Heintzen and Vieter reversed the process, placed the sound generator against the thoracic wall and picked up the signals inside the heart cavities. The cardiac chambers and great vessels transmitted sound waves within the tested frequencies range of 50–1000 Hz. The transmitted sound waves were of constant intensity during cardiac standstill as well as in postmortem animal studies. Cardiac action modified the amplitude of the sound waves transmitted from chest wall to the cardiac chambers and great vessels; the recorded pattern showed striking variations of sound conductivity of different shapes in the different heart chambers and vessels (minimal changes in the venae cavae or pulmonary artery, marked changes in the right ventricle). These studies suggest that sound transmission is related to cardiac factors such as alteration of thickness, stiffness, compliance or elasticity of chamber walls, and to extracardiac factors such as variations in location of the heart within the thorax in health and disease.

**Turbulence**

Fluid mechanical aspects of blood flow, and in particular, turbulent blood flow, have been the subjects of increasing investigative interest during the past decade. Stein and Sabbah measured point velocity in the ascending aorta of patients using a catheter mounted high-film anemometer probe; turbulent flow occurred consistently in the ascending aorta of individuals with abnormal aortic valves, and occurred within the ascending aorta of normal subjects under circumstances such as high cardiac output states. The magnitude of turbulence, judged by energy of the fluctuations (turbulent energy density), was highest in subjects with aortic stenosis, where turbulence was observed throughout the ascending aorta and in the innominate artery.

Sabbah and Stein demonstrated an association between turbulent blood flow and systolic ejection murmurs (velocity measurement combined with ICSP; Millar manometer). Intra-arterial ejection murmurs were always found to be associated with turbulent or highly disturbed flow, whereas in the absence of intra-arterial sound during ejection only minor flow disturbances were found. This study demonstrated a linear relation between sound energy density and turbulent energy density, and between sound intensity and turbulent power supply. When power generated by turbulence exceeded 3 ergs/sec per cm² the murmurs were audible at the chest wall; the clinical gradation of murmur intensity increased as the power of turbulence increased.

**Events of the Cardiac Cycle and Ventricular Performance**

The events of the cardiac cycle, derived intervals and indices have been studied extensively since the early delineation of the temporal sequence of electrical and mechanical events, and pressure pulse definition. Catheter manometry has been used: 1) to determine the relation between directly measured isovolumic contraction time and externally measured pre-ejection period and isovolumic contraction time; 2) to measure right ventricular systolic time intervals, their relation to respiration, heart rate and left ventricular systolic time intervals; 3 to correlate external systolic intervals with internal indices of left ventricular function in man; 4) in combination with aortic flow velocity measurements to compare left ventricular function indices derived from velocity measurements with conventional function indices derived from left ventricular pressure and quantitative cineangiography; 5) to assess normal...
ventricular ejection dynamics in man with emphasis on physiologic impulse gradients, and the relationships of intervals of both flow velocity and pressure events to cardiovascular sound production;\textsuperscript{221} and 6) to assess the effects of chronic pressure and volume overloading on right ventricular systolic time intervals.\textsuperscript{222} These are not all ICP studies per se, but are a representative sampling of many studies emphasizing the direction and evolution of manometry, pressure, flow and velocity recording, with the inevitable contributions and overlap of such studies to the understanding and evolution of ICSP studies in man.

**Perspective**

The science of cardiovascular acoustics is dependent on the accuracy and timing of measurements and recordings, and upon the methods with which correlations are established. The clinical auscultor functions in this sensory and scientific milieu. Ideally, he or she improves and develops with experience, additional layers of knowledge and information, response to critical analysis, and the stimulation provided by infusions of fresh material. During the past three decades ICSP studies have contributed to clinical auscultation in a variety of ways, stimulating a reassessment of traditional auscultatory tenets. The clinical auscultor has been, and will continue to be, influenced by multiple cardiovascular investigative and diagnostic methods.

The exploratory phase of ICSP analysis lies behind us. The future of ICSP studies will be influenced by the use of multisensor catheters\textsuperscript{22} or miniature transducers providing multiple and simultaneous sound, pressure, flow and velocity signals from right and left heart, at rest and during physiologic pharmacologic stresses, with telemetry, signal processing and minicomputers designed for human hemodynamic research, during acute investigative or chronic implantation. ICSP studies may also evolve in the direction of assessment of cardiac function, since the character of heart sounds is altered by disease, and alterations of cardiac material wall properties may result in altered ability to generate and propagate sound.\textsuperscript{223}

**Acknowledgment**

The contributions and wisdom of so many colleagues, many of whom comprise the bibliography, and personal associates including J. M. Ryan, Mary E. Fontana, R. F. Leighton, C. Bush, J. Kilman, W. Molnar, R. F. Lewis, J. V. Warren, R. S. Goodwin, G. Reiser, a generation of Cardiology Fellows at Ohio State, and the assistance of J. A. Martin, are gratefully acknowledged.

**References**

10. Allard EM: Sound and pressure signals obtained from a single intracardiac transducer. IRE Trans Bio-Med Elec BME-9, Number 2, 1962
15. Barritt DW, Davies DH: Direct recording of sounds and pressures within the heart. Br Heart J 25: 549, 1963
50. Shah PM, Mori M, MacCanon DM, Luisada AA: Hemodynamic cor-
Intracardiac phonocardiography: intracardiac sound and pressure in man.
C F Wooley

Circulation. 1978;57:1039-1054
doi: 10.1161/01.CIR.57.6.1039
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1978 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/57/6/1039.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/