Pressoreceptor-Autonomic Oscillation: A Probable Cause of Vasomotor Waves

ARTHUR C. GUYTON and JEFF W. HARRIS

From the Department of Physiology and Biophysics, School of Medicine, University of Mississippi
University, Mississippi

IN A RECENT study of blood pressure response to intermittent flow and outflow of blood from the circulation (1), it was observed that after suddenly ceasing outflow and then beginning immediately the inflow of blood there usually followed in normal animals a series of damped oscillations in the blood pressure. This effect also occurred when the inflow of blood was suddenly stopped and was followed by outflow. However, following progressive stages of pressoreceptor denervation, these oscillations became less pronounced and were not demonstrable after total pressoreceptor denervation. Furthermore, after total spinal anesthesia, the waves were not evident. Therefore, the hypothesis was offered that these waves are due to pressoreceptor-sympathetic oscillation, and it was further supposed, because of similar periodicities of these waves and vasomotor waves found in dogs, that vasomotor waves might have the same origin. The present study adds additional observations in support of this hypothesis which was only briefly mentioned before.

METHODS

First, a search through more than a hundred old records was made for vasomotor waves. These included a large number of records on pressoreceptor denervated animals, animals with total spinal anesthesia, animals following major thoracic surgery, animals following various degrees of transfusion and hemorrhage, and animals receiving constant infusions of epinephrine.

Second, by a series of different procedures the conditions for production of good vasomotor waves in the records were studied. Each procedure will be presented separately along with the results.

In all of the experiments, blood pressure has been recorded by use of a mercury manometer system in conjunction with either heparin or citrate anticoagulant. In order to demonstrate the vasomotor waves with clarity, the respiratory waves were in many instances greatly damped by an adjustable clamp on the blood pressure recording tube to the manometer. To minimize further the effects of respiratory waves a very rapid respirator (around once every 2 seconds) was connected via tracheal cannula to the animals, and the animals were overventilated sufficiently to suppress

Received for publication September 25, 1950.

1 This investigation was supported by a research grant from the National Heart Institute, of the National Institutes of Health, U. S. Public Health Service, Bethesda, Md.
their own involuntary respiratory efforts. Also, in several of the animals, the phrenic nerves were cut.

All animals received sodium pentobarbital anesthesia.

RESULTS

Analysis of Previous Records. In the analysis of the old records several points of importance were noted as follows:

In records from 16 animals which had total spinal anesthesia and 22 animals with total pressoreceptor denervation, no vasomotor waves were found.

In 36 animals which had been subjected to opening of the chest cage followed by extensive cannulation of the venous inflow of the heart so that venous resistance could be exactly controlled, very marked vasomotor waves were often observed, sometimes as great as 30 mm. Hg (fig. 1, upper record). Indeed, these interfered greatly with studies in progress.

In 16 animals which had been bled approximately 25 per cent of their total blood volume, waves almost invariably appeared when blood pressure fell to between 50 and 80 mm. Hg, and in one of these animals, which was known to have been under very light anesthesia, the vasomotor waves became persistent over a period of half an hour with a pressure differential of 30 mm. Hg (fig. 1, lower record). When small transfusions of blood had been given to these previously hemorrhaged animals, short periods of damped oscillations followed with the period of these oscillations ranging approximately between 15 and 30 seconds.

Thus, in 2 groups of animals, both of which had received severe circulatory trauma, very large vasomotor waves appeared to develop spontaneously.

Effect of Hemorrhage on Vasomotor Waves. The effect of various degrees of hemorrhage was specifically tested in 6 heparinized dogs by removing and reinjecting various quantities of blood through a plastic catheter inserted down an external jugular vein into the right auricle. In all of these animals the vasomotor waves increased in height as the mean blood pressure fell into the range between 50 and 80 mm. Hg. This was found particularly true when the pressure remained at this level for at least 30 minutes. Furthermore, small transfusions into the animals frequently set off trains of damped oscillations even though no waves might have been present at the moment.

Effect of Sodium Pentobarbital Anesthesia on Vasomotor Waves. It was the general impression in all of the experiments that the vasomotor waves became much more prominent as the anesthesia wore off. However, this impression was specifically tested in 2 animals by giving deeply anesthetizing doses of sodium pentobarbital (30 mg/kg.) and studying the waves over several hours. In both of these, there were no waves at first, but gradually over a period of 2 hours the waves increased until the usual vasomotor waves of normal records appeared.

