SYMPOSIUM ON CARDIOVASCULAR SOUND

GUEST EDITOR: VICTOR A. MCKUSICK, M.D.

I. Mechanisms

MODERATOR: HANS H. HECHT, M.D., Salt Lake City, Utah

Valve Mechanics

ROBERT F. RUSHMER, M.D., Seattle, Wash.

Cardiovascular sound may be divided into 2 categories, namely, murmurs that result from turbulence in streams of blood flowing so rapidly that the critical Reynolds number is exceeded and, heart sounds that represent vibrations resulting from abrupt changes in the velocity of blood movement. Since closure of the heart valves suddenly arrests or reverses the movement of blood, normal valve function undoubtedly contributes to the production of heart sounds.

This discussion is limited to the structure and function of the atrioventricular valves, since I have not studied the semilunar valves directly. Each atrioventricular valve consists of 2 broad cusps attached at opposite sides of a large oval opening. Chordae tendineae enter the structure of the valve cusps at or near their edges to prevent eversion of the cusps when ventricular pressure is high (fig. 1). The chordae tendineae of the mitral valve insert primarily into 2 papillary muscles. The tricuspid valve is supported by chordae tendineae from 3 papillary muscles inserting into 2 main cusps and a large intermediary cusp. Thus, the structure and function of the 2 atrioventricular valves are sufficiently similar that only the mitral valve will be considered in detail.

According to traditional concepts, an advancing gush of blood thrusts the atrioventricular valves widely open during early ventricular diastole. They are believed to be partially closed after atrial systole and clamped shut by a retrograde surge of blood at the onset of ventricular systole. These concepts have been derived primarily from observations and direct photography of valve action in isolated hearts, and from correlations of heart sounds with mechanical and electric events of the cardiac cycle. Cinefluorographic observations of the motion of the mitral valve cusps in intact dogs did not confirm these concepts. Such motion pictures showed the edges of the mitral valve cusps only slightly separated during ventricular filling. No abrupt movement of the valves toward the atrium was noted at the onset of ventricular systole. Indeed, the edges of the valve cusps and valve rings were observed to move toward the apex of the ventricle during systole.

The contrast between the wide valve excursions in isolated hearts and the restricted valve movements in intact animals may be explained by some recent experimental observations. One factor determining the amount of valve movement would be the degree of slack in the cusps and chordae tendineae. The amount of slack would, in turn, depend upon the size of the ventricular cavities. Roentgenographic evidence has been presented that the heart of a dog shrinks significantly when the thorax is opened, and gradually regains its normal dimensions after repair of the thoracotomy. In intact dogs, the ventricles normally function at larger diastolic and systolic dimensions, so that throughout the cardiac cycle, the movements of the valves may be restrained by tension exerted by chordae tendineae. It is quite possible that normal ventricular filling is accomplished by the rush of blood through a rather narrow aperture between the valve cusps.

Similarly, there is some evidence that closure

* The motion pictures shown in conjunction with this presentation are available for loan.

This symposium was held in Cincinnati on October 26, 1956. The morning program, devoted to a consideration of mechanisms, appears in this issue and the afternoon program on clinical aspects will appear in next month's issue.
I. MECHANISMS

Fig. 1. Note that each papillary muscle is attached by chordae tendineae to each cusp of the mitral valve. The fibers of each chorda tendinea fan out in the substance of the cusp curtain.

of the atrioventricular valves does not result solely from a retrograde surge of blood. To produce such a displacement of blood, the dimensions of the ventricle would have to decrease as the ventricular pressure rises. Instead, the length, circumference, and internal diameter of the left ventricle all abruptly expand during the initial phase of ventricular systole. These observations indicate that early contraction of papillary muscles and trabeculae carneae draw the atrioventricular valves toward the ventricular apex, closing the valves, distending the ventricular walls, and producing the initial rise in ventricular pressure. Since the chordae tendineae from each papillary muscle are inserted into each of the 2 main valve cusps, contraction of papillary muscles would tend to draw the valves together (fig. 1). Contraction of the trabeculae carneae would draw the valve ring toward the apex. Both these actions would
tend to elevate intraventricular pressure while distending the ventricular walls. Thus, contraction of papillary muscles may play an important role in atroventricular valve closure when the sequence of ventricular excitation is normal.

Modifications in traditional concepts that are prompted by these studies are important in visualizing the origin of heart sounds, the changes in heart sounds owing to valvular disease, the requirements for plastic reconstruction of atroventricular valves, and the applicability of studies of valve function in isolated or exposed hearts.

Discussion

Dr. Aldo A. Luisada (Chicago, Ill.): The concept that there is no remarkable ballooning of the atroventricular valves into the atrium in ventricular systole is entirely consistent with recordings of pressure and volume events in the atria.

Dr. McKusick (Baltimore, Md.): There is interesting work demonstrating atroventricular regurgitation in animals with atrial fibrillation. The results corroborate the view that atrial systole normally plays a role in the closure of the atroventricular valves. Furthermore, the data on the intensity of the first sound in relation to P-R interval are pertinent. Figure 2 shows data from a dog with surgically produced complete heart block.

These observations, seemingly so well accounted for by the experiments of Henderson and Johnson and of Dean must find other explanation if Rushmer is correct in concluding that excursion of movement of the mitral cusps is in general small. Is it not possible that with the clips applied to the margin of the cusp, Rushmer has indeed demonstrated little movement? May not, however, the main portion of the cuspal curtain be considerably more mobile? Current thinking about the valvular contribution to the heart sounds is more along the
line of tensing of the valve curtain than of actual collision of the margins of the cusps. The "inrolling" of the valve in the wake of atrial systole may be accompanied by rather little motion at the margin of the cusp.

CINEMATOGRAPHIC STUDIES OF NORMAL AND ABNORMAL HUMAN VALVES

ROBERT P. GLOVER, M.D., PHILADELPHIA, PA.

The presentation consisted of motion pictures of functioning heart valves in autopsy hearts. Ventricular function was simulated by means of a pump. The mitral valve in particular was studied and mitral regurgitation was the main object of study. The effect of surgical procedures was demonstrated. Some views of the aortic valve were also provided.

Discussion

Dr. McKusick: In the specimen with considerable mitral stenosis the pictures seemed to corroborate the generally accepted idea of the origin of the mitral opening snap. The aortic leaflet of the mitral valve appeared to billow abruptly toward the ventricle at the time that would correspond to early diastole and to the time that the opening snap occurs.

