Observations on the Interatrial Pressure Gradients in Man

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It was possible to calculate pressure gradients across the interatrial septum in several cases of congenital heart disease. Gradients in cases of interatrial septal defect are similar to those found in animals with artificially produced defects. The data are used to form a rounded picture of the hemodynamics of interatrial septal defect. In pulmonic stenosis with interatrial communication, reversal of the usual left-to-right gradient may occur only during atrial systole. Under these circumstances it is often possible to distinguish a patent foramen ovale with competent valve from an interatrial septal defect.

Atrial hemodynamics have been extensively studied in animals\textsuperscript{1–7} with or without interatrial communications. Despite the widespread use of right heart catheterization, there is still a paucity of such information in man.

During routine right heart catheterization of several patients with congenital heart disease, passage of the catheter through interatrial communications made it possible to record pressure pulses from both atria. An analysis of these curves, insofar as it provides information on atrial hemodynamics in man, forms the basis of this report.

Methods

The data consisted of atrial pressure pulses from 14 cases with congenital interatrial communications. Seven of these sets of curves were unsuitable for detailed analysis because of artefacts or large respiratory variations. However, the data from these discarded cases lend themselves to the same interpretation as the seven analyzed in detail.

The atrial pressure curves were recorded from each atrium in quick succession, using the Sanborn capacitance manometer (fig. 1). A simultaneously recorded electrocardiogram (lead II) served as a time reference. The patients were supine and breathing quietly. The zero level was 5 cm. dorsal to the angle of Louis. Blood samples were obtained in each case from both atria. The presence and magnitude of right-to-left shunting of blood in the atria were determined by comparing the oxygen content of left atrial or systemic arterial blood with that of pulmonary venous blood. Where the latter was not available, 95 per cent saturation was assumed. Left-to-right shunting of blood in the atria was indicated by the high oxygen content of right atrial blood relative to caval blood. The pressure pulses and blood samples from other chambers and vessels were used to complete the hemodynamic picture and to arrive at a final diagnosis.

The pressure differences between the left and right atrial curves during several heart cycles were determined for each 0.04 second, using the summit of the QRS as a zero time reference point. In each case, the cycle lengths of the atrial curves selected were identical and were, as far as could be determined, from the same phase of the respiratory cycle. The results were plotted as graphs representing the cyclic interatrial pressure gradients. Examples of these are shown in figures 2 to 8. The general similarity of the graphs from cases of interatrial septal defect indicates that there is validity to this analysis despite the errors inherent in pressure recording through a catheter due to movement of the heart\textsuperscript{1} or to the variable position of the catheter opening relative to the direction of blood flow.\textsuperscript{2}

The atrial pressure pulses were used as recorded and have not been expressed as effective atrial pressures by subtraction of the simultaneous intrathoracic pressure near the respective atria.\textsuperscript{3,4} It is unlikely that a significant difference between the intrathoracic pressures around each atrium exists at any instant\textsuperscript{5}.\textsuperscript{6} Although reports to the contrary have appeared,\textsuperscript{7,8} the latter possibility, and the difficulty of matching right and left atrial pressure pulses from exactly the same phase of the respiratory cycle, mean that the phasic pressure differences recorded are not likely to be absolutely correct. However, in patients such as ours, where breathing was slow and shallow, respiratory pressure variations were slight and the graphs are considered to be accurate enough for study.

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Results

1. Interatrial Septal Defects, Uncomplicated or with Pulmonary Hypertension

The first three cases (figs. 2 to 4) had normal or almost normal pulmonary pressures, large left-to-right shunts and very small right-to-left shunts. The fourth (fig. 5) had a high pulmonary arterial pressure and the left-to-right shunt was less marked.

In all four cases the pressure gradient through each cardiac cycle is by and large from left to right, with the maximum gradient during atrial systole. There is a more sustained but less marked peak during ventricular systole, the period of rapid atrial inflow,12 and this reaches its maximum during the "V" wave of the atrial pulse. The left-to-right pressure gradient drops when the A-V valves open and remains small until the next atrial systole. The time of opening of the A-V valves could be estimated within about 0.02 second. This occurred at 0.48 second in figure 2, at 0.48 and 1.20 seconds in figure 3 (best seen here on account of the slower rate), 0.8 second in figure 4 and 0.56 second in figure 5. The pressure gradient is least either early in atrial systole or just after it. Each graph, except that of figure 4 where the gradient reaches zero, shows reversal of the gradient at one or both of these times. The blood oxygen data of each case

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Fig. 1. Atrial pressure pulses from a case of valvular pulmonic stenosis with a patent foramen ovale. Left: right atrial pressure pulse. Right: left atrial pressure pulse. Electrocardiogram: lead II.

