Cardiovascular Dynamics of Vasovagal Reactions in Man

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Various aspects of normal and abnormal circulatory adjustments in health and disease have been studied by many investigators. However, there has been little definitive physiologic evaluation of a commonly occurring disturbance in cardiovascular regulatory mechanisms in man, i.e., the common faint or "vasovagal syncope." This is due to difficulties in obtaining measurements of blood flow during rapid changes in state as well as the undesirability of allowing the circulatory collapse to continue for any prolonged period of time. It would appear, however, that studies which would elucidate the pathophysiologic mechanisms of this condition as it occurs spontaneously would add important information concerning the regulation of the circulation.

This study describes the cardiovascular dynamics of vasovagal reactions (vasovagal syncope sine syncope) of moderate degrees which occurred in 2 patients during cardiac catheterization. Fortuitously, the reactions occurred after control data were obtained and before the performance of various maneuvers designed to alter the circulatory state. Syncope did not occur in these subjects, perhaps because they were in the supine position and the reactions were not severe enough.

The term "vasovagal" is used in this presentation because the reactions qualitatively resembled those described by others. The use of this term does not imply knowledge regarding basic causative mechanisms, data for which are not adequately available in this study, but is simply an attempt to conform to common terminology.

Methods

Right heart catheterization was being performed in the 2 subjects of this report as part of another investigation. The patients were in the resting recumbent states. Premedication was not given. A double-lumen cardiac catheter was introduced into the pulmonary artery from the left median basilic vein. An indwelling arterial needle (Cournand) was inserted into the right brachial artery. Pressures were obtained with Statham strain-gage transducers and recorded on a multichannel oscillographic photographic recorder. Mean pressures were obtained by electric integration of the pressure pulses. The point of zero reference for measurements of intracardiac pressures was taken at 5 cm. below the angle of Louis. Standard lead I of the electrocardiogram was constantly monitored. In subject A, cardiac output was determined by the standard direct Fick method. The catheter tip was then advanced to the pulmonary "wedge" position, pressures recorded, and the tip withdrawn to the pulmonary artery. At that point, the vasovagal reaction occurred. In subject B, control cardiac outputs were determined once by the direct Fick method and twice by the indicator dilution method, according to Hamilton and co-workers.

In the latter method, known amounts of dye (Cardiogreen) were injected rapidly into the pulmonary artery through the catheter and continuous time-concentration curves of dye were obtained from the peripheral (brachial) artery blood using a cuvette densitometer in conjunction with a constant flow system. The volume of blood between the point of injection and the site of sampling (including all temporally related sites) was calculated as the product of cardiac output and mean circulation time (central blood volume). Several minutes following the last blood flow determination, the vasovagal reaction occurred.

Total pulmonary vascular and total peripheral arterial resistances were calculated according to standard formulae, using the Poiseuille equation, where

\[
\text{resistance} = \frac{\text{arterial mean pressure}}{\text{rate of blood flow}}
\]

*Colson Model 103 Cuvette Densitometer and Colson Model 105-S Constant Flow System.*
Resistance is expressed as dynes/sec./cm. \(^6\) by the use of conversion factors.\(^*\)

No unusual difficulties were encountered in these subjects during the procedures and prior to the onset of the reactions. There was no pain, no excessive or difficult manipulations of the catheter or arterial needle, and no significant blood loss. Neither patient demonstrated undue anxiety or emotional disturbances. Dry runs had been performed the day before catheterization to familiarize the patient with the laboratory and with anticipated procedures. The vasovagal reactions occurred suddenly and unexpectedly.

The reactions were not severe, as indicated by the degrees of systemic arterial hypotension and bradycardia, and therefore were permitted to continue without immediate therapeutic intervention. Measurements of physiologic parameters, as described before, were repeated at frequent intervals. In subject A, right heart pressures were not recorded during the initial 60 to 70 minutes due to technical difficulties. Further manipulations, especially of the catheter, were specifically avoided to permit the reactions to pursue their courses without the risk of further complications or changes, thereby minimizing possibilities of additional variables. Pulmonary "wedge" pressures and calculated pulmonary "arteriolar" resistances were thus deliberately sacrificed.

