Oscillation of Blood Flow and Vascular Resistance During Mayer Waves

By Thomas Killip, III, M.D.

In experimental animals in poor condition, slow spontaneous oscillations in blood pressure may often be observed (fig. 1). Termed Mayer waves, after the description by Sigmund Mayer in 1876, they are slower than the respiratory rate. Small Mayer waves often develop in animals bled to an arterial pressure between 60 and 80 mm. Hg. Bilateral carotid clipping will usually exaggerate the pressure rise which may reach an amplitude of 80 mm. Hg or more with each wave. Vagotomy reduces the amplitude of the waves, as does breathing pure oxygen. They are abolished by sinus nerve block, inactivation of the carotid chemoreceptors, or sympathetic blockade.

It has long been postulated that Mayer waves are due to rhythmic change in vasomotor function, but evidence to support this thesis has been scant. The experiments described herein were designed to determine whether Mayer waves are accompanied by an oscillation of vascular resistance. Blood flow was measured in different vascular beds and the changes in resistance calculated. The data indicate that Mayer waves are accompanied by rhythmic fluctuations in vascular resistance which vary regionally.

Methods

Experiments were performed on cats anesthetized with chloralose intravenously (60 to 80 mm./Kg.) and tracheotomized. Heart rate was recorded with an interval recorder. Blood flows were measured with a drop flow meter. Vessels were cannulated with polyethylene tubing and the animal heparinized. The drop chamber and tubing were enclosed in a water jacket maintained at 38 C. The rate of formation of drops was recorded by an ordinate writer connected to a polygraph. The ordinate writer is so constructed that the height of rise of the marking pen is inversely proportional to the flow rate. Thus, when perfusion pressure is held constant, the rise of the marking pen is directly related to the resistance to blood flow in the region being perfused.

For measuring flow in the great vessels, the abdominal aorta and inferior vena cava were approached retroperitoneally through a flank incision and cannulated just caudal to the renal vessels. Venous pressure in the inferior vena cava was held constant, between 3 and 6 mm. Hg, by allowing blood from the venous flow meter to drip from a
Mayer waves and oscillation of respiration. Arterial pressure fluctuates 50 mm. Hg at a frequency of 3.6 per minute. Note that cyclical changes in respiration slightly precede those of blood pressure.

Arterial inflow was measured in muscle, skin, kidney, and small intestine. In all experiments, flow in muscle was measured simultaneously with at least one other organ flow. In a few experiments, all four flows were determined simultaneously. A hind leg was skinned with electrocautery, circulation to the paw occluded with a tight ligature above the ankle, and the femoral or iliac artery cannulated for muscle flow. Flow to skin was measured via cannulation of the dorsal vein or artery of the paw. When the vein was utilized, collateral veins draining the paw were ligated. No difference in results was apparent between use of the artery or vein. For renal flow, the renal artery was cannulated after carefully dissecting away the renal nerves. A large mesenteric artery serving the ileum was chosen for measuring gut inflow and the nerves dissected from the vessel.

In order to maintain a constant perfusion pressure to the organs in which flow was being recorded, despite large changes in systemic pressure, the inflow side of the drop chamber was connected to a special stopcock which in turn received arterial blood from the iliac or femoral artery opposite the skinned leg. The stopcock had multiple outlets which allowed measurement of arterial pressure proximal (systemic) and distal (perfusion) to a variable occluding screw and which permitted simultaneous perfusion of four drop chambers at the same pressure. Arterial pressures were measured with Statham strain gauges. Respiration was recorded from intratracheal or right atrial pressure.

Initially, Mayer waves were produced by repeated hemorrhage and transfusion. In not every animal, however, were the waves of sufficient amplitude to permit analysis of the records. It was then found that a combination of hemorrhage and graded carotid occlusion reliably resulted in Mayer waves of 40 mm. Hg or more amplitude. In the later experiments, both common carotids were perfused from an arterial source via a second variable stopcock. After hemorrhage sufficient to lower the arterial blood pressure below 80 to 100 mm. Hg, setting the screw clamp somewhere between partial and complete closure was followed by the development of large and usually persistent Mayer waves. When the carotid screw clamp was opened, permitting normal flow, the waves disappeared.