In 3 additional experiments, the reverse effect of increasing anesthesia was observed. In each of these animals, the waves were already well developed as a result of light anesthesia and hemorrhage. Successive small increments of sodium pentobarbital gradually reduced the waves to zero. Death occurred at a still deeper stage of an-
esthesia in 1 of the animals (fig. 2), but in 2 of them the depth of anesthesia was carried to the point that oscillations ceased though death did not ensue.

Production of Damped Oscillations in Blood Pressure Records. A number of different types of sudden changes in circulation equilibrium were tested in order to determine how trains of damped oscillations might be produced. In general, it was found that almost any change which raises or lowers blood pressure momentarily may cause oscillations provided the animal is not too deeply anesthetized. Among the different effective methods have been the following: 1) one-second stimulation of either vagus nerve with a strong tetanizing current; 2) one-second stimulation of either intact carotid sinus or the central end of the sectioned carotid sinus nerve; 3) very hard pressure on the abdomen for a few seconds; 4) a sudden blast of positive air pressure into the lungs; 5) closure of the tracheal cannula for a few seconds so that the animal strains for breath; 6) sudden blow on the animal’s chest. Over 100 such damped oscillation records were recorded in 13 different dogs with invariable success. Four of these records, elicited by different stimuli, are shown in figure 3.

Effect of Pressoreceptor Denervation on Damped Oscillations. Using any one of the various stimuli which may produce a series of damped oscillations, the effect of progressive pressoreceptor denervation on these oscillations was studied in 11 dogs. The surgery except for actual denervation was completed prior to beginning the experiments. Denervations of the aortic pressoreceptors were accomplished by vagal section at the level of the carotid sinuses, and the sinuses were denervated by stripping in all directions for an inch. Regardless of which area was denervated first, the procedure being varied from one experiment to the next, damped oscillations of progressively less intensity occurred (fig. 4). (Though there was prone to be a fall in blood pressure in these experiments, presumably due to the circulatory insults necessary to elicit damped oscillations, there often occurred the usual rising pressure associated with pressoreceptor denervation, and the effects on the oscillations were exactly the same as those noted in this figure.) No oscillations of constant periodicity could be elicited after total denervation.

Effect of Pressoreceptor Denervation on Sustained Vasomotor Waves. The effect of pressoreceptor denervation in 4 animals with sustained waves of at least 15 mm. pressure differential and of at least 20 minutes duration was determined. In each case, the large waves disappeared as illustrated in figure 5, though there were still other very weak waves present in the records. These were usually so irregular that no definite periodicity could be established, but the lower record of figure 5 shows waves having a vaguely recurrent period of between 45 and 50 seconds; these possibly could be analogous to the ‘splenic waves’ of Barcroft (2). However, the record of figure 5 illustrates one of the best series of such waves that could be found in over 8 hours of records from 12 pressoreceptor denervated animals. (The mean blood pressure in the experiment of figure 5 rose from 94 mm. Hg to 107 mm. Hg as a result of the denervation. This animal had been bled previously approximately 20 per cent of his blood volume in order to produce the waves. Therefore, only a slight rise in blood pressure was to be expected because the circulatory system was already in a state of vasoconstriction. The denervations in this group of animals were performed in less than 4 minutes with essentially no bleeding nor trauma because the vagi and carotid sinuses had been exposed prior to beginning the study of the vasomotor waves.)
Reaction Time of Blood Pressure Following Electrical Stimulation of a Carotid Sinus. Because a hypothesis of pressoreceptor sympathetic oscillation has been advanced, and because any type of oscillation implies a time delay somewhere in the control circuit, it is desirable to know the reaction time of blood pressure to carotid sinus pressoreceptor stimulation. In 15 trials, this time was found to average 13 seconds between the end of a 2 second stimulus and the lowest point of the blood pressure response.

Fig. 1. Very strong vaso-motor waves found in animals with severe circulatory trauma and low blood pressure. Upper record was observed in a dog following complete cannulation of the great veins and right auricle for study of venous resistance. Lower record was observed in a lightly anesthetized dog one hour after hemorrhage of 25 per cent of his blood volume. (Time, 5 seconds.)

Fig. 2. Effect of Sodium Pentobarbital anesthesia on the vaso-motor waves. An additional dose of 1.0 mg/kg. of sodium pentobarbital was injected at each arrow. The final 'steps' in the record are declines in blood pressure as a result of the drug rather than waves. (Time, 5 seconds.)

Periods of Damped Oscillations and of Vasomotor Waves. The average period of oscillation in 42 damped oscillation records was found to be 24.1 seconds. The average period in 28 records of spontaneous, sustained vasomotor waves was found to be 25.2 seconds, and the individual records varied between 11 and 40 seconds.