It should be kept in mind that, although much valuable information pertaining to gross defects of the atrioventricular valves, either stenosis or regurgitation, can be obtained by this method, it is impossible to reproduce precisely the normal function of the atrioventricular valves. Participation of the contracting muscular ring, the role of contraction of the papillary muscles as suggested by Rushmer, and particularly the role of atrial systole are not, and cannot easily be, represented in this system. On the other hand, function of the semilunar valves can be quite precisely reproduced in a model set-up.

ORIGIN OF THE HEART SOUNDS

JOHN J. KELLY, JR., M.D., BROOKLYN, N.Y.

Shortly after Laennec introduced the art of auscultation, authorities were in general agreement that the second heart sound results from the sudden tensing of the semilunar leaflets as these valves close at the end of systole. No such agreement was met in explaining the origin of the first sound. Two leading opinions have resulted; one ascribes the sound to the tensing of the atrioventricular valves and their chordae tendineae, and the other felt that the vibration of the contracting ventricular muscle mass dominates the first sound.

Phonocardiographers usually describe 4 components of the first heart sound. The first element, which is found in normal subjects, is composed of low-pitched, faint, in fact usually inaudible vibrations. The second element, which is composed of audible higher frequency oscillations, begins from 0.02 to 0.06 second after the QRS in normal subjects. This component dominates the first sound at the apex. The third element occurs from 0.07 to 0.12 second after the Q wave. This component is louder at the base of the heart over the great vessels than at the apex. It occurs with the beginning of ejection in the aorta and pulmonary arteries. When the vessels are dilated this element may be very loud as described in a "systolic click." The "fourth element" of the phonocardiographers is composed of inaudible low-frequency vibrations.

The mode of production of the second element of the first heart sound has been controversial. Because it occurs in normal subjects synchronous with the beginning of ventricular contraction, it was thought to result from muscular vibrations. Earlier experiments of Dock demonstrated the disappearance of the heart sounds of an exposed dog heart when venous inflow was halted. Phonocardiographic studies relating the intensity of the first heart sound to the P-R interval implied that the first sound is caused by the sudden tensing of the atrioventricular leaflets, and that its intensity is governed to a large degree by the position of these structures at the onset of ventricular contraction. These findings failed to convert the protagonists for the muscle theory.

Studies of patients with mitral stenosis have settled this problem. The time between the Q wave and first rapid vibration of the first sound (Q-1 interval) varies between 0.02 and 0.06 second if patients with bundle-branch block and mitral stenosis are excluded. In individuals with mitral stenosis, the Q-1 intervals may be
We have attempted to evaluate the contribution of the tricuspid valve to the first sound by studying subjects with left bundle-branch block. In these individuals the right ventricle should contract first.* Onset of right ventricular contraction could be determined by the systolic deflection of an apex cardiogram or by cardiac catheterization. Splitting of the first sound was found in only 6 of 25 subjects although splitting of the second sound occurred in 20 of 25. In 5 instances a sound was found that was simultaneous with the onset of right ventricular contraction. Hence it would appear that the tricuspid contributes little to the first sound in this group. Gallops were recorded in 10 of 25 cases, 8 of the gallops occurring in presystole. The frequent association of presystolic gallop with bundle-branch block contributes to the illusion of a split first sound.†

Third heart sounds have been variously explained as due to sudden tensing of the atrioventricular valves at the end of rapid ventricular filling, to the impact of the heart against the chest wall, and to the audible vibrations of the muscular fibers when the ventricular limit of stretch is reached. This latter theory rests upon the presumption that a thick ventricular mass would respond to sudden tensing with a sound. This has been critically tested by Dock21 who was unable to produce a sound by tensing a strip of ventricle, whereas the atrioventricular valves and strips of pericardium give off loud sounds when similarly tested.

It seems reasonable that both normal third heart sounds and gallops have a common mode of production and that a gallop is an exaggerated third heart sound.22 We believe that they are best explained by a momentary tensing of the atrioventricular valves resulting from a reflux that follows rapid ventricular inflow.

**Discussion**

**DR. WILLIAM LIKOFF (Philadelphia, Pa.):** If the first heart sound is delayed, and if our ob-

---

* Ed.: However, by simultaneous right and left heart catheterizations Braunstein and Morrow20 could demonstrate no asynchronism in left bundle-branch block.

† The vexing question of splitting of the first sound in bundle-branch block was discussed further in the afternoon program.
I. MECHANISMS

**Fig. 4.** Top. Record obtained on a middle-aged man with proved mitral stenosis. The electric-mechanical interval (E.M.) is demonstrated to be .04 second by the systolic deflection of the apex impulse. This was confirmed by direct measurement of ventricular pressure at operation. The first sound in the absence of mitral stenosis occurs at this time. In this instance the first sound begins .09 second after the beginning of the QRS. Note the deflections of the apex beat simultaneous with the first sound.

**Fig. 5.** Bottom. Trace obtained from subject with proved mitral stenosis. Atrial fibrillation with varying R-R intervals present. When the preceding diastole is long, the Q-1 is short and when diastole is short, the Q-1 lengthens. A long diastole allows better left atrial emptying and consequently a lowering of the left atrial pressure.

[Ed.: Dr. Likoff and his collaborators23 have come to the conclusions (1) that the presystolic murmur is due to vibrations of the mitral valve in billowing toward the atrium—not to vibrations produced by the forcing of blood through the orifice with atrial systole, and (2) that the presystolic murmur is in fact systolic. These conclusions cannot be reconciled with recordings of the presystolic murmur that show its beginning well before the QRS of the electrocardiogram. With prolonged P-R intervals the "presystolic" murmur remains with the P wave and occurs even longer before the QRS. The question of whether this murmur is in actuality systolic is in part confused by the failure to distinguish electric and mechanical systole of the ventricle. It is true that the presystolic murmur continues into the first portion of electric systole...]

[End of text]
of the left ventricle. However, although it is an atriosystolic murmur, it can scarcely be considered a ventriculosystolic murmur."

Dr. Luisada: In the past, slow vibrations initiating the first sound were considered a residuum of the effects of atrial contraction. This has been shown to be incorrect, since these vibrations persist in atrial fibrillation. However, in measuring the Q-S₁ interval the first rapid vibrations, not these slow ones, are used.