Fig. 2. Cyclic pressure gradient across the interatrial septum in a case of uncomplicated interatrial septal defect (left atrial pressure—right atrial pressure in mm. Hg). A left-to-right pressure gradient is present when the graph is below the zero line, and the gradient is reversed when the graph is above the zero line. R = summit of the QRS of the electrocardiogram; a = period of atrial systole.

Fig. 3. Cyclic pressure gradient across the interatrial septum in a case of uncomplicated interatrial septal defect. Conventions as in figure 2.
indicated a small right-to-left shunt. Thus, despite the fact that the left atrial mean pressure exceeded the right, there was evidence of small transient reversals both of the gradient and of the flow through the defect in all cases. The inadequacy of mean pressures in the study of the intimate hemodynamics of the atria is obvious, and is again stressed here.

The present graphs do not differ significantly from those of dogs with artificial interatrial septal defects. The drop in left-to-right gradient on opening of the A-V valves and the transient reversal of this gradient before or after atrial systole are seen in both human and animal curves. However, in animal experiments the left-to-right gradient is most often described as smallest in the middle or at the end of atrial systole rather than at the beginning and end. This difference between man and the dog is more apparent than real and depends on the conventions used in identifying the time of events in this part of the cycle. In all our cases where it could be clearly defined, and contrary to reports by other investigators, the right atrial "a" waves begin 0.02 to 0.03 second before the left, and reach their peak that much sooner. This is also observed in curves obtained from dogs and would be expected to reduce or reverse the left-to-right gradient at the beginning of atrial systole. The manner of spread of the impulse from the sinus node explains the asynchrony between the left and right atrial contraction.

2. Valvular Pulmonic Stenosis Associated with Interatrial Communication

The left-to-right gradient, which is accentuated during atrial systole when interatrial septal defect is the significant lesion, is by contrast markedly reversed in figure 6 except at the very end of atrial systole. During the rest of the cycle there is a left-to-right pressure gradient. Because of the rapid heart rate in this case, the effect of opening of the A-V valves is obscured by the simultaneous occurrence of atrial systole. The right-to-left shunt in this case was sufficient to account for a thirteen per cent difference between the oxygen contents of the pulmonary venous and brachial arterial blood samples, but there was no evidence of a left-to-right shunt on careful sampling of the right atrium, despite the marked and prolonged left-to-right gradient. (The mean gradient was left to right, but the only shunt was right to left.) It is deduced from the latter fact that the interatrial communication through which the catheter passed is a patent foramen ovale.

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FIG. 4. Cyclic pressure gradient across the interatrial septum in a case of interatrial septal defect with mild pulmonary arterial hypertension. Conventions as in figure 2.

FIG. 5. Cyclic pressure gradient across the interatrial septum in a case of interatrial septal defect with moderately severe pulmonary arterial hypertension. Conventions as in figure 2.

FIG. 6. Cyclic pressure gradient across the interatrial septum in a case of severe valvular pulmonic stenosis with a patent foramen ovale. Conventions as in figure 2.
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Figure 7. Cyclic pressure gradient across the interatrial septum in a case of severe valvular pulmonic stenosis with an interatrial communication in early right heart failure. Conventions as in figure 2.

Figure 7 shows the interatrial pressure gradient in a similar case. There was very severe valvular pulmonic stenosis with early right heart failure as evidenced by an elevated right ventricular end-diastolic pressure. In this case, the right atrial pressure is higher than the left through most of the cycle, and, like the previous case, it is most marked during atrial systole. Only for a short time at the moment of the A-V valve opening (0.68 second) when, under the circumstances, right ventricular inflow would be most free, is there a left-to-right gradient. This graph indicates that the shunt, if any, is right to left during most of the cycle. In this case, the shunt was large enough to cause overt cyanosis; evidence of a left-to-right shunt was completely lacking.