In subject A, the hypotensive state persisted for 140 minutes. Atropine sulfate, 0.4 mg., was then administered directly into the pulmonary artery through the catheter, and measurements were continued for the next 60 minutes. In subject B, the reaction appeared to recede spontaneously over a 35- to 40-minute period.

**Results**

Although the changes which occurred during the vasovagal reactions in the 2 subjects were similar in most aspects, there were certain differences. These were apparently related to dissimilar initial physiologic states. For the sake of clarity, therefore, the results will be described separately for each subject.

**Subject A (Figure 1)**

Subject A was a 36-year-old Negress who had mild hypertension of unknown duration. Her medical history and physical examination were otherwise negative. She had never received antihypertensive therapy.

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\(^*\)1,332, conversion factor from mm. Hg to dynes per cm. \(^{-2}\).

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**Figure 1**

Subject A. Cardiovascular dynamics during control period, during vasovagal reaction, and after administration of atropine. Under arterial pressures, the symbol \(x\) denotes mean pressure. Under cardiac index, the symbol \(F\) denotes determination by Fick method and \(D\) by indicator dilution method.

**Control Physiologic Data**

Mild systemic arterial hypertension was present. Total peripheral resistance was increased. A mild tachycardia and a slight decrease in stroke volume were present. Other physical parameters listed in figure 1, as well as oxygen consumption, ventilation, and arterial-mixed venous oxygen difference, were normal.

**Vasovagal Reaction Period**

**Clinical Features.** Manifestations suggesting autonomic dysfunction occurred suddenly. These included nausea, retching, sweating, pallor, restlessness, light-headedness, and weakness. They lasted for a short period, however, regressing after 15 minutes. Only weakness persisted. With the exception of bradycardia, the electrocardiogram (standard lead 1) did not change. The physiologic disturbances lasted considerably longer than the clinical disturbances.
**Physiologic Data.** There were abrupt falls in systemic arterial pressures and heart rates, followed by more gradual declines to their lowest levels during the ensuing 20 to 30 minutes. Pulse pressures were generally decreased. Central vascular pressures did not change with the exception of slightly lower pulmonary artery systolic pressures. Cardiac indices and stroke volumes were considerably reduced. Total peripheral and pulmonary vascular resistances (calculated) increased. After 50 minutes, heart rate rose to control levels without significant changes in vascular pressures, flows, or resistances. It is of interest that as the heart rose, stroke volume decreased further. This suggested that the latter was primarily responsible for the persistence of the abnormalities in cardiodynamics.

There were no changes in the electromechanical intervals and in the characteristics of the pressure pulses of the brachial artery, pulmonary artery and right ventricle.

**Following the Administration of 0.4 mg. Atropine Sulfate into Pulmonary Artery**

**Early Phase.** An immediate rise in heart rate occurred, exceeding control levels by 14 per cent. This was associated with no change in cardiac index, indicating that a further reduction in stroke volume had occurred as a result of the tachycardia. Systemic arterial pressure increased slightly, but was still 15 per cent below control levels. Central vascular pressures, vascular resistances, and central blood volume did not change.

**Late Phase.** The cardiovascular dynamics present during the early phase of the atropine period persisted for approximately 52 minutes. Systemic pressures, cardiac index, and vascular resistances then attained control levels. Heart rate continued at its accelerated rate. Therefore, the rise in cardiac output was a result of an increase in stroke volume, although not to control values. The continued reduction in stroke volume at this time could be attributed to the increased heart rate since cardiac output was normal. Central vascular pressures did not change. Central blood volume increased somewhat from its low level, although it was still not higher than it had been during the initial phase of the reaction. This is difficult to explain, although it is generally appreciated that there is a relatively large error inherent in the calculation of this volume, and that differences of less than approximately 20 per cent may not be statistically significant albeit they may be important physiologically.