Dr. Aubrey Leatham (London): Just a plea to remember the normal ventricular asynchrony, that there are 2 ventricles and 2 sets of heart sounds and that if, as phonocardiographers, you want to split the heart sounds into 4 components, then in fact you have to split them into 8, which heaven forbid!

Dr. Rushmer: It disturbs me to hear discussions that imply the valves are vibrating alone or the chordae tendineae are vibrating alone. One must have a restoring force and a mass to produce sound. The ballooning of the valve with closure will cause overstretching and the tense valve will cause the blood to move in the opposite direction. This movement would give you the first half cycle of a vibration. But, what is going to cause the blood to move back again in the other direction and produce the multiple vibrations we record? It seems clear, to me at least, that no part of the heart is not vibrating. Basically the vibration of a system—valves, blood, wall, etc.—is involved. Consequently, when we try to isolate valves, parts of valves, or chordae, and produce sounds, I think we are off on the wrong tangent.

Dr. Samuel A. Talbot (Baltimore, Md.): I believe that in a chamber with compliant walls, there can occur local pressure fluctuations and that it is not necessary to think of the wall and the blood vibrating as a whole. Localized oscillatory mechanisms are admissible, involving local masses, local elastic properties, and local tensions. However, we must remember that no valve leaflet can move without there being considerable motion of the blood coupled with it.

In the experiments of Dock and in connection with the abrupt billowing of the mitral curtain mentioned earlier by Dr. McKusick as the probable mechanism of the mitral opening snap, it is important to keep in mind the difference between the snapping of a towel or the billowing of a sail in air, and of a valve in blood. Useful as the analogy is, the tremendously greater viscosity and density of blood, with loading of the valve cusps thereby, imposes an important difference. We should think in terms of local pressure transients—fluctuations in mean hydrostatic pressure—associated with changes in the momentum of blood.

The Gallop Sounds

Studies of the Mechanism of Production

Peter T. Kuo, M.D., Philadelphia, Pa.

The mechanism of the gallop sound was studied previously in this laboratory with the aid of the electrokymograph. A wave of rapid lateral movement of the left ventricular wall was recorded in 28 patients with severe hypertension, heart failure, and a diastolic gallop rhythm. Simultaneous phonocardiographic and electrokymographic recordings showed that the gallop sound occurred 0.01 to 0.04 second before the end of the wave of lateral movement of the ventricular wall and not after its completion. This abnormal kymographic pattern returned to normal after the patients had regained cardiac compensation and had lost the gallop sound. These observations are compatible with the view that an impact or sudden stretch of the ventricular wall is the chief cause of production of the diastolic gallop sound.*

The technics of right and left heart catheterization have made it possible to investigate further the origin of the gallop sound. In the present study, the time relationships of the gallop sound to atrial, superior vena caval, and jugular pressure pulses of the same subject were compared. Apex cardiograms were also studied in this series of 14 patients with gallop sounds. Both the piezo-electric pick-up and the Lilly capacitance manometer were employed in the recording of the apex beats.

No venous reflux wave was demonstrated in

* Ed.: Brady and Taubman also used electrokymography but arrived at a different conclusion.
the pressure curves taken directly from the right or the left atrium at the
time the gallop sound occurred. A delay of 0.16 to 0.20 second
in the transmission of the venous pulse wave from the atrium to the jugular vein was
observed in these patients.

A sharp dip (inflection) following an initial
upswing is often recorded in the apex beat
when a piezo-electric pick-up is used. This
artificial wave of apical retraction can be eliminated
by the use of the amplifying system of
the Lilly capacitance manometer.

Simultaneous right atrial and ventricular
pressures were obtained in 4 patients with
right heart failure associated with a right-sided
gallop. The record showed that in all 4 patients
the gallop sound occurred at the peak of the atrial “a” wave, while the right atrial pressures
were 3.0 to 10.8 mm. Hg higher than those of
the right ventricle.

Simultaneous recordings of the left atrial and ventricular pressures through 2 separate cathe ters were obtained in 10 patients with
mitral insufficiency and a left-sided gallop
sound. The gallop sounds were recorded in
these patients when their left atrial pressures
were 3.2 to 18.4 mm. Hg higher than the ven-
tricular pressures.

It is unlikely that either the mitral or the
tricuspid valves could close and vibrate while
there is a sustained elevation of the atrial pres-
sure over the ventricular pressure at the time of the gallop sound.

[Ed.: It is possibly important, in the design of
experiments on the genesis of gallop sounds
and in the reports of such experiments, to keep
protodiastolic (ventricular or third sound) gallops distinct from presystolic (atrial or
fourth sound) gallops. We do not know that
the mechanism in the 2 is identical. Certainly
the clinical setting in which each occurs is, with
some overlap, distinctive: Presystolic gallops
tend to accompany pulmonary and systemic
arterial hypertension, aortic and pulmonary
stenosis, conditions of systolic ventricular over-
load. Protodiastolic gallops more often are as-
associated with myocardial failure or mitral re-
gurgitation, conditions of diastolic ventricular
overload, relative or absolute.]

Discussion

DR. FRANKLIN D. JOHNSTON (Ann Arbor,
Mich.): I was very much interested, in Dr.
kuo’s paper, to see the low-frequency vibra-
tions that correlate with the audible gallop
sounds. Many times you can see and feel gal-
llops when they are not actually audible. The
reason is obvious when you look at the low-
frequency records. The vibrations are far below
the major peaks in intensity or below the audi-
ble range. This simply emphasizes the impor-
tance of looking and feeling in the area of the
“point of maximum impulse.” Sometimes you
are able to demonstrate beautifully to students
a double apex impulse that goes along with a
gross presystolic vibration, when you cannot
hear the presystolic sound at all.

DR. LUISADA: I think that from a clinical
standpoint it is important for this group to
give some directives, of a semantic order, as to
what is a sound and what is a murmur. A sound
is very short, consisting of either 1 or 2 vibra-
tions. When longer it should be called a mur-
mur. If this is correct, then the heart sounds are
not sounds at all but rather short murmurs; we
call them sounds or tones just by habit.

DR. P. A. ONGLEY (Boston, Mass.): What
grounds do you have for deciding to call 1 or 2
vibrations a sound and more a murmur? Should not intensity and frequency be con-
sidered in some manner?

MR. MAURICE RAPPAPORT (Boston, Mass.):
Obviously the heart sounds, take the third
sound as an example, are not pure tones. If one
puts it in a variable filter and gradually attenu-
ates the low frequencies, then one will record,
not the usual coarse vibrations, but a relatively
high frequency sound that for obvious reasons
has many vibrations. What would you call a
murmur and what a sound? The number of vi-
braions is dependent on the characteristics of
your recording system!