3. Interventricular Septal Defect and Patent Foramen Ovale

Figure 8 shows the interatrial pressure gradient in a case of interventricular septal defect and patent foramen ovale associated with a moderate pulmonary hypertension. The left-to-right atrial pressure gradient is very marked and reversal occurs to a slight degree only at the end of atrial systole in two of the three heart cycles shown. The left-to-right gradient is augmented during the period of rapid atrial filling, and then rises sharply again during atrial systole. This graph may be considered as an exaggeration of the graphs of interatrial septal defect shown before. Despite the marked left-to-right gradient, no shunt was evident in either direction. Thus, the interatrial communication was a patent foramen ovale.

Discussion

The present observation that mean pressure is higher in the left atrium than in the right in patients with uncomplicated interatrial septal defect is in agreement with others. This is also true in normal dogs. The creation of an interatrial septal defect moderate in size in the dog does not alter this relationship, although the gradient is lessened somewhat because of an increase in right atrial pressure. Thus, it would seem reasonable to assume that left atrial pressure usually exceeds right atrial pressure in normal man.

A number of mechanisms may account for the pressure differences between the atria. These include:

1. The different pressure-volume characteristics of the two atria, suggested on anatomic grounds in man, both with and without interatrial septal defects, and proved directly in dogs and to some extent in man.

Both in the dog and in man, the left atrium has a smaller cavity and a thicker wall than the right.

2. The smaller capacity of the venous system draining into the left atrium than into the right so that each increment of volume causes a greater increment of pressure in the pulmonary veins and left atrium than in the cavae and right atrium.

3. The greater extent and greater peripheral resistance of the systemic circuit as compared with the pulmonary circuit may mean that right ventricular contraction exerts a greater vis a tergo effect on venous return than does left ventricular contraction.

4. Variations in the movement of the A-V junction on the two sides may result in higher pressure in the left atrium than in the right during ventricular systole.

5. The smaller area of the mitral orifice compared to the tricuspid, as well as the thicker wall and smaller cavity of the left ventricle compared to the right, have been considered as the basis of a greater resistance to inflow into the left ventricle than into the right.

This last point led to the suggestion that the left-to-right gradient across the interatrial septum in uncomplicated interatrial septal defect should be small before the A-V valves.
open and should increase afterwards.\textsuperscript{19} We have observed exactly the reverse. Since in the normal human heart the blood flow is equal through the mitral and tricuspid valves, it is possible, but unproved, that the pressure is higher in the left atrium than in the right during ventricular filling. However, in the presence of an interatrial septal defect, the unequal ventricular inflows may, in part, nullify this difference through some rise in right ventricular filling pressure, and there is some evidence for this in man\textsuperscript{25} and in the dog.\textsuperscript{5} Certainly, the present data in cases of interatrial septal defect show that filling pressures in the two ventricles approach each other. The pressures in both atria fall when the A-V valves open but the fall is greater in the left atrium. This was found in such curves from dogs\textsuperscript{1} but was not marked in another study on man.\textsuperscript{20}

It is generally agreed that the minute flow of blood in uncomplicated interatrial septal defect may be considered in the following terms: (1) There is a large left-to-right flow of blood through the defect.\textsuperscript{14-16, 18, 26, 27} Although the cephalad position of the left atrium with respect to the right has not been generally accepted as a factor contributing to the left to right shunt,\textsuperscript{29} there is some support for the idea.\textsuperscript{29} (2) The minute flow through one atrium is the same as that of the other and both vary directly with the size of the shunt. (3) Systemic minute-flow, and with it venous return to the right atrium, is often reduced.\textsuperscript{3, 19} (4) Despite the greatly increased flow through all chambers except the left ventricle, there is no demonstrable deviation in pressure from the normal except for the possible rise in right ventricular end-diastolic pressure.\textsuperscript{24}

At present there is no way of directly measuring flow through an interatrial septal defect instant by instant during a cardiac cycle, but it may be presumed that the magnitude of the shunt does vary cyclically. In the absence of direct measurement, logical conclusions concerning such cyclic flow changes may be drawn from the available data, including the cyclic pressure gradient across the interatrial septum, but cannot, of course, be regarded as proved. It is possible, for example, that intangible factors such as changes in the size of the interatrial defect during the cardiac cycle may alter the relationship between flow and the pressure gradient across the septum to a significant degree. Here, such a relationship must be regarded as constant. One concept of cyclic flow across the interatrial septum in cases of uncomplicated interatrial septal defect may be expressed as follows:

