The Limits of Right Ventricular Compensation Following Acute Increase in Pulmonary Circulatory Resistance

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The ability of the right ventricle to compensate as the pulmonary artery is constricted appears to be determined by four major factors: (1) there occurs the well-known increased force of contraction as the right heart becomes distended; (2) the adequacy of the coronary circulation determines to a great extent the degree of pulmonary arterial constriction which can occur before failure occurs; (3) the circulatory reflexes apparently aid the compensation to a moderate extent; and (4) the greater the blood volume, the greater is the limit of compensation before right ventricular failure occurs.

The effects on the dynamics of circulation of progressive pulmonary embolism and progressive constriction of the pulmonary artery have been investigated numerous times. These previous investigations have demonstrated clearly the following basic principles of right ventricular compensation when pulmonary resistance is increased: First, even the slightest pulmonary embolism or slightest constriction of the pulmonary artery causes an increase in the pulmonary arterial pressure proximal to the constriction but little change in the pulmonary arterial pressure distal to the constriction. Second, for the first few ensuing heart beats following acute increase in pulmonary circulatory resistance, the right ventricle progressively dilates, and there occurs a concurrent increase in the right ventricular systolic pressure associated at first with only minor changes in end-diastolic pressure but followed later, as the right ventricle fails, by a pronounced rise in the end-diastolic pressure. Third, it has been pointed out in several studies that the pulmonary artery must be occluded approximately 60 per cent of its total cross-sectional area before the right ventricular end-diastolic pressure and the systemic venous pressure begin to rise perceptibly. It is at this same stage that the cardiac output begins to fail.

The present paper has a two-fold purpose: (1) to present quantitative curves which depict the progressive reactions of various parts of the circulatory system as pulmonary arterial resistance is increased, (2) to analyze various factors affecting the limit of compensation and to gain some idea of the relative importance of these factors. The four factors studied specifically have been: (1) the initial tension of the right ventricular myocardium as indicated by the end-diastolic pressure; (2) the coronary blood supply; (3) the blood volume; and (4) the sympathetic reflexes.

METHODS

Twenty-nine mongrel dogs anesthetized with sodium pentobarbital and heparinized with 3 mg. of heparin per kilogram were used in these studies. One to four weeks prior to experimentation a plastic tubular loop was placed around the pulmonary artery. One end of the plastic tube was fixed anteriorly around one of the ribs, and the other end, after encircling the artery, was brought out of the chest cage posteriorly through a stab wound. Because of the smooth, nonwettable nature of the constraining tube, a sinus tract developed in the postoperative animal along the course of the tube protruding from the back. It was found possible to pull the tube at any time, thereby constricting the pulmonary artery. By pushing the plastic tube back into the sinus tract this immediately released the constriction of the pulmonary artery. Very fine variations of pulmonary arterial constriction could be effected, as will be illustrated in subsequent figures. Indeed, by attaching a rubber band to the end of the plastic tube and stretching this to a desired length, any degree of strain could be imposed on the vessel, thus affecting the degree of constriction.

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constant tension could be applied over prolonged periods of time to the loop constricting the pulmonary artery.

Pressure measurements were made through venous catheters inserted variously into the right atrium, right ventricle, and pulmonary artery proximal to the constriction and distal to the constriction. Systemic arterial pressure was recorded with a mercury manometer, and pulsatile pressures were recorded with the Sanborn electromanometer. The zero pressure point was considered to be one-third the thickness of the chest behind the anterior sternal margin. This zero pressure point has been found in studies from this laboratory to represent a reasonable approximation of the mean position of the right atrium in the dog's chest.

In order to eliminate circulatory reflexes, approximately one-half of the animals were, during the course of each experiment, converted into areflex animals by a method that has been followed many times in this laboratory. To do this, all spinal nervous outflow is paralyzed by the injection into the spinal canal of 200 mg. of procaine or 150 mg. of metycaine dissolved in 20 cc. of saline. This causes an immediate fall in arterial pressure to approximately 40 to 50 mm. Hg and causes complete cessation of respiration. Artificial respiration is then instituted by means of tracheal cannula or electrophrenic respiration, and the blood pressure is brought to normal by continuous infusion of epinephrine at a rate averaging approximately 0.00045 mg. per kilogram per minute.

Cardiac outputs were performed by the usual direct Fick method.