Successful experiments with the development of Mayer waves of large amplitude were achieved in 17 cats (fig. 1). The average Mayer wave was 56 mm. Hg in amplitude (range 25 to 105 mm.) developing from a base systemic pressure of 70 mm. Hg (range 45 to 100 mm.), with a frequency of 3.0/min. (range 1.6 to 4.3/min.). There was no correlation between amplitude and frequency or between base systemic pressure and amplitude. When the waves were small, minor adjustment of blood volume by bleeding or transfusing a few ml. of blood frequently resulted in a striking increase in amplitude. Partial carotid occlusion had a similar effect. Mayer waves were invariably accompanied by cyclical variations in respiration in spontaneously breathing animals (figs. 1 and 2). The respiratory cycles varied with the same frequency as the Mayer waves, although slightly out of phase. The maximum depth

\[ \text{FIGURE 1} \]

\[ \text{FIGURE 2} \]
Mayer waves and aortic flow during constant aortic perfusion pressure. Note oscillation of flow and pressure. Striking decrease in flow reflects marked increase in vascular resistance with each arterial pressure wave.

The fluctuations in arterial pressure were associated with a parallel rise and fall in calculated vascular resistance during constant perfusion pressure in the lower half of the body (fig. 3). In four experiments with
Regional vascular resistance during Mayer waves—Data averaged from experiments in which regional blood flow was measured during constant perfusion pressure. See text for details. Ordinates: pressure in mm. Hg and resistance in units. Note hierarchy of resistance change in muscle, intestine, skin, and no resistance change in kidney.

Mayer waves averaging 60 mm. Hg (range 45 to 65 mm. Hg), resistance in the hind-quarters averaged a 230 per cent increase (range 160 per cent to 282 per cent) as the pressure rose. Any procedure which abolished the waves, such as transfusion or excessive bleeding, cutting the vagi, or reducing the degree of carotid occlusion also abolished the resistance oscillation. Rhythmic fluctuations in resistance were observed only in the presence of Mayer waves.

The pattern of blood flow during Mayer waves varied in the four regions investigated (fig. 4). With Mayer waves of large amplitude, muscle blood flow decreased during the pressure rise and increased during the pressure fall. Blood flow in the small intestine showed a similar response, but the changes were less pronounced. Skin blood flow usually increased modestly during the pressure rise. Renal blood flow was markedly sensitive and varied directly with the arterial pressure.

Regional vasoconstrictor responses during Mayer waves were compared quantitatively with constant perfusion pressure (fig. 5). Muscle vascular resistance increased in 12 experiments, an average of 276 per cent (range 206 per cent to 440 per cent) from trough to pressure peak. Vascular resistance in small intestine increased an average of 210 per cent in four experiments (range 179 per cent to 280 per cent). Skin resistance increased 136 per cent in five animals (range 112 per cent to 199 per cent). Kidney showed no change in resistance. In none of eight experiments was there any evidence of renal vasoconstriction during Mayer waves.

Because of the possibility that nerve damage accounted for the observed differences in vascular resistance, the nerves accompanying the intestinal and renal artery were stimulated at the end of each experiment at frequencies ranging from 1 to 16 per second. One or two nerves accompanying the artery were selected, divided, and the distal end stimulated. In every case, stimulation at low frequency produced vasoconstriction in the gut or kidney. Frequency response curves had the classical form but were shifted to the right since only a few of the nerves to the organ were being stimulated. Stimulation in the region of the celiac ganglion also produced renal vasoconstriction.

In three experiments in which blood flow had been measured during Mayer waves, the effect of asphyxia was observed. Perfusion pressure was held constant during tracheal occlusion, although systemic blood pressure rose considerably. During asphyxia there was marked vasoconstriction in the muscle, gut, and skin, as well as kidney. The constrictor response during asphyxia is interpreted as further evidence that the innervation to the organs studied was intact.