Blood enters the atria from the cavae or pulmonary veins continuously during the cardiac cycle except during atrial systole, and venous return is much greater to the left atrium than to the right in the presence of an uncomplicated interatrial septal defect. Venous return is augmented for a time after atrial systole, both to the left\textsuperscript{11, 15, 30} and to the right atrium.\textsuperscript{32} This is attributed to relaxation of the atria, and, in the case of the reduced right atrial inflow, to the intrathoracic pressure changes resulting from expulsion of blood from the thorax by left ventricular ejection. At this time the left-to-right pressure gradient across the interatrial septum is large, and this gradient is maintained, despite the defect, by the constantly replenished reservoir of blood present in the left atrium and its tributaries. The large sustained left atrial inflow and the high left-to-right interatrial pressure gradient therefore suggest that the left-to-right shunt is large, particularly since the A-V valves are closed during this part of the cardiac cycle. The fact that in the experimental animal the creation of a septal defect of moderate size leaves the pressure gradient between the atria virtually unaffected supports this idea, ruling against resistance to flow through the defect as being an important cause of the pressure gradient; this fact further suggests that the left atrium and its tributaries do not at this time contain more than their usual blood volume, the excess having passed through the defect. The greater distensibility of the right atrium allows this excess to collect with little or no rise in right atrial pressure.

About the time that the A-V valves open, the left-to-right pressure gradient decreases rather abruptly and may disappear. It follows that the opening of the A-V valves nullifies or minimizes the factors which were responsible
for the pressure gradient. This is the period of rapid filling of the ventricles when almost all the blood which will make up the systemic flow is entering the left ventricle from the left atrium. The left atrium now has an additional outlet through which a large flow is occurring and venous return is unchanged or reduced. This combination of factors along with the fall in the interatrial pressure gradient indicates that flow through the interatrial septal defect is reduced during the period of rapid inflow of the ventricles. The systolic murmur of uncomplicated interatrial septal defect may be due to the occurrence of most of the shunt during the relatively brief period of ventricular systole.

The foregoing interpretation is in keeping with the radiologic and autopsy observations that the right atrium in cases of uncomplicated interatrial septal defect may be markedly dilated while the left atrium is little altered from the normal. The greater the proportion of the total flow across the interatrial septum in systole, the more dilated the right atrium should be since the excess blood has no runoff while the A-V valves are closed. Thus, the two atria are affected differently by an interatrial septal defect despite the fact that minute flow through each is the same. The basis for such a difference is better appreciated by some consideration of cyclic variations in flow through and between the atria.

The earlier occurrence of right atrial systole as compared with left causes a transient reversal of the pressure gradient across the interatrial septum (figs. 2, 3 and 5). It is likely that much of the small but well-documented right-to-left shunt occurs at this time. During the remainder of atrial systole there is a marked left-to-right pressure gradient. Reversal of the pressure gradient after atrial systole is seen in figures 2 and 3 and is also described by others. Some of the right-to-left shunting may occur at this time.

Apart from the hemodynamics of interatrial septal defect during a typical cardiac cycle, normal and forced respiration play a large role dynamically in artificial interatrial septal defects of animals. Although undoubtedly important, this has not been worked out in man.

The right atrial pressure pulse curve shown in figure 1 and used for figure 6 is seen especially in cases of valvular pulmonic stenosis with intact ventricular septum. The precise cause of the augmented “a” wave has not been fully explained.

Consideration of figure 6 with the accompanying blood oxygen data indicates that the cyanosis seen in such cases often has its basis in an intermittent rise in right above left atrial pressure during atrial systole and is not simply due to a general rise in right atrial pressure. Furthermore, venous blood enters the left atrium from the right through a patent foramen ovale with a competent valve rather than through an interatrial septal defect. The valve prevents left-to-right flow of blood while left atrial pressure exceeds the right.

As surgical technics for closure of interatrial defects are more widely applied, it will become important to distinguish preoperatively between interatrial septal defect and a patent foramen ovale in these cases, particularly when cyanosis is present. Such a distinction may be made when the catheter enters the left atrium and a left-to-right pressure gradient is found, in the absence of evidence of left-to-right shunting of blood; or, failing to enter the left atrium, by finding (1) cyanosis or arterial desaturation, (2) a large “a” wave in the right atrial pressure pulse associated with low pressure level during the rest of the cycle and (3) no left-to-right shunt.