Results

Compensatory Changes in Right Ventricular Pressure Caused by Increased Pulmonary Resistance

Figure 1 illustrates the effect of increasing the pulmonary resistance on the mean right ventricular pressure, the mean pulmonary arterial pressure proximal to the constriction, the mean pulmonary arterial pressure distal to the constriction, the mean right atrial pressure, and the mean systemic arterial pressure. The curves of this figure have been constructed as an algebraic average of 22 similar curves obtained in 14 normal dogs. In each instance, the increasing pulmonary resistance was applied progressively and very slowly requiring three to five minutes for completion of each entire set of curves.

The compensatory changes in mean right ventricular pressure were exactly as expected and agreed with the previous results of others.
pulmonary arterial constriction. The rise in pressure proximal to the constriction occurred concurrently with the rise in right ventricular pressure, but the distal pulmonary arterial pressure did not fall perceptibly until the right ventricle was no longer able to compensate for the increased pulmonary arterial resistance. As noted below, it is this same point at which cardiac output began to decrease.

**Effect of Progressive Pulmonary Arterial Constriction on Systemic Arterial Pressure and Cardiac Output**

Figure 1 illustrates that the fall in systemic arterial pressure did not occur to any major extent until the right ventricle could not compensate further. Figure 2 illustrates the relationship of systemic arterial pressure and cardiac output to other changes in the circulation during progressive pulmonary artery constriction. In most of the dogs with their reflexes still intact the systemic arterial pressure and the cardiac output increased in the early phases of pulmonary arterial constriction. Averaging the results from all dogs, the systemic arterial pressure increased 10 mm. Hg, and in one animal the cardiac output increased approximately 20 per cent.

**Coronary Blood Supply as a Possible Limiting Factor in Right Ventricular Compensation**

Fineberg and Wiggers pointed out on theoretic grounds that as the pulmonary resistance increases and consequently causes a decrease in systemic arterial pressure, the decreasing coronary arterial pressure undoubtedly depresses the ability of the right ventricle to compensate. Though direct measurements of coronary blood flow during progressive pulmonary arterial constriction have not been made, there were in the present studies indications that Fineberg and Wiggers' conclusions are correct.

First, if pulmonary arterial constriction causes a decreased systemic arterial pressure and this in turn causes the pressure of the right ventricle to decrease because of poor coronary blood flow, then this effect would further decrease the flow of blood through the pulmonary system into the left heart, thus creating a vicious circle. Such a vicious circle apparently was operative in all of the present experiments, for, once the right ventricular pressure began to fall, even without further occlusion of the pulmonary artery, the pressure continued to fall to the point of complete right ventricular standstill. Secondly, attempts were made to stabilize the systemic arterial pressure at various levels below normal. By very critical adjustment of the degree of occlusion, it was possible to stabilize the systemic arterial pressure at levels above approximately 60 mm. Hg. Any time the level of systemic arterial pressure fell below this value, progressive deterioration of right ventricular compensation ensued even though the degree of pulmonary arterial constriction remained constant.

Also, in 19 dogs the pulmonary artery was suddenly and totally occluded 62 times. This
total occlusion was maintained over variable periods of time. If the occlusion lasted only one to two seconds, the circulatory pressures returned to normal immediately after termination of occlusion. If the occlusion was maintained for 60 to 90 seconds, the heart could not recover, illustrating that it had become greatly weakened. Figure 3 illustrates the recovery of systemic arterial pressure following total occlusion of the pulmonary artery for variable periods of time. It will be noted that immediately after blood is allowed to flow through the pulmonary artery after a prolonged occlusion, the systemic arterial pressure rises to a short plateau. The level of this plateau is lower, and its length is more prolonged the longer the period of pulmonary arterial occlusion. Furthermore, the systemic arterial pressure rises from this plateau up to a normal value approximately at the same time that the heart was calculated to have begun receiving sufficient coronary blood supply to offset the period of ischemia. That this step phenomenon in the recovery of systemic arterial pressure was not a result of reflexes was indicated by the fact that the same phenomenon occurred in 16 occlusions in six areflex dogs.

Role of the Circulatory Reflexes in Right Ventricular Compensation

In order to determine the difference between normal animals and animals which do not have intact circulatory reflexes, 12 areflex dogs were prepared as described under “methods.” The following differences in the reaction of these dogs and normal dogs were noted: As illustrated in figure 2, right ventricular pressure measurements, as measured before and after the animal was rendered areflex, illustrated that the normal animal was capable of an average of 27 per cent greater compensatory rise in ventricular pressure than was true in the areflex animal. Also shown in figure 2 is the relative effect of pulmonary arterial constriction on cardiac output in the normal and in the areflex animal, illustrating that the normal animal was capable of maintaining its cardiac output at a normal or supernormal level for a much longer period of time during progressive pulmonary arterial constriction than was the areflex animal.