*Figure 3*

Regional vascular resistance during Mayer waves. Data averaged from experiments in which regional blood flow was measured during constant perfusion pressure. See text for details. Ordinates: pressure in mm. Hg and resistance in units. Note hierarchy of resistance change in muscle, intestine, skin, and no resistance change in kidney.
BLOOD FLOW DURING MAYER WAVES

Discussion
The present study has shown that Mayer waves are accompanied by cyclical variations in respiratory movements, blood flow, and resistance to blood flow, but no change in heart rate. Possible limitations of the experimental techniques merit discussion. The anesthesia may have influenced the results. Chloralose has been shown to reduce baroreceptor function and alter the effect of sinus nerve stimulation in the cat. With another agent or in the unanesthetized animal, a different pattern of cardiovascular response with Mayer waves may occur.

Measurement of blood flow required dissection and cannulation of the artery supplying blood to the region under study. Less than 10 per cent of the sympathetic vasoconstrictor activity in thigh muscle is interrupted by ligation of the femoral artery. What fraction of the constrictor fibers is in the adventitia of arteries to skin, kidney, and gut is not known. The nerves of the kidney and gut are intimately related to their respective arteries, and undoubtedly some were damaged during the insertion of the cannula. However, since stimulation of the nerves to the kidneys and gut produced striking vasoconstriction at the termination of the experiments, and since asphyxia caused extreme vasoconstriction in all vascular beds cannulated, it is unlikely that nerve damage adversely affected the results.

Maintenance of a constant perfusion pressure lowered mean blood flow and exaggerated the decrease in regional flow as vascular resistance increased during Mayer waves. The added resistance of the screw clamp accentuated the systemic pressure rise and fall. These alterations may have influenced the observed fluctuations in flow and resistance. The decreased flow might have produced sufficient local metabolic change to cause a vasodilation, similar to reactive hyperemia, thus distorting the actual resistance change. The increased amplitude of the waves might have altered the distribution of blood flow. To minimize these possibilities, constant perfusion pressure was limited to the vascular bed under study.

Comparison of records obtained with both constant perfusion pressure and systemic perfusion pressure revealed similar oscillations in calculated resistance. It is considered unlikely, therefore, that the constant local perfusion pressure significantly affected the experimental results.

Mayer waves appear to be reflex in origin. Andersson et al. eliminated them in cats by sinus nerve section or selective destruction of the chemoreceptors. They postulated that Mayer waves are the result of an oscillation between baroreceptor and chemoreceptor functions. Guyton et al. demonstrated that epidural sympathetic blockade or pressoreceptor denervation obliterate Mayer waves in the dog. They also proposed an oscillation between the pressoreceptors and autonomic reflex vasoconstriction as an explanation.

The failure of heart rate to change during Mayer waves is of interest since baroreceptor stimulation during the pressure rise would be expected to cause bradycardia. In the cat, the tachycardia of systemic anoxia is unaffected by changes in the oxygen content of carotid body perfusate, although stimulation of the chemoreceptors by cyanide causes a prompt increase in heart rate. Since chloralose depresses baroreceptor function in the cat, the constant heart rate observed in the present experiments suggests that the baroreceptors are less important in the genesis of Mayer waves than has been proposed. Following cerebral compression or increased cerebral spinal fluid pressure, large Mayer waves develop which are unaffected by carotid and aortic denervation. A direct role for the vasoconstrictor center or some other area in the brain in the genesis of Mayer waves cannot be ruled out.

The cyclical variation in respiratory depth and rate in the spontaneously breathing animals may be a reflection of the rhythmic chemoreceptor discharge known to accompany Mayer waves. That the respiratory variation is not necessary for the blood pressure oscillations is shown by their occurrence during constant positive pressure ventilation. The respiratory cycles slightly precede the blood...
pressure waves, as does the increase in the intensity of discharge of the chemoreceptor nerves.11 This suggests that the ventilatory mechanism reacts faster to a common stimulus than does the vascular system.