DR. McKUSICK: I cannot quite see that a
distinction between murmurs and sounds is pos-
sible or has any significance. The French
apparently are not puzzled by this, since bruit is
used to refer to both. The title of Calo’s book
is Les bruits du coeur et des vaisseaux (1950). The
title selected for this symposium was inten-
Impacts

especially when a gallop sound is present and the physician believes he is dealing with mitral stenosis. The reason for proposing 2 vibrations for a sound was purely arbitrary. If you feel differently, all right; but let’s agree on something.

Mr. George N. Webb (Baltimore, Md.): On the basis of frequency-amplitude-time characteristics cardiovascular sound can be broken down into 3 instead of 2 categories: Firstly, impacts—transients, occurring at the time of valve closures; secondly, murmurs, which occur at constriction; and thirdly, vibrations that are musical in nature. The number of waves—1, 2, 3, or 30—is irrelevant. When we talk about sounds we should talk of what the ear interprets. The oscillogram is inadequate for displaying the characteristics by which the ear distinguishes the 3 categories. The ear is superior. The spectral phonocardiogram illustrates, inadequately as yet, the time-amplitude-frequency characteristics on the basis of which the ear makes its distinctions.

Murmurs in Relation to Turbulence and Eddy Formation in the Circulation

D. A. McDonald, M.D., London, England

The discussion of the hydrodynamic causes of murmurs produced in the circulation must necessarily be speculative because there has been relatively little fundamental physical research into the problems of noise generation in liquids.

There are 2 main types of fluid flow regimes in steady flow conditions—laminar, or stream-line, flow and turbulent flow. The conditions for the breakdown of laminar to turbulent flow were first studied in detail by Osborne Reynolds. The Reynolds number is defined as the product of the velocity of flow, the diameter of the tube and the reciprocal of the kinematic viscosity* \( \left( \frac{V \times D}{\mu} \right) \). When the Reynolds number exceeds 2,000,† laminar flow usually becomes unstable and turbulence occurs. This simple statement, however, is empirical and only applies to established steady flow in a long pipe. That is, it does not apply in any precise way to pulsatile flow or to flow conditions near the entrance of a tube (fig. 6).

In the circulation of mammals the situations where murmurs are to be found all have markedly pulsatile flow and, in the case of the root of the aorta, also concern flow within the “entrance length.” In a film on the nature of flow in the veins (Streamline Flow in Veins – D. A. McDonald and E. P. W. Helps, produced by the Wellcome Film Unit, Burroughs Wellcome) it was shown that the deviations from classical streamline flow were almost entirely due to the formation of eddies.

Laminar flow is completely silent and although it is probable that turbulent flow is accompanied by the generation of sound, it is rarely detectable on the outside of the tube in which the flow is taking place. In air streams the loudest noise generation occurs with large eddy formation.§ In view of the fact that the classical sites for murmurs—the cardiac valves and arteriovenous fistulas (the ductus arteriosus is functionally of this type)—are undoubtedly sites where many eddies are formed, it seems to be a reasonable hypothesis that the 2 phenomena are causally related.

* Kinematic viscosity is absolute viscosity divided by density.
† Ed.: Values of about 1000 are found elsewhere in the biological literature (e.g., ref. 3), merely because radius, not diameter, is used in the Reynolds formula by some workers.
‡ A copy of this film is available from the American Heart Association.
§ Ed.: In the original presentation “vortex-formation” was used throughout. As brought out in the discussion (see below), it may be preferable to substitute “eddy” for “vortex.”
I. MECHANISMS

Fig. 6. The drawings illustrate the "entrance length," before the flow pattern—turbulent or laminar—is established. In the case of laminar flow, the drawing attempts to represent the parabolic velocity profile with most rapid flow at the center of the pipe.

To produce sound loud enough to be heard outside the body it is probable that some solid structure must be vibrated by the disturbed flow. The chordae tendineae of the ventricle, the valve cusps, and even the vessel walls are the structures probably involved. Dawes, Mott, and Widdicombe showed, for example, that the ductus arteriosus murmur was always accompanied by a palpable vibration of the wall of the pulmonary artery. Frequency analyses of murmurs, as in McKusick's work, might be most helpful in the analysis of this problem as it is to be expected that murmurs originating in the vibration of such solid structures will have a low fundamental frequency, whereas sound arising from the fluid itself would be expected to have higher frequency components. Cavitation, the formation and collapse of gas bubbles in the circulation (fig. 7), is also a possible source of sound—probably of high frequencies.

To summarize, the search for the causation of murmurs should be directed under the following headings:

1. Sound generated within the fluid itself.
   1. Due to turbulence.
   2. Due to eddy formation.
3. Due to cavitation—this may arise de novo or in association with eddies.

II. Sound generated by the vibration of solid structures.
1. Valve margins or chordae tendineae.
2. Jet formation impinging on a vessel wall. Ductus arteriosus and arteriovenous fistulas are the most obvious examples but jets may play a role in the root of the aorta.

III. Resonance in solid structures as a response to sound generated in the fluid. (This merely emphasizes that the separation of groups I and II is largely artificial.)

Discussion

DR. EUGENE LEPESCHKIN (Burlington, Vt.): I was interested in the remark of Dr. McDonald that the Reynolds number theoretically exceeds the critical value normally in the aorta; yet we know that normal flow does not produce murmurs. I wonder whether one explanation may be that it takes time for turbulence to develop.
Once a vibration develops, resonance occurs, further turbulence is facilitated, and so on. High velocity flow in the aorta may be present for too short a time for turbulence to develop.

**Principles of Fluid Flow as Seen in the Jerrard-Burton Demonstration**

**David H. Lewis, M.D., Philadelphia, Pa.**

The model* originally described by Jerrard and Burton clearly demonstrates laminar and turbulent flow, the parabolic velocity profile of laminar flow, and the nature of eddy currents. We have used it in lectures on hemodynamics to different groups and all have appreciated the opportunity of seeing things previously only read about. A complete description of the modified device has been given by Burton and need not be repeated here. It is essentially a flow tube made of plastic with straight portions, bends, and a point of constriction. The nature of the flow pattern is demonstrated by marking the axial stream with dye. Eddy currents are seen when sawdust particles are put in the water.