DISCUSSION

Pressoreceptor-Autonomic Mechanism as an Oscillatory System. Weiner has outlined in mathematical detail the requirements for oscillation in its various forms (3), but presented in simple terms, there are 2 essential requirements in order for
Fig. 3. Damped oscillations in the blood pressure records caused by various factors which momentarily change the blood pressure. These records were obtained respectively from top downwards by the following procedures: momentary distention of the lungs with a blast of air, momentary pressure on the abdomen, 2-second tetanizing stimulus of the right vagus, 2-second tetanizing stimulus of the right carotid sinus. (Time, 5 seconds.)

Fig. 4. Effect of progressive pressoreceptor denervation on damped oscillations resulting from distention of the lungs with air for a few seconds. From above downwards the records represent: control, after stripping left carotid sinus, after stripping right carotid sinus, after section of left vagus, after section of right vagus. (Time, 5 seconds.)

Fig. 5. Effect of pressoreceptor denervation on sustained blood pressure oscillations. Upper record shows waves which had arisen spontaneously and had been sustained for over 30 minutes. Lower record is from same animal 5 minutes later after total pressoreceptor denervation. (Time, 5 seconds.)

oscillation to occur: First, there must be a negative reflex mechanism which tends to return a given system toward the mean operating level whenever it is displaced from that mean. Second, there must be a time delay after excitation of the reflex mechanism before the negative response occurs. However, oscillations caused by such a
system may exist in waxing, sustained, or damped forms depending on the relative driving force of the reflex as opposed to the various dampening factors at any given instant.

The pressoreceptor-autonomic mechanism fulfills the 2 requirements for oscillations because, first, this mechanism tends to return the arterial pressure toward the mean whatever the pressure might be at a given instant, and, second, there is a time delay in the response after stimulation of the pressoreceptors. Therefore, the system may be explained as follows: High pressure in the arterial system stimulates the pressoreceptors, this excites the vagi and inhibits the sympathetics, the blood pressure falls, and it continues to fall even after the mean level is reached because of the time delay in the response. Then, low blood pressure decreases the pressoreceptor stimulation; this in turn causes a resultant excitation of the sympathetics and inhibition of the vagi. The blood pressure rises once again, and the cycle begins over. Because this system satisfies the necessary requirements for oscillation, it is essential that pressoreceptor-autonomic oscillatory waves be present in blood pressure records at least in the damped form and possibly in the sustained and waxing forms. Furthermore, because the pressoreceptor mechanism is not a weak one, it is almost certain, from theoretical considerations, that these oscillations should be of sufficient intensity to be easily observed. The question simply remains: are the damped and sustained waves recorded in this study due to this oscillatory mechanism or to some other factor? The following observations seem pertinent:

The time delay in the pressoreceptor reflex is probably due to 2 factors: first, the delay of nerve impulses between the pressoreceptors and the autonomic nerve endings, and, second, the delay in humoral response once the impulses reach the nerve endings. Because it has been found that the pressoreceptor reflex to the vagi is relatively rapid (4), it is highly possible that the same speed of nerve activity exists for the sympathetic component of the system and that the major delay is in the sympathetic humoral response.

In the present experiments, the time delay of the carotid sinus reflex was found to be approximately 13 seconds. Therefore, the period of a half cycle in pressoreceptor-autonomic oscillation should be approximately this same interval, and the period of an entire cycle should be approximately 26 seconds. The average period of the damped oscillations in this study was found to be 24.1 seconds while the average period of the sustained oscillations was found to be 25.2 seconds.

Even when the pressoreceptor reflex system is in a weakened condition as the result of pentobarbital anesthesia, damped oscillations can still be produced in the records by any factor that suddenly raises or lowers blood pressure. This is in accord with the mathematical observation that only damped oscillations can be produced when the reflex mechanism is weak in relationship to the dampening factors. On the other hand, not until the anesthesia becomes light do waves appear in the sustained state. This is in agreement with the necessity for the negative reflex mechanism to be of at least a certain power before sustained waves can exist.

Still another observation which indicates the correctness of the oscillation hypothesis is that progressive section of the pressoreceptor nerves causes the waves in damped oscillation records to dampen progressively more rapidly and not to exist at
all after total section of the nerves. Furthermore, section of these same nerves during the course of very large sustained waves causes disappearance of the waves. Finally, total anesthesia of the sympathetics, the major efferent limb of the pressoreceptor reflex, causes a complete abrogation of the waves—both the spontaneous waves and the damped waves excited by inflow and outflow of blood (1). This is also in accord with the findings of Green et al. that Traube-Hering waves are due to rhythmic changes in vasomotor tone (5).