**Subject B (Figure 2)**

Subject B was a 48-year-old Negro male who had severe hypertension. Left ventricular failure (clinically) had been present for several years. Physical examination revealed blood pressure 190/140 mm. Hg, no systemic venous vascular congestion, and moderate left ventricular hypertrophy. Electrocardiogram confirmed left ventricular hypertrophy. He had never received antihypertensive therapy.

**Control Physiologic Data**

Severe systemic arterial hypertension was present. The clinical evidence of left heart failure was physiologically supported by decreased cardiac indices, elevated arterial-mixed venous oxygen difference, and moderate pulmonary arterial hypertension. Alteration in right ventricular function was present as indicated by an increased end-diastolic pressure. Total peripheral and pulmonary vascular resistances were markedly elevated. Central blood volumes were moderately increased. A mild tachycardia and a moderate decrease in stroke output were present. Oxygen consumption and ventilation were normal.

**Vasovagal Reaction Period**

**Clinical Features.** Clinical manifestations in regard to onset, symptoms, duration, and the electrocardiographic complexes (standard lead I) were similar to those of subject A. Again, the physiologic disturbances lasted longer than the clinical disturbances, although weakness persisted for some time.

**Physiologic Data.** There were abrupt decreases in systemic arterial pressures and heart rates. At the same time, pulmonary artery and right ventricular pressures fell considerably, reaching normal levels. Cardiac index, stroke volume, and central blood volume fell markedly. Total peripheral resistance rose and pulmonary vascular resistance de-
VASOVAGAL REACTIONS

clined. The cardiovascular hemodynamics then returned gradually in a direction toward control levels during the period of observation, although only heart rate attained control values (at 27 minutes).

There were no changes in the electromechanical intervals and in the characteristics of the pressure pulses of the brachial artery, pulmonary artery and right ventricle.

Additional Information

Sensitivity to vagal stimulatory maneuvers was evaluated in each patient at some date after cardiac catheterization. The following were performed: carotid sinus stimulation, eyeball compression, gagging, and production of cutaneous pain. Responses were completely negative with respect to blood pressure, heart rate, electrocardiogram and clinical symptomatology.

Discussion

The reactions are described as occurring spontaneously in the sense that drugs, venesection, tourniquets, postural changes, carotid sinus pressure, and other such maneuvers were not utilized as precipitating aids. The stimulus responsible for the occurrence of the reactions in our subjects is not apparent. Psychic stimuli such as fright, pain, emotions, experience of physiologic tests or instruments, and sight of blood are well known causes and could have been contributing factors. Excessive stimulation of circulatory system receptors by the catheter or the indwelling arterial needle could also have been involved. A host of pressoreflexes arising from stimulation of receptors located in many areas of the cardiovascular and pulmonary systems have been described. For present purposes, however, one need only consider that the abnormal physiologic reactions occurred as a result of excessive or abnormal reflex reactions (whatever the initial stimulus or receptor may have been), unadulterated by preparatory maneuvers which by themselves affect cardiovascular dynamics.

It is to be noted that the hypotension levels of pressure referred to were not truly hypotensive per se, but rather, as related to control values. The levels during the reactions were the acutely abnormal pressures and denoted, therefore, acute alterations in cardiovascular dynamics.

The striking feature in our subjects was the considerable decline in cardiac output during the vasovagal reactions. It was this physiologic event which was primarily responsible for the reduction in arterial pressure. The roles played by heart rate and stroke volume in the production of decreased blood flow were different. Bradycardia and reduced stroke output occurred during the initial phases of the reactions. In each subject, heart rate increased to control levels during this period, while stroke volume did not change (subject A) or increased only slightly (subject B). Changes in minute volume paralleled those of stroke volume, both remaining considerably diminished. In subject A, atropine resulted in an immediate tachycardia, but no change in cardiac output and a further decrease in stroke output. Only 45 minutes later did cardiac output (as well as arterial pres-
sure) rise to control levels concomitant with an increase in stroke volume. The latter was still somewhat reduced at that time, however, probably as a simple reciprocal relationship to the tachycardia (since minute volume was normal). The data indicate, therefore, that the reduction in stroke volume was the predominant cause of the decreased cardiac output, and that heart rate influenced cardiodynamics to a minor degree.