Its use in teaching fluid dynamics was described in the original communication and amplified by Lewis. For the purposes of this symposium 2 concepts are germane. First are the factors determining the velocity of flow. It is shown both from the demonstration and from theoretical considerations that the velocity (V) at any point (y) along the radius of the tube is dependent upon the pressure drop along the tube (P1 - P2), the radius (r), the length (l), and the viscosity of the fluid (η). The formula for this relationship is

\[ V_y = (P_2 - P_1) \left( \frac{1}{4l} \right) \left( \frac{1}{\eta} \right) (r^2 - y^2) \]

In the condition where y = r, that is, considering the velocity at the wall of the tube, it can be seen that the velocity here is zero. In laminar flow there is a layer of fluid that coats the wall of the vessel and is stationary. The actual flow of fluid is therefore over this outermost layer and not over the wall of the vessel itself. In laminar flow, as pointed out in engineering texts on fluid dynamics, the roughness of the wall does not affect the nature of the flow so long as it remains laminar. For the physician this point is in keeping with the present concept that roughness of vessel walls and valve surfaces is not in itself sufficient to cause murmurs.

The second point to be considered is implicit in the Reynolds number. This dimensionless expression quantifies the transition from laminar to turbulent flow and for the physician indicates the conditions necessary for the genesis of murmurs. It is usually expressed as follows:

\[ Re = \frac{\rho \bar{V} r}{\eta} \]

where Re is the Reynolds number, ρ the density of the fluid, \( \bar{V} \) mean linear velocity of flow, and r and η as before, radius and viscosity, respectively. There is an element of confusion here for those who see the demonstration. It is pointed out that the larger the Reynolds number the greater is the likelihood of turbulence. It seems as though turbulence should be more likely the greater the radius, and yet just the opposite is pointed out by the demonstration. The element of confusion is the concept of mean linear velocity, which is seldom used in circulatory physiology. By substituting for mean velocity the volume rate of flow (\( \dot{Q} \)), which is equal to the product of mean linear velocity and cross-sectional area, the confusion is dispelled. The Reynolds number then becomes

\[ Re = \frac{\rho \dot{Q}}{\pi r \eta} \]

since \( \dot{Q} = \bar{V} \pi r^2 \).

This revised expression predicts that turbulence and the production of murmurs may occur with an increase in the volume rate of flow as in exercise, with a decrease in radius of the vessel as in valvular stenosis, and with a decrease in viscosity as in anemia.

**Discussion**

**Dr. McDonald:** There is some precise information bearing on the influence of roughness of the wall of the tube on flow pattern. In general, for 2 flow situations with identical Reynolds
number, turbulence is more likely to occur in a tube with a roughened lining than one with a smooth lining. In other words, the critical (transitional) Reynolds number is likely to be lower in a tube with rough lining.

It should be pointed out that the model you have shown does not demonstrate turbulence in the very narrow portion where velocity is greatest, but beyond it in an area where you get very large eddy formation. Heavy vortex formation due to a jet may look like turbulence.

**Dr. Rushmer:** Would Dr. McDonald expand on the distinction between turbulence and vortex formation?

**Dr. McDonald:** In turbulence all the fluid particles are moving at random but the disturbances occur through a small latitude. In vortices one is really dealing with laminar flow that has a circular motion. Any vortex, such as a whirlpool, has a pressure drop in its center. In the whirlpool this pressure drop creates the dent in the center. The pressure drop in vortices may be related to sound generation. Actually I would prefer to use the term “eddy” rather than “vortex” in the situation under discussion.

**Transients as a Mechanism in the Production of Heart Sounds and Murmurs**

**Simon Rodbard, M.D. Buffalo, N.Y.**

This study,† extending over the past several years, has been based on the theses (1) that hydrodynamic factors generate discrete bursts or transients that fuse to produce the heart sounds and murmurs and (2) that if these transients could be recorded and timed, significant new information concerning cardiac function would become available.

**Heart Sounds.** During the early part of the first heart sound, successive transients are generated by closure of the tricuspid and mitral valves. After a brief interval, related to the period of isometric contraction, other bursts appear, representing opening of the pulmonary and aortic valves. Such bursts also generate low-frequency vibrations of great energy and long persistence that fuse, producing the usual irregular phonocardiographic trace. Vibration analyzers of the Bell type (spectral phonocardiograph) do not provide the time resolution required to separate such transients.

To separate and time the transients in heart sounds, specially designed high-pass filters were used, thereby eliminating the commonly used frequencies (below 1,000 c.p.s.). The remaining signal was amplified, recorded on magnetic tape, and displayed by means of a cathode ray oscilloscope camera, using time-expansion techniques (figs. 8 and 9).

With this method, cardiac as well as arterial sounds evoked a succession of irregularly spaced spikes that were constant in timing from beat to beat. Similar transients were obtained with intracardiac microphones (fig. 10).

**Murmurs.** An analysis of the acoustic phenomena accompanying flow through soft-walled vessels (fig. 11) led to a similar approach to murmurs. Thus, flow at critical velocities through a soft tube repetitively raises and lowers the distending pressure acting on the wall (in accordance with the principle outlined by Bernoulli), causing recurrent closure and producing particular sequences of transient bursts.* Hydrodynamic studies show the repetition rate of closing to be a function of (1) inlet pressure head, (2) outlet head, (3) vessel diameter, and (4) stiffness of wall. The parameters of such flow, determined by appropriate model experiments, provide a basis for analysis of murmurs in terms of pressure differences across valves, as well as of the nature of the orifice or vessels through which the flow is taking place. Rapid repetition rates (high pitch) are related to higher driving heads with relatively wide orifices and increased flow. The amplitude of the transient is in general related to the pressure head driving the fluid through the opening, and to the acoustic distance of the generator of the impulse.

The principles outlined are illustrated by

---

* A motion picture (taken at 4,000 frames per second) of the recurrent closing and opening of the vocal cords and of elastic valves and tubes was shown. The film can be obtained from Dr. Rodbard.

---

* Aided by a grant from the Heart Association of Erie County, N.Y.
† See references 31-35.
Fig. 8. Seven consecutive heart beats, recorded at the pulmonic area on a normal subject, are aligned so that each QRS complex begins on the same vertical line. The first heart sound, which was relatively quiet, is represented by only a single small transient noted by the arrow at 119 milliseconds after the onset of the QRS complex. The second sound which was much louder shows a series of transients the first of which is not marked but is followed by a series that recurs consistently in each succeeding beat. In particular the transients at 400, 415, and 430 milliseconds can be clearly seen to rise above the noise level. These transients, representing very high frequencies of the order of about 5,000, may be associated with specific vibration-producing events occurring within the chest.