From the above considerations, it seems probable that the waves which have been studied are due to pressoreceptor-autonomic oscillation. In the original statement of this hypothesis (1) it was stated as pressoreceptor-sympathetic oscillation. However, simply on theoretical grounds, it seems reasonable to modify the statement so that the parasympathetics may also be included. Yet, the fact that even damped oscillations fail to appear after total spinal anesthesia indicates that the parasympathetic component is certainly very weak.

Influence of Hemorrhage on Intensity of the Oscillations. The fact that hemorrhage makes the oscillations greater than normal cannot be explained on the basis of present data. Furthermore, why do the very intense oscillations of 30 mm Hg noted a number of times in these experiments not occur in normal animals and in normal human beings? Even though the pressoreceptor mechanism is a powerful one, it undoubtedly is opposed in the normal animal by powerful dampening factors. The effect of fluid shifts as a stabilizing influence on blood pressure has been discussed previously (1) and compared with the pressoreceptor stabilizing effect. This ability of the circulation to shift fluids from the tissues to the circulation and in the opposite direction undoubtedly does exert at least some dampening effect on the oscillation of blood pressure, and the previous studies indicate that this effect is much more rapid and more quantitatively important than has been generally expected to be the case. It has, furthermore, been shown that hemodilution following hemorrhage does not occur significantly unless the animal is in a well hydrated state (6–8). Therefore, it seems at least possible that hemorrhage causes a relatively rapid depletion of the tissue fluid stores which are normally available for purposes of hemodilution and thereby diminishes the dampening effect of this fluid shift mechanism on the blood pressure oscillations.

Waves in the Blood Pressure Records Other Than Pressoreceptor-Autonomic Oscillations. The irregular waves existing in the records after complete pressoreceptor denervation failed to establish any striking pattern, though there did occur a number of weak waves having a period of about 45 seconds, these waves frequently appearing in series of 2 to 5 at a time. It is possible that these waves represent the 'splenic waves' which Barcroft claims to be a distinct entity (2). However, the possibility that other oscillatory systems exist should be strongly considered. For instance, the response of blood pressure to medullary ischemia is a negative reflex mechanism with a time delay somewhat longer than the time delay of the pressoreceptors (9, 10). This could very easily cause these 45-second waves or some of the other waves with relatively long periods. It is almost certain that oscillatory waves from this mechanism do exist under appropriate conditions because the 2 conditions for oscillation are satisfied.
Identity of the Pressoreceptor-Autonomic Oscillatory Waves. The waves that have been considered in these studies are those found in almost all blood pressure records from dogs and variously called Traube-Hering waves, Mayer waves, vaso-motor waves, and alpha waves (5, 11, 12). (Possibly the 'splenic waves' should also be included in this group even though they are considered by some to be of different origin (13)). The period of these waves has been reported as short as 10 seconds in man up to 83 seconds for the splenic waves of cats (2). In the present series of animals, the periods varied from 11 seconds up to 40 seconds in the different dogs. It seems quite reasonable that all these waves may be due to the same effect, with the possible exception of the 'splenic waves,' and that the variations in periodicity may result from variations in experimental animals and experimental conditions.

SUMMARY

The blood pressure waves commonly known as Traube-Hering or vasomotor waves have been studied in relation to the pressoreceptor-autonomic reflex system. These waves were found to be greatly intensified approximately 30 minutes to an hour after moderate but not lethal hemorrhage. It was found in over 100 individual attempts that a short series of damped waves could always be elicited in the blood pressure records of normal animals by any factor which would cause the blood pressure to rise or fall momentarily, thereby upsetting the equilibrium of the pressoreceptor control system.

Deep sodium pentobarbital anesthesia was found to abolish the spontaneous, sustained waves and to depress greatly the damped waves. Complete spinal anesthesia was found to abolish both sustained and damped waves. Complete denervation of the pressoreceptors of the carotid sinuses and those supplied by the vagi was found to eliminate both the sustained and the damped waves.

The principles of oscillation as applied to this problem have been briefly discussed, and the conditions under which damped or sustained oscillations may be expected to occur have been pointed out. On the basis of these principles and the experimental findings summarized above, it is concluded that the waves under consideration are probably due to pressoreceptor-autonomic oscillation and that the oscillations are probably the same as Traube-Hering, Mayer, alpha, and vasomotor waves. Irregular waves, much weaker and of different periodicities from those of pressoreceptor-autonomic oscillations, were found to occur after pressoreceptor denervation. It is suggested that these waves might result from oscillatory cycles in other time delay blood pressure regulatory systems such as the system responsible for the medullary ischemic reflex.

REFERENCES