In the areflex animal, recovery of the heart following total occlusion of the pulmonary artery was greatly impaired. When the pulmonary artery was occluded in areflex dogs for an average period of approximately 20 to 30 seconds, recovery of the heart would not ensue even though the proocclusion systemic arterial pressures had been sustained at completely normal values by continuous infusion of epinephrine. This period of 20 to 30 seconds compares with 60 to 90 seconds during which total pulmonary occlusion had to be maintained in the normal animal before recovery would not ensue.

To study the effect of epinephrine on the ability of the right heart to compensate for increased pulmonary arterial resistance, varying rates of epinephrine infusion were given to areflex animals, and the maximal compensatory ability of the heart was studied. Figure 4 depicts graphically the relationship of maximal ventricular compensatory pressure to the initial systemic arterial pressure which was varied in the areflex dogs by varying the rate of epinephrine infusion. It will be noted that

![Graph](Fig. 4. Effect of increasing the control level of systemic arterial pressure on the ability of the right ventricle to compensate. The different levels of systemic pressure were effected by changing the rate of epinephrine infusion into areflex dogs.)
Epinephrine does markedly increase the maximal pressure to which the right ventricle can compensate.

Two other experiments on normal dogs illustrated probable effects of circulatory reflexes on right ventricular compensation. First, when the pulmonary artery was suddenly and totally occluded the maximal rise in right ventricular pressure was only approximately one-half the maximal rise which occurred when the pulmonary arterial constriction was effected slowly over a period of four to five minutes.

Second, when the pulmonary artery was rapidly compressed, but only partially so, and the degree of occlusion was maintained at a constant degree following this rapid partial occlusion, it was found that the right ventricular compensatory pressure rose to about one-half its final value immediately after the occlusion and then rose gradually to a higher level, reaching a plateau at approximately 30 to 45 seconds after partial occlusion. This prolonged rise was not observed in areflex animals. When the partial occlusion was sufficient to depress the systemic arterial pressure, a progressive rise in systemic arterial pressure occurred during the first minute following the partial constriction even though the degree of occlusion remained constant. This recovery of systemic pressure following sudden partial occlusion of the pulmonary artery did not occur in the areflex animals.

The Effect of Increased Fluid Volume on Maximal Right Ventricular Pressure During Progressive Pulmonary Artery Constriction

In two normal dogs and in two areflex dogs transfusions of 500 cc. of blood were given in a period of approximately one minute immediately prior to slow occlusion of the pulmonary artery. As illustrated in figure 5, the maximal right ventricular pressure was greater after the transfusion than immediately prior to transfusion, averaging 61 per cent greater following the four transfusions, and there was no significant difference in the responses of the normal and areflex animals.

Discussion

The present study obviously has confirmed previous studies on massive pulmonary embolism and progressive pulmonary arterial constriction. Of especial importance, however, has been the attempt to determine the importance of the different factors noted in the introduction which determine the degree of maximal compensation which the right ventricle can attain.

The inherent ability of the myocardium to react to initial stretch has been demonstrated so often and is so well accepted that this factor in itself does not need further discussion. Instead, it is the relationship of this inherent ability to the other three factors that still requires clarification.

The effect of coronary blood flow on the ability of the right heart to compensate is obvious, for every investigator who has studied curves of heart contraction has recognized immediately the variability of these curves with varying states of coronary blood supply. In the present study the rapid deterioration of right ventricular contraction, once the pulmonary artery was constricted beyond the point of maximal right ventricular compensation, indicates that the coronary blood flow is a very important limiting factor on the degree of right ventricular compensation which can be attained.

Recent studies by Case and associates using special heart preparations in which the coronary blood supply remained constant throughout the experiments illustrated that the compensatory curve of right ventricular pressure against increasing load can be greatly depressed by insufficient coronary blood supply. Therefore, it is reasonable to believe that the rapid deterioration of right heart function in the present experiments, after a certain degree of pulmonary artery constriction, was due to sudden diminishment of coronary blood supply. This tendency for a weakened heart to...
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diminish its own coronary blood supply and thereby create a vicious circle of deterioration is undoubtedly one of the most important aspects of heart disease, though unfortunately it is very difficult to obtain adequate controlled quantitative observations on this mechanism.

The experiments on areflex animals in the present study emphasize the importance of the circulatory reflexes as one of the compensatory factors during progressive constriction of the pulmonary artery. The beneficial effect of sympathetic reflexes on heart contraction is demonstrated by the inability of the heart in the areflex animal to recover easily following total occlusion of the pulmonary artery. Also, the over-all ability of the circulatory reflexes to aid in right ventricular compensation to progressive pulmonary arterial constriction was illustrated by the fact that the maximal compensatory rise in pressure was 27 per cent greater in the normal animal than in the areflex animal even though the control pressures were the same.