Studies, with reference to aortic stenotic murmurs in man, in specially designed models (fig. 12). High-velocity flow produces transients as discrete repetitive openings and closings of the valves, which generate the transient spikes. The notches on the upstroke of the arterial pressure pulse wave correspond in time to the occurrence of the acoustic transients. Similar results in man have been obtained by use of a sphygmomanometer cuff to produce varying degrees of “stenosis” of the brachial artery.

The results show that high frequencies present in heart sounds and murmurs may be displayed as discrete transients. These require further investigation to determine their clinical utility.

Discussion

Mr. H. Kenneth Wiskind (Baltimore, Md.): Dr. Rodbard’s remarks are very interesting. However, I do not think we can dismiss turbulence as a murmur producer and it is otherwise of significance in cardiovascular physiology even if, as Dr. Rodbard asserts, it plays a minor role in cardiovascular sound. Therefore I would like to make a few remarks about turbulent flow.

The Critical Reynolds Number. With respect to the problem of transition from laminar to turbulent flow, the critical Reynolds number 2,000 is usually mentioned. The number 2,000 has importance only in a restricted sense. Let us consider flow from a reservoir into a pipe (fig. 6). It is important to distinguish between the pipe entrance conditions and what we call fully developed turbulent pipe flow. It is for the latter type of flow that the Reynolds number 2,000 is a reasonable criterion.

The importance of the Reynolds number lies in its use as a comparison of various flow situations, insuring that for any given situation, consistent with the basic description of the model, the dynamic state of the flow and hence its propensity for transition will be the same.
Fig. 9. Similar tracings taken at the cardiac apex on the same day show 3 transients in the first heart sound and 6 in the second.

Fig. 10. Transients recorded by means of a barium titanate crystal catheter microphone inserted into the heart of a dog through the jugular vein and vena cava. Frequencies below 1,000 cycles per minute were eliminated by filter. The sounds are arranged with the scale at zero milliseconds (M.S.) placed at the onset of the Q of the electrocardiogram recorded simultaneously. The first heart sound, indicated by a series of transients, is followed by a second series of transients that increase in amplitude and then fade out. The second heart sound is not clearly determined. A presystolic sound, which was also heard at the apex, is illustrated by the several transients at the right end of each record at about 475 M.S. of the cardiac cycle.
Fig. 11. Flow through a soft-walled tube using pressure heads of 140, 75, and 33 cm. of water respectively. The horizontal axis gives the delivery in milliliters per second. The vertical axis represents the degree of constriction of the tube, induced by the air pressure in the glass cuff surrounding the soft-walled tube. The numbers adjacent to the 3 lines represent the repetition rate of closing and opening of the tube, as determined by stroboscope.

The upper trace shows the changes in delivery as the constriction (cuff pressure) is modified in a system with a driving head of 140 cm. of water. No effect on flow (70 ml. per second) was seen at cuff pressures from zero to 20 cm. of water. As the cuff pressure increased to 25 cm. of water, the flow fell to 60 ml. per second and the wall was observed by stroboscope to be closing repetitively 13 times each second. Increases in cuff pressure further reduced flow and increased rates of closure in a fairly consistent fashion. When cuff pressure was approximately equal to pressure head, flow fell below 5 ml. per second and closing and opening of the tube was no longer apparent. Similar data for pressure heads of 75 and 33 cm. of water are also given. The data show that the repetition rate becomes faster with either increasing pressure head or increasing degree of narrowing.

despite widely varying pipe diameters, velocities, and fluids as characterized by their kinematic viscosity. One of the consequences of this concept is the possibility of gaining a large amount of information about transition in different fluids, with a variety of pipe sizes, and over a range of velocities, from a relatively limited amount of experimentation.

The significant features of the model to which the critical Reynolds number of 2,000 is applicable are (1) straight pipe, (2) fully developed flow, i.e., without change in pattern along the pipe, and (3) steady, i.e., nonpulsatile, flow. These features obtain at a distance downstream from the pipe entrance such that the entrance conditions no longer have an effect on the flow (fig. 6). In this region experimental evidence shows that if the Reynolds number is below approximately 2,000 the flow will be laminar and above 2,000, the flow will be turbulent.

In considering flow situations in which there
is a departure from the basic model, the critical (i.e., transitional) Reynolds number may very well depart greatly from 2,000. Therefore, in the consideration of the flow in the base of the aorta (which for the sake of the argument being presented can be compared to the flow at the pipe entrance in the model) it becomes higher than 2,000 because the effect of the pipe walls has not had sufficient opportunity to create fully developed pipe flow (fig. 6). Other departures from the above basic model that appear in the cardiovascular system are unsteady (i.e., pulsatile) blood flow, the arch of the aorta, the relative high elasticity of the “pipe,” the state of the blood flow entering the pipe, roughness of the pipe, and obstructions in the flow.

I do not wish to imply that these departures mean that transition in blood flow cannot be predicted. I merely wish to point out that the complexities present in physiologic flows do not permit the quantitative application of results from the simplified model. However, research on the problem of transition has made significant advances in recent years and it seems reasonable that such studies applied to blood flow would be fruitful. For the present the Reynolds number can be expected to give only qualitative information.

**Sound Generation from Turbulence.** Turbulent flow in a free field can generate sound. This mechanism is the “demon” of the jet airplane noise problem. However, the jet of an airplane is essentially air moving at high speeds, while in the case of cardiovascular sound there is relatively low speed of movement of blood. These 2 different situations produce sounds of greatly different magnitudes. A quantitative indication of the difference can be obtained by considering the efficiency of conversion of flow energy to acoustic energy in the 2 cases. The fluid flow energy is converted into turbulent energy and then into acoustic energy and the ratio of acoustic energy to flow energy is given by \( \eta \left( \frac{V}{c} \right)^5 \), where \( V \) is a mean flow speed, \( c \) is the speed of sound in the medium and \( \eta \) is a constant of proportionality which from laboratory measurements with air jets has been determined to be approximately \( 10^{-4} \). \( V/c \) is the Mach number, which can be high in the jets of airplanes, but since the speed of sound in blood is relatively high and the speed of blood flow relatively low, the Mach number in blood is usually low. The fact that the efficiency is proportional to the fifth power of the Mach number indicates the great sensitivity between Mach number and sound generation. Workers in underwater acoustics usually regard turbulence as a negligible factor in sound generation.