Since a probe-patent foramen ovale is usually closed and dynamically insignificant, the routine catheterization of a heart without defects other than patent foramen ovale, or with other dynamically insignificant defects, could by chance reveal the normal human left atrial pressure curve, something which has been recorded only in open-chested man with the distortion attendant upon recording under these conditions. Such curves obtained in open-chested man without heart disease are roughly similar in contour to left atrial pressure curves from patients with uncomplicated interatrial septal defects and to the left atrial curves recorded in dogs.

From figure 7 it is impossible to be certain whether the short period of left-to-right pressure gradient gave rise to an undetectable
left-to-right shunt through an interatrial septal defect, or whether shunting was prevented by the valve of a patent foramen ovale. The difficulty of determining whether or not a competent valve is present under these circumstances is also illustrated in reported cases in which the right atrial pressure apparently exceeded the left throughout the cardiac cycle. 

Certain differences exist between the interatrial pressure gradients of congenital pulmonic stenosis with interatrial communication and those of acute artificial pulmonic stenosis produced in animals along with an interatrial septal defect. Right atrial pressure in the animal is greatest just before the opening of the A-V valves while in the patient it is greatest during atrial systole. Thus, reversal of the left-to-right gradient takes place during one part of the cardiac cycle in a clinical case and at a different time in the experimental analogue. This may be accounted for by dilatation and hypertrophy of the right atrium in congenital pulmonic stenosis which is absent in the acute experimental animal.

The case shown in figure 8 is a clear example of a patent foramen ovale with a competent valve since, with a marked left-to-right atrial pressure gradient, no evidence of a left-to-right shunt was found. A large left-to-right shunt through the interventricular septal defect brings about greatly increased venous return to the left atrium and a decreased return to the right atrium. The left atrium is deprived of the extra outlet present in interatrial septal defect. Since the pressures in the two atria in this case are completely independent, the graph of figure 8 may represent the cyclic pressure difference between the two atria in man. More likely, as shown in animal work, the normal pressure difference is exaggerated by the previously mentioned factors, in contrast to its being reduced by an interatrial septal defect.

This analysis shows how the plotting of the cyclic pressure difference between the left and right atrium during the heart cycle may afford a valuable means of studying the cardiology of interatrial septal defect in man as it does in the experimental animal. It permits the evaluation of chronic factors not operative in acute animal experiments. It offers a method whereby a patent foramen ovale in association with other lesions may be recognized on routine catheterization.

**Summary**

1. The cyclic pressure gradient across the atrial septum was determined in seven cases of congenital heart disease.

2. In general, there is good agreement between data on man and those obtained during animal experiments. The difference found depends on the chronicity of the lesions.

3. Apart from mean pressure differences between the atria in interatrial septal defect, it was shown that pressure fluctuations occurring during one cycle could result in transient reversals of the gradient and so explain the slight arterial desaturation found in these cases.

4. The importance of the cyclic fluctuations in flow, as contrasted with mean flow, has been discussed in connection with the hemodynamics of interatrial septal defect. The striking influence of other congenital lesions on flow through interatrial communications was demonstrated.

5. It is established on dynamic grounds as a result of these studies that the distinction may be made between a patent foramen ovale and
an interatrial septal defect in the living patient even without catheterization of the left atrium.

**Sumario Español**

1. La pendiente cíclica de presión a través del septo atrial fue determinada en siete casos de enfermedad congénita cardiaca.

2. En general, hay bastante acuerdo entre los datos en el hombre y aquellos obtenidos durante experimentos en animales. La diferencia encontrada depende en la cronicidad de las lesiones.

3. Aparte de diferencias en presión entre los atrios en defectos del septo atrial, se demostró que las fluctuaciones en presión que ocurrieron durante un ciclo podían resultar en reveses transitorios de la pendiente y así explicar la ligera desaturación arterial encontrada en estos casos.

4. La importancia de la fluctuación cíclica en el fluir, al compararse con el fluir promedio, se ha discutido en conexión con la hemodinámica de defectos del septo interatrial. La influencia marcada de otras lesiones congénitas en el fluir a través de comunicaciones interatriales fue demostrada.

5. Se ha establecido en bases dinámicas como resultado de estos estudios que la distinción puede hacerse entre un foramen ovale patente y un defecto del septo atrial en el paciente vivo sin necesidad del cateterismo del atrio izquierdo.

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