The mechanisms whereby stroke volume was reduced cannot be adequately determined on the basis of observations in only 2 subjects. Various maneuvers which would have offered information in this regard could have been performed. However, in view of the limited availability of this type of case material and the lack of information concerning the cardiodynamics of spontaneous reactions, it was deemed advisable to study the reactions in their pure form and without the influence of additional variables. Possible mechanisms include: (1) a redistribution of blood volume from the central vascular bed to peripheral vessels due to systemic vasodilation (primarily venous), resulting in a reduction in venous return and, thereby, in the amount of blood available to the heart; and (2) reflex inhibition of myocardial contractility.

The striking decreases of the initially elevated pulmonary arterial and right ventricular pressures to normal in subject B are in direct contrast to the lack of large changes in lesser circulation pressures in subject A. However, these differences may be explained by the volume elasticity properties of the heart chambers and pulmonary vessels. The general contours of pressure-flow curves of these structures are characterized by upward convexities when pressure is plotted on the vertical axis. When pressures are initially normal, changes in flow produce minimal changes in pressure. In contrast, small changes in flow may accomplish great changes in pressure when the latter is initially elevated.

The increase in total peripheral resistance during the vasovagal reactions in each of our subjects does not by itself indicate increased arteriolar tone, but rather, a decrease in luminal area or caliber. In general, caliber varies indirectly with the active (smooth muscle dependent) vascular tone and directly with the intravascular force (blood flow or volume) tending to distend the vessel, the result depending on the balance between these 2 factors. Therefore, a rise in peripheral resistance (or a decrease in luminal caliber) may occur in the presence of a decline in vasomotor tone if the distending force (blood flow or volume) decreases to a greater degree. It appears that this was the combination of events in our subjects. In addition, arterial pressure is ordinarily maintained in the presence of a reduced cardiac output by a compensatory rise in arteriolar tone (and peripheral resistance). The declines in blood pressures in our subjects again suggest that compensatory arteriolar constriction was impeded by decreases in arteriolar tone, and that the passive tension properties (elastic tissue dependent) of the vessel wall were responsible for some reduction in luminal area as the distending force (cardiac output) decreased.

The ineffectiveness of atropine in restoring cardiodynamics in subject A suggests that inhibition of efferent sympathetic impulses was the major etiologic factor in the vasovagal reaction, rather than an increase in parasympathetic activity. Other workers have also indicated the importance of the sympathetic system in this, as well as in related conditions. This would also be pertinent in terms of therapy, namely, that sympathomimetic agents may be more specific in improving cardiovascular dynamics in this condition.

Summary

The dynamics of vasovagal reactions which occurred in 2 patients during right heart catheterization were studied. Both subjects initially had systemic hypertension with corresponding increases in peripheral resistances. Subject B had considerably decreased blood flow, moderately elevated pulmonary artery and right ventricular end-diastolic pressures, and elevated central blood volume. These parameters were normal in subject A.

The characteristic features of the reactions were appreciable declines in cardiac outputs
VASOVAGAL REACTIONS

coincident with decreased systemic arterial systolic, diastolic, and pulse pressures, decreased heart rates, and slight increases in calculated peripheral resistances. Stroke volumes were moderately reduced. A slight decrease in pulmonary artery systolic pressure occurred in subject A. In subject B, pulmonary artery and right ventricular end-diastolic pressures declined to normal and central blood volume decreased moderately. The return of heart rate to control values had no significant effects on the other physiologic parameters.

The data demonstrate that reductions in cardiac output, due primarily to decreased stroke outputs, were predominantly responsible for the arterial hypotensions during the vasovagal reactions in these 2 subjects. The ineffectiveness of atropine in restoring hemodynamics in one subject suggested the importance of inhibition of efferent sympathetic activity in the etiology of this reaction. The failure of peripheral resistance to compensate for decreased blood flow suggested inhibition of arteriolar tone.

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