Nevertheless, there are other mechanisms by which turbulent flow can produce sound. One such situation might be turbulent flow

---

**Fig. 12.** Cuttings from an experiment on a circulation model showing a relation between the anacrotic incisura and the degree of constriction of a soft-walled outflow tract. The cuff pressure for each strip is given as 0, 50, 75, 100, 125, 150, and 175 cm. of water respectively. A specially designed pump raised the pressure in the “ventricle” sufficient to eject a constant stroke output in each beat; a diastolic notch is seen near the peak of the pulse wave as the “aortic valve” closes at the end of ejection. The sound trace is given above. At cuff pressures of 0 and 50 cm. of water, the “aortic pressure” rises smoothly with ejection and no murmur is recorded. As the cuff pressure (stenosis) increases to 75 cm. of water, notches appear in the first portion of the upstroke of the “arterial pulse wave” and these are synchronous with the brief chatter of the stenosed outflow tract. With greater constriction the anacrotic notching of the “pulse wave” is more evident, the repetition rate increases and the accompanying bruit is prolonged. With severe stenosis the anacrotic incisura is even more notable, and the repetition action and bruit become holosystolic.
I. MECHANISMS

along an elastic panel or wall such as may exist in the aorta. In this configuration the turbulent pressure fluctuations can drive the wall which may then transmit this energy to the surface of the body where it appears as sound. However, this mechanism depends on a number of factors that require study before it can be established as a producer of cardiovascular sound.

Cavitation. It is important to think of cavitation as the appearance of bubbles, not only of the vapor phase of the liquid—water in the case of blood—but also of so-called entrained gases—in the case of blood, nitrogen, oxygen, and carbon dioxide. As they grow and collapse, bubbles of the first type, vapor bubbles, radiate noise with wide-band frequency composition (including low frequencies). Gas-entrained bubbles, on the other hand, radiate sound by excitation of their natural frequency. The compressibility of the gas in the bubble behaves as a spring. The bubble has a natural frequency of oscillation. A bubble can be excited, that is, made to oscillate around its natural size and at its natural frequency, in the process of origination, of coalescing with another bubble, and of splitting into 2 bubbles, and finally in collapsing. The natural frequency of gas-entrained bubbles is given by

$$f_0 = \frac{1}{2\pi R^2} \frac{3kP}{\rho}$$

where $R$ is the radius of the tube, $k$ is the ratio of specific heats of the gas entrained, $P$ is the hydrostatic pressure in the liquid and $\rho$ is the density of the liquid. Using approximate values pertinent to this discussion one arrives at $f_0 = 330/R$ where $R$ is in centimeters and $f_0$ in cycles per second. If we consider the average radius of a bubble in the cardiovascular system to be about 1 mm., the formula yields a natural frequency of 3,300 c.p.s., a level far above that of significant components of murmurs. It follows that, if cavitation plays any role in the genesis of murmurs, vapor bubbles, not gas-entrained bubbles, are involved. The interplay between elastic wall and vibrations of wide-frequency composition—resonance, if you will—might result in murmurs with the frequency composition we in fact encounter.

It seems appropriate to make a further remark here on the origination of the cavitation bubble. The usually employed concept is that when a liquid moves rapidly enough, its static pressure may be lowered to a level below the vapor pressure and vapor bubbles appear. People concerned with this problem often either calculate or measure mean flow velocities and on this information found a judgment of the likelihood of cavitation. However, the correct conditions for the birth of a bubble need only occur in a small local region. Bubbles can appear in local areas of high velocity such as in flow around an obtuse sharp corner or in the center of a vortex, despite the fact that the mean velocity of the flow would not suggest cavitation.

Interpretation of Surface Sounds. The last comment I would like to make is on the problem of interpreting the sounds that reach the surface of the body. The body is a complex structure of which the most unusual feature from the acoustic standpoint is the fact that there is blood which is relatively incompressible within vessels that are of relatively elastic materials. As a result the transmission of the sound is very strongly dependent upon the mechanical properties of the tissues. These problems must be taken into consideration in experimental work in models and also in attempting to relate disturbances in the blood stream to sounds appearing at the surface of the body. The work of von Gierke and Oestreicher emphasizes that the transmission of sound in living tissues is complex.

Dr. Lepeschkin: The work of Dr. Rodbard links the 2 factors in the formation of murmurs: turbulence and resonance of the wall. I have found that a given amount of turbulence may not produce an audible murmur in a glass wall, but will when the flow is in a soft Tygon or polyethylene plastic tube.

Dr. McDonald: In the formula $\eta \left(\frac{V}{c}\right)^2$, what would be the significance of defining $c$, not as the speed of sound in a free liquid medium, but as the speed of sound in an incompressible fluid in an elastic tube, that is in a model comparable to the aorta?

Mr. Wiskind: That is an interesting point,
Dr. McDonald. The elasticity of the aorta contributes a “compressible” nature to blood flow. It causes pressure waves to travel down the aorta relatively slowly, let us say 8 M. per second, whereas the speed of pressure propagation in blood is 1,500 M. per second. Hence, a Mach number for the aorta using 8 M. per second for c might turn out to be indicative of the energy radiated from turbulent flow in the aorta. However, this remark is pure conjecture, its only significance being that, if energy is radiated from disturbances in blood flow, then the mechanical properties of surrounding tissues play an important part in determining its characteristics.

Mr. Webb: What happens, Dr. Rodbard, when you give a liquid, or chest-like, “surround” to the generator in your model?

Dr. Rodbard: There is sufficient energy for transmission of the sound to the surface of such a surround.

A word on the question of turbulence and murmurs. Homogeneous turbulence, that is, the variety produced when the critical Reynolds number is exceeded, does not produce murmurs of the coarse variety heard in aortic or pulmonic stenosis, at compressed arteries and at other sites. The sound produced by such turbulence is higher pitched than any biological sounds except the most high-pitched murmurs as in aortic insufficiency. The sounds produced by cavitation are also of a very high-pitched hissing quality and can hardly be responsible for the rumbling murmurs. I believe that good evidence supports the concept that the most common cause of murmurs will be shown to be due to repetitive closings and openings (“fitter”) of the valves of the heart.