Whether oscillation of vascular resistance is the only factor controlling the pulse pressure of Mayer waves cannot be determined from the present data since cardiac function was not measured. It is possible that rhythmic alteration of myocardial contractility and cardiac output may contribute. If venous return to the right heart lags behind the arterial pressure fluctuation, as was true for flow in the inferior vena cava, then a changing cardiac output might either augment or depress the pressure rise, depending on the frequency of the waves and the degree of lag.

Few data comparing vasoconstriction in two or more regions to the same afferent stimulus are available. Rein found that during carotid occlusion, muscle had the most active reflex vasoconstriction and kidney the least, while gut was intermediate.10 Bernthal and Schwind showed more intense vasoconstriction in muscle and skin than in the gut during carotid body stimulation.17 McGiff and Aviado have recently reported that anoxia and carotid occlusion have a greater effect on femoral than on renal vascular resistance.18 In the cat, bulbar stimulation is associated with more intense vasoconstriction in muscle than in skin or kidney.19

Measurement of regional blood flow and resistance during Mayer waves has provided an opportunity to observe dynamic changes during a fluctuating central stimulus of presumably constant peak intensity. Since the evidence indicates that Mayer waves are reflex in origin, the varying pattern of vascular resistance may be interpreted as indirect evidence for inherent regional differences in the central control of the peripheral vascular system. The greater vasoconstrictor activity of muscle and gut confirms the experience of other workers. Failure to demonstrate renal vasoconstriction during Mayer waves is of interest in view of the long-standing debate about the role of the kidney in reflex blood flow distribution.

The ultimate vasoconstrictor response to a central stimulus must depend upon an interaction between local and central mechanisms. As the animals were bled and arterial pressure fell, blood flows fell to very low values (fig. 4). What role local factors, perhaps influenced by anaerobic metabolism, may play in relation to central stimuli in the regional flow and resistance changes observed in Mayer waves cannot be determined from the present data.

Summary

In cats anesthetized with chloralose, Mayer waves developed following graded hemorrhage and, in some, partial carotid occlusion. The average Mayer wave was 56 mm Hg in amplitude rising from a base systemic pressure of 70 mm Hg at a frequency of 3.0 per minute. Rhythmic fluctuation of respiratory depth and frequency paralleled but slightly preceded the blood pressure change. There was no significant variation in heart rate during Mayer waves.

Flow in the abdominal aorta and vena cava varied inversely with systemic pressure. A flow lag of four to six seconds in the vena cava behind that in the aorta during Mayer waves was probably related to circulation time.

Blood flow was measured in muscle, small intestine, skin, and kidney. During the pressure rise of each Mayer wave, blood flow decreased in muscle more than in gut. Cutaneous flow increased moderately. Renal flow varied directly with the arterial pressure. Changes in vascular resistance were evaluated by holding perfusion pressure constant and measuring regional blood flow. During Mayer waves, muscle vascular resistance increased 276 per cent, intestinal resistance increased 210 per cent, and cutaneous resistance rose 136 per cent. Renal vascular resistance did not change.

Since Mayer waves are apparently reflexogenic in origin, the data are interpreted as evidence for regional differences in the pattern of central reflex control of the peripheral vascular system.
Acknowledgment

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Addendum

Since this paper was prepared for publication, B. Löfving (Cardiovascular adjustments induced from increased muscle blood flow and passive increase in renal blood flow during Mayer waves. He states in skin and gut to a lesser extent than in muscle. Limgren, M.D., and Professor Borje Uvnäs for in-

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The following suggestions are made on the basis of observations under the electron microscope: (1) The location and ultramicroscopic structures of the cardiac nerves suggest that axon reflexes are untenable; all branching of the finest nerve fibers is a separation of preformed individual protoaxons, never a dividing of a common stem, as required to mediate an axon reflex. (2) The ability of a muscle to do heavy work can be mathematically stated as a function of the type of sarcomeres found within its muscle fibers. (3) Muscle fibrils of cardiac muscle and the fibrils of other types of striated muscle exhibit no basic differences. (4) The inner surface of the capillary is scalloped, and long ribbon-like extensions from the endothelial wall may stretch deep into the bloodstream within the capillary lumen. The pictures and techniques for preparation of heart specimens are included in this monograph.
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