It should be noted specifically that it is not the normal tonic sympathetic impulses which are responsible for greater right ventricular compensation in normal dogs than in areflex dogs, but it is the increase in sympathetic impulses as a result of reflexes during pulmonary constriction which is important. In other words, if $\Delta S$ is the increase in sympathetic discharge and $\Delta C$ is the increase in pulmonary constriction, in areflex dogs $\Delta S/\Delta C$ is zero, whereas in the normal dogs $\Delta S/\Delta C$ is strongly positive as is illustrated by the compensatorily elevated systemic arterial pressure immediately following release from pulmonary arterial constriction in the normal animal.

The reason why increased blood volume raises the maximum level to which the right ventricular pressure can compensate is not so clear as are the other factors. Yet, by allusion to a few simple differential analyses, an attempt will be made to explain the mechanism: It is a well-accepted fact that, as the load on the right heart increases, back pressure effects cause the right ventricle to stretch and the right ventricular pressure to increase. In order for this stretch to occur, the right ventricular end-diastolic pressure, and consequently the right atrial pressure, must increase. Furthermore, the degree of right ventricular stretch increases directly with the increase in right atrial pressure. On the other hand, it has been shown in this laboratory and by Starr that cessation of heart function by fibrillation or otherwise can cause a maximum rise in right atrial pressure to only 10 to 14 mm. Hg. In fact, in the present experiments, slow constriction of the pulmonary artery in 22 dogs caused an average rise in right atrial pressure to a level of only 12 mm. Hg before return of blood to the heart completely ceased.

Thus, pulmonary constriction causes two effects which affect the degree of right ventricular compensation: First, pressure in the right atrium directly increases the stretch and the force of contraction. Second, the rising right atrial pressure opposes the return of blood to the heart, and the diminishing cardiac output eventually leads to coronary ischemia which in turn diminishes the force of contraction of the right ventricle. Equating these effects in accord with the usual theory of differential analysis, one finds that progressive pulmonary constriction should cause continual increase in right ventricular pressure until the negative coronary ischemia factor becomes quantitatively equal to the positive myocardial stretch factor, and when these two factors are equal the maximal level of right ventricular compensation will have been reached.

Transfusion (as has been shown in this laboratory and by Huckabee and co-workers) builds up the pressure of blood throughout the circulatory system, and this pressure can overcome to a certain extent the tendency of right atrial pressure to diminish venous return to the heart. Consequently, increased blood volume presumably delays the development of coronary ischemia during progressive pulmonary constriction. Therefore, following transfusion, the right ventricle can develop considerably greater force of contraction before the negative coronary ischemia factor overbalances the positive myocardial stretch factor. This precise effect, with an average increase in right ventricular compensation of 61 per cent, was observed in all of the experiments, thus illustrating that increased blood
volume can aid in overcoming at least this one type of cardiac insufficiency.

The rise in the systemic arterial pressure occurring in most of the present experiments during early stages of pulmonary arterial occlusion confirms the observations of Gibbon and Churchill and Fineberg and Wiggers who have mentioned this effect. One wonders what the cause of this effect might be. The pulmonary arterial pressoreceptors might provide a clue to this phenomenon, for it is possible that even a slight decrease in the distal pulmonary arterial pressure might initiate a sufficient pressoreceptor reflex to cause a rise in the systemic arterial pressure rather than simply to moderate the fall in systemic arterial pressure, which is the usual function of pressoreceptors. However, if this is true, it indicates that the pulmonary pressoreceptor reflexes of dogs are much more powerful than have been suspected and perhaps play a very important role in blood pressure control.

**SUMMARY**

Quantitative, average curves showing the dynamic response of right ventricular pressure and other circulatory pressures to progressive pulmonary arterial constriction have been presented.

It has been pointed out and discussed that at least four different major factors determine the maximal compensatory pressure that can be developed by the right ventricle in response to progressive pulmonary arterial constriction. These are: first, the well-known intrinsic ability of the myocardium to react with increasing force of contraction in response to increasing initial stretch; second, the integrity of the coronary blood supply; third, the ability of the circulatory reflexes to increase the force of contraction of the right ventricle; and, fourth, the quantity of blood which is available to elevate the right ventricular end-diastolic pressure.

The fact that slight pulmonary arterial constriction usually increases systemic arterial pressure and cardiac output to levels even above normal has been pointed out.

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