Mr. Wiskind: The frequency content of the pressure fluctuations in fully developed turbulent pipe flow is of the order of magnitude of $\frac{V}{D}$ where $V$ is the mean velocity of flow and $D$ is the pipe diameter. Hence, for a 150 cm. per second velocity of blood flow in a 1-cm. aorta the dominant frequency content of the turbulent fluctuations would be about 150 c.p.s. This rough rule is based on a great many experimental data in the literature. In some crude experiments in our laboratory I also found the above to be approximately true.

**Editorial Summary and Comments**

The details of valve mechanics continue to be shrouded in some perplexities. Rushmer’s observation of minimal movement of the mitral cusps in the intact animal will require consideration in connection with the genesis of the first heart sound. Rushmer suggests that contraction of the papillary muscles may contribute to closure of the atrioventricular valves. Gradually the predominantly valvular origin of the first and second sound is attaining general acceptance. Attention is being directed to the origin of the diastolic gallop sounds. Here, too, valvular and myocardial schools are in evidence.

The discussion on mechanisms in the genesis of murmurs should serve to emphasize at least 3 points: 1. Turbulence and murmurs cannot be equated in a direct manner. In our present state of knowledge the formula for the Reynolds number is useful solely as a catalog of some of the factors controlling murmur production. 2. Murmurs are produced through a complex interplay between the disturbed flow and the wall or other boundary structures. 3. Cavitation, i.e., bubble formation, as a result of local drops in pressure, should be investigated as a basis for cardiovascular sound.

**Summario e Commentos Editorial in Interlingua**

Le detalios del mecanica valvular continua esser obscurece per certe perplexitatis. Le observation de Rushmer del minime movimento del cusipes mitral in le animal intacte va requirer consideration en connexion con le genese del prime sono cardiae. Rushmer suggere que le contraction del musculos papilar pot contribuer al clausura del valvulas atrioventricular. Le origine predominantemente valvular del prime e del secunde sono attinge gradualmente un acceptation general. Attention nune es dirigite al origine del diastolic sonos de galopo. Etiam hie le scholas valvular e myocardic se manifesta.

Le discussion super mechanismos in le
I. MECHANISMS

289

genese de murmures debe servir a sublinear 3
punctos al minus: 1. Turbulentia e murmure
non pot esser equate de un manera directe.
In le presente stato de nostre saper le formula
pro le numero Reynolds servi solmente como
un catalogo de certes del factores que regula
le production de murmures. 2. Murmures es
produite por un complexe interaction inter le
fluxo disturbate e le pariete o altre structuras
limitante. 3. Cavitation, i.e., formation de
dellas como resultato de local caditas in
pression, debe esser investigate como un del
bases de sonos cardiovascular.

ACKNOWLEDGMENT

In preparing this symposium for publication, the
editor, Dr. McKusick, had the assistance of Drs.
S. H. Boyer IV, Robert P. Grant, Hans H. Hecht,
J. O’Neal Humphries, Andrew Kerr, Jr., Simon
Rodbard, Robert F. Rushmer, and Samuel A.
Taibot.

REFERENCES

1. Rushmer, R. F.: Cardiac Diagnosis: A Physiologic
2. Reynolds, O.: An experimental investigation of the
circumstances which determine whether the
motion of water shall be direct or sinuus, and
of the law of resistance in parallel channels.
3. Coulter, N. A., Jr., and Pappenheimer, J. R.: 
Development of turbulence in flowing blood.
features of the normal mitral valve and associated
5. Sokoloff, L., Elster, S. K., and Righthand, N.: 
Sclerosis of the chordae tendineae of the mitral
6. Brock, R. C.: The surgical and pathological
anatomy of the mitral valve. Brit. Heart J. 14:
489, 1952.
7. Henderson, Y., and Johnson, F. E.: Two modes
of closure of the heart valves. Heart 4: 69, 1912.
8. Dean, A. L., Jr.: The movements of the mitral
cusps in relation to the cardiac cycle. Am. J.
9. Essex, H. E., Smith, H. L., and Baldes, E. J.: 
M. B.: The movement of aortic and pulmonary
valves studied post-mortem by colour cine-
11. Rushmer, R. F., Finlayson, B. L., and Nash,
A. A.: Movements of the mitral valve. Circu-
12. —, —, and —: Shrinkage of the heart in anes-
thetized, thoracotomized dogs. Circulation
Mitral incompetence in experimental auricular
14. Beard, O. W., and Decherd, G. M., Jr.: Vari-
tions in the first heart sound in complete A-V
15. Shearn, M. A., Tarr, E., and Ryland, D. A.: 
The significance of changes in amplitude of the
first heart sound in children with A-V block.
Circulation 7: 839, 1953.
16. Davila, J. C., Trout, R. G., Sunner J. E., and
Glover, R. P.: A simple mechanical pulse
duplicator for cinematography of cardiac valves
17. Dock, W.: Mode of production of the first heart
18. Kelly, J. J., Jr.: Diagnostic value of phono-
sequence of ventricular contraction in bundle
branch block. Presented at meeting of American
Heart Association, Cincinnati, Oct. 28, 1956.
20. Dock, W.: Heart Sounds, Cardiac Pulsations, and
Coronary Disease. (Porter Lectures, 1955.) Law-
rence, Kansas, University of Kansas Press, 1956.
21. —, Granell, F., and Taubman, F.: The physi-
ologic third heart sound: its mechanism and
relation to protodiastolic gallop. Am. Heart J.
22. Nichols, H. T., Likoff, W., Goldberg, H., and
Fuchs, M.: The genesis of the “prespysiotico”
murmur in mitral stenosis. Am. Heart J. 52:
379, 1956.
23. Counihan, T., Messer, A. L., Rappaport, M. B.,
and Sprague, H. B.: The initial vibrations of the
The mechanism of gallop sounds, studied with the
35: 1306, 1951.
motion of the heart border in subjects with
gallop rhythm or third heart sounds. Am.
26. Dawes, G. S., Mott, J. C., and Widdicombe,
J. G.: The cardiac murmur from the patent
ductus arteriosus in newborn lambs. J. Physiol.
27. Jerrard, W., and Burton, A. C.: Demonstra-
tion of hemodynamic principles in particular of
I. Mechanisms
VICTOR A. MCKUSICK and HANS H. HECHT

Circulation. 1957;16:270-290
doi: 10.1161/01.CIR.16.2.270
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1957 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/16/2